26 The Urinary System

Learning Outcomes

These Learning Outcomes correspond by number to this chapter's sections and indicate what you should be able to do after completing the chapter.

26-1 Identify the **components of the urinary system**, and describe the **functions** it performs.

26-2 Describe the **location and structural features of the kidneys**, identify **major blood vessels** associated with each kidney, trace the **path of blood flow through a kidney**, describe the **structure of a nephron**, and identify the **functions of each region of the nephron and collecting system**.

26-3 Describe the **basic processes responsible for urine formation**.

26-4 Describe the factors that influence **glomerular filtration pressure** and the **rate of filtrate formation**.

26-5 Identify the **types and functions of transport mechanisms** found along each segment of the **nephron**, explain the **role of countercurrent multiplication**, describe **hormonal influence on the volume and concentration of urine**, and describe the **characteristics of a normal urine sample**.

26-6 Describe the **structures and functions of the ureters, urinary bladder, and urethra**, discuss the **voluntary and involuntary regulation of urination**, and describe the **micturition reflex**.

26-7 Describe the **effects of aging on the urinary system**.

26-8 Give examples of **interactions between the urinary system and other organ systems** studied so far.

Clinical Notes

Spotlight

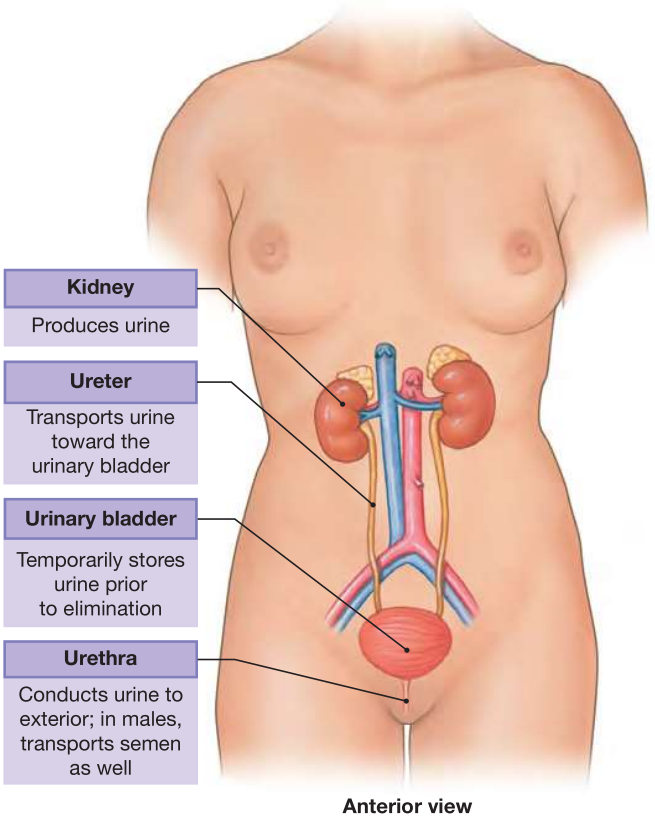
An Introduction to the Urinary System

The urinary system removes most physiological wastes. In this chapter, we consider the functional organization of the urinary system and describe how the kidneys remove metabolic waste products from the circulation to produce urine. We also explain the major regulatory mechanisms controlling urine production and concentration, and identify how urine is transported to the urinary bladder and released from the body through the urinary tract passageways.

26-1 Consisting of the kidneys, ureters, urinary bladder, and urethra, the urinary system has three primary functions

The **urinary system** (Figure 26–1) has three major functions: (1) *excretion*, the removal of organic waste products from body fluids; (2) *elimination*, the discharge of these waste products into the environment; and (3) homeostatic regulation of the volume and solute concentration of blood plasma.

Figure 26–1 An Introduction to the Urinary System. An anterior view of the urinary system, showing the positions of its components.



The two **kidneys** perform the excretory functions of the urinary system. These organs produce **urine,** a fluid containing water, ions, and small soluble compounds. Urine leaving the kidneys flows along the **urinary tract,** which consists of paired tubes called **ureters** (ū-RĒ-terz), to the **urinary bladder,** a muscular sac for temporary storage of urine. On leaving the urinary bladder, urine passes through the **urethra** (ū-RĒ-thra), which conducts the urine to the exterior.

The urinary bladder and the urethra eliminate urine. This process is called **urination** or **micturition** (mik-choo-RISH-un). In this process, the muscular urinary bladder contracts and forces urine through the urethra and out of the body. ATLAS: Embryology Summary 20: The Development of the Urinary System

The urinary system removes waste products generated by cells throughout the body, but it has several other essential homeostatic functions that are often overlooked. They include the following:

- *Regulating blood volume and blood pressure*, by adjusting the volume of water lost in urine, releasing erythropoietin, and releasing renin.
- *Regulating plasma concentrations of sodium, potassium, chloride, and other ions*, by influencing the quantities lost in urine. The kidneys also control calcium ion levels through the synthesis of calcitriol.
- *Helping to stabilize blood pH*, by controlling the loss of hydrogen ions and bicarbonate ions in urine.
- *Conserving valuable nutrients*, by preventing their loss in urine while removing organic wastes—especially nitrogenous wastes such as *urea* and *uric acid*.
- *Assisting the liver* in detoxifying poisons and, during starvation, deaminating amino acids so that other tissues can metabolize them.

These activities are carefully regulated to keep the composition of blood within acceptable limits. A disruption of any one of them has immediate consequences and can be fatal.

Checkpoint

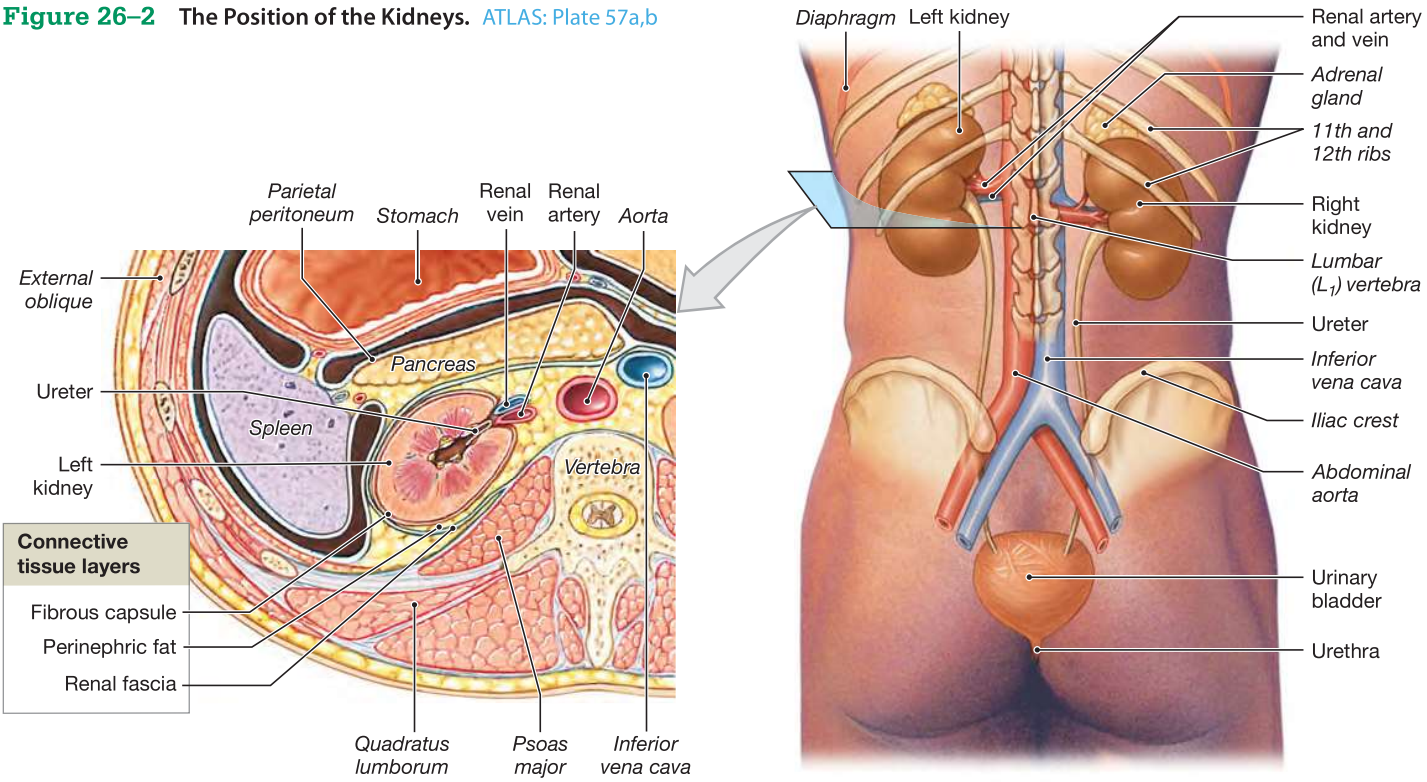
1. Name the three major functions of the urinary system.
2. Identify the components of the urinary system.
3. Define micturition.

See the blue Answers tab at the back of the book.

26-2 Kidneys are highly vascular structures containing functional units called nephrons, which perform filtration, reabsorption, and secretion

The kidneys are located on either side of the vertebral column, between vertebrae T_{12} and L_3 (Figure 26–2a). The left kidney

Figure 26–2 **The Position of the Kidneys.** ATLAS: Plate 57a,b



a A posterior view of the trunk

b A superior view of a transverse section at the level indicated in part (a)

lies slightly superior to the right kidney. The right kidney is slightly inferior due to the position of the right lobe of the liver.

The superior surface of each kidney is capped by an adrenal gland. The kidneys and adrenal glands lie between the muscles of the posterior body wall and the parietal peritoneum, in a retroperitoneal position (**Figure 26–2b**).

Tips & Tricks

To visualize the kidneys' retroperitoneal positions, think of each kidney as a picture on the body wall that got covered over by wallpaper (the parietal peritoneum).

The position of the kidneys in the abdominal cavity is maintained by (1) the overlying peritoneum, (2) contact with adjacent visceral organs, and (3) supporting connective tissues. Three concentric layers of connective tissue protect and stabilize each kidney (**Figure 26–2b**):

1. The **fibrous capsule,** a layer of collagen fibers that covers the outer surface of the entire organ.
2. The **perinephric fat capsule,** a thick layer of adipose tissue that surrounds the fibrous capsule.
3. The **renal fascia,** a dense, fibrous outer layer that anchors the kidney to surrounding structures. Collagen fibers extend outward from the fibrous capsule through the perinephric fat to this layer. Posteriorly, the renal fascia fuses with the deep fascia surrounding the muscles of the body wall. Anteriorly, the renal fascia forms a thick layer that fuses with the peritoneum.

In effect, each kidney hangs suspended by collagen fibers from the renal fascia and is packed in a soft cushion of adipose tissue. This arrangement prevents the jolts and shocks of day-to-day living from disturbing normal kidney function. If the suspensory fibers break or become detached, a slight bump or hit can displace the kidney and stress the attached vessels and ureter. This condition is called a *floating kidney*. It may cause pain or other problems from the distortion of the ureter or blood vessels during movement.

A typical adult kidney is reddish-brown and about 10 cm (4 in.) long, 5.5 cm (2.2 in.) wide, and 3 cm (1.2 in.) thick (**Figures 26–3** and **26–4**). Each kidney weighs about 150 g (5.25 oz). The **hilum,** a prominent medial indentation, is the point of entry for the *renal artery* and *renal nerves*. The hilum is also the point of exit for the *renal vein* and the ureter.

Sectional Anatomy of the Kidneys

The fibrous capsule covering the outer surface of the kidney also lines the **renal sinus,** an internal cavity within the kidney (**Figure 26–4a**). The fibrous capsule is bound to the outer surfaces of the structures within the renal sinus. In this way, it stabilizes the positions of the ureter and of the renal blood vessels and nerves.

Figure 26–3 The Gross Anatomy of the Urinary System. The abdominopelvic cavity (with the digestive organs removed), showing the kidneys, ureters, urinary bladder, and blood supply to the urinary structures. ATLAS: Plates 61a; 62a,b

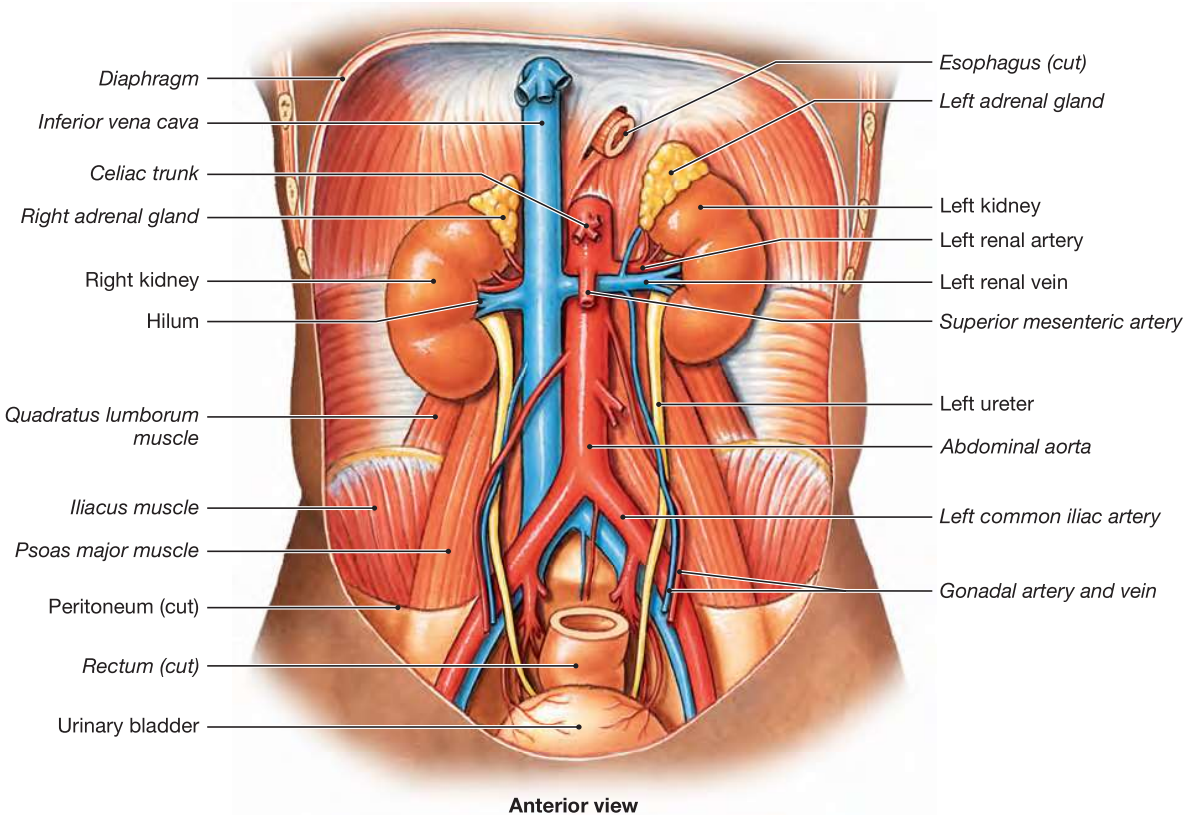
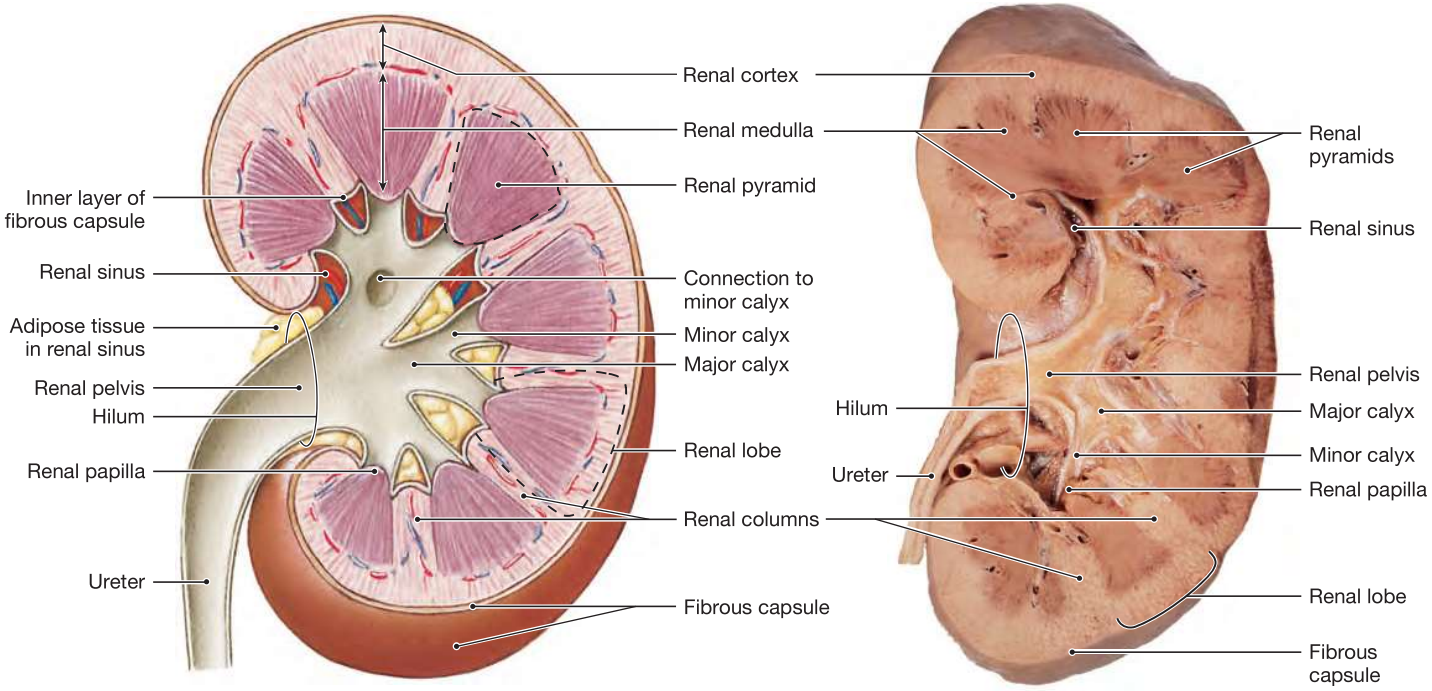


Figure 26–4 The Structure of the Kidney. ATLAS: Plates 57a,b; 61b



a A diagrammatic view of a frontal section through the left kidney

b A frontal section of the left kidney

The kidney itself has an outer cortex and an inner medulla. The **renal cortex** is the superficial portion of the kidney, in contact with the fibrous capsule. The cortex is reddish brown and granular.

The **renal medulla** consists of 6 to 18 distinct triangular structures called **renal pyramids.** The base of each pyramid abuts the cortex. The tip of each pyramid—a region known as the **renal papilla**—projects into the renal sinus. Each pyramid has a series of fine grooves that converge at the papilla. Adjacent renal pyramids are separated by bands of cortical tissue called **renal columns,** which extend into the medulla. The columns have a distinctly granular texture, similar to that of the cortex. A **renal lobe** consists of a renal pyramid, the overlying area of renal cortex, and adjacent tissues of the renal columns.

Urine is produced in the renal lobes. Ducts within each renal papilla discharge urine into a cup-shaped drain called a **minor calyx** (KĀ-liks). Four or five minor calyces (KAL-i-sēz) merge to form a **major calyx,** and two or three major calyces combine to form the **renal pelvis,** a large, funnel-shaped chamber. The renal pelvis fills most of the renal sinus and is connected to the ureter, which drains the kidney.

Urine production begins in microscopic, tubular structures called *nephrons* (NEF-ronz) in the cortex of each renal lobe. Each kidney has roughly 1.25 million nephrons, with a combined length of about 145 km (85 miles).

Blood Supply and Innervation of the Kidneys

Your kidneys receive 20–25 percent of your total cardiac output. In normal, healthy individuals, about 1200 mL of blood flow through the kidneys each minute—a phenomenal amount of blood for organs with a combined weight of less than 300 g (10.5 oz)!

Each kidney receives blood through a **renal artery.** This vessel originates along the lateral surface of the abdominal aorta near the level of the superior mesenteric artery (**Figure 21–25a**, pp. 744–745). As it enters the renal sinus, the renal artery provides blood to the **segmental arteries** (**Figure 26–5a**). Segmental arteries further divide into a series of **interlobar arteries.** These arteries radiate outward through the renal columns between the renal pyramids. The interlobar arteries supply blood to the **arcuate** (AR-kū-āt) **arteries,** which arch along the boundary between the cortex and medulla of the kidney. Each arcuate artery gives rise to a number of **cortical radiate arteries,** also called *interlobular arteries*. They supply the cortical portions of the adjacent renal lobes. Branching from each cortical radiate artery are numerous **afferent arterioles.** These vessels deliver blood to the capillaries supplying individual nephrons (**Figure 26–5b,c**).

After passing through the capillaries of the nephrons, blood enters a network of venules and small veins that converge on the **cortical radiate veins,** also called *interlobular veins* (**Figure 26–5a,c**). The cortical radiate veins deliver blood to **arcuate veins.** These veins in turn empty into **interlobar veins,** which drain directly into the **renal vein.** There are no segmental veins.

The kidneys and ureters are innervated by **renal nerves.** Most of the nerve fibers involved are sympathetic postganglionic fibers from the celiac plexus and the inferior splanchnic nerves. ↩ pp. 522, 531 A renal nerve enters each kidney at the hilum and follows the branches of the renal arteries to reach individual nephrons. The sympathetic innervation (1) adjusts rates of urine formation by changing blood flow and blood pressure at the nephron; and (2) stimulates the release of renin, which ultimately restricts losses of water and salt in the urine by stimulating reabsorption at the nephron. When a substance is reabsorbed, it is "reclaimed," eventually reentering the blood.

Clinical Note

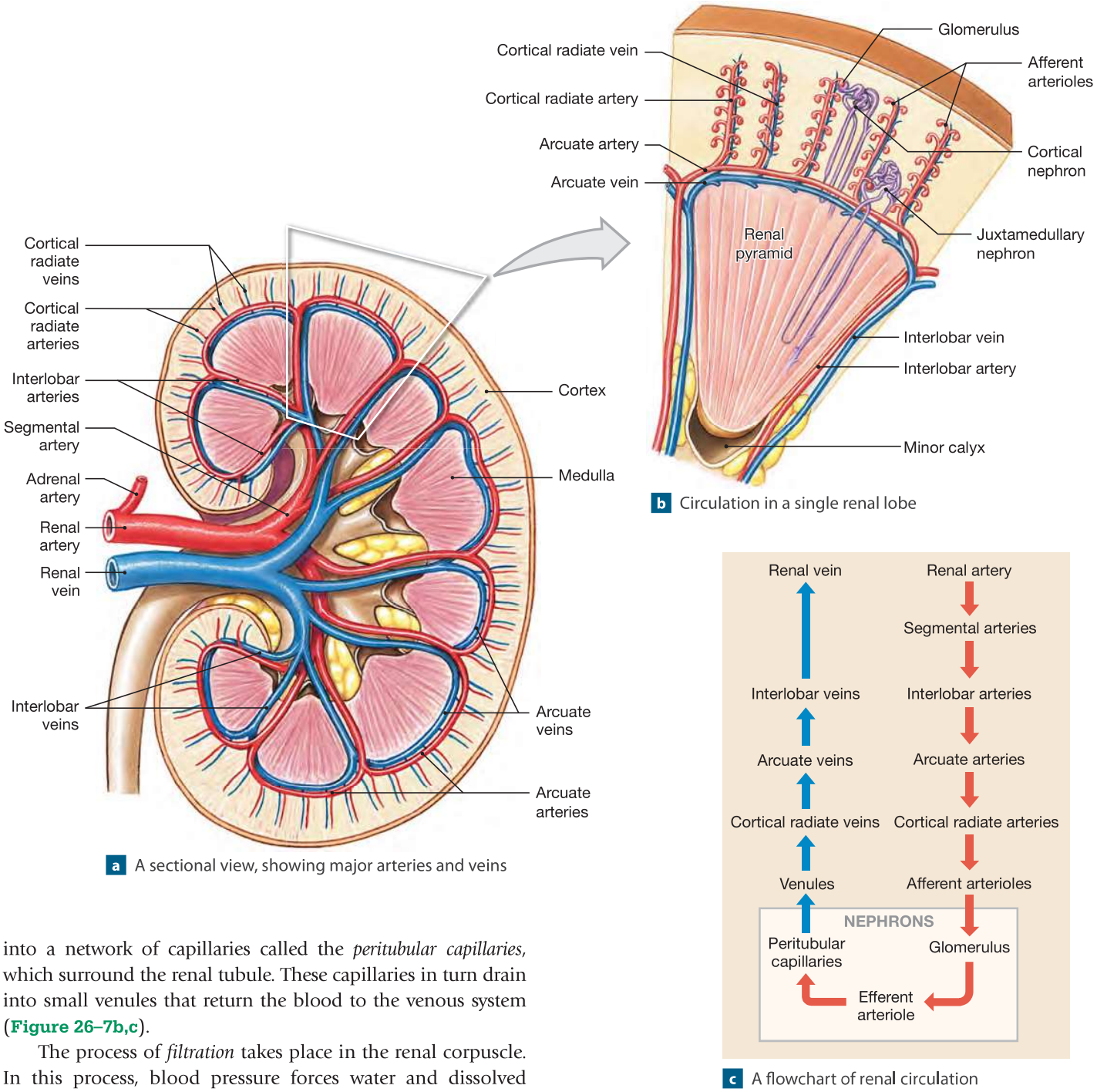
Analysis of Renal Blood Flow The rate of blood flow through the kidneys can be estimated by administering the compound *para-aminohippuric acid (PAH)*, which is removed at the nephrons and eliminated in urine. Virtually all the PAH contained in the blood that arrives at the kidneys is removed before the blood departs in the renal veins. Renal blood flow can thus be approximated by comparing plasma concentrations of PAH with the amount secreted in urine. In practice, however, it is usually easier to measure the glomerular filtration rate (p. 969).

