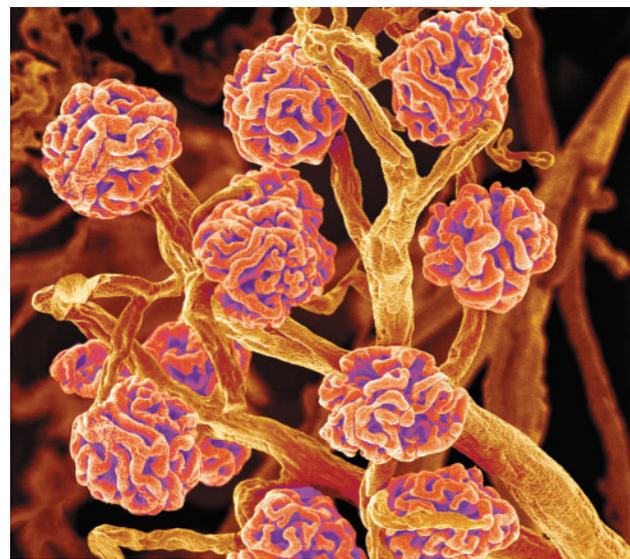


The Urinary System



Animals living in an aquatic environment face little risk of becoming dehydrated. However, animals that started to spend more time on dry land millions of years ago needed mechanisms to conserve water and prevent dehydration. The organ system that performs this function in humans—the **urinary system**—is the topic of this chapter. The organs of the urinary system are organs of **excretion**—they remove wastes and water from the body. Specifically, the urinary system “cleans the blood” of *metabolic wastes*, which are substances produced by the body that it cannot use for any purpose. However, as you will learn in this chapter, the urinary system does far more: This system is also essential for removing toxins, maintaining homeostasis of many factors (including blood pH and blood pressure), and producing erythrocytes. Read on to discover how the urinary system is vital to your body’s homeostasis.

MODULE

24.1

Overview of the Urinary System

Learning Outcomes

1. List and describe the organs of the urinary system.
2. Describe the major functions of the kidneys.

The urinary system is composed of the paired *kidneys* and the *urinary tract*. The **kidneys** filter the blood to remove metabolic wastes and then modify the resulting fluid, which allows these organs to maintain fluid, electrolyte, acid-base, and blood pressure homeostasis. This process produces **urine**, a fluid that consists of water, electrolytes, and metabolic wastes. Then the remaining organs of the urinary system—those of the urinary tract—transport, store, and eventually eliminate urine from the body. In this module, we first examine the basic structures of the urinary system, and then turn to the functional roles of the kidneys.

Overview of Urinary System Structures

As you can see in **Figure 24.1**, the kidneys resemble their namesake, the kidney bean, in both shape and color. The kidneys are situated against the posterior abdominal wall and are *retroperitoneal* (reh'-troh-pair-ih-ton-EE-ul; *retro-* = “behind”) organs, meaning they are located posterior to the peritoneal membranes. Note, however, that the two kidneys differ slightly in position—the left kidney extends from about T12 to L3, whereas the right kidney sits slightly lower on the abdominal wall because of the position of the liver. The superior portions

24.1	Overview of the Urinary System	941
24.2	Anatomy of the Kidneys	943
24.3	Overview of Renal Physiology	951
24.4	Renal Physiology I: Glomerular Filtration	951
24.5	Renal Physiology II: Tubular Reabsorption and Secretion	960
24.6	Renal Physiology III: Regulation of Urine Concentration and Volume	968
24.7	Putting It All Together: The Big Picture of Renal Physiology	974
24.8	Urine and Renal Clearance	974
24.9	Urine Transport, Storage, and Elimination	976

Photo: This scanning electron micrograph shows glomeruli, the filtering units of the kidneys.

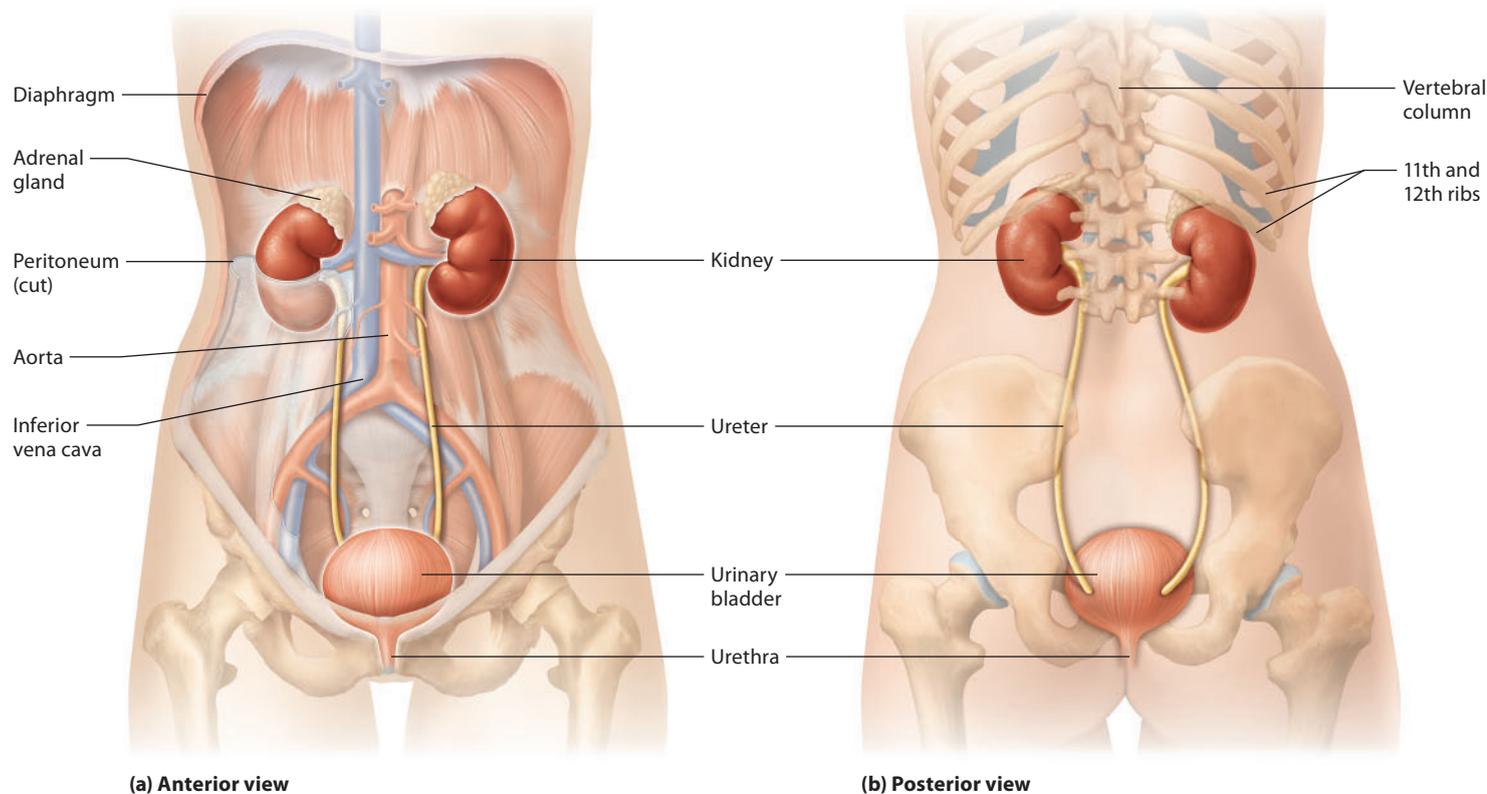


Figure 24.1 Organs of the urinary system in a female.



of both kidneys are partially protected by the 11th and 12th pairs of ribs. Each kidney is capped by an adrenal gland (*ad-* = “near,” *ren-* = “kidney”); these glands perform endocrine functions and secrete a variety of hormones (see Chapter 16).

The **urinary tract** is composed of the paired *ureters* (YOOR-eh-terz), the *urinary bladder*, and the *urethra* (yoo-REE-thrah). Urine leaves each kidney through one of the two ureters, tubes that run along the posterior body wall, connecting the kidneys with the hollow urinary bladder. The bladder, which stores the urine, sits on the floor of the pelvic cavity. Urine is expelled from the body through the tube called the urethra, which connects the urinary bladder with the outside of the body.

Quick Check

1. What are the organs of the urinary system?

Overview of Kidney Function

◀ Flashback

1. What are three factors that determine blood pressure? (p. 670)
2. What is erythropoietin, and what is its main function? (p. 727)

The regulation of homeostasis by the urinary system takes place in the kidneys, so let’s take a quick look at what the kidneys do and how they do it. The kidneys perform the following functions:

- **Removal of metabolic wastes.** As we have discussed, the kidneys filter the blood, removing metabolic wastes. These wastes are eliminated from the body via the urine.
- **Regulation of fluid and electrolyte balance.** The kidneys regulate blood solute concentration, or osmolarity, by conserving or eliminating water and electrolytes such as sodium, potassium, and calcium ions.
- **Regulation of acid-base balance.** The kidneys assist in the long-term regulation of blood pH by conserving or eliminating hydrogen (H^+) and bicarbonate (HCO_3^-) ions.
- **Maintenance of blood pressure.** The kidneys directly influence systemic blood pressure through their control of blood volume. Additionally, they secrete an enzyme that influences both blood volume and peripheral resistance.
- **Regulation of erythropoiesis.** The kidneys regulate red blood cell production in the bone marrow by releasing the hormone *erythropoietin* (eh-rith'-row-POY-eh-tin; see Chapter 19).
- **Performing other metabolic functions.** The kidneys play many important metabolic roles, including detoxifying substances in the blood, activating vitamin D, and making new glucose through the process of *gluconeogenesis* (glew'-koh-nee-oh-JEN-eh-sis).

Quick Check

- 2. List the basic functions of the kidneys.

Apply What You Learned

- 1. Inflammation of the peritoneal membranes, or *peritonitis*, can cause dysfunction of multiple organs in the abdominal cavity. Would you expect peritonitis to impact the kidneys? Explain.
- 2. Explain why a patient with long-term renal failure might have a decreased number of erythrocytes in his or her blood.

See answers in Appendix A.

MODULE

24.2

Anatomy of the Kidneys**Learning Outcomes**

1. Describe the external structure of the kidney, including its location, support structures, and covering.
2. Trace the path of blood flow through the kidneys.
3. Identify the major structures and subdivisions of the renal corpuscle, renal tubules, and renal capillaries.
4. Describe the histological structure of the proximal tubule, nephron loop, distal tubule, and collecting system, and trace the pathway of filtrate flow through these tubules.
5. Compare and contrast cortical and juxtamedullary nephrons.

Let's now take a closer look at the anatomy of the kidneys. In this module, we explore first the external and internal anatomy of the kidneys. We then turn our attention to the structure and basic roles of the kidneys' functional units: the *nephrons* (NEF-ronz; *nepbro-* = "kidney"). We conclude the module with an examination of the two main types of nephrons.

External Anatomy of the Kidneys

The kidneys are held in place on the posterior body wall and protected by three external layers of connective tissue (**Figure 24.2**). From superficial to deep, these layers are as follows:

- **Renal fascia.** The **renal fascia** (FASH-ee-ah) is a layer of dense irregular connective tissue that anchors each kidney to the peritoneum and to the fascia covering the muscles of the posterior abdominal wall.
- **Adipose capsule.** The middle and thickest layer, called the **adipose capsule**, consists of adipose tissue that wedges each kidney in place and shields it from physical shock. During prolonged starvation, the body uses the fatty acids in the adipose capsule of the kidney for fuel. This causes the kidney to droop, a condition called *nephroptosis* (nef-rop-TOH-sis; *-ptosis* = "drooping").
- **Renal capsule.** The **renal capsule** is an extremely thin layer of dense irregular connective tissue that covers the exterior of each kidney like plastic wrap. It protects the kidney from infection and physical trauma.

Without its connective tissue coverings, a typical adult kidney is about the size of a large bar of soap (11 cm long, 6 cm wide,

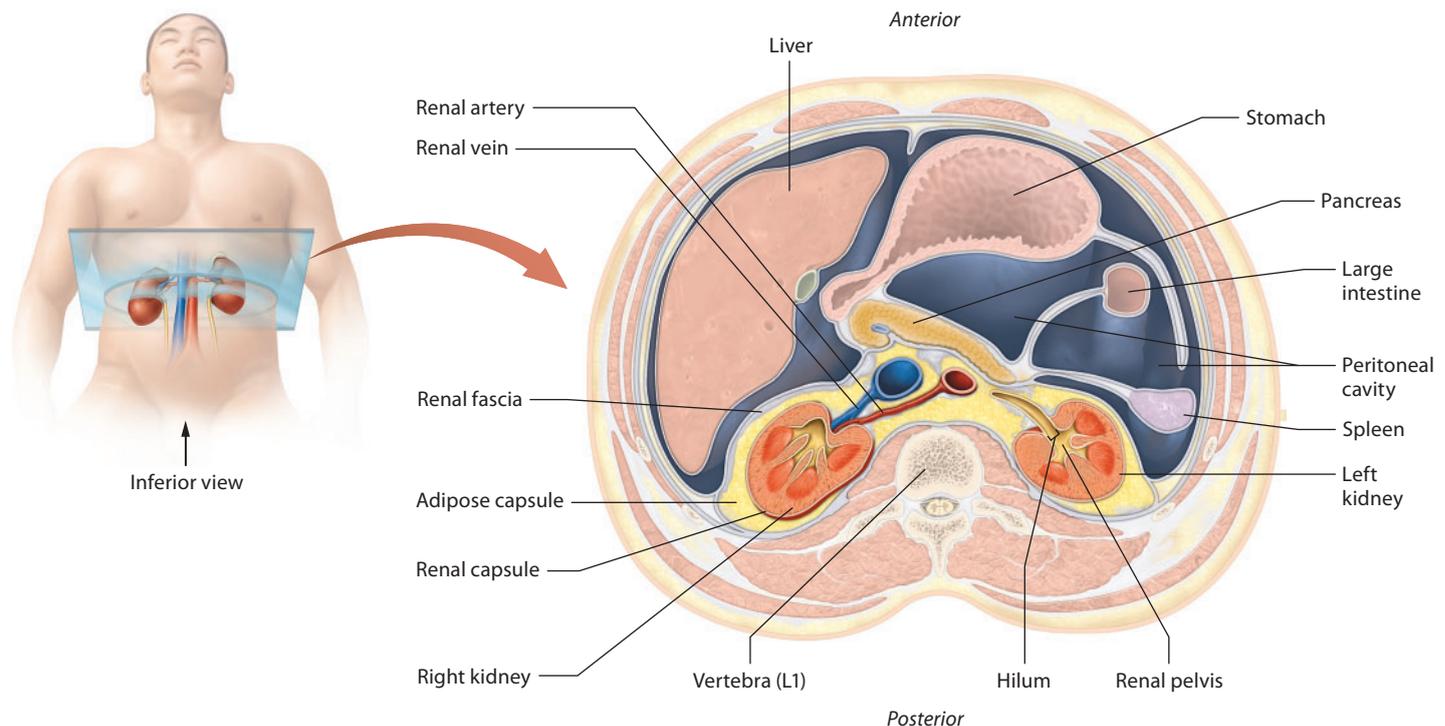


Figure 24.2 Position and external structure of the kidneys. Note that you are looking at an inferior view of this transverse section of the trunk.

and 3 cm thick), and weighs about 150 grams. On the medial surface we find an opening called the **hilum** (HY-lum), through which the *renal artery*, *renal vein*, renal nerves, and ureter enter and exit the kidney. The hilum opens to a central cavity called the **renal sinus**, which is lined by the renal capsule and filled with urine-draining structures and adipose tissue. This connective tissue anchors the ureter, blood vessels, and nerves in place.

Quick Check

- 1. What are the three connective tissue coverings of the kidney?

Internal Anatomy of the Kidneys

A frontal section of the kidney reveals the three distinct regions of this organ: the outermost **renal cortex**, the middle **renal medulla**, and the inner **renal pelvis** (Figure 24.3a). Together, the renal cortex and the renal medulla make up the urine-forming portion of the kidney. The renal pelvis and associated structures drain urine that the cortex and medulla have formed.

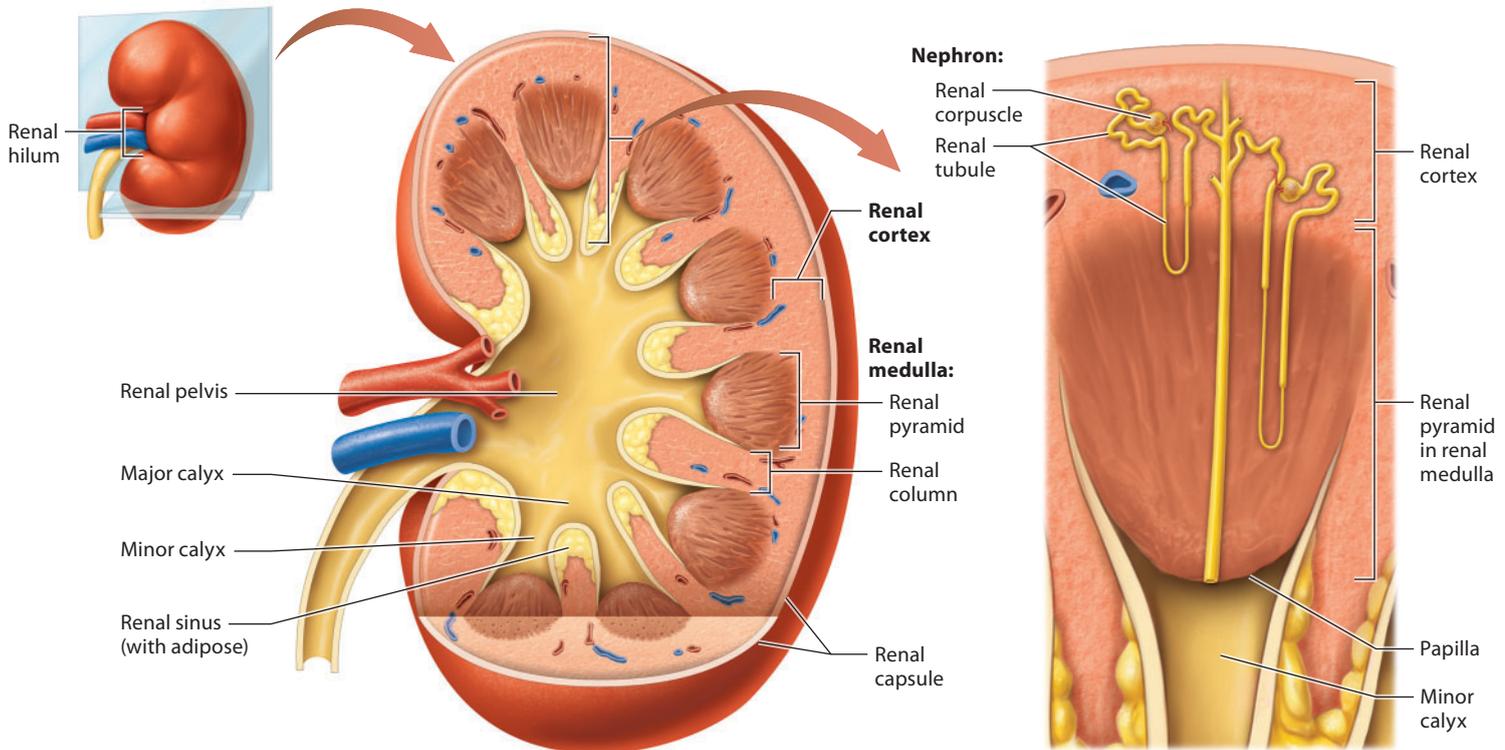
Notice in Figure 24.3a that the renal cortex is reddish-brown. This is due to its rich blood supply—it houses 90–95% of the kidney’s blood vessels. At specific points, extensions of the renal cortex called **renal columns** pass through the renal medulla toward the renal pelvis. The renal columns house blood vessels

that branch from the renal artery as they travel to the outer portion of the cortex.

Within the renal medulla we also find cone-shaped **renal pyramids** (or *medullary pyramids*), which are separated from one another by a renal column on each side. Notice that the renal pyramids are darker in color and appear striped, reflecting that they are made up of parallel bundles of small tubes, with fewer blood vessels than in the renal cortex.

The renal cortex and renal medulla of each kidney contain over one million microscopic filtering structures called **nephrons**. Nephrons are the functional units of the kidney—each one is capable of filtering the blood and producing urine. Figure 24.3b shows the basic structure of a nephron, which consists of two main components: the globe-shaped *renal corpuscle*, and a long, snaking tube of epithelium called the *renal tubule*. Notice how these components are arranged in the kidney. The renal corpuscle and the majority of the renal tubule reside in the renal cortex, whereas varying amounts of the renal tubule dip into the renal medulla.

The tip of each renal pyramid tapers into a slender **papilla** (pah-PIL-ah; *papil-* = “nipple”), which borders on the first urine-draining structure, a cup-shaped tube called a **minor calyx** (KAY-lik; plural *calyces*, KAL-ih-seez). Urine from three to four minor calyces drains into a larger **major calyx** (shown in Figure 24.3a). Two to three major calyces, in turn, drain urine into the large collecting chamber that is the renal pelvis, which leads into the ureter. Smooth muscle tissue in the walls of the calyces and renal pelvis contracts to help propel urine toward the ureter. Both the calyces and the renal pelvis reside in the renal sinus.



(a) Kidney, frontal section

(b) Section of the renal cortex and renal pyramid showing nephrons

Figure 24.3 Internal anatomy of the kidney, including the nephron.

Quick Check

- 2. What are the three regions of the kidney, and how do they differ structurally?
- 3. What is the functional unit of the kidney?

Blood Supply of the Kidneys**Flashback**

1. How is blood delivered to and drained from a typical capillary bed? (p. 670)
2. What are the major arteries and veins that supply and drain the kidneys? (p. 683)

The kidneys receive approximately one-fourth of the total cardiac output—about 1200 ml per minute—from the right and left **renal arteries**, which branch from the abdominal aorta. The renal arteries fan out into ever-smaller vessels as they pass through the renal sinus to the renal columns and cortex. **Figure 24.4** traces the path of blood flow through the kidney. From largest to smallest, the arteries shown in Figure 24.4 are as follows: **1 Renal artery** → **2 Segmental artery** → **3 Interlobar artery** → **4 Arcuate artery** → **5 Interlobular (cortical radiate) artery**.

You learned in the blood vessels chapter that systemic capillary beds are fed by arterioles and drained by venules (see Chapter 18). But in the kidneys, we find an unusual capillary bed that is both fed and drained by arterioles (Figure 24.4b). In the kidney's renal cortex, the interlobular arteries branch into tiny **afferent arterioles** (*affer-* = “to carry toward”), which feed a ball-shaped capillary bed called the **glomerulus** (gloh-MAIR-yoo-lus; *glom-* = “ball”). The glomerulus, which consists of glomerular capillaries and supporting cells, is part of the renal corpuscle of the nephron. The glomerular capillaries are then drained by a second arteriole called the **efferent arteriole** (*effer-* = “to carry away”). The efferent arteriole feeds a second capillary bed known as the **peritubular capillaries**, which together form a plexus or network around the renal tubule of each nephron. The order of this part of the system is as follows: **6 Afferent arteriole** → **7 Glomerulus** → **8 Efferent arteriole** → **9 Peritubular capillaries**.

The venous route of blood out of the kidney parallels the arterial path. Groups of peritubular venules unite into a series of progressively larger venous vessels. The sequence, from smallest to largest (see Figure 24.4), is as follows: **10 Interlobular vein** → **11 Arcuate vein** → **12 Interlobar vein** → **13 Renal vein**. Note that no segmental veins are present in the kidneys; the interlobar veins merge in the renal sinus to form the large **renal vein**. The renal vein then exits the kidney through the hilum and empties into the inferior vena cava.

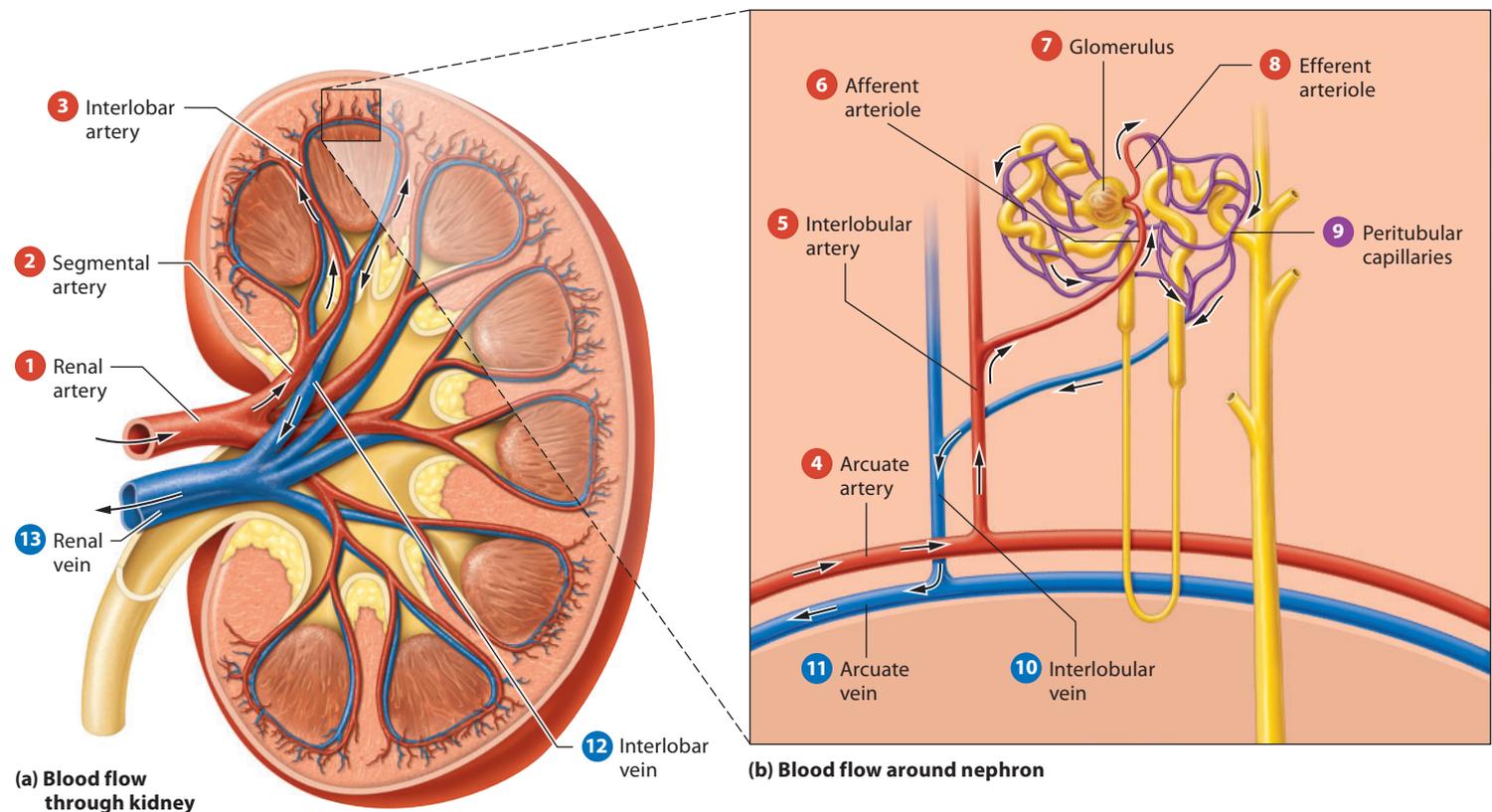


Figure 24.4 Blood flow through the kidney.



Quick Check

- 4. Trace the sequence of blood flow through the kidneys from the renal artery to the renal vein.
- 5. How does the arrangement of capillary beds in the kidneys differ from those elsewhere in the body?

