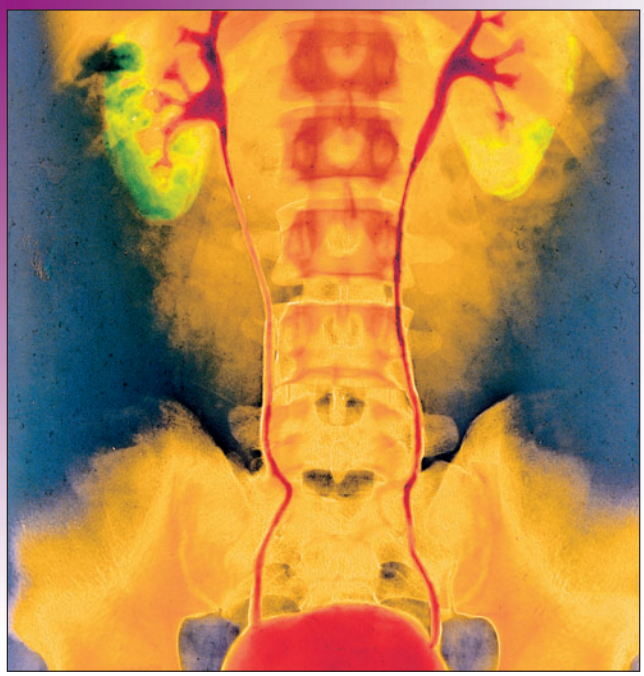


The kidneys (*green*), ureters, and urinary bladder (*red*) of a healthy person (colorized X ray)

CHAPTER

23

The Urinary System

CHAPTER OUTLINE

INSIGHTS

Brushing Up

To understand this chapter, it is important that you understand or brush up on the following concepts:
- Osmosis, tonicity, and osmolarity (pp. 107–109)
- Carrier-mediated transport mechanisms, especially symports and antiports (pp. 109–110)
- Osmotic diuresis (p. 669)
- Blood pressure, resistance, and flow (p. 733)
- Capillary filtration and reabsorption (p. 761)

The urinary system is well known for eliminating wastes from the body, but its role in homeostasis goes far beyond that. The kidneys also detoxify poisons, synthesize glucose, and play indispensable roles in controlling electrolyte and acid-base balance, blood pressure, erythrocyte count, and the P_{O_2} and P_{CO_2} of the blood. The urinary system thus has a very close physiological relationship with the endocrine, circulatory, and respiratory systems, covered in the preceding chapters.

Anatomically, the urinary system is closely associated with the reproductive system. In many animals the eggs and sperm are emitted through the urinary tract, and the two systems have a shared embryonic development and adult anatomical relationship. This is reflected in humans, where the systems develop together in the embryo and, in the male, the urethra continues to serve as a passage for both urine and sperm. Thus the urinary and reproductive systems are often collectively called the *urogenital (U-G) system,* and *urologists* treat both urinary and reproductive disorders. We examine the anatomical relationship between the urinary and reproductive systems in chapter 27, but the physiological link to the circulatory and respiratory systems is more important to consider at this time.

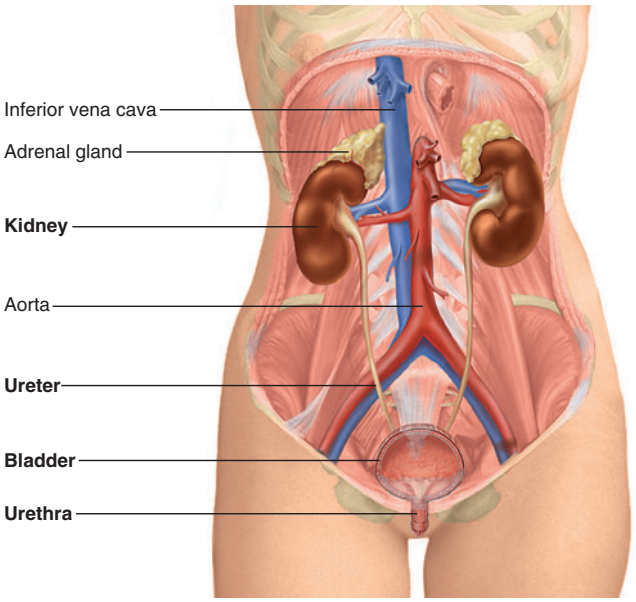


Figure 23.1 The Urinary System. Organs of the urinary system are indicated in boldface.

Functions of the Urinary System

Objectives

When you have completed this section, you should be able to

- name and locate the organs of the urinary system;
- list several functions of the kidneys in addition to urine formation;
- name the major nitrogenous wastes and identify their sources; and
- define *excretion* and identify the systems that excrete wastes.

The **urinary system** consists of six organs: two **kidneys,** two **ureters,** the **urinary bladder,** and the **urethra** (fig. 23.1). Most of our focus in this chapter is on the kidneys.

Functions of the Kidneys

Metabolism constantly produces a variety of waste products that can poison the body if not eliminated. The most fundamental role of the kidneys is to eliminate these wastes and homeostatically regulate the volume and composition of the body fluids. All of the following processes are aspects of kidney function:

- They filter blood plasma, separate wastes from the useful chemicals, and eliminate the wastes while returning the rest to the bloodstream.
- They regulate blood volume and pressure by eliminating or conserving water as necessary.
- They regulate the osmolarity of the body fluids by controlling the relative amounts of water and solutes eliminated.
- They secrete the enzyme *renin,* which activates hormonal mechanisms that control blood pressure and electrolyte balance.
- They secrete the hormone *erythropoietin,* which controls the red blood cell count and oxygen-carrying capacity of the blood.
- They function with the lungs to regulate the P_{CO_2} and acid-base balance of the body fluids.
- They contribute to calcium homeostasis through their role in synthesizing calcitriol (vitamin D) (see chapter 7).
- They detoxify free radicals and drugs with the use of peroxisomes.
- In times of starvation, they carry out *gluconeogenesis;* they *deaminate* amino acids (remove the $-NH_2$ group), excrete the amino group as ammonia (NH_3), and synthesize glucose from the rest of the molecule.

Nitrogenous Wastes

A **waste** is any substance that is useless to the body or present in excess of the body's needs. A **metabolic waste,** more specifically, is a waste substance produced by the body. Thus the food residue in feces, for example, is a waste but not a metabolic waste, since it was not produced by the body and, indeed, never entered the body's tissues.

Metabolism produces a great quantity of wastes that are lethal to cells if allowed to accumulate. Some of the

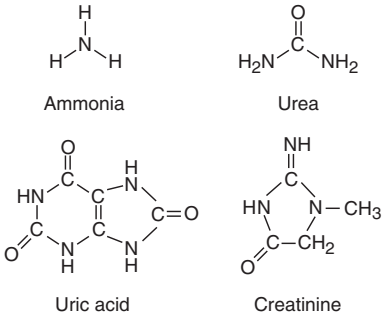


Figure 23.2 The Major Nitrogenous Wastes.
How is each of these wastes produced in the body?

most toxic examples are small nitrogen-containing compounds called **nitrogenous wastes** (fig. 23.2). About 50% of the nitrogenous waste is **urea,** a by-product of protein catabolism. Proteins are broken down to amino acids, and then the $-NH_2$ group is removed from each amino acid. The $-NH_2$ forms ammonia, which is exceedingly toxic but which the liver quickly converts to urea, a less harmful waste:

$$2\ NH_3 + CO_2 \rightarrow H_2N{-}\overset{\overset{O}{\|}}{C}{-}NH_2 + H_2O$$

Other nitrogenous wastes in the urine include **uric acid** and **creatinine** (cree-AT-ih-neen), produced by the catabolism of nucleic acids and creatine phosphate, respectively. Although less toxic than ammonia and less abundant than urea, these wastes are far from harmless.

The level of nitrogenous waste in the blood is typically expressed as **blood urea nitrogen (BUN).** The urea concentration is normally 7 to 18 mg/dL. An abnormally elevated BUN is called **azotemia**[1] (AZ-oh-TEE-me-uh) and may indicate renal insufficiency. Azotemia may progress to **uremia** (you-REE-me-uh), a syndrome of diarrhea, vomiting, dyspnea, and cardiac arrhythmia stemming from the toxic effects of nitrogenous wastes. Convulsions, coma, and death can follow within a few days. Unless a kidney transplant is available, renal failure requires *hemodialysis* to remove nitrogenous wastes from the blood (see insight 23.4, p. 907).

Excretion

Excretion is the process of separating wastes from the body fluids and eliminating them. It is carried out by four organ systems:

1. The respiratory system excretes carbon dioxide, small amounts of other gases, and water.
2. The integumentary system excretes water, inorganic salts, lactic acid, and urea in the sweat.
3. The digestive system not only *eliminates* food residue (which is not a process of excretion) but also actively *excretes* water, salts, carbon dioxide, lipids, bile pigments, cholesterol, and other metabolic wastes.
4. The urinary system excretes a broad variety of metabolic wastes, toxins, drugs, hormones, salts, hydrogen ions, and water.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

1. State four functions of the kidneys other than forming urine.
2. List four nitrogenous wastes and their metabolic sources.
3. Name some wastes eliminated by three systems other than the urinary system.

Anatomy of the Kidney

Objectives

When you have completed this section, you should be able to

- identify the major external and internal features of the kidney;
- trace the flow of fluid through the renal tubules;
- trace the flow of blood through the kidney; and
- describe the nerve supply to the kidney.

Gross Anatomy

The kidneys lie against the posterior abdominal wall at the level of vertebrae T12 to L3. The right kidney is slightly lower than the left because of the space occupied by the liver above it. Each kidney weighs about 160 g and measures about 12 cm long, 5 cm wide, and 2.5 cm thick—about the size of a bar of bath soap. The lateral surface is convex while the medial surface is concave and has a slit, the **hilum,** where it receives the renal nerves, blood vessels, lymphatic vessels, and ureter. The left adrenal gland rests on the superior pole of that kidney, while the right adrenal gland is more medial, between the hilum and pole. The kidneys, adrenal glands, ureters, and urinary bladder are retroperitoneal—they lie between the peritoneum and body wall (fig. 23.3).

The kidney is protected by three layers of connective tissue: (1) a fibrous **renal**[2] **fascia,** immediately deep to the parietal peritoneum, which binds the kidney and associated organs to the abdominal wall; (2) the **adipose capsule,** a layer of fat that cushions the kidney and holds it in place;

[1] *azot* = nitrogen + *emia* = blood condition

[2] *ren* = kidney + *al* = pertaining to

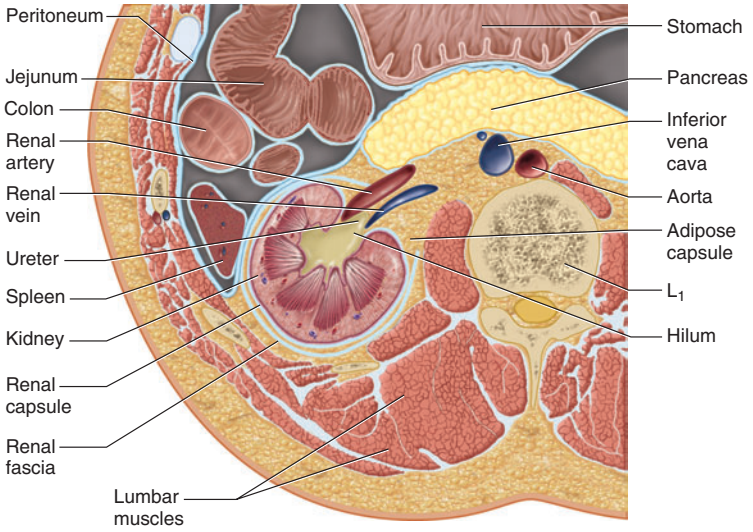


Figure 23.3 Location of the Kidney. Cross section of the abdomen at the level of vertebra L1.
Why is the kidney described as retroperitoneal? Name another retroperitoneal organ in this figure.

and (3) the **renal capsule,** a fibrous sac that is anchored at the hilum and encloses the rest of the kidney like a cellophane wrapper, and protects the kidney from trauma and infection. Collagen fibers extend from the renal capsule, through the fat, to the renal fascia. The renal fascia is fused with the peritoneum on one side and the deep fascia of the lumbar muscles on the other. Thus the kidneys are suspended in place. Nevertheless, they drop about 3 cm when you go from a supine to a standing position, and under some circumstances they become detached and drift even lower, with pathological results (see nephroptosis, or "floating kidney," in table 23.3 at the end of this chapter).

The renal parenchyma—the glandular tissue that forms the urine—appears C-shaped in frontal section. It encircles a medial space, the **renal sinus,** occupied by blood and lymphatic vessels, nerves, and urine-collecting structures. Adipose tissue fills the remaining space and holds these structures in place (fig. 23.4).

