Chapter 26: The Urinary System

An Overview of the Urinary System, p. 952

Objective
1. Identify the components of the urinary system and describe the functions it performs.

**Figure 26-1**
- The urinary system 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.
- The excretory functions of the urinary system are performed by the two kidneys—organs that 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, to the urinary bladder, a muscular sac for temporary storage of urine. On leaving the urinary bladder, urine passes through the urethra, which conducts the urine to the exterior.
- The urinary bladder and the urethra are responsible for the elimination of urine, a process called urination or micturition. In this process, contraction of the muscular urinary bladder forces urine through the urethra and out of the body. In addition to removing waste products generated by cells throughout the body, the urinary system has several other essential homeostatic functions that are often overlooked, including 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 controlling the quantities lost in urine and controlling 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 excretion in urine while excreting organic waste products—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 break them down. These activities are carefully regulated to keep the composition of blood within acceptable limits.

The Kidneys, p. 952

Objectives
1. Describe the location and structural features of the kidneys.
2. Identify the major blood vessels associated with each kidney and trace the path of blood flow through a kidney.
3. Describe the structure of the nephron and outline the processes involved in the formation of urine.

**Figure 26-2**
- The kidneys are located on either side of the vertebral column, between vertebrae T12 and L3. The left kidney lies slightly superior to the right kidney. The superior surface of each kidney is capped by an adrenal gland. The kidneys and adrenal glands lie between the muscles of the dorsal body wall and the parietal peritoneum, in a retroperitoneal position.
- 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. Each kidney is protected and stabilized by three concentric layers of connective tissue:
  - The renal capsule, a layer of collagen fibers that covers the outer surface of the entire organ.
  - The adipose capsule, a thick layer of adipose tissue that surrounds the renal capsule.
The renal fascia, a dense, fibrous outer layer that anchors the kidney to surrounding structures. Collagen fibers extend outward from the renal capsule through the adipose capsule to this layer.

- 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. 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, and the point of exit for the renal vein and the ureter.

Sectional Anatomy of the Kidneys

Figure 26-3

Figure 26-4

- The fibrous renal capsule covering the outer surface of the kidney also lines the renal sinus, an internal cavity within the kidney.
- The renal capsule is bound to the outer surfaces of the structures within the renal sinus, stabilizing the positions of the ureter and of the renal blood vessels and nerves. 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 renal capsule. The cortex is reddish brown and granular.
- The renal medulla consists of 6 to 18 distinct conical or triangular structures called renal pyramids. The base of each pyramid abuts the cortex, and 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 production occurs in the renal lobes. Ducts within each renal papilla discharge urine into a cup-shaped drain called a minor calyx. Four or five minor calyces merge to form a major calyx, and two or three major calyces combine to form the renal pelvis, a large, funnelshaped chamber.
- The renal pelvis, which fills most of the renal sinus, is connected to the ureter, which drains the kidney. Urine production begins in microscopic, tubular structures called nephrons 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

Figure 26-5

- Your kidneys receive 20–25 percent of your total cardiac output. In normal, healthy individuals, about 1200 ml of blood flows through the kidneys each minute.
- Each kidney receives blood through a renal artery, which originates along the lateral surface of the abdominal aorta near the level of the superior mesenteric artery. As it enters the renal sinus, the renal artery provides blood to the segmental arteries.
- Segmental arteries further divide into a series of interlobar arteries, which radiate outward through the renal columns between the renal pyramids. The interlobar arteries supply blood to the arcuate arteries, which arch along the boundary between the cortex and medulla of the kidney.
- Each arcuate artery gives rise to a number of interlobular arteries, which supply the cortical portions of the adjacent renal lobes. Branching from each interlobular artery are numerous afferent arterioles, which deliver blood to the capillaries supplying individual nephrons.
- From the capillaries of the nephrons, blood enters a network of venules and small veins that converge on the interlobular veins. The interlobular veins deliver blood to arcuate veins; these 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. A
renal nerve enters each kidney at the hilum and follows the tributaries 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.

**The Nephron**

**Figure 26-6**

- Each nephron consists of a renal tubule and a renal corpuscle.
- The renal tubule is a long tubular passageway which may be 50 mm (1.97 in.) in length. It begins at the renal corpuscle, a spherical structure consisting of Bowman’s capsule, a cup-shaped chamber approximately 200 in diameter, and a capillary network known as the glomerulus.
- Blood arrives at the renal corpuscle by way of an afferent arteriole. This arteriole delivers blood to the glomerulus, which consists of about 50 intertwining capillaries. The glomerulus projects into Bowman’s capsule much as the heart projects into the pericardial cavity.
- Blood leaves the glomerulus in an efferent arteriole and flows into a network of capillaries, the peritubular capillaries, that surround the renal tubule. These capillaries in turn drain into small venules that return the blood to the venous system. The renal corpuscle is the site where the process of filtration occurs.
- 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. 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 is responsible for three crucial functions: (1) reabsorbing all the useful organic nutrients that enter the filtrate, (2) reabsorbing more than 90 percent of the water in the filtrate, and (3) secreting into the tubule any waste products that failed to enter the renal corpuscle through filtration at the glomerulus.
- The renal tubule has two convoluted (coiled or twisted) segments—the proximal convoluted tubule (PCT) and the distal convoluted tubule (DCT)—separated by a simple U-shaped tube called the loop of Henle.
- The convoluted segments are in the cortex, and the loop of Henle extends at least partially into the medulla.