The Nephron

Recall that the kidneys remove waste products from the blood and help to regulate blood volume and blood pressure, ion levels, and blood pH. In the kidneys, the functional units—the smallest structures that can carry out all the functions of a system—are the **nephrons** (NEF-ronz). Each nephron consists of a renal corpuscle and a renal tubule (**Figure 26–6**). The **renal corpuscle** (KOR-pus-ul) is a spherical structure consisting of the *glomerular* (Bowman's) *capsule*, a cup-shaped chamber approximately 200 μm in diameter, and a capillary network known as the *glomerulus*. The **renal tubule** is a long tubular passageway which may be 50 mm (1.97 in.) in length. It begins at the renal corpuscle.

Blood arrives at the renal corpuscle by way of an afferent arteriole. This arteriole delivers blood to the **glomerulus** (glo-MER-ū-lus; plural, *glomeruli*), which consists of about 50 intertwining capillaries. The glomerulus projects into the glomerular capsule much as the heart projects into the pericardial cavity. Blood leaves the glomerulus in an **efferent arteriole.** It flows

Figure 26–5 **The Blood Supply to the Kidneys.** ATLAS: Plates 53c,d; 61a–c



a A sectional view, showing major arteries and veins

b Circulation in a single renal lobe

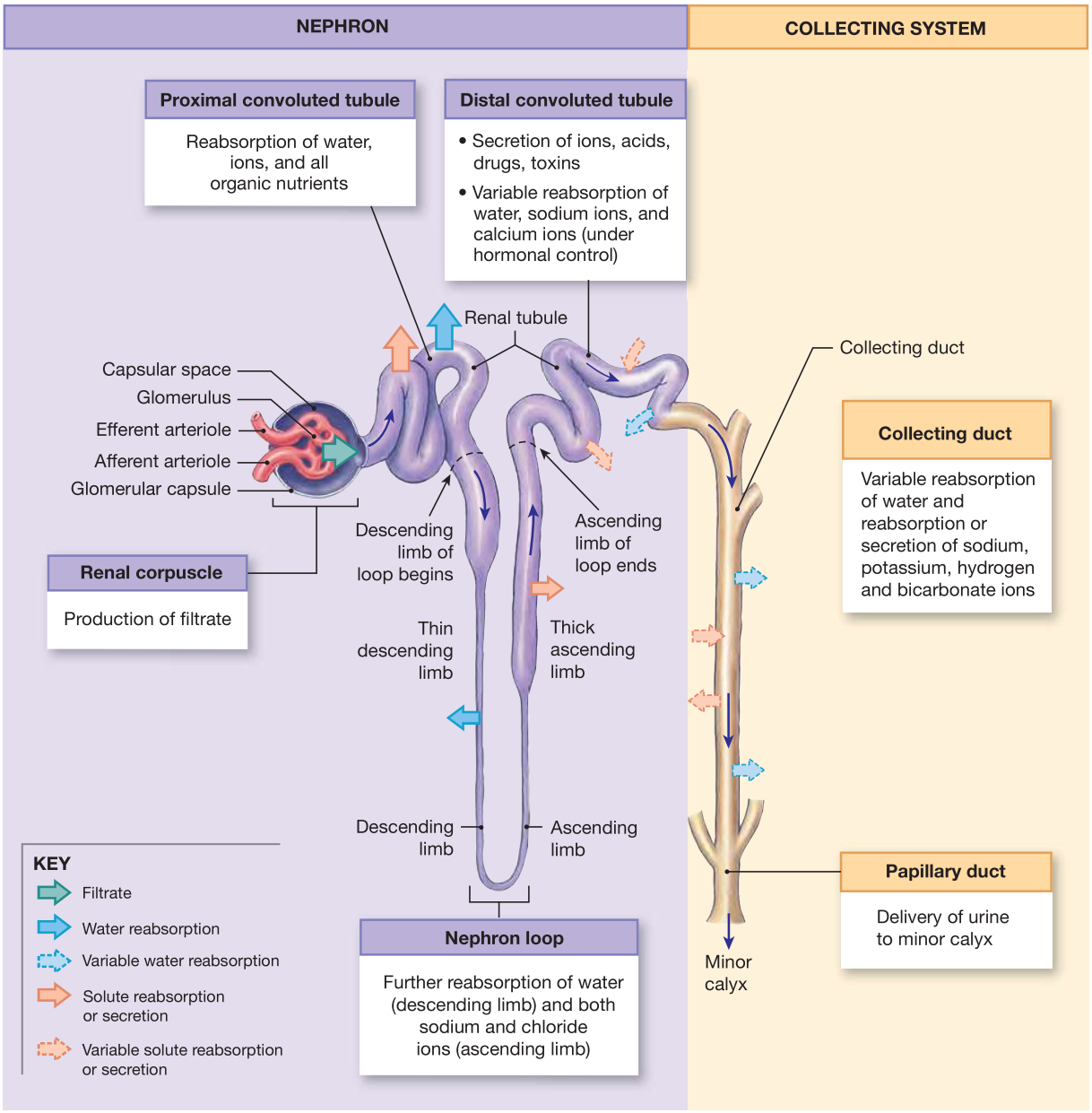
c A flowchart of renal circulation

into a network of capillaries called the *peritubular capillaries*, which surround the renal tubule. These capillaries in turn drain into small venules that return the blood to the venous system (**Figure 26–7b,c**).

The process of *filtration* takes place in the renal corpuscle. In this process, blood pressure forces water and dissolved solutes out of the glomerular capillaries and into a chamber—the *capsular space*—that is continuous with the lumen of the renal tubule (**Figure 26–6**). Filtration produces an essentially protein-free solution, known as a **filtrate,** that is otherwise similar to blood plasma. From the renal corpuscle, filtrate enters the renal tubule, which has three crucial functions: (1) reabsorbing all the useful organic nutrients in the filtrate; (2) reabsorbing more than 90 percent of the water in the filtrate; and (3) secreting into the tubule lumen any waste products that did not pass into the filtrate at the glomerulus.

The renal tubule has two convoluted (coiled or twisted) segments—the *proximal convoluted tubule* (PCT) and the *distal convoluted tubule* (DCT). They are separated by a simple U-shaped tube, the *nephron loop*, also called the *loop of Henle*

Figure 26–6 The Functional Anatomy of a Representative Nephron and the Collecting System. The major functions of each segment of the nephron (purple) and the collecting system (tan) are noted. The nephron has been significantly shortened, and some components rearranged in space, in this representational figure.



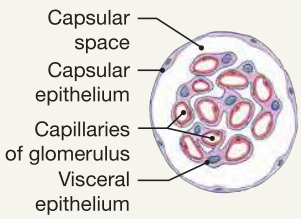
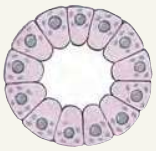
(HEN-lē). The convoluted segments lie in the cortex of the kidney, and the nephron loop dips at least partially into the medulla. For clarity, the nephron shown in **Figure 26–6** has been shortened and straightened.

The regions of the nephron vary by structure and function. As it travels along the tubule, the filtrate, now called **tubular fluid,** gradually changes in composition. The changes that take place and the characteristics of the urine that result are due to the activities under way in each segment of the nephron. **Figure 26–6** and **Table 26–1** survey the regional specializations.

Tips & Tricks

In the nephron, the terms *proximal tubule* and *distal tubule* refer to how far along the renal tubule these structures are situated from the renal corpuscle. Think of *proximal* (nearer the renal corpuscle) as being first, and *distal* (farther from the renal corpuscle) as being last.

Table 26–1 The Organization of the Nephron and Collecting System

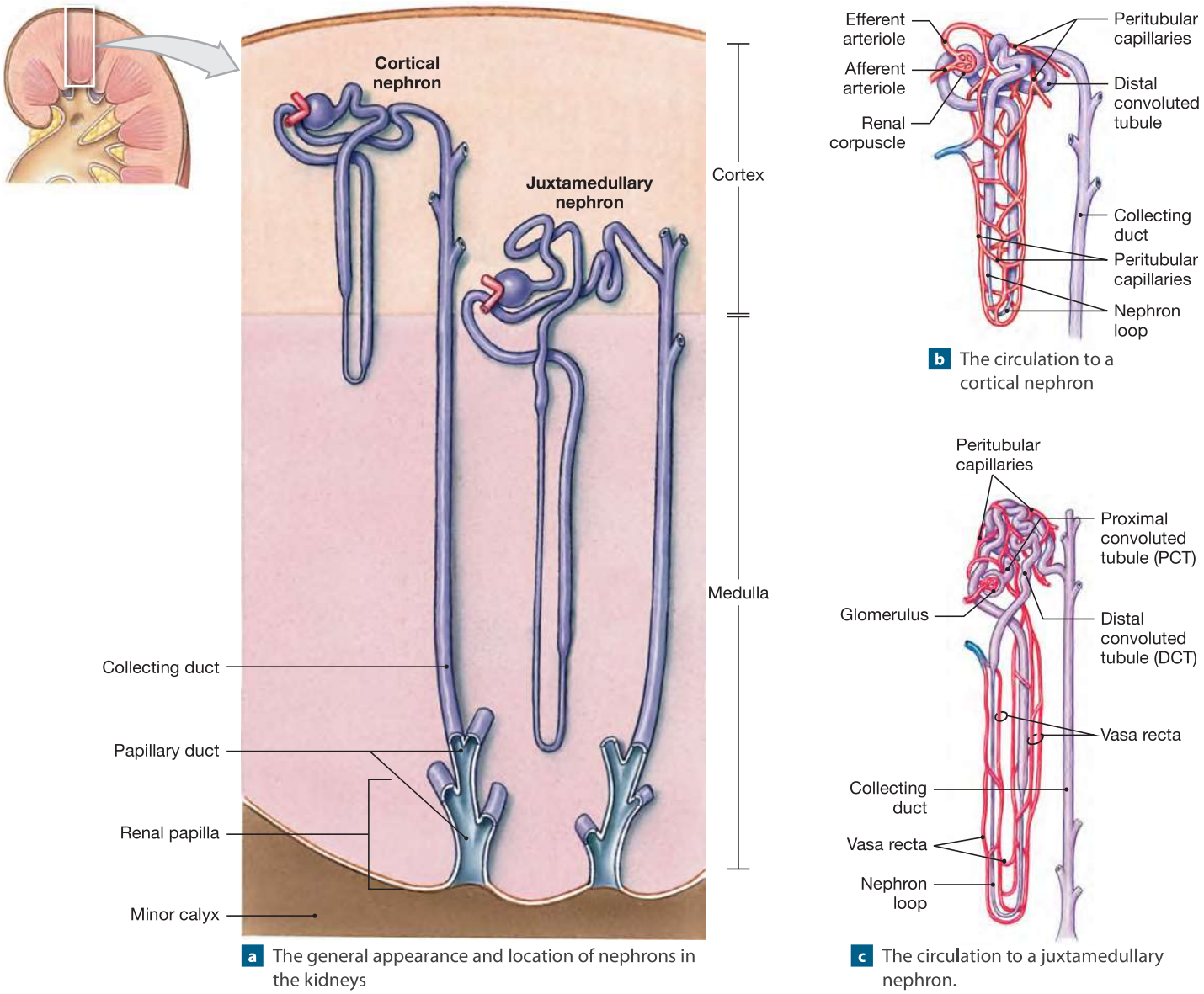
Region	Histological Characteristics	Length	Diameter	Primary Function
NEPHRON				
Renal corpuscle 	Glomerulus (capillary knot), mesangial cells, and dense layer, enclosed by the glomerular capsule; visceral epithelium (podocytes) and capsular epithelium separated by capsular space	150–250 μm (spherical)	150–250 μm	Filtration of plasma
Renal tubule				
Proximal convoluted tubule (PCT) 	Cuboidal cells with microvilli	14 mm	60 μm	Reabsorption of ions, organic molecules, vitamins, water; secretion of drugs, toxins, acids
Nephron loop 	Squamous or low cuboidal cells	30 mm		
			15 μm	Descending limb: reabsorption of water from tubular fluid
			30 μm	Ascending limb: reabsorption of ions; assists in creation of a concentration gradient in the medulla
Distal convoluted tubule (DCT) 	Cuboidal cells with few if any microvilli	5 mm	30–50 μm	Reabsorption of sodium ions and calcium ions; secretion of acids, ammonia, drugs, toxins
COLLECTING SYSTEM				
Collecting duct 	Cuboidal to columnar cells	15 mm	50–100 μm	Reabsorption of water, sodium ions; secretion or reabsorption of bicarbonate ions or hydrogen ions
Papillary duct 	Columnar cells	5 mm	100–200 μm	Conduction of tubular fluid to minor calyx; contributes to concentration gradient of the medulla

Each nephron empties into the **collecting system,** a series of tubes that carry tubular fluid away from the nephron. *Collecting ducts* receive this fluid from many nephrons. Each collecting duct begins in the cortex and descends into the medulla, carrying fluid to a *papillary duct* that drains into a minor calyx.

Nephrons from different locations differ slightly in structure. Roughly 85 percent of all nephrons are **cortical nephrons,** located almost entirely within the superficial cortex of the kidney (**Figure 26–7a,b**). In a cortical nephron, the nephron loop is relatively short, and the efferent arteriole delivers blood to a network of **peritubular capillaries,** which surround the entire renal tubule. These capillaries drain into small venules that carry blood to the cortical radiate veins (**Figure 26–5c**).

The remaining 15 percent of nephrons, termed **juxtamedullary** (juks-tuh-MED-u-lār-ē; *juxta,* near) **nephrons,** have long nephron loops that extend deep into the medulla (**Figure 26–7a,c**). In juxtamedullary nephrons, the peritubular capillaries are connected to the **vasa recta** (*vasa,* vessel + *recta,* straight)—long, straight capillaries that parallel the nephron loop.

Figure 26–7 The Locations and Structures of Cortical and Juxtamedullary Nephrons.



a The general appearance and location of nephrons in the kidneys

b The circulation to a cortical nephron

c The circulation to a juxtamedullary nephron.

Cortical nephrons perform most of the reabsorptive and secretory functions of the kidneys because they are more numerous than juxtamedullary nephrons. However, as you will see later in the chapter, it is the juxtamedullary nephrons that enable the kidneys to produce concentrated urine.

Next let's examine the structure of each segment of a representative nephron.

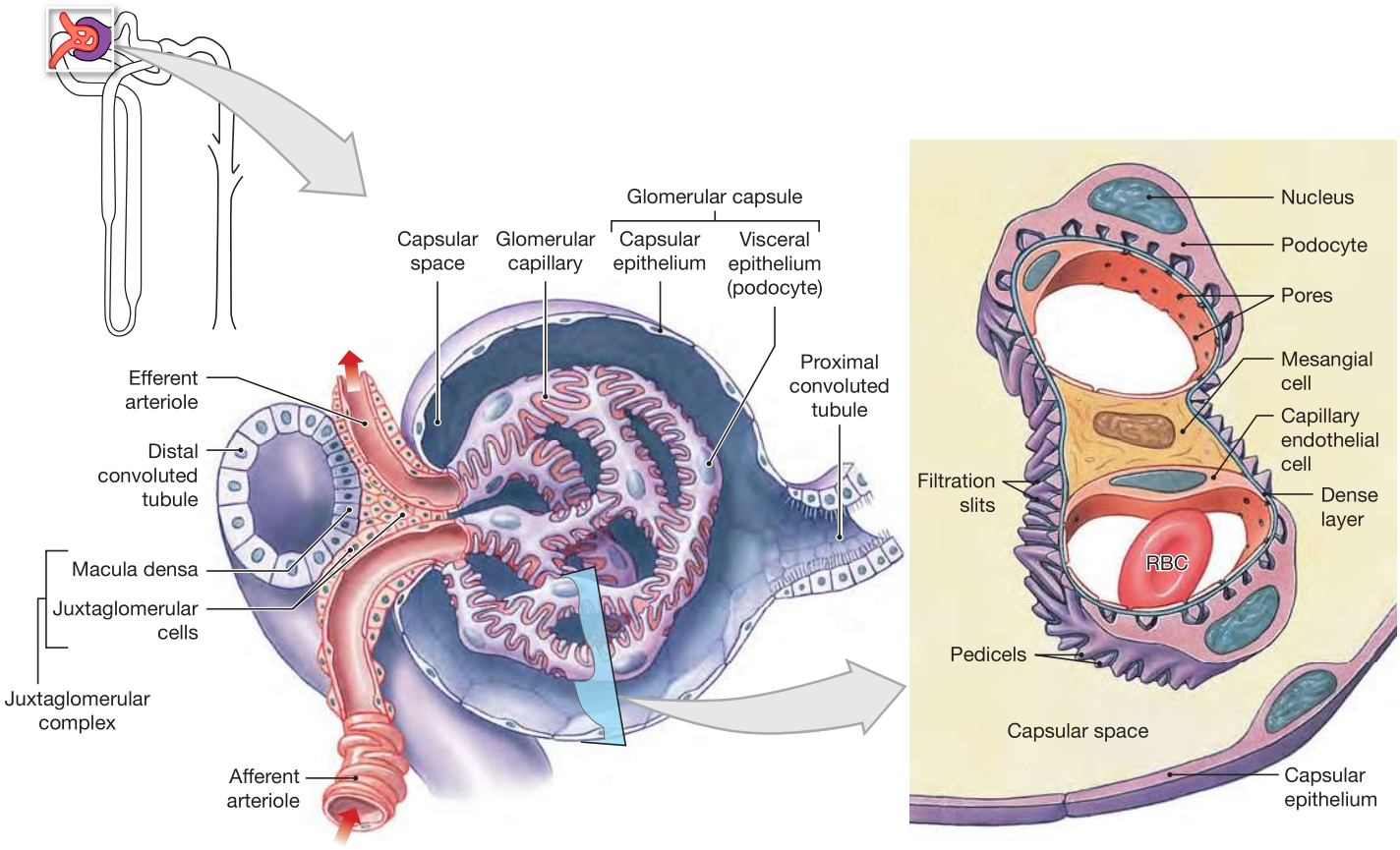
The Renal Corpuscle

Each renal corpuscle (Figure 26–8) is 150–250 μm in diameter. It includes both the **glomerular capsule** and the capillary network of the *glomerulus* (Figure 26–8a). The glomerular capsule is connected to the initial segment of the renal tubule and forms the outer wall of the renal corpuscle. It encapsulates the glomerular capillaries.

The outer wall of the capsule is lined by a simple squamous **capsular epithelium** (Figure 26–8a). This layer is continuous with the **visceral epithelium**, which covers the glomerular capillaries. The **capsular space** separates the capsular and visceral epithelia. The two epithelial layers are continuous where the glomerular capillaries are connected to the afferent arteriole and efferent arteriole.

The visceral epithelium consists of large cells with complex processes, or "feet," that wrap around the specialized *dense layer* of the glomerular capillaries. These unusual cells are called **podocytes** (PŌ-dō-sīts; *podos*, foot + *-cyte*, cell). Their feet are

Figure 26–8 The Renal Corpuscle.



a Important structural features of a renal corpuscle

b This cross section through a segment of the glomerulus shows the components of the filtration membrane of the nephron.

Clinical Note

Glomerulonephritis

Glomerulonephritis (glo-mer-ū-lō-nef-RĪ-tis) is an inflammation of the glomeruli that affects filtration in the kidneys. The condition is often an *immune complex disorder*, which may develop after an infection involving *Streptococcus* bacteria. ↩ p. 801 The kidneys are not the sites of infection, but as the immune system responds, the number of circulating antigen–antibody complexes skyrockets. These complexes are small enough to pass through the dense layer, but too large to fit through the filtration slits of the filtration membrane. The complexes clog up the filtration mechanism, and filtrate production drops. Any condition that leads to a massive immune response, including viral infections and autoimmune disorders, can cause glomerulonephritis.

known as **pedicels** (**Figure 26–8b**). Materials passing out of the blood at the glomerulus must be small enough to pass between the narrow gaps, called **filtration slits,** between adjacent pedicels.

Mesangial cells are special supporting cells that lie between adjacent capillaries. Actin-like filaments in these cells enable them to contract. In this way these cells control capillary diameter and the rate of capillary blood flow. Several substances, including angiotensin II, vasopressin, and histamine, affect mesangial cell contraction. ↩ p. 625 Some evidence suggests that these cells also make renin.

The glomerular capillaries are fenestrated capillaries. That is, their endothelium contains large-diameter pores (**Figure 26–8b**). The dense layer differs from that found in the basement membrane of other capillary networks in that it may encircle more than one capillary.

Together, the fenestrated endothelium, the dense layer, and the filtration slits form the *filtration membrane*. During filtration, blood pressure forces water and small solutes across this membrane and into the capsular space. The larger solutes, especially plasma proteins, do not pass through.

Filtration at the renal corpuscle is both effective and passive, but it has one major drawback: In addition to metabolic wastes and excess ions, useful compounds such as glucose, free fatty acids, amino acids, vitamins, and other solutes also enter the capsular space. These substances are recaptured before filtrate leaves the kidneys. Much of this reabsorption takes place in the proximal convoluted tubule.

The Proximal Convoluted Tubule

Recall that the renal tubule consists of three segments: the proximal convoluted tubule, the nephron loop, and the distal convoluted tubule. The **proximal convoluted tubule (PCT)** is the first segment (**Figure 26–6**). Its entrance lies almost directly opposite the point where the afferent and efferent arterioles connect to the glomerulus. The lining of the PCT is a simple cuboidal epithelium whose apical surfaces have microvilli (**Table 26–1**). The tubular cells reabsorb organic nutrients, ions, water, and plasma proteins (if present) from the tubular fluid and release them into the **peritubular fluid,** the interstitial fluid surrounding the renal tubule. The reabsorbed substances in the peritubular fluid eventually reenter the blood. *Reabsorption* is the primary function of the PCT, but the epithelial cells can also secrete substances into the lumen of the renal tubule.

The Nephron Loop (Loop of Henle)

The PCT makes an acute bend that turns the renal tubule toward the renal medulla. This turn leads to the **nephron loop,** or *loop of Henle* (**Figure 26–7**). We can divide the nephron loop into a **descending limb** and an **ascending limb.** Fluid in the descending limb flows toward the renal pelvis. Fluid in the ascending limb flows toward the renal cortex. Each limb contains a **thick segment** and a **thin segment.** The terms *thick* and *thin* refer to the height of the epithelium, not to the diameter of the lumen: Thick segments have a cuboidal epithelium. A squamous epithelium lines the thin segments (**Table 26–1**).

The thick descending limb has functions similar to those of the PCT: It pumps sodium and chloride ions out of the tubular fluid. The effect of this pumping is most noticeable in the medulla, where the long ascending limbs of juxtamedullary nephrons create unusually high solute concentrations in peritubular fluid. The thin segments are freely permeable to water, but not to solutes. Water moves out of these segments, helping to concentrate the tubular fluid.

The Distal Convoluted Tubule

The thick ascending limb of the nephron loop ends where it forms a sharp angle near the renal corpuscle. The **distal convoluted tubule (DCT),** the third segment of the renal tubule, begins there. The initial portion of the DCT passes between the afferent and efferent arterioles (**Figure 26–8a**).

In sectional view, the DCT differs from the PCT in that the DCT has a smaller diameter and its epithelial cells lack microvilli (**Table 26–1**). The DCT is an important site for three vital processes: (1) the active secretion of ions, acids, drugs, and toxins into the tubule; (2) the selective reabsorption of sodium ions and calcium ions from tubular fluid; and (3) the selective reabsorption of water, which assists in concentrating the tubular fluid.

The Juxtaglomerular Complex. The epithelial cells of the DCT near the renal corpuscle are taller than those elsewhere along the DCT, and their nuclei are clustered together. This region is called the **macula densa** (MAK-ū-la DEN-sa) (**Figure 26–8a**). The cells of the macula densa are closely associated with unusual smooth muscle fibers in the wall of the afferent arteriole. These fibers are known as **juxtaglomerular cells.** Together, the macula densa and juxtaglomerular cells form the **juxtaglomerular complex (JGC),** an endocrine structure that secretes the hormone *erythropoietin* and the enzyme *renin*. ↩ p. 624

The Collecting System

The distal convoluted tubule, the last segment of the nephron, opens into the collecting system (**Figure 26–6**). Individual nephrons drain into a nearby **collecting duct.** Several collecting ducts then converge into a larger **papillary duct,** which in turn empties into a minor calyx. The epithelium lining the collecting system is typically columnar (**Table 26–1**).

The collecting system does more than simply transport tubular fluid from the nephrons to the renal pelvis. It also adjusts the fluid's composition and determines the final osmotic concentration and volume of urine, the final product. We consider these activities of the collecting system later in the chapter.

Checkpoint

4. **Which portions of the nephron are in the renal cortex?**
5. **Why don't plasma proteins pass into the capsular space under normal circumstances?**
6. **Damage to which part of the nephron would interfere with the hormonal control of blood pressure?**

See the blue Answers tab at the back of the book.