The parenchyma is divided into two zones: an outer **renal cortex** about 1 cm thick and an inner **renal medulla** facing the sinus. Extensions of the cortex called **renal columns** project toward the sinus and divide the medulla into 6 to 10 **renal pyramids.** Each pyramid is conical, with a broad base facing the cortex and a blunt point called the **renal papilla** facing the sinus. One pyramid and the overlying cortex constitute one *lobe* of the kidney.

The papilla of each renal pyramid is nestled in a cup called a **minor calyx**[3] (CAY-lix), which collects its urine. Two or three minor calices (CAY-lih-seez) converge to form a **major calyx,** and two or three major calices converge in the sinus to form the funnel-like **renal pelvis.**[4] The ureter is a tubular continuation of the renal pelvis that drains the urine down to the urinary bladder.

The Nephron

Each kidney contains about 1.2 million functional units called **nephrons** (NEF-rons) (fig. 23.5). If you can understand the function of one nephron, you will understand nearly everything about the function of the kidney. A nephron consists of two principal parts: a *renal corpuscle* where the blood plasma is filtered and a long *renal tubule* that processes this filtrate into urine.

The Renal Corpuscle

The **renal corpuscle** (fig. 23.6) consists of a ball of capillaries called a **glomerulus**[5] (glo-MERR-you-lus), enclosed in a two-layered **glomerular (Bowman's**[6]**) capsule.** The parietal (outer) layer of the capsule is a simple squamous epithelium, while the visceral layer consists of elaborate cells called **podocytes**[7] wrapped around the capillaries. The podocytes are described in detail later. The fluid that filters from the glomerular capillaries, called the **glomerular filtrate,** collects in the **capsular space** between the

[3] *calyx* = cup

[4] *pelvis* = basin
[5] *glomer* = ball + *ulus* = little
[6] Sir William Bowman (1816–92), British physician
[7] *podo* = foot + *cyte* = cell

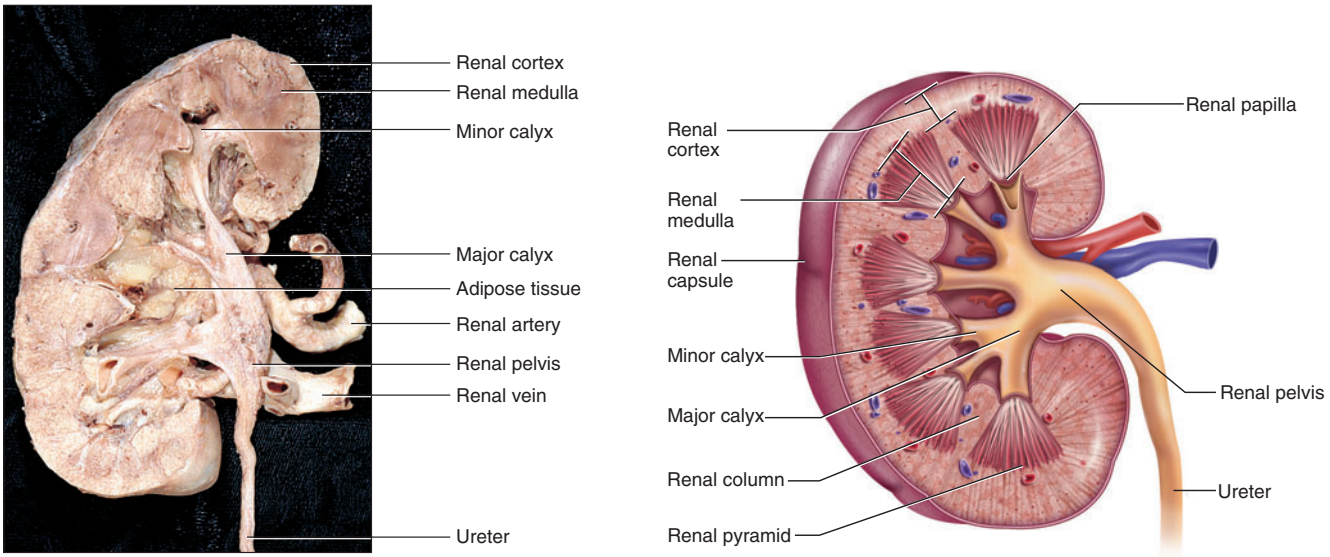


Figure 23.4 **Gross Anatomy of the Kidney.** (*a*) Photograph of a frontal section. (*b*) Major anatomical features.

parietal and visceral layers and then flows into the renal tubule on one side of the capsule.

The Renal Tubule

The **renal (uriniferous[8]) tubule** is a duct that leads away from the glomerular capsule and ends at the tip of a medullary pyramid. It is about 3 cm long and divided into four major regions: the *proximal convoluted tubule, nephron loop, distal convoluted tubule,* and *collecting duct* (see fig. 23.5). Only the first three of these are parts of an individual nephron; the collecting duct receives fluid from many nephrons. Each region of the renal tubule has unique physiological properties and roles in the production of urine.

The Proximal Convoluted Tubule The **proximal convoluted tubule (PCT)** arises from the glomerular capsule. It is the longest and most coiled of the four regions and thus dominates histological sections of renal cortex. The PCT has a simple cuboidal epithelium with prominent microvilli (a brush border), which attests to the great deal of absorption that occurs here. The microvilli give the epithelium a distinctively shaggy look in tissue sections.

The Nephron Loop After coiling extensively near the renal corpuscle, the PCT straightens out and forms a long U-shaped **nephron loop (loop of Henle[9]).** The first portion of the loop, the **descending limb,** passes from the cortex into the medulla. At its deep end it turns 180° and forms an **ascending limb** that returns to the cortex. The nephron loop is divided into thick and thin segments. The **thick segments** have a simple cuboidal epithelium. They form the initial part of the descending limb and part or all of the ascending limb. The cells here are heavily engaged in active transport of salts, so they have very high metabolic activity and are loaded with mitochondria. The **thin segment** has a simple squamous epithelium. It forms the lower part of the descending limb, and in some nephrons, it rounds the bend and continues partway up the ascending limb. The cells here have low metabolic activity but are very permeable to water.

The Distal Convoluted Tubule When the nephron loop returns to the cortex, it coils again and forms the **distal convoluted tubule (DCT).** This is shorter and less convoluted than the PCT, so fewer sections of it are seen in histological sections. It has a cuboidal epithelium with smooth-surfaced cells nearly devoid of microvilli. The DCT is the end of the nephron.

The Collecting Duct The DCTs of several nephrons drain into a straight tubule called the **collecting duct,** which passes down into the medulla. Near the papilla, several collecting ducts merge to form a larger **papillary duct;** about 30 of these drain from each papilla into its minor calyx. The collecting and papillary ducts are lined with simple cuboidal epithelium.

The flow of fluid from the point where the glomerular filtrate is formed to the point where urine leaves the

[8] *urin* = urine + *fer* = to carry
[9] Friedrich G. J. Henle (1809–85), German anatomist

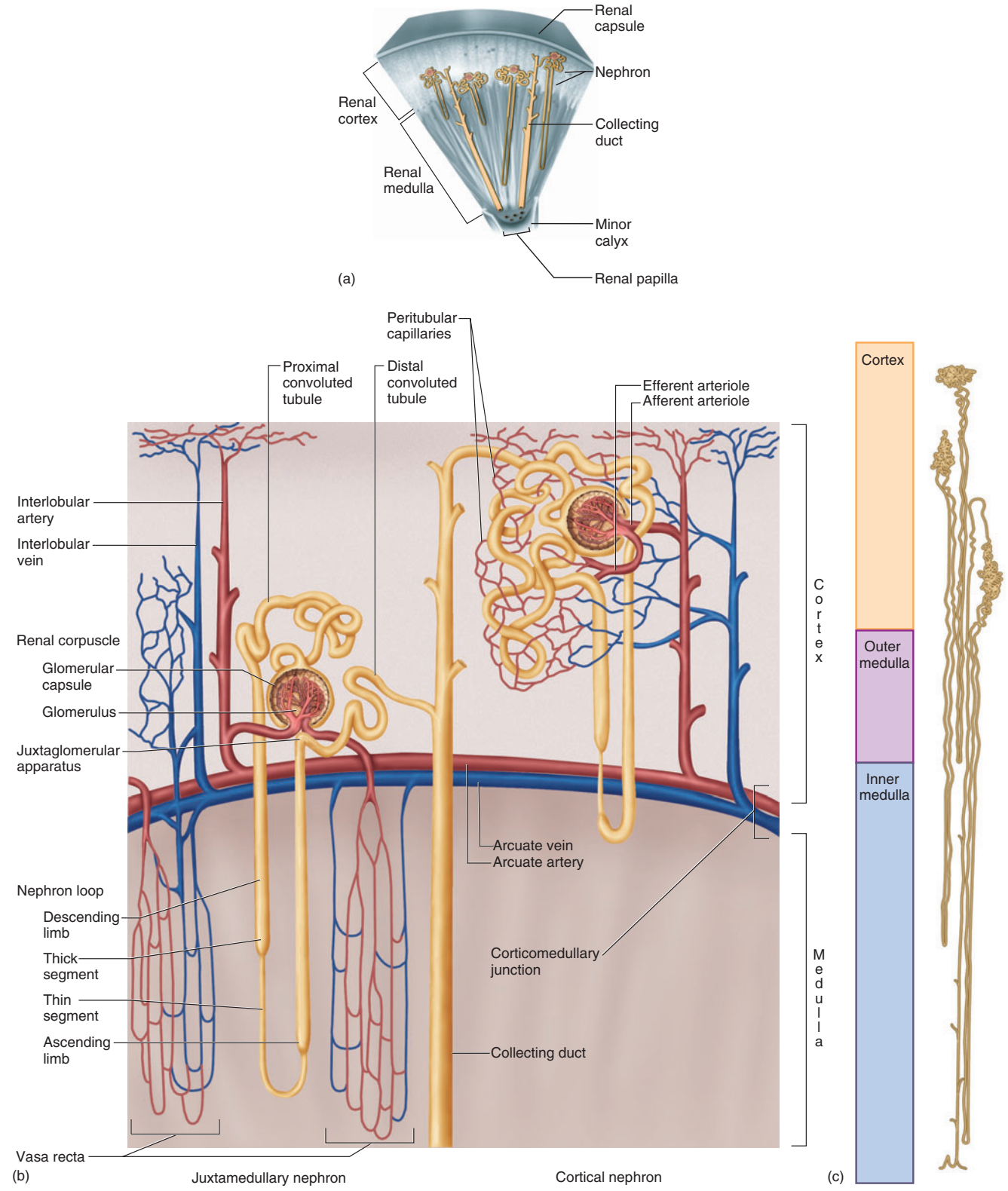


Figure 23.5 Structure of the Nephron. (*a*) Location of the nephrons in one wedge-shaped lobe of the kidney. (*b*) Structure of two nephrons. For clarity, vasa recta are shown only on the *left* and peritubular capillaries only on the *right*. Note that juxtamedullary nephrons are closer to the corticomedullary junction and have longer nephron loops than cortical nephrons. Vasa recta come only from the nephrons closest to the medulla. (*c*) The true proportions of the nephron loops relative to the convoluted tubules.

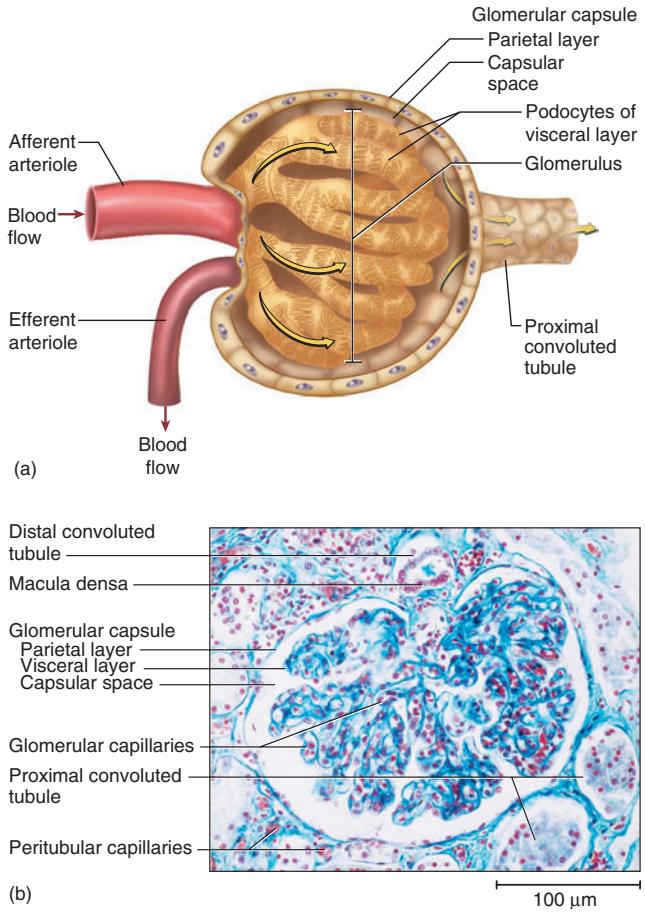


Figure 23.6 The Renal Corpuscle. (*a*) Anatomy of the corpuscle; (*b*) light micrograph.

body is: glomerular capsule → proximal convoluted tubule → nephron loop → distal convoluted tubule → collecting duct → papillary duct → minor calyx → major calyx → renal pelvis → ureter → urinary bladder → urethra.