**Table 26-1**

- 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 occur and the characteristics of the urine that results vary with the activities under way in each segment of the nephron.
- 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.

**Figure 26-7**

- 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.
- In a cortical nephron, the loop of Henle 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 interlobular veins.
- The remaining 15 percent of nephrons, termed juxtamedullary nephrons, have long loops of Henle that extend deep into the medulla. In these nephrons, the peritubular capillaries are connected to the vasa recta—long, straight capillaries that parallel the loop of Henle.
• Because they are more numerous than juxtamedullary nephrons, cortical nephrons perform most of the reabsorptive and secretory functions of the kidneys. However, it is the juxtamedullary nephrons that enable the kidneys to produce concentrated urine.

**Keys**
- The kidneys remove waste products from the blood; they also assist in the regulation of blood volume and blood pressure, ion levels, and blood pH. Nephrons are the primary functional units of the kidneys.

**The Renal Corpuscle**

**Figure 26-8**
- Each renal corpuscle is 150–250 in diameter. It includes both a region known as Bowman’s capsule and the capillary network of the glomerulus.
- Connected to the initial segment of the renal tubule, Bowman’s capsule forms the outer wall of the renal corpuscle and encapsulates the glomerular capillaries. The glomerulus is surrounded by Bowman’s capsule, much as the heart is surrounded by the pericardial cavity.
- The outer wall of the capsule is lined by a simple squamous parietal epithelium. This layer is continuous with the visceral epithelium, which covers the glomerular capillaries.
- The capsular space separates the parietal 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 lamina densa of the glomerular capillaries.
- These unusual cells are called podocytes, and their feet are known as pedicels. Materials passing out of the blood at the glomerulus must be small enough to pass between the narrow gaps, or filtration slits, between adjacent pedicels.
- The glomerular capillaries are fenestrated capillaries—that is, their endothelium contains large-diameter pores. The lamina densa differs from that found in the basal lamina of other capillary networks in that it may encircle more than one capillary. Special supporting cells that lie between adjacent capillaries play a role in controlling their diameter and thus in the rate of capillary blood flow.
- Together, the fenestrated endothelium, the lamina densa, 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, are excluded.
- Filtration at the renal corpuscle is both effective and passive, but it has one major limitation: In addition to metabolic wastes and excess ions, compounds such as glucose, free fatty acids, amino acids, vitamins, and other solutes also enter the capsular space. These potentially useful materials are recaptured before filtrate leaves the kidneys; much of the reabsorption occurs in the proximal convoluted tubule.

**The Proximal Convoluted Tubule**

**Table 26-1**
- The proximal convoluted tubule (PCT) is the first segment of the renal tubule. The entrance to the PCT 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 bear microvilli. The tubular cells absorb 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.
- Reabsorption is the primary function of the PCT, but the epithelial cells can also secrete substances into the lumen.

**The Loop of Henle**
- The PCT makes an acute bend that turns the renal tubule toward the renal medulla. This turn leads to the loop of Henle, or nephron loop. The loop of Henle can be divided into a descending limb and an ascending limb.
• Fluid in the descending limb flows toward the renal pelvis, and that in the ascending limb flows toward the renal cortex. Each limb contains a thick segment and a thin segment.
• 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 movement out of these segments helps concentrate the tubular fluid.

The Distal Convoluted Tubule
• The thick ascending limb of the loop of Henle 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. In sectional view, the DCT differs from the PCT in that the DCT has a smaller diameter and its epithelial cells lack microvilli.
• The DCT is an important site for three vital processes: (1) the active secretion of ions, acids, drugs, and toxins, (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 Apparatus
• 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.
• 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 apparatus (JGA), an endocrine structure that secretes the hormone erythropoietin and the enzyme renin.

The Collecting System
• The distal convoluted tubule, the last segment of the nephron, opens into the collecting system. 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.
• In addition to transporting tubular fluid from the nephron to the renal pelvis, the collecting system adjusts the fluid’s composition and determines the final osmotic concentration and volume of urine.

Principles of Renal Physiology, p. 961

Objectives
1. Discuss the major functions of each portion of the nephron and collecting system.
2. Identify and describe the major factors responsible for the production of urine.
3. Describe the normal characteristics, composition, and solute concentrations of a representative urine sample.
• 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. Three organic waste products are noteworthy:
  o Urea. Urea is the most abundant organic waste. You generate roughly 21 g of urea each day, most of it through the breakdown of amino acids.
  o Creatinine. Creatinine is generated in skeletal muscle tissue through the breakdown of creatine phosphate, a high-energy compound that plays an important role in muscle contraction. Your body generates roughly 1.8 g of creatinine each day, and virtually all of it is excreted in urine.
- **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 and can be eliminated only while dissolved in urine. As a result, their removal is accompanied by 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. (Methods of reporting solute concentrations are discussed 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**

**Table 26-2**

- To perform their functions, the kidneys rely on three distinct processes:
  - **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.
  - **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 occurs after filtrate has left the renal corpuscle. Most of the reabsorbed materials are nutrients the body can use. Whereas filtration occurs solely based on size, reabsorption is a selective process involving either simple diffusion or the activity of carrier proteins in the tubular epithelium. Water reabsorption occurs passively, through osmosis.
  - **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 provides a backup process for filtration, can further lower the plasma concentration of undesirable materials. Secretion is often the primary method of excretion for some compounds, including many drugs.