Microanatomy of the Kidney: The Nephron and Collecting System

◀ Flashback

1. What are fenestrated capillaries? (p. 686)

As you learned in this module, most of the functions of the kidneys occur in their tiny nephrons (Figure 24.5). Nephrons filter the blood and modify the filtered fluid as it passes through the renal tubules. This fluid then leaves the nephron and drains into the tubules of the *collecting system* (which are not considered part of the nephron), where it is further modified until it finally becomes urine. Let's take a closer look at each of these components.

The Nephron

As we introduced earlier, the nephron has two main divisions: the renal corpuscle and the renal tubule. Both structures are composed of multiple parts.

The Renal Corpuscle The **renal corpuscle** is responsible for filtering the blood. Each globe-shaped renal corpuscle consists of two parts: the glomerulus and an outer sheath of epithelial tissue called the **glomerular capsule** (or Bowman's capsule; Figure 24.6). The glomerulus is a group of looping fenestrated capillaries. These capillaries are called fenestrated because of the large pores, or *fenestrations* (*fenestre-* = “window”), present within their plasma membranes and between their endothelial cells. These fenestrations, which make the capillaries extremely “leaky,” or permeable, form a main part of the filtering structure of the renal corpuscle.

Surrounding the glomerulus is the double-layered glomerular capsule, which consists of an outer *parietal layer* (pah-RY-eh-tal) and an inner *visceral layer*. The parietal layer is a globelike extension of the renal tubule consisting of simple squamous epithelium. The visceral layer consists of modified epithelial cells called **podocytes** (POH-doh-sytz; *podo-* = “foot”) that wrap around the glomerular capillaries. Extending from each podocyte are extensions called *foot processes*, or *pedicels* (PED-ih-selz). Pedicels weave together to form **filtration slits**, which make up another part of the renal corpuscle's filtering structure. Between the parietal and visceral layers we find a hollow region, or lumen, called the **capsular space**, which is continuous with the beginning of the renal tubule lumen.

The podocytes and fenestrated glomerular capillaries form part of a complex membrane (the filtering structure we mentioned earlier) that filters blood flowing through the glomerulus. This structure allows a large volume of fluid to be filtered from the blood (which we discuss in the next module). The fluid

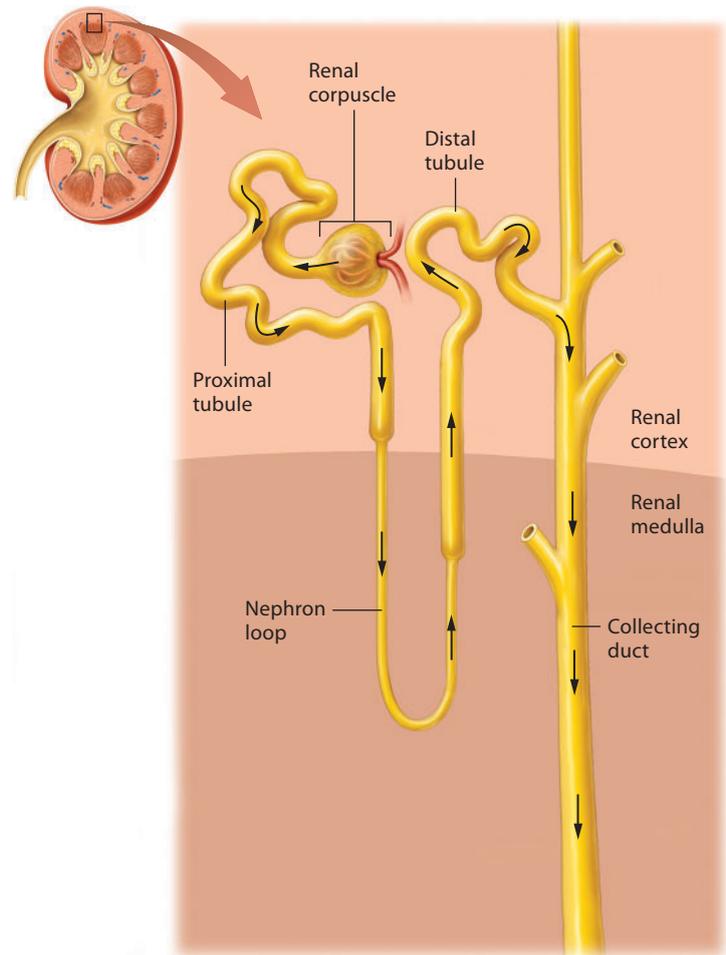


Figure 24.5 A generalized nephron and collecting system.



that passes through the filter to leave the glomerular capillaries, which is known as *filtrate*, first enters the capsular space, then flows into the renal tubule lumen.

The Renal Tubule Newly formed filtrate flows from the capsular space into the “pipes” of the nephron: the renal tubule. The renal tubule is a winding tube responsible for modifying the filtrate. It has three regions: the proximal tubule, nephron loop, and distal tubule, each of which differs in structure and function (Figure 24.7).

1. **Proximal tubule.** The initial and longest segment of the renal tubule through which filtrate flows is the **proximal tubule**; it consists of simple cuboidal epithelial cells with prominent microvilli. This part of the tubule has both convoluted (coiled) and straight sections, which is why this text uses the broader term proximal tubule (rather than proximal convoluted tubule). The many microvilli projecting into the lumen of the proximal tubule form a *brush border*, so named because the fine projections resemble the bristles on a brush. This border greatly increases surface area.

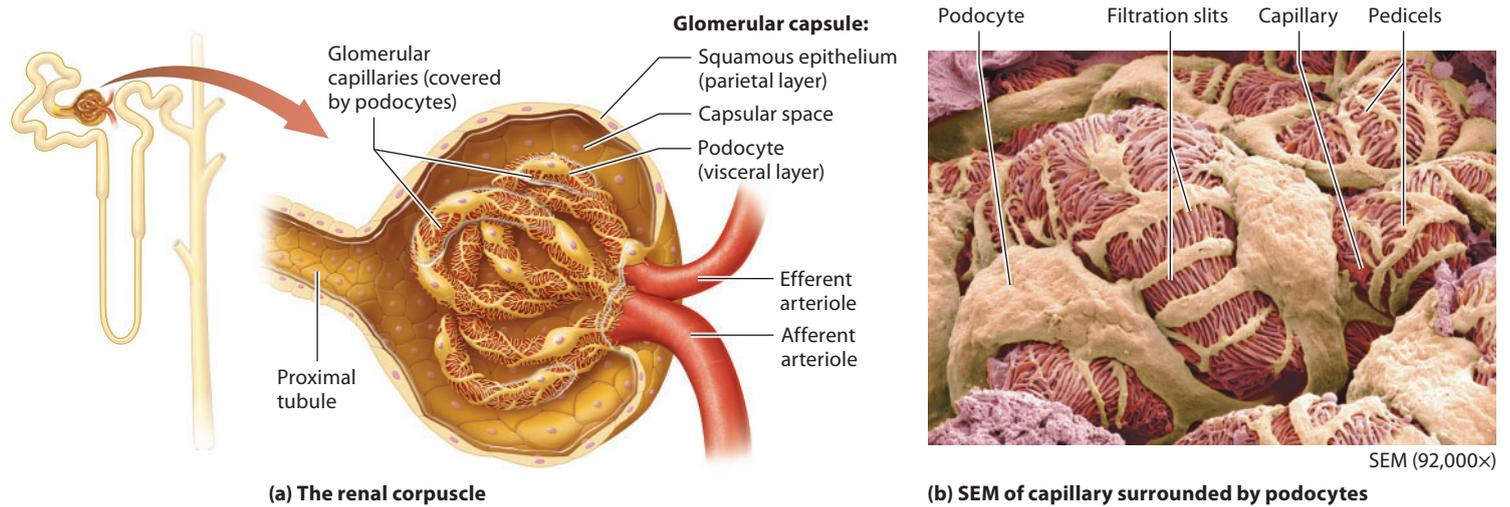


Figure 24.6 The renal corpuscle.

2. **Nephron loop (loop of Henle).** The remaining filtrate flows on to the **nephron loop**, also known as the **loop of Henle**, which is the only part of the renal tubule that dips into the renal medulla. The nephron loop has two limbs: The **descending limb** travels toward the renal medulla, turns 180°, and becomes the **ascending limb**, which climbs back toward the renal cortex. The descending limb is composed of simple squamous epithelium, and thus is often called the **thin descending limb**. In some nephrons this thin segment also forms the bend region and part of the ascending limb, so there is also a **thin ascending limb**. However, the majority of the ascending limb is composed of thicker simple cuboidal epithelium, and is therefore referred to as the **thick ascending limb**.

3. **Distal tubule.** The final segment through which the filtrate passes in the renal tubule is the **distal tubule**. (Again, this text uses the broader term, as this segment of the tubule has both convoluted and straight sections.) Like the proximal tubule, the distal tubule is composed of simple cuboidal epithelium. However, the distal tubule lacks a brush border.

The Juxtaglomerular Apparatus

At the transition point between the ascending limb of the nephron loop and the distal tubule, we find a tightly packed group of cells called the **macula densa** (MAK-yoo-lah DEN-sah; “dense spot”). The macula densa comes into contact with modified smooth muscle cells in the afferent and efferent arterioles, known

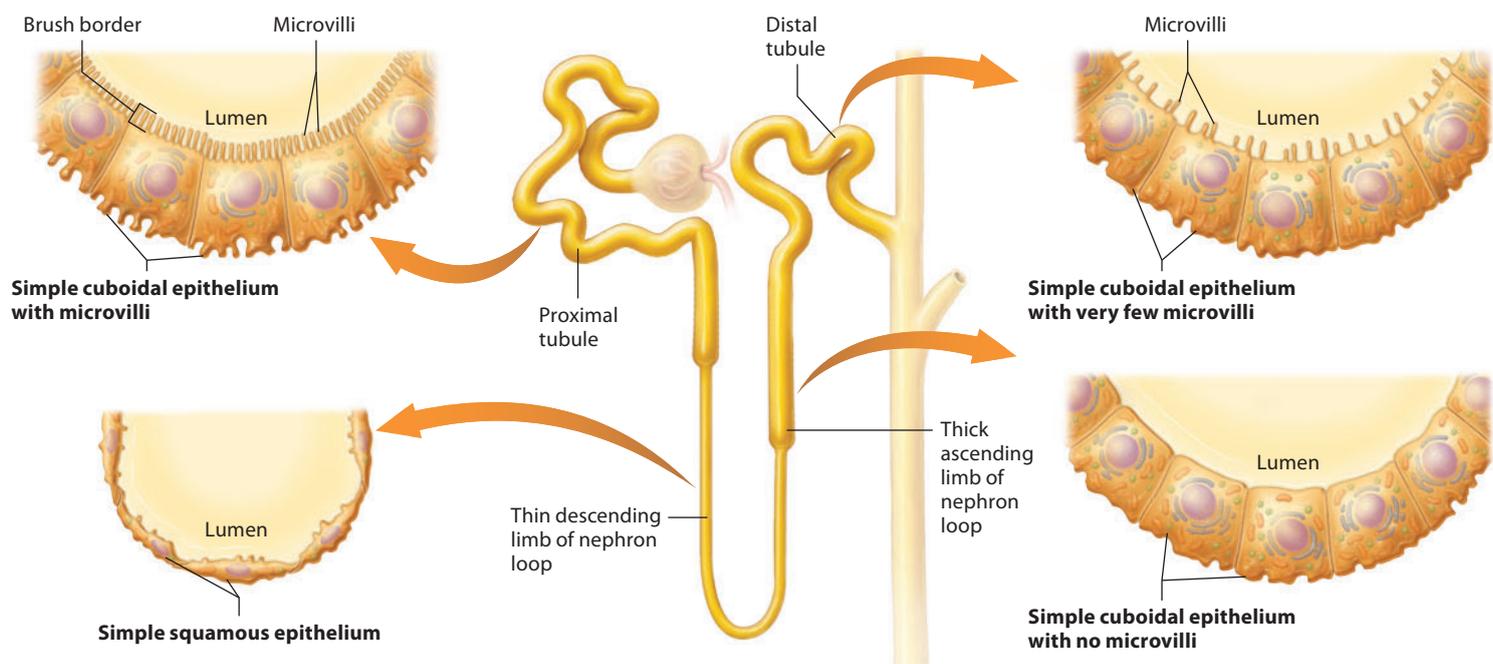


Figure 24.7 Structural characteristics of the renal tubule.

as **juxtaglomerular (JG) cells** (juks'-tah-gloh-MAIR-yoo-lar; *juxta-* = “next to”). Together, the macula densa and JG cells form a structure called the **juxtaglomerular apparatus (JGA)**, which regulates blood pressure and glomerular filtration rate (**Figure 24.8**). We will revisit the JGA in Module 24.4.

The Collecting System

The nephron ends where filtrate in the distal tubule empties into the **collecting system**, another series of structurally and functionally distinct tubules that further modify the filtrate as it passes through them. Most of the collecting system consists of simple cuboidal or columnar epithelium with few microvilli (**Figure 24.9**).

The collecting system consists of the cortical collecting duct and the medullary collecting system. The distal tubule empties filtrate into the first part of the collecting system, the **cortical collecting duct**, which is found within the renal cortex. The cortical collecting duct is made up of simple cuboidal epithelial cells. Note that each cortical collecting duct drains several distal tubules. As the cortical collecting duct passes into the renal medulla, it becomes the **medullary collecting duct**. Deep within the renal medulla, several medullary collecting ducts empty filtrate into a larger **papillary duct**. The papillary duct contains low columnar epithelial cells. The **medullary collecting system** includes the medullary collecting ducts and the papillary ducts. When the filtrate reaches the end of the papillary duct, it is urine. The urine exits at the papilla of the renal pyramid into a minor calyx. The formation of crystals within the tubules of the collecting system can block the flow of filtrate and lead to intense pain. You can find out more about this condition in *A&P in the Real World: Nephrolithiasis*.

Quick Check

- 6. What are the two components of the renal corpuscle?
- 7. Trace the pathway filtrate takes through the nephron and collecting system from the capsular space to the papillary duct.

Types of Nephrons

The previous discussion simplified the nephron by presenting a “generalized” version of it. However, the kidneys actually contain two types of nephrons that are distinguished by both the structure and function of their nephron loops and the organization of the peritubular capillaries. These two types are labeled **cortical** and **juxtamedullary** (juk'-stah-MED-yoo-lair-ee).

About 80% of nephrons are **cortical nephrons**, so named because they are located primarily in the renal cortex (**Figure 24.10a**). The renal corpuscles of cortical nephrons are situated in the **outer** renal cortex, and they have very short nephron loops that either just dip into the superficial part of the renal medulla or never leave the cortex. Peritubular capillaries supply blood to the nephron loops of cortical nephrons (although they exchange materials through the interstitial fluid rather than directly).

The other, less numerous, type of nephron in the kidney is the **juxtamedullary nephron**. Notice in **Figure 24.10b** that the renal corpuscle of the juxtamedullary nephron sits close to the boundary between the renal cortex and the renal medulla. In addition, it has a long nephron loop that burrows deeply into the renal medulla. Here the loop is surrounded by a ladder-like network of capillaries called the **vasa recta** (VAY-zah REK-tah; “straight vessels”) which arises from the efferent arteriole. Like the

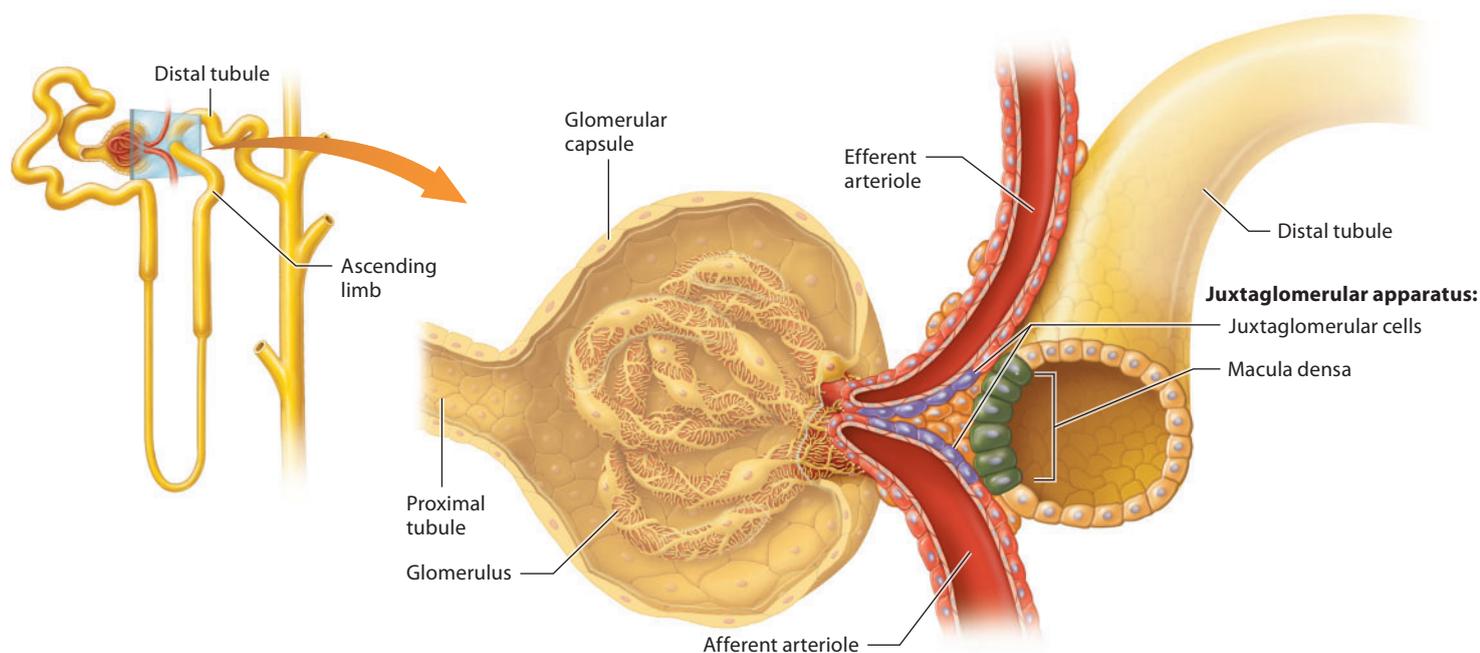


Figure 24.8 The juxtaglomerular apparatus.

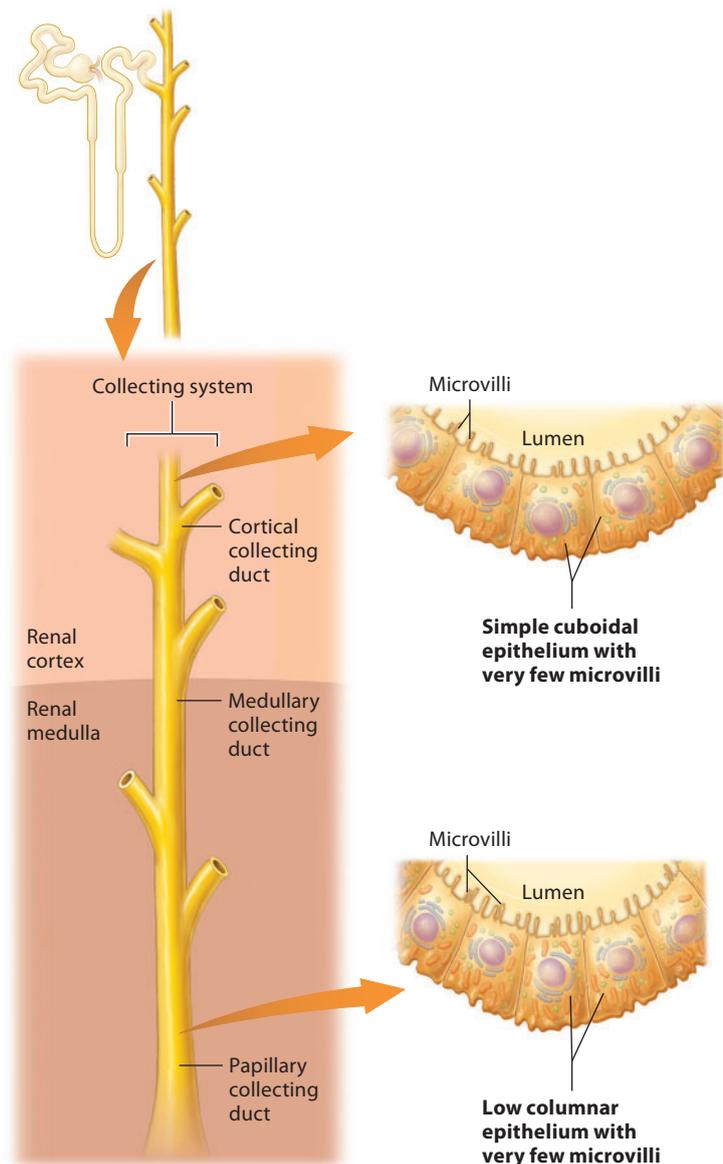


Figure 24.9 Structural characteristics of the collecting system.

peritubular capillaries, the vasa recta empty into interlobular veins. Notice that the portion of the nephron that lies in the cortex is surrounded by branches of the peritubular capillaries from the neighboring cortical nephrons. This unique structure allows the juxtamedullary nephrons to function as part of a system that controls the volume and concentration of urine, concepts we will discuss in Module 24.6.

Apply What You Learned

1. Predict the effects of a condition that results in gradual loss of microvilli from the proximal tubule.
2. Predict the potential effects of abnormally narrow renal arteries, a condition called *renal artery stenosis*, on the ability of the kidneys to carry out their functions.

See answers in Appendix A.

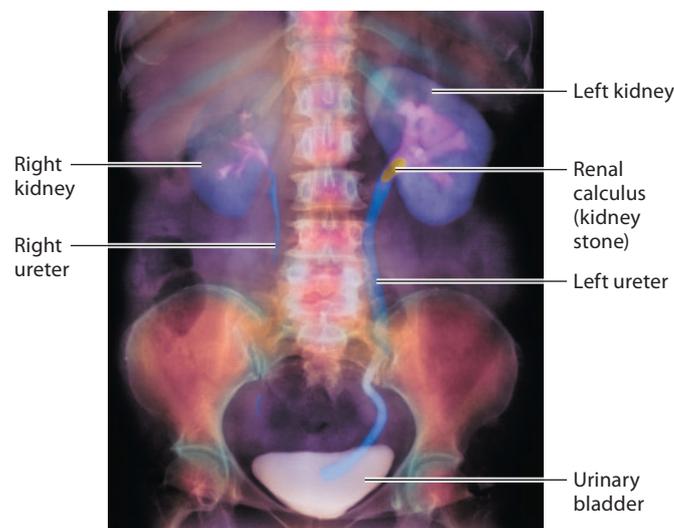


Nephrolithiasis

The condition known as **nephrolithiasis** (nef'-roh-lith-EYE-ah-sis; *lith-* = “stone”) is characterized by the formation of **renal calculi** (KAL-kyoo-lye), commonly known as *kidney stones*. Renal calculi are crystalline structures composed most commonly of calcium oxalate salts. They form when the concentrations of these ions, as well as solutes such as sodium ions, hydrogen ions, and uric acid, are present in the filtrate in higher than normal amounts. This condition is known as *supersaturation*, and supersaturated ions are more likely to come out of solution and crystallize. Risk factors for supersaturation include dehydration; a diet high in fat, animal protein, and salt; and obesity.

Typically, the crystals form in the nephron loop, distal tubule, and/or collecting system. Most crystals simply pass unnoticed into the urine. However, sometimes the crystals adhere to the epithelium of the tubules, particularly in the collecting system, and form *seed crystals* that lead to the formation of stones. The stones may remain in the collecting system or may break off and lodge in the calyces, renal pelvis, and ureter. Stones lodged within the urinary system cause the most common symptom of nephrolithiasis: severe pain, known as *renal colic*, that radiates from the lumbar region to the pubic region. Other symptoms include blood in the urine, sweating, nausea, and vomiting.

Nephrolithiasis can be diagnosed in several ways, including computed tomography scans and an **intravenous pyelogram** (PY-loh-gram; *pyelo-* = “pelvis”), or **IVP**. An IVP is a radiograph of the urinary system that uses a contrast medium such as iodine to reveal the structure of the renal pelvis, the major and minor calyces, and the ureters and urinary bladder. An example of an IVP with a renal calculus blocking the left ureter is shown here:



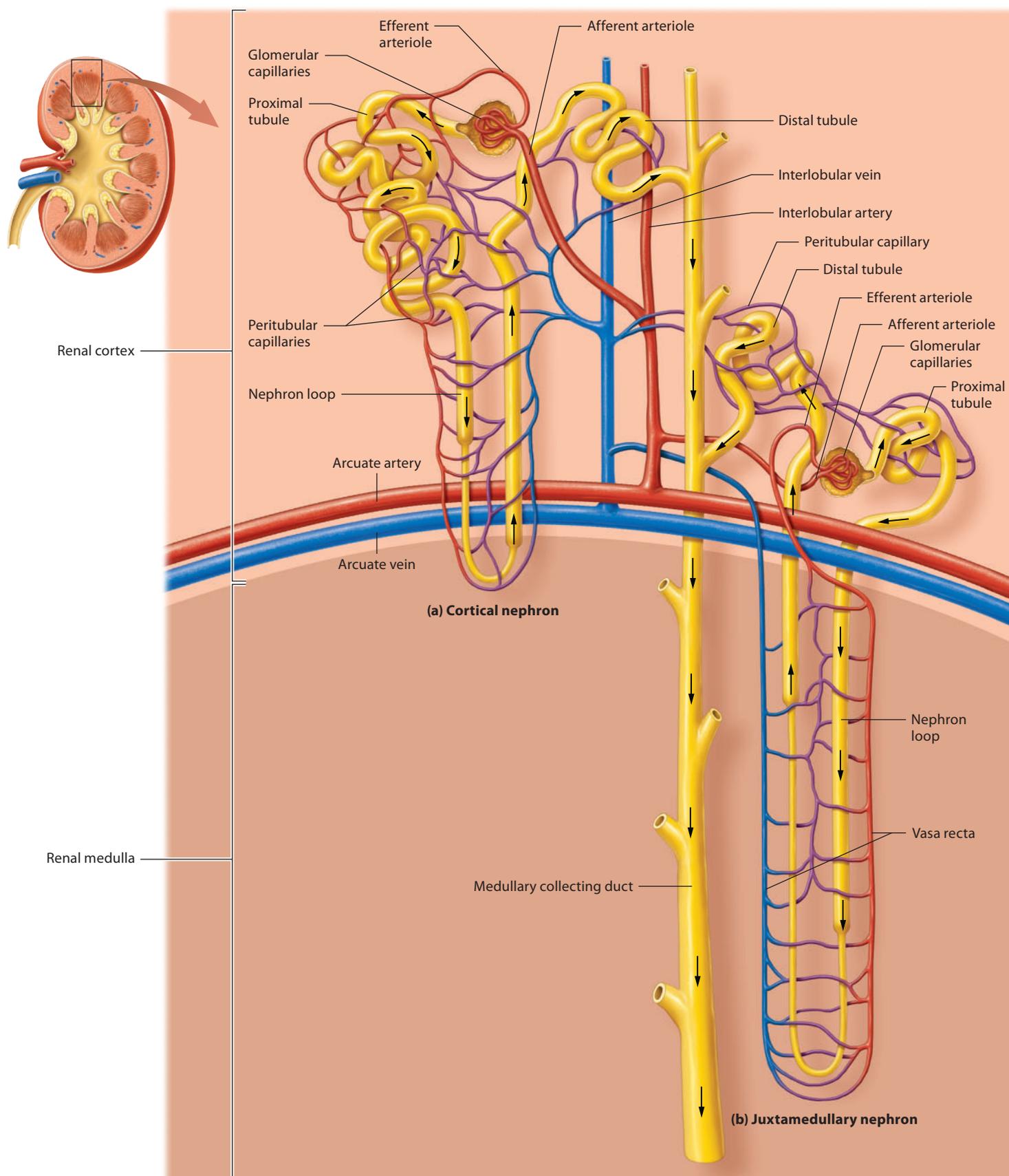


Figure 24.10 Cortical and juxtamedullary nephrons.