Cortical and Juxtamedullary Nephrons

Nephrons just beneath the renal capsule, close to the kidney surface, are called **cortical nephrons.** They have relatively short nephron loops that dip only slightly into the outer medulla before turning back (see fig. 23.5*b, c*) or turn back even before leaving the cortex. Some cortical nephrons have no nephron loops at all. Nephrons close to the medulla are called **juxtamedullary**[10] **nephrons.** They have very long nephron loops that extend to the apex of the renal pyramid. As you will see later, nephron loops are responsible for maintaining a salinity gradient in the medulla that helps the body conserve water. Although only 15% of the nephrons are juxtamedullary, they are almost solely responsible for maintaining this gradient.

Blood Supply

Although the kidneys account for only 0.4% of the body weight, they receive about 21% of the cardiac output (the *renal fraction*). This attests to their importance in controlling blood volume and composition.

The larger divisions of the renal circulation are shown in figure 23.7*a*. Each kidney is supplied by a **renal artery** (occasionally two or more) arising from the aorta. Just before or after entering the hilum, the renal artery divides and eventually gives rise to a few **interlobar arteries.** One interlobar artery penetrates each renal column and travels between the pyramids to the *corticomedullary junction,* the boundary between the cortex and medulla. Here it branches again to form the **arcuate arteries,** which make a sharp 90° bend and travel along the base of the pyramid. Each arcuate artery gives rise to several **interlobular arteries,** which pass upward into the cortex.

The finer branches of the renal circulation are shown in figure 23.5*b*. As an interlobular artery ascends through the cortex, a series of **afferent arterioles** arise from it like the limbs of a pine tree. Each afferent arteriole supplies blood to one nephron and ends in the glomerulus described earlier. The glomerulus is drained by an **efferent arteriole.**

The afferent and efferent arterioles penetrate one side of the glomerular capsule together. Just outside the capsule, they contact the first part of the distal convoluted tubule and with it, form a **juxtaglomerular** (JUX-tuh-glo-MER-you-lur) **apparatus.** This is a device that enables a nephron to monitor and stabilize its own performance and compensate for fluctuations in blood pressure. It will be described in detail when we consider renal autoregulation.

The efferent arteriole leads next to a plexus of **peritubular capillaries,** named for the fact that they form a network around the renal tubules. Blood flows from the peritubular capillaries to, in order, the **interlobular veins, arcuate veins, interlobar veins,** and **renal vein,** which travel parallel to the arteries of the same names. The renal vein leaves the hilum and drains into the inferior vena cava.

The renal medulla receives only 1% to 2% of the total renal blood flow, supplied by a network of vessels called the **vasa recta.**[11] In the juxtamedullary nephrons, the efferent arterioles descend immediately into the medulla and give rise to the vasa recta instead of giving rise to peritubular capillaries. The capillaries of the vasa

[10] *juxta* = next to

[11] *vasa* = vessels + *recta* = straight

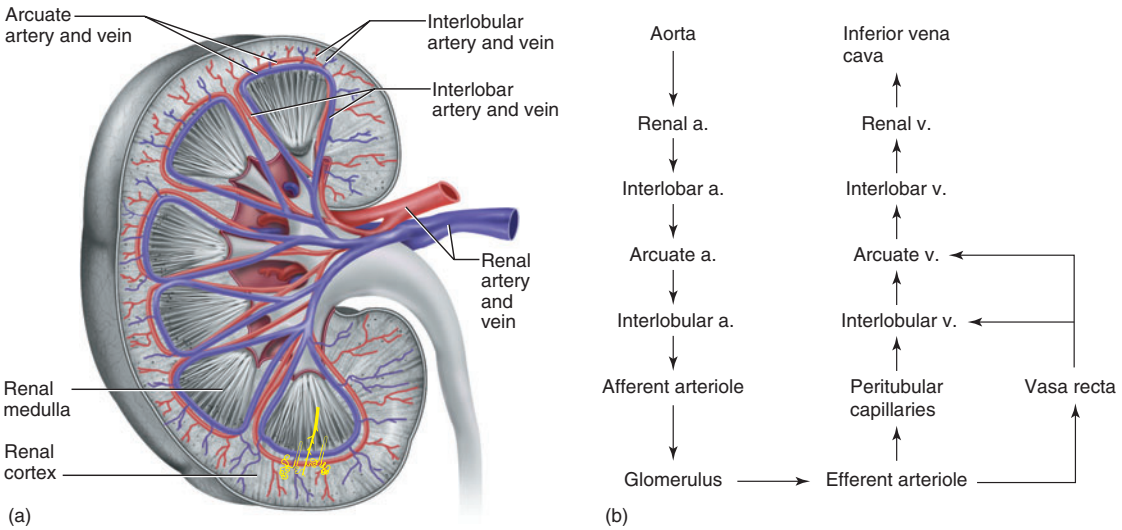


Figure 23.7 Renal Circulation. (*a*) The larger blood vessels of the kidney. (*b*) Flow chart of renal circulation. The pathway through the vasa recta (instead of peritubular capillaries) applies only to the juxtamedullary nephrons.

recta lead into venules that ascend and empty into the arcuate and interlobular veins. The route of renal blood flow is summarized in figure 23.7*b*.

Think About It

Can you identify a portal system in the renal circulation?

Nerve Supply

The **renal nerves** arise from the superior mesenteric ganglion (see p. 568) and enter the hilum of each kidney. They follow branches of the renal artery to reach individual nephrons. These nerves consist mostly of sympathetic fibers that regulate the blood flow into and out of each nephron, and thus control the rate of filtration and urine formation. If the blood pressure falls, they also stimulate the nephron to secrete renin, which ultimately restores blood pressure by mechanisms described later.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

4. Arrange the following in order from the most numerous to the least numerous structures in a kidney: glomeruli, major calices, minor calices, interlobular arteries, interlobar arteries.
5. Trace the path taken by one red blood cell from the renal artery to the renal vein.
6. Consider one molecule of urea in the urine. Trace the route that it took from the point where it left the bloodstream to the point where it left the body.

Urine Formation I: Glomerular Filtration

Objectives

When you have completed this section, you should be able to

- describe the glomerular filtration membrane and how it excludes blood cells and proteins from the filtrate;
- explain the forces that promote and oppose glomerular filtration, and calculate net filtration pressure if given the magnitude of these forces; and
- describe how the nervous system, hormones, and the kidney itself regulate glomerular filtration.

The kidney converts blood plasma to urine in three stages: glomerular filtration, tubular reabsorption and secretion, and water conservation (fig. 23.8). As we trace fluid through the nephron, we will refer to it by different names that reflect its changing composition: (1) The fluid in the capsular space, called **glomerular filtrate,** is similar to blood plasma except that it has almost no protein. (2) The fluid from the proximal convoluted tubule through the distal convoluted tubule will be called **tubular fluid.** It differs from the glomerular filtrate because of substances removed and added by the tubule cells. (3) The fluid will be called **urine** once it enters the collecting duct.

The Filtration Membrane

Glomerular filtration, discussed in this section, is a special case of the capillary fluid exchange process described in chapter 20. It is a process in which water and some

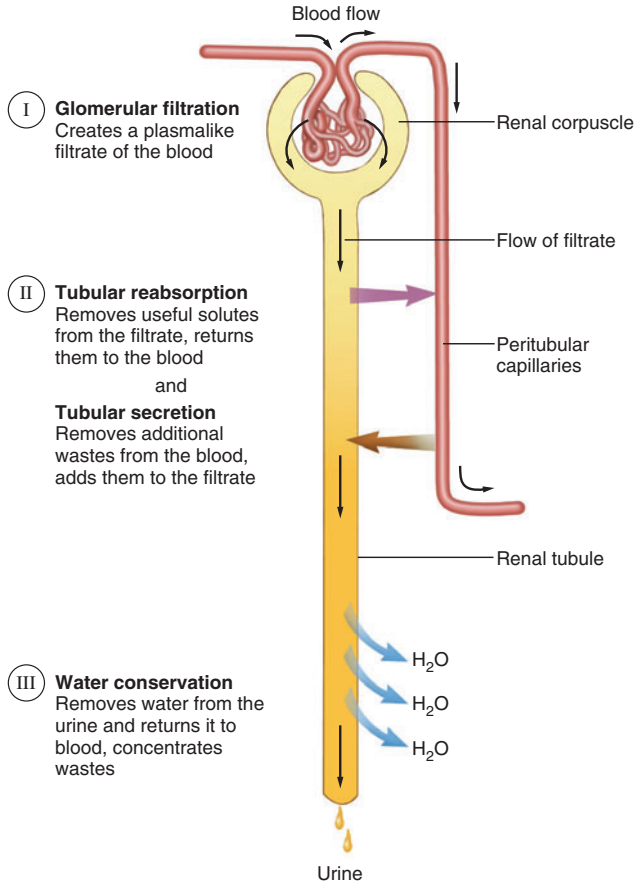


Figure 23.8 **Basic Steps in the Formation of Urine.**

solutes in the blood plasma pass from the capillaries of the glomerulus into the capsular space of the nephron. To do so, fluid passes through three barriers that constitute the **filtration membrane** (fig. 23.9):

1. **The fenestrated endothelium of the capillary.** Endothelial cells of the glomerular capillaries are honeycombed with large pores about 70 to 90 nm in diameter (see fig. 20.6, p. 752). They are much more permeable than endothelial cells elsewhere, although their pores are small enough to exclude blood cells from the filtrate.
2. **The basement membrane.** This membrane consists of a proteoglycan gel. For large molecules to pass through it is like trying to pass sand through a kitchen sponge. A few particles may penetrate its small spaces, but most are held back. On the basis of size alone, the basement membrane would exclude any molecules larger than 8 nm. Some smaller molecules, however, are also held back by a negative electrical charge on the proteoglycans. Blood albumin is slightly less than 7 nm in diameter, but it is also negatively charged and thus repelled by the basement membrane. While the blood plasma is 7% protein, the glomerular filtrate is only 0.03% protein. It has traces of albumin and smaller polypeptides, including some hormones.
3. **Filtration slits.** The podocytes of the glomerular capsule are shaped somewhat like octopi, with bulbous cell bodies and several thick arms. Each arm has numerous little extensions called **pedicels**[12]**(foot processes)** that wrap around the capillaries and interdigitate with each other, like wrapping your hands around a pipe and lacing your fingers together. The pedicels have negatively charged **filtration slits** about 30 nm wide between them, which are an additional obstacle to large anions.

Almost any molecule smaller than 3 nm can pass freely through the filtration membrane into the capsular space. This includes water, electrolytes, glucose, fatty acids, amino acids, nitrogenous wastes, and vitamins. Such substances have about the same concentration in the glomerular filtrate as in the blood plasma. Some substances of low molecular weight are retained in the bloodstream because they are bound to plasma proteins that cannot get through the membrane. For example, most calcium, iron, and thyroid hormone in the blood are bound to plasma proteins that retard their filtration by the kidneys. The small fraction that is unbound, however, passes freely through the filtration membrane and appears in the urine.

Kidney infections and trauma can damage the filtration membrane and allow albumin or blood cells to filter through. Kidney disease is sometimes marked by the presence of protein (especially albumin) or blood in the urine—conditions called **proteinuria (albuminuria)** and **hematuria,** respectively. Distance runners and swimmers often experience temporary proteinuria and hematuria. Strenuous exercise greatly reduces perfusion of the kidneys, and the glomerulus deteriorates under the prolonged hypoxia, thus leaking protein and sometimes blood into the filtrate.