- Together, these processes produce a fluid that is very different from other body fluids.

**Filtration**

- In filtration, hydrostatic pressure forces water through membrane pores, and solute molecules small enough to pass through those pores are carried along. Filtration occurs as larger solutes and suspended materials are left behind.
- In the body, the heart pushes blood around the cardiovascular system and generates hydrostatic pressure. Filtration occurs across the walls of capillaries as water and dissolved materials are pushed into the interstitial fluids of the body.
- 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, a 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.

**Types of Carrier-Mediated Transport**

- In previous chapters, we considered four major types of carrier-mediated transport:
  - In **facilitated diffusion,** a carrier protein transports a molecule across the cell membrane without expending energy. 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. Exchange pumps and other carrier proteins are active along the kidney
tubules. Active transport mechanisms can operate despite an opposing concentration gradient.

- In **cotransport**, carrier protein activity is not directly linked to the hydrolysis of ATP. 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 mechanisms are responsible for the reabsorption of organic and inorganic compounds from the tubular fluid.

- **Countertransport** resembles cotransport in all respects, except that the two transported ions move in opposite directions. Countertransport mechanisms operate 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:
  - **A Specific Substrate Binds to a Carrier Protein That Facilitates Movement across the Membrane.**
  - **A Given Carrier Protein Typically Works in One Direction Only.** In facilitated diffusion, that direction is determined by the concentration gradient of the substance being transported. 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.
  - **The Distribution of Carrier Proteins Can Vary among Portions of the Cell Surface.** Transport between tubular fluid and interstitial fluid involves two steps—the material must enter the cell at its apical surface and then leave the cell and enter the peritubular fluid at the cell’s basolateral surface. Each step involves a different carrier protein.
  - **The Membrane of a Single Tubular Cell Contains Many Types of Carrier Protein.** Each cell can have multiple functions, and a cell that reabsorbs one compound can secrete another.
  - **Carrier Proteins, Like Enzymes, Can Be Saturated.** When an enzyme is saturated, further increases in substrate concentration have no effect on the rate of reaction. When a carrier protein is saturated, further increases in substrate concentration have no effect on the rate of transport across the cell membrane. For any substance, the concentration at saturation is called the transport maximum or tubular maximum. The saturation of carrier proteins involved in tubular secretion seldom occurs in healthy individuals, but carriers involved in tubular reabsorption are often at risk of saturation, especially during the absorptive state following a meal.

### Tm 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 will exceed the reabsorptive abilities of the nephron, so 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 concentrations in tubular fluid exceed the threshold of the tubular cells, so glucose appears in urine. The presence of glucose in urine is a condition called **glucosuria**.
- 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.
- 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.

### An Overview of Renal Function

#### Figure 26-9

#### Table 26-4
- Most regions perform a combination of reabsorption and secretion, but the balance between the two processes shifts from one region to another:
  - Filtration occurs exclusively in the renal corpuscle, across the filtration membrane.
  - Water and solute reabsorption occurs primarily along the proximal convoluted tubules, but also elsewhere along the renal tubule and within the collecting system.
  - Active secretion occurs primarily at the proximal and distal convoluted tubules.
  - The loops of Henle—especially the long loops of the juxtamedullary nephrons—and the collecting system interact to regulate the final volume and solute concentration of the urine.
- 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 will occur within a few days unless medical assistance is provided.
- The major differences between the two types of nephron are that the loop of Henle of a cortical nephron is shorter and does not extend as far into the medulla as does the loop of Henle of a juxtamedullary nephron.
- The long loop of Henle in a juxtamedullary nephron extends deep into the renal pyramids, where it plays a vital role in water conservation and the formation of concentrated urine.
- The osmotic concentration, or osmolality, of a solution is the total number of solute particles in each liter. Osmolarity is usually expressed 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. Ion concentrations are often reported in milliequivalents per liter (mEq L), whereas the concentrations of large organic molecules are usually reported in grams or milligrams per unit volume of solution (typically, mg or g per dl).

### Renal Physiology: Filtration at the Glomerulus, p. 965

**Objective**

1. List and describe the factors that influence filtration pressure and the rate of filtrate formation.
   - Filtration occurs 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, which has three components: (1) the capillary endothelium, (2) the lamina densa, and (3) the filtration slits.
   - Glomerular capillaries are fenestrated capillaries with pores ranging from 60 to 100 nm (0.06 to ) 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 lamina densa 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, which is small enough to prevent the passage of most small plasma proteins.