26-3 Different segments of the nephron form urine by filtration, reabsorption, and secretion

Most people don't commonly think of it this way, but the goal of urine production is to maintain homeostasis by regulating

the volume and composition of blood. This process involves the excretion of solutes—specifically, metabolic waste products. Our bodies form three important organic waste products:

1. *Urea.* Urea is the most abundant organic waste. You generate approximately 21 g of urea each day, most of it through the breakdown of amino acids.
2. *Creatinine.* Skeletal muscle tissue generates creatinine through the breakdown of *creatine phosphate*, a high-energy compound that plays an important role in muscle contraction. ↩ p. 305 Your body generates roughly 1.8 g of creatinine each day. Virtually all of it is excreted in urine.
3. *Uric Acid.* **Uric acid** is a waste product formed during the recycling of the nitrogenous bases from RNA molecules. You produce approximately 480 mg of uric acid each day.

These waste products are dissolved in the bloodstream. They can be eliminated only when dissolved in urine. For this reason, their removal involves an unavoidable water loss. The kidneys are usually capable of producing concentrated urine with an osmotic concentration of 1200–1400 mOsm/L, more than four times that of plasma. (We discuss methods of reporting solute concentrations in a later section.) If the kidneys were unable to concentrate the filtrate produced by glomerular filtration, fluid losses would lead to fatal dehydration in a matter of hours. The kidneys also ensure that the fluid that *is* lost does not contain potentially useful organic substrates that are present in blood plasma, such as sugars or amino acids. These valuable materials must be reabsorbed and retained for use by other tissues.

Basic Processes of Urine Formation

In forming urine, the kidneys use three distinct processes that we have already mentioned:

1. *Filtration.* In **filtration,** blood pressure forces water and solutes across the wall of the glomerular capillaries and into the capsular space. Solute molecules small enough to pass through the filtration membrane are carried by the surrounding water molecules.
2. *Reabsorption.* **Reabsorption** is the removal of water and solutes from the filtrate, and their movement across the tubular epithelium and into the peritubular fluid. Reabsorption takes place after filtrate has left the renal corpuscle. Most of the reabsorbed materials are nutrients the body can use. Filtration takes place solely based on size, but reabsorption is a selective process. Reabsorption involves either simple diffusion or the activity of carrier proteins in the tubular epithelium. The reabsorbed substances in the peritubular fluid eventually reenter the blood. Water reabsorption takes place passively, through osmosis.
3. *Secretion.* **Secretion** is the transport of solutes from the peritubular fluid, across the tubular epithelium, and into the tubular fluid. Secretion is necessary because filtration does not force all the dissolved materials out of the plasma. Tubular secretion, which removes substances from the blood, can further lower the plasma concentration of undesirable materials. It provides a backup process for filtration. Secretion is often the primary method of preparing compounds, including many drugs, for excretion.

Together, these processes produce a fluid that is very different from other body fluids. **Table 26–2** shows the efficiency of the renal system by comparing the concentrations of some substances in urine and plasma.

Tips & Tricks

Secretion by the urinary system takes place when cells produce and then discharge substances into the urine, whereas *excretion* is the elimination of wastes from the body in the form of urine, sweat, and feces.

An Overview of Renal Function

Figure 26–9 summarizes the general functions of the various segments of the nephron and collecting system in the formation of urine. Most regions carry out a combination of reabsorption and secretion. Note that the balance between the two processes shifts from one region to another.

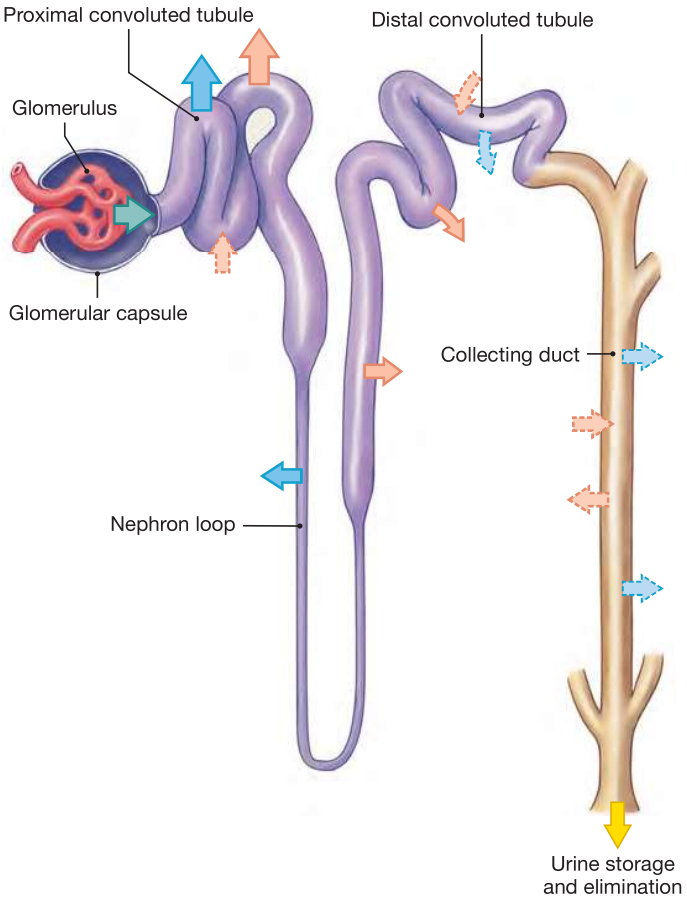
Normal kidney function can continue only as long as filtration, reabsorption, and secretion function within relatively narrow limits. A disruption in kidney function has immediate effects on the composition of the circulating blood. If both kidneys are affected, death follows within a few days unless medical assistance is provided.

Before we take a closer look at the functions of the individual portions of the nephron, let's briefly examine each of the three major processes involved in urine formation.

Table 26–2 Normal Laboratory Values for Solutes in Plasma and Urine

Solute	Plasma	Urine
IONS (mEq/L)		
Sodium (Na^+)	135–145	40–220
Potassium (K^+)	3.5–5.0	25–100
Chloride (Cl^-)	100–108	110–250
Bicarbonate (HCO_3^-)	20–28	1–9
METABOLITES AND NUTRIENTS (mg/dL)		
Glucose	70–110	0.009
Lipids	450–1000	0.002
Amino acids	40	0.188
Proteins	6000–8000	0.000
NITROGENOUS WASTES (mg/dL)		
Urea	8–25	1800
Creatinine	0.6–1.5	150
Ammonia	<0.1	60
Uric acid	2–6	40

Figure 26–9 An Overview of Urine Formation.



Filtration

In filtration, hydrostatic pressure forces water through membrane pores, and solute molecules small enough to pass through those pores are carried along. Filtration takes place as larger solutes and suspended materials are left behind. We can see filtration in action in a drip coffee machine. Gravity forces hot water through the filter, and the water carries a variety of dissolved compounds into the pot. The large coffee grounds never reach the pot, because they cannot fit through the pores of the filter. In other words, they are "filtered out" of the solution; the coffee we drink is the filtrate.

In the body, the heart pushes blood around the cardiovascular system and generates hydrostatic pressure. As you have seen, filtration takes place across the walls of capillaries as water and dissolved materials are pushed into the interstitial fluids of the body (see **Figure 21–12**, p. 723). In some sites (for example, the liver), the pores are so large that even plasma proteins can enter the interstitial fluids. At the renal corpuscle, however, the specialized filtration membrane restricts the passage of even the smallest circulating proteins.

Reabsorption and Secretion

The processes of reabsorption and secretion at the kidneys involve a combination of diffusion, osmosis, channel-mediated diffusion, and carrier-mediated transport. We considered diffusion and osmosis in several other chapters. Here we briefly review carrier-mediated transport mechanisms.

Types of Carrier-Mediated Transport. In previous chapters, we looked at four major types of *carrier-mediated transport:*

- In *facilitated diffusion,* a carrier protein transports a molecule across the plasma membrane without expending energy (see **Figure 3–18**, p. 91). Such transport always follows the concentration gradient for the ion or molecule transported.
- *Active transport* is driven by the hydrolysis of ATP to ADP on the inner membrane surface (see **Figure 3–19**, p. 92). Exchange pumps and other carrier proteins are active along the kidney tubules. Active transport can operate despite an opposing concentration gradient.
- In *cotransport,* carrier protein activity is not directly linked to the hydrolysis of ATP (see **Figure 3–20**, p. 93). Instead, two substrates (ions, molecules, or both) cross the membrane while bound to the carrier protein. The movement of the substrates always follows the concentration gradient of at least one of the transported substances. Cotransport is used for the reabsorption of organic and inorganic compounds from the tubular fluid.
- *Countertransport* resembles cotransport, except that the two transported ions move in *opposite* directions (see **Figures 23–24**, p. 847, and **24–14**, p. 881). Countertransport operates in the PCT, DCT, and collecting system.

Characteristics of Carrier-Mediated Transport. All carrier-mediated processes share five features that are important for an understanding of kidney function:

1. *A specific substrate binds to a carrier protein that facilitates movement across the membrane.*
2. *A given carrier protein typically works in one direction only.* In facilitated diffusion, the concentration gradient of the substance being transported determines that direction. In active

transport, cotransport, and countertransport, the location and orientation of the carrier proteins determine whether a particular substance is reabsorbed or secreted. The carrier protein that transports amino acids from the tubular fluid to the cytoplasm, for example, will not carry amino acids back into the tubular fluid.

3. *The distribution of carrier proteins can vary among portions of the cell surface.* Transport between tubular fluid and interstitial fluid involves two steps. First, the material enters the cell at its apical surface. Then the material leaves the cell at its basolateral surface and enters the peritubular fluid. Each step involves a different carrier protein. For example, the apical surfaces of cells along the proximal convoluted tubule contain carrier proteins that bring amino acids, glucose, and many other nutrients into these cells by sodium-linked cotransport. In contrast, the basolateral surfaces contain carrier proteins that move those nutrients out of the cell by facilitated diffusion.
4. *The membrane of a single tubular cell contains many types of carrier proteins.* Each cell can have multiple functions. A cell that reabsorbs one compound can secrete another.
5. *Carrier proteins, like enzymes, can be saturated.* Recall that when an enzyme is *saturated*, further increases in substrate concentration have no effect on the rate of reaction. ↩ p. 53 Likewise, when a carrier protein is saturated, further increases in substrate concentration have no effect on the rate of transport across the plasma membrane. For any substance, the concentration at saturation is called the **transport maximum (T_m)** or *tubular maximum*. In healthy individuals, carrier proteins involved in tubular secretion seldom become saturated. However, carriers involved in tubular reabsorption are often at risk of saturation, especially during the absorptive state following a meal.

T_m and the Renal Threshold. Normally, any plasma proteins and nutrients, such as amino acids and glucose, are removed from the tubular fluid by cotransport or facilitated diffusion. If the concentrations of these nutrients rise in the tubular fluid, the rates of reabsorption increase until the carrier proteins are saturated. A concentration higher than the transport maximum exceeds the reabsorptive abilities of the nephron. In this case, some of the material will remain in the tubular fluid and appear in the urine. The transport maximum thus determines the **renal threshold**—the plasma concentration at which a specific compound or ion begins to appear in the urine.

The renal threshold varies with the substance involved. The renal threshold for glucose is approximately 180 mg/dL. When plasma glucose concentrations exceed 180 mg/dL glucose appears in urine; this condition is called *glycosuria*. After you have eaten a meal rich in carbohydrates, your plasma glucose levels may exceed the T_m for a brief period. The liver quickly lowers circulating glucose levels, and very little glucose is lost in your urine. However, chronically elevated plasma and urinary glucose concentrations are highly abnormal. (Glycosuria is one of the key signs of diabetes mellitus. ↩ p. 623)

The renal threshold for amino acids is lower than that for glucose. Amino acids appear in urine when plasma concentrations exceed 65 mg/dL. Plasma amino acid levels commonly exceed the renal threshold after you have eaten a protein-rich meal, causing some amino acids to appear in your urine. This condition is termed **aminoaciduria** (am-i-nō-as-i-DOO-rē-uh).

T_m values for water-soluble vitamins are relatively low. As a result, you excrete excess quantities of these vitamins in urine. (This is typically the fate of water-soluble vitamins in daily supplements.) Cells of the renal tubule ignore a number of other compounds in the tubular fluid. As water and other compounds are removed, the concentrations of the ignored materials in the tubular fluid gradually rise. **Table 26–3** lists some substances that are actively reabsorbed or secreted by the renal tubules, as well as several that are not transported at all.

Ways of Expressing Osmotic Concentration. The osmotic concentration, or *osmolarity*, of a solution is the total number of solute particles in each liter. ↩ p. 89 We usually express osmolarity in **osmoles** per liter (Osm/L) or **milliosmoles** per liter (mOsm/L). If each liter of a fluid contains 1 mole of dissolved particles, the solute concentration is 1 Osm/L, or 1000 mOsm/L. Body fluids have an osmotic concentration of about 300 mOsm/L. In comparison, that of seawater is about 1000 mOsm/L. That of fresh water is about 5 mOsm/L.

Ion concentrations are often reported in *milliequivalents* per liter (mEq/L). Milliequivalents indicate the number of positive or negative charges in solution, rather than the number of solutes; multiply mmol/L by the charges on each ion to get mEq/L. For example, each sodium ion bears one charge only, so

Table 26–3 Tubular Reabsorption and Secretion

Reabsorbed	Secreted	No Transport Mechanism
Ions	**Ions**	Urea
Na^+, Cl^-, K^+	K^+, H^+, Ca^{2+},	Water
Ca^{2+}, Mg^{2+},	PO_4^{3-}	Urobilinogen
SO_4^{2-}, HCO_3^-		Bilirubin
	Wastes	
	Creatinine	
Metabolites	Ammonia	
Glucose	Organic acids and bases	
Amino acids		
Proteins		
Vitamins	**Miscellaneous**	
	Neurotransmitters (ACh, NE, E, dopamine)	
	Histamine	
	Drugs (penicillin, atropine, morphine, many others)	

for Na^+, 1 mmol/L = 1 mEq/L; for Ca^{2+}, each ion bears two charges, so 1 mmol/L = 2 mEq/L. The concentrations of large organic molecules are usually reported in grams, milligrams, or micrograms per unit volume of solution (typically, per dL).

Cortical and Juxtamedullary Nephrons. In the next sections, we proceed along the nephron to consider the formation of filtrate and the changes in the composition and concentration of the filtrate as it passes along the renal tubule. Most of what follows applies equally to cortical and juxtamedullary nephrons. The functions of the renal corpuscle and of the proximal and distal convoluted tubules are the same in all nephrons. The major difference between the two types of nephron is that the nephron loop of a cortical nephron is shorter. Note that it does not extend as far into the medulla as does the nephron loop of a juxtamedullary nephron (**Figure 26–7a**).

The long nephron loop in a juxtamedullary nephron extends deep into the renal pyramids. There it plays a key role in water conservation and the formation of concentrated urine. This process is vitally important, affecting the tubular fluid produced by every nephron in the kidney. For this reason, we use a juxtamedullary nephron as our example. **Table 26–4** summarizes the functions of the various parts of the nephron.

Checkpoint

7. **Identify the three distinct processes of urine formation in the kidney.**
8. **What occurs when the plasma concentration of a substance exceeds its tubular maximum?**

See the blue Answers tab at the back of the book.

Table 26–4 Renal Structures and Their Function

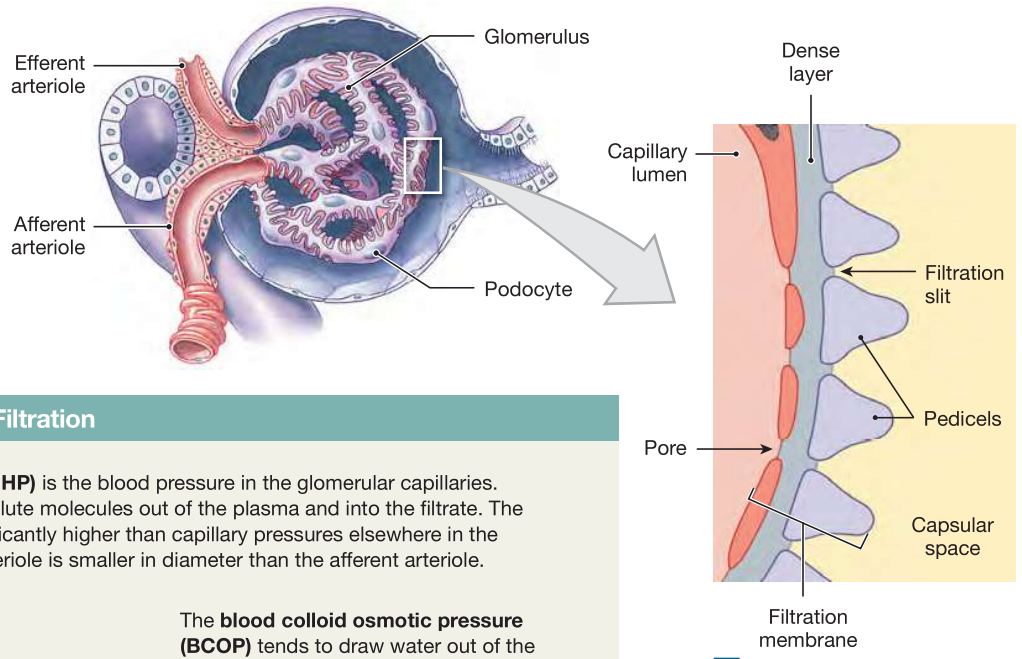
Segment	General Functions	Specific Functions	Mechanisms
Renal corpuscle	*Filtration* of plasma; generates approximately 180 L/day of filtrate similar in composition to blood plasma without plasma proteins	*Filtration* of water, inorganic and organic solutes from plasma; retention of plasma proteins and blood cells	Glomerular hydrostatic (blood) pressure working across capillary endothelium, dense layer, and filtration slits
Proximal convoluted tubule (PCT)	*Reabsorption* of 60%–70% of the water (108–116 L/day), 99%–100% of the organic substrates, and 60%–70% of the sodium and chloride ions in the original filtrate	*Active reabsorption*: Glucose, other simple sugars, amino acids, vitamins, ions (including sodium, potassium, calcium, magnesium, phosphate, and bicarbonate)	Carrier-mediated transport, including facilitated transport (glucose, amino acids), cotransport (glucose, ions), and countertransport (with secretion of H^+)
		Passive reabsorption: Urea, chloride ions, lipid-soluble materials, water	Diffusion (solutes) or osmosis (water)
		Secretion: Hydrogen ions, ammonium ions, creatinine, drugs, and toxins (as at DCT)	Countertransport with sodium ions
Nephron loop	*Reabsorption* of 25% of the water (45 L/day) and 20%–25% of the sodium and chloride ions present in the original filtrate; creation of the concentration gradient in the medulla	*Reabsorption*: Sodium and chloride ions	Active transport via Na^+–K^+/2 Cl^- transporter
		Water	Osmosis
Distal convoluted tubule (DCT)	*Reabsorption* of a variable amount of water (usually 5%, or 9 L/day), under ADH stimulation, and a variable amount of sodium ions, under aldosterone stimulation	*Reabsorption*: Sodium and chloride ions	Cotransport
		Sodium ions (variable)	Countertransport with potassium ions; aldosterone-regulated
		Calcium ions (variable)	Carrier-mediated transport stimulated by parathyroid hormone and calcitriol
		Water (variable)	Osmosis; ADH regulated
		Secretion: Hydrogen ions, ammonium ions	Countertransport with sodium ions
		Creatinine, drugs, toxins	Carrier-mediated transport
Collecting system	*Reabsorption* of a variable amount of water (usually 9.3%, or 16.8 L/day) under ADH stimulation, and a variable amount of sodium ions, under aldosterone stimulation	*Reabsorption*: Sodium ions (variable)	Countertransport with potassium or hydrogen ions; aldosterone-regulated
		Bicarbonate ions (variable)	Diffusion, generated within tubular cells
		Water (variable)	Osmosis; ADH-regulated
		Urea (distal portions only)	Diffusion
		Secretion: Potassium and hydrogen ions (variable)	Carrier-mediated transport
Peritubular capillaries	*Redistribution* of water and solutes reabsorbed in the cortex	Return of water and solutes to the general circulation	Osmosis and diffusion
Vasa recta	*Redistribution* of water and solutes reabsorbed in the medulla and stabilization of the concentration gradient of the medulla	Return of water and solutes to the general circulation	Osmosis and diffusion

26-4 Hydrostatic and colloid osmotic pressures influence glomerular filtration pressure, which in turn affects the glomerular filtration rate

Filtration takes place in the renal corpuscle as fluids move across the wall of the glomerulus and into the capsular space. The process of **glomerular filtration** involves passage across a filtration membrane. Recall that this membrane has three components: (1) the capillary endothelium, (2) the dense layer, and (3) the filtration slits (**Figures 26–8b** and **26–10**).

Glomerular capillaries are fenestrated capillaries with pores ranging from 60 to 100 nm (0.06 to 0.1 μm) in diameter. These openings are small enough to prevent the passage of blood cells, but they are too large to restrict the diffusion of solutes, even those the size of plasma proteins. The dense layer

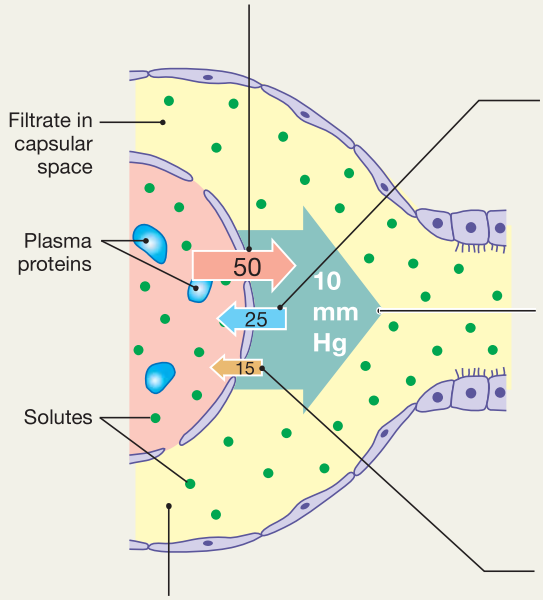
Figure 26–10 Glomerular Filtration.



a The glomerular filtration membrane

Factors Controlling Glomerular Filtration

The **glomerular hydrostatic pressure (GHP)** is the blood pressure in the glomerular capillaries. This pressure tends to push water and solute molecules out of the plasma and into the filtrate. The GHP, which averages 50 mm Hg, is significantly higher than capillary pressures elsewhere in the systemic circuit, because the efferent arteriole is smaller in diameter than the afferent arteriole.



The **capsular colloid osmotic pressure** is usually 0 because few, if any, plasma proteins enter the capsular space.

The **blood colloid osmotic pressure (BCOP)** tends to draw water out of the filtrate and into the plasma; it thus opposes filtration. Over the entire length of the glomerular capillary bed, the BCOP averages about 25 mm Hg.

The **net filtration pressure (NFP)** is the net pressure acting across the glomerular capillaries. It represents the sum of the hydrostatic pressures and the colloid osmotic pressures. Under normal circumstances, the net filtration pressure is approximately 10 mm Hg. This is the average pressure forcing water and dissolved materials out of the glomerular capillaries and into the capsular space.

Capsular hydrostatic pressure (CsHP) opposes GHP. CsHP, which tends to push water and solutes out of the filtrate and into the plasma, results from the resistance of filtrate already present in the nephron that must be pushed toward the renal pelvis. The difference between GHP and CsHP is the *net hydrostatic pressure (NHP)*.

b Net filtration pressure

is more selective: Only small plasma proteins, nutrients, and ions can cross it. The filtration slits are the finest filters of all. Their gaps are only 6–9 nm wide. These gaps are small enough to prevent the passage of most small plasma proteins. As a result, under normal circumstances only a few plasma proteins—such as albumin molecules, with an average diameter of 7 nm—can cross the filtration membrane and enter the capsular space. However, plasma proteins are all that stay behind, so the filtrate contains dissolved ions and small organic molecules in roughly the same concentrations as in plasma.

Filtration Pressures

We discussed the major forces that act across capillary walls in Chapters 21 and 22. (You may find it helpful to review **Figures 21–12** and **21–13**, pp. 723, 724, before you proceed.) The primary factor involved in glomerular filtration is basically the same one that governs fluid and solute movement across capillaries throughout the body. This factor is the balance between *hydrostatic pressure*, or fluid pressure, and *colloid osmotic pressure*, or pressure due to materials in solution, on either side of the capillary walls.

Hydrostatic Pressure

Blood pressure is low in typical systemic capillaries. The reason is that capillary blood flows into the venous system, where resistance is fairly low. However, at the glomerulus, blood leaving the glomerular capillaries flows into an efferent arteriole, whose diameter is *smaller* than that of the afferent arteriole. For this reason, the efferent arteriole offers considerable resistance. Relatively high pressures are needed to force blood into it. As a result, glomerular pressures are similar to those of small arteries. These pressures average about 50 mm Hg, instead of the 35 mm Hg typical of peripheral capillaries. Glomerular hydrostatic pressure (GHP), capsular hydrostatic pressure (CsHP), blood colloid osmotic pressure (BCOP), and net filtration pressure (NFP) are shown in **Figure 26–10**.

Capsular hydrostatic pressure (CsHP) opposes glomerular hydrostatic pressure. This pressure results from the resistance to flow along the nephron and the conducting system. (Before additional filtrate can enter the capsule, some of the filtrate already present must be forced into the PCT.) The CsHP averages about 15 mm Hg.