Filtration Pressure

Glomerular filtration follows the same principles that govern filtration in other blood capillaries (see pp. 761–762), but there are significant differences in the magnitude of the forces involved:

- The blood hydrostatic pressure (BHP) is much higher here than elsewhere—about 60 mmHg compared with 10 to 15 mmHg in most other capillaries. This results from the fact that the afferent arteriole is substantially

[12] *pedi* = foot + *cel* = little

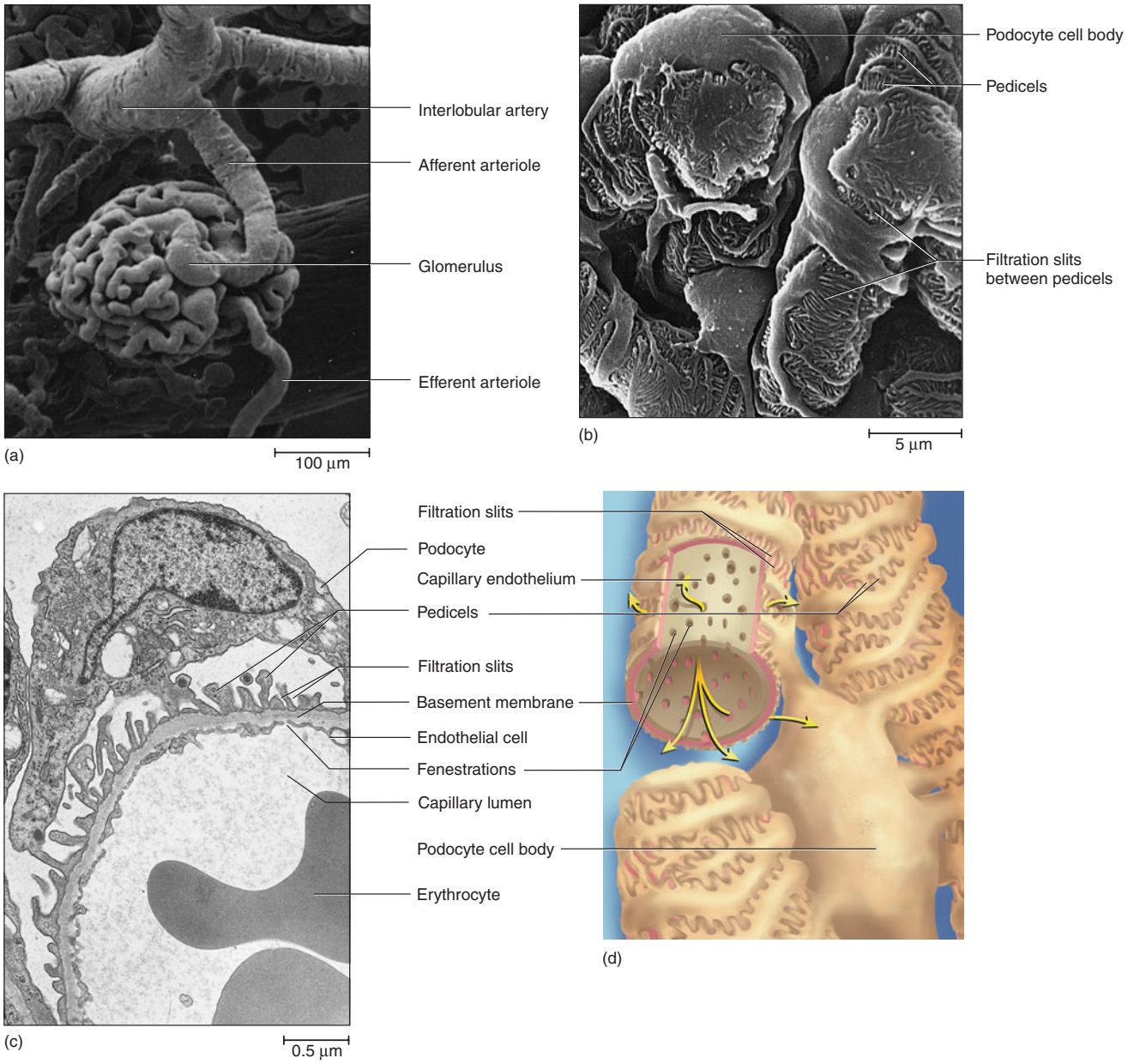


Figure 23.9 Structure of the Glomerulus. (*a*) A resin cast of the glomerulus and nearby arteries (SEM). (*b*) Blood capillaries of the glomerulus closely wrapped in the spidery podocytes that form the visceral layer of the glomerular capsule (SEM). (*c*) A blood capillary and podocyte showing fenestrations and filtration slits (TEM). (*d*) The production of glomerular filtrate by the passage of fluid through the fenestrations and filtration slits. (*a*) From R. G. Kessel and R. H. Kardon, *Tissues and Organs: A Text-Atlas of Scanning Electron Microscopy* (W. H. Freeman, 1979).
Which is larger, the efferent arteriole or the afferent arteriole? How does the difference affect the function of the glomerulus?

larger than the efferent arteriole, giving the glomerulus a large inlet and small outlet (fig. 23.9*a*).

- The hydrostatic pressure in the capsular space is about 18 mmHg, compared with the slightly negative interstitial pressures elsewhere. This results from the high rate of filtration occurring here and the continual accumulation of fluid in the capsule.
- The colloid osmotic pressure (COP) of the blood is about the same here as anywhere else, 32 mmHg.
- The glomerular filtrate is almost protein-free and has no significant COP. (This can change markedly in kidney diseases that allow protein to filter into the capsular space.)

On balance, then, we have a high outward pressure of 60 mmHg, opposed by two inward pressures of 18 and 32 mmHg (fig. 23.10), giving a net filtration pressure (NFP) of

$$60_{out} - 18_{in} - 32_{in} = 10\ mmHg_{out}$$

In most blood capillaries, the BHP drops low enough at the venous end that osmosis overrides filtration and the capillaries reabsorb fluid. Although BHP also drops along the course of the glomerular capillaries, it remains high enough that these capillaries are engaged solely in filtration. They reabsorb little or no fluid.

The high blood pressure in the glomeruli makes the kidneys especially vulnerable to hypertension, which can have devastating effects on renal function. Hypertension ruptures glomerular capillaries and leads to scarring of the kidneys *(nephrosclerosis).* It promotes atherosclerosis of the renal blood vessels just as it does elsewhere in the body and thus diminishes renal blood supply. Over time, hypertension often leads to renal failure.

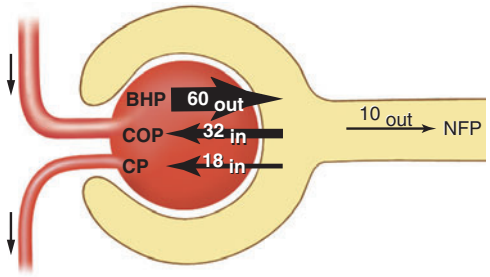
Glomerular Filtration Rate

Glomerular filtration rate (GFR) is the amount of filtrate formed per minute by the two kidneys combined. For every 1 mmHg of net filtration pressure, the kidneys produce about 12.5 mL of filtrate per minute. This value, called the *filtration coefficient (K_f),* depends on the permeability and surface area of the filtration barrier. K_f is about 10% lower in women than in men. For the reference male,

$$GFR = NFP \times K_f = 10 \times 12.5 = 125\ mL/min$$

In the reference female, the GFR is about 105 mL/min.

This is a rate of 180 L/day in males and 150 L/day in females—impressive numbers considering that this is about 50 to 60 times the amount of blood plasma in the body and equally exceeds the amount of filtrate produced by all other capillaries combined. Obviously only a small portion of this is eliminated as urine. An average adult reabsorbs 99% of the filtrate and excretes 1 to 2 L of urine per day.



Blood hydrostatic pressure (BHP)	60 mmHg out
Colloid osmotic pressure (COP)	–32 mmHg in
Capsular pressure (CP)	–18 mmHg in
Net filtration pressure (NFP)	10 mmHg out

Figure 23.10 **The Forces Involved in Glomerular Filtration.**

Regulation of Glomerular Filtration

GFR must be precisely controlled. If it is too high, fluid flows through the renal tubules too rapidly for them to reabsorb the usual amount of water and solutes. Urine output rises and creates a threat of dehydration and electrolyte depletion. If GFR is too low, fluid flows sluggishly through the tubules, they reabsorb wastes that should be eliminated in the urine, and azotemia may occur. The only way to adjust GFR from moment to moment is to change glomerular blood pressure. This is achieved by three homeostatic mechanisms: renal autoregulation, sympathetic control, and hormonal control.

Renal Autoregulation

Renal autoregulation is the ability of the nephrons to adjust their own blood flow and GFR without external (nervous or hormonal) control. It enables them to maintain a relatively stable GFR in spite of changes in arterial blood pressure. If the mean arterial pressure (MAP) rose from 100 to 125 mmHg and there were no renal autoregulation, urine output would increase from the normal 1 to 2 L/day to more than 45 L/day. Because of renal autoregulation, however, urine output increases only a few percent even if MAP rises as high as 160 mmHg. Renal autoregulation thus helps to ensure stable fluid and electrolyte balance in spite of the many circumstances that substantially alter one's blood pressure. There are two mechanisms of autoregulation: the myogenic mechanism and tubuloglomerular feedback.

The Myogenic Mechanism This mechanism of stabilizing the GFR is based on the tendency of smooth muscle to contract when stretched. When arterial blood pressure rises, it stretches the afferent arteriole. The arteriole constricts, and thus prevents blood flow into the glomerulus from changing very much. Conversely, when blood pressure

falls, the afferent arteriole relaxes and allows blood to flow more easily into the glomerulus. Either way, glomerular blood flow and filtration remain fairly stable.

Tubuloglomerular Feedback In this mechanism, the juxtaglomerular apparatus (JGA) monitors the fluid entering the distal convoluted tubule and adjusts the GFR to maintain homeostasis. An understanding of this mechanism requires a closer look at the components of the JGA (fig. 23.11).

1. The **juxtaglomerular (JG) cells** are enlarged smooth muscle cells found in the afferent arteriole and to some extent in the efferent arteriole. When stimulated by the macula densa (discussed next), they dilate or constrict the arterioles. They also contain granules of renin, which they secrete in response to a drop in blood pressure. This initiates negative feedback mechanisms, described later, that raise blood pressure.
2. The **macula densa**[13] is a patch of slender, closely spaced epithelial cells at the start of the distal convoluted tubule (DCT), directly across from the JG cells.
3. **Mesangial**[14] **cells** are found in the cleft between the afferent and efferent arterioles and among capillaries of the glomerulus. Their role is not yet clearly understood, but they are connected to the macula densa and JG cells by gap junctions and perhaps mediate communication between those cells.

The details of tubuloglomerular feedback are still obscure. If GFR rises, however, it increases the flow of tubular fluid and the rate of NaCl reabsorption. The macula densa apparently senses variations in flow or fluid composition and secretes a paracrine messenger that stimulates the juxtaglomerular cells. Contraction of the juxtaglomerular cells constricts the afferent arteriole, thus reducing GFR to normal. The mesangial cells amid the glomerular capillaries may also contract, constricting the capillaries and reducing filtration (fig. 23.12). Conversely, if GFR falls, the macula densa may secrete a different messenger causing the afferent arteriole and mesangial cells to relax, blood flow to increase, and GFR to rise back to normal.

Think About It

Describe or diagram a negative feedback loop similar to figure 23.12 to show how the macula densa could compensate for a drop in systemic blood pressure.

Two important points must be noted about renal autoregulation. First, it does not completely prevent changes in the GFR. Like any other homeostatic mechanism, it maintains a *dynamic equilibrium;* the GFR fluctuates within narrow limits. Changes in blood pressure do affect the GFR and urine output. Second, renal autoregulation cannot compensate for extreme blood pressure variations. Over a MAP range of 90 to 180 mmHg, the GFR remains quite stable. Below 70 mmHg, however, glomerular filtration and urine output cease. This can happen in hypovolemic shock (p. 765).

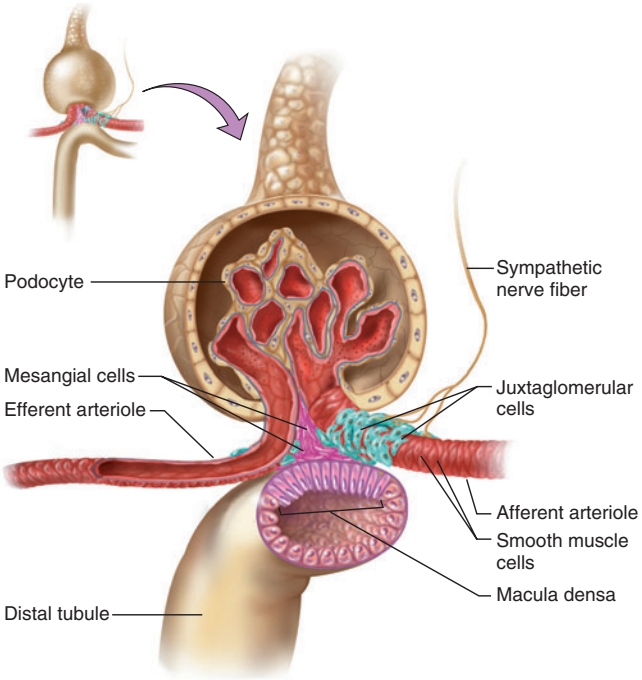


Figure 23.11 **The Juxtaglomerular Apparatus.**

Sympathetic Control

Sympathetic nerve fibers richly innervate the renal blood vessels. In strenuous exercise or acute conditions such as circulatory shock, the sympathetic nervous system and adrenal epinephrine constrict the afferent arterioles. This reduces GFR and urine production, while redirecting blood from the kidneys to the heart, brain, and skeletal muscles, where it is more urgently needed. Under such conditions, GFR may be as low as a few milliliters per minute.