**Filtration Pressures**
• The primary factor involved in glomerular filtration is basically the same as that governing fluid and solute movement across capillaries throughout the body: the balance between hydrostatic pressure (fluid pressure) and colloid osmotic pressure (pressure due to materials in solution) on either side of the capillary walls.

• **Hydrostatic Pressure** 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 is significantly higher than capillary pressures elsewhere in the systemic circuit, due to the arrangement of vessels at the glomerulus.

• Blood pressure is low in typical systemic capillaries because capillary blood flows into the venous system, where resistance is relatively low. At the glomerulus, blood leaving the glomerular capillaries flows into an efferent arteriole, whose diameter is smaller than that of the afferent arteriole.

• The efferent arteriole thus offers considerable resistance, so relatively high pressures are needed to force blood into it. Glomerular pressures are similar to those of small arteries, averaging about 50 mm Hg instead of the 35 mm Hg typical of peripheral capillaries.

• **Glomerular hydrostatic pressure** is opposed by the capsular hydrostatic pressure (CsHP), which tends to push water and solutes out of the filtrate and into the plasma. This pressure results from the resistance to flow along the nephron and the conducting system. 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. Net hydrostatic pressure can be calculated as follows:
  
  o **Colloid Osmotic Pressure** The colloid osmotic pressure of a solution is the osmotic pressure resulting from the presence of suspended proteins.
  
  o 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.

**Figure 26-10**

• **Filtration Pressure** The filtration pressure (FP) at the glomerulus is the difference between the hydrostatic pressure and the colloid osmotic pressure acting across the glomerular capillaries. This is the average pressure forcing water and dissolved materials out of the glomerular capillaries and into the capsular spaces. Problems that affect 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—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.

• When necessary, a more accurate GFR determination can be performed by using the complex carbohydrate inulin, which 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 (50 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.

• The glomerular filtration rate depends on the filtration pressure across glomerular capillaries. Any factor that alters the filtration pressure therefore alters the GFR, thereby affecting kidney function.
Control of the GFR

- Glomerular filtration is the vital first step essential to all other kidney functions. If filtration does not occur, waste products are not excreted, pH control is jeopardized, and an important mechanism for regulating blood volume is lost.
- 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.
- Autoregulation of the GFR Autoregulation maintains an adequate GFR despite changes in local blood pressure and blood flow. Maintenance of the GFR is accomplished by changing the diameters of afferent arterioles, efferent arterioles, and glomerular capillaries. The most important regulatory mechanisms stabilize the GFR when systemic blood pressure declines.
  - A reduction in blood flow and a decline in glomerular blood pressure trigger (1) dilation of the afferent arteriole, (2) relaxation of supporting cells and dilation of the glomerular capillaries, and (3) constriction of the efferent arteriole. This combination increases blood flow and elevates glomerular blood pressure to normal levels.
  - As a result, filtration rates remain relatively constant. 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).
  - There are three triggers for the release of renin by the juxtaglomerular apparatus (JGA): (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 tributaries; (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 stimuli are often interrelated.
  - Because the tubular fluid is then in the ascending limb of the loop of Henle longer, the concentration of sodium and chloride ions in the tubular fluid reaching the macula densa and DCT becomes abnormally low.
  - At the nephron, angiotensin II causes the constriction of the efferent arteriole, further elevating glomerular pressures and filtration rates. Angiotensin II also directly stimulates the reabsorption of sodium ions and water at the PCT.
  - At the adrenal glands, angiotensin II stimulates the secretion of aldosterone by the adrenal cortex. The aldosterone then accelerates sodium reabsorption in the DCT and cortical portion of the collecting system.
  - In the CNS, angiotensin II (1) causes the sensation of thirst; (2) triggers the release of antidiuretic hormone (ADH), stimulating the reabsorption of water in the distal portion of the DCT and the collecting system; and (3) increases sympathetic motor tone, mobilizing the venous reserve, increasing cardiac output, and stimulating peripheral vasoconstriction.
  - In peripheral capillary beds, angiotensin II causes a brief but powerful vasoconstriction of arterioles and precapillary sphincters, elevating 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, and this promotes fluid losses that help return blood
volume to normal levels. If the elevation in blood volume is severe, hormonal factors further increase the GFR and accelerate fluid losses in the urine.

- **Natriuretic peptides** are released in response to the stretching of the walls of the heart by increased blood volume or blood pressure. These hormones are released by the heart: atrial natriuretic peptide (ANP) is released by the atria, and brain natriuretic peptide (BNP) is released by the ventricles.
  - Among their other effects, the natriuretic peptides trigger the dilation of afferent arterioles and constriction of efferent arterioles. This mechanism elevates glomerular pressures and increases the GFR.
  - The natriuretic peptides also increase tubular reabsorption of sodium ions, and the net result is increased urine production and decreased blood volume and pressure.

- **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 one direct effect on the GFR: It produces a powerful vasoconstriction of afferent arterioles, decreasing the GFR and slowing the production of filtrate.
  - When the sympathetic division alters regional patterns of blood circulation, blood flow to the kidneys is often affected.
  - 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.