The *net hydrostatic pressure (NHP)* is the difference between the glomerular hydrostatic pressure, which tends to push water and solutes out of the bloodstream, and the capsular hydrostatic pressure, which tends to push water and solutes into the bloodstream. We can calculate net hydrostatic pressure as follows:

$$\text{NHP} = (\text{GHP} - \text{CsHP}) = (50 \text{ mm Hg} - 15 \text{ mm Hg}) = 35 \text{ mm Hg}$$

Colloid Osmotic Pressure

The *colloid osmotic pressure* of a solution is the osmotic pressure resulting from suspended proteins. Under normal conditions, very few plasma proteins enter the capsular space, so no opposing colloid osmotic pressure exists within the capsule. However, if the glomeruli are damaged by disease or injury, and plasma proteins begin passing into the capsular space, a *capsular colloid osmotic pressure* is created that promotes filtration and increases fluid losses in urine.

Net Filtration Pressure

The net filtration pressure (NFP) at the glomerulus is the difference between the net hydrostatic pressure and the blood colloid osmotic pressure acting across the glomerular capillaries. Under normal circumstances, we can summarize this relationship as

$$\text{NFP} = \text{NHP} - \text{BCOP}$$

or

$$\text{NFP} = 35 \text{ mm Hg} - 25 \text{ mm Hg} = 10 \text{ mm Hg}$$

This is the average pressure forcing water and dissolved materials out of the glomerular capillaries and into the capsular spaces (**Figure 26–10b**). Problems that affect the net filtration pressure can seriously disrupt kidney function and cause a variety of clinical signs and symptoms.

The Glomerular Filtration Rate

The **glomerular filtration rate (GFR)** is the amount of filtrate the kidneys produce each minute. Each kidney contains about 6 m^2—some 64 square feet—of filtration surface, and the GFR averages an astounding *125 mL per minute*. This means that roughly 10 percent of the fluid delivered to the kidneys by the renal arteries leaves the bloodstream and enters the capsular spaces.

A *creatinine clearance test* is often used to estimate the GFR. Creatinine results from the breakdown of creatine phosphate in muscle tissue and is normally eliminated in urine. Creatinine enters the filtrate at the glomerulus and is not reabsorbed in significant amounts. By monitoring the creatinine concentrations in blood and the amount excreted in urine in a 24-hour period, a clinician can easily estimate the GFR.

Consider, for example, a person who eliminates 84 mg of creatinine each hour and has a plasma creatinine concentration of 1.4 mg/dL. The GFR is equal to the amount secreted divided by the plasma concentration, so this person's GFR is

$$\frac{84 \text{ mg/h}}{1.4 \text{ mg/dL}} = 60 \text{ dL/h} = 100 \text{ mL/min}.$$

The GFR is usually reported in milliliters per minute.

The value 100 mL/min is only an approximation of the GFR. The reason is that up to 15 percent of creatinine in the

urine enters by means of active tubular secretion. When necessary, a more accurate GFR can be obtained by using the complex carbohydrate *inulin*. This compound is not metabolized in the body and is neither reabsorbed nor secreted by the kidney tubules.

In the course of a single day, the glomeruli generate about 180 liters (48 gal) of filtrate, roughly 70 times the total plasma volume. But as filtrate passes through the renal tubules, about 99 percent of it is reabsorbed. You should now appreciate the significance of tubular reabsorption!

The glomerular filtration rate depends on the net filtration pressure across glomerular capillaries. Any factor that alters the net filtration pressure also alters the GFR and affects kidney function. One of the most significant factors is a drop in renal blood pressure. If blood pressure at the glomeruli drops by 20 percent (from 50 mm Hg to 40 mm Hg), kidney filtration ceases, because the net filtration pressure is 0 mm Hg. For this reason, the kidneys are sensitive to changes in blood pressure that have little or no effect on other organs. Hemorrhaging, shock, and dehydration are relatively common clinical conditions that can cause a dangerous decline in the GFR and lead to acute renal failure (p. 986).

Control of the GFR

Glomerular filtration is the vital first step for all other kidney functions. If filtration does not take place, waste products are not excreted, pH control is jeopardized, and an important mechanism for regulating blood volume is lost. It should be no surprise that a variety of regulatory mechanisms ensure that GFR remains within normal limits.

Filtration depends on adequate blood flow to the glomerulus and on the maintenance of normal filtration pressures. Three interacting levels of control stabilize GFR: (1) *autoregulation*, at the local level; (2) *hormonal regulation*, initiated by the kidneys; and (3) *autonomic regulation*, primarily by the sympathetic division of the autonomic nervous system.

26

Autoregulation of the GFR

Autoregulation (local blood flow regulation) maintains an adequate GFR despite changes in local blood pressure and blood flow. *Myogenic mechanisms*—how arteries and arterioles react to an increase or decrease in blood pressure—play a role in the autoregulation of blood flow. Changes to the diameters of afferent arterioles, efferent arterioles, and glomerular capillaries maintain GFR. The most important regulatory mechanisms stabilize the GFR when systemic blood pressure drops (**Figure 26–11**).

The GFR also remains relatively constant when systemic blood pressure rises. A rise in renal blood pressure stretches the walls of afferent arterioles, and the smooth muscle cells respond by contracting. The reduction in the diameter of afferent arterioles decreases glomerular blood flow and keeps the GFR within normal limits.

Hormonal Regulation of the GFR

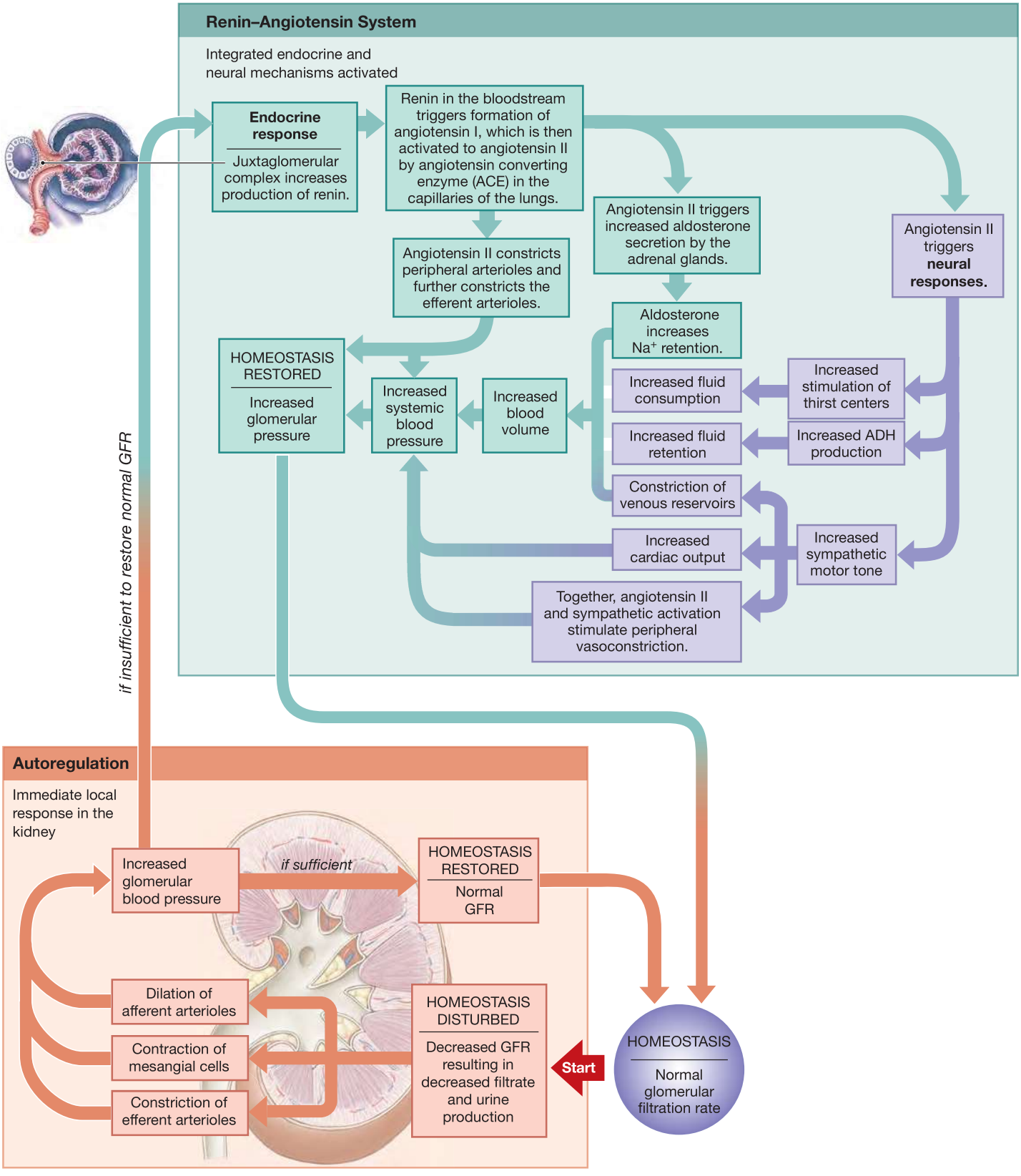
The GFR is regulated by the hormones of the renin–angiotensin system and the natriuretic peptides (ANP and BNP). We introduced these hormones and their actions in Chapters 18 and 21. ↩ pp. 624–626, 731–732 There are three triggers for the release of renin by the juxtaglomerular complex (JGC). They are (1) a decline in blood pressure at the glomerulus as the result of a decrease in blood volume, a fall in systemic pressures, or a blockage in the renal artery or its branches; (2) stimulation of juxtaglomerular cells by sympathetic innervation; or (3) a decline in the osmotic concentration of the tubular fluid at the macula densa.

These triggers are often interrelated. For example, a decline in systemic blood pressure reduces the glomerular filtration rate, while baroreceptor reflexes cause sympathetic activation. Meanwhile, a reduction in the GFR slows the movement of tubular fluid along the nephron. As a result, the tubular fluid is in the ascending limb of the nephron loop longer, and the concentration of sodium and chloride ions in the tubular fluid reaching the macula densa and DCT becomes abnormally low.

Figure 26–11 provides a general overview of the response of the renin–angiotensin system to a decline in GFR. A drop in GFR leads to the release of renin by the juxtaglomerular complex. Renin converts the inactive protein angiotensinogen to angiotensin I. Angiotensin I is also inactive but is then converted to angiotensin II by **angiotensin-converting enzyme (ACE).** This conversion takes place primarily in the capillaries of the lungs. Angiotensin II acts at the nephron, adrenal glands, and in the CNS. In peripheral capillary beds, angiotensin II causes a brief but powerful vasoconstriction of arterioles and precapillary sphincters, raising arterial pressures throughout the body. The combined effect is an increase in systemic blood volume and blood pressure and the restoration of normal GFR.

If blood volume rises, the GFR increases automatically. This increase promotes fluid losses that help return blood volume to normal levels. If the rise in blood volume is severe, hormonal factors further increase the GFR and speed up fluid losses in the urine. As noted in Chapter 18, the heart releases *natriuretic peptides* when increased blood volume or blood pressure stretches the walls of the heart. The atria release atrial natriuretic peptide (ANP), and the ventricles release brain natriuretic peptide (BNP). ↩ pp. 626, 731 Among their other effects, these hormones trigger the dilation of afferent arterioles and the constriction of efferent arterioles. This mechanism raises glomerular pressures and increases the GFR. The natriuretic peptides also decrease sodium reabsorption at the renal tubules. The net result is increased urine production and reduced blood volume and pressure.

Figure 26–11 The Response to a Reduction in the GFR.



Autonomic Regulation of the GFR

Most of the autonomic innervation of the kidneys consists of sympathetic postganglionic fibers. (The role of the few parasympathetic fibers in regulating kidney function is not known.) Sympathetic activation has a direct effect on the GFR. It produces a powerful vasoconstriction of afferent arterioles, which decreases the GFR and slows the production of filtrate. In this way, the sympathetic activation triggered by an acute fall in blood pressure or a heart attack overrides the local regulatory mechanisms that act to stabilize the GFR. As the crisis passes and sympathetic tone decreases, the filtration rate gradually returns to normal.

When the sympathetic division alters regional patterns of blood circulation, blood flow to the kidneys is often affected. For example, the dilation of superficial vessels in warm weather shunts blood away from the kidneys. As a result, glomerular filtration declines temporarily. The effect becomes especially pronounced during strenuous exercise. As the blood flow to your skin and skeletal muscles increases, kidney perfusion gradually decreases. These changes may be opposed, with variable success, by autoregulation at the local level.

At maximal levels of exertion, renal blood flow may be less than 25 percent of normal resting levels. This reduction can create problems for endurance athletes. Metabolic wastes build up over the course of a long event. *Proteinuria* (protein in the urine) commonly occurs after such events because the glomerular cells have been injured by prolonged hypoxia (low oxygen levels). If the damage is substantial, *hematuria* (blood in the urine) occurs. Hematuria develops in roughly 18 percent of marathon runners. The cause is trauma to the bladder epithelium from the shocks of running. Proteinuria and hematuria generally disappear within 48 hours as the glomerular tissues are repaired. However, a small number of marathon and ultramarathon runners experience *acute renal failure*, with permanent impairment of kidney function.

Checkpoint

9. **What nephron structures are involved in filtration?**
10. **List the factors that influence net filtration pressure.**
11. **List the factors that influence the rate of filtrate formation.**
12. **How would a decrease in blood pressure affect the GFR?**

See the blue Answers tab at the back of the book.

26-5 Countercurrent multiplication and the influence of antidiuretic hormone and aldosterone affect reabsorption and secretion

Reabsorption recovers useful materials that have entered the filtrate. Secretion ejects waste products, toxins, or other undesirable solutes that did not leave the bloodstream at the glomerulus. Both processes take place in every segment of the nephron except the renal corpuscle. Their relative importance changes from segment to segment.

Reabsorption and Secretion at the PCT

The cells of the proximal convoluted tubule normally reabsorb 60–70 percent of the volume of the filtrate produced in the renal corpuscle. The reabsorbed materials enter the peritubular fluid, diffuse into peritubular capillaries, and are quickly returned to the circulation.

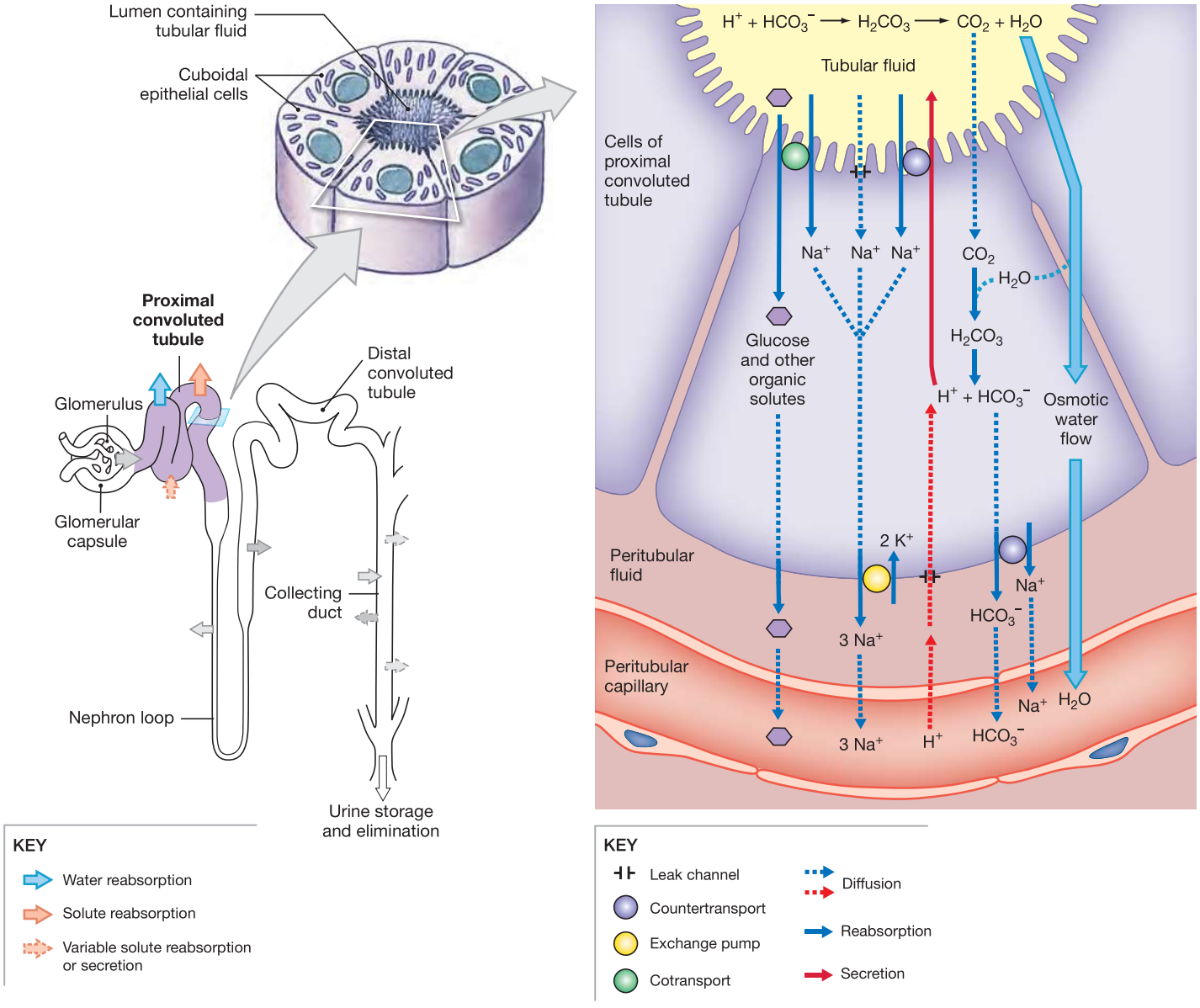
The PCT has five major functions:

1. *Reabsorption of Organic Nutrients.* Under normal circumstances, before the tubular fluid enters the nephron loop, the PCT reabsorbs more than 99 percent of the glucose, amino acids, and other organic nutrients in the fluid. This reabsorption involves a combination of facilitated transport and cotransport.
2. *Active Reabsorption of Ions.* The PCT actively transports several ions, including sodium, potassium, and bicarbonate ions (**Figure 26–12**), plus magnesium, phosphate, and sulfate ions. Although the ion pumps involved are individually regulated, they may be influenced by circulating ion or hormone levels. For example, angiotensin II stimulates Na^+ reabsorption along the PCT. By absorbing carbon dioxide, the PCT indirectly recaptures about 90 percent of the bicarbonate ions from tubular fluid. Bicarbonate is important in stabilizing blood pH. We examine this process further in Chapter 27.
3. *Reabsorption of Water.* The reabsorptive processes have a direct effect on the solute concentrations inside and outside the tubules. The filtrate entering the PCT has the same osmotic concentration as that of the surrounding peritubular fluid. As reabsorption proceeds, the solute concentration of tubular fluid decreases, and that of peritubular fluid and adjacent capillaries increases. Osmosis then pulls water out of the tubular fluid and into the peritubular fluid. Along the PCT, this mechanism results in the reabsorption of roughly 108 liters of water each day.
4. *Passive Reabsorption of Ions.* As active reabsorption of ions takes place and water leaves tubular fluid by osmosis, the concentration of other solutes in tubular fluid increases above that in peritubular fluid. If the tubular cells are permeable to them, those solutes move across the tubular cells and into the peritubular fluid by passive diffusion. Urea, chloride ions, and lipid-soluble materials may diffuse out of the PCT in this way. Such diffusion further reduces the solute concentration of the tubular fluid and promotes additional water reabsorption by osmosis.
5. *Secretion.* Active secretion also takes place along the PCT. Because the DCT carries out comparatively little reabsorption, we will consider secretory mechanisms when we discuss the DCT.

Sodium ion reabsorption plays an important role in all of these processes. Sodium ions may enter tubular cells by diffusion through Na^+ leak channels; by the sodium-linked cotransport of glucose, amino acids, or other organic solutes; or by countertransport for hydrogen ions (**Figure 26–12**). Once inside the tubular cells, sodium ions diffuse toward the basement membrane. The plasma membrane in this area contains sodium–potassium exchange pumps that eject sodium ions in exchange for extracellular potassium ions. Reabsorbed sodium ions then diffuse into the adjacent peritubular capillaries.

The reabsorption of ions and compounds along the PCT involves many different carrier proteins. Some people have an inherited inability to manufacture one or more of these carrier proteins. For this reason, these individuals are unable to recover specific solutes from tubular fluid. In *renal glycosuria* (glī-kō-SOO-rē-uh), for example, a defective carrier protein makes it impossible for the PCT to reabsorb glucose from tubular fluid.

Figure 26–12 Transport Activities at the PCT. Sodium ions may enter a tubular cell from the filtrate by diffusion, cotransport, or countertransport. The sodium ions are then pumped into the peritubular fluid by the sodium–potassium exchange pump. Other reabsorbed solutes may be ejected into the peritubular fluid by separate active transport mechanisms. The absorption of bicarbonate is indirectly associated with the reabsorption of sodium ions and the secretion of hydrogen ions.



The Nephron Loop and Countercurrent Multiplication

Roughly 60–70 percent of the volume of filtrate produced at the glomerulus has been reabsorbed before the tubular fluid reaches the nephron loop. In the process, useful organic substrates and many mineral ions have been reclaimed. The nephron loop reabsorbs about half of the remaining water and two-thirds of the remaining sodium and chloride ions. This reabsorption takes place efficiently according to the principle of countercurrent exchange. We introduced this principle in Chapter 25 in our discussion of heat conservation mechanisms. ↩ p. 945

The thin descending limb and the thick ascending limb of the nephron loop lie very close together. They are separated only by peritubular fluid. The exchange between these segments is called **countercurrent multiplication.** *Countercurrent* refers to the fact that the exchange takes place between fluids moving in opposite directions: Tubular fluid in the descending limb flows toward the renal pelvis, while tubular fluid in the ascending limb flows toward the cortex. *Multiplication* refers to the fact that the effect of the exchange increases as movement of the fluid continues.

The two parallel limbs of the nephron loop have very different permeability characteristics. The thin descending limb is permeable to water but relatively impermeable to solutes. The thick ascending limb is relatively impermeable to both water and solutes, but it contains active transport mechanisms that pump sodium and chloride ions from the tubular fluid into the peritubular fluid of the medulla.

A quick overview of countercurrent multiplication will help you make sense of the details:

- Sodium and chloride are pumped out of the thick ascending limb and into the peritubular fluid.
- This pumping action raises the osmotic concentration in the peritubular fluid around the thin descending limb.
- The result is an osmotic flow of water out of the thin descending limb and into the peritubular fluid. This loss of water increases the solute concentration in the thin descending limb.
- The arrival of the highly concentrated solution in the thick ascending limb speeds up the transport of sodium and chloride ions into the peritubular fluid of the medulla.

Notice that this process is a simple positive feedback loop. Solute pumping at the ascending limb leads to higher solute concentrations in the descending limb, which then bring about increased solute pumping in the ascending limb.

We can now take a closer look at the mechanics of the process. **Figure 26–13a** diagrams ion transport across the epithelium of the thick ascending limb. Active transport at the apical surface moves sodium, potassium, and chloride ions out of the tubular fluid. The carrier is called a $\mathbf{Na^+–K^+/2\ Cl^-}$ transporter, because each cycle of the pump carries a sodium ion, a potassium ion, and two chloride ions into the tubular cell. Then cotransport carriers pump potassium and chloride ions into the peritubular fluid. However, potassium ions are removed from the peritubular fluid as the sodium–potassium exchange pump pumps sodium ions out of the tubular cell. The potassium ions then diffuse back into the lumen of the tubule through potassium leak channels. The net result is that Na^+ and Cl^- enter the peritubular fluid of the renal medulla.

The removal of sodium and chloride ions from the tubular fluid in the ascending limb raises the osmotic concentration of the peritubular fluid around the thin descending limb (**Figure 26–13b**). Recall that the thin descending limb is permeable to water but not to solutes. As tubular fluid travels deeper into the medulla within the thin descending limb, osmosis moves water into the peritubular fluid. Solutes remain behind. As a result, the tubular fluid at the turn of the nephron loop has a higher osmotic concentration than it did at the start.

The pumping mechanism of the thick ascending limb is highly effective. Almost two-thirds of the sodium and chloride ions that enter it are pumped out of the tubular fluid before that fluid reaches the DCT. In other tissues, differences in solute concentration are quickly resolved by osmosis. However, osmosis cannot take place across the wall of the thick ascending limb, because the epithelium there is impermeable to water. Thus, as Na^+ and Cl^- are removed, the solute concentration in the tubular fluid declines. Tubular fluid arrives at the DCT with an osmotic concentration of only about 100 mOsm/L. This value is one-third the concentration of the peritubular fluid of the renal cortex.