MODULE

24.3

Overview of Renal Physiology

Learning Outcomes

1. List the three major processes in urine formation and describe where each occurs in the nephron and collecting system.

Nephrons carry out three basic physiologic processes that allow the kidneys to perform their homeostatic functions: *filtration*, *reabsorption*, and *secretion*. These functions, illustrated in **Figure 24.11**, are as follows:

- **Glomerular filtration.** The first process performed by the nephron is to filter the blood, a process known as **glomerular filtration**. This takes place as blood passes through the membrane of the glomerular capillaries and some of the plasma is filtered into the surrounding glomerular space. This filter is selective based on size, so it holds back cells and most proteins, which remain in the blood, but allows some of the smaller substances—including water, electrolytes (such as sodium and potassium ions), acids and bases (such as hydrogen and bicarbonate ions), organic molecules, and metabolic wastes—to exit the blood and enter the glomerular capsule. The fluid and solutes that enter the capsular space of the nephron form the **filtrate**, also known as *tubular fluid*.
- **Tubular reabsorption.** The next process the nephron performs is to modify the filtrate as it flows through the tubules. Much of this modification involves reclaiming substances from the filtrate, such as water, glucose, amino acids, and electrolytes, and returning them to the blood. This process is known as **tubular reabsorption**. The nephron is able to reabsorb the majority of water and solutes filtered by the glomerular membrane. Most reabsorption takes place in the proximal tubule and nephron loop. However, some more precisely controlled reabsorption also occurs in the distal tubule and collecting ducts; this process allows the nephron to vary the amounts of different substances reabsorbed to maintain homeostasis as the needs of the body change.
- **Tubular secretion.** The filtrate is also modified by a process known as **tubular secretion**, which is essentially tubular reabsorption in the reverse direction. Notice in **Figure 24.11** that during tubular secretion substances are moved from the peritubular capillary blood into the filtrate to eventually be excreted. Secretion happens all along the tubule, although different substances may be secreted more in one area than another. Tubular secretion helps maintain electrolyte and acid-base homeostasis and removes toxins from the blood that did not enter the filtrate via filtration.

In the next two modules, Modules 24.4 and 24.5, we examine each of these processes and how they contribute to the overall function of the kidneys and urinary system. In Module 24.6 we see how these processes allow the kidneys to control the volume and concentration of urine produced.

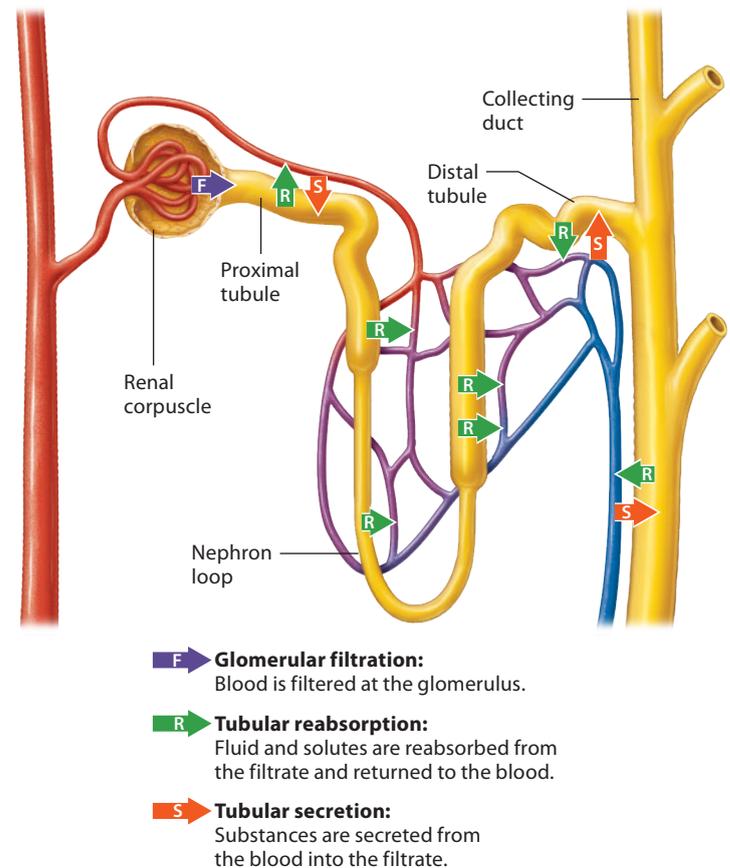


Figure 24.11 Three physiological processes carried out by the kidneys.

Quick Check

1. What happens during glomerular filtration?
2. How do tubular reabsorption and tubular secretion differ?

MODULE

24.4

Renal Physiology I: Glomerular Filtration

Learning Outcomes

1. Describe the structure of the filtration membrane.
2. Define the glomerular filtration rate (GFR) and state its average value.
3. Describe the hydrostatic and colloid osmotic forces that favor and oppose filtration.
4. Predict specific factors that will increase or decrease GFR.
5. Describe the myogenic and tubuloglomerular feedback mechanisms.
6. Describe the role of each of the following in the control of GFR: renin-angiotensin-aldosterone system, atrial natriuretic peptide, and sympathetic nervous system activity.

The mechanical process of filtration is easy to picture—you witness it every time you drain cooked spaghetti into a colander. When you “filter” the spaghetti, you cause the filtrate (water and small solutes) to pass through a filter (the colander) and leave large substances (the noodles) behind. A similar process occurs in the kidneys with glomerular filtration—the membrane in the renal corpuscle, known as the *filtration membrane*, forms a filter that allows filtrate to pass through, but leaves relatively large substances behind in the blood.

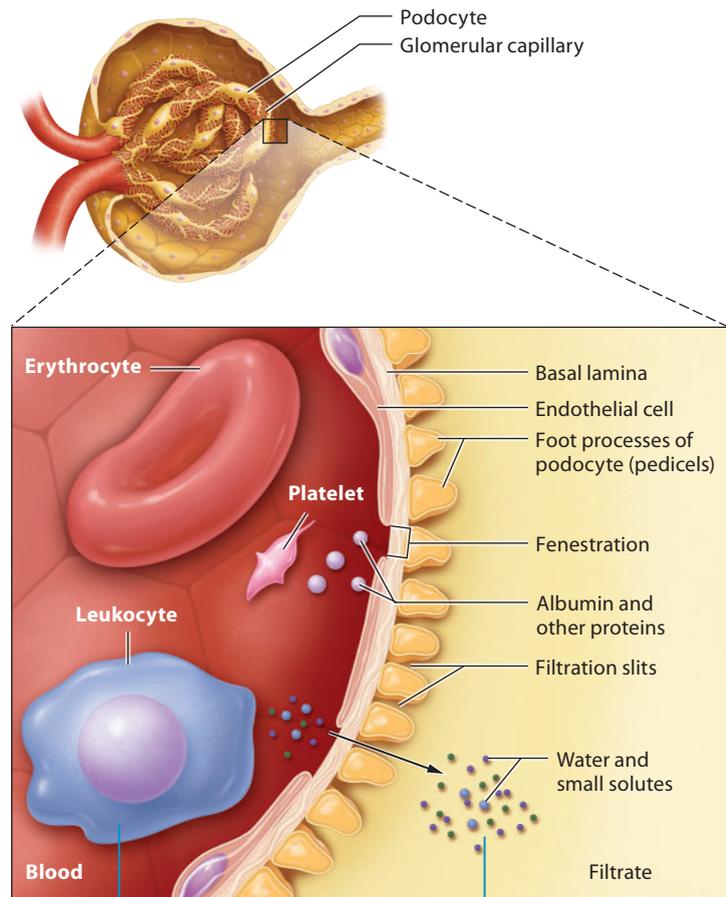
In this module we examine the structure of the filtration membrane and the mechanical process of filtration. We then take a look at the factors that determine the rate at which filtrate is formed, a value known as the *glomerular filtration rate*. We conclude by discussing how the body tightly regulates the glomerular filtration rate and how this in turn enables the kidneys to maintain many aspects of homeostasis.

The Filtration Membrane and the Filtrate

The inner part of the glomerular capsule consists of three layers that act as barriers, or filters; together these layers are called the **filtration membrane**. This membrane is made up of the glomerular capillary endothelial cells, a basal lamina, and podocytes (the visceral layer of the glomerular capsule) (Figure 24.12). Let’s look at each of these layers, from deep to superficial (the direction of filtrate flow), more closely:

1. **Fenestrated glomerular capillary endothelial cells.** Like all capillaries, the glomeruli are composed of endothelial cells. Recall, however, that the glomerular endothelial cells are **fenestrated**; they have pores that make them leakier than most capillaries. The gaps between the glomerular endothelial cells are relatively large (about 70–100 nm) but are still small enough to prevent blood cells and platelets from exiting the capillaries.
2. **Basal lamina.** This thin layer of extracellular matrix gel separates the glomerular endothelial cells from the podocytes. Collagen fibers within the basal lamina form a meshwork that acts like a colander, preventing substances with a diameter greater than 8 nm from entering the capsular space. This effectively blocks the passage of most plasma proteins. In addition, the collagen fibers have negative charges that repel negatively charged plasma proteins, even those smaller than 8 nm in diameter.
3. **Podocytes (visceral layer of the glomerular capsule).** The podocytes composing the visceral layer of the glomerular capsule make up the third and finest filter in the filtration membrane. Note in Figure 24.12 that their finger-like pedicels wrap around the glomerular capillaries and interlace to form filtration slits. These narrow slits allow only substances with a diameter less than 6–7 nm to enter the capsular space. Albumin, the most prevalent plasma protein, has a diameter of 7.1 nm, so it is normally prevented from entering the filtrate.

The fluid and solutes that pass through the filtration membrane and enter the capsular space make up the filtrate. The size of the pores in this membrane determines the composition of



Formed elements and most proteins in blood are too large to fit through the filtration slits.

Water and small solutes are small enough to pass through the filtration slits and enter the filtrate.

Figure 24.12 Filtration and the filtration membrane.



the filtrate. Observe in Figure 24.12 that the filtration membrane allows water and small dissolved solutes, including glucose, electrolytes, very small proteins, and amino acids, to leave the blood and enter the capsular space, but prevents the exit of formed elements, such as cells and platelets, and most proteins. Another important substance filtered from the blood is a group of molecules known as *nitrogenous wastes*. These molecules include *urea* and *ammonium ions* (NH_4^+), waste products of protein metabolism; *creatinine*, a waste product of the creatine kinase reaction that occurs in muscle cells and other body cells; and *uric acid*, a waste product of nucleic acid metabolism. All are relatively small molecules that pass easily through the pores of the filtration membrane.

The percentage of plasma that passes through the filtration membrane to enter the capsular space and become filtrate is called the *filtration fraction*. An average filtration fraction is 20%, which means that about one-fifth of the plasma that flows through the glomerulus exits the blood and enters the capsular space. The filtration fraction is so large because of the looping arrangement of the glomerular capillaries. This looping increases their surface area dramatically—if you were to stitch


CORE PRINCIPLE
Structure-Function

all of the surfaces of the filtration membranes of one kidney together, their combined area would be about 6 m^2 (about the size of a small bedroom)! In an example of the Structure-Function Core Principle (p. 25), this large surface area makes filtration through this stack of ever-finer filters a very efficient process.

Quick Check

- 1. What are the three components of the filtration membrane?
- 2. What is the function of the filtration membrane?
- 3. Which substances are found in the filtrate?

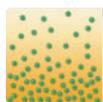
The Glomerular Filtration Rate (GFR)

◀ Flashback

1. Define osmosis. (p. 75)
2. What is colloid osmotic pressure? (p. 690)
3. What is vascular resistance? (p. 689)

Filtrate is formed at the remarkably rapid rate of about 125 ml/min. This value, the amount of filtrate formed by both kidneys in 1 minute, is known as the **glomerular filtration rate (GFR)**. Over the course of a day, the kidneys produce about 180 liters of filtrate (to put this into perspective, imagine filling your gastrointestinal tract with a similar volume by drinking 90 2-liter bottles of soda in one day!). This is an impressive feat, considering that we have only about 3 liters of plasma. Therefore, your entire plasma volume is filtered by your kidneys about 60 times per day.

The kidneys are able to filter blood so efficiently in part because the glomerular capillaries are remarkably permeable.


CORE PRINCIPLE
Gradients

However, even with fenestrated capillaries, filtration will happen only if a pressure gradient is present to push water and solutes through the filtration membrane (an example of the Gradients Core Principle, p. 26). In this section we discuss the forces that allow this process to occur.

Filtration Pressures

Let's first review the two forces that drive fluid movement in a typical capillary bed:

- **Hydrostatic pressure.** *Hydrostatic pressure* is the force of a fluid on the wall of its container. In the case of blood capillaries, hydrostatic pressure is equal to the blood pressure, and it tends to push water *out* of the capillary and into the interstitial space.
- **Colloid osmotic pressure.** *Colloid osmotic pressure (COP)* is the pressure created by proteins (primarily albumin) in the plasma. The osmotic gradient created by these proteins pulls water *into* the capillaries by osmosis.

Recall that these two forces work together in a capillary bed to determine the *net filtration pressure (NFP)* of the bed (see Chapter 18). The net filtration pressure determines the direction of water movement between the capillaries and the interstitial fluid. Simply stated, water moves out of the capillary if hydrostatic pressure is higher than COP, or into the capillary if COP is higher than hydrostatic pressure.

Net Filtration Pressure at the Glomerulus

We can apply these same two principles to the glomerular capillaries. However, the situation is slightly more complex in the glomerulus, because we have a third force to factor in: the hydrostatic pressure of the fluid in the capsular space. Let's examine each of these forces, which are shown in **Figure 24.13**:

- **Glomerular hydrostatic pressure.** The **glomerular hydrostatic pressure (GHP)**, which is largely determined by the systemic blood pressure, measures about 50 mm Hg. This pressure is considerably higher than that of a typical capillary bed (which ranges from 17 to 35 mm Hg). This is because blood leaving such a capillary bed enters a low-resistance venule, whereas blood leaving the glomerulus enters a high-resistance efferent arteriole. This arteriole's high resistance is due to its smooth muscle and its small diameter—notice in Figure 24.13 that the diameter of the efferent arteriole is smaller than that of the afferent arteriole. This causes blood to back up and push against the walls of the glomerular capillaries, which *favors* its movement through the filtration membrane.
- **Glomerular colloid osmotic pressure.** Like the COP in typical capillaries, the **glomerular colloid osmotic pressure (GCOP)** is created by the presence of proteins such as albumin in the plasma. The GCOP averages about 30 mm Hg, slightly higher than the COP in a typical capillary bed, because the blood in the glomerulus is a bit more concentrated. The reason for this is that water leaves the glomerular blood rapidly through the filtration membrane, which causes any solutes left in the blood to increase in concentration. The GCOP *opposes* filtration, “pulling” on water to hold it in the glomerular capillaries.

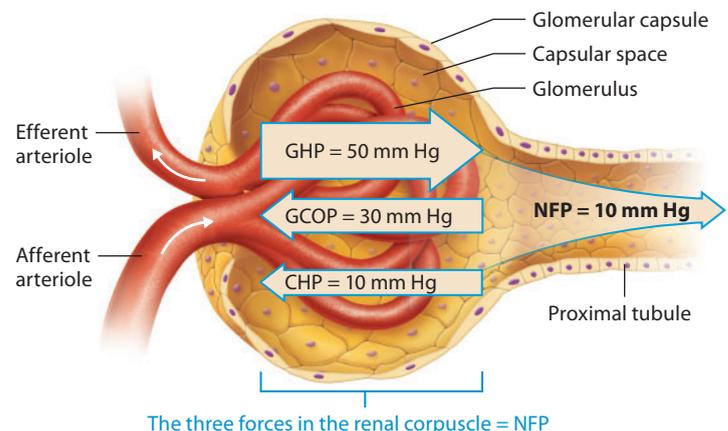


Figure 24.13 Net filtration pressure in the glomerular capillaries.



Play animation
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- **Capsular hydrostatic pressure.** Like an emptying kitchen sink with the faucet turned on, the water in the capsular space can only drain into the renal tubule so quickly. The rapidly accumulating filtrate inside the capsular space of a nephron builds up a hydrostatic pressure of its own, called the **capsular hydrostatic pressure (CHP)**. This pressure (about 10 mm Hg) tries to push water into the glomerular capillaries and so *opposes* filtration.

We can combine these three forces to yield the glomerular **net filtration pressure (NFP)**, the total pressure gradient available to drive water across the filtration membrane and into the capsular space. To find the glomerular NFP, we subtract the two forces that oppose filtration (GCOP and CHP) from the one that favors filtration (GHP):

$$\begin{aligned} \text{NFP} &= \text{GHP} - (\text{GCOP} + \text{CHP}) \\ &= 50 \text{ mm Hg} - (30 \text{ mm Hg} + 10 \text{ mm Hg}) \\ &= 10 \text{ mm Hg} \end{aligned}$$

So, we find a net filtration pressure of about 10 mm Hg in the glomerular capillaries. This pressure, combined with the leakiness of the glomerular capillaries and their large surface area, yields the GFR of about 125 ml/min. To gain perspective on this, compare the GFR to the rate at which systemic capillary beds lose water—about 1.5 ml/min, quite a significant difference.

Many conditions can impact the GFR. One common condition is discussed in *A&P in the Real World: Glomerulonephritis*.

Quick Check

- 4. What is the GFR?
- 5. Which three pressures combine to determine the net filtration pressure? Which pressure(s) promote filtration? Which pressure(s) oppose filtration?

Factors That Affect the Glomerular Filtration Rate

◀ Flashback

1. What are the primary functions of the hormones angiotensin-II and atrial natriuretic peptide? (p. 610)
2. What happens to a blood vessel when blood pressure increases and the vessel is stretched? (p. 671)

Glomerular filtration is essentially the “gatekeeper” of renal physiology because it begins the process of waste removal. The GFR determines how rapidly the blood is cleansed of metabolic wastes, how effectively the kidneys can carry out both tubular reabsorption and secretion, and how well the kidneys are able to maintain homeostasis in the body. For these reasons, factors that impact the GFR influence all functions of the kidney.

Several factors regulate and impact the GFR. These factors may originate within the kidney itself or may be due to the function of systems outside the urinary system. The internal mechanisms are called *autoregulation*, and have to do with maintaining

the GFR. The external factors, including neural and hormonal factors, are part of broader systems that work to maintain systemic blood pressure and affect the GFR in doing so. We discuss each of these factors in the upcoming sections. But first let’s look at the physical changes that are used by all of these mechanisms to control the GFR.

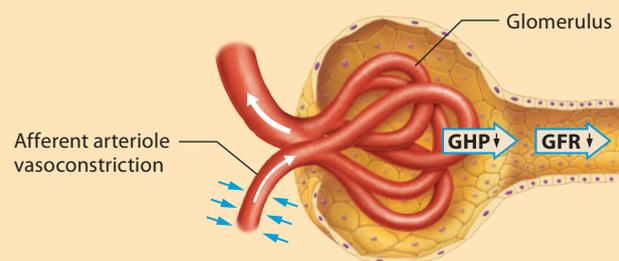
ConceptBOOST >>>

How Changes in Arteriolar Diameter Influence the GFR

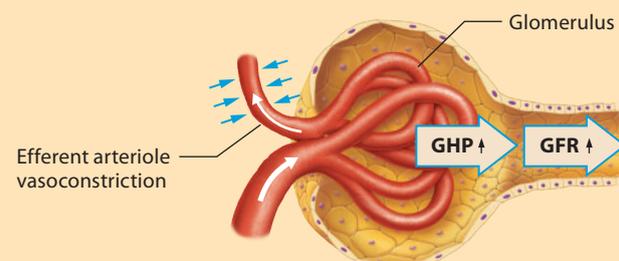
As we discussed earlier, filtration will occur only when a net pressure gradient in the glomerulus drives fluid out of the blood and into the capsular space. The size of this gradient determines how much filtration takes place—a small gradient will lead to only minimal filtration, whereas a large gradient leads to heavy filtration. Several factors determine the size of the pressure gradient in the glomerulus, but one of the most easily adjustable factors is the diameter of the afferent (entering) and efferent (leaving) arterioles. When either arteriole constricts or dilates, this changes the glomerular hydrostatic pressure (GHP), and therefore the entire net pressure gradient also changes.

You can think of blood flowing in and out of the glomerulus as being similar to water flowing in and out of a sink, where the afferent arteriole is the faucet, the basin is the glomerulus, and the efferent arteriole is the drainpipe. Keep this analogy in mind as we explore how this mechanism works:

- Vasoconstriction of the afferent arteriole “turns down the faucet.” This allows less blood to flow into the glomerulus, which decreases the GHP and the GFR:

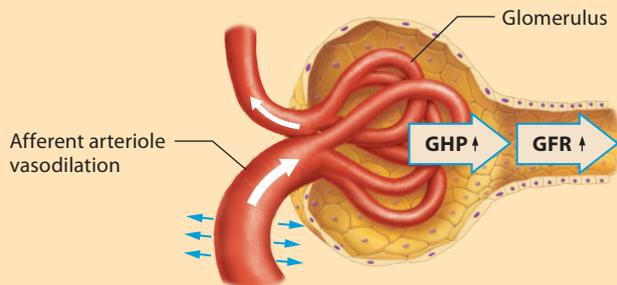


- Vasoconstriction of the efferent arteriole “clogs the drain.” This causes blood to back up within the glomerulus, which increases the GHP and thus increases the GFR:

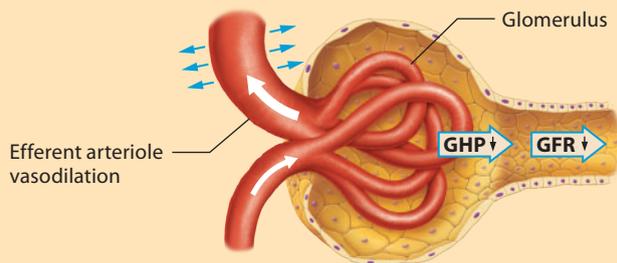


Vasodilation has the opposite effects:

- Vasodilation of the afferent arteriole “turns up the faucet.” This increases the GHP and the GFR:



- Vasodilation of the efferent arteriole “unclogs the drain,” allowing increased flow out of the glomerulus. This decreases the GHP and the GFR:



In the upcoming sections, you'll see that the main mechanisms the body uses to control or maintain GFR work by causing one or more of these physical changes. ■

mechanisms to control GFR that we discussed in the Concept Boost. It occurs in the following way:

- An *increase* in systemic blood pressure stretches the afferent arteriole and leads to an increase in GFR. This leads the muscle cells to contract, constricting the arteriole. Vasoconstriction of the afferent arteriole decreases the blood flow through the glomerulus (“turns down the faucet”), which decreases glomerular hydrostatic pressure and the GFR back to normal levels.
- A *decrease* in the systemic blood pressure causes the afferent arteriole to be less stretched, decreasing the GFR and making its smooth muscle cells relax. The resulting vasodilation of the arteriole increases the blood flow and the glomerular hydrostatic pressure (“turns up the faucet”), and the GFR increases back to normal levels.

The myogenic mechanism acts rapidly—it can restore the normal GFR within seconds of even a significant change in blood pressure. Note, however, that these mechanisms can restore the GFR over a systolic blood pressure range of about 80–180 mm Hg (a normal range for systolic pressure is 100–120 mm Hg). If the systolic blood pressure goes higher than 180 mm Hg, the afferent arteriole can't constrict any further to restore the GFR. Similarly, if systolic blood pressure drops below this range, the afferent arteriole is unable to dilate enough to restore the GFR to normal levels.

Tubuloglomerular Feedback The second autoregulatory mechanism of the kidneys is *tubuloglomerular feedback* (too'-byoo-low-gloh-MAIR-yoo-lar), so named because the macula densa of the distal renal tubule (see Figure 24.8) is part of a negative feedback loop that controls pressure in the glomerulus. As it's currently understood, the mechanism of tubuloglomerular feedback is related to the concentration of NaCl in the

Autoregulation of the GFR

Because the GHP is mostly the result of systemic blood pressure, it seems logical that a change in systemic blood pressure would alter the GHP and so the GFR. However, this is *not* the case. The GFR remains relatively constant over wide ranges of systemic blood pressure because of the process known as **autoregulation**, local responses initiated and maintained by the kidneys. In an example of the Feedback Loops Core Principle (p. 21), autoregulation consists of two negative feedback processes: the *myogenic mechanism* and *tubuloglomerular feedback*.



CORE PRINCIPLE
Feedback Loops

The Myogenic Mechanism Recall that an increase in blood pressure stretches a blood vessel, which triggers its smooth muscle cells to vasoconstrict (see Chapter 18). This decreases the amount of blood flowing through the vessel, which in turn minimizes the stretch imposed on the vessel. We find a similar phenomenon in the blood vessels of the kidney, which is termed the **myogenic mechanism** (my-oh-JEN-ik; *myo-* = “muscle,” *-genic* = “producing”). The myogenic mechanism works by using the same



Glomerulonephritis

Glomerulonephritis (gloh-mair-yoo-loh-nef-RY-tiss) is a common condition that involves damage to and destruction of the glomeruli, with

resulting inflammation of the glomerular capillaries and the glomerular basement membrane. Recall that the major hallmarks of inflammation are both increased blood flow and increased capillary permeability. This increases the GHP and causes the filtration membrane to become excessively leaky, leading to the loss of blood cells and proteins to the urine. As nephrons are further damaged and destroyed by the inflammation, the GFR decreases, which triggers compensatory mechanisms that further increase the GHP to maintain the GFR. This causes additional loss of cells and proteins to the urine. Eventually, these mechanisms are insufficient to restore the GFR, and toxic substances can accumulate in the blood. This condition may eventually lead to complete renal failure, in which the GFR is insufficient for the kidneys to perform their functions.

filtrate. The basic feedback loop proceeds by the following steps:

1. If the GFR increases, the volume of filtrate flowing through the renal tubule increases.
2. The increased filtrate volume makes the filtrate flow more rapidly through the tubules. This leads to an increased delivery of sodium and chloride ions to the macula densa cells in the distal tubule, causing them to absorb more of these ions from the filtrate.
3. In an example of the Cell-Cell Communication Core Principle (p. 27), the macula densa cells release chemicals (which researchers are currently trying to identify) that diffuse through the interstitial fluid to the afferent arteriole, which they trigger to constrict.
4. The macula densa cells signal the renin-containing JG cells to reduce their release of renin, leading to a decreased renal production of angiotensin-II and dilation of the efferent arteriole.
5. The GFR decreases back toward normal.



CORE PRINCIPLE
Cell-Cell Communication

Conversely, a decrease in the GFR is thought to have the opposite effect—fewer sodium and chloride ions are delivered to the macula densa cells, causing the afferent arteriole to dilate and the efferent arterioles to constrict. This increases the glomerular hydrostatic pressure and restores the GFR.

With both the myogenic mechanism and tubuloglomerular feedback at work, the GFR remains remarkably consistent through changes in blood pressure, which happen with some frequency. For example, every time you sneeze or get up off the couch, your blood pressure changes momentarily. However, these mechanisms are insufficient to maintain GFR when dealing with very large changes in blood pressure. If systolic blood pressure rises above 180 mm Hg, the GFR and urine output will increase dramatically. Conversely, if systolic blood pressure drops below about 70 mm Hg, glomerular filtration will cease because the compensatory mechanisms cannot create an NFP that favors filtration. At this point, no urine will be produced, a life-threatening condition called *anuria* (an-YOO-ree-ah; “absence of urine formation”).

Quick Check

- 6. What happens to the GFR when the afferent arteriole constricts? What happens to the GFR when it dilates?
- 7. How does tubuloglomerular feedback affect the GFR?