The Renin-Angiotensin Mechanism

When blood pressure drops, the sympathetic nerves also stimulate the juxtaglomerular cells to secrete the enzyme **renin** (REE-nin). Renin acts on a plasma protein, *angiotensinogen,* to remove a fragment called angiotensin I, a chain of 10 amino acids. In the lungs and kidneys, **angiotensin-converting enzyme (ACE)** removes two more

[13] *macula* = spot, patch + *densa* = dense
[14] *mes* = in the middle + *angi* = vessel

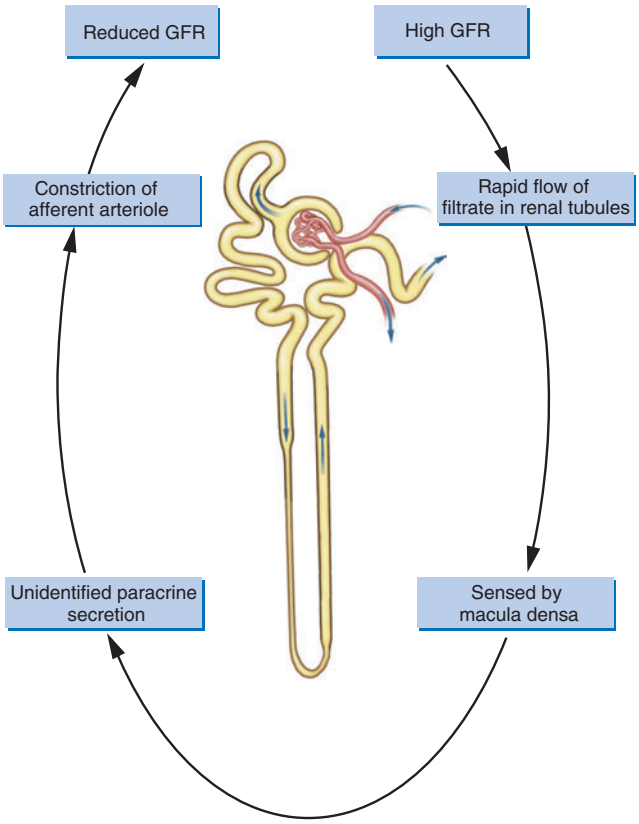


Figure 23.12 **Negative Feedback Control of Glomerular Filtration Rate.**

amino acids, converting it to **angiotensin II,** a hormone with multiple effects (fig. 23.13):

- It stimulates widespread vasoconstriction, which raises the MAP throughout the body.
- It constricts both the afferent and efferent arterioles. The net effect of this is to reduce GFR and water loss.
- It stimulates the secretion of antidiuretic hormone, which promotes water reabsorption.
- It stimulates the adrenal cortex to secrete aldosterone, which in turn promotes sodium and water retention.
- It stimulates the sense of thirst and encourages water intake.

Some of these effects are explained more fully later in this chapter and in chapter 24.

Think About It

What do you predict would be the effect of ACE inhibitors (see p. 759) on the tubular reabsorption of water by the kidneys?

To summarize the events thus far: Glomerular filtration occurs because the high blood pressure of the glomerular capillaries overrides reabsorption. The filtration membrane allows most plasma solutes into the capsular space while retaining formed elements and protein in the bloodstream. Glomerular filtration is maintained at a fairly steady rate of about 125 mL/min in spite of variations in systemic blood pressure. This stability is achieved by renal autoregulation, sympathetic control, and hormonal control.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

7. Name the four major processes in urine production.
8. Trace the movement of a urea molecule from the blood to the capsular space, and name the barriers it passes through.
9. Calculate the net filtration pressure in a patient whose blood COP is only 10 mmHg because of hypoproteinemia. Assume other relevant variables to be normal.
10. Assume a person is moderately dehydrated and has low blood pressure. Describe the homeostatic mechanisms that would help the kidneys maintain a normal GFR.

Urine Formation II: Tubular Reabsorption and Secretion

Objectives

When you have completed this section, you should be able to

- describe how the renal tubules reabsorb useful solutes from the glomerular filtrate and return them to the blood;
- describe how the tubules secrete solutes from the blood into the tubular fluid; and
- describe how the nephron regulates water excretion.

Conversion of the glomerular filtrate to urine involves the removal and addition of chemicals by tubular reabsorption and secretion, to be described in this section. Here we trace the course of the tubular fluid through the nephron, from proximal convoluted tubule through distal convoluted tubule, and see how the filtrate is modified at each point along the way. Refer to figure 23.8 to put these processes into perspective.

The Proximal Convoluted Tubule

The proximal convoluted tubule (PCT) reabsorbs about 65% of the glomerular filtrate, while it also removes some substances from the blood and secretes them into the tubule for disposal in the urine. The importance of the PCT is reflected in its relatively great length and prominent microvilli, which increase its absorptive surface area. Its cells also contain abundant large mitochondria that provide

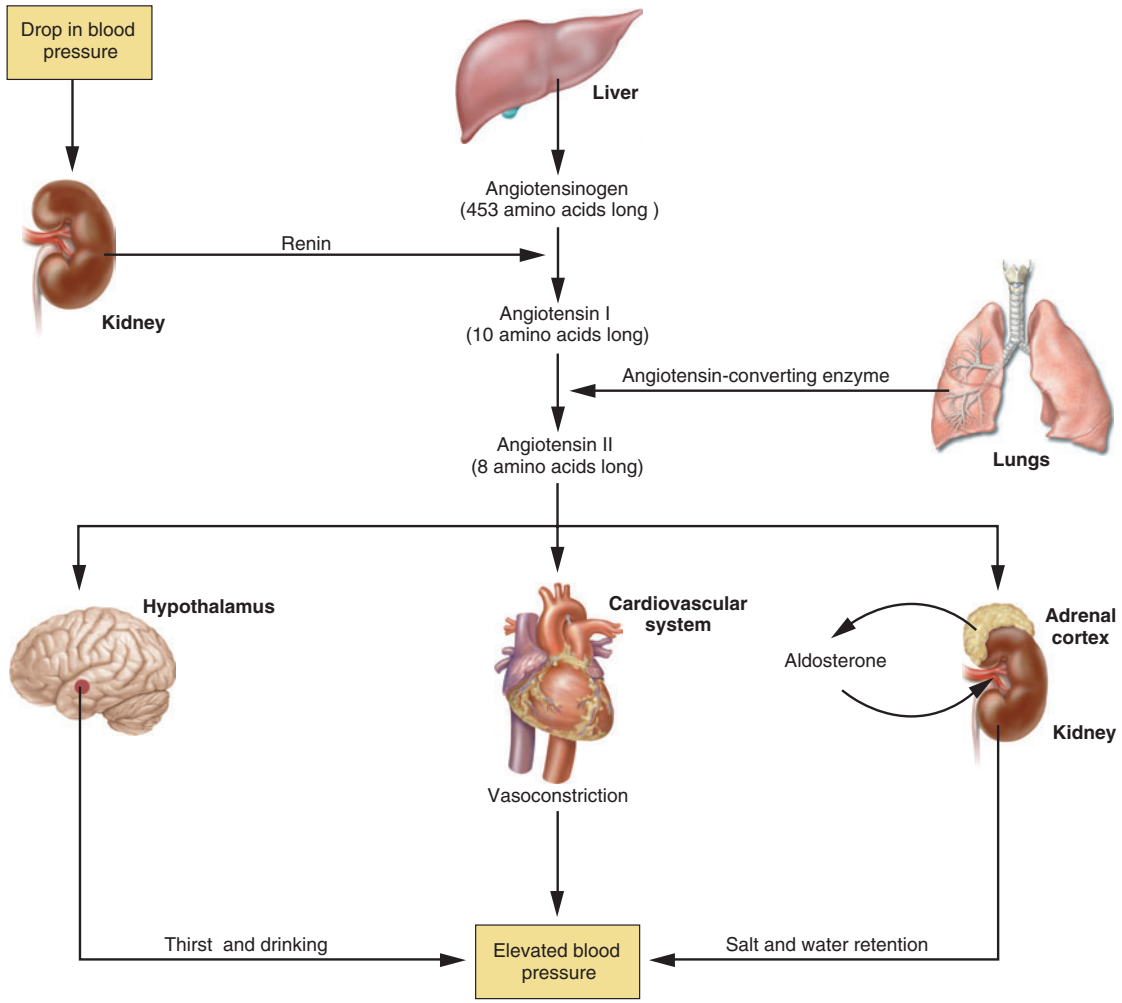


Figure 23.13 **The Renin-Angiotensin-Aldosterone Mechanism.** This chain of events is activated by a drop in blood pressure and acts to raise it again.

ATP for active transport. Your PCTs alone account for about 6% of your resting ATP and calorie consumption.

Tubular reabsorption is the process of reclaiming water and solutes from the tubular fluid and returning them to the blood. The PCT reabsorbs a greater variety of chemicals than any other part of the nephron. There are two routes of reabsorption: (1) the **transcellular**[15] **route,** in which substances pass through the cytoplasm and out the base of the epithelial cells and (2) the **paracellular**[16] **route,** in which substances pass between the epithelial cells. The "tight" junctions between tubule epithelial cells are quite leaky and allow significant amounts of water, minerals, urea, and other matter to pass between the cells. Either way, such materials enter the extracellular fluid (ECF) at the base of the epithelium, and from there they are taken up by the peritubular capillaries. In the following discussion and figure 23.14, we examine mechanisms for the reabsorption of water and some individual solutes.

Sodium Sodium reabsorption is the key to everything else, because it creates an osmotic and electrical gradient that drives the reabsorption of water and the other solutes. Sodium, the most abundant cation in the glomerular filtrate, is reabsorbed by both the transcellular and paracellular routes. It has a concentration of 140 mEq/L in the fluid entering the PCT and only 12 mEq/L in the cytoplasm of the

[15] *trans* = across
[16] *para* = next to

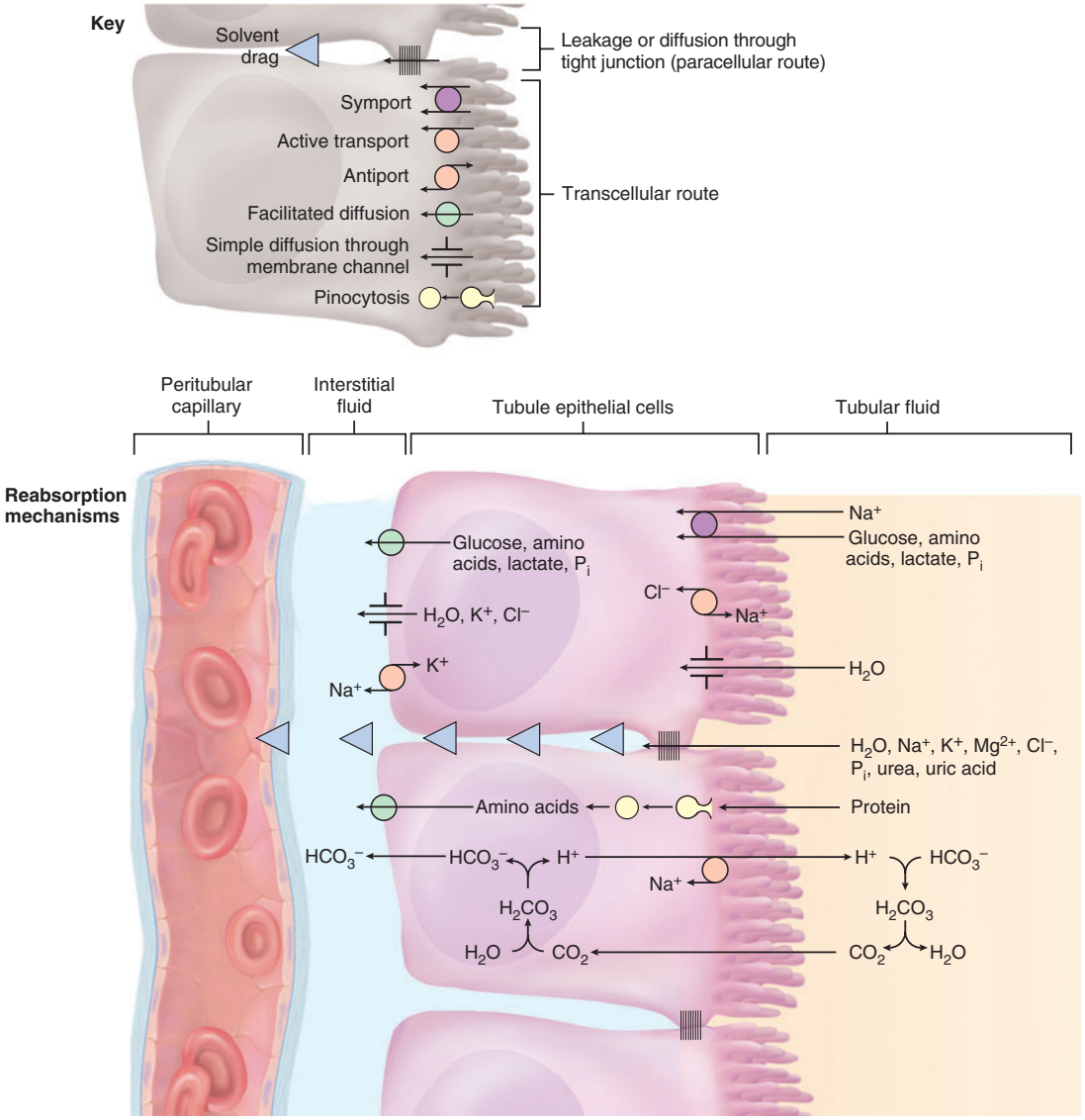


Figure 23.14 **Mechanisms of Reabsorption in the Proximal Convoluted Tubule.**
How would increased Na^+ reabsorption affect the pH of the urine? Why?

epithelial cells. Thus there is a steep concentration gradient favoring its facilitated diffusion into the epithelial cells.