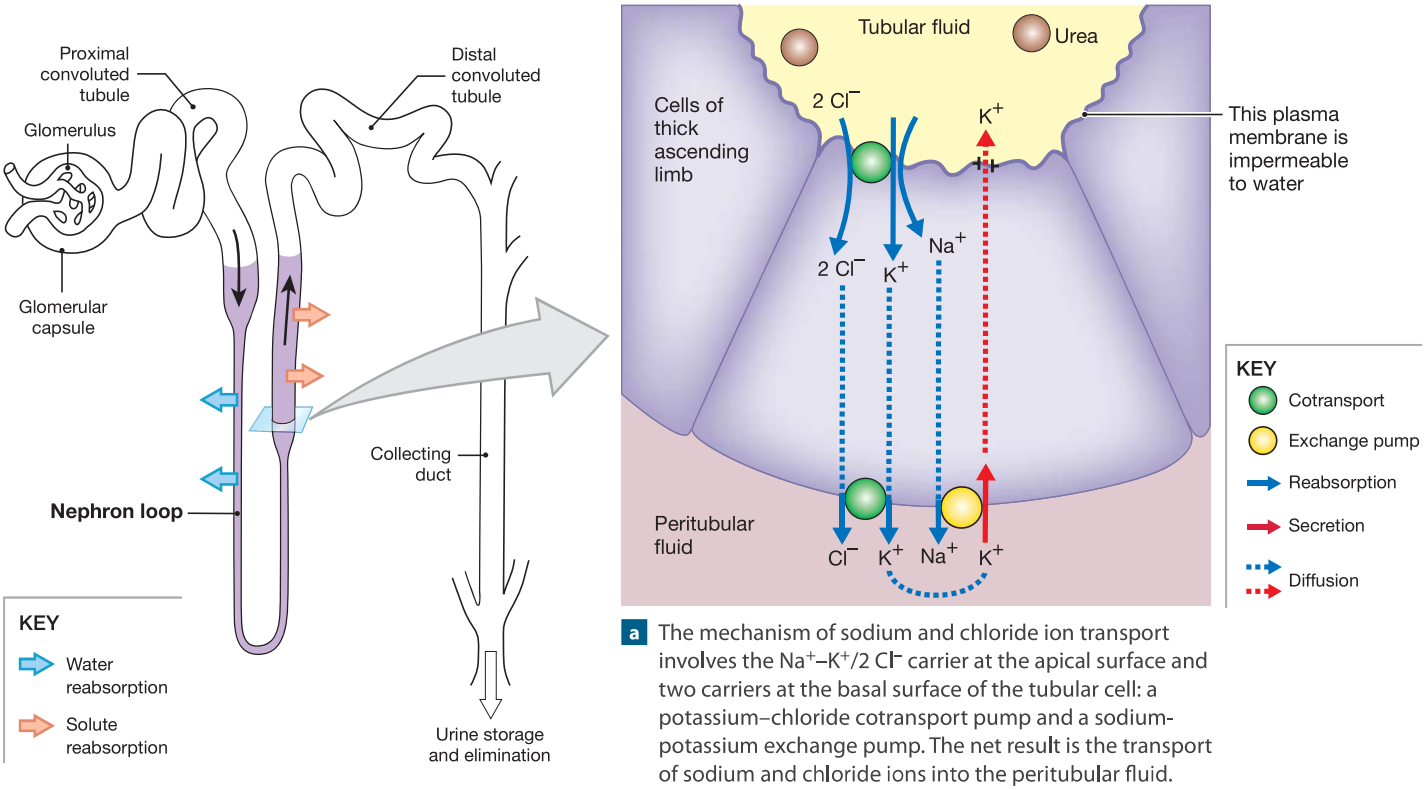
The rate of ion transport across the thick ascending limb is proportional to an ion's concentration in tubular fluid. As a result, more sodium and chloride ions are pumped into the medulla at the start of the thick ascending limb, where NaCl concentrations are highest, than near the cortex. This regional difference in the rate of ion transport is the basis of the concentration gradient within the medulla.

The Concentration Gradient of the Medulla

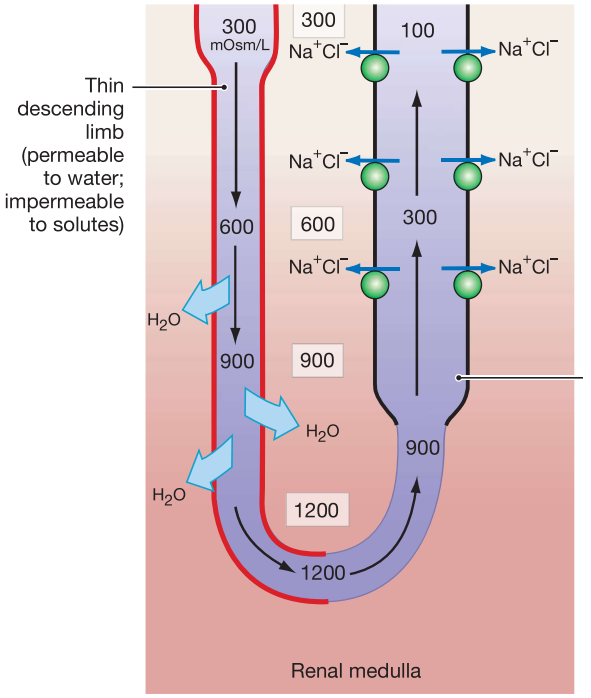
Normally, the maximum solute concentration of the peritubular fluid near the turn of the nephron loop is about 1200 mOsm/L (**Figure 26–13b**). Sodium and chloride ions pumped out of the loop's ascending limb account for roughly two-thirds of that gradient (750 mOsm/L). The rest of the concentration gradient results from the presence of urea.

To understand how urea arrives in the medulla, let's look ahead to events in the last segments of the collecting system (**Figure 26–13c**). The thick ascending limb of the nephron loop, the DCT, and the collecting ducts are all impermeable to urea. As water is reabsorbed, the concentration of urea gradually rises

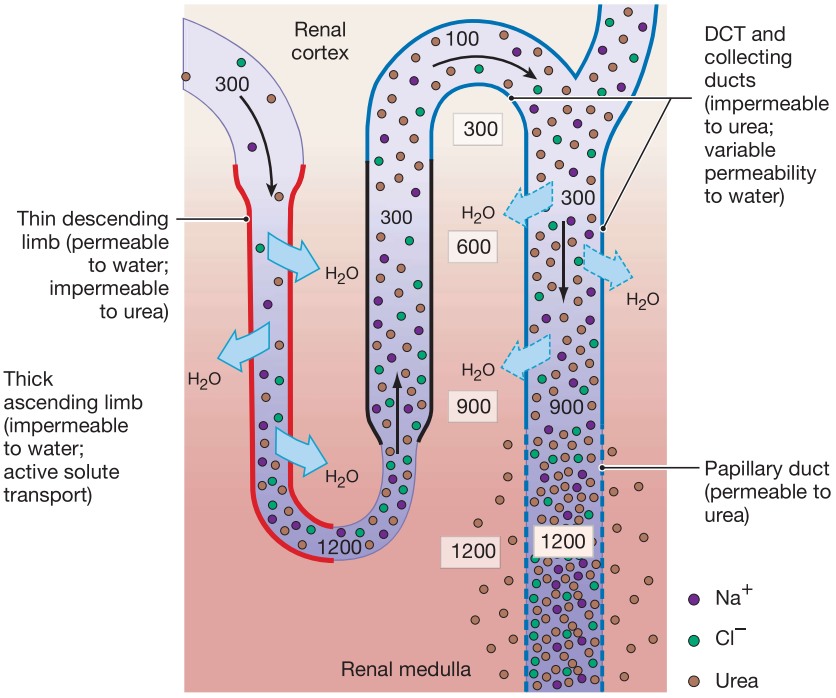
Figure 26–13 Countercurrent Multiplication and Concentration of Urine.



a The mechanism of sodium and chloride ion transport involves the Na^+–K^+/2 Cl^- carrier at the apical surface and two carriers at the basal surface of the tubular cell: a potassium–chloride cotransport pump and a sodium-potassium exchange pump. The net result is the transport of sodium and chloride ions into the peritubular fluid.



b Transport of NaCl along the ascending thick limb results in the movement of water from the descending limb.



c The permeability characteristics of both the loop and the collecting duct tend to concentrate urea in the tubular fluid and in the medulla. The nephron loop, DCT, and collecting duct are impermeable to urea. As water reabsorption occurs, the urea concentration rises. The papillary ducts' permeability to urea accounts for roughly one-third of the solutes in the deepest portions of the medulla.

in the tubular fluid. When the tubular fluid reaches the papillary duct, it typically contains urea at a concentration of about 450 mOsm/L. Because the papillary ducts are permeable to urea, the urea concentration in the deepest parts of the medulla also averages 450 mOsm/L.

Benefits of Countercurrent Multiplication

The countercurrent mechanism performs two functions:

1. It efficiently reabsorbs solutes and water before the tubular fluid reaches the DCT and collecting system.
2. It establishes a concentration gradient that permits the passive reabsorption of water from the tubular fluid in the collecting system. Circulating levels of antidiuretic hormone (ADH) regulate this reabsorption.

In summary, countercurrent multiplication is a way to either concentrate or dilute urine. The tubular fluid entering the descending limb of the nephron loop has an osmotic concentration of roughly 300 mOsm/L, due primarily to the presence of ions such as Na^+ and Cl^-. The concentration of organic wastes, such as urea, is low. About half of the tubular fluid entering the nephron loop is then reabsorbed along the thin descending limb. Two-thirds of the Na^+ and Cl^- is reabsorbed along the thick ascending limb. As a result, the DCT receives a reduced volume of tubular fluid with an osmotic concentration of about 100 mOsm/L. Urea and other organic wastes, which were not pumped out of the thick ascending limb, now represent a significant proportion of the dissolved solutes.

Reabsorption and Secretion at the DCT

As we have just seen, the composition and volume of tubular fluid change dramatically as it flows from the capsular space to the distal convoluted tubule. Only 15–20 percent of the initial filtrate volume reaches the DCT. The concentrations of electrolytes and organic wastes in the arriving tubular fluid no longer resemble the concentrations in blood plasma. Selective reabsorption or secretion, primarily along the DCT, makes the final adjustments in the solute composition and volume of the tubular fluid.

Reabsorption at the DCT

Throughout most of the DCT, the tubular cells actively transport Na^+ and Cl^- out of the tubular fluid (**Figure 26–14a**). Tubular cells along the distal portions of the DCT also contain ion pumps that reabsorb tubular Na^+ in exchange for another cation (usually K^+) (**Figure 26–14b**). The hormone *aldosterone*, produced by the adrenal cortex, controls the Na^+ channels and the ion pump. This hormone stimulates the synthesis and incorporation of sodium channels and sodium ion pumps in plasma membranes along the DCT and collecting duct. The net result is a reduction in the number of sodium ions lost in urine.

However, sodium ion conservation is associated with potassium ion loss. Prolonged aldosterone stimulation can therefore produce *hypokalemia*, a dangerous reduction in the plasma K^+ concentration. The secretion of aldosterone and its actions on the DCT and collecting system are opposed by the natriuretic peptides (ANP and BNP).

The DCT is also the primary site of Ca^{2+} reabsorption. Circulating levels of parathyroid hormone and calcitriol regulate this process. pp. 614–615

Secretion at the DCT

The blood entering the peritubular capillaries still contains a number of potentially undesirable substances that did not cross the filtration membrane at the glomerulus. In most cases, the concentrations of these materials are too low to cause physiological problems. However, any ions or compounds in peritubular capillaries will diffuse into the peritubular fluid. If those concentrations become too high, the tubular cells may absorb these materials from the peritubular fluid and secrete them into the tubular fluid. **Table 26–3** lists some of the substances secreted into tubular fluid by the proximal and distal convoluted tubules.

The rate of K^+ and H^+ secretion rises or falls in response to changes in their concentrations in peritubular fluid. The higher their concentration in the peritubular fluid, the higher the rate of secretion. Potassium and hydrogen ions merit special attention, because their concentrations in body fluids must be maintained within narrow limits.

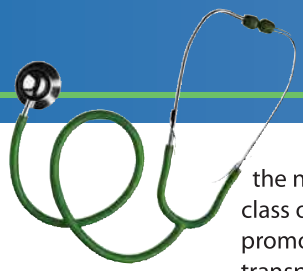
Potassium Ion Secretion. **Figure 26–14a, b** diagrams the mechanism of K^+ secretion. In effect, tubular cells trade sodium ions in the tubular fluid for excess potassium ions in body fluids. Potassium ions are removed from the peritubular fluid in exchange for sodium ions from the tubular fluid. These potassium ions diffuse into the lumen of the DCT through potassium leak channels at the apical surfaces of the tubular cells.

Hydrogen Ion Secretion. Hydrogen ion secretion is also associated with the reabsorption of sodium. **Figure 26–14c** depicts two routes of secretion. Both involve the generation of carbonic acid by the enzyme *carbonic anhydrase*. pp. 844, 881 Hydrogen ions generated by the dissociation of the carbonic acid are secreted by sodium-linked countertransport in exchange for Na^+ in the tubular fluid. The bicarbonate ions diffuse into the peritubular fluid and then into the bloodstream. There they help prevent changes in plasma pH.

Hydrogen ion secretion acidifies the tubular fluid while elevating the pH of the blood. Hydrogen ion secretion speeds up

Clinical Note

Diuretics



You take one to go one

Diuresis (dī-ū-RĒ-sis; *dia*, through + *ouresis*, urination) is the elimination of urine. *Urination* is an equivalent term in a general sense, but *diuresis* typically indicates the production of a large volume of urine. **Diuretics** (dī-ū-RET-iks) are drugs that promote the loss of water in urine. The usual goal in diuretic therapy is to reduce blood volume, blood pressure, extracellular fluid volume, or all three. The ability to control renal water losses with relatively safe and effective diuretics has saved the lives of many people, especially those with high blood pressure or congestive heart failure.

Diuretics have many mechanisms of action. However, all such drugs affect transport activities or water reabsorption along the nephron and collecting system. For example, consider the class of diuretics called *thiazides* (THĪ-uh-zīdz). These drugs promote water loss by reducing sodium and chloride ion transport in the proximal and distal convoluted tubules.

Diuretic use for nonclinical reasons is on the rise. For example, some bodybuilders take large doses of diuretics to improve muscle definition temporarily. Some fashion models or horse jockeys do the same to reduce body weight for brief periods. This practice of "cosmetic dehydration" is extremely dangerous and has caused several deaths due to electrolyte imbalance and consequent cardiac arrest.

when the pH of the blood falls. This can happen in *lactic acidosis*, which can develop after exhaustive muscle activity, or *ketoacidosis*, which can develop in starvation or diabetes mellitus. ↩ p. 935 The combination of H^+ removal and HCO_3^- production by the kidneys plays an important role in the control of blood pH. Because one of the secretory pathways is aldosterone sensitive, aldosterone stimulates H^+ secretion. Prolonged aldosterone stimulation can cause *alkalosis*, or abnormally high blood pH.

In Chapter 25, we noted that the production of lactic acid and ketone bodies during the postabsorptive state can cause acidosis. Under these conditions, the PCT and DCT deaminate amino acids in reactions that strip off the amino groups ($—NH_2$). The reaction sequence ties up H^+ and yields both **ammonium ions** (NH_4^+) and HCO_3^-. As indicated in **Figure 26–14c**, the ammonium ions are then pumped into the tubular fluid by sodium-linked countertransport, and the bicarbonate ions enter the bloodstream by way of the peritubular fluid.

Tubular deamination thus has two major benefits. It provides carbon chains suitable for catabolism. It also generates bicarbonate ions that add to the buffering capacity of plasma.

Reabsorption and Secretion along the Collecting System

The collecting ducts receive tubular fluid from many nephrons and carry it toward the renal sinus, through the concentration gradient in the medulla. The normal amount of water and solute loss in the collecting system is regulated in two ways:

- By aldosterone, which controls sodium ion pumps along most of the DCT and the proximal portion of the collecting system. As we have noted, these actions are opposed by the natriuretic peptides.
- By ADH, which controls the permeability of the DCT and collecting system to water. The secretion of ADH is suppressed by the natriuretic peptides, and this—combined with the effects of natriuretic peptide on aldosterone secretion and action—can dramatically increase urinary water losses.

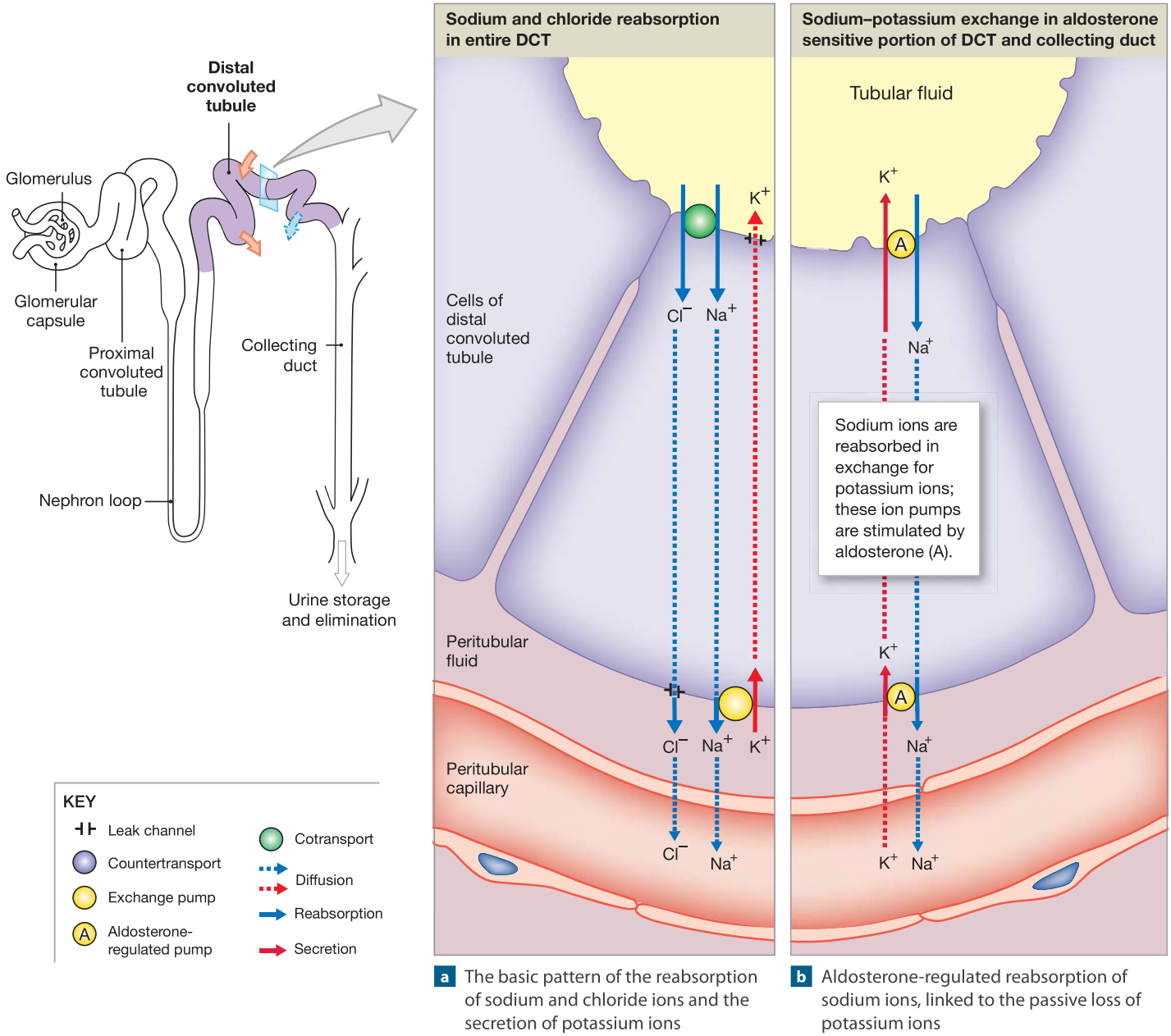
The collecting system also has other reabsorptive and secretory functions. Many of them are important to the control of body fluid pH.

Reabsorption in the Collecting System

The collecting system reabsorbs sodium ions, bicarbonate ions, and urea as follows:

- *Sodium Ion Reabsorption.* The collecting system contains aldosterone-sensitive ion pumps that exchange Na^+ in tubular fluid for K^+ in peritubular fluid (**Figure 26–14b**).
- *Bicarbonate Reabsorption.* Bicarbonate ions are reabsorbed in exchange for chloride ions in the peritubular fluid (**Figure 26–14c**).
- *Urea Reabsorption.* The concentration of urea in the tubular fluid entering the collecting duct is relatively high. The fluid entering the papillary duct generally has the same osmotic concentration as that of interstitial fluid of the medulla—about 1200 mOsm/L—but contains a much higher concentration of urea. As a result, urea tends to diffuse out of the tubular fluid and into the peritubular fluid in the deepest portion of the medulla.

Figure 26–14 Tubular Secretion and Solute Reabsorption at the DCT.



a The basic pattern of the reabsorption of sodium and chloride ions and the secretion of potassium ions

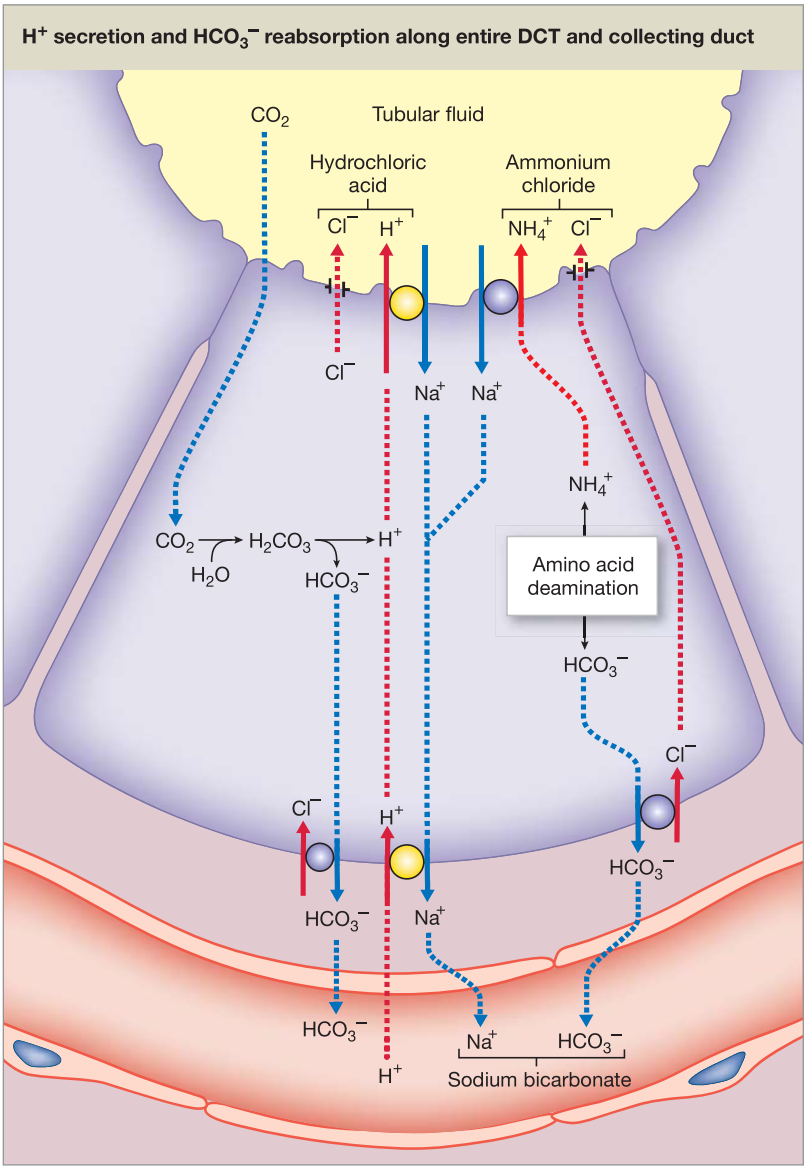
b Aldosterone-regulated reabsorption of sodium ions, linked to the passive loss of potassium ions

Secretion in the Collecting System

The collecting system is important in controlling the pH of body fluids through the secretion of hydrogen or bicarbonate ions. If the pH of the peritubular fluid drops, carrier proteins pump hydrogen ions into the tubular fluid and reabsorb bicarbonate ions that help restore normal pH. If the pH of the peritubular fluid rises (a much less common event), the collecting system secretes bicarbonate ions and pumps hydrogen ions into the peritubular fluid. The net result is that the body eliminates a buffer and gains hydrogen ions that lower the pH. We examine these responses in more detail in Chapter 27, when we consider acid–base balance.

The Control of Urine Volume and Osmotic Concentration

Urine volume and osmotic concentration are regulated through the control of water reabsorption. Water is reabsorbed by osmosis along the proximal convoluted tubule and the descending limb of the nephron loop. The water permeabilities of these re-



c Hydrogen ion secretion and the acidification of urine occur by two routes. The central theme is the exchange of hydrogen ions in the cytoplasm for sodium ions in the tubular fluid, and the reabsorption of the bicarbonate ions generated in the process.

gions cannot be adjusted. As a result, water reabsorption takes place wherever the osmotic concentration of the peritubular fluid is greater than that of the tubular fluid. The ascending limb of the nephron loop is impermeable to water. In the distal convoluted tubule and collecting system, 1–2 percent of the volume of water in the original filtrate is recovered during sodium ion reabsorption. All these water movements represent *obligatory water reabsorption* because they cannot be prevented. This reabsorption usually recovers 85 percent of the volume of filtrate.

The volume of water lost in urine depends on how much of the remaining water in the tubular fluid is reabsorbed along the DCT and collecting system. (This remaining water represents 15 percent of the filtrate volume, or approximately 27 liters per day.) The amount reabsorbed can be precisely controlled by a process called *facultative water reabsorption*. Precise control is possible because these segments are relatively impermeable to water except in the presence of ADH. This hormone causes special *water channels*, or *aquaporins*, to be inserted in the apical plasma membranes. These water channels dramatically enhance the rate of osmotic water movement. The higher the circulating levels of ADH, the greater the number of water channels, and the greater the water permeability of these segments.