Hormonal Effects on the GFR

Recall that *hormones* are chemical messengers released into the bloodstream that regulate the functions of other cells (see Chapter 16). Like the two autoregulatory mechanisms, hormones that affect the GFR do so by adjusting the glomerular hydrostatic pressure. However, hormones affect the GFR as part of a larger system that regulates systemic blood pressure. One hormone that regulates the GFR is *angiotensin-II* (an'-jee-oh-TEN-sin), a component of the *renin-angiotensin-aldosterone system*. Another

set of regulating hormones consists of the *natriuretic peptides* (nay'-tree-er-ET-ik; *natri-* = “sodium”) produced by the heart. First let’s examine the former hormone system.

The Renin-Angiotensin-Aldosterone System The **renin-angiotensin-aldosterone system (RAAS)** is a complex system whose primary function is to maintain systemic blood pressure; it preserves the GFR as a secondary effect. Therefore, it acts on much more than just the afferent and/or efferent arterioles of the glomeruli. The RAAS also significantly impacts tubular reabsorption in the nephron and collecting system in order to influence electrolyte balance and blood volume, in addition to causing changes within the body as a whole.

This system may be triggered into action by three conditions: (1) stimulation from neurons of the sympathetic nervous system, (2) low glomerular hydrostatic pressure, or (3) stimulation from the macula densa cells as part of tubuloglomerular feedback. Note that often the system is “turned on” by a combination of these three factors.

The RAAS proceeds by the following steps, illustrated in **Figure 24.14**:

- 1 **Systemic blood pressure decreases, causing a decrease in the GFR.**
- 2 **JG cells release renin.** Decreased blood flow through the afferent arteriole triggers the JG cells to release the enzyme **renin** (REE-nin) into the bloodstream.
- 3 **Renin converts angiotensinogen to angiotensin-I.** Renin circulates until it encounters an inactive protein produced by the liver called **angiotensinogen** (an'-jee-oh-ten-SIN-oh-jen). Renin catalyzes the conversion of angiotensinogen to a product with minimal activity, **angiotensin-I (A-I)**.
- 4 **ACE converts angiotensin-I to the active angiotensin-II.** A-I circulates through the blood until it encounters an enzyme called **angiotensin-converting enzyme (ACE)**, which is made by cells such as the endothelial cells in the lungs. ACE converts A-I to its active form, **angiotensin-II (A-II)**.

A-II has several different, simultaneous effects that influence both systemic blood pressure and the GFR, including:

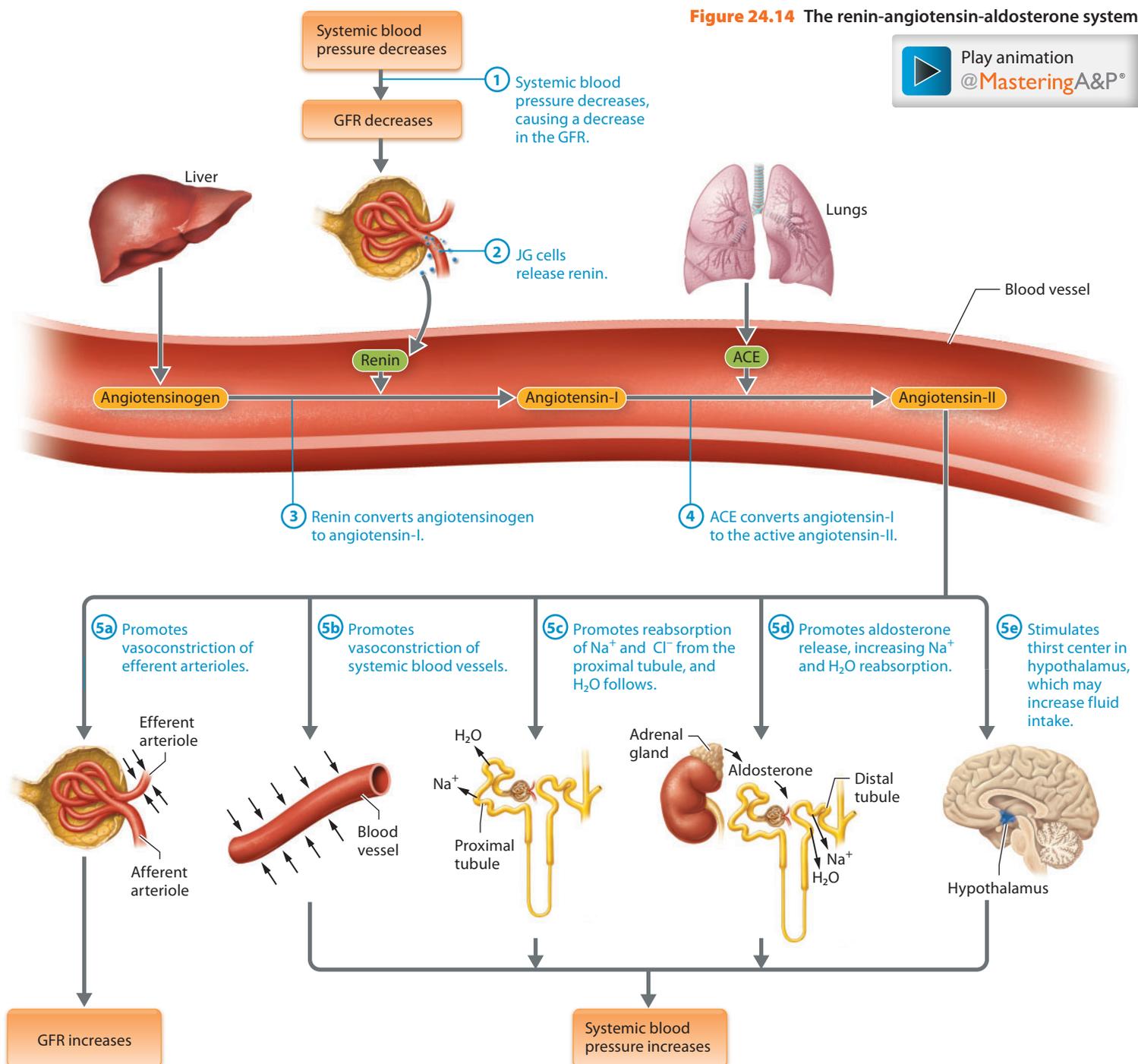
- 5a **Promotes vasoconstriction of efferent arterioles.** A-II constricts all of the renal blood vessels, but it has a greater effect on the efferent arterioles than on the afferent arterioles. This “clogs the drain,” raising glomerular hydrostatic pressure. This increased pressure, in turn, increases the GFR to maintain the filtration rate despite the reduced blood flow.
- 5b **Promotes vasoconstriction of systemic blood vessels.** A-II is a powerful vasoconstrictor of nearly all systemic vessels (it causes effects more than 40 times stronger than those of norepinephrine). This vasoconstriction increases peripheral resistance, which in turn increases systemic blood pressure.
- 5c **Promotes reabsorption of sodium and chloride ions from the proximal tubule, and water follows.** One of the most powerful effects of A-II on blood pressure comes from its role in renal tubule reabsorption (covered in Module 24.5). In the proximal tubule, A-II promotes reabsorption of both

sodium and chloride ions from the filtrate, which in turn causes reabsorption of water by osmosis. This increases blood volume, which raises blood pressure.

- 5d** Promotes aldosterone release, leading to increased sodium ion and water reabsorption. A-II stimulates the adrenal glands to release the hormone **aldosterone** (al-DOHS-ter-own). Aldosterone acts on the distal tubule and parts of the collecting system to increase sodium ion reabsorption from the filtrate. If ADH is present, water follows by osmosis, so this action increases blood volume, and therefore blood pressure.

- 5e** Stimulates thirst. Another effect of A-II is to stimulate the thirst centers in the hypothalamus. This can increase fluid intake, which would increase blood volume.

The RAAS maintains blood pressure over both the short and long term. The vasoconstriction produced by A-II is nearly immediate—blood pressure rises within seconds of exposure to A-II. However, this vasoconstriction lasts only 2–3 minutes. Long-term blood pressure control comes from the retention of sodium ions and water from the filtrate. Notice that the effects of



the RAAS on both vasoconstriction and sodium ion reabsorption allow the body to increase systemic blood pressure while preserving the GFR.

In addition to its effects on blood pressure, the RAAS is also critical to maintaining sodium ion balance. When the sodium ion level decreases in the plasma, and so in the filtrate, the macula densa cells stimulate renin secretion from the JGA cells, and more sodium ions are reabsorbed into the blood from the filtrate in the renal tubules. When the plasma sodium ion level increases, renin secretion decreases, and the kidneys excrete more sodium ions. The RAAS is so effective at this task that sodium ion intake can increase up to 50 times and the level of sodium ions in the plasma will remain relatively unchanged. See *A&P in the Real World: The RAAS and Hypertension* for information on how the effects of the RAAS can be modified to treat high blood pressure.

Atrial Natriuretic Peptide Recall that certain cells of the atria in the heart produce the hormone **atrial natriuretic peptide (ANP)** (see Chapter 16). ANP, which is released when the volume of blood in the atria increases, acts to lower blood volume and blood pressure and thereby reduce the workload of the heart. One of the ways that ANP accomplishes this task is by increasing the GFR. ANP dilates the afferent arterioles and constricts the efferent arterioles of the glomeruli, a combination that “turns up the faucet” and “clogs the drain.” This increases the glomerular hydrostatic pressure, raising the GFR. High GFR leads to more fluid loss and therefore decreases blood volume and effectively lowers blood pressure. Note that ANP is part of a system that works to decrease the systemic blood pressure; it simply happens to do so by impacting the GFR. We consider the other effects of ANP on the kidney in Module 24.5.

Quick Check

- 8. Describe the basic steps of the renin-angiotensin-aldosterone system.
- 9. What are the effects of the RAAS on the GFR?
- 10. What are the effects of ANP on the GFR?

Neural Regulation of the GFR

Neural control of the GFR is chiefly mediated by the sympathetic division of the autonomic nervous system. As with the hormonal systems just described, the sympathetic nervous system affects the GFR as part of a larger system to control systemic blood pressure. Sympathetic neurons release norepinephrine during times of increased sympathetic activity, which causes constriction of most systemic blood vessels, including the afferent arterioles, and so elevates systemic blood pressure. You might think this should decrease glomerular hydrostatic pressure and the GFR, but the sympathetic effect on the GFR isn't quite that simple. Instead, its impact depends on how much it is stimulated:

- If the level of sympathetic stimulation is low (e.g., during mild exercise such as walking), sympathetic neurons trigger

the JG cells to release renin. This leads to the formation of a low level of A-II, which raises systemic blood pressure and increases the GFR.

- If the level of sympathetic stimulation is high (e.g., during strenuous exercise or severe blood loss), a large amount of renin is secreted, and the blood concentration of A-II increases dramatically. A high level of A-II will actually *constrict* both the afferent and efferent arterioles of the glomeruli, decreasing the filtration rate. This is especially important in cases of severe hypotension and dehydration, as it helps the body to minimize fluid loss and preserve blood volume and blood pressure. In these cases, perfusion of muscle tissue and vital organs (brain, heart, etc.) takes precedence over filtration in the kidneys.

Table 24.1 summarizes the autoregulatory, hormonal, and neural mechanisms that control the GFR.

Quick Check

- 11. How does the sympathetic nervous system affect the GFR at both low and high levels of stimulation?

Renal Failure

If a person's GFR decreases, he or she may enter **renal failure**, a condition in which the kidneys are unable to carry out their vital functions. Many conditions may lead to renal failure, including factors that decrease blood flow to the kidneys, diseases of the kidneys themselves, and anything that obstructs urine outflow from the kidneys. Short-term renal failure, which is known as *acute renal failure* or *acute kidney injury*, is common among hospitalized patients and may resolve completely with treatment of the underlying cause. Some people develop *chronic* (long-term) *renal failure*, which is defined as a decrease in GFR lasting 3 months or longer.

The biggest risk factors for the development of chronic renal failure are diabetes mellitus and hypertension. Symptoms depend on the severity of the renal failure, and those with mild renal failure might not notice any symptoms. As renal function declines, patients experience fatigue, edema, nausea, and loss of appetite. Severe renal failure, in which the GFR is less than 50% of normal, results in a condition known as **uremia** (yoo-REEM-ee-ah). Uremia is characterized by a buildup of waste products and fluid, electrolyte, and acid-base imbalances. Untreated, it can lead to coma, seizures, and death.

When a patient develops the signs and symptoms of uremia, **dialysis** (dy-AL-ah-sis) treatment may be initiated. There are two types of dialysis. The first is **hemodialysis**, which temporarily removes an individual's blood and passes it through a filter that removes metabolic wastes and extra fluid, and normalizes electrolyte and acid-base balance. Hemodialysis must be performed three times per week at a dialysis clinic. The second type is **peritoneal dialysis**, in which dialysis fluid is placed

TABLE 24.1 SUMMARY OF CONTROL OF THE GLOMERULAR FILTRATION RATE

Stimulus	Responding Mechanism	Main Effect(s)	Effect on GFR
Autoregulation			
Increased stretching of the afferent arteriole (due to increased blood pressure)	Myogenic mechanism	• Vasoconstriction of the afferent arteriole	Decrease
Increased sodium ion delivery to the macula densa cells (due to increased GFR)	Tubuloglomerular feedback	• Vasoconstriction of the afferent arteriole • Vasodilation of the efferent arteriole	Decrease
Hormonal Mechanisms			
Sympathetic nervous system activated; decreased GFR; decreased systemic blood pressure	Renin-angiotensin-aldosterone system	• Vasoconstriction of the efferent arteriole • Systemic vasoconstriction • Reabsorption of sodium ions from the filtrate in the proximal tubule • Release of aldosterone • Reabsorption of water	Increase (decrease at high levels of activation)
Increased systemic blood pressure	Atrial natriuretic peptide	• Vasodilation of the afferent arteriole • Vasoconstriction of the efferent arteriole • Decreased reabsorption of sodium ions • Increased water loss	Increase
Neural Mechanisms			
Multiple	Sympathetic nervous system	• Constriction of all vessels, including the afferent and efferent arterioles • Stimulates RAAS	Decrease (increase at low levels of activation)

into the peritoneal cavity, allowed to circulate for several hours, and then drained. A patient is able to undergo peritoneal dialysis nightly at home, so this is often the preferred treatment for individuals needing long-term dialysis.

Apply What You Learned

- 1. Ms. Douglas has advanced liver disease; because her liver is no longer able to produce plasma proteins, her colloid osmotic pressure has decreased. Predict the effects that this loss of pressure will have on the net filtration pressure and the GFR in her nephrons.
- 2. Certain drugs that treat high blood pressure cause vasodilation of systemic arteries and arterioles, including those in the kidneys. What effect would these drugs have on the GFR? How would the myogenic mechanism and tubuloglomerular feedback respond to this change in the GFR?
- 3. Mr. Adams is taking an ACE inhibitor and an angiotensin-receptor blocker, both drugs that block the RAAS, for his high blood pressure. He complains that when he tries to engage in physical activity, he feels faint. He is asked to exercise on a treadmill, and his blood pressure remains very low when he exercises, rather than rising with his level of physical activity. Explain how his medications could be causing his current problem.

See answers in Appendix A.



The RAAS and Hypertension

Because the effects of the RAAS on systemic blood pressure are so potent, three classes of drugs have been developed that act on this system to reduce blood pressure:

- **ACE inhibitors**, a class of drugs developed from snake venom, block angiotensin-converting enzyme, and therefore inhibit the conversion of angiotensin-I to angiotensin-II.
- **Angiotensin-receptor blockers** block the angiotensin receptors on the cells of blood vessels and the proximal tubule, preventing vasoconstriction and sodium ion and water reabsorption, respectively.
- **Aldosterone antagonists** block the effects of aldosterone on the distal tubule and decrease reabsorption of sodium ions and water; this leads to a diuretic (“water-losing”) effect.

Although these drugs are useful in the treatment of hypertension, blocking the formation or actions of angiotensin-II can decrease the GFR. Typically, the GFR will noticeably decrease only in those patients with pre-existing renal disease, but all patients should be monitored for this potential adverse effect.

Renal Physiology II: Tubular Reabsorption and Secretion

Learning Outcomes

1. Describe how and where water, organic compounds, and ions are reabsorbed in the nephron by both passive and active processes.
2. Describe the location(s) in the nephron where tubular secretion occurs.
3. Compare and contrast tubular reabsorption and secretion, with respect to direction of solute movement, strength of concentration gradients, and energy required.
4. Describe how the renin-angiotensin-aldosterone system, antidiuretic hormone, and atrial natriuretic peptide each work to regulate reabsorption and secretion.

Because of the high rate of filtrate formation, the kidneys have to work to reclaim most of the filtrate and return it to the bloodstream. Recall that this occurs by the process of *tubular reabsorption* in the nephrons and collecting ducts. Of the 180 liters of water filtered by the kidneys every day, only about 1.8 liters (1%) ultimately leave the body as urine, which means that the kidneys are very efficient at reclaiming water. In addition, about 99% of the solutes filtered are subsequently reabsorbed. Given the magnitudes of these quantities, it's not surprising that the kidneys use approximately 20% of the body's ATP at rest.

Since our kidneys reabsorb so much of what they filter, you may wonder why our bodies need to filter blood through the kidneys at all. First of all, certain waste products are not reabsorbed. In addition, in spite of the high GFR, some waste substances do not pass through the filtration membranes of the glomeruli and therefore don't enter the filtrate. This necessitates the process of *tubular secretion*, which occurs in the renal tubules and collecting ducts at the same time as tubular reabsorption. Certain substances are secreted into the filtrate; these nonreabsorbed and secreted substances are often toxic when present in high concentrations, and the high GFR and process of secretion ensure their rapid clearance from the body. In addition, the presence of a large volume of filtrate in the nephrons gives the kidneys precise control over the homeostasis of fluid, electrolyte, and acid-base balance. If substances are not needed, they are excreted with the urine. If they are needed, they will be reabsorbed into the blood.

In the upcoming sections, we examine the processes of tubular reabsorption and secretion more closely. We also trace the filtrate as it flows through the different parts of the nephron and collecting system, and discuss how it changes in both composition and concentration to finally become urine.

Principles of Tubular Reabsorption and Secretion

◀ Flashback

1. What are tight junctions, and what are their functions? (p. 127)
2. What are facilitated diffusion, primary active transport, and secondary active transport? (p. 76)

This section looks at how substances move between the inside of the renal tubule and the surrounding peritubular capillaries. We also examine how solute and water movement are driven by either active or passive transport processes. Let's start by reviewing some of the principles we've learned that we can now apply to tubular reabsorption and secretion.

Paracellular and Transcellular Transport Routes

When discussing the movement of solutes and water, we first need to discuss exactly where and how the substances are moved. As you can see in **Figure 24.15**, in tubular reabsorption, substances must pass from the filtrate in the lumen (inside) of the tubule across or between the tubule cells, into the interstitial fluid, and finally across or between the endothelial cells of the peritubular capillaries to re-enter the blood. In tubular secretion, substances move in the opposite direction. But exactly how do these substances cross the tubule cells?

As you learned in the histology chapter, substances can be transported by two different routes across epithelia: paracellular or transcellular (see Figure 4.6). For a quick review, these processes are described as follows:

- **Paracellular route.** On the paracellular route (*para-* = “beside”), substances pass *between* adjacent tubule cells. The tight junctions between the tubule cells are just leaky enough to allow some substances such as small ions and water to move passively between them, particularly in the proximal tubule.
- **Transcellular route.** On the transcellular route (*trans-* = “across”), substances such as glucose and amino acids must move *through* the tubule cells. A reabsorbed substance first crosses the *apical* membrane of the tubule cell (the membrane facing the tubule lumen), then travels through the cytosol, and finally exits the cell through the *basolateral* membrane (the side of the membrane facing the interstitial fluid).

Transport along the paracellular route is passive, requiring no energy in the form of ATP, because substances move with their concentration gradients via diffusion or osmosis. The same is true for certain substances taking the transcellular route. However, other substances moving along the transcellular route travel against their concentration gradients and thus require energy, either directly or indirectly, from ATP. Secretion is an active process, so it must occur via the transcellular route across the tubule cell membrane.

Reabsorbed substances that have entered into the interstitial fluid may then cross the endothelial cells of the blood vessel and enter the blood. These substances can follow the same routes into the capillary

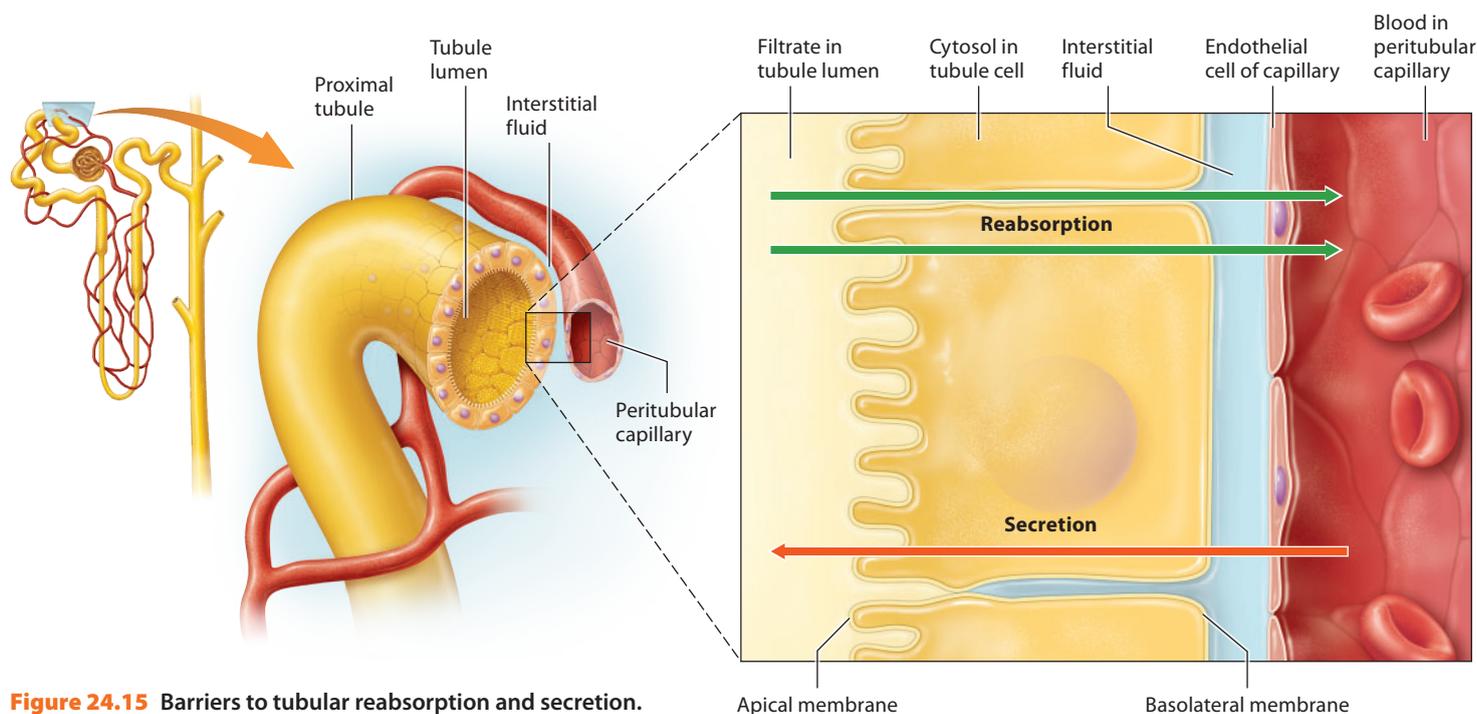


Figure 24.15 Barriers to tubular reabsorption and secretion.

that they followed to exit the tubule—they may take the paracellular route or the transcellular route. Generally, these processes are passive, and solutes move by diffusion and water by osmosis.

Carrier-Mediated Transport and the Transport Maximum

Most of the substances that are reabsorbed and secreted via the transcellular route require the use of a carrier protein in the tubule cell plasma membrane. Recall that there are three ways in which cells use carrier proteins to transport substances (see Chapter 3):

- *facilitated diffusion*, in which a carrier protein passively transports a substance with its concentration gradient, without using energy from ATP (an example of the Gradients Core Principle, p. 26);
- *primary active transport*, in which a carrier protein “pump” directly uses ATP to move a substance against its concentration gradient; and
- *secondary active transport*, in which a concentration gradient set up by a primary active transport pump is used to drive the transport of a second substance against its concentration gradient via another carrier protein.

There are two types of active transport carrier proteins: *antiport pumps* (or *antiporters*) move two or more substances in opposite directions, and *symport pumps* (or *symporters*) move two or more substances in the same direction (see Chapter 3). Both have a limited number of sites on which they can transport substances, much as a train has only a certain number of seats for passengers. If all of their sites become filled, the carrier proteins are said to be **saturated**, as they have reached their

transport maximum (T_M). Any substances unable to bind to their carrier proteins will likely not be transported and will end up in the urine. This is what happens to glucose in diabetes mellitus, as discussed in *A&P in the Real World: Glycosuria*.

Quick Check

1. What are the two routes of reabsorption and secretion?
2. List the three types of transport processes that involve carrier proteins in the renal tubule and collecting system.



Glycosuria

The transport maximum (T_M) becomes especially important with substances such as glucose that “fill seats” fairly rapidly in the carriers of the proximal tubule cells. If too much glucose is in the filtrate, the T_M will be reached before all of the glucose is reabsorbed and glucose will appear in the urine, a condition called *glycosuria* (gly'-koh-SOOR-ee-ah). Glycosuria is commonly seen with the disorder **diabetes mellitus**, a condition characterized by defects in the production of or response to the pancreatic hormone *insulin*. Insulin causes most cells to take in glucose; in its absence, these cells are unable to bring glucose into their cytosol. This leads to a high level of circulating blood glucose, or *hyperglycemia*, which causes excessive amounts of glucose to be present in the filtrate and therefore ultimately in the urine.

Reabsorption and Secretion in the Proximal Tubule

Flashback

1. What is the function of the Na^+/K^+ pump? In which direction(s) does it move sodium and potassium ions? (p. 79)
2. What is the function of the carbonic acid–bicarbonate ion buffer system? (p. 49)

The remainder of this module follows the filtrate from the capsular space through the nephron as it is modified by tubular reabsorption and secretion. We start, of course, with the proximal tubule. Recall that the cells of the proximal tubule have prominent microvilli that provide these cells with a large surface area. This facilitates the remarkably rapid reabsorption that occurs in this very active segment of the renal tubule. In fact, the proximal tubule is the most metabolically active part of the nephron, as most of the filtrate is reabsorbed here—its Na^+/K^+ pumps alone consume about 6% of the body's ATP at rest. In addition to all of this reabsorption, a great deal of secretion takes place in the proximal tubule as well. The following sections examine the changes that the filtrate undergoes in the proximal tubule; we discuss first reabsorption and then secretion.

The main roles of the proximal tubule in reabsorption from the filtrate back to the blood are as follows:

- reabsorption of a large percentage of electrolytes, including sodium, chloride, potassium, sulfate, and phosphate ions, an activity that is vital for electrolyte homeostasis;

- reabsorption of nearly 100% of nutrients such as glucose, amino acids, and other organic substances (e.g., lactic acid, water-soluble vitamins);
- reabsorption of many of the bicarbonate ions, which is critical for acid-base homeostasis; and
- reabsorption of about 65% of the water, which is required for maintenance of the body's fluid homeostasis.

Let's look more closely at each of these roles.

Sodium Ion Reabsorption

We begin with the reabsorption of sodium ions, because this process turns out to be the key to reabsorbing many other substances in the proximal tubule. First, the majority of sodium ion reabsorption occurs through sodium ion leak channels on the apical surface of the proximal tubule cell, driven by its concentration gradient. Then, for active transport by the transcellular route, the cells of the proximal tubule have three types of carrier proteins for sodium ions in their apical membranes:

- carrier proteins specific for sodium ions that enable facilitated diffusion of sodium ions from the filtrate into the tubule cells,
- Na^+ symporters that bring sodium ions from the filtrate into the cells with other solutes (such as glucose), and
- Na^+/H^+ antiporters that bring sodium ions into the cells while secreting hydrogen ions into the filtrate.