**Keys**

- Roughly 180 L of filtrate is produced at the glomeruli each day, and that represents 70 times the total plasma volume. Almost all of that fluid volume must be reabsorbed to avoid fatal dehydration.

**Renal Physiology: Reabsorption and Secretion, p. 969**

**Objectives**

1. Identify the types of transport mechanisms found along the nephron and discuss the reabsorptive or secretory functions of each segment of the nephron and collecting system.
2. Explain the role of countercurrent multiplication in the formation of a concentration gradient in the renal medulla.
3. Describe how antidiuretic hormone and aldosterone influence the volume and concentration of urine.

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

**Reabsorption and Secretion at the PCT**

**Figure 26-12**

- 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 and diffuse into peritubular capillaries.
- The PCT has five major functions:
  - **Reabsorption of Organic Nutrients.** Under normal circumstances, before the tubular fluid enters the loop of Henle, 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.
  - **Active Reabsorption of Ions.** The PCT actively transports several ions, including sodium, potassium, and bicarbonate ions, plus magnesium, phosphate, and sulfate ions. The ion pumps involved are individually regulated and may be influenced by
The Loop of Henle and Countercurrent Multiplication

- The thin peritubular exchange. Fluid. Reabsorbed roughly 60–70 percent of the bicarbonate ions from tubular fluid. Bicarbonate is important in stabilizing blood pH.
- 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 transport activities proceed, 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.
- Passive Reabsorption of Ions. As active reabsorption of ions occurs 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 will 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.
- Secretion. Active secretion also occurs along the PCT. Because the DCT performs comparatively little reabsorption, we will consider secretory mechanisms when we discuss the DCT.
  - Sodium ion reabsorption plays an important role in all of the foregoing processes. Sodium ions may enter tubular cells by diffusion through leak channels; by the sodium-linked cotransport of glucose, amino acids, or other organic solutes; Na⁺-Na⁺ or by countertransport for hydrogen ions.
  - 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 and are therefore unable to recover specific solutes from tubular fluid.

The Loop of Henle 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 loop of Henle. In the process, useful organic substrates and many mineral ions have been reclaimed. The loop of Henle reabsorbs roughly half of the water, and two-thirds of the sodium and chloride ions, remaining in the tubular fluid.
  - This reabsorption is performed efficiently according to the principle of countercurrent exchange.
  - The thin descending limb and the thick ascending limb of the loop of Henle are very close together, separated only by peritubular fluid. The exchange that occurs between these segments is called countercurrent multiplication. Countercurrent refers to the fact that the exchange occurs between fluids moving in opposite directions: Tubular fluid in the descending limb flows toward the renal pelvis, whereas 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 segments of the loop of Henle have very different permeability characteristics. The thin descending limb is permeable to water but relatively impermeable to solutes. The thick ascending limb, which is relatively impermeable to both water and solutes, contains active transport mechanisms that pump sodium and chloride ions from the tubular fluid into the peritubular fluid of the medulla.
    - Sodium and chloride are pumped out of the thick ascending limb and into the peritubular fluid.
    - This pumping action elevates 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, increasing the solute concentration in the thin descending limb.
The arrival of the highly concentrated solution in the thick ascending limb accelerates the transport of sodium and chloride ions into the peritubular fluid of the medulla. Solute pumping at the ascending limb leads to higher solute concentrations in the descending limb, which then result in accelerated solute pumping in the ascending limb.

**Figure 26-13**

- Active transport at the apical surface moves sodium, potassium, and chloride ions out of the tubular fluid. The carrier is called a \( \text{Na}^+ - \text{K}/2 \text{Cl} \) transporter, because each cycle of the pump carries a sodium ion, a potassium ion, and two chloride ions into the tubular cell. Potassium and chloride ions are pumped into the peritubular fluid by cotransport carriers.
- 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 removal of sodium and chloride ions from the tubular fluid in the ascending limb elevates the osmotic concentration of the peritubular fluid around the thin descending limb. Because the thin descending limb is permeable to water but impermeable to solutes, as tubular fluid travels deeper into the medulla along the thin descending limb, osmosis moves water into the peritubular fluid. Solutes remain behind, so the tubular fluid reaching the turn of the loop of Henle 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.
- As \( \text{Na}^+ \) and \( \text{Cl}^- \) 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, 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.
- 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 loop of Henle is about 1200 mOsm L. 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. The thick ascending limb of the loop of Henle, the DCT, and the collecting ducts are impermeable to urea. As water is reabsorbed, the concentration of urea gradually rises. The tubular fluid reaching the papillary duct 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:
  - It efficiently reabsorbs solutes and water before the tubular fluid reaches the DCT and collecting system.
  - It establishes a concentration gradient that permits the passive reabsorption of water from the tubular fluid in the collecting system. This reabsorption is regulated by circulating levels of antidiuretic hormone (ADH).

*Reabsorption and Secretion at the DCT*

**Figure 26-14**

- 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, and 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 and out of the tubular fluid. Tubular cells along the distal portions of the DCT also contain ion pumps that reabsorb tubular Na⁺ in exchange for another cation (usually K⁺).