As noted earlier in this chapter, the tubular fluid arriving at the DCT has an osmotic concentration of only about 100 mOsm/L. In the presence of ADH, osmosis takes place. Water moves out of the DCT until the osmotic concentration of the tubular fluid equals that of the surrounding cortex (roughly 300 mOsm/L).

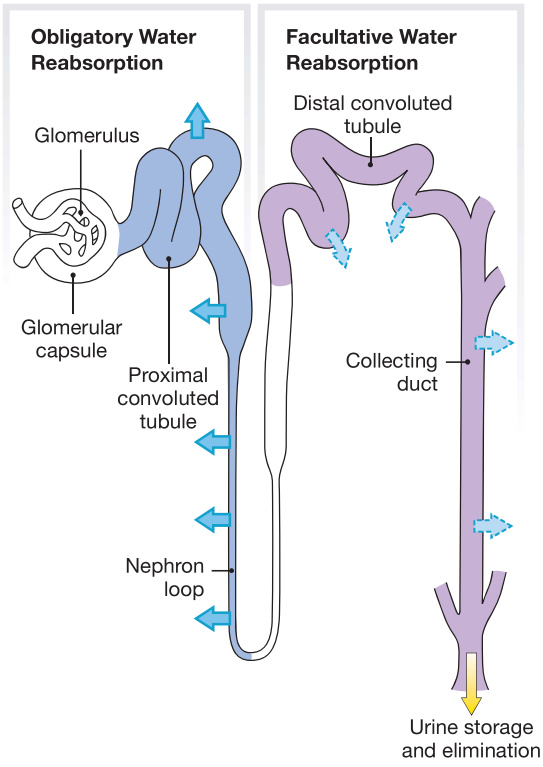
The tubular fluid then flows along the collecting duct, which passes through the concentration gradient of the medulla. Additional water is then reabsorbed. The urine reaching the minor calyx has an osmotic concentration closer to 1200 mOsm/L. Just how closely the osmotic concentration approaches 1200 mOsm/L depends on how much ADH is present.

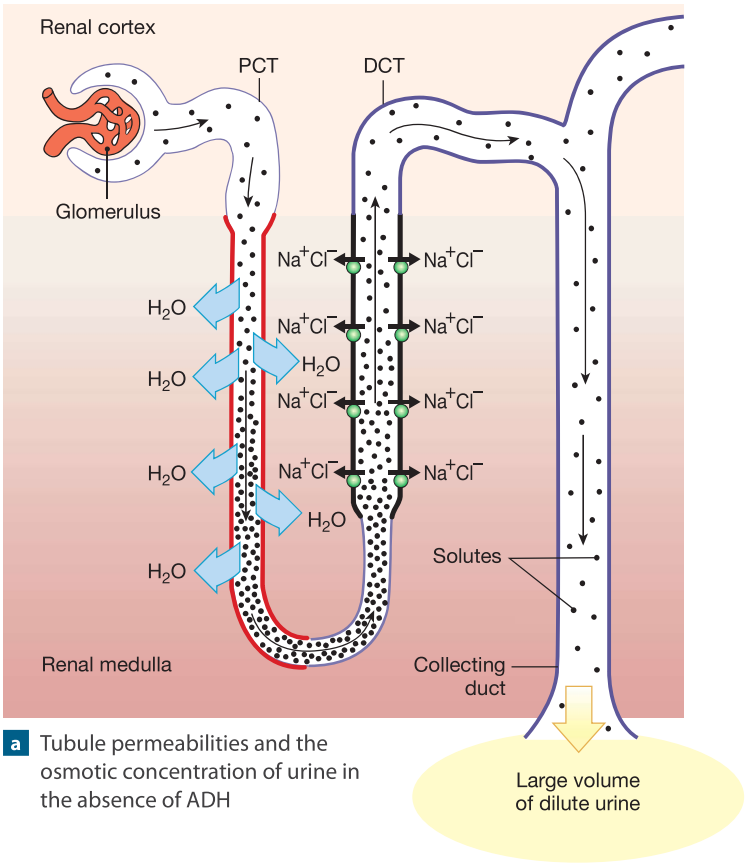
Figure 26–15 diagrams the effects of ADH on the DCT and collecting system. In the absence of ADH (**Figure 26–15a**), water is not reabsorbed in these segments, so all the fluid reaching the DCT is lost in the urine. The individual then produces large amounts of very dilute urine. That is just what happens in cases of *diabetes insipidus.* ↩ p. 608 In this condition, urinary water losses may reach 24 liters (6.3 gal) per day and the urine osmotic concentration is 30–400 mOsm/L.

As ADH levels rise (**Figure 26–15b**), the DCT and collecting system become more permeable to water. As a result, the amount of water reabsorbed increases. At the same time, the osmotic concentration of the urine climbs. Under maximum ADH stimulation, the DCT and collecting system become so permeable to water that the osmotic concentration of the urine equals that of the deepest portion of the medulla. Note that the concentration of urine can never *exceed* that of the medulla, because the concentrating mechanism relies on osmosis.

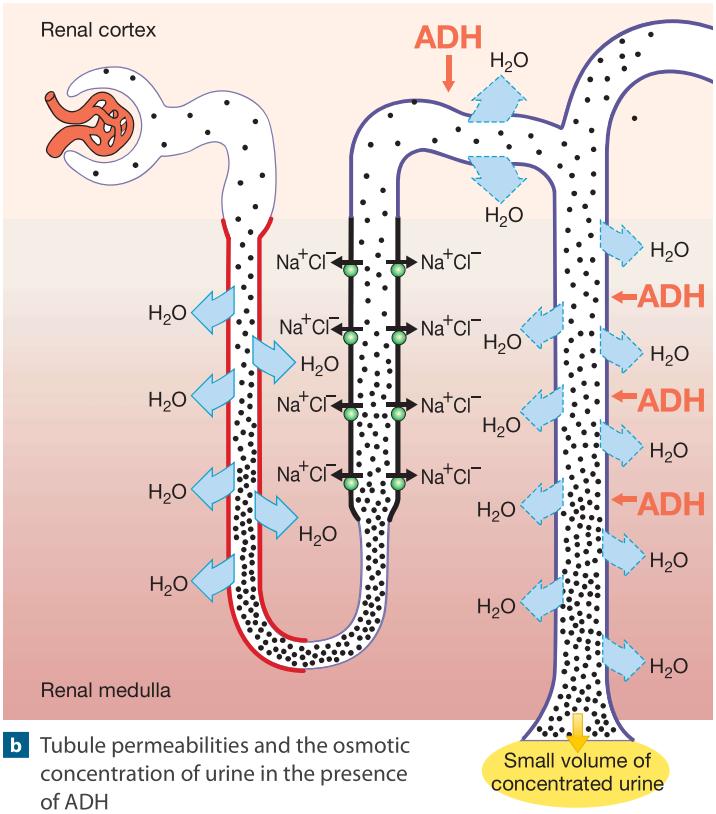
The hypothalamus continuously secretes ADH at low levels. For this reason, the DCT and collecting system always have

Figure 26–15 The Effects of ADH on the DCT and Collecting Duct.

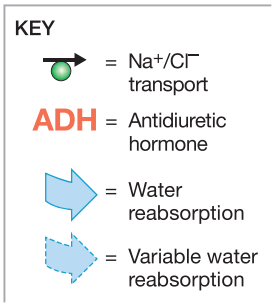




a Tubule permeabilities and the osmotic concentration of urine in the absence of ADH



b Tubule permeabilities and the osmotic concentration of urine in the presence of ADH



a significant degree of water permeability. At these low ADH levels, the DCT reabsorbs roughly 9 liters of water per day, or about 5 percent of the original volume of filtrate produced by the glomeruli. At normal ADH levels, the collecting system reabsorbs about 16.8 liters per day, or about 9.3 percent of the original volume of filtrate. A healthy adult typically produces 1200 mL of urine per day (about 0.6 percent of the filtrate volume). Its osmotic concentration is 800–1000 mOsm/L.

The effects of ADH are opposed by those of the natriuretic peptides, ANP and BNP. These hormones stimulate the production of a large volume of relatively dilute urine. This water loss reduces plasma volume to normal.

The Function of the Vasa Recta

The solutes and water reabsorbed in the renal medulla must be returned to the bloodstream without disrupting the concentration gradient. This return is the function of the vasa recta. Recall that the vasa recta are long, straight capillaries that parallel the long nephron loop of juxtamedullary nephrons.

Blood entering the vasa recta from the peritubular capillaries has an osmotic concentration of approximately 300 mOsm/L. As the blood descends into the medulla, it gradually increases in osmotic concentration as the solute concentration in the peritubular fluid rises. This increase in blood osmotic concentration involves both solute absorption and water loss. Solute absorption predominates, however, because the plasma proteins limit the osmotic flow of water out of the blood. ↩ p. 723

Blood ascending toward the cortex gradually decreases in osmotic concentration as the solute concentration of the peritubular fluid declines. Again, this decrease involves both solute diffusion and osmosis. In this case osmosis predominates, because the presence of plasma proteins does not oppose the osmotic flow of water into the blood.

The net results are that (1) some of the solutes absorbed in the descending portion of the vasa recta do not diffuse out in the ascending portion and (2) more water moves into the ascending portion of the vasa recta than moves out in the descending portion. Thus, the vasa recta carries both water and solutes out of the medulla. Under normal conditions, the removal of solutes and water by the vasa recta precisely balances the rates of solute reabsorption and osmosis in the medulla.

The Composition of Normal Urine

As we have seen, more than 99 percent of the 180 liters of filtrate produced each day by the glomeruli is reabsorbed. It never reaches the renal pelvis for elimination. General characteristics of the remaining filtrate—normal urine—are listed in **Table 26–5**. However, the composition of the urine produced each day varies with the metabolic and hormonal events under way.

Table 26–5 General Characteristics of Normal Urine

Characteristic	Normal Range
pH	4.5–8 (average: 6.0)
Specific gravity	1.003–1.030
Osmotic concentration (osmolarity)	855–1335 mOsm/L
Water content	93%–97%
Volume	700–2000 mL/day
Color	Clear yellow
Odor	Varies with composition
Bacterial content	None (sterile)

The composition and concentration of urine are two related but distinct properties. The *composition* of urine reflects the filtration, reabsorption, and secretion activities of the nephrons. Some compounds (such as urea) are neither actively excreted nor reabsorbed along the nephron. In contrast, organic nutrients are completely reabsorbed. Other compounds, such as creatinine, are missed by filtration but are actively secreted into the tubular fluid.

Filtration, reabsorption, and secretion determine the identities and amounts of materials excreted in urine. The *concentration* of these materials in a given urine sample depends on the osmotic movement of water across the walls of the tubules and collecting ducts. Because the composition and concentration of urine vary independently, you can produce a small volume of concentrated urine or a large volume of dilute urine and still excrete the same amount of dissolved materials. For this reason, physicians who are interested in a detailed assessment of renal function commonly analyze the urine produced over a 24-hour period rather than a single urine sample.

Urinalysis is the analysis of a urine sample. It is an important diagnostic tool, even in high-technology medicine. A standard urinalysis includes an assessment of the color and appearance of urine. These two characteristics can be determined without specialized equipment. In the 17th century, physicians classified the taste of the urine as sweet, salty, and so on, but quantitative analytical tests have long since replaced the taste-bud assay.

Normal urine is a clear, sterile solution. Its yellow color comes from the pigment urobilin. The kidneys generate this pigment from the urobilinogens produced by intestinal bacteria and absorbed in the colon (see **Figure 19–5**, p. 647). The characteristic odor of urine is due to the evaporation of small molecules, such as ammonia. Other substances not normally present, such as acetone or other ketone bodies, can also impart a distinctive smell.

Table 26–6 gives some typical values obtained from urinalysis. **Spotlight Figure 26–16** provides a summary of kidney function showing the major steps in the reabsorption of water and the production of concentrated urine.

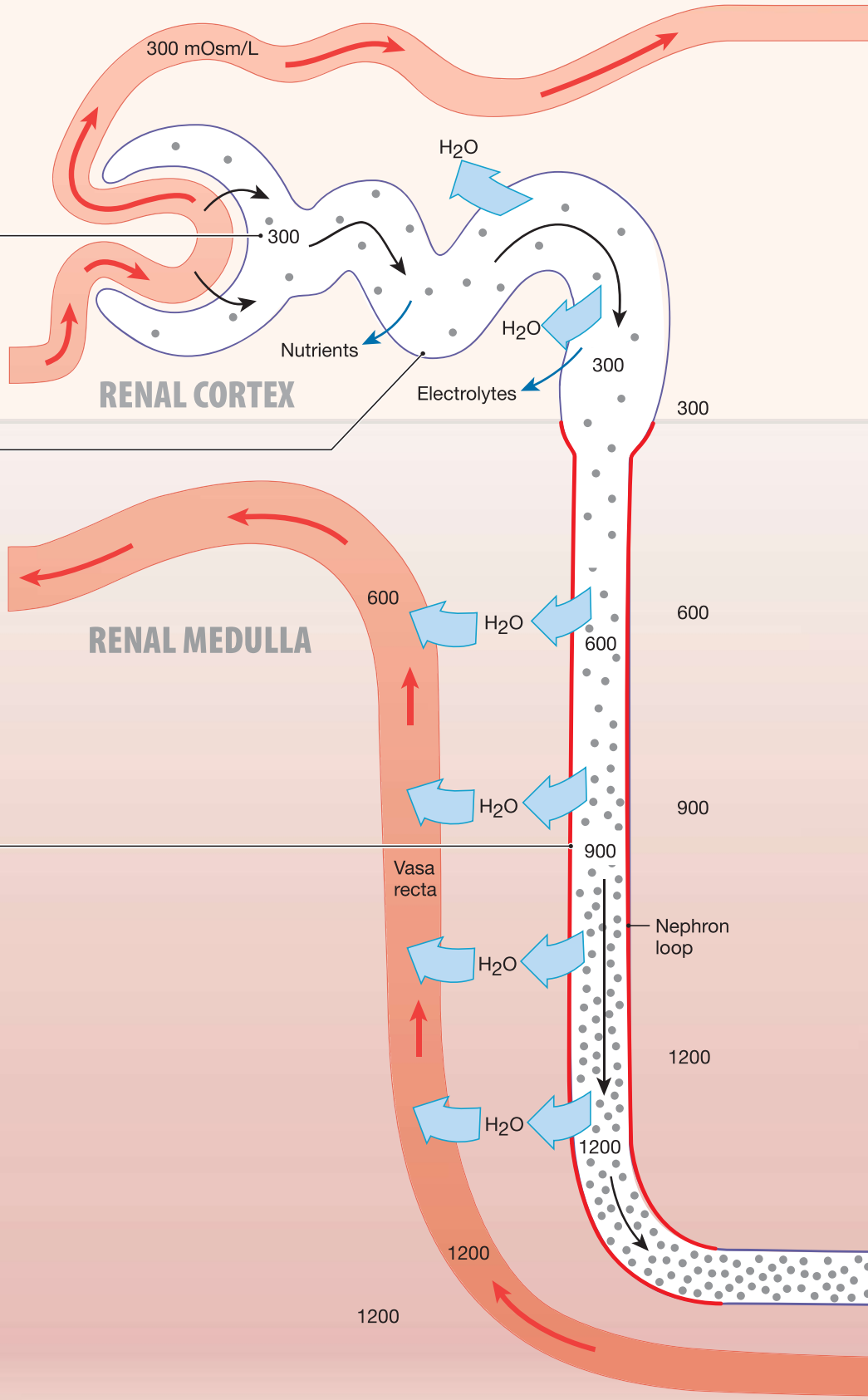
Spotlight

Figure 26–16
Summary of Renal Function

1 The filtrate produced at the renal corpuscle has the same osmotic concentration as plasma—about 300 mOsm/L. It has the same composition as blood plasma but does not contain plasma proteins.

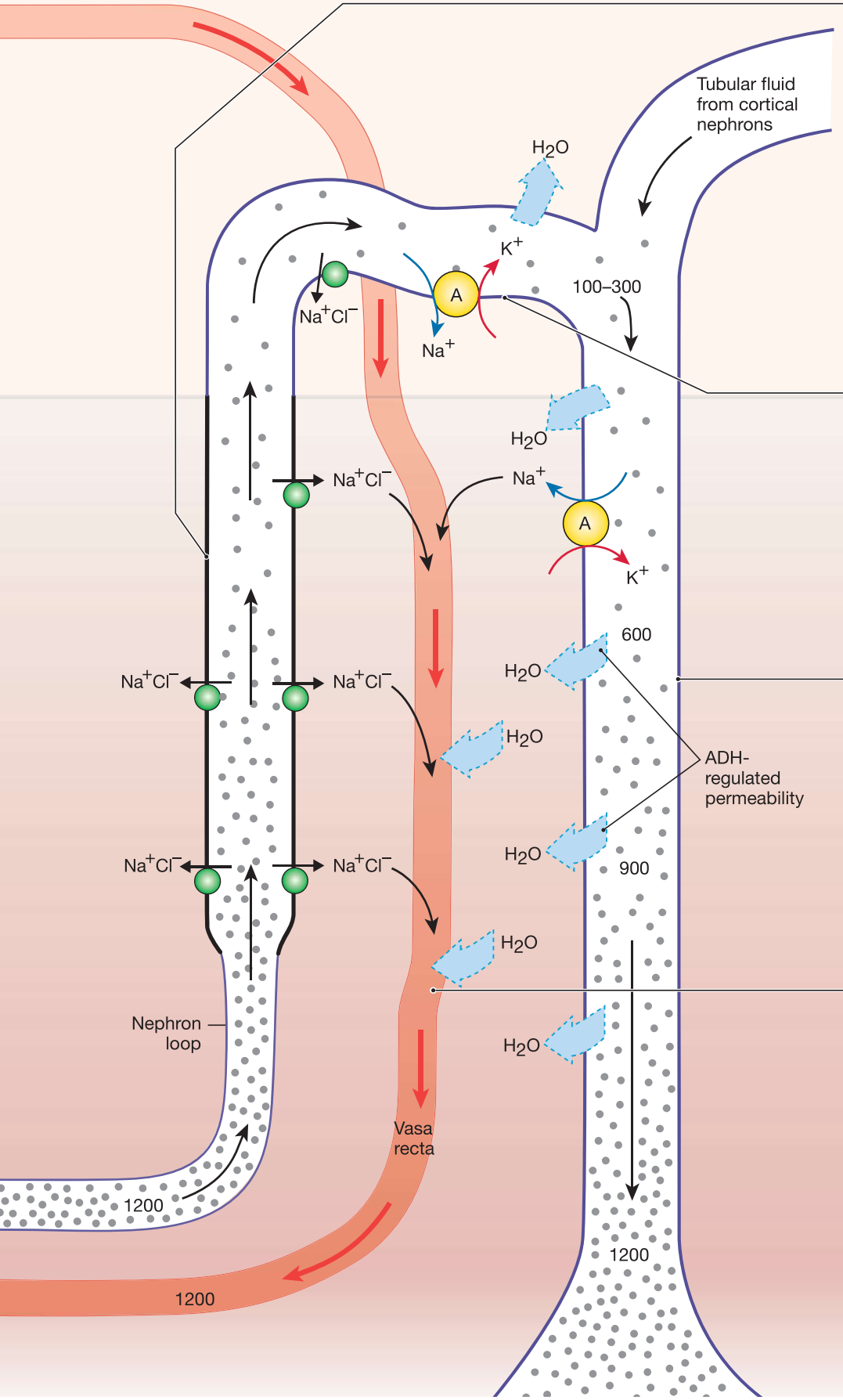
2 In the proximal convoluted tubule (PCT), the active removal of ions and organic nutrients produces a continuous osmotic flow of water out of the tubular fluid. This reduces the volume of filtrate but keeps the solutions inside and outside the tubule isotonic. Between 60 and 70 percent of the filtrate volume is absorbed here.

3 In the PCT and descending limb of the nephron loop, water moves into the surrounding peritubular fluids, leaving a small volume of highly concentrated tubular fluid. This reduction occurs by obligatory water reabsorption.



KEY

- = Water reabsorption
- = Variable water reabsorption
- = Na^+/Cl^- transport
- (A) = Aldosterone-regulated pump



4 The thick ascending limb is impermeable to water and solutes. The tubule cells actively transport Na^+ and Cl^- out of the tubule, thereby lowering the osmotic concentration of the tubular fluid. Because just Na^+ and Cl^- are removed, urea accounts for a higher proportion of the total osmotic concentration at the end of the nephron loop.

5 The final adjustments in the composition of the tubular fluid occur in the DCT and the collecting system. The osmotic concentration of the tubular fluid can be adjusted through active transport (reabsorption or secretion).

6 The final adjustments in the volume and osmotic concentration of the tubular fluid are made by controlling the water permeabilities of the distal portions of the DCT and the collecting system. The level of exposure to ADH determines the final urine concentration.

7 The vasa recta absorbs the solutes and water reabsorbed by the nephron loop and the collecting ducts. By transporting these solutes and water into the bloodstream, the vasa recta maintains the concentration gradient of the renal medulla.

Table 26–6 Typical Values Obtained from Standard Urinalysis

Compound	Primary Source	Daily Elimination*	Concentration	Remarks
NITROGENOUS WASTES				
Urea	Deamination of amino acids by liver and kidneys	21 g	1.8 g/dL	Rises if negative nitrogen balance exists
Creatinine	Breakdown of creatine phosphate in skeletal muscle	1.8 g	150 mg/dL	Proportional to muscle mass; decreases during atrophy or muscle disease
Ammonia	Deamination by liver and kidney, absorption from intestinal tract	0.68 g	60 mg/dL	
Uric acid	Breakdown of purines	0.53 g	40 mg/dL	Increases in gout, liver diseases
Hippuric acid	Breakdown of dietary toxins	4.2 mg	350 μg/dL	
Urobilin	Urobilinogens absorbed at colon	1.5 mg	125 μg/dL	Gives urine its yellow color
Bilirubin	Hemoglobin breakdown product	0.3 mg	20 μg/dL	Increase may indicate problem with liver elimination or excess production; causes yellowing of skin and mucous membranes in jaundice
NUTRIENTS AND METABOLITES				
Carbohydrates		0.11 g	9 μg/dL	Primarily glucose; *glycosuria* develops if T_m is exceeded
Ketone bodies		0.21 g	17 μg/dL	Ketonuria may occur during postabsorptive state
Lipids		0.02 g	0.002 mg/dL	May increase in some kidney diseases
Amino acids		2.25 g	188 μg/dL	Note relatively high loss compared with other metabolites due to low T_m; excess *(aminoaciduria)* indicates T_m problem
IONS				
Sodium		4.0 g	40–220 mEq/L	Varies with diet, urine pH, hormones, etc.
Potassium		2.0 g	25–100 mEq/L	Varies with diet, urine pH, hormones, etc.
Chloride		6.4 g	110–250 mEq/L	
Calcium		0.2 g	17 mg/dL	Hormonally regulated (PTH/CT)
Magnesium		0.15 g	13 mg/dL	
BLOOD CELLS†				
RBCs		130,000/day	100/mL	Excess *(hematuria)* indicates vascular damage in urinary system
WBCs		650,000/day	500/mL	Excess *(pyuria)* indicates renal infection or inflammation

*Representative values for a 70-kg (154-lb) male.
† Usually estimated by counting the cells in a sample of sediment after urine centrifugation.

Checkpoint

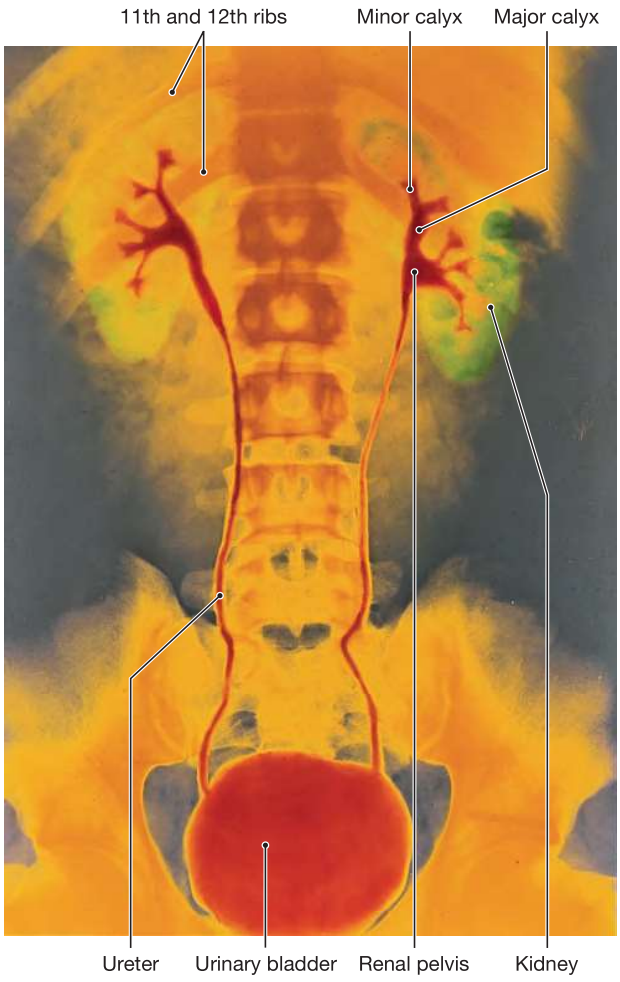
13. What effect would increased amounts of aldosterone have on the K^+ concentration in urine?
14. What effect would a decrease in the Na^+ concentration of filtrate have on the pH of tubular fluid?
15. How would the lack of juxtamedullary nephrons affect the volume and osmotic concentration of urine?
16. Why does a decrease in the amount of Na^+ in the distal convoluted tubule lead to an increase in blood pressure?