In the first half of the proximal convoluted tubule, sodium is absorbed by several symport proteins that simultaneously bind glucose, amino acids, phosphate, or lactate and transport them into the cell. In addition, H^+ ions are generated within the cell by the reaction $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$, and then an Na^+-H^+ antiport in the membrane transports H^+ out of the cell and Na^+ in. (The fate of the HCO_3^- is explained shortly.) In the second half of the proximal tubule, the organic molecules in the tubular fluid have been largely depleted by reabsorption, but the chloride ion concentration is high. Thus, in this part of the tubule, Na^+ crosses the epithelium with Cl^- through both transcellular and paracellular routes.

Sodium uptake is possible only because the Na^+ concentration in the tubule cells is much lower than in the tubular fluid. But with all this Na^+ entering the tubule cells, how does its cytoplasmic concentration remain so low? Why doesn't the inflow of Na^+ stop? The

answer is that Na^+-K^+ pumps in the basal and lateral plasma membrane continually pump Na^+ out of the cell and into the extracellular fluid beneath the tubule epithelium. The transport of Na^+ and other Na^+-linked solutes through the apical plasma membrane thus exemplifies *secondary active transport,* because even though the cotransport proteins here do not use ATP, they depend on the ATP-consuming Na^+-K^+ pumps in the basolateral part of the cell.

Chloride Chloride is reabsorbed through both the paracellular and transcellular routes. Its reabsorption is favored by two factors: (1) negative chloride ions tend to follow the positive sodium ions by electrical attraction, and (2) water reabsorption raises the Cl^- concentration in the tubular fluid, thereby creating a gradient favorable to Cl^- reabsorption, especially in the second half of the tubule. In the transcellular route, Cl^- is apically absorbed by various antiports that exchange Cl^- for other anions. A K^+-Cl^- symport transports the chloride ions out the basolateral cell surfaces.

Bicarbonate Substantial amounts of bicarbonate ion (HCO_3^-) are filtered out of the blood by the glomerulus, and yet the urine is usually bicarbonate-free. Thus it would seem as if all the bicarbonate is reabsorbed by the nephron, but this is only an appearance. Bicarbonate ions do not actually cross the apical plasma membranes of the tubule cells. However, the tubule cells generate bicarbonate and hydrogen ions internally by the reaction of CO_2 and water. The hydrogen ions are pumped into the tubular fluid by the Na^+-H^+ antiport mentioned earlier, and neutralize the HCO_3^- in the tubule. The bicarbonate ions are pumped out the base of the cell and enter the blood. Thus one HCO_3^- disappears from the tubule fluid as one new HCO_3^- appears in the blood, and the net effect is the same as if an HCO_3^- ion had actually crossed the epithelium from tubular fluid to blood.

Other Electrolytes Potassium, magnesium, and phosphate (P_i) ions diffuse through the paracellular route with water. Phosphate is also cotransported into the epithelial cells with Na^+ as noted earlier. Some calcium is reabsorbed through the paracellular route in the proximal tubule, but most Ca^{2+} absorption occurs later in the nephron, as we will see then. Sulfates and nitrates are not reabsorbed; thus they pass in the urine.

Glucose Glucose is cotransported with Na^+ by carriers called **sodium-glucose transport proteins (SGLTs).** It is then removed from the basolateral surface of the cell by facilitated diffusion. Normally all glucose in the tubular fluid is reabsorbed and there is none in the urine.

Nitrogenous Wastes Urea diffuses through the tubule epithelium with water. The nephron as a whole reabsorbs 40% to 60% of the urea in the tubular fluid, but since it reabsorbs 99% of the water, urine has a substantially higher urea concentration than blood or glomerular filtrate. When blood enters the kidney, its urea concentration is about 20 mg/dL; when it leaves the kidney, it is typically down to 10.4 mg/dL. Thus the kidney removes about half of the urea, keeping its concentration down to a safe level but not completely clearing the blood of it.

The PCT reabsorbs nearly all the uric acid entering it, but later parts of the nephron secrete it back into the tubular fluid. Creatinine is not reabsorbed at all. It is too large to diffuse through water channels in the plasma membrane, and there are no transport proteins for it. Therefore, all creatinine filtered by the glomerulus is excreted in the urine.

Other Organic Solutes Some apical Na^+ carriers also bind and transport amino acids and lactate. Peptide hormones, other small peptides, and small amounts of larger proteins filter through the glomerulus. Although their rate of filtration is low, it would amount to a protein loss of 7.2 g/day if the protein were not reabsorbed. PCT cells partially degrade proteins to smaller peptides by means of enzymes on their brush border, then absorb the peptides and break them down the rest of the way to amino acids. Amino acids, lactate, and other small organics leave the basal side of the cell by facilitated diffusion.

Water The kidneys reduce about 180 liters of glomerular filtrate to 1 or 2 liters of urine each day, so obviously water reabsorption is a significant function. About two-thirds of the water is reabsorbed by the PCT. The reabsorption of all the salt and organic solutes as just described makes the tubule cells and surrounding tissue fluid hypertonic to the tubular fluid. Water follows the solutes by osmosis through both the paracellular and transcellular routes. Transcellular absorption occurs by way of water channels called **aquaporins** in the plasma membrane.

Because the PCT reabsorbs proportionate amounts of solutes and water, the osmolarity of the tubular fluid remains unchanged in the PCT. Elsewhere in the nephron, the amount of water reabsorption is continually modulated by hormones according to the body's state of hydration. In the PCT, however, water is reabsorbed at a constant rate called **obligatory water reabsorption.**

Uptake By the Peritubular Capillaries

After water and solutes leave the basal surface of the tubule epithelium, they are reabsorbed by the peritubular capillaries, thus returning to the bloodstream. The mechanisms of capillary absorption are osmosis and solvent drag. Three factors promote osmosis into these capillaries: (1) The accumulation of reabsorbed fluid around the basolateral sides of the epithelial cells creates a high interstitial fluid pressure that tends to drive water into the capillaries. (2) The narrowness of the efferent arteriole lowers the blood hydrostatic pressure (BHP) from 60 mmHg in the glomerulus to only 8 mmHg in the peritubular capillaries,

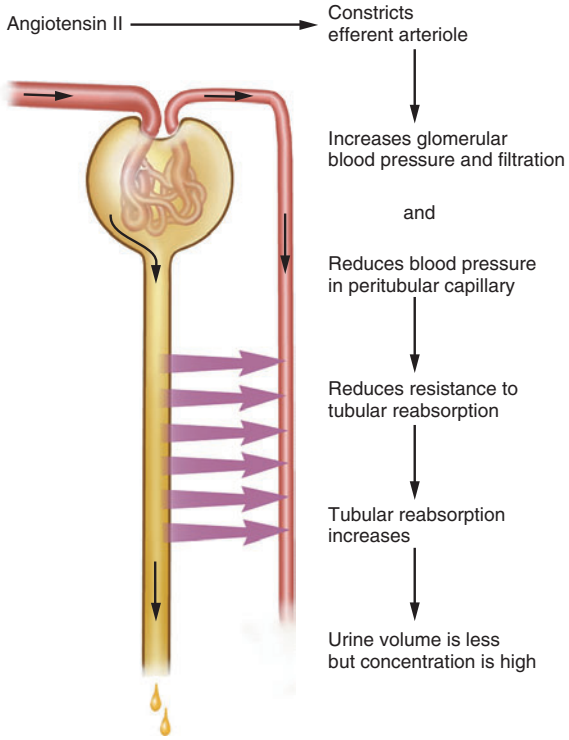


Figure 23.15 **The Effect of Angiotensin II on Urine Volume and Concentration.**

so there is less capillary resistance to reabsorption here than in most systemic capillaries (fig. 23.15). (3) As blood passes through the glomerulus, a lot of water is filtered out but nearly all of the protein remains in the blood. Therefore, the blood has an elevated colloid osmotic pressure (COP) by the time it leaves the glomerulus. With a high COP and low BHP in the capillaries and a high hydrostatic pressure in the tissue fluid, the balance of forces in the peritubular capillaries strongly favors reabsorption. Water on the basal side of the tubular epithelium therefore passes into the capillaries. The dissolved solutes enter the capillaries by **solvent drag**—the water "drags" these solutes into the capillary with it.

The Transport Maximum

There is a limit to the amount of solute that the renal tubule can reabsorb because there are a limited number of transport proteins in the plasma membranes. If all the transporters are occupied as solute molecules pass through, some solute will escape reabsorption and appear in the urine. The maximum rate of reabsorption is the *transport maximum (T_m),* which is reached when the transporters are saturated (see p. 109). Each organic solute reabsorbed by the renal tubule has its own T_m. For glucose, for example, T_m = 320 mg/min. Glucose normally enters the renal tubule at a rate of 125 mg/min, well within the T_m; thus all of it is reabsorbed. But when the plasma concentration of glucose reaches a *threshold* of about 220 mg/dL, more glucose is filtered than the tubule can reabsorb, and we begin to see the excess glucose in the urine, a condition called **glycosuria**[17] (GLY-co-soo-ree-uh). In untreated diabetes mellitus, the plasma glucose concentration may exceed 400 mg/dL, so glycosuria is one of the classic signs of this disease.

Tubular Secretion

Tubular secretion is a process in which the renal tubule extracts chemicals from the capillary blood and secretes them into the tubular fluid (see fig. 23.8). Tubular secretion in the distal convoluted tubule is discussed shortly. In the proximal convoluted tubule and nephron loop, it serves two purposes:

1. **Waste removal.** Urea, uric acid, bile acids, ammonia, catecholamines, and a little creatinine are secreted into the tubule. Tubular secretion of uric acid compensates for its reabsorption earlier in the PCT and accounts for all of the uric acid in the urine. Tubular secretion also clears the blood of pollutants, morphine, penicillin, aspirin, and other drugs. One reason that so many drugs must be taken three or four times a day is to keep pace with this rate of clearance and maintain a therapeutically effective drug concentration in the blood.
2. **Acid-base balance.** Tubular secretion of hydrogen and bicarbonate ions serves to regulate the pH of the body fluids. The details are discussed in chapter 24.

The Nephron Loop

The primary function of the nephron loop is to generate a salinity gradient that enables the collecting duct to concentrate the urine and conserve water, as discussed later. But in addition, the loop reabsorbs about 25% of the Na^+, K^+, and Cl^- and 15% of the water in the glomerular filtrate. Cells in the thick segment of the loop have proteins in the apical membranes that simultaneously bind 1 Na^+, 1 K^+, and 2 Cl^- from the tubular fluid and cotransport them into the cytoplasm. These ions leave the basolateral cell surfaces by active transport of Na^+ and diffusion of K^+ and Cl^-. Potassium reenters the cell by means of the Na^+-K^+ pump and then reenters the tubular fluid, but NaCl remains in the tissue fluid of the renal medulla. The thick segment of the loop is impermeable to water; thus water cannot follow the

[17] *glycos* = sugar + *uria* = urine condition

reabsorbed electrolytes, and tubular fluid becomes very dilute by the time it passes from the nephron loop into the distal convoluted tubule.