• The ion pump and the channels involved are controlled by the hormone aldosterone, produced by the adrenal cortex. Aldosterone stimulates the synthesis and incorporation of sodium ion pumps and sodium channels in cell membranes along the DCT and collecting duct.

• The rate of sodium reabsorption is regulated by circulating levels of parathyroid hormone and calcitriol.

• Secretion at the DCT The blood entering peritubular capillaries still contains a number of potentially undesirable substances that did not cross the filtration membrane at the glomerulus.

• The rate of secretion rises or falls in response to changes in the concentration of sodium in the peritubular fluid, the higher their concentration in the peritubular fluid, the higher the rate of secretion.

• Potassium Ion Secretion Potassium ions diffuse into the lumen through potassium channels at the apical surfaces of the tubular cells. In effect, tubular cells trade sodium ions in the tubular fluid for excess potassium ions in body fluids.

• Hydrogen Ion Secretion Hydrogen ion secretion is also associated with the reabsorption of sodium. Both involve the generation of carbonic acid by the enzyme carbonic anhydrase.

  • Hydrogen ions generated by the dissociation of the carbonic acid are secreted by sodium-linked countertransport in exchange for sodium. The bicarbonate ions diffuse into the peritubular fluid and then into the bloodstream, where they help prevent changes in plasma pH.

  • Hydrogen ion secretion acidifies the tubular fluid while elevating the pH of the blood. Hydrogen ion secretion accelerates when the pH of the blood falls—as in lactic acidosis, which can develop after exhaustive muscle activity, or ketoacidosis, which can develop in starvation or diabetes mellitus.

  • The combination of removal and production at the kidneys plays an important role in the control of blood pH. Because one of the secretory pathways is aldosterone sensitive, aldosterone stimulates secretion. Prolonged aldosterone stimulation can cause alkalois, or abnormally high blood pH.

  • Under these conditions, the PCT and DCT deaminate amino acids in reactions that strip off the amino groups. The reaction sequence ties up and yields both ammonium ions. The ammonium ions are then pumped into the tubular fluid by sodiumlinked 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, and it generates bicarbonate ions that add to the buffering capabilities 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:
The Control of Urine Volume and Osmotic Concentration

- By aldosterone, which controls sodium ion pumps along most of the DCT and the proximal portion of the collecting system. 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 its effects on aldosterone secretion and action—can dramatically increase urinary water losses. The collecting system also has other reabsptive and secretory functions, many of which are important to the control of body fluid pH.

- Reabsorption in the Collecting System Important examples of solute reabsorption in the collecting system include the following:
  - Sodium Ion Reabsorption. The collecting system contains aldosterone-sensitive ion pumps that exchange in tubular fluid for in peritubular fluid.
  - Bicarbonate Reabsorption. Bicarbonate ions are reabsorbed in exchange for chloride ions in the peritubular fluid.
  - 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.

- Secretion in the Collecting System The collecting system is an important site for the control of body fluid pH by means of the secretion of hydrogen or bicarbonate ions.
  - If the pH of the peritubular fluid declines, 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.

**Keys**

- Reabsorption involves a combination of diffusion, osmosis, channel-mediated diffusion, and active transport. Many of these processes are independently regulated by local or hormonal mechanisms. The primary mechanism governing water reabsorption can be described as “water follows salt.” Secretion is a selective, carrier-mediated process.

**The Control of Urine Volume and Osmotic Concentration**

**Figure 26-15**

- Urine volume and osmotic concentration are regulated through the control of water reabsorption. Water is reabsorbed by osmosis in the proximal convoluted tubule and the descending limb of the loop of Henle.
  - The water permeabilities of these regions cannot be adjusted, and water reabsorption occurs whenever the osmotic concentration of the peritubular fluid exceeds that of the tubular fluid.
  - The ascending limb of the loop of Henle is impermeable to water, but 1–2 percent of the volume of water in the original filtrate is recovered during sodium ion reabsorption in the distal convoluted tubule and collecting system.
  - Because these water movements cannot be prevented, they represent obligatory water reabsorption, which usually recovers 85 percent of the volume of filtrate produced. The volume of water lost in urine depends on how much of the water in the remaining tubular fluid (15 percent of the filtrate volume, or roughly 27 liters per day) is reabsorbed along the DCT and collecting system.
  - The amount 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 the appearance of special water channels in the apical cell membranes, dramatically enhancing 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.

- The tubular fluid arriving at the DCT has an osmotic concentration of only about 100 mOsml L. In the presence of ADH, osmosis occurs, and water moves out of the DCT until the osmotic concentration of the tubular fluid equals that of the surrounding cortex (roughly 300 mOsml L).
- The tubular fluid then flows along the collecting duct, which passes through the concentration gradient of the medulla. Additional water is then reabsorbed, and the urine reaching the minor calyx has an osmotic concentration closer to 1200 mOsml L.
- Just how closely the osmotic concentration approaches 1200 mOsml L depends on how much ADH is present. In the absence of ADH, 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.
- Under maximum ADH stimulation, the DCT and collecting system become so permeable to water that the osmotic concentration of the urine is equal to 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, and the DCT and collecting system always have a significant degree of water permeability. The DCT normally 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 roughly 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), with an osmotic concentration of 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, soon restoring plasma volume to normal.
- **Diuresis** is the elimination of urine. Whereas **urination** is an equivalent term in a general sense, diuresis typically indicates the production of a large volume of urine. **Diuretics** are drugs that promote the loss of water in urine. The usual goal in diuretic therapy is a reduction in 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 individuals, especially those with high blood pressure or congestive heart failure.