See the blue Answers tab at the back of the book.

26-6 Urine is transported via the ureters, stored in the bladder, and eliminated through the urethra, aided by the micturition reflex

Filtrate modification and urine production end when the fluid enters the renal pelvis. The urinary tract (the ureters, urinary bladder, and urethra) transports, stores, and eliminates urine. A **pyelogram** (PĪ-el-ō-gram) is an image of the urinary system (**Figure 26–17**). It is obtained by taking an x-ray of the kidneys

Figure 26–17 A Pyelogram. This posterior view of urinary system structures was color-enhanced. ATLAS: Plate 62b



after a radiopaque dye has been administered intravenously. Such an image provides an orientation to the relative sizes and positions of the main structures. Note that the sizes of the minor and major calyces, the renal pelvis, the ureters, the urinary bladder, and the proximal portion of the urethra are somewhat variable. These regions are lined by a *transitional epithelium* that can tolerate cycles of distension and contraction without damage. ↩ p. 116

The Ureters

The ureters are a pair of muscular tubes that extend from the kidneys to the urinary bladder—a distance of about 30 cm (12 in.). Each ureter begins at the funnel-shaped renal pelvis (**Figure 26–4**). The ureters extend inferiorly and medially, passing over the anterior surfaces of the *psoas major muscles* (**Figure 26–3**). The ureters are retroperitoneal and are firmly attached to the posterior abdominal wall. The paths taken by the ureters in men and women are different, due to variations in the nature, size, and position of the reproductive organs. In males, the base of the urinary bladder lies between the rectum and the pubic symphysis (**Figure 26–18a**). In females, the base of the urinary bladder sits inferior to the uterus and anterior to the vagina (**Figure 26–18b**).

The ureters penetrate the posterior wall of the urinary bladder without entering the peritoneal cavity. They pass through the bladder wall at an oblique angle. The **ureteral openings** are slit-like rather than rounded (**Figure 26–18c**). This shape helps prevent the backflow of urine toward the ureter and kidneys when the urinary bladder contracts.

Histology of the Ureters

The wall of each ureter consists of three layers (**Figure 26–19a**): (1) an inner mucosa, made up of a transitional epithelium and the surrounding lamina propria; (2) a middle muscular layer made up of longitudinal and circular bands of smooth muscle; and (3) an outer connective tissue layer that is continuous with the fibrous capsule and peritoneum. About every 30 seconds, a peristaltic contraction begins at the renal pelvis. As it sweeps along the ureter, it forces urine toward the urinary bladder.

The Urinary Bladder

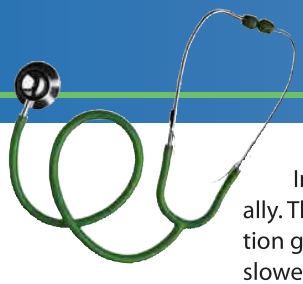
The urinary bladder is a hollow, muscular organ that serves as a temporary reservoir for urine (**Figure 26–18c**). The dimensions of the urinary bladder vary with its state of distension. A full urinary bladder can contain as much as a liter of urine.

A layer of peritoneum covers the superior surfaces of the urinary bladder. Several peritoneal folds assist in stabilizing its position. The **median umbilical ligament** extends from the anterior, superior border toward the umbilicus (navel). The **lateral umbilical ligaments** pass along the sides of the bladder to the umbilicus. These fibrous cords are the vestiges of the two *umbilical arteries*, which supplied blood to the placenta during embryonic and fetal development. ↩ p. 755 The urinary bladder's posterior, inferior, and anterior surfaces lie outside the peritoneal cavity. In these areas, tough ligamentous bands anchor the urinary bladder to the pelvic and pubic bones.

In sectional view, the mucosa lining the urinary bladder is usually thrown into folds, or **rugae**, that disappear as the bladder fills. The triangular area bounded by the openings of the ureters and the entrance to the urethra makes up a region called the **trigone** (TRĪ-gōn) of the urinary bladder. There, the mucosa is smooth and very thick. The trigone acts as a funnel that channels urine into the urethra when the urinary bladder contracts.

The urethral entrance lies at the apex of the trigone, at the most inferior point in the urinary bladder. The region surrounding the urethral opening is known as the **neck** of the urinary bladder. It contains a muscular **internal urethral sphincter.** The smooth muscle fibers of this sphincter provide involuntary control over the discharge of urine from the blad-

Clinical Note



Renal Failure and Kidney Transplantation

Waiting lists outpace organ donations

Renal failure occurs when the kidneys become unable to perform the excretory functions needed to maintain homeostasis. When kidney filtration slows for any reason, urine production declines. As the decline continues, signs and symptoms of renal failure appear because water, ions, and metabolic wastes are retained. Virtually all systems in the body are affected. Fluid balance, pH, muscular contraction, metabolism, and digestion are disturbed. The individual generally becomes hypertensive; anemia develops due to a decline in erythropoietin production; and CNS problems can lead to sleeplessness, seizures, delirium, and even coma.

Acute renal failure occurs when renal ischemia, urinary obstruction, trauma, or exposure to nephrotoxic drugs causes filtration to slow suddenly or stop. The reduction in kidney function takes place over a few days and may persist for weeks. Sensitized individuals can also develop acute renal failure after an allergic response to antibiotics or anesthetics. Most deaths associated with acute renal failure are caused by the underlying non-renal disease. With supportive treatment, the kidneys may regain partial or complete function. (With supportive treatment, the mortality rate is approximately 50 percent.)

In *chronic renal failure*, kidney function deteriorates gradually. The associated problems accumulate over years. This condition generally cannot be reversed. Its progression can only be slowed, and symptoms of *end-stage renal failure* eventually develop. The symptoms of end-stage and acute renal failure can be relieved by *hemodialysis*, a treatment that "cleanses" the blood by serving as a substitute for normal kidney functioning. However, this treatment is not a cure.

Probably the most satisfactory solution to the problem of end-stage renal failure, in terms of overall quality of life, is **kidney transplantation.** This procedure involves implanting a new kidney from a living donor or a cadaver. Of the 16,829 kidneys transplanted in 2009, 6387 came from living donors. The rest came from cadavers. In 2010, 91,294 people were on the kidney waiting list. The recipient's nonfunctioning kidney(s) may be removed, especially if an infection is present. The transplanted kidney and ureter are usually placed retroperitoneally in the pelvic cavity (within the iliac fossa). The ureter is connected to the recipient's urinary bladder.

The success rate for kidney transplantation varies, depending on how aggressively the recipient's T cells attack the donated organ and whether infection develops. The one-year success rate is now 89 percent when a cadaver kidney is used, and 95.1 percent when the kidney comes from a living donor. The use of kidneys from close relatives significantly improves the chances that the transplant will succeed. Immunosuppressive drugs are given to reduce tissue rejection. Unfortunately, this treatment also lowers the recipient's resistance to infection or cancer.

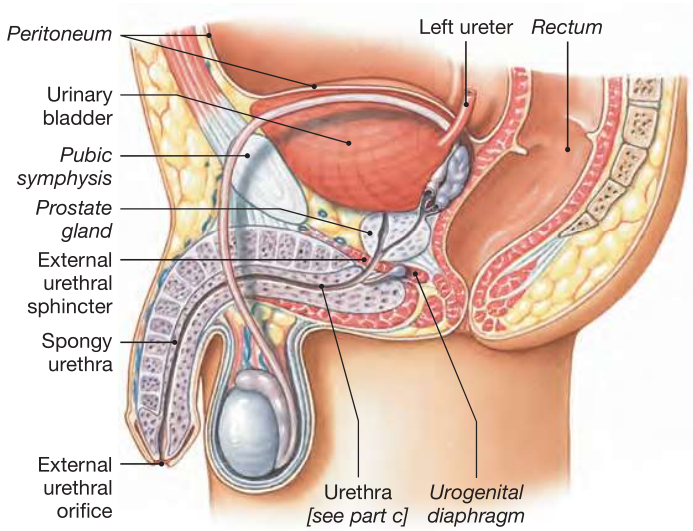
der. The urinary bladder is innervated by postganglionic fibers from ganglia in the hypogastric plexus and by parasympathetic fibers from intramural ganglia that are controlled by branches of the pelvic nerves.

Histology of the Urinary Bladder

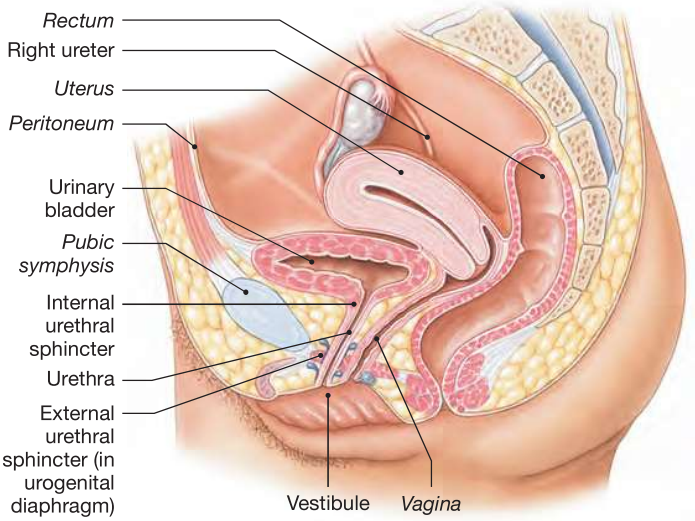
The wall of the urinary bladder contains mucosa, submucosa, and muscularis layers (**Figure 26–19b**). The muscularis layer consists of inner and outer layers of longitudinal smooth muscle, with a circular layer between the two. Together, these layers form the powerful **detrusor** (de-TROO-sor) **muscle** of the urinary bladder. When this muscle contracts, it compresses the urinary bladder and expels urine into the urethra.

The Urethra

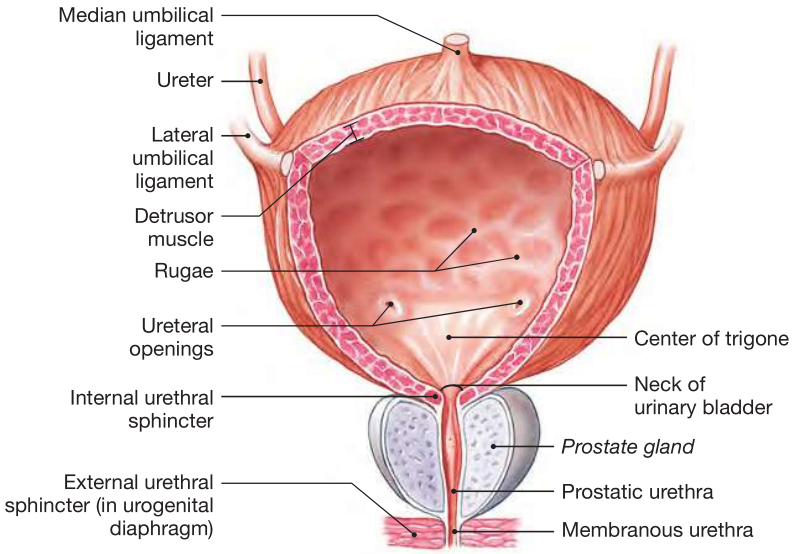
The urethra extends from the neck of the urinary bladder and transports urine to the exterior of the body. The urethrae of males and females differ in length and in function. In males, the urethra extends from the neck of the urinary bladder to the tip of the penis (**Figure 26–18a,c**). This distance may be



a Male



b Female



c Urinary bladder in male

Figure 26–18 Organs for the Conduction and Storage of Urine. ATLAS: Plates 62b; 64; 65

18–20 cm (7–8 in.). We can subdivide the male urethra into three portions: the prostatic urethra, the membranous urethra, and the spongy urethra. The **prostatic urethra** passes through the center of the prostate gland. The **membranous urethra** includes the short segment that penetrates the *urogenital diaphragm*, the muscular floor of the pelvic cavity. The **spongy urethra,** or *penile* (PĒ-nīl) *urethra*, extends from the distal border of the urogenital diaphragm to the external opening, or **external urethral orifice,** at the tip of the penis. In females, the urethra is very short. It extends 3–5 cm (1–2 in.) from the bladder to the vestibule (**Figure 26–18b**). The external urethral orifice is near the anterior wall of the vagina.

In both sexes, where the urethra passes through the urogenital diaphragm, a circular band of skeletal muscle forms the **external urethral sphincter.** This muscular band acts as a valve. The external urethral sphincter is under voluntary control through the perineal branch of the pudendal nerve. This sphincter has a resting muscle tone and must be voluntarily relaxed to permit micturition.

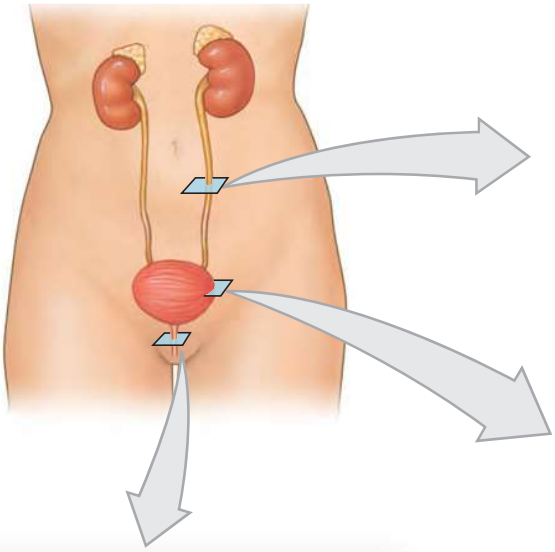
Tips & Tricks

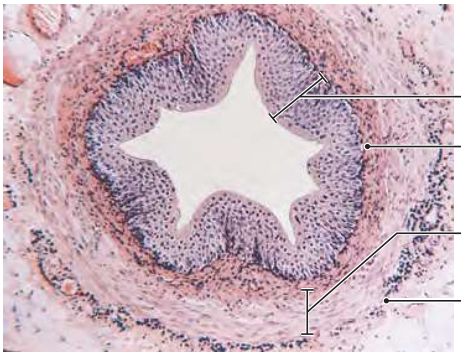
To remember that the urethra is the urinary tract's conduit to the exterior, proclaim, "Eureka! Your urine! It's coming out the urethra!"

Histology of the Urethra

The urethral lining consists of a stratified epithelium that varies from transitional epithelium at the neck of the urinary bladder, to stratified columnar epithelium at the midpoint, to stratified squamous epithelium near the external urethral orifice. The lamina propria is thick and elastic. The mucosa is folded into longitudinal creases (**Figure 26–19c**). Mucin-secreting cells are located in the epithelial pockets. In males, the epithelial mucous glands may form tubules that extend into the lamina propria. Connective tissues of the lamina propria anchor the urethra to surrounding structures. In females, the lamina propria contains an extensive network of veins. Concentric layers of smooth muscle surround the entire complex.

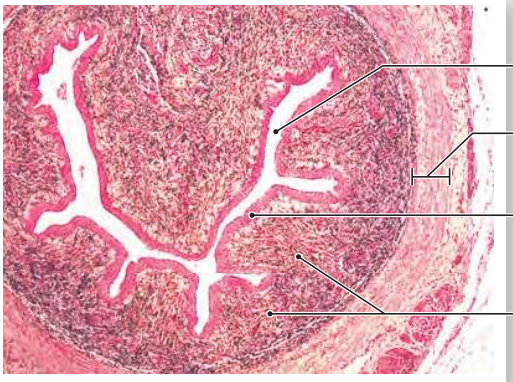
Figure 26–19 The Histology of the Organs That Collect and Transport Urine.





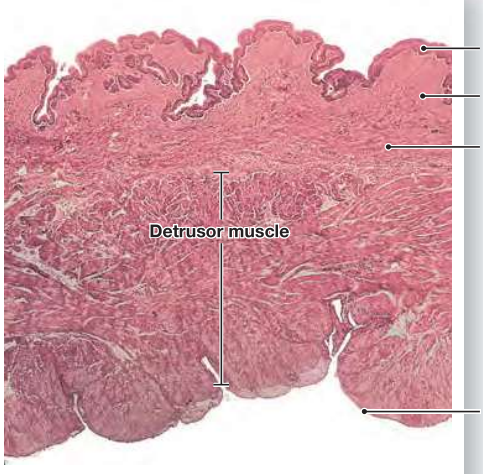
Ureter LM × 65

a A transverse section through the ureter



Female urethra LM × 50

c A transverse section through the female urethra. A thick layer of smooth muscle surrounds the lumen.



Urinary bladder LM × 36

b The wall of the urinary bladder

26

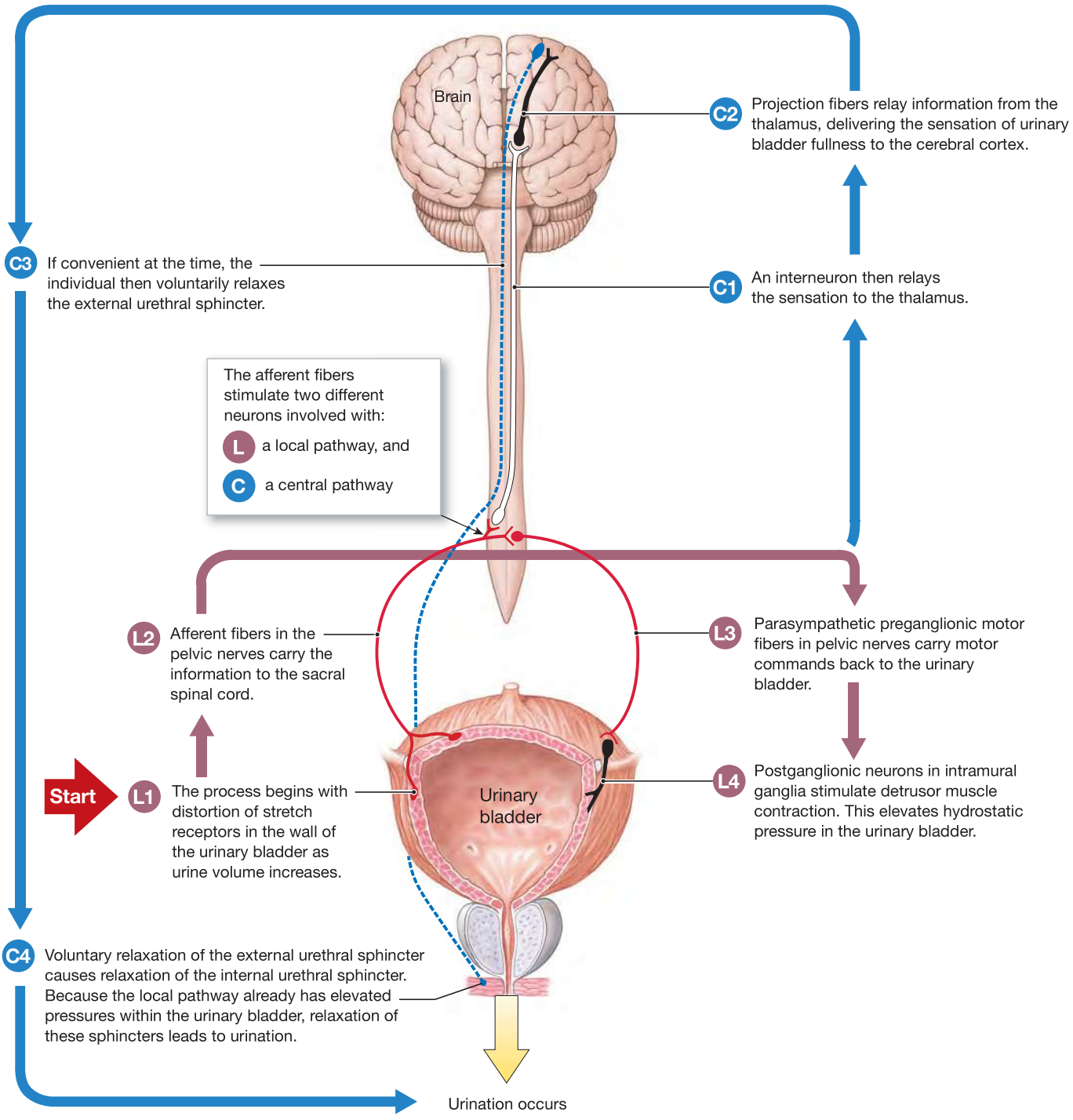
The Micturition Reflex and Urination

As we have seen, urine reaches the urinary bladder by peristaltic contractions of the ureters. The process of urination is coordinated by the **micturition reflex** (Figure 26–20).

As the bladder fills with urine, stretch receptors in the bladder wall are stimulated. Afferent fibers in the pelvic nerves carry impulses to the sacral spinal cord. The increased level of activity in the fibers (1) facilitates parasympathetic motor neurons in the sacral spinal cord and (2) stimulates interneurons that relay sensations to the thalamus and then, through projection fibers, to the cerebral cortex. As a result, you become aware of the fluid pressure in your urinary bladder.

The urge to urinate generally appears when your bladder contains about 200 mL of urine. As Figure 26–20 shows, the micturition reflex begins when the stretch receptors provide adequate stimulation to parasympathetic preganglionic motor neurons. A further increase in bladder volume begins the cycle again, usually within an hour. Each increase in urinary volume leads to an increase in stretch receptor stimulation that makes the sensation more acute. Once the volume exceeds 500 mL, the bladder contractions triggered by the micturition reflex may generate enough pressure to force open the internal urethral sphincter. This opening leads to a reflexive relaxation of the external urethral sphincter. Urination takes place despite voluntary opposition or potential inconvenience. At the end of a typical micturition, less than 10 mL of urine remains in the bladder.

Figure 26–20 The Micturition Reflex.



Infants lack voluntary control over urination, because the necessary corticospinal connections have yet to be established. Accordingly, "toilet training" before age 2 often involves training the parent to anticipate the timing of the reflex rather than training the child to exert conscious control.

Incontinence (in-KON-ti-nens) is the inability to control urination voluntarily. Trauma to the internal or external urethral sphincter can contribute to incontinence in otherwise healthy adults. For example, some mothers develop *stress incontinence* if childbirth overstretches and damages the sphincter muscles. In

Clinical Note — Urinary Obstruction

A different kind of stone blasting

Local blockages of the collecting ducts or ureters can result from *casts*—small blood clots, epithelial cells, lipids, or other materials that form in the collecting ducts. Casts are commonly eliminated in urine and are visible in microscopic analyses of urine samples. **Renal calculi** (KAL-kū-lī), or *kidney stones*, form within the urinary tract from calcium deposits, magnesium salts, or crystals of uric acid. The condition is called *nephrolithiasis* (nef-rō-li-THĪ-uh-sis; *nephros*, kidney; *lithos*, stone). The blockage of the ureter by a stone or by other means (such as external compression) creates **urinary obstruction.** This problem is serious because, in addition to causing pain, it reduces or prevents filtration in the affected kidney by elevating the capsular hydrostatic pressure.

Calculi are generally visible on an x-ray. If peristalsis and fluid pressures cannot dislodge them, they must be either surgically removed or destroyed. One nonsurgical procedure involves disintegrating the stones with a *lithotripter*, a device originally developed from machines used to de-ice airplane wings. Lithotripters focus sound waves on the stones, breaking them into smaller fragments that can be passed in the urine. Another nonsurgical approach is the insertion of a catheter armed with a laser that can shatter calculi with intense light beams.

this condition, elevated intra-abdominal pressures—caused, for example, by a cough or sneeze—can overwhelm the sphincter muscles, causing urine to leak out. Incontinence can also develop in older individuals due to a general loss of muscle tone.

Damage to the central nervous system, the spinal cord, or the nerve supply to the urinary bladder or external urethral sphincter can also produce incontinence. For example, incontinence commonly accompanies Alzheimer disease or spinal cord damage. In most cases, the affected individual develops an *automatic bladder*. The micturition reflex remains intact, but voluntary control of the external urethral sphincter is lost, so the person cannot prevent the reflexive emptying of the urinary bladder. Damage to the pelvic nerves can abolish the micturition reflex entirely, because those nerves carry both afferent and efferent fibers of this reflex arc. The urinary bladder then becomes greatly distended with urine. It remains filled to capacity while the excess urine flows into the urethra in an uncontrolled stream. The insertion of a catheter is often needed to facilitate the discharge of urine.

Checkpoint

17. **What effect would a high-protein diet have on the composition of urine?**
18. **Obstruction of a ureter by a kidney stone would interfere with the flow of urine between which two points?**
19. **The ability to control the micturition reflex depends on your ability to control which muscle?**

See the blue Answers tab at the back of the book.