Each of these three carrier proteins transports sodium ions down its concentration gradient into the tubule cell. This concentration gradient isn't present naturally—it is created by

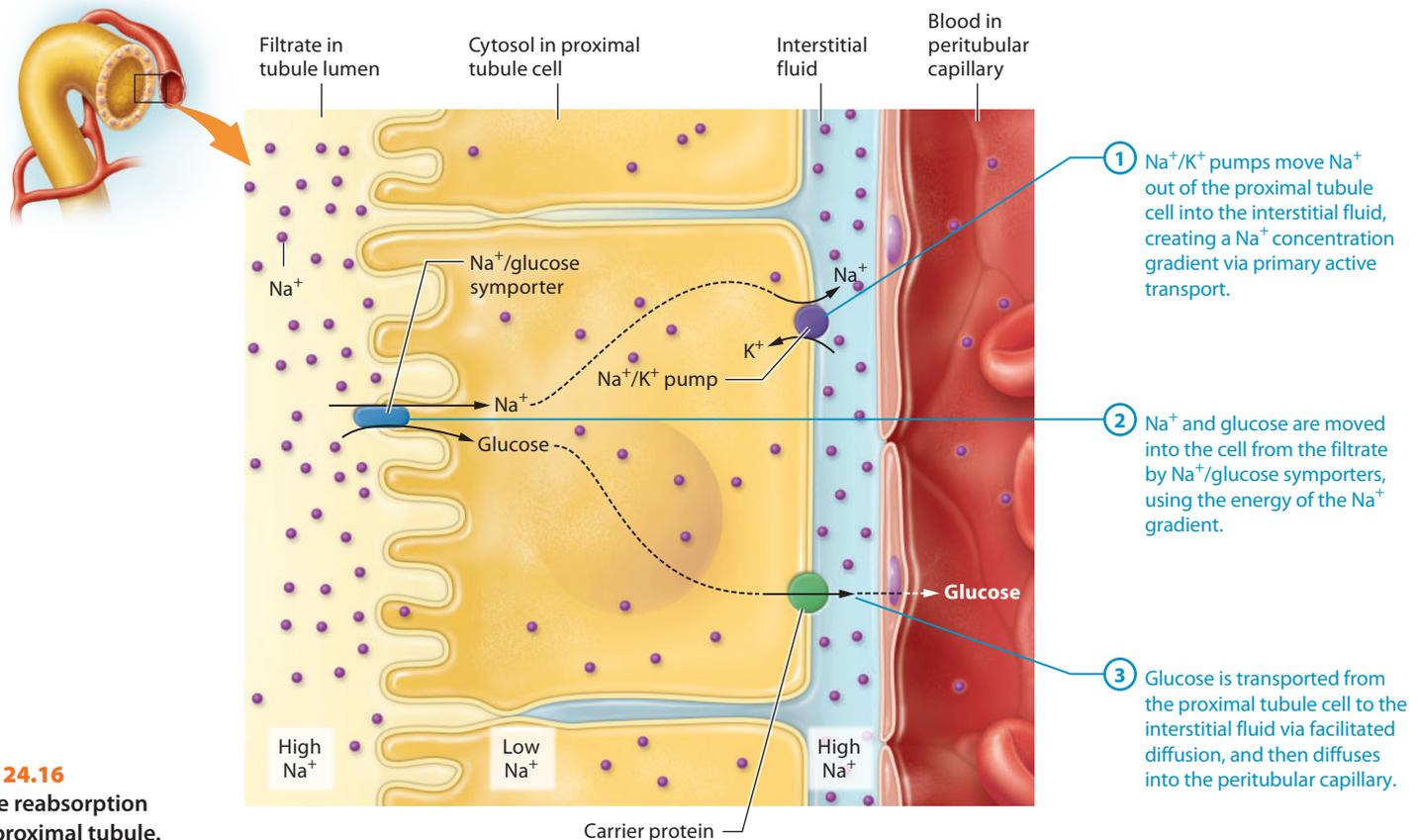


Figure 24.16
Glucose reabsorption in the proximal tubule.

Na^+/K^+ pumps in the basolateral membrane that continually pump sodium ions out of the tubule cells and into the interstitial fluid. These pumps create a relatively low sodium ion concentration in the proximal tubule cells (about 12 milliosmoles, or mOsm), whereas the sodium ion concentration in the filtrate is higher (about 142 mOsm). This concentration gradient is critical for the secondary active transport of many other solutes.

Most activity in the proximal tubule occurs without any outside control. Exceptions occur, such as parathyroid hormone decreasing phosphate ion reabsorption. In addition, the Na^+/K^+ pumps in the basolateral membrane become more active in the presence of angiotensin-II, which explains how this hormone increases sodium ion reabsorption from proximal tubule cells.

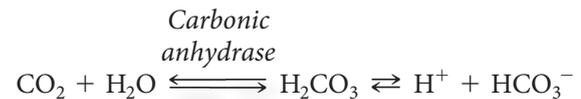
Reabsorption of Organic Solutes and Ions

The cells of the first half of the proximal tubule contain both Na^+/K^+ pumps and $\text{Na}^+/\text{glucose symporters}$. The symporters use the sodium ion gradient created by the pumps to carry both glucose and sodium ions from the filtrate into the tubule cell, an example of secondary active transport (Figure 24.16). Once in the cell, glucose is transported via facilitated diffusion into the interstitial fluid, where it diffuses into the peritubular capillaries. Other symporters in the apical membrane of the proximal tubule cells function in a similar fashion, allowing the secondary active transport of sodium ions and another solute, such as an ion (e.g., SO_4^{-2} or HPO_4^{-2}) or an organic solute (e.g., amino acids or lactic acid).

The reabsorption of sodium ions also leads to the reabsorption of anions such as chloride ions in another way, too. As sodium ions are passively transported out of the tubule lumen, the lumen accumulates a net negative charge. This creates an electrical gradient that pushes the negatively charged chloride ions across the epithelium through the paracellular route. These chloride ions similarly follow sodium ions into the interstitial fluid and into the plasma, as well.

Bicarbonate Ion Reabsorption

Bicarbonate ion reabsorption from the proximal tubule involves principles that you learned in the chemistry chapter about the carbonic acid–bicarbonate buffer system (see Chapter 2). Recall that carbon dioxide (CO_2) in the blood reacts with water (H_2O) to produce carbonic acid (H_2CO_3); this reaction is catalyzed by the enzyme *carbonic anhydrase* (CA). Newly formed carbonic acid spontaneously dissociates into bicarbonate (HCO_3^-) and hydrogen (H^+) ions. The complete reaction is as follows:



Remember that carbonic anhydrase also catalyzes the reverse reaction, turning carbonic acid into carbon dioxide and water.

Bicarbonate reabsorption from the proximal tubule occurs in a roundabout way (Figure 24.17). The process somewhat resembles a game of “fetch”: The cell “tosses” hydrogen ions into the

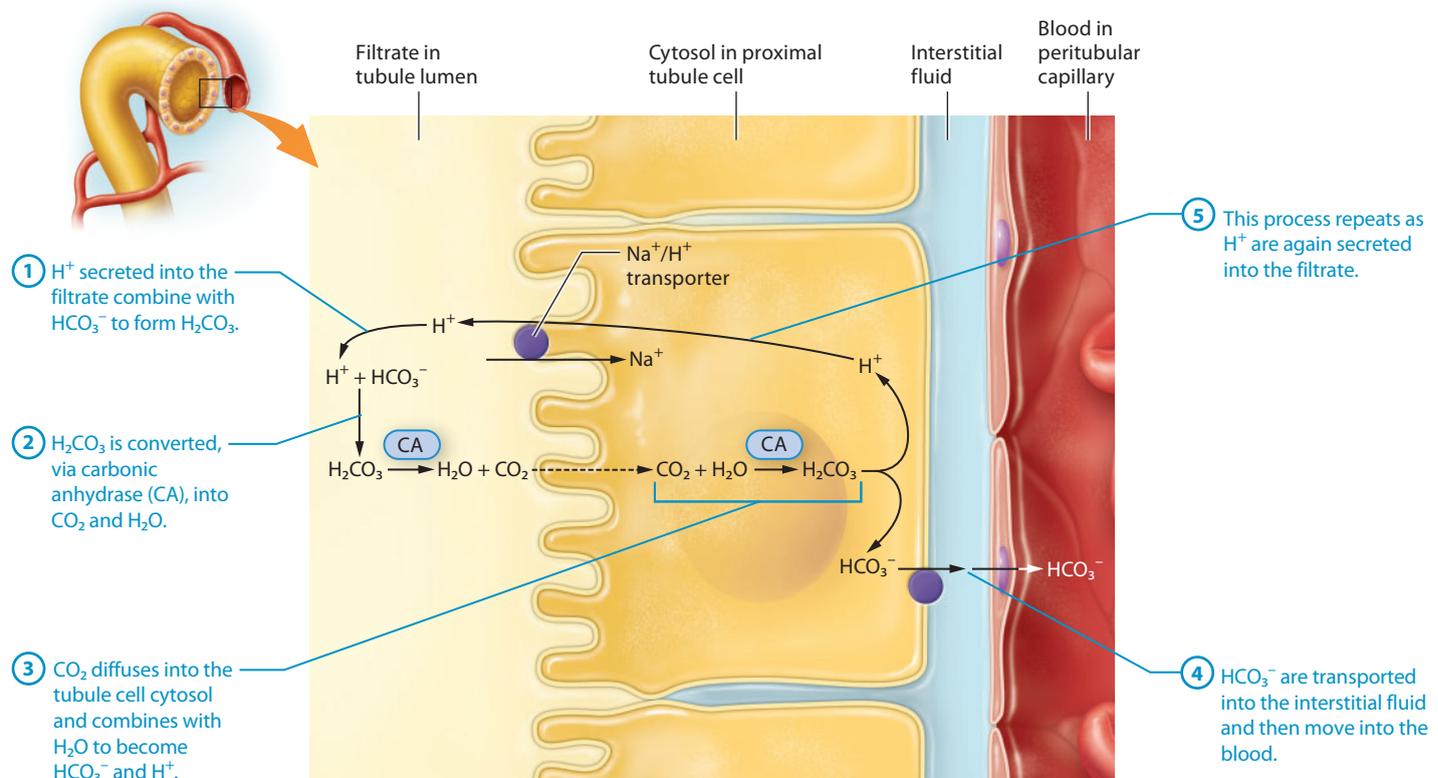


Figure 24.17 Bicarbonate ion reabsorption in the proximal tubule.

filtrate, and the hydrogen ion “fetches” a bicarbonate ion, which is then brought back into the cell. This toss is accomplished with the help of another carrier protein: the Na^+/H^+ antiporter. This carrier protein transports sodium ions into the cell while secreting hydrogen ions from the cell into the filtrate. Here’s how the process unfolds:

- 1 **Hydrogen ions secreted into the filtrate combine with bicarbonate ions to form carbonic acid.** Hydrogen ions are secreted from the cytosol of the proximal tubule cell into the filtrate by the Na^+/H^+ antiporter. The H^+ react with HCO_3^- in the filtrate to form H_2CO_3 .
- 2 **Carbonic acid is converted, via carbonic anhydrase, to carbon dioxide and water.** Carbonic anhydrase on the apical plasma membrane of the tubule cell catalyzes the conversion of H_2CO_3 into CO_2 and H_2O .
- 3 **Carbon dioxide diffuses into the tubule cell cytosol and combines with water to become bicarbonate and hydrogen ions.** CO_2 diffuses into the cytosol of the tubule cell with its concentration gradient. Carbonic anhydrase within the cell catalyzes the conversion of CO_2 and H_2O into H_2CO_3 , which then dissociates into HCO_3^- and H^+ .
- 4 **Bicarbonate ions are transported into the interstitial fluid and then move into the blood.** The HCO_3^- is transported across the basolateral membrane to enter the interstitial fluid and then diffuses into the peritubular capillaries.
- 5 **The process repeats as hydrogen ions are again secreted into the filtrate.** Hydrogen ions are again secreted into the filtrate by the Na^+/H^+ antiporter, and the process is repeated.

Though this process may seem complicated, it is effective and allows the cells of the proximal tubule to reabsorb about 90% of the bicarbonate ions from the filtrate. This is a key component of the body’s ability to maintain the pH of the blood within a very specific range, 7.35–7.45 (see Chapter 25).

Obligatory Water Reabsorption and Its Effect on Other Electrolytes

By the time the filtrate has reached the second half of the proximal tubule, many of the sodium ions as well as glucose and other organic molecules have been reabsorbed. This creates a gradient favoring the passive movement of water by osmosis out of the filtrate along both the paracellular and transcellular routes. Remember that in osmosis, water moves to the solution with a higher solute concentration.

This type of water reabsorption is called **obligatory water reabsorption**, because water is “obliged” to follow solute movement (Figure 24.18). A kind of water channel in the plasma membrane called an **aquaporin** (ah-kwah-POUR-in) greatly enhances rapid water reabsorption. These channels, which are located in both the apical and basolateral membranes of proximal tubule cells, allow water to move through these cells via the transcellular route.

As obligatory water reabsorption continues, the concentration of solutes, such as potassium, calcium, and magnesium ions, rises in the filtrate. This creates a concentration gradient that favors their diffusion into or between the proximal tubule cells. Notice that in this process, active reabsorption of solutes stimulates further reabsorption of water by osmosis. This in turn stimulates passive reabsorption of other solutes.

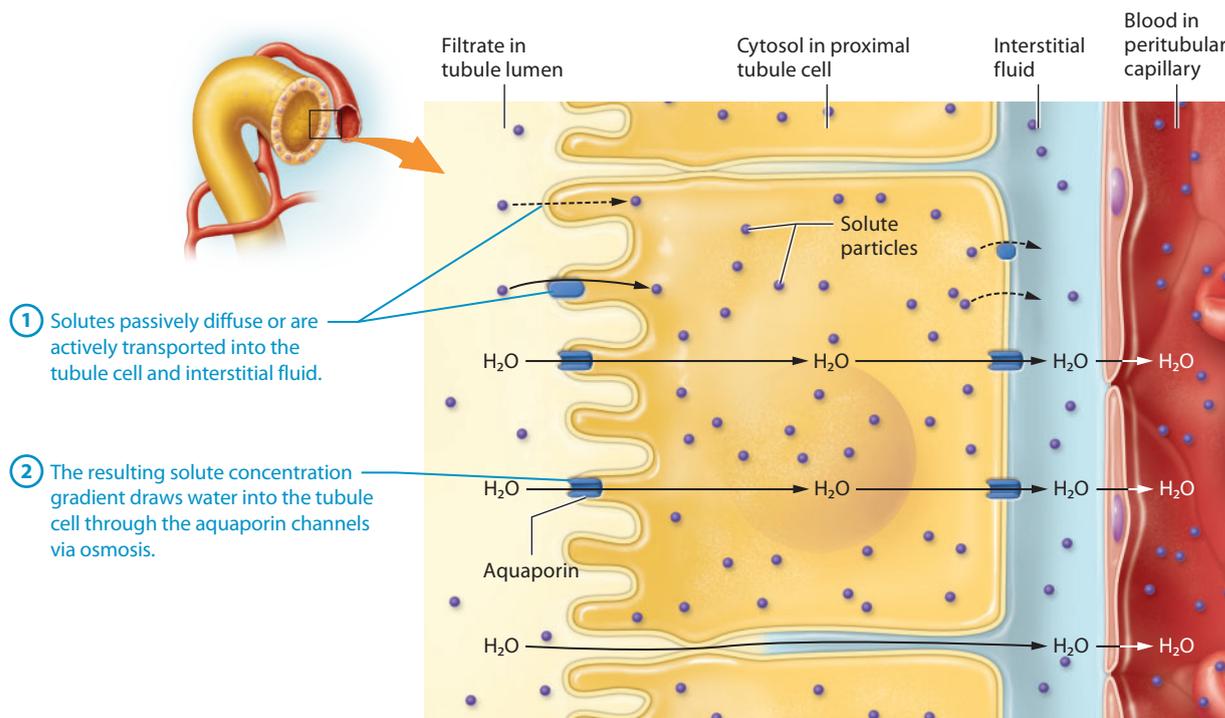


Figure 24.18 Obligatory water reabsorption in the proximal tubule.

Secretion in the Proximal Tubule

In addition to the hydrogen ion secretion we discussed earlier, other substances are secreted into the filtrate by the proximal tubule cells, including many nitrogenous waste products and drugs. In the first half of the proximal tubule, most of the uric acid in the filtrate is reabsorbed, but nearly all of it is secreted back into the filtrate in the second half of the tubule. Additionally, ammonium ions (NH_4^+), creatinine, and small amounts of urea are also secreted. Drugs such as penicillin and morphine have significant renal secretion. These drugs must be taken often (typically 3–5 times per day), because medicine lost through renal secretion must be replaced in order to maintain relatively consistent blood levels.

Quick Check

- 3. Which substances are reabsorbed from the proximal tubule? Which of these substances are reabsorbed using the sodium ion gradient?
- 4. What is obligatory water reabsorption?

Reabsorption in the Nephron Loop

By the time the filtrate reaches the nephron loop, it barely resembles the original filtrate—about 60–70% of the electrolytes and water have been reabsorbed from the filtrate and returned to the blood, in addition to most of the organic solutes such as glucose and amino acids. As the filtrate flows through the nephron loop, it undergoes further losses: Approximately 20% of the total water, 25% of the total sodium and chloride ions, and a significant portion of the remaining ions are reabsorbed and returned to the blood.

In the proximal tubule, you saw that water reabsorption is proportional to solute reabsorption. For this reason, the filtrate in the proximal tubule has the same concentration, or *osmolarity*, as the interstitial fluid, about 300 mOsm. In the nephron loop, however, the filtrate's osmolarity changes as it flows through the loop. This is due to the differing permeabilities in the ascending and descending limbs of the nephron loop.

The thin descending limb of the nephron loop is freely permeable to water, but much less permeable to solutes such as sodium and chloride ions. So water can move out of the thin descending limb cells by osmosis, but few solutes follow. This causes the osmolarity of the filtrate to increase as it passes down the descending limb and rounds the bend of the loop.

The cells of the thick ascending limb are impermeable to water, but they transport NaCl into the tubule cells with the use of $\text{Na}^+/\text{K}^+/2\text{Cl}^-$ **symporters**. This secondary active transport system brings one sodium, one potassium, and two chloride ions into the tubule cell, relying on the Na^+/K^+ pump on the basolateral membrane to create a favorable sodium ion gradient. Remember that the Na^+/K^+ pumps drive potassium ions back *into* the tubule cell, so there isn't much net reabsorption of potassium ions in this process. As filtrate passes through the ascending limb, it loses solutes and gradually becomes less concentrated as ions are pumped into the interstitial fluid. These differing permeabilities in the two limbs and the changing concentration of the filtrate are part of a

larger system that allows for extensive water reabsorption from the filtrate in both the loop and the collecting system, which we cover in Module 24.6.

Quick Check

- 5. How do the permeabilities of the two limbs of the nephron loop differ?
- 6. What is reabsorbed from the filtrate in the nephron loop?

Reabsorption and Secretion in the Distal Tubule and Collecting System

By the time the filtrate enters the first part of the distal tubule, about 85% of the water and 90% of the sodium ions have been reabsorbed. For this reason, the rate of filtrate flow in this part of the tubule is significantly lower (about 20 ml/min) than it was in the early proximal tubule (about 120 ml/min). As you learned earlier, the cells of the distal tubule lack microvilli. This reflects the



CORE PRINCIPLE Structure-Function

Structure-Function Core Principle (p. 25)—most of the water reabsorption has already taken place, and so the cells do not require

microvilli to perform their functions of reabsorbing much of the remaining water and solutes. Even though so much reabsorption has taken place, if we excreted the remaining water and sodium ions in the urine, we would still lose about 29 liters of water and a significant portion of our sodium ions every day. This situation would be incompatible with life. Reabsorption of the remaining water and sodium ions, then, is still critical.

The early distal tubule is structurally and functionally similar to the ascending limb of the nephron loop. However, the latter portion of the distal tubule is very similar to the cortical collecting duct, so we discuss them together here. Then we examine the medullary collecting system, which differs structurally and functionally from these other areas.

The Late Distal Tubule and Cortical Collecting Duct: Hormone Regulation

Cells of the late distal tubule and cortical collecting duct have hormone receptors that determine their function; the number and types of these receptors vary with hormone stimulation. The majority of their activity is therefore regulated by hormones in order to fine-tune water, electrolyte, and acid-base balance. For this reason, the water reabsorption here is called **facultative water reabsorption**, because water is reabsorbed in accordance with the body's needs (*facultative* means “able to adapt to a need”). The hormones involved in facultative water reabsorption as well as water and electrolyte balance include the following:

- **Aldosterone.** Aldosterone is a steroid hormone synthesized and released by the adrenal cortex that interacts with the DNA of cells to increase their permeability to sodium ions and the number of their Na^+/K^+ pumps. Both actions increase the reabsorption of sodium ions from the filtrate

and the secretion of potassium ions into the filtrate. Note that these actions also indirectly cause reabsorption of water and chloride ions, because as sodium ions are reabsorbed, water and chloride ions passively follow (if antidiuretic hormone is present, as discussed next). Aldosterone also stimulates secretion of hydrogen ions into the filtrate by specialized cells called *intercalated cells*.

- **Antidiuretic hormone.** Recall that **antidiuretic hormone (ADH)** is made by the hypothalamus and released from the posterior pituitary gland (see Chapter 16). Note that *diuresis* (dy-yoo-REE-sis) refers to losing body water to the urine, and a *diuretic* is an agent that promotes diuresis. An *anti-diuretic*, therefore, refers to an agent that causes water retention and reduces urine output. ADH exerts these effects by causing aquaporins to be inserted into the cells' apical membranes, permitting rapid water reabsorption. In the absence of ADH, the cells of the late distal tubule and cortical collecting duct are barely permeable to water, and a larger volume of water is lost in the urine.
- **Atrial natriuretic peptide (ANP).** ANP triggers *natriuresis* (nay'-tree-yoo-REE-sis), or urinary excretion of sodium ions. It also appears to inhibit release of ADH and aldosterone, causing fewer sodium ions (and also less water) to be reabsorbed, and so more sodium ions and water to appear in the urine.

The Medullary Collecting System

As filtrate flows through the medullary collecting ducts and the papillary ducts, this is the kidney's last chance to regulate fluid, electrolyte, and acid-base balance before the filtrate becomes urine. The cells of the medullary collecting system have the following properties:

- They are impermeable to water in the absence of ADH. However, in the presence of ADH, they reabsorb large volumes of water.
- They are permeable to urea, which allows some urea to move down its concentration gradient into the interstitial fluid.
- Intercalated cells in this region actively secrete hydrogen ions from the interstitial fluid into the filtrate against a very high concentration gradient; they can increase the concentration of hydrogen ions in the filtrate about 900 times.

In addition, the cells of the medullary collecting system continue to reabsorb ions such as sodium and chloride from the filtrate. We revisit the medullary collecting system in Module 24.6, as it is part of a mechanism that allows the kidneys to concentrate urine and conserve water.

Quick Check

- 7. How does aldosterone impact reabsorption and secretion in the late distal tubule and cortical collecting duct?
- 8. How does ADH influence water reabsorption? In which parts of the nephron and collecting system does ADH act?

How Tubular Reabsorption and Secretion Maintain Acid-Base Balance

Variable reabsorption and secretion of hydrogen and bicarbonate ions contribute to pH homeostasis of the extracellular fluids, including blood. Thus far, you have seen two examples of acid-base regulation throughout the renal tubule and collecting system: The cells of the proximal tubule secrete hydrogen ions as a way to reabsorb bicarbonate ions, and the intercalated cells of the late distal tubule and collecting system actively secrete hydrogen ions under the influence of aldosterone. Another mechanism in renal tubule cells is stimulated when the pH of the blood becomes abnormal. If the pH of the blood *decreases*, making it too acidic, enzymes in the tubule cells will remove the amino group ($-\text{NH}_2$) from the amino acid glutamine in the cytosol. In doing this, the cells generate two ammonia molecules (NH_3) and two bicarbonate ions. The ammonia is then secreted, and the bicarbonate ions are reabsorbed. In the filtrate, the ammonia molecules bind and buffer hydrogen ions to form the ammonium ion (NH_4^+). Both ammonia buffering and bicarbonate ion reabsorption help to raise the pH of the blood back to normal. If the pH of the blood *increases*, making it too alkaline, the tubule cells will reabsorb fewer bicarbonate ions from the filtrate, excreting them in the urine and lowering the pH of the blood.

Putting It All Together: The Big Picture of Tubular Reabsorption and Secretion

As you've seen, both tubular reabsorption and secretion are vital functions, and enormous quantities of water and solutes cross the tubule cells every day. Filtrate entering the proximal tubule contains water; ions such as sodium, potassium, chloride, calcium, and bicarbonate; and organic solutes such as glucose, amino acids, and metabolic wastes. By the time the filtrate leaves the papillary ducts to become urine, most of the water and solutes have been reclaimed. In **Figure 24.19** we summarize the substances that are filtered, reabsorbed, and secreted by the nephrons and collecting system of the kidneys.

The final product that exits the papillary ducts is urine; the properties of this fluid are discussed in Module 24.7.

Apply What You Learned

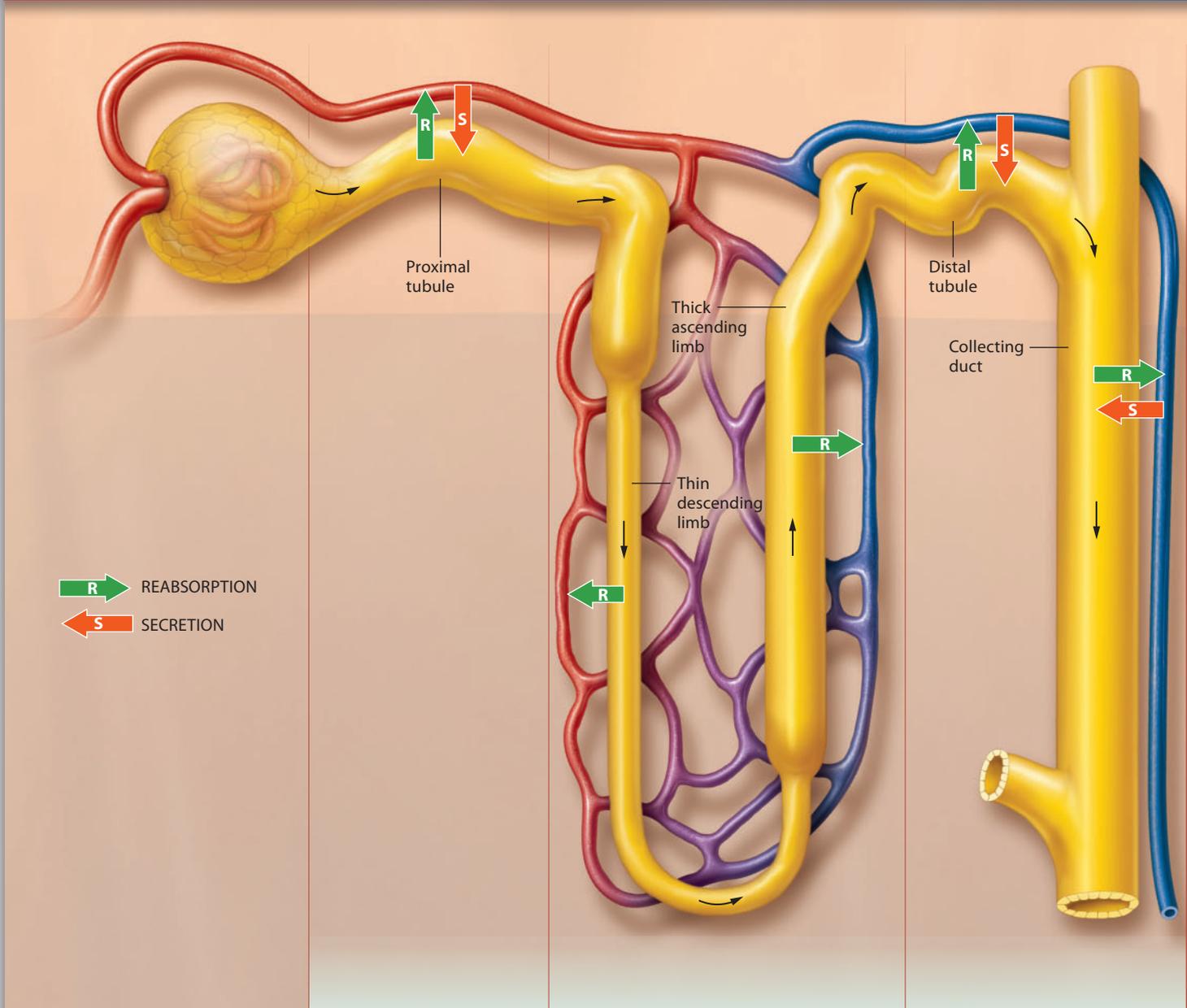
- 1. You discover a new toxin that blocks the reabsorption of all sodium ions from the proximal tubule. What effect would this drug have on the reabsorption of water and other electrolytes from this tubule?
- 2. What effect would this toxin have on the reabsorption of glucose and bicarbonate?
- 3. Respiratory conditions can cause chronic *hypoventilation* that leads to a decreased blood pH. Predict how the kidneys will respond to this change in pH.