**The Function of the Vasa Recta**

- The solutes and water reabsorbed in the medulla must be returned to the general circulation without disrupting the concentration gradient. This return is the function of the **vasa recta**.
- Blood entering the vasa recta has an osmotic concentration of approximately 300 mOsm L. The blood descending into the medulla 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, but solute absorption predominates, because the plasma proteins limit osmotic flow out of the blood.
- Blood flowing toward the cortex gradually decreases in osmotic concentration as the solute concentration of the peritubular fluid declines. Again, this decrease involves a combination of solute diffusion and osmosis, but 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 is moved out in the descending portion.
- 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**
More than 99 percent of the 180 liters of filtrate produced each day by the glomeruli is reabsorbed and never reaches the renal pelvis.

The composition and concentration of urine are two related but distinct properties. The composition of urine reflects the filtration, absorption, and secretion activities of the nephrons. Some compounds (such as urea) are neither actively excreted nor reabsorbed along the nephron.

Organic nutrients are completely reabsorbed, and other compounds, such as creatinine, that are missed by the filtration process are actively secreted into the tubular fluid. The concentration of these components in a given urine sample depends on the osmotic movement of water across the walls of the tubules and collecting ducts.

Normal urine is a clear, sterile solution. Its yellow color results from the presence of the pigment urobin, generated in the kidneys from the urobilinogens produced by intestinal bacteria and absorbed in the colon.

The evaporation of small molecules, such as ammonia, accounts for the characteristic odor of urine. Other substances not normally present, such as acetone or other ketone bodies, can also impart a distinctive smell.

Table 26-6

| Urinalysis, the analysis of a urine sample, is a diagnostic tool of considerable importance, even in high-technology medicine. A standard urinalysis includes an assessment of the color and appearance of urine, two characteristics that can be determined without specialized equipment. |

Figure 26-16

Summary: Renal Function

Step 1 The filtrate produced at the renal corpuscle has the same osmotic concentration as does plasma—about 300 mOsm L. It has the composition of blood plasma, minus the plasma proteins.

Step 2 In the PCT, the active removal of ions and organic substrates produces a continuous osmotic flow of water out of the tubular fluid. This process reduces the volume of filtrate but keeps the solutions inside and outside the tubule isotonic.

  o Between 60 and 70 percent of the filtrate volume has been reabsorbed before the tubular fluid reaches the descending limb of the loop of Henle.

Step 3 In the PCT and descending limb of the loop of Henle, water moves into the surrounding peritubular fluids, leaving a small volume (15–20 percent of the original filtrate) of highly concentrated tubular fluid. The reduction in volume has occurred by obligatory water reabsorption.

Step 4 The thick ascending limb is impermeable to water and solutes. The tubular cells actively transport and out of the tubular fluid, thereby lowering the osmotic concentration of tubular fluid without affecting its volume.

  o The tubular fluid reaching the distal convoluted tubule is hypotonic relative to the peritubular fluid, with an osmotic concentration of only about 100 mOsm L.

  o Urea accounts for a significantly higher proportion of the total osmotic concentration at the end of the loop than it did at the start of it.

Step 5 The final adjustments in the composition of the tubular fluid are made in the DCT and the collecting system.
Although the DCT and collecting duct are generally impermeable to solutes, the osmotic concentration of tubular fluid can be adjusted through active transport (reabsorption or secretion).

- Some of these transport activities are hormonally regulated.

- **Step 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.
  - These segments are relatively impermeable to water unless exposed to ADH. Under maximum ADH stimulation, urine volume is at a minimum, and urine osmotic concentration is equal to that of the peritubular fluid in the deepest portion of the medulla (roughly 1200 mOsm L).

- **Step 7** The vasa recta absorbs solutes and water reabsorbed by the loop of Henle and the collecting ducts, thereby maintaining the concentration gradient of the medulla.

### Urine Transport, Storage, and Elimination, p. 982

**Objectives**
1. Describe the structures and functions of the ureters, urinary bladder, and urethra.
2. Discuss the voluntary and involuntary regulation of urination and describe the micturition reflex.

**Figure 26-17**
- Filtrate modification and urine production end when the fluid enters the renal pelvis. The urinary tract (the ureters, urinary bladder, and urethra) is responsible for the transport, storage, and elimination of urine.
- 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, because these regions are lined by a [transitional epithelium](#) that can tolerate cycles of distension and contraction without damage.