26-7 Age-related changes affect kidney function and the micturition reflex

In general, aging is associated with an increased incidence of kidney problems. One example—*nephrolithiasis*, the formation of calculi, or kidney stones—is described in the Urinary Obstruction Clinical Note. Other age-related changes in the urinary system include the following:

- *A Decline in the Number of Functional Nephrons.* The total number of kidney nephrons drops by 30–40 percent between ages 25 and 85.
- *A Reduction in the GFR.* This reduction results from fewer glomeruli, cumulative damage to the filtration apparatus in the remaining glomeruli, and diminished renal blood flow.
- *A Reduced Sensitivity to ADH.* With age, the distal portions of the nephron and collecting system become less responsive to ADH. Water and sodium ions are reabsorbed at a reduced rate, and more sodium ions are lost in urine.
- *Problems with the Micturition Reflex.* Three factors are involved in such problems: (1) The sphincter muscles lose muscle tone and become less effective at voluntarily retaining urine. This leads to incontinence, often involving a slow leakage of urine. (2) The ability to control micturition can be lost due to a stroke, Alzheimer disease,

or other CNS problems affecting the cerebral cortex or hypothalamus. (3) In males, *urinary retention* may develop if the prostate gland enlarges and compresses the urethra, restricting the flow of urine.

Checkpoint

20. **List four age-related changes in the urinary system.**
21. **Define nephrolithiasis.**
22. **Describe how incontinence may develop in an elderly person.**

See the blue Answers tab at the back of the book.

26-8 The urinary system is one of several body systems involved in waste excretion

The urinary system excretes wastes produced by other body systems, but it is not the only organ system involved in excretion. Indeed, the urinary, integumentary, respiratory, and digestive systems are together regarded as an anatomically diverse **excretory system** whose components perform all the excretory functions that affect the composition of body fluids:

- *Integumentary System.* Water losses and electrolyte losses in sensible perspiration can affect the volume and composition of the plasma. The effects are most apparent when losses are extreme, such as during peak sweat production. Small amounts of metabolic wastes, including urea, also are eliminated in perspiration.
- *Respiratory System.* The lungs remove the carbon dioxide generated by cells. Small amounts of other compounds, such as acetone and water, evaporate into the alveoli and are eliminated when you exhale.
- *Digestive System.* The liver excretes small amounts of metabolic waste products in bile. You lose a variable amount of water in feces.

These excretory activities have an impact on the composition of body fluids. The respiratory system, for example, removes carbon dioxide from the body. Note that the excretory functions of these systems are not regulated as closely as are those of the kidneys. Under normal circumstances, the effects of integumentary and digestive excretory activities are minor compared with those of the urinary system.

Figure 26–21 summarizes the functional relationships between the urinary system and other systems. We explore many of these relationships further in Chapter 27 when we consider major aspects of fluid, pH, and electrolyte balance.

Checkpoint

23. **Identify the role the urinary system plays for all other body systems.**
24. **Name the components of the body's excretory system.**

See the blue Answers tab at the back of the book.

Related Clinical Terms

azotemia: The condition characterized by excessive urea or other nitrogen-containing compounds in the blood.
continuous ambulatory peritoneal dialysis (CAPD): A maintenance system of peritoneal dialysis in which a catheter is fixed in place in the patient to permit fluid to drain into and out of the peritoneal cavity by gravity.
cystocele: Condition that occurs when the supportive tissue between a woman's bladder and vaginal wall weakens, stretches, and allows the bladder to bulge into the vagina.
cystoscopy: Diagnostic procedure using an optical instrument called a cystoscope that is inserted through the urethra to visually examine the bladder and lower urinary tract, to collect urine samples, or to view the prostate gland.
enuresis: Involuntary urination, especially that of a child while asleep.
glucosuria: Condition characterized by the excretion of glucose in the urine, often in elevated quantities. This condition is also called glycosuria.
hemodialysis: A technique in which an artificial membrane is used to regulate the composition of blood when kidney function is seriously impacted.
nephroptosis: Condition in which the kidney is displaced downward from its usual and normal position; also called a floating kidney.
nephrotic syndrome: A kidney disorder that causes one to excrete excessive protein in the urine.
nephrotoxin: A toxin that has a specific harmful effect on the kidney.
nocturnal enuresis: Involuntary urination while asleep; also called nocturia or bedwetting.
polycystic kidney disease: An inherited abnormality that affects the development and structure of kidney tubules.
shock-wave lithotripsy: A noninvasive technique used to pulverize kidney stones by passing high-pressure shock waves through a water-filled tub in which the patient sits.
urologist: Physician who specializes in functions and disorders of the urinary system.

SYSTEM INTEGRATOR

Body System → Urinary System

Urinary System → Body System

Integumentary
Sweat glands assist in elimination of water and solutes, especially sodium and chloride ions; keratinized epidermis prevents excessive fluid loss through skin surface; epidermis produces vitamin D_3, important for the renal production of calcitriol

Kidneys eliminate nitrogenous wastes; maintain fluid, electrolyte, and acid–base balance of blood that nourishes the skin
Integumentary Page 165

Skeletal
Axial skeleton provides some protection for kidneys and ureters; pelvis protects urinary bladder and proximal portion of urethra

Conserves calcium and phosphate needed for bone growth
Skeletal Page 275

Muscular
Sphincter controls urination by closing urethral opening; muscle layers of trunk provide some protection for urinary organs

Removes waste products of protein metabolism; assists in regulation of calcium and phosphate concentrations
Muscular Page 369

Nervous
Adjusts renal blood pressure; monitors distension of urinary bladder and controls urination

Kidneys eliminate nitrogenous wastes; maintain fluid, electrolyte, and acid–base balance of blood, which is critical for neural function
Nervous Page 543

Endocrine
Aldosterone and ADH adjust rates of fluid and electrolyte reabsorption by kidneys

Kidney cells release renin when local blood pressure drops and erythropoietin (EPO) when renal oxygen levels fall
Endocrine Page 632

Cardiovascular
Delivers blood to glomerular capillaries, where filtration occurs; accepts fluids and solutes reabsorbed during urine production

Releases renin to elevate blood pressure and erythropoietin to accelerate red blood cell production
Cardiovascular Page 759

Lymphatic
Provides adaptive defenses against urinary tract infections

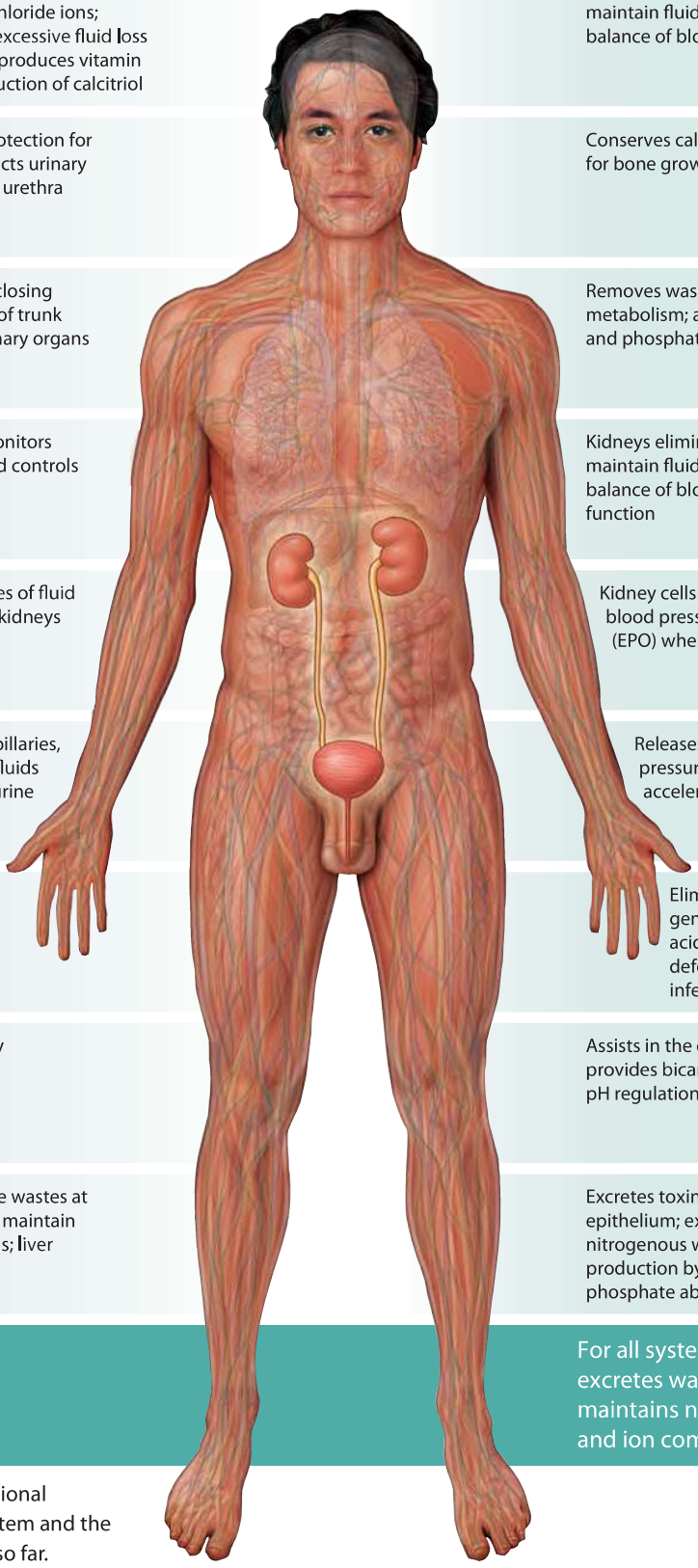
Eliminates toxins and wastes generated by cellular activities; acid pH of urine provides innate defense against urinary tract infections
Lymphatic Page 807

Respiratory
Assists in the regulation of pH by eliminating carbon dioxide

Assists in the elimination of carbon dioxide; provides bicarbonate buffers that assist in pH regulation
Respiratory Page 857

Digestive
Absorbs water needed to excrete wastes at kidneys; absorbs ions needed to maintain normal body fluid concentrations; liver removes bilirubin

Excretes toxins absorbed by the digestive epithelium; excretes bilirubin and nitrogenous wastes from the liver; calcitriol production by kidneys aids calcium and phosphate absorption along digestive tract
Digestive Page 910



The URINARY System

For all systems, the urinary system excretes waste products and maintains normal body fluid pH and ion composition.

Reproductive Page 1072

Figure 26–21 diagrams the functional relationships between the urinary system and the other body systems we have studied so far.

Chapter Review

Study Outline

26-1 Consisting of the kidneys, ureters, urinary bladder, and urethra, the urinary system has three primary functions p. 954

1. The three major functions of the **urinary system** are *excretion*, the removal of organic waste products from body fluids; *elimination*, the discharge of these waste products into the environment; and homeostatic regulation of the volume and solute concentration of blood plasma. Other homeostatic functions include regulating blood volume and pressure by adjusting the volume of water lost and releasing hormones; regulating plasma concentrations of ions; helping to stabilize blood pH; conserving nutrients; assisting the liver in detoxifying poisons; and, during starvation, deaminating amino acids so that they can be catabolized by other tissues.
2. The urinary system includes the **kidneys,** the **ureters,** the **urinary bladder,** and the **urethra.** The kidneys produce **urine,** a fluid containing water, ions, and soluble compounds. During **urination (micturition),** urine is forced out of the body. *(Figure 26–1)*

26-2 Kidneys are highly vascular structures containing functional units called nephrons, which perform filtration, reabsorption, and secretion p. 954

3. The left kidney extends superiorly slightly more than the right kidney. Both kidneys and the adrenal gland that overlies each are retroperitoneal. *(Figures 26–1, 26–2, 26–3)*
4. The **hilum,** a medial indentation, provides entry for the *renal artery* and *renal nerves* and exit for the *renal vein* and the ureter. *(Figures 26–3, 26–4)*
5. The superficial portion of the kidney, the cortex, surrounds the **medulla.** The ureter communicates with the **renal pelvis,** a chamber that branches into two **major calyces.** Each major calyx is connected to four or five **minor calyces,** which enclose the **renal papillae.** *(Figure 26–4)*
6. The blood supply to the kidneys includes the **renal, segmental, interlobar, arcuate,** and **cortical radiate arteries.** *(Figure 26–5)*
7. The **renal nerves,** which innervate the kidneys and ureters, are dominated by sympathetic postganglionic fibers.
8. The **nephron** is the basic functional unit in the kidney. It consists of the **renal corpuscle** and **renal tubule.** The renal tubule is long and narrow and divided into the *proximal convoluted tubule*, the *nephron loop*, and the *distal convoluted tubule*. **Filtrate** is produced at the renal corpuscle. The nephron empties **tubular fluid** into the **collecting system,** consisting of **collecting ducts** and **papillary ducts.** *(Figures 26–6, 26–7)*
9. Nephrons produce filtrate; reabsorb organic nutrients, water, and ions; and secrete into the tubular fluid various waste products. *(Table 26–1)*
10. Roughly 85 percent of the nephrons are **cortical nephrons,** located in the renal cortex. **Juxtamedullary nephrons** are closer to the renal medulla, with their *nephron loops* extending deep into the **renal pyramids.** *(Figure 26–7)*
11. Blood travels from the efferent arteriole to the **peritubular capillaries** and the **vasa recta.** *(Figure 26–7)*
12. The renal tubule begins at the renal corpuscle, which includes a knot of intertwined capillaries called the **glomerulus,** surrounded by the **glomerular capsule.** Blood arrives at the glomerulus via the **afferent arteriole** and departs in the **efferent arteriole.** *(Figure 26–8)*
13. At the glomerulus, **podocytes** cover the **dense layer** of the capillaries that project into the **capsular space.** The **pedicels** of the podocytes are separated by narrow **filtration slits. Mesangial cells** lie between adjacent capillaries and control capillary diameter. *(Figure 26–8)*
14. The **proximal convoluted tubule (PCT)** actively reabsorbs nutrients, plasma proteins, and ions from the filtrate. These substances are released into the **peritubular fluid,** which surrounds the nephron. *(Figure 26–6)*
15. The **nephron loop,** also called the **loop of Henle,** includes a **descending limb** and an **ascending limb.** Each limb contains a **thick segment** and a **thin segment.** The ascending limb delivers fluid to the **distal convoluted tubule (DCT),** which actively secretes ions, toxins, and drugs, and reabsorbs sodium ions from the tubular fluid. *(Figures 26–6, 26–7)*

26-3 Different segments of the nephron form urine by filtration, reabsorption, and secretion p. 963

16. Urine production maintains homeostasis by regulating blood volume and composition. In the process, organic waste products—notably urea, creatinine, and uric acid—are excreted.
17. Urine formation involves **filtration, reabsorption,** and **secretion.**
18. Four types of *carrier-mediated transport (facilitated diffusion, active transport, cotransport,* and *countertransport)* are involved in modifying filtrate. The saturation limit of a carrier protein is its **transport maximum,** which determines the **renal threshold**—the plasma concentration at which various compounds will appear in urine. *(Table 26–2)*
19. The transport maximum determines the renal threshold for the reabsorption of substances in tubular fluid. *(Table 26–3)*
20. Most regions of the nephron perform a combination of reabsorption and secretion. *(Figure 26–9; Table 26–4)*

26-4 Hydrostatic and colloid osmotic pressures influence glomerular filtration pressure, which in turn affects the glomerular filtration rate p. 968

21. **Glomerular filtration** occurs as fluids move across the wall of the glomerulus into the capsular space in response to the **glomerular hydrostatic pressure (GHP)**—the hydrostatic (blood) pressure in the glomerular capillaries. This movement is opposed by the **capsular hydrostatic pressure (CsHP)** and by the **blood colloid osmotic pressure (BCOP).** The **net filtration pressure (NFP)** at the glomerulus is the difference between the blood pressure and the opposing capsular and osmotic pressures. *(Figure 26–10)*
22. The **glomerular filtration rate (GFR)** is the amount of filtrate produced in the kidneys each minute. Any factor that alters the filtration pressure acting across the glomerular capillaries will change the GFR and affect kidney function.

23. A drop in filtration pressures stimulates the **juxtaglomerular complex (JGC)** to release renin and erythropoietin. *(Figure 26–11)*
24. Sympathetic activation (1) produces a powerful vasoconstriction of the afferent arterioles, decreasing the GFR and slowing the production of filtrate; (2) alters the GFR by changing the regional pattern of blood circulation; and (3) stimulates the release of renin by the juxtaglomerular complex. *(Figure 26–11)*

26-5 Countercurrent multiplication and the influence of antidiuretic hormone and aldosterone affect reabsorption and secretion p. 972

25. Glomerular filtration produces a filtrate with a composition similar to blood plasma, but with few, if any, plasma proteins.
26. The cells of the PCT normally reabsorb sodium and other ions, water, and almost all the organic nutrients that enter the filtrate. These cells also secrete various substances into the tubular fluid. *(Figure 26–12)*
27. Water and ions are reclaimed from tubular fluid by the nephron loop. A concentration gradient in the renal medulla encourages the osmotic flow of water out of the tubular fluid. The **countercurrent multiplication** between the ascending and descending limbs of the nephron loop helps create the osmotic gradient in the medulla. As water is lost by osmosis and the volume of tubular fluid decreases, the urea concentration rises. *(Figure 26–13)*
28. The DCT performs final adjustments by actively secreting or absorbing materials. Sodium ions are actively absorbed, in exchange for potassium or hydrogen ions discharged into tubular fluid. Aldosterone secretion increases the rate of sodium reabsorption and potassium loss. *(Figure 26–14)*
29. The amount of water and solutes in the tubular fluid of the collecting ducts is further regulated by aldosterone and ADH secretions. *(Figure 26–14)*
30. Urine volume and osmotic concentration are regulated by controlling water reabsorption. Precise control over this occurs via *facultative water reabsorption*. *(Figure 26–15)*
31. Normally, the removal of solutes and water by the vasa recta precisely balances the rates of reabsorption and osmosis in the renal medulla.
32. More than 99 percent of the filtrate produced each day is reabsorbed before reaching the renal pelvis. *(Table 26–5)*
33. *Urinalysis* is the chemical and physical analysis of a urine sample. *(Table 26–6)*
34. Each segment of the nephron and collecting system contributes to the production of concentrated urine. *(Spotlight Figure 26–16; Table 26–4)*

26-6 Urine is transported via the ureters, stored in the bladder, and eliminated through the urethra, aided by the micturition reflex p. 984

35. Urine production ends when tubular fluid enters the renal pelvis. The rest of the urinary system transports, stores, and eliminates urine. *(Figure 26–17)*
36. The ureters extend from the renal pelvis to the urinary bladder. Peristaltic contractions by smooth muscles move the urine along the tract. *(Figures 26–18, 26–19)*
37. The urinary bladder is stabilized by the **middle umbilical ligament** and the **lateral umbilical ligaments.** Internal features include the **trigone**, the **neck,** and the **internal urethral sphincter.** The mucosal lining contains prominent **rugae** (folds). Contraction of the **detrusor muscle** compresses the urinary bladder and expels urine into the urethra. *(Figures 26–18, 26–19)*
38. In both sexes, where the urethra passes through the *urogenital diaphragm*, a circular band of skeletal muscles forms the **external urethral sphincter,** which is under voluntary control. *(Figure 26–18)*
39. Urination is coordinated by the **micturition reflex**, which is initiated by stretch receptors in the wall of the urinary bladder. Voluntary urination involves coupling this reflex with the voluntary relaxation of the external urethral sphincter, which allows the opening of the **internal urethral sphincter.** *(Figure 26–20)*

26-7 Age-related changes affect kidney function and the micturition reflex p. 990

40. Aging is generally associated with increased kidney problems. Age-related changes in the urinary system include (1) declining numbers of functional nephrons, (2) reduced GFR, (3) reduced sensitivity to ADH, and (4) problems with the micturition reflex. (**Urinary retention** may develop in men whose prostate gland is enlarged.)

26-8 The urinary system is one of several body systems involved in waste excretion p. 991

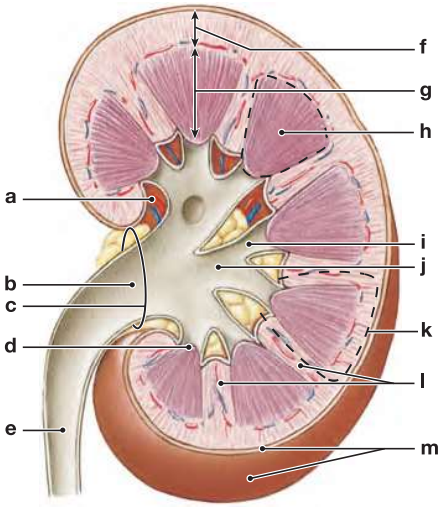
41. The urinary system is the major component of an anatomically diverse *excretory system* that includes the integumentary system, the respiratory system, and the digestive system.

Review Questions

See the blue Answers tab at the back of the book.

LEVEL 1 Reviewing Facts and Terms

1. Identify the structures of the kidney in the following diagram.



(a) _____
(b) _____
(c) _____
(d) _____
(e) _____
(f) _____
(g) _____
(h) _____
(i) _____
(j) _____
(k) _____
(l) _____
(m) _____

2. The basic functional unit of the kidney is the
   (a) nephron.
   (b) renal corpuscle.
   (c) glomerulus.
   (d) nephron loop.
   (e) filtration unit.
3. The process of urine formation involves all of the following, *except*
   (a) filtration of plasma.
   (b) reabsorption of water.
   (c) reabsorption of certain solutes.
   (d) secretion of wastes.
   (e) secretion of excess lipoprotein and glucose molecules.
4. The glomerular filtration rate is regulated by all of the following, *except*
   (a) autoregulation.
   (b) sympathetic neural control.
   (c) cardiac output.
   (d) angiotensin II.
   (e) the hormone ADH.
5. The distal convoluted tubule is an important site for
   (a) active secretion of ions.
   (b) active secretion of acids and other materials.
   (c) selective reabsorption of sodium ions from the tubular fluid.
   (d) all of these.
6. Changing the diameters of the afferent and efferent arterioles to alter the GFR can be an example of _____ regulation.
   (a) hormonal
   (b) autonomic
   (c) autoregulation
   (d) a, b, and c
7. What is the primary function of the urinary system?
8. What structures are components of the urinary system?
9. Trace the pathway of the protein-free filtrate from where it is produced in the renal corpuscle until it drains into the renal pelvis in the form of urine. (Use arrows to indicate the direction of flow.)
10. Name the segments of the nephron distal to the renal corpuscle, and state the function(s) of each.
11. What is the function of the juxtaglomerular complex?
12. Using arrows, trace a drop of blood from its entry into the renal artery until its exit via a renal vein.
13. Name and define the three distinct processes involved in the production of urine.
14. What are the primary effects of angiotensin II on kidney function and regulation?
15. Which parts of the urinary system are responsible for the transport, storage, and elimination of urine?

LEVEL 2 Reviewing Concepts

16. When the renal threshold for a substance exceeds its tubular maximum,
   (a) more of the substance will be filtered.
   (b) more of the substance will be reabsorbed.
   (c) more of the substance will be secreted.
   (d) the amount of the substance that exceeds the tubular maximum will be found in the urine.
   (e) both a and d occur.
17. Sympathetic activation of nerve fibers in the nephron causes
   (a) the regulation of glomerular blood flow and pressure.
   (b) the stimulation of renin release from the juxtaglomerular complex.
   (c) the direct stimulation of water and Na^+ reabsorption.
   (d) all of these.
18. Sodium reabsorption in the DCT and in the cortical portion of the collecting system is accelerated by the secretion of
   (a) ADH.
   (b) renin.
   (c) aldosterone.
   (d) erythropoietin.
19. When ADH levels rise,
   (a) the amount of water reabsorbed increases.
   (b) the DCT becomes impermeable to water.
   (c) the amount of water reabsorbed decreases.
   (d) sodium ions are exchanged for potassium ions.

20. The control of blood pH by the kidneys during acidosis involves
    (a) the secretion of hydrogen ions and reabsorption of bicarbonate ions from the tubular fluid.
    (b) a decrease in the amount of water reabsorbed.
    (c) hydrogen ion reabsorption and bicarbonate ion loss.
    (d) potassium ion secretion.
21. How are proteins excluded from filtrate? Why is this important?
22. What interacting controls stabilize the glomerular filtration rate (GFR)?
23. What primary changes occur in the composition and concentration of filtrate as a result of activity in the proximal convoluted tubule?
24. Describe two functions of countercurrent multiplication in the kidney.
25. Describe the micturition reflex.

LEVEL 3 Critical Thinking and Clinical Applications

26. In a normal kidney, which of the following conditions would cause an increase in the glomerular filtration rate (GFR)?
    (a) constriction of the afferent arteriole
    (b) a decrease in the pressure of the glomerulus
    (c) an increase in the capsular hydrostatic pressure
    (d) a decrease in the concentration of plasma proteins in the blood
    (e) a decrease in the net glomerular filtration process
27. In response to *excess* water in the body,
    (a) antidiuretic hormone is secreted by the adenohypophysis.
    (b) the active transport mechanisms in the ascending limb of the nephron loop cease functioning.
    (c) the permeability of the distal convoluted tubules and collecting ducts to water is decreased.
    (d) the permeability of the ascending limb of the nephron loop is increased.
    (e) the glomerular filtration rate is reduced.
28. Sylvia is suffering from severe edema in her arms and legs. Her physician prescribes a diuretic (a substance that increases the volume of urine produced). Why might this help alleviate Sylvia's problem?
29. David's grandfather suffers from hypertension. His doctor tells him that part of his problem stems from renal arteriosclerosis. Why would this cause hypertension?
30. *Mannitol* is a sugar that is filtered, but not reabsorbed, by the kidneys. What effect would drinking a solution of mannitol have on the volume of urine produced?
31. The drug *Diamox* is sometimes used to treat mountain sickness. Diamox inhibits the action of carbonic anhydrase in the proximal convoluted tubule. Polyuria (the elimination of an unusually large volume of urine) is a side effect associated with the medication. Why does polyuria occur?

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