The Distal Convoluted Tubule and Collecting Duct

Fluid arriving in the DCT still contains about 20% of the water and 7% of the salts from the glomerular filtrate. If this were all passed as urine, it would amount to 36 L/day, so obviously a great deal of fluid reabsorption is still to come. A distinguishing feature of these parts of the renal tubule is that unlike the PCT and nephron loop, they are subject to hormonal control—particularly by aldosterone, atrial natriuretic peptide, antidiuretic hormone, and parathyroid hormone. There are two kinds of cells in the DCT and collecting duct. The **principal cells** are the more abundant; they have receptors for these hormones and are involved chiefly in salt and water balance. The **intercalated cells** are fewer in number. They have a high density of mitochondria, reabsorb K^+, secrete H^+ into the tubule lumen, and are involved mainly in acid-base balance, as discussed in chapter 24.

Aldosterone

Aldosterone, the "salt-retaining hormone," is a steroid secreted by the adrenal cortex. A drop in blood Na^+ concentration or a rise in K^+ concentration directly stimulates aldosterone secretion. A drop in blood pressure does so indirectly—it stimulates the kidney to secrete renin, this leads to the production of angiotensin II, and angiotensin II stimulates aldosterone secretion (see fig. 23.13). The mechanism of aldosterone action on the kidney tubule is detailed in the following chapter, but its general effect is to cause the DCT and cortical portion of the collecting duct to reabsorb more Na^+ (which is followed by Cl^- and water) and to secrete more K^+. Thus the urine volume is reduced, and it contains more K^+ but less NaCl. Salt and water reabsorption helps to maintain blood volume and pressure.

Atrial Natriuretic Peptide

Atrial natriuretic peptide (ANP) is secreted by the atrial myocardium of the heart in response to high blood pressure. ANP has four actions that result in the excretion of more salt and water in the urine, thus reducing blood volume and pressure:

1. It dilates the afferent arteriole and constricts the efferent arteriole, thus increasing the glomerular filtration rate.
2. It antagonizes the angiotensin-aldosterone mechanism by inhibiting the adrenal cortex from secreting aldosterone and inhibiting the kidney from secreting renin.
3. It inhibits the secretion of ADH by the pituitary and the action of ADH on the kidney.
4. It inhibits NaCl reabsorption by the collecting duct.

Antidiuretic Hormone

Antidiuretic hormone (ADH) is secreted by the posterior lobe of the pituitary gland in response to dehydration and rising blood osmolarity. Its mechanism of action is explained later in more detail. Briefly, it makes the collecting duct more permeable to water, so water in the tubular fluid reenters the tissue fluid and bloodstream rather than being lost in the urine.

Parathyroid Hormone

Parathyroid hormone (PTH) promotes calcium reabsorption by the ascending limb of the nephron loop and the DCT. PTH is secreted when the plasma Ca^{2+} concentration falls below normal, and acts to minimize further loss of Ca^{2+} in the urine. PTH also inhibits phosphate reabsorption by the proximal convoluted tubule, thus increasing the urinary output of phosphate. This prevents phosphate from binding with plasma calcium and precipitating in the bone and other tissues. PTH also promotes magnesium reabsorption, and stimulates the kidney to complete the synthesis of calcitriol (see chapter 7).

In summary, the PCT reabsorbs about 65% of the glomerular filtrate and returns it to the blood of the peritubular capillaries. Much of this reabsorption occurs by osmotic and cotransport mechanisms linked to the active transport of sodium ions. The nephron loop reabsorbs another 25% of the filtrate, although its primary role, detailed later, is to aid the function of the collecting duct. The DCT reabsorbs more sodium, chloride, and water, but its rates of reabsorption are subject to control by hormones, especially aldosterone and ANP. These tubules also extract drugs, wastes, and some other solutes from the blood and secrete them into the tubular fluid. The DCT essentially completes the process of determining the chemical composition of the urine. The principal function left to the collecting duct is to conserve body water.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

11. The reabsorption of water, Cl^-, and glucose by the PCT are all linked to the reabsorption of Na^+, but in three very different ways. Contrast these three mechanisms.
12. Explain why a substance appears in the urine if its rate of glomerular filtration exceeds the T_m of the renal tubule.
13. Contrast the effects of aldosterone and ANF on the renal tubule.

Urine Formation III: Water Conservation

Objectives

When you have completed this section, you should be able to

- explain how the collecting duct and antidiuretic hormone regulate the volume and concentration of urine; and
- explain how the kidney maintains an osmotic gradient in the renal medulla that enables the collecting duct to function.

The kidney serves not just to eliminate metabolic waste from the body but to prevent excessive water loss in doing so, and thus to support the body's fluid balance. As the kidney returns water to the tissue fluid and bloodstream, the fluid remaining in the renal tubule becomes more and more concentrated. In this section, we examine the kidney's mechanisms for conserving water and concentrating the urine.

The Collecting Duct

The collecting duct (CD) begins in the cortex, where it receives tubular fluid from numerous nephrons. As it passes through the medulla, it usually reabsorbs water and concentrates the urine. When urine enters the upper end of the CD, it has a concentration of 100 to 300 mOsm/L, but by the time it leaves the lower end, it can be up to four times as concentrated. This ability to concentrate wastes and control water loss was crucial to the evolution of terrestrial animals such as ourselves (see insight 23.1).

Two facts enable the collecting duct to produce such hypertonic urine: (1) the osmolarity of the extracellular fluid is four times as high deep in the medulla as it is in the cortex, and (2) the medullary portion of the CD is more permeable to water than to NaCl. Therefore, as urine passes down the CD through the increasingly salty medulla, water leaves the tubule by osmosis, most NaCl and other wastes remain behind, and the urine becomes more and more concentrated (fig. 23.16).

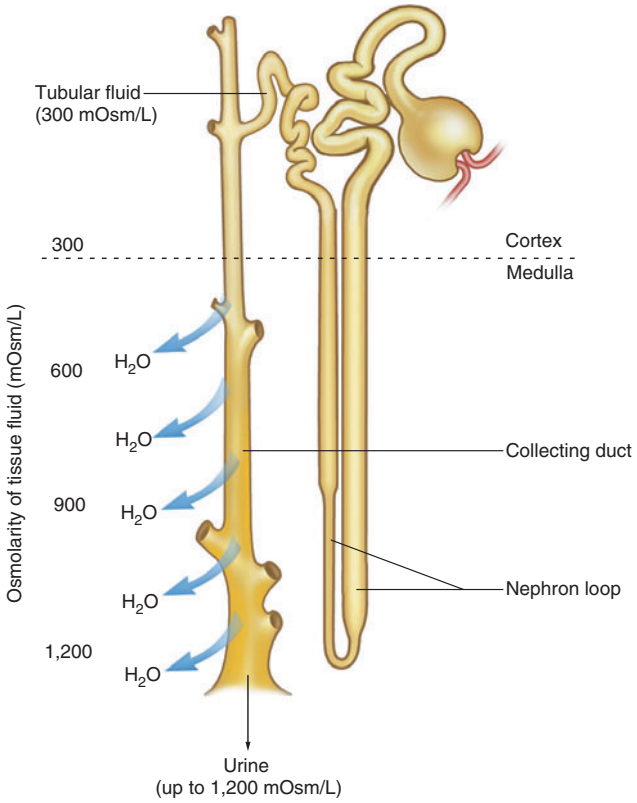


Figure 23.16 Water Reabsorption by the Collecting Duct. Note that the osmolarity of the tissue fluid increases fourfold from 300 mOsm/L in the cortex to 1,200 mOsm/L deep in the medulla. When the collecting duct has open water channels, water leaves the duct by osmosis and urine concentration increases.

Insight 23.1 Evolutionary Medicine

The Kidney and Life on Dry Land

Physiologists first suspected that the nephron loop plays a role in water conservation because of their studies of a variety of animal species. Animals that must conserve water have longer, more numerous nephron loops than animals with little need to conserve it. Fish and amphibians lack nephron loops and produce urine that is isotonic to their blood plasma. Aquatic mammals such as beavers have short nephron loops and only slightly hypertonic urine.

But the kangaroo rat, a desert rodent, provides an instructive contrast. It lives on seeds and other dry foods and need never drink water. The water produced by its aerobic respiration is enough to meet its needs because its kidneys are extraordinarily efficient at conserving water. They have extremely long nephron loops and produce urine that is 10 to 14 times as concentrated as their blood plasma (compared with about 4 times, at most, in humans).

Comparative studies thus suggested a hypothesis for the function of the nephron loop and prompted many years of difficult research that led to the discovery of the countercurrent multiplier mechanism for water conservation. This shows how comparative anatomy provides suggestions and insights into function and why physiologists do not study human function in isolation from other species.

Control of Water Loss

Just *how* concentrated the urine becomes depends on the body's state of hydration. For example, if you drink a large volume of water, you will soon produce a large volume of hypotonic urine. This response is called *water diuresis*[18] (DY-you-REE-sis). Under such conditions, the cortical

[18] *diuresis* = passing urine

portion of the CD reabsorbs NaCl but is impermeable to water. Thus salt is removed from the urine, water stays in the CD, and urine concentration may be as low as 50 mOsm/L.

Dehydration, on the other hand, causes your urine to be scanty and more concentrated. The high blood osmolarity of a dehydrated person stimulates the release of ADH from the posterior lobe of the pituitary gland. ADH induces the renal tubule cells to synthesize aquaporins (water-channel proteins) and install them in the plasma membrane, so more water can pass through the epithelial cells. The CD then reabsorbs more water, which is carried away by the peritubular capillaries. Urine output is consequently reduced. By contrast, when you are well hydrated, ADH secretion falls and the tubule cells remove aquaporins from the plasma membrane. Water is then less able to escape the tubule, so it remains in the duct and you produce abundant, dilute urine.

In extreme cases, the blood pressure of a dehydrated person is low enough to reduce the glomerular filtration rate. When the GFR is low, fluid flows more slowly through the renal tubules and there is more time for tubular reabsorption. Less salt remains in the urine as it enters the collecting duct, so there is less opposition to the osmosis of water out of the duct and into the ECF. More water is reabsorbed and less urine is produced.

The Countercurrent Multiplier

The ability of the CD to concentrate urine depends on the salinity gradient of the renal medulla. It may seem surprising that the ECF is four times as salty deep in the medulla as it is in the cortex. We would expect the salt to diffuse toward the cortex until it was evenly distributed through the kidney. However, there is a mechanism that overrides this—the nephron loop acts as a **countercurrent multiplier,** which continually recaptures salt and returns it to the deep medullary tissue. It is called a *multiplier* because it multiplies the salinity deep in the medulla and a *countercurrent* mechanism because it is based on fluid flowing in opposite directions in two adjacent tubules—downward in the descending limb and upward in the ascending limb. The countercurrent multiplier works as follows:

1. The thin segment of the descending limb is very permeable to water but not to NaCl. Therefore, as the tubular fluid descends into the increasingly salty medulla, more and more water leaves the descending limb while NaCl remains in the tubule. As the fluid reaches the lower end of the loop, it has a concentration of about 1,200 mOsm/L.
2. Most or all of the ascending limb (its thick segment), by contrast, is impermeable to water, but actively cotransports Na^+, K^+, and Cl^- into the ECF. This keeps the osmolarity of the renal medulla high. Since water remains in the tubule, the tubular fluid becomes more and more dilute as it approaches the cortex. It is about 100 mOsm/L at the top of the loop.

The essence of the *countercurrent* mechanism is that the two limbs of the nephron loop are close enough to influence each other through a positive feedback relationship, as shown in figure 23.17.

The collecting duct also helps to maintain the osmotic gradient (fig. 23.18). Its lower end is somewhat permeable to urea, which diffuses down its concentration gradient, out of the duct and into the tissue fluid. Some of this urea enters the descending thin segment of the nephron loop and travels to the distal convoluted tubule. Neither the thick segment of the loop nor the distal tubule is permeable to urea, so urea remains in the tubules and returns to the collecting duct. Combined with new urea being added continually by the glomerular filtrate, urea becomes more and more concentrated in the fluid of the collecting duct, and still more diffuses out into the medulla. Thus there is a continual recycling of urea from the collecting duct to the medulla and back. Urea accounts for about 40% of the high osmolarity deep in the medulla.

The Countercurrent Exchange System

The renal medulla must have a blood supply to meet its metabolic needs, and this creates a potential problem—capillaries of the medulla could carry away the urea and salt that produce the high osmolarity. The vasa recta that supply the medulla, however, form a countercurrent system of their own that prevents this from happening. Blood flows in opposite directions in adjacent parallel capillaries. These capillaries form a **countercurrent exchange system.** Blood in the vasa recta exchanges water for salt as it flows downward into the deep medulla—water diffuses out of the capillaries and salt diffuses in. As the blood flows back toward the cortex, the opposite occurs; it exchanges salt for water. Thus, the vasa recta give the salt back and do not subtract from the osmolarity of the medulla. Indeed, they absorb more water on the way out than they unload on the way in; they carry away the water reabsorbed from the urine by the collecting duct and nephron loop.