See answers in Appendix A.

The Big Picture of Tubular Reabsorption and Secretion

Figure 24.19

Play animation
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R → REABSORPTION
← **S** SECRETION

TUBULAR SEGMENTS	PROXIMAL TUBULE	NEPHRON LOOP		DISTAL TUBULE AND COLLECTING DUCT
		Thin descending limb	Thick ascending limb	
SUBSTANCES REABSORBED → R	<ul style="list-style-type: none"> • 65% of H₂O in the filtrate • Nearly 100% of glucose, amino acids, and other organic solutes • About 90% of bicarbonate ions (HCO₃⁻) • 65% or more of Na⁺, K⁺, Ca²⁺, Cl⁻, and Mg²⁺ 	<ul style="list-style-type: none"> • 20% of H₂O in the filtrate 	<ul style="list-style-type: none"> • 25% of Na⁺ and Cl⁻ 	<ul style="list-style-type: none"> • Most of remaining H₂O • Nearly all of the remaining Na⁺, Cl⁻, and Ca²⁺ • Bicarbonate ions (HCO₃⁻)
SUBSTANCES SECRETED ← S	<ul style="list-style-type: none"> • Hydrogen ions (H⁺) • Nitrogenous wastes such as uric acid • Some drugs 			<ul style="list-style-type: none"> • K⁺ and H⁺ (regulated by hormones)

Renal Physiology III: Regulation of Urine Concentration and Volume

Learning Outcomes

1. Explain why the differential permeability of specific sections of the renal tubule is necessary to produce concentrated urine.
2. Predict specific conditions that cause the kidneys to produce dilute versus concentrated urine.
3. Explain the role of the nephron loop, the vasa recta, and the countercurrent mechanism in the concentration of urine.

In the previous two modules on renal physiology, we followed the path of the filtrate from its formation via glomerular filtration to its modification in the renal tubules and collecting system by reabsorption and secretion. Now we are moving on to discuss the variable water reabsorption in the late distal tubule and collecting system, and the impact of this on urine concentration and volume.

As you learned in the previous module, about 85% of water reabsorption in the kidney is obligatory—water is “obliged” by osmosis to follow solutes that have been reabsorbed. The last 15% of water reabsorption is facultative water reabsorption, which is adjusted by hormones to meet the body’s needs and maintain fluid homeostasis. Facultative water reabsorption is what determines final urine concentration and volume. In this module, we examine how the kidneys adjust facultative water reabsorption to produce either dilute or concentrated urine, and the role that hormones, particularly ADH, play in this process.

Osmolarity of the Filtrate

Let’s first trace the filtrate through the nephron and follow how its osmolarity can change on its way to becoming urine. The filtrate that exits the blood and enters the renal tubule initially is *iso-osmotic*, or equally osmotic, to the plasma at 300 mOsm. Recall that in the nephron loop, however, the filtrate’s osmolarity changes because of the differing permeabilities of its ascending and descending limbs.

The thin descending limb of the nephron loop is permeable to water but not solutes, as you learned, so water flows from the filtrate to the interstitial fluid by osmosis, but very few solutes follow. This causes the filtrate to become progressively more concentrated as it travels down the loop. By the time it reaches the bottom of the loop, on average it is approximately 900 mOsm, about three times more concentrated than plasma.

As the filtrate enters the thick ascending limb, sodium and other ions are pumped out of the filtrate and into the interstitial fluid. However, because this part of the limb is virtually impermeable to water, water can’t follow these solutes. So the concentration

of the filtrate decreases as it moves up the ascending limb of the loop. By the time the filtrate exits the thick ascending limb and moves into the distal tubule, its osmolarity is generally less than that of filtrate at the same level in the thin descending limb. In the early distal tubule, ions continue to leave the filtrate while water stays behind, and the concentration of the filtrate decreases even further, to about 100 mOsm, or three times *less* concentrated than plasma.

Once the filtrate enters the late distal tubule and collecting system, facultative water reabsorption may begin, so the concentration of the filtrate varies with the amount of water reabsorbed. If less water is reabsorbed, the concentration of the filtrate remains low as it passes through the late distal tubule and collecting system. The end result is the production of *dilute urine*, or urine with a concentration less than 300 mOsm. If, however, more water is reabsorbed, the concentration of the filtrate progressively increases as it passes through the late distal tubule and collecting system. The end result is the production of *concentrated urine*, or urine with a concentration greater than 300 mOsm. The upcoming sections examine the means by which both dilute urine and concentrated urine are produced.

Quick Check

- 1. How does the concentration of the filtrate change as it passes through the renal tubule and collecting system?
- 2. What are concentrated urine and dilute urine?

Production of Dilute Urine

The kidneys produce dilute urine when the solute concentration of the body’s extracellular fluid is too low (which means the extracellular fluid contains excessive water) (**Figure 24.20**). The filtrate entering the late distal tubule is already less concentrated than the surrounding interstitial fluid. For this reason, the kidneys simply have to not reabsorb any additional water from the filtrate, or “turn off” facultative water reabsorption, to produce dilute urine. This is accomplished through a reduction in ADH release, which renders the late distal tubule and collecting system essentially impermeable to water.

Note that the distal tubule and collecting system continue to reabsorb sodium and chloride ions from the filtrate, so the number of solutes in the filtrate decreases while the amount of water remains the same. This causes the concentration of the filtrate to progressively decrease as it passes through the collecting system. When the amount of water in the extracellular fluid is greatly in excess, the osmolarity of the urine can fall as low as 50 mOsm, which is only one-sixth the osmolarity of plasma.

Typically, the volume of urine produced also increases when the urine is very dilute. As you learned, the normal volume of urine produced is about 1.8 liters per day. However, this value can increase dramatically when ADH secretion is low. Note that urine volume is also influenced by many factors, including fluid intake, general health, diet, and blood pressure. It is also impacted by **diuretics**, which act on various parts of the renal tubule to block reabsorption of water or solutes and promote diuresis.

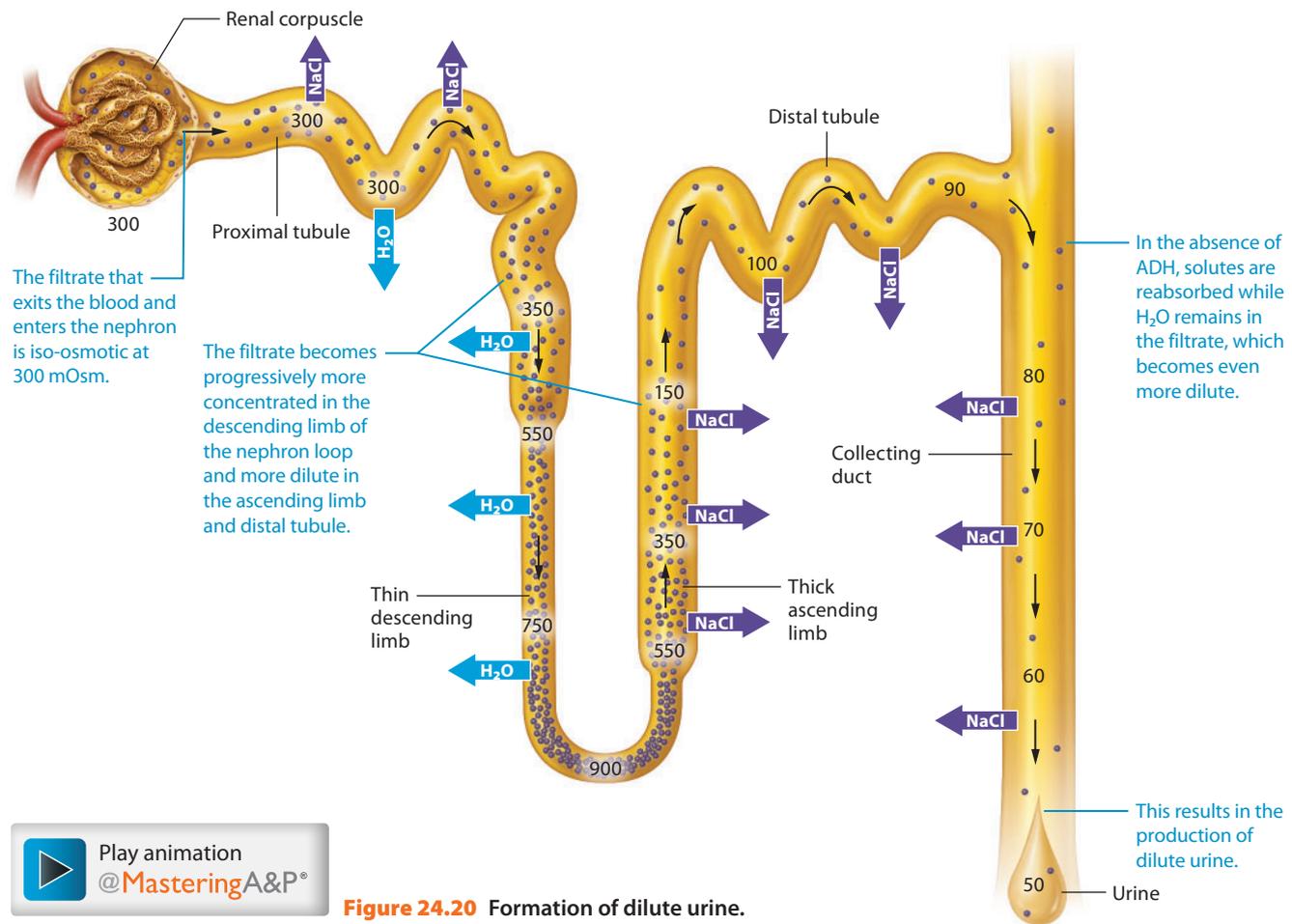


Figure 24.20 Formation of dilute urine.

Quick Check

- 3. Under what condition do the kidneys produce dilute urine?
- 4. How do the kidneys produce dilute urine?

The Countercurrent Mechanism and the Production of Concentrated Urine

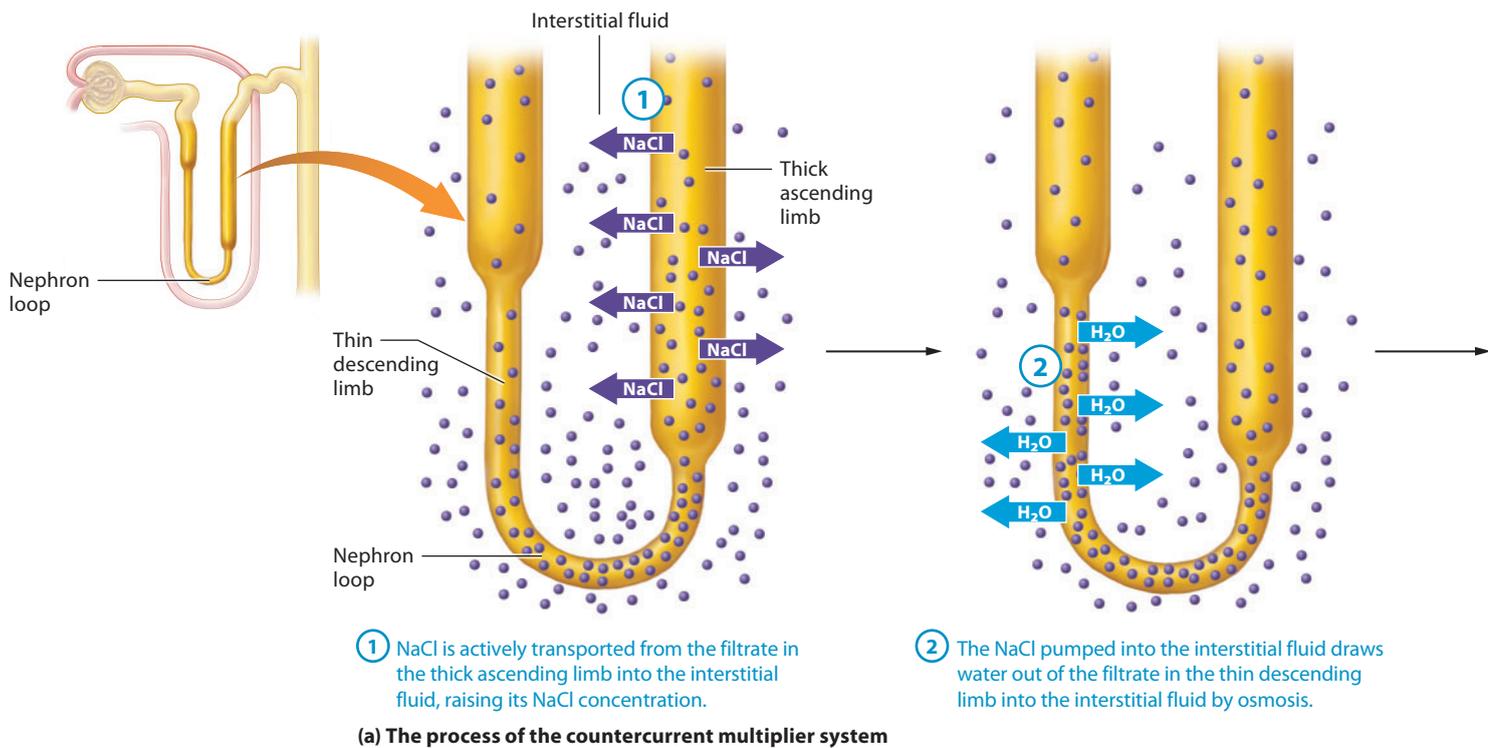
Our kidneys are quite effective at conserving water and can produce urine with a concentration up to about 1200 mOsm. (This is impressive, but the kidneys of the Australian desert hopping mouse can produce urine with a concentration as high as 10,000 mOsm!) Concentrated urine results from “turning on” facultative water reabsorption in the late distal tubule and collecting system by the release of ADH. However, facultative water reabsorption requires more than simply the presence of ADH. Recall that water reabsorption happens only by osmosis, and osmosis, being a passive process, will occur only if a concentration gradient is present to drive it. This means that facultative water reabsorption takes place



only if the interstitial fluid surrounding the nephron is *more* concentrated than the filtrate (an example of the Gradients Core Principle, p. 26).

The interstitial fluid within the renal cortex has about the same osmolarity as the interstitial fluid elsewhere in the body, approximately 300 mOsm. The filtrate entering the late distal tubule and cortical collecting duct has an osmolarity of about 100 mOsm, so it is less concentrated than the interstitial fluid. This creates a small but significant gradient to drive water reabsorption. However, by the time the filtrate enters the medullary collecting duct, its osmolarity has risen to a value about equal to that of interstitial fluid, and the gradient disappears. Therefore osmosis will not take place unless the nephrons work to create a concentration gradient within the renal medulla. This gradient, known as the **medullary osmotic gradient**, starts at 300 mOsm at the cortex/medulla border, and increases as we go deeper into the medulla. Within the deepest regions of the renal medulla, it reaches a concentration of about 1200 mOsm, four times more concentrated than plasma.

The medullary osmotic gradient is created and maintained by a system called the **countercurrent mechanism**, which is a type of mechanism that involves the exchange of materials or heat between fluids flowing in opposite directions. In the kidneys, this mechanism consists of three factors: (1) a *countercurrent multiplier* system in the nephron loops of juxtamedullary nephrons, (2) the recycling of urea in the medullary collecting ducts, and (3) a *countercurrent exchanger* in the vasa recta.



(a) The process of the countercurrent multiplier system

Figure 24.21 The countercurrent multiplier in the nephron loop.



The Nephron Loop and the Countercurrent Multiplier

Recall that there are two types of nephrons: cortical and juxtamedullary. Up to this point in the chapter, we have been discussing the physiology of both types of nephron. Now, however, we shift our attention specifically to the physiology of juxtamedullary nephrons—those with long nephron loops that descend deeply into the renal medulla. Within these long nephron loops we find a system called the **countercurrent multiplier**, which helps to create the medullary osmotic gradient.

In this system, the term *countercurrent* refers to the fact that the filtrate in the two limbs of the nephron loop flows in opposite directions—the filtrate in the descending limb flows toward the renal pelvis, and the filtrate in the ascending limb flows back up toward the renal cortex. Although the two limbs do not directly touch, they are close enough to influence each other. The term *multiplier* means that the effect increases, or multiplies, as the process proceeds due to the input of energy from ATP.

As depicted in **Figure 24.21a**, the system works like this:

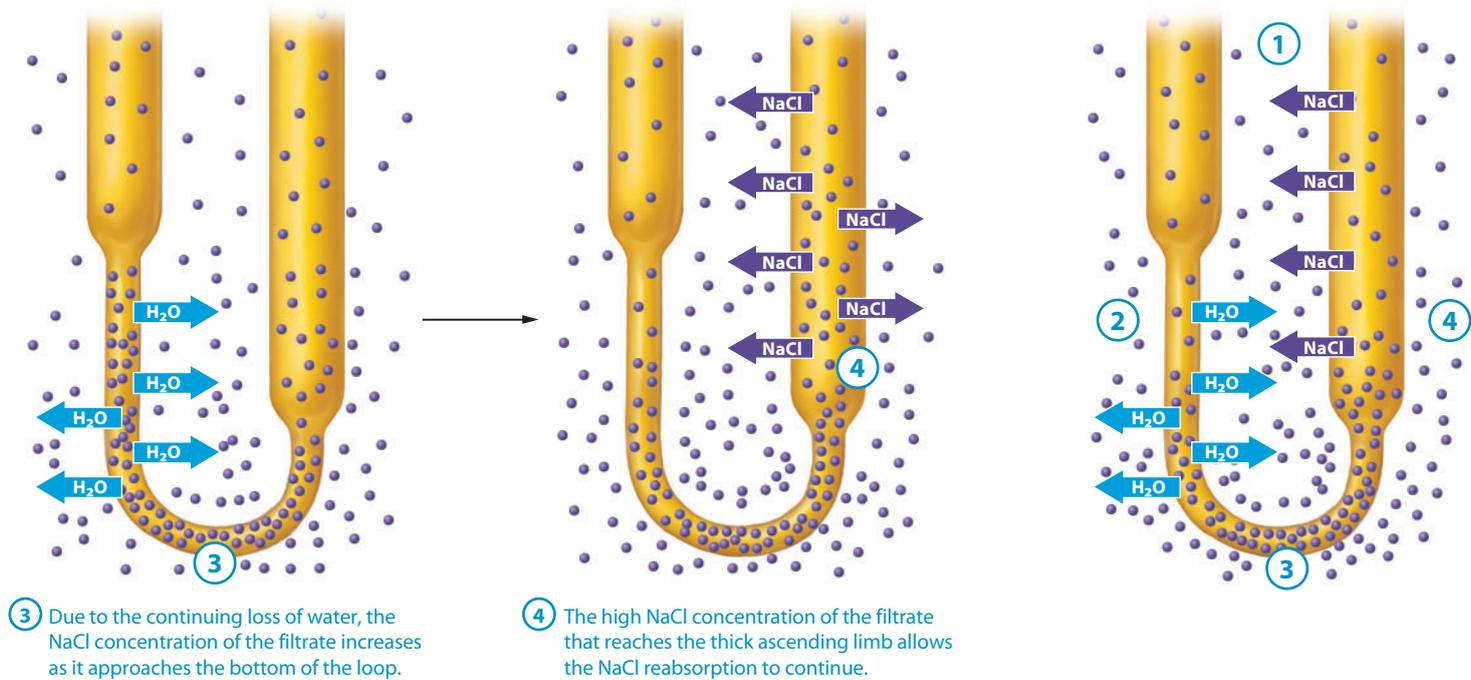
- 1 NaCl is actively transported from the filtrate in the thick ascending limb into the interstitial fluid, raising its NaCl concentration.** $\text{Na}^+/\text{K}^+/\text{2Cl}^-$ symporters pump NaCl from the cells of the thick ascending limb into the interstitial fluid. This increases the interstitial fluid's osmolarity.
- 2 The NaCl pumped into the interstitial fluid draws water out of the filtrate in the thin descending limb into the interstitial fluid by osmosis.** The concentrated interstitial

fluid creates an osmotic gradient that draws water from the filtrate in the thin descending limb into the interstitial fluid.

- 3 Due to the continuing loss of water, the NaCl concentration of the filtrate increases as it approaches the bottom of the loop.** As water leaves the filtrate in the thin descending limb, NaCl remains, so the filtrate becomes progressively more concentrated as it reaches the bottom of the nephron loop.
- 4 The high NaCl concentration of the filtrate that reaches the thick ascending limb allows the NaCl reabsorption to continue.** The filtrate reaches the thick ascending limb with a very high NaCl concentration. This is key because the symporters in the thick ascending limb will work only if the filtrate has a high NaCl concentration. The symporters then begin pumping NaCl into the interstitial fluid, and we return to step **1**.

All of these steps are occurring constantly; we separated them here for simplicity. You can see how the process works in **Figure 24.21b**.

The interstitial fluid is most concentrated in the deepest part of the renal medulla because the amount of NaCl pumped out of the thick ascending limb is proportional to its concentration in the filtrate, and its concentration is highest at the base of the loop. As the filtrate moves up the thick ascending limb and NaCl is pumped out, the NaCl concentration in the filtrate decreases and less NaCl can be pumped into the interstitial fluid.



(b) The countercurrent multiplier

ConceptBOOST >>>>

Demystifying the Countercurrent Multiplier

Let's be honest: The countercurrent multiplier is a difficult concept for everyone to understand at first. To demystify it, first remember that this process has two main functions:

- to reabsorb about 15–25% of the remaining water and electrolytes in the filtrate, and
- to create a steep concentration gradient in the deepest parts of the renal medulla that allows water reabsorption from the medullary collecting ducts by osmosis.

The second thing to remember is that this is a *positive feedback loop*, meaning that its effects amplify. The countercurrent multiplier is actually a two-part positive feedback loop. In the first part, sodium and chloride ions that are reabsorbed from the ascending limb increase the amount of water that is reabsorbed from the descending limb. In the second part, as more water is reabsorbed from the descending limb, the concentration of sodium and chloride ions in the ascending limb increases. The higher the concentration of sodium and chloride ions in the ascending limb, the more that are pumped out in the first part of the loop. So, both parts amplify one another, allowing the system to perform its two main functions. ■

The Medullary Collecting System and Urea Recycling

A second factor that helps to create the medullary osmotic gradient is the permeability of the medullary collecting system to urea. As water is reabsorbed from the filtrate, urea becomes more concentrated in the remaining fluid. In the medullary collecting ducts and papillary ducts, urea follows its concentration gradient and passively diffuses out of the filtrate and into the interstitial fluid, further concentrating the medullary interstitial fluid. Some urea then enters the thin descending limb, so it continuously recycles. Note that the urea diffusing out of the medullary collecting duct constitutes only a small amount of the total urea; much of the urea remains in the filtrate and is excreted in the urine.

The Vasa Recta and the Countercurrent Exchanger

The steep medullary osmotic gradient created by the countercurrent multiplier and urea recycling is maintained by the vasa recta, the capillaries surrounding the nephron loops of juxtamedullary nephrons. The vasa recta act as a special kind of vascular system called a **countercurrent exchanger**. Like the limbs of the nephron loop, the vasa recta descend into the renal medulla, and then, following a hairpin turn, ascend toward the renal cortex. This arrangement of countercurrent flow, the blood flowing in the opposite direction from the filtrate, enables them to exchange substances.

Let's take a closer look at how countercurrent exchange works—it's illustrated in **Figure 24.22**. First notice that the blood within the vasa recta has a concentration of about 300 mOsm as it enters the renal medulla (to the right of the nephron, as shown in the figure). This means that ① as the blood descends into the medulla it is hypo-osmotic to the interstitial fluid. As we saw earlier, this situation causes water to leave the blood and enter the interstitial fluid by osmosis. In addition, more NaCl is present in the interstitial fluid than in the blood, which causes NaCl to diffuse from the interstitial fluid into the blood. The blood in the vasa recta continues to pick up NaCl and lose water as it descends deeper into the renal medulla. By the time the blood reaches the deepest part of the medulla, it has a concentration of about 1200 mOsm.

However, ② as the vasa recta ascend through the medulla, the gradient is reversed—the blood is now hyperosmotic to

the interstitial fluid, and the opposite process occurs. NaCl now diffuses out of the blood and back into the interstitial fluid, and water moves by osmosis from the interstitial fluid into the blood. Notice what has happened here: All of the NaCl that was removed from the interstitial fluid by the blood in the descending limb of the vasa recta was “exchanged,” or put back into the interstitial fluid by the blood in the ascending limb of the vasa recta. By the time the vasa recta exit the renal medulla, the blood has approximately the same concentration (about 300 mOsm) it had upon entering the renal medulla. The return of the blood to its initial osmolarity is critical, because it allows the vasa recta to deliver oxygen and nutrients to the cells of the medulla without depleting the medullary osmotic gradient necessary for water reabsorption and the production of concentrated urine. Note that

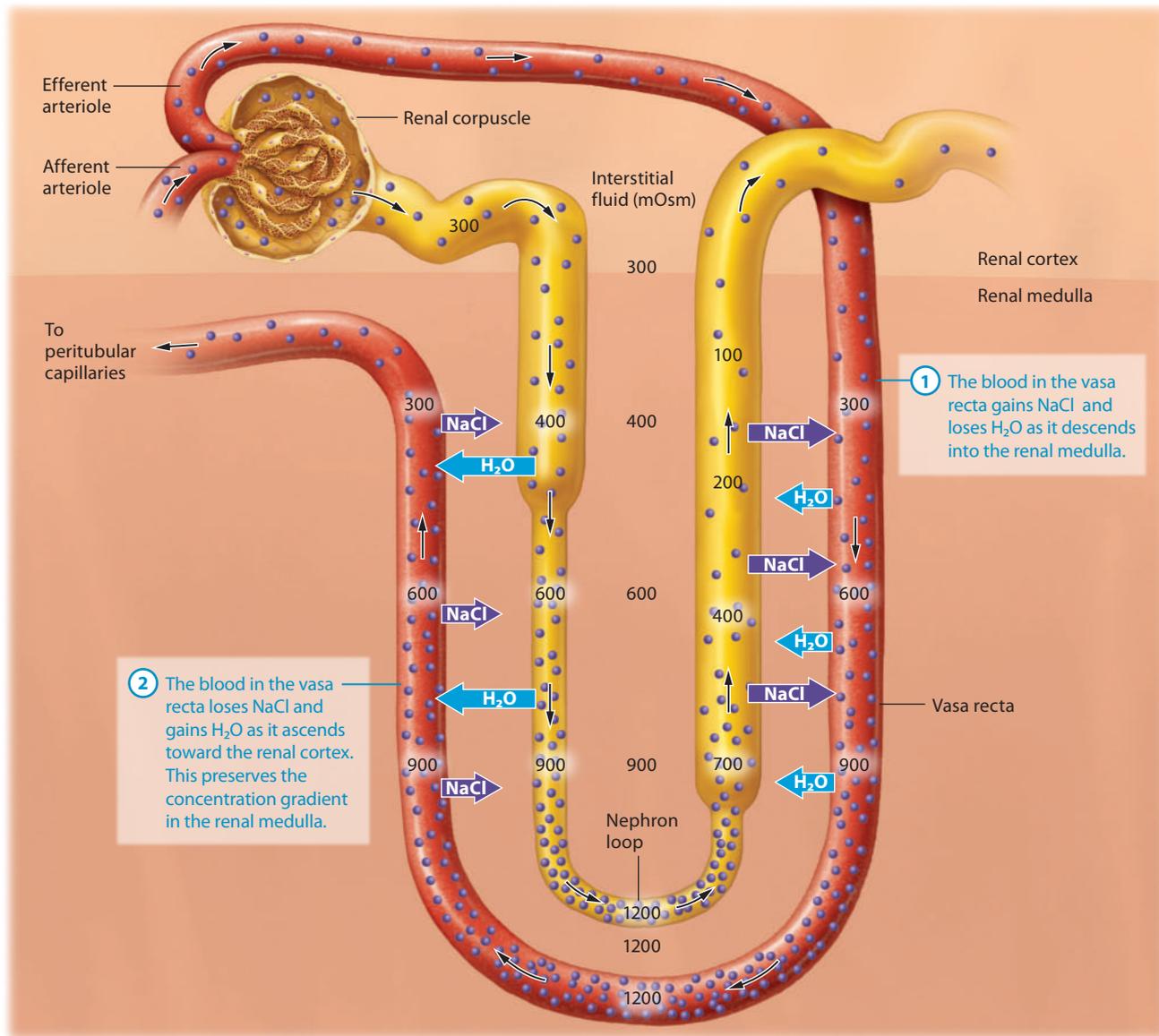


Figure 24.22 The countercurrent exchanger in the vasa recta.