**The Ureters**

**Figure 26-18**
- 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.
- The ureters extend inferiorly and medially, passing over the anterior surfaces of the *psosas* major muscles. The ureters are retroperitoneal and are firmly attached to the posterior abdominal wall.
- 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, and the ureteral openings are slitlike rather than rounded. 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: (1) an inner mucosa, comprising 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 renal capsule and peritoneum.
- About every 30 seconds, a peristaltic contraction begins at the renal pelvis and sweeps along the ureter, forcing urine toward the urinary bladder.

**The Urinary Bladder**
• The urinary bladder is a hollow, muscular organ that functions as a temporary reservoir for the storage of urine. The dimensions of the urinary bladder vary with its state of distension, but a full urinary bladder can contain as much as a liter of urine.
• The superior surfaces of the urinary bladder are covered by a layer of peritoneum; several peritoneal folds assist in stabilizing its position.
• The middle 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.
• 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 constitutes a region called the trigone of the urinary bladder.
• 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, known as the neck of the urinary bladder, contains a muscular internal urethral sphincter, or sphincter vesicae. The smooth muscle fibers of this sphincter provide involuntary control over the discharge of urine from the bladder.
• 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.

Figure 26-19
• Histology of the Urinary Bladder The wall of the urinary bladder contains mucosa, submucosa, and muscularis layers. The muscularis layer consists of inner and outer layers of longitudinal smooth muscle, with a circular layer between the two. Collectively, these layers form the powerful detrusor muscle of the urinary bladder. Contraction of this muscle compresses the urinary bladder and expels its contents into the urethra.

The Urethra
• The urethra extends from the neck of the urinary bladder 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, a distance that may be 18–20 cm (7–8 in.). The male urethra can be subdivided into three portions: the prostatic urethra, the membranous urethra, and the spongy urethra.
  o 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 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, extending 3–5 cm (1–2 in.) from the bladder to the vestibule. 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, which is under voluntary control via the perineal branch of the pudendal nerve, has a resting muscle tone and must be voluntarily relaxed to permit micturition.
• Histology of the Urethra The urethral lining consists of a stratified epithelium that varies from transitional at the neck of the urinary bladder, to stratified columnar at the midpoint, to stratified squamous near the external urethral orifice.
• The lamina propria is thick and elastic, and the mucous membrane is thrown into longitudinal folds. 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, and the entire complex is surrounded by concentric layers of smooth muscle.

The Micturition Reflex and Urination

Figure 26-20
• Urine reaches the urinary bladder by peristaltic contractions of the ureters. The process of urination is coordinated by the micturition reflex.
• Stretch receptors in the wall of the urinary bladder are stimulated as the bladder fills with urine. Afferent fibers in the pelvic nerves carry the impulses generated 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.
  o The urge to urinate generally appears when the bladder contains about 200 ml of urine. The micturition reflex begins to function when the stretch receptors have provided adequate stimulation to parasympathetic preganglionic motor neurons.
  o Action potentials carried by efferent fibers within the pelvic nerves then stimulate ganglionic neurons in the wall of the urinary bladder.
  o These neurons in turn stimulate sustained contraction of the detrusor muscle.
  o This contraction elevates fluid pressure in the urinary bladder, but urine ejection does not occur unless both the internal and external urethral sphincters are relaxed.
  o An awareness of the fullness of the urinary bladder depends on interneurons that relay information from stretch receptors to the thalamus and from the thalamus to the cerebral cortex.
  o The relaxation of the external urethral sphincter occurs under voluntary control; when the external urethral sphincter relaxes, so does the internal urethral sphincter, and urination occurs.
  o If the external urethral sphincter does not relax, the internal urethral sphincter remains closed, and the urinary bladder gradually relaxes. A further increase in bladder volume begins the cycle again, usually within an hour.
  o 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.
  o This opening leads to a reflexive relaxation of the external urethral sphincter, and urination occurs despite voluntary opposition or potential inconvenience. At the end of a typical micturition, less than 10 ml of urine remains in the bladder.
• Infants lack voluntary control over urination, because the necessary corticospinal connections have yet to be established.
• Incontinence is the inability to control urination voluntarily. Trauma to the internal or external urethral sphincter can contribute to incontinence in otherwise healthy adults.

Aging and the Urinary System
• In general, aging is associated with an increased incidence of kidney problems.
• Age-related changes in the urinary system include the following:
  o A Decline in the Number of Functional Nephrons. The total number of kidney nephrons drops by 30–40 percent between ages 25 and 85.
  o 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.
o A Reduced Sensitivity to ADH. With age, the distal portions of the nephron and collecting system become less responsive to ADH. Reabsorption of water and sodium ions occurs at a reduced rate, and more sodium ions are lost in urine.

o 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 after a stroke, Alzheimer’s disease, or other CNS problems affecting the cerebral cortex or hypothalamus. (3) In males, urinary retention may develop if enlargement of the prostate gland compresses the urethra and restricts the flow of urine.

- The urinary system 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:
  o 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.
  o 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.
  o Digestive System. The liver excretes small amounts of metabolic waste products in bile, and you lose a variable amount of water in feces. These excretory activities have an impact on the composition of body fluids.