To summarize what we have studied in this section, the collecting duct can adjust water reabsorption to produce urine as hypotonic as 50 mOsm/L or as hypertonic as 1,200 mOsm/L, depending on the body's need for water conservation or removal. In a state of hydration, ADH is not secreted and the cortical part of the CD reabsorbs salt without reabsorbing water; the water remains to be excreted in the dilute urine. In a state of dehydration, ADH is secreted, the medullary part of the CD reabsorbs water, and the urine is more concentrated. The CD

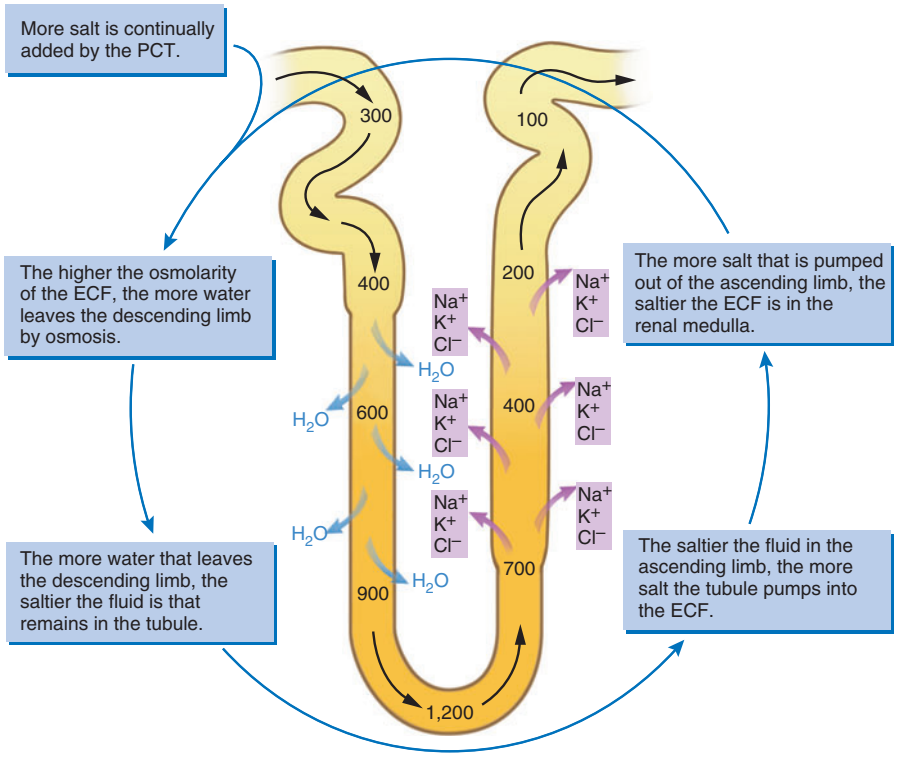


Figure 23.17 **The Countercurrent Multiplier of the Nephron Loop.**

is able to do this because it passes through a salinity gradient in the medulla from 300 mOsm/L near the cortex to 1,200 mOsm/L near the papilla. This gradient is produced by a countercurrent multiplier of the nephron loop, which concentrates NaCl in the lower medulla, and by the diffusion of urea from the collecting duct into the medulla. The vasa recta are arranged as a countercurrent exchange system that enables them to supply blood to the medulla without subtracting from its salinity gradient. Figure 23.19 summarizes the major solutes reabsorbed and secreted in each part of the renal tubule. Table 23.1 summarizes the hormones that affect renal function.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

14. Predict how ADH hypersecretion would affect the sodium concentration of the urine, and explain why.
15. Concisely contrast the role of the countercurrent multiplier with that of the countercurrent exchanger.
16. How would the function of the collecting duct change if the nephron loop did not exist?

Urine and Renal Function Tests

Objectives

When you have completed this section, you should be able to

- describe the composition and properties of urine; and
- carry out some calculations to evaluate renal function.

Medical diagnosis often rests on determining the current and recent physiological state of the tissues. No two fluids are as valuable for this purpose as blood and urine. **Urinalysis,** the examination of the physical and chemical properties of urine, is therefore one of the most routine procedures in medical examinations. The principal characteristics of urine and certain tests used to evaluate renal function are described here.

Composition and Properties of Urine

The basic composition and properties of urine are as follows:

- **Appearance.** Urine varies from almost colorless to deep amber, depending on the body's state of hydration. The yellow color of urine is due to **urochrome,** a pigment produced by the breakdown of

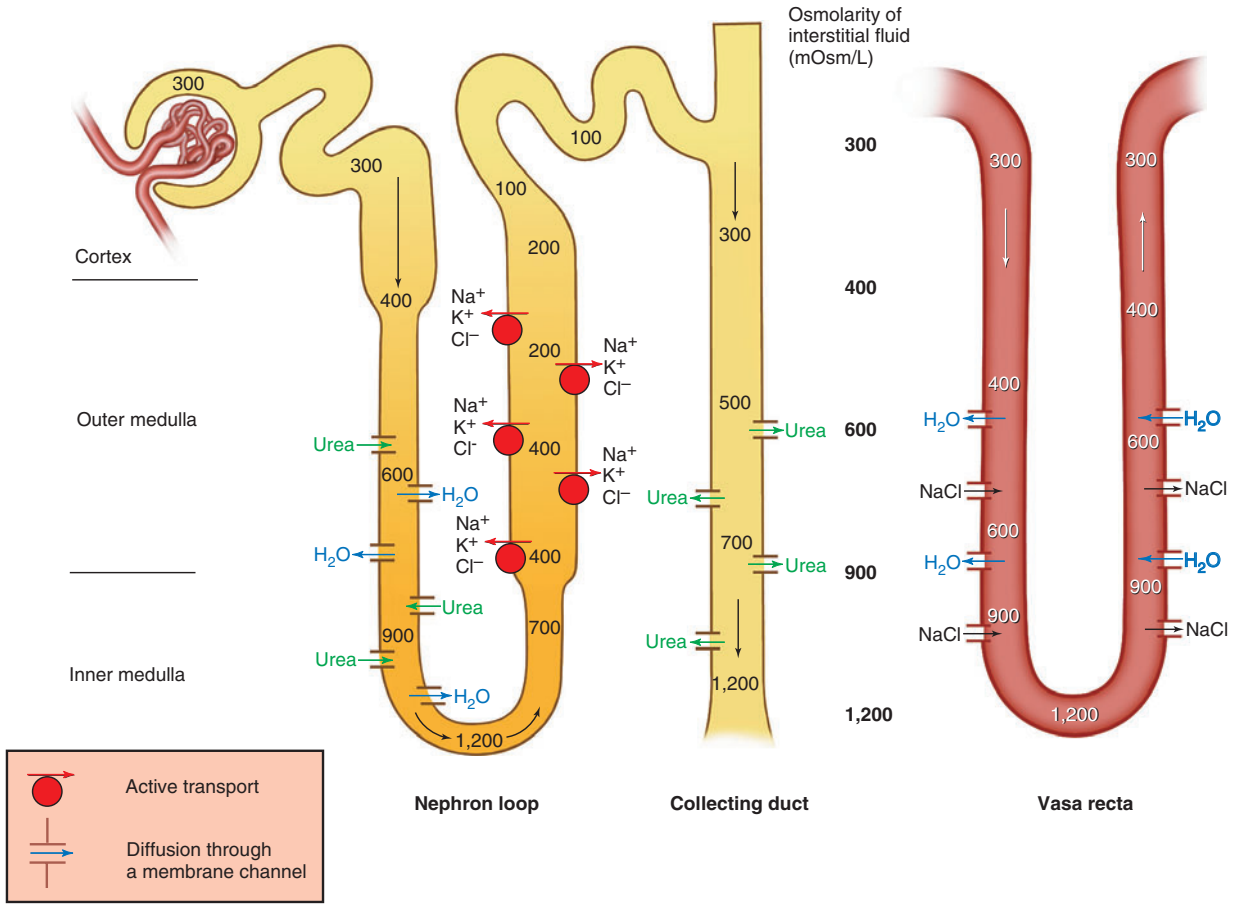


Figure 23.18 **The Relationship of the Nephron Loop, Vasa Recta, and Collecting Duct in Maintaining the Osmolarity of the Renal Medulla.**

hemoglobin from expired erythrocytes. Pink, green, brown, black, and other colors result from certain foods, vitamins, drugs, and metabolic diseases. Urine is normally clear but turns cloudy upon standing because of bacterial growth. Pus in the urine **(pyuria)** makes it cloudy and suggests kidney infection. Blood in the urine (hematuria) may be due to a urinary tract infection, trauma, or kidney stones. Cloudiness or blood in a urine specimen sometimes, however, simply indicates contamination with semen or menstrual fluid.

- **Odor.** Fresh urine has a distinctive but not repellent odor. As it stands, however, bacteria multiply, degrade urea to ammonia, and produce the pungent odor typical of stale wet diapers. Asparagus and other foods can impart distinctive aromas to the urine. Diabetes mellitus gives it a sweet, "fruity" odor of acetone. A "mousy" odor suggests phenylketonuria (PKU), and a "rotten" odor may indicate urinary tract infection.
- **Specific gravity.** This is a ratio of the density (g/mL) of a substance to the density of distilled water. Distilled water has a specific gravity of 1.000, and urine ranges from 1.001 when it is very dilute to 1.028 when it is very concentrated. Multiplying the last two digits of the specific gravity by a proportionality constant of 2.6 gives an estimate of the grams of solid matter per liter of urine. For example, a specific gravity of 1.025 indicates a solute concentration of 25 × 2.6 = 65 g/L.
- **Osmolarity.** Urine can have an osmolarity as low as 50 mOsm/L in a very hydrated person or as high as 1,200 mOsm/L in a dehydrated person. Compared with the osmolarity of blood (300 mOsm/L), then, urine can be either hypotonic or hypertonic under different conditions.
- **pH.** The pH of urine ranges from 4.5 to 8.2 but is usually about 6.0 (mildly acidic). The regulation of urine pH is discussed extensively in chapter 24.

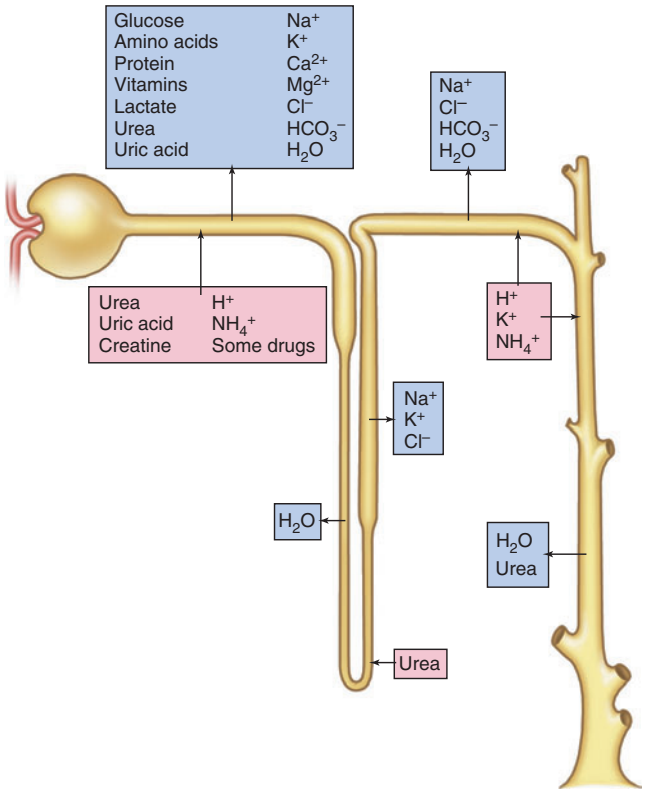


Figure 23.19 **Solutes Reabsorbed (*blue*) and Secreted (*pink*) in Different Portions of the Renal Tubule.**

- **Chemical composition.** Urine averages 95% water and 5% solutes by volume. Normally, the most abundant solute is urea, followed by sodium chloride, potassium chloride, and lesser amounts of creatinine, uric acid, phosphates, sulfates, and traces of calcium, magnesium, and sometimes bicarbonate (table 23.2). Urine contains a trace of bilirubin from the breakdown of hemoglobin and related products, and urobilin, a brown oxidized derivative of bilirubin. It is abnormal to find glucose, free hemoglobin, albumin, ketones, or more than a trace of bile pigments in the urine; their presence is sometimes an indicator of disease.

Urine Volume

An average adult produces 1 to 2 L of urine per day. An output in excess of 2 L/day is called diuresis or **polyuria**[19] (POL-ee-YOU-ree-uh). Fluid intake and some drugs can temporarily increase output to as much as 20 L/day. Chronic diseases such as diabetes (see next) can do so over a long term. **Oliguria**[20] (oll-ih-GUE-ree-uh) is