Figure 24.22 is a simplified model, as numerous vasa recta and nephrons are actually in proximity to each other in the kidney.

How the Countercurrent Mechanism Produces Concentrated Urine

The countercurrent system is complicated, so let's take the time to summarize its function. First, keep in mind that the entire homeostatic function of this system is to conserve water for the body when needed. Water can be reabsorbed from collecting ducts only if ADH is present and a concentration gradient is there to drive osmosis. This medullary osmotic gradient doesn't exist on its own, so the kidneys must create and maintain it in the following ways:

- The countercurrent multiplier of the thick ascending limb establishes the medullary interstitial gradient by pumping NaCl into the interstitial fluid.
- Continued solute reabsorption, including urea recycling, from the filtrate in the medullary collecting duct adds to the gradient.
- The countercurrent exchanger of the vasa recta allows perfusion of the inner medulla while maintaining the medullary interstitial gradient.

Let's look at **Figure 24.23** to see how these combine to produce concentrated urine:

- 1 **When filtrate enters the cortical collecting duct in the renal medulla, there is no osmotic gradient between the filtrate and the interstitial fluid, so no water is reabsorbed.** Filtrate entering the renal medulla has the same concentration as the interstitial fluid, so no gradient is present to drive water reabsorption.
- 2 **In the presence of ADH, the concentrated medullary interstitial fluid creates a gradient for water reabsorption from the filtrate in the medullary collecting duct.** The interstitial fluid in the renal medulla is more concentrated than the filtrate. So as the filtrate passes deeper into the renal medulla through the medullary collecting duct, if ADH is present, water is drawn into the interstitial fluid by osmosis, thanks to the aquaporins and the medullary osmotic gradient. Water is reabsorbed until the filtrate and interstitial fluid are iso-osmotic.
- 3 **Deeper into the medulla, interstitial fluid is more concentrated, so water reabsorption continues from the medullary collecting duct.** The process continues because the interstitial fluid becomes progressively more concentrated in the deep renal medulla, allowing continued water reabsorption.
- 4 **Concentrated urine is produced.** This process produces urine with a concentration up to 1200 mOsm. We cannot make more concentrated urine, because after this point there is no longer a gradient to drive osmosis.

To find out what happens to the concentration of urine when too much ADH is secreted, see *A&P in the Real World: SIADH* on page 974.

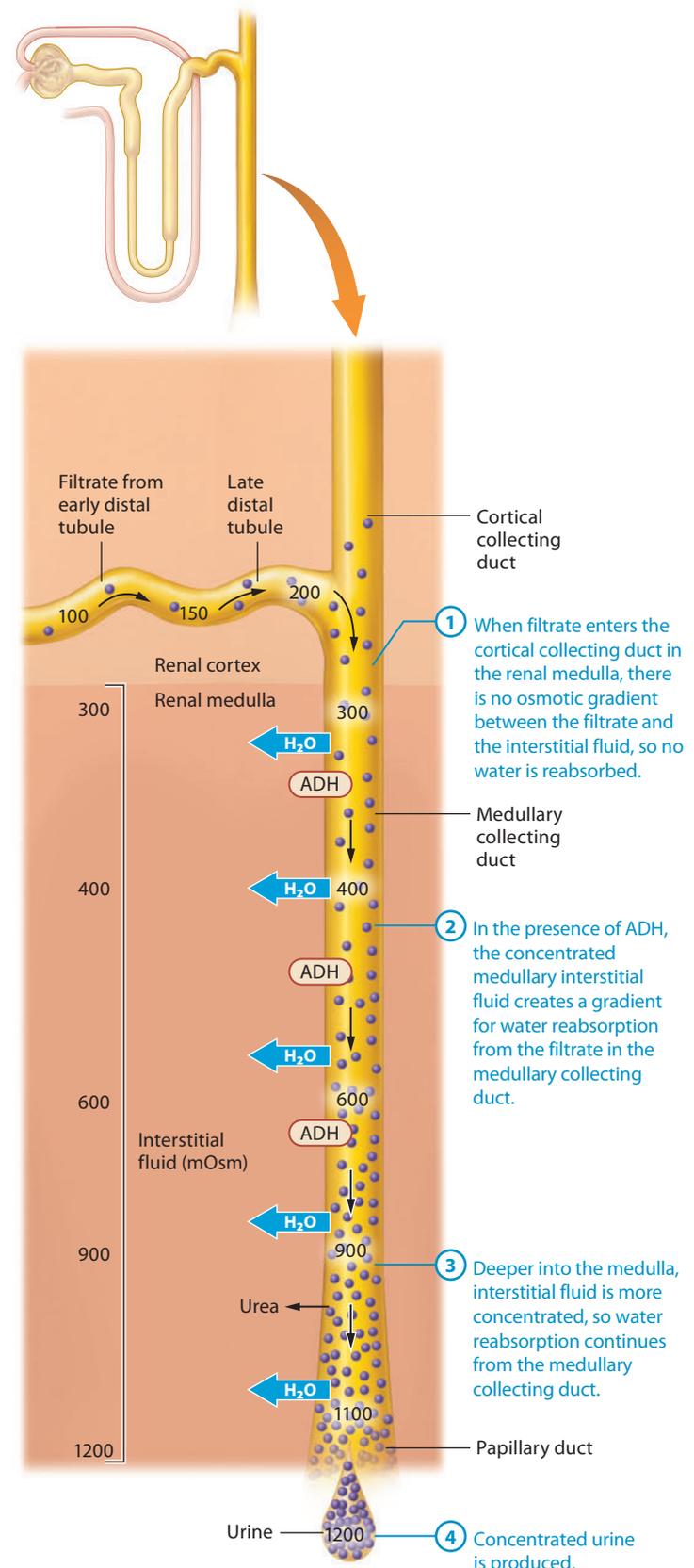


Figure 24.23 Formation of concentrated urine.





SIADH

The condition known as **syndrome of inappropriate ADH secretion**, or **SIADH**, is characterized by the secretion of excess antidiuretic hormone. SIADH has multiple causes, including ADH-secreting tumors (certain lung tumors are especially prone to this). Regardless of the cause, the result is the same: excessive fluid retention leading to a decreased plasma osmolarity and a high urine osmolarity.

Quick Check

- 5. What three factors allow the kidney to produce and maintain the medullary osmotic gradient?
- 6. How is concentrated urine produced?

Apply What You Learned

- 1. Alcohol inhibits the release of ADH. Predict how this inhibition will influence urine volume and concentration.
- 2. Drugs called *loop diuretics* block the $\text{Na}^+/\text{K}^+/\text{2Cl}^-$ symporters in the thick ascending limb of the nephron loop.
 - a. Predict the effect these drugs will have on water reabsorption from the thin descending limb of the nephron loop.
 - b. Predict the effect these drugs will have on the gradient in the renal medulla, and the resulting effect on water reabsorption from the medullary collecting system. How will this impact urine volume?

See answers in Appendix A.

MODULE

24.7

Putting It All Together: The Big Picture of Renal Physiology

Learning Outcomes

1. Describe the overall process by which blood is filtered and filtrate is modified to produce urine.

Let's now take a big picture look at all of the processes involved in renal physiology. We can break these processes down into six broad steps that are outlined in **Figure 24.24**. Note that Figure 24.24 shows the production of concentrated urine only.

Apply What You Learned

- 1. Glomerulonephritis, or inflammation of the glomerulus, results in excessively leaky glomerular capillaries and damaged glomeruli. The damaged and destroyed glomeruli cause the GFR to decrease. Which compensatory mechanisms would you expect to be triggered, and what effects would they have?
- 2. Certain diuretics block the effects of carbonic anhydrase in the proximal tubule. Predict the effects these drugs would have on the pH of the blood. How might the kidneys compensate for this?

See answers in Appendix A.

MODULE

24.8

Urine and Renal Clearance

Learning Outcomes

1. Explain how the physical and chemical properties of a urine sample are determined and relate these properties to normal urine composition.
2. Explain how filtration, reabsorption, and secretion determine the rate of excretion of any solute.
3. Explain how renal clearance rate can be used to measure GFR.

In the previous modules, we discussed how blood is filtered and how filtrate is modified as it flows through the nephron and collecting system. Now we take a look at the final product that exits the papillary ducts and is excreted by the body: the urine. In this module, we examine the components of normal urine and how abnormalities in the urine can signify problems in the kidneys and elsewhere in the body. We also explore another way in which the health of the kidneys may be assessed, through a value known as *renal clearance*.

Urine Composition and Urinalysis

As you learned in earlier modules, urine is the fluid that remains after tubular reabsorption and secretion have taken place. It normally contains water; sodium, potassium, chloride, and hydrogen ions; phosphates; sulfates; and metabolic waste products such as urea, creatinine, ammonia, and uric acid. It may also contain trace amounts of bicarbonate, calcium, and magnesium ions.

Because certain conditions cause abnormalities in the urine, an analysis of the urine, or **urinalysis**, can be a valuable tool in the diagnosis of disease. The factors examined in a typical urinalysis are as follows:

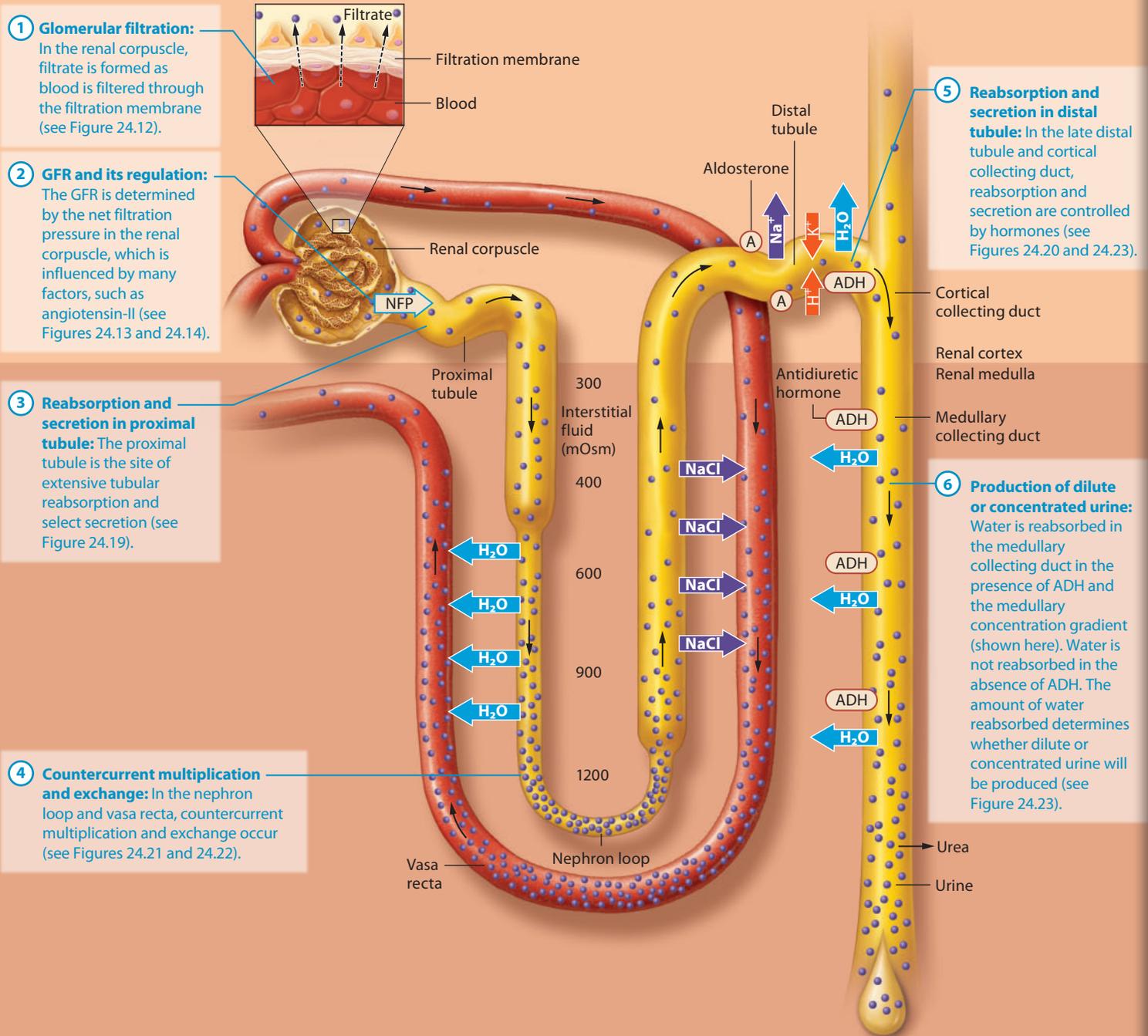
- **Color.** Urine is colored by a yellow pigment called *urochrome* (YER-oh-kroh-m), a breakdown product of hemoglobin. The more concentrated the urine, the less water is present, so the

The Big Picture of Renal Physiology

Figure 24.24



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same amount of urochrome makes the urine darker yellow. The color of urine may also be altered by certain foods, vitamins, drugs, and food dyes, or by the presence of blood.

- **Translucency.** Regardless of color, urine should always be translucent (you should be able to see light through it). Cloudy urine typically indicates an infection but may also indicate that the urine contains large quantities of protein.
- **Odor.** Recently voided urine should have a mild odor. If urine is allowed to sit out, however, bacteria metabolize the urea in the urine to produce ammonia, giving it a stronger odor. The odor of urine may also be altered by certain disease states, such as diabetes mellitus or infection, or by eating certain foods, such as asparagus.
- **pH.** The pH of urine is normally around 6.0—slightly acidic—but it can range from 4.5 to 8.0. The reason for the minimum pH of 4.5 is that the H^+ transport pumps in the distal tubule and collecting system cannot pump against a higher hydrogen ion gradient than this.
- **Specific gravity.** Specific gravity compares the amount of solutes in a solution to the amount in deionized water. Deionized water has no solutes and is assigned a specific gravity of 1.0; because urine has solutes, its specific gravity will be higher than that of water. This value typically ranges from 1.001 (very dilute urine) to 1.035 (very concentrated urine).

Other properties of urine, such as the presence and relative levels of certain solutes, are analyzed with urinalysis test strips. These strips are dipped in the urine, and their chemical indicators change color in the presence of specific substances. Substances commonly tested for in this way include blood, protein, leukocytes, and glucose. If the kidneys are functioning properly, these substances should not be present in urine in significant amounts.

Quick Check

- 1. What is the normal composition of urine?
- 2. What are its normal characteristics?

Renal Clearance

Evaluation of renal function is very important in clinical settings to monitor the health of the kidneys. Although urinalysis may provide valuable clues about renal function, a more complete assessment is provided by measuring the rate at which the kidneys remove a substance from the blood, a process known as **renal clearance**. The renal clearance of the chemical is then used to estimate the GFR. Renal clearance and GFR both are measured in the same units: milliliters of plasma per minute.

For a substance to provide an accurate measure of renal clearance and the GFR, the substance should be completely filtered and neither reabsorbed nor secreted. Substances secreted by renal tubules have a renal clearance greater than their GFR, whereas those that are reabsorbed have a renal clearance less than their GFR. To measure renal clearance, we therefore have a limited group of substances from which to choose. Two such commonly used substances are creatinine and inulin.

Creatinine, as you learned earlier, is a waste product of the metabolism of muscle and other cells. Nearly all of the creatinine produced is excreted by the kidneys. When the kidneys are impaired, the level of creatinine in the blood tends to rise. Generally, a plasma creatinine level above 1.2 mg/dl (milligrams per deciliter) is considered abnormal, but this varies with age, gender, and body mass. Creatinine excretion may be used to estimate the GFR by comparing the amount of creatinine excreted in the urine to the plasma concentration of creatinine. The main difficulty with using creatinine as an indicator of glomerular filtration is that between 15% and 50% of creatinine in the urine arrived there via secretion, not filtration. So a patient with a very low GFR may still have a nearly normal result from this test.

A more accurate assessment of the GFR can be obtained using the substance *inulin* (IN-yoo-lin). Inulin (not to be confused with the hormone insulin) is a complex carbohydrate found in plants such as garlic and artichokes that is filtered by the glomerulus, but is neither reabsorbed nor secreted by the renal tubule or collecting system. The GFR may be measured by injecting inulin and comparing its excretion in the urine to its plasma concentration.

Quick Check

- 3. What is renal clearance, and what is it used to estimate?

Apply What You Learned

- 1. The condition known as metabolic acidosis is characterized by a decreased blood pH from the accumulation of metabolic acids. Predict the effects this condition will have on the pH of the urine. What effect would you expect the opposite condition, metabolic alkalosis, to have on the urine pH?
- 2. Dietary supplementation with creatine phosphate is popular among athletes for its supposed performance-enhancing effects. What effect would creatine phosphate supplementation have on the amount of creatinine in the blood, and therefore the amount of creatinine that the kidneys must excrete?

See answers in Appendix A.

MODULE

24.9

Urine Transport, Storage, and Elimination

Learning Outcomes

1. Identify and describe the structure and functions of the ureters, urinary bladder, and urethra.
2. Relate the anatomy and histology of the bladder to its function.
3. Compare and contrast the male and female urinary tracts.
4. Describe the micturition reflex.
5. Describe voluntary and involuntary neural control of micturition.

Newly formed urine drains from the papillary ducts to minor calyces, then to major calyces, and finally to a renal pelvis. The renal pelvis then drain urine into the organs of the urinary tract. In this module, we examine the structure and function of the organs of the urinary tract. We conclude with a look at the process by which urine is expelled from the body, *micturition* (mik-choo-RISH-un).

Anatomy of the Urinary Tract

◀ Flashback

1. What are the properties of transitional epithelium? (p. 135)

The urinary tract consists of the two ureters, the urinary bladder, and the urethra (Figure 24.25a). The upcoming sections examine their anatomy and histology and the differences between the male and female urinary tracts.

Ureters

The **ureters** transport urine from the kidneys to the urinary bladder. The ureters are generally about 25–30 cm long and 3–4 mm in diameter in an adult. They begin at roughly the level of the second lumbar vertebra, travel behind the peritoneum, and empty into the urinary bladder.

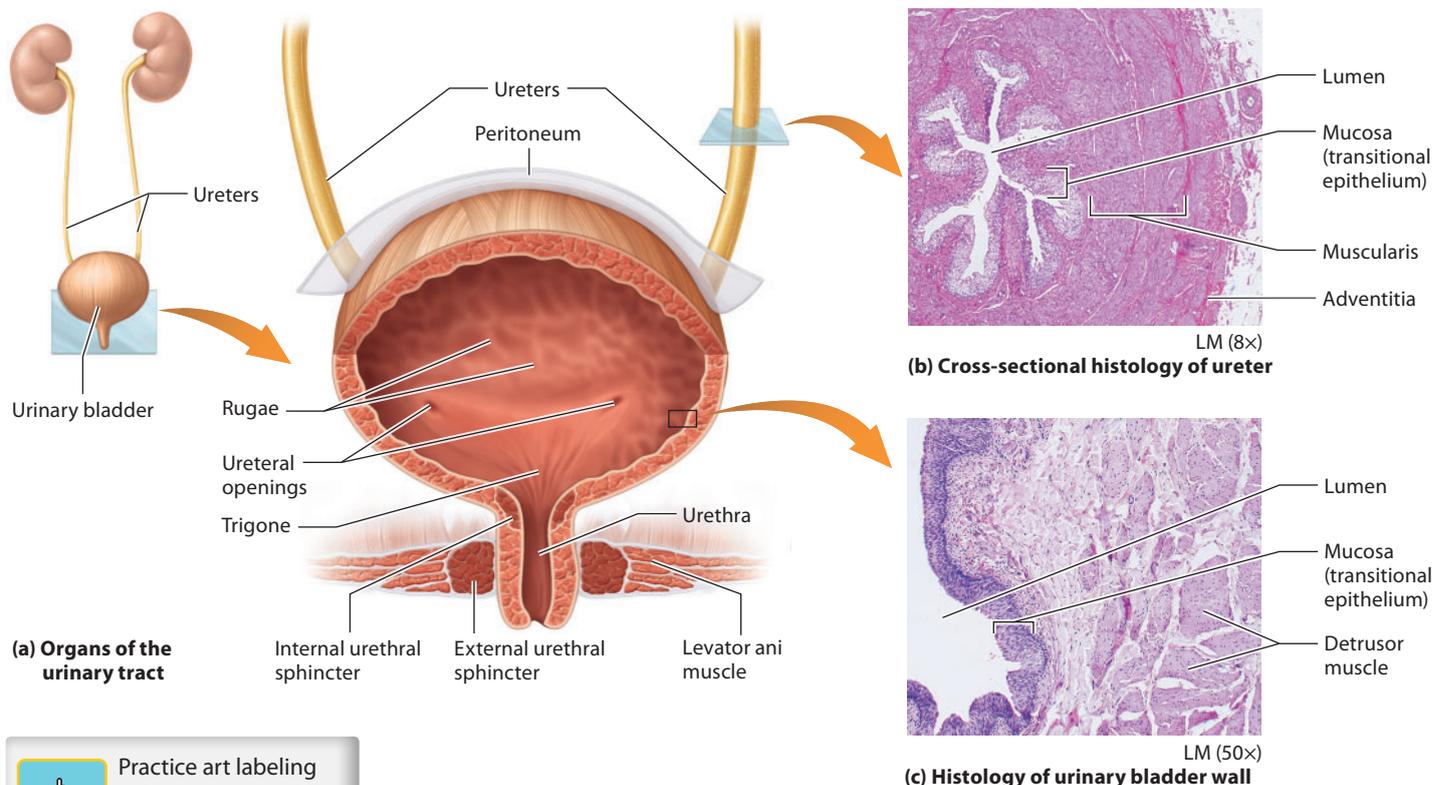
Like any hollow organ, the ureters have a multilayered wall. The three layers are named as follows, from superficial to deep (Figure 24.25b):

1. **Adventitia.** This superficial layer, known as the **adventitia** (ad-ven-TISH-uh), is fibrous connective tissue that supports the ureters.
2. **Muscularis.** The middle layer is the **muscularis**, and it consists of smooth muscle. Like the smooth muscle of the alimentary canal, the smooth muscle in the muscularis contracts rhythmically via *peristalsis* to propel urine toward the urinary bladder. Waves of peristalsis course through the muscularis as often as five times per minute, depending on the rate of urine production.
3. **Mucosa.** The innermost layer is the **mucosa**, a mucous membrane composed of transitional epithelium and its underlying basal lamina. As you learned in Chapter 4, transitional epithelium is stratified with cells that can change from having a dome shape to being squamous. This property allows the epithelium to expand and recoil.

The ureters drain posteriorly into the inferior urinary bladder. In this region a mechanism prevents urine from flowing backward through the ureter. As each ureter passes along the posterior urinary bladder, it travels obliquely through a “tunnel” in the bladder wall. As urine collects in the bladder, the pressure rises and compresses this tunnel, pinching the ureter closed and preventing backflow of urine.

Urinary Bladder

The **urinary bladder** is a hollow, distensible organ that sits on the floor of the pelvic cavity, suspended by a fold of parietal peritoneum.



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Figure 24.25 Anatomy of the urinary tract.

It collapses when empty, but when distended, it becomes pear-shaped, and can hold up to about 700–800 ml of urine in males (slightly less in females because of the position of the uterus).

Like the ureters, the wall of the urinary bladder has three tissue layers (**Figure 24.25c**). From superficial to deep, these layers are as follows:

1. **Adventitia.** The adventitia, the most superficial layer, is composed of areolar connective tissue. On the superior surface of the urinary bladder is an additional serosa, which is a fold of the parietal peritoneum.
2. **Detrusor muscle.** The middle tissue layer is composed of smooth muscle known as the **detrusor muscle** (dee-TROO-sor; “to push down”). The muscle fibers are arranged into inner longitudinal, middle circular, and outer longitudinal layers. The detrusor muscle forms a circular band around the opening of the urethra, called the **internal urethral sphincter**, shown in **Figure 24.25a**.
3. **Mucosa.** The mucosa is composed of transitional epithelium with an underlying basal lamina. It is a mucous membrane that produces mucus to protect the bladder epithelium from urine. When the bladder is not full, folds of mucosa called *rugae* (ROO-gee) are visible. What would happen if this mucus was not present? See *A&P in the Real World: Interstitial Cystitis* to find out.

Notice that the floor of the urinary bladder contains a triangular area called the **trigone** (TRY-gohn; “triangle”). The trigone lacks rugae and appears smooth because its mucosa is tightly bound to the underlying muscularis. The two posterior corners of the trigone are formed by the two ureteral orifices (openings). These orifices have mucosal flaps that act as valves to prevent backflow of urine during elimination. The apex of the trigone is formed by the opening to the urethra, the **internal urethral orifice**.



Interstitial Cystitis

Inadequate mucus production by the mucosa of the urinary bladder can cause the disease *interstitial cystitis* (sis-TY-tis; IC). This condition allows the acid and other toxic substances in the urine to damage the underlying mucosa and other tissues. IC is characterized by frequent urination and pelvic pain resulting from mucosal ulcerations. The underlying cause of IC is unknown, and unfortunately it responds poorly to treatment. Over the long term, IC can lead to bladder scarring and contraction.

Notice in **Figure 24.26** that the position of the urinary bladder differs in males and females. In males, it is anterior to the rectum; in females, it is anterior to the vagina and inferior to the uterus.

Urethra

The **urethra** is the terminal portion of the urinary tract; it drains urine from the urinary bladder to the outside of the body. Like the rest of the urinary tract, the urethra has an outer adventitia, middle muscularis, and inner mucosa. It begins at the internal urethral orifice in the urinary bladder, which is surrounded by the internal urethral sphincter. This sphincter remains closed unless urine is being eliminated. A second urethral sphincter, the **external urethral sphincter**, is formed from the *levator ani muscle* (leh-VAY-ter AY-nai; sometimes called the *urogenital diaphragm*), the muscular floor of the pelvic cavity. This sphincter is composed of skeletal muscle and is under voluntary control. There is no sphincter at the external orifice to the urethra in either males or females.

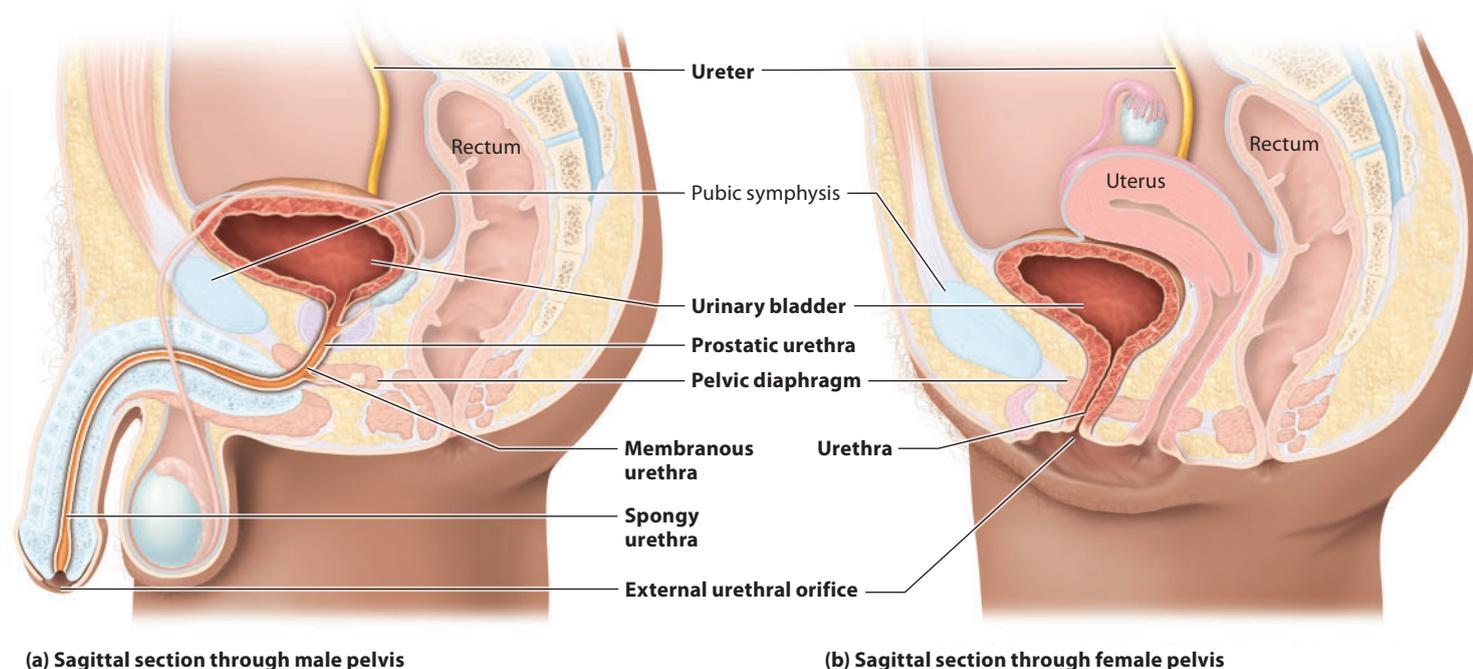


Figure 24.26 Comparison of urinary tract anatomy in the male and female.

The urethra differs in males and females structurally, as shown in Figure 24.26, which means that functional differences must exist as well. The female urethra is shorter (about 4 cm in length) and opens at the **external urethral orifice** between the vagina and the clitoris. It serves exclusively as a passage for urine.

The male urethra is considerably longer (about 20 cm in length) and consists of three regions:

1. **Prostatic urethra.** As the urethra exits the urinary bladder, it passes through the *prostate gland*, which sits inferior to the urinary bladder. This section of the urethra is called the **prostatic urethra**.
2. **Membranous urethra.** The shortest segment, known as the **membranous urethra**, passes through the levator ani muscle.
3. **Spongy urethra.** The longest segment of the male urethra, the **spongy urethra**, passes through the penis to the external urethral orifice. It is called the spongy urethra because it passes through an erectile body of the penis called the *corpus spongiosum*.

The location of the male urethra allows it to serve a dual purpose: It transports both urine and semen (see Chapter 26).

Quick Check

- 1. What are the three tissue layers of the organs of the urinary tract?
- 2. What are the functions of the ureters and urinary bladder?
- 3. How does the urethra differ structurally and functionally in males and females?

Micturition

◀ Flashback

1. What are afferent and efferent neurons? (p. 478)
2. What is a reflex arc? (p. 508)

Micturition, also called urination or voiding, is the discharge of urine from the urinary bladder to the outside of the body. It is activated by a reflex arc called the **micturition reflex**, which is mediated by the parasympathetic nervous system. This reflex arc is carried out by three components: (1) stretch receptors in the wall of the urinary bladder, (2) sensory afferent nerve fibers that convey this information to the sacral portion of the spinal cord (S2 and S3), and (3) parasympathetic efferent fibers that travel to the detrusor muscle and internal sphincter of the urinary bladder.

Micturition is shown in **Figure 24.27**. When urine fills the bladder and stretches its walls ①, the micturition reflex occurs. In infants and young children, this involuntary reflex is the primary mechanism by which the urinary bladder is emptied. This reflex arc has two basic steps:

- ② Stretch receptors send a signal via sensory afferent fibers to the sacral portion of the spinal cord.
- ③ Parasympathetic efferent fibers stimulate the detrusor muscle to contract and the internal urethral sphincter to relax, causing micturition.

As children mature, however, pathways develop between these parasympathetic neurons and the brain that allow control over the external urethral sphincter. At this point, micturition is predominantly controlled by the **micturition center** in the pons,

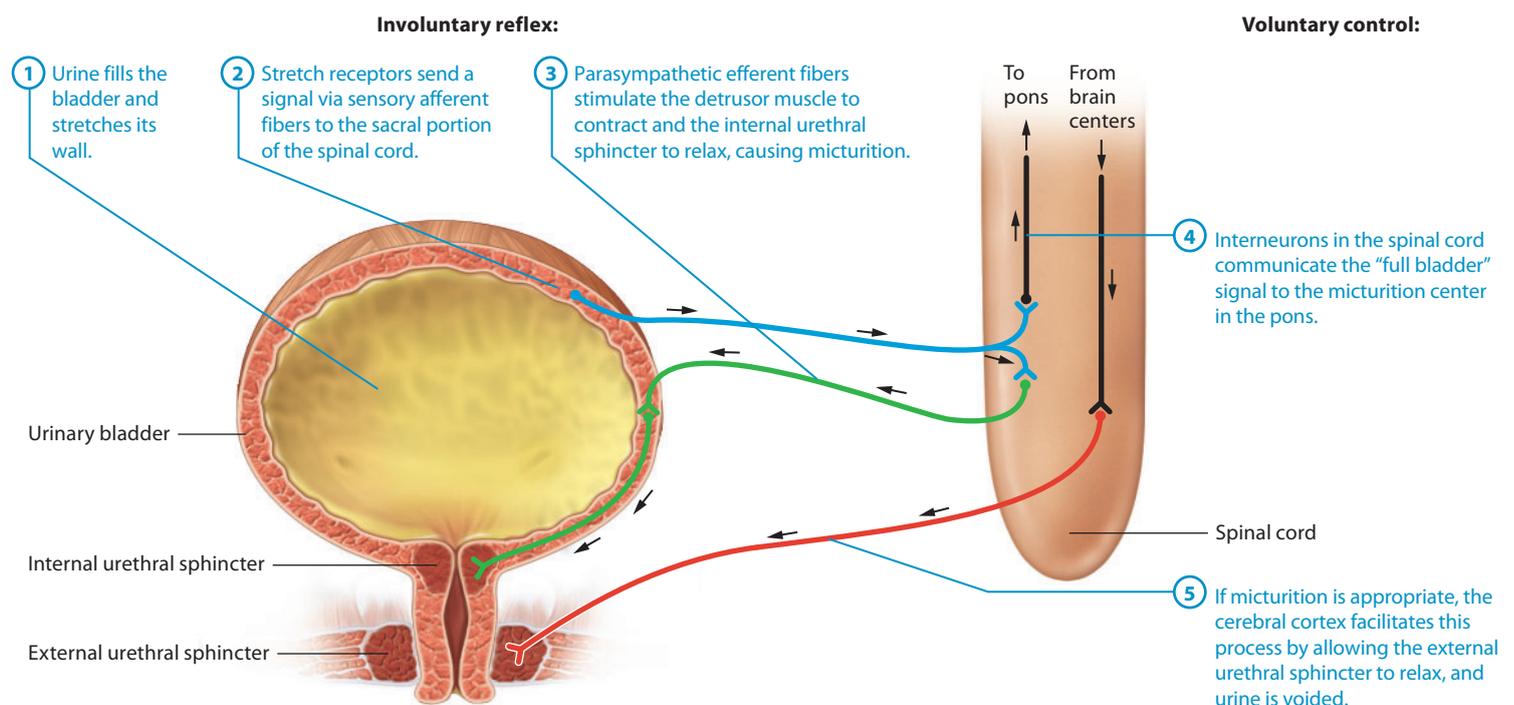


Figure 24.27 Micturition.

making the process voluntary. When the bladder is full, two additional steps then occur simultaneously with the involuntary process (see Figure 24.27):

- 4 Interneurons in the spinal cord communicate the “full bladder” signal to the micturition center in the pons.
- 5 If micturition is appropriate, the cerebral cortex facilitates this process by allowing the external urethral sphincter to relax, and urine is voided.

If micturition is not appropriate, then the detrusor muscle relaxes, the internal and external urethral sphincters remain closed, and the urge to urinate passes. The reflex generally initiates again within about an hour. This cycle repeats until the sensation of having to urinate becomes more acute. By the time about 500–600 ml has accumulated in the urinary bladder, the urge to urinate becomes too strong, voluntary control over the external urethral

sphincter is lost, and micturition occurs. After micturition, the bladder contains only about 10 ml of urine.

Quick Check

- 4. What are the steps of the micturition reflex?
- 5. How is micturition consciously controlled?

Apply What You Learned

- 1. Predict what would happen if the epithelium of the urinary tract were made of simple squamous epithelium instead of transitional epithelium.
- 2. How would a spinal cord injury above the level of S1–S2 affect micturition in that patient? How would the situation change if the injury were below S1–S2?

See answers in Appendix A.

CHAPTER SUMMARY

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MODULE 24.1

Overview of the Urinary System 941

- The organs of the **urinary system** are the **kidneys** and the ureters, urinary bladder, and urethra. (Figure 24.1, p. 942)

 Practice art-labeling exercise: Figure 24.1.

- The kidneys remove waste products from the blood and produce and expel **urine**; regulate fluid, electrolyte, and acid-base balance, blood pressure, and erythrocyte production; and perform other metabolic functions.

MODULE 24.2

Anatomy of the Kidneys 943

- The kidneys are paired retroperitoneal organs with three layers of protective coverings. (Figure 24.2, p. 943)
- Each kidney consists of over one million functional units called **nephrons**.
- Internally, the kidney consists of three regions: the superficial **renal cortex**, which houses blood vessels and most parts of the

nephrons; the middle **renal medulla**, which consists of triangular **renal pyramids** that are separated by **renal columns**; and the innermost **renal pelvis** and **major** and **minor calyces**, which form drainage and collection areas for urine. (Figure 24.3, p. 944)

 Practice art-labeling exercise: Figure 24.3.

- The kidney is supplied by the large **renal artery**, which branches multiple times as it passes from the renal pelvis to the renal cortex. In the renal cortex, each tiny **afferent arteriole** feeds a **glomerulus**, which is then drained by an **efferent arteriole**. The efferent arteriole feeds a second capillary bed, the **peritubular capillaries**. These vessels lead into a series of veins that drain into the **renal vein**. (Figure 24.4, p. 945)

 Practice art-labeling exercise: Figure 24.4.

- Nephrons are made up of two main parts: (Figure 24.5, p. 946)
 - The first part of the nephron is the **renal corpuscle**, which consists of the **glomerulus** and the surrounding **glomerular capsule**. The glomerular capsule has a parietal layer consisting of simple squamous epithelium and an inner visceral layer consisting of **podocytes**. (Figure 24.6, p. 947)
 - The second part of the nephron is the renal tubule, which consists of the **proximal tubule**, the **nephron loop**, and the **distal tubule**. (Figure 24.7, p. 947)

 Practice art-labeling exercise: Figure 24.5.

- The **juxtaglomerular apparatus** is a specialized region of the nephron where a group of cells located at the transition point between the nephron loop and the distal tubule **macula densa** come into contact with the **JG cells** of the afferent arteriole. (Figure 24.8, p. 948)
- Nephrons drain into the **collecting system**, which consists of the **cortical collecting ducts** and the **medullary collecting system**; the latter includes the **medullary collecting ducts** and **papillary ducts**. A papillary duct drains into a minor calyx. (Figure 24.9, p. 949)

- There are two types of nephrons: **cortical nephrons**, which have short nephron loops, and **juxtamedullary nephrons**, which have long nephron loops that dip deeply into the renal medulla and are surrounded by capillaries called the **vasa recta**. (Figure 24.10, p. 950)

 [Play Interactive Physiology tutorial on Urinary System: Anatomy Review.](#)

MODULE 24.3

Overview of Renal Physiology 951

- Nephrons carry out three basic physiological processes: (Figure 24.11, p. 951)
 - **Glomerular filtration** is performed by the renal corpuscles as blood passes through the glomerulus, resulting in the production of **filtrate**.
 - **Tubular reabsorption** is the process by which solutes and water are reclaimed from the filtrate and re-enter the blood.
 - **Tubular secretion** is the process by which substances are removed from the blood and transported into the filtrate.

MODULE 24.4

Renal Physiology I: Glomerular Filtration 951

- Three barriers to filtration constitute the **filtration membrane**: the glomerular capillary endothelial cells, the basal lamina of the glomerulus, and the podocytes (visceral layer of the glomerular capsule). The filtration membrane permits the passage of small molecules into the filtrate, but does not permit larger molecules, such as proteins and the formed elements of blood, to pass. (Figure 24.12, p. 952)

 [Play animation on filtration: Figure 24.12.](#)

- The rate at which filtrate is formed is called the **glomerular filtration rate (GFR)**; it averages about 125 ml/min. The GFR is determined by the net filtration pressure (NFP) in the glomerulus, which is the sum of the forces that favor filtration (glomerular hydrostatic pressure) and those that oppose filtration (colloid osmotic pressure and capsular hydrostatic pressure). The NFP averages about 10 mm Hg. (Figure 24.13, p. 953)

 [Play animation on net filtration pressure: Figure 24.13.](#)

- Maintenance of the GFR is crucial to homeostasis of fluid, electrolyte, and acid-base balance.
 - The kidneys can autoregulate to maintain the GFR by the **myogenic mechanism** and **tubuloglomerular feedback**. Both mechanisms maintain the GFR by modifying the diameter of the glomerular afferent arterioles.
 - The **renin-angiotensin-aldosterone system (RAAS)** works to maintain the GFR as part of the larger process of maintaining systemic blood pressure. The RAAS culminates in the formation of the protein **angiotensin-II**, which increases glomerular hydrostatic pressure through greater constriction of the efferent arterioles to preserve the GFR, stimulates sodium ion and water reabsorption from the proximal tubule, causes systemic vasoconstriction, and triggers aldosterone release to increase systemic blood pressure. (Figure 24.14, p. 957)

 [Play animation on the renin-angiotensin-aldosterone system: Figure 24.14.](#)

- **Atrial natriuretic peptide** increases the GFR by dilating the afferent arteriole.
- The sympathetic nervous system decreases the GFR by causing vasoconstriction of the afferent arterioles.
- The ways in which the GFR is controlled are summarized in Table 24.1 (p. 959).

 [Play Interactive Physiology tutorial on Urinary System: Glomerular Filtration.](#)

MODULE 24.5

Renal Physiology II: Tubular Reabsorption and Secretion 960

- To be reabsorbed, substances must pass from the filtrate in the tubule lumen, past the tubule cells into the interstitial space, where they then diffuse through the cells of the capillary walls into the blood. Substances may cross the tubule cells by passing *between* the cells (the **paracellular route**) or *through* them (the **transcellular route**). Substances are secreted only through the transcellular route. (Figure 24.15, p. 961)
- Reabsorption and secretion occur in the renal tubule and collecting system:
 - In the proximal tubule, sodium ion reabsorption drives **obligatory water reabsorption**, reabsorption of many solutes, and hydrogen ion secretion. About 65% of the water, much of the HCO_3^- , nearly all of the amino acids and glucose, and variable amounts of electrolytes are reabsorbed here. (Figure 24.16, p. 962; Figure 24.17, p. 963; Figure 24.18, p. 964)
 - In the nephron loop, another 15–20% of the water and 20–25% of the NaCl are reabsorbed.

 [Play Interactive Physiology tutorial on Urinary System: Early Filtrate Processing.](#)

- The late distal tubule and cortical collecting ducts are relatively impermeable to water and solutes unless influenced by hormones.
 - **Aldosterone** causes reabsorption of sodium ions and secretion of potassium and hydrogen ions.
 - **Antidiuretic hormone (ADH)** stimulates the reabsorption of water through the formation of **aquaporin** channels.
- The medullary collecting system reabsorbs most of the remaining water from the filtrate under the influence of ADH. These ducts also reabsorb many of the ions by diffusion and secrete hydrogen ions by primary active transport.
- The pH of the blood is regulated by adjusting the secretion of hydrogen ions and the reabsorption of bicarbonate ions.

 [Play Interactive Physiology tutorial on Urinary System: Late Filtrate Processing.](#)

- The big picture of tubular reabsorption and secretion is shown in Figure 24.19 (p. 967).

 [Play animation on tubular reabsorption and secretion: Figure 24.19.](#)

MODULE 24.6

Renal Physiology III: Regulation of Urine Concentration and Volume 968

- **Facultative water reabsorption** in the late distal tubule and collecting system determines the concentration and volume of urine that the kidneys produce. If less water is reabsorbed, dilute urine is produced. If more water is reabsorbed, concentrated urine is produced.
- Dilute urine is produced by decreasing the release of ADH, which causes less water to be reabsorbed. (Figure 24.20, p. 969)

 [Play animation on the formation of dilute urine: Figure 24.20.](#)

- The ability to produce concentrated urine relies on two factors: ADH acting on the late distal tubule and collecting system to cause reabsorption of water and a **medullary osmotic gradient** in the interstitial fluid of the renal medulla that drives the reabsorption of water by osmosis.
 - The medullary osmotic gradient is created by the **countercurrent multiplier** in the nephron loops of juxtamedullary nephrons, whereby NaCl is pumped out of the thick ascending limb of the loop into the interstitial fluid and water moves out of the thin descending limb into the interstitial fluid by osmosis. (Figure 24.21, pp. 970–971)

 [Play animation on the countercurrent multiplier: Figure 24.21.](#)

- Urea passively diffuses into the interstitial fluid from the medullary collecting system, which contributes to the medullary osmotic gradient.
- The vasa recta maintain the gradient by acting as a **countercurrent exchanger**. These vessels remove NaCl from the interstitial fluid as they descend into the renal medulla and then redeposit the NaCl and absorb water as they ascend into the renal cortex. (Figure 24.22, p. 972)

 [Play animation on the countercurrent exchanger: Figure 24.22.](#)

- The result of the medullary osmotic gradient in the presence of ADH is continued water reabsorption and a low volume of concentrated urine. (Figure 24.23, p. 973)

 [Play animation on the formation of concentrated urine: Figure 24.23.](#)

MODULE 24.7

Putting It All Together: The Big Picture of Renal Physiology 974

- The big picture of renal physiology is shown in Figure 24.24 (p. 975).

 [Play animation on the big picture of renal physiology: Figure 24.24.](#)

MODULE 24.8

Urine and Renal Clearance 974

- Urine is composed of mostly water with solutes such as electrolytes and metabolic wastes.
- Renal function may be assessed by measuring the rate at which certain substances are removed from the blood by the kidney, known as **renal clearance**, as a way to estimate GFR. Commonly measured substances include creatinine and inulin.

MODULE 24.9

Urine Transport, Storage, and Elimination 976

- The ureters, urinary bladder, and urethra comprise the **urinary tract**. (Figure 24.25, p. 977)

 [Practice art-labeling exercise: Figure 24.25.](#)

- The **ureters** are muscular tubes that undergo peristalsis to propel urine toward the urinary bladder.
- The wall of the **urinary bladder** consists of three layers: the inner **mucosa**, made of transitional epithelium; the middle **detrusor muscle**; and the outer **adventitia**. The inferior portion of the urinary bladder is called the **trigone**.
- The **urethra** contains two sphincters: the involuntary **internal urethral sphincter** and the voluntary **external urethral sphincter**. The longer male urethra contains three regions and serves as a conduit for both urine and semen. The shorter female urethra serves as a passageway only for urine. (Figure 24.26, p. 978)
- **Micturition** is the process whereby urine is voided from the urinary bladder through the urethra. It occurs via the **micturition reflex**, mediated by the parasympathetic nervous system, though typically under voluntary control. (Figure 24.27, p. 979)

ASSESS WHAT YOU LEARNED

See answers in Appendix A.

LEVEL 1 Check Your Recall

1. What are the four main organs of the urinary system?
2. Which of the following is not a physiological process carried out by the kidneys?
 - a. Blood pressure regulation
 - b. Tubular reabsorption
 - c. Tubular secretion
 - d. Glomerular filtration
 - e. All of the above are physiological processes carried out by the kidneys.
3. Mark the following statements as true or false. If a statement is false, correct it to make a true statement.
 - a. The kidneys are retroperitoneal and covered by three layers of connective tissue.
 - b. Internally, the kidneys consist of an outer renal medulla, a middle renal pelvis, and an inner renal cortex.

- c. The first capillary bed of the kidneys is the peritubular capillaries, which are fed by the afferent arteriole and drained by the efferent arteriole.
- d. Filtrate flows from the renal corpuscle to the distal tubule, the nephron loop, the proximal tubule, and into the collecting system.
4. Cortical and juxtamedullary nephrons differ in the:
- lengths of their nephron loops.
 - structure of the capillaries surrounding them.
 - structure of their renal corpuscles.
 - Both a and b are correct.
 - Both b and c are correct.
5. Describe the structure of the filtration membrane.
6. Which of the following substances would pass through the filtration membrane to become part of the filtrate under normal circumstances? (Circle all that apply.)
- | | |
|-----------------|----------------|
| a. Sodium ions | e. Leukocytes |
| b. Albumin | f. Amino acids |
| c. Glucose | g. Urea |
| d. Erythrocytes | |
7. Fill in the blanks: Glomerular hydrostatic pressure _____ filtration; colloid osmotic pressure and capsular hydrostatic pressure _____ filtration.
- | | |
|--------------------|-------------------|
| a. favors; favor | c. favors; oppose |
| b. opposes; oppose | d. opposes; favor |
8. Fill in the blanks for the following statements:
- When the GFR decreases, the macula densa releases chemicals to _____ the afferent arteriole.
 - The sympathetic nervous system _____ the blood vessels supplying the kidney to _____ the glomerular filtration rate.
 - The enzyme _____ is released by JG cells in response to a decrease in the GFR.
 - The enzyme _____ converts angiotensin-I to angiotensin-II.
 - Generally, angiotensin-II _____ systemic blood pressure while _____ the GFR.
9. Which of the following is *false* about the GFR?
- The GFR averages about 120 ml/min.
 - The GFR increases when the afferent arteriole dilates.
 - The GFR decreases when the efferent arteriole constricts.
 - The GFR decreases when the afferent arteriole constricts.
10. The route by which substances are reabsorbed by crossing through the cells of the renal tubule and collecting system is known as the:
- paracellular route.
 - transcellular route.
 - primary active transport route.
 - secondary active transport route.
11. Mark the following statements as true or false. If a statement is false, correct it to make a true statement.
- Sodium ions and glucose are cotransported into the proximal tubule cell by secondary active transport.
 - The distal tubule reabsorbs sodium ions and secretes potassium and hydrogen ions in response to ADH.
 - Sodium ion reabsorption creates a gradient that helps drive the reabsorption of water and many other solutes from the proximal tubule.
 - ADH triggers water reabsorption from the nephron loop.
 - Obligatory water reabsorption occurs in the distal tubule and collecting system.
12. Dilute urine is produced when decreased levels of _____ are secreted:
- aldosterone
 - atrial natriuretic peptide
 - ADH
 - none of the above
13. Which of the following conditions does not contribute to the creation and/or maintenance of the medullary osmotic gradient?
- The countercurrent exchanger of the vasa recta
 - The countercurrent multiplier of the nephron loops of cortical nephrons
 - The countercurrent multiplier of the nephron loops of juxtamedullary nephrons
 - The permeability of the medullary collecting system to urea and other ions
14. Fill in the blanks: The kidneys produce _____ urine when the osmolarity of the body's fluids increases. They produce _____ urine when the osmolarity of the body's fluids decreases.
15. Normal urine should have which of the following properties? Circle all that apply.
- Translucency
 - Yellowish pigment
 - Cloudy appearance
 - pH less than 4.5
16. The GFR may be estimated by measuring the rate at which certain substances are removed from the blood, which is known as:
- renal clearance.
 - plasma creatinine.
 - glomerular hydrostatic pressure.
 - inulin estimation.
17. Fill in the blanks for each of the following statements:
- The process by which urine is eliminated is called _____, and it is mediated by reflexes involving the _____ nervous system.
 - The mucosa of the organs of the urinary tract is lined with _____ epithelium.
 - The three layers of smooth muscle in the urinary bladder are known as the _____ muscle.
 - The female urethra provides a passageway for _____, whereas the male urethra provides a passageway for _____ and _____.

LEVEL 2 Check Your Understanding

1. Predict the effects the following scenarios would have on glomerular filtration:
 - a. Having excess proteins in the blood, increasing colloid osmotic pressure
 - b. Having low arterial blood pressure (hypotension)
 - c. Having high arterial blood pressure (hypertension)
2. Trace the pathway taken by a molecule of urea through the kidney from the glomerulus to the renal pelvis if the urea is recycled.
3. Explain why urinary tract infections, which involve the urethra and urinary bladder, are much more common in females than males.
4. Why must the kidneys establish a concentration gradient in the interstitial fluid of the renal medulla in order to produce concentrated urine?

LEVEL 3 Apply Your Knowledge**PART A: Application and Analysis**

1. Drugs that treat hypertension, or high blood pressure, have the following actions. Discuss the potential effects of each of these drug actions on the functions of the kidneys. Might any of these drugs cause adverse effects? If so, what are the potential adverse effects of each drug type?
 - a. Blocking the action of aldosterone on the kidneys
 - b. Blocking the receptor for angiotensin-II on blood vessels, including the vessels of the kidney

c. Blocking the $\text{Na}^+/\text{Cl}^-/2\text{K}^+$ transport pumps in the thick ascending limb of the nephron loop

2. Mr. Wu is a patient with kidney disease who presents to your clinic for monitoring. You notice on his chart that his GFR was estimated through inulin administration to be about 35 ml/min. What does this tell you about the health of his kidneys? Mr. Wu is taking a medication that is normally excreted from the body in the urine. You order blood work and find that the concentration of this medication in his plasma is much higher than normal. How does his decreased GFR explain the elevated level of medication in his plasma?
3. Deana is a 4-year-old girl with a rare genetic defect that causes the Na^+ /glucose symporters in the proximal tubule to reabsorb less glucose and sodium ions than normal. Predict the effects this defect will have on the composition and volume of Deana's urine. Explain why you would expect to see increased activity of the tubuloglomerular feedback and the renin-angiotensin-aldosterone systems in Deana's kidneys.

PART B: Make the Connection

4. Explain how each of the drugs in question 1 from this section would lower blood pressure. (*Connects to Chapter 17*)
5. What might it mean if you found a high concentration of urobilinogen in your patient's urine? (*Hint: Consider the source of urobilinogen.*) (*Connects to Chapter 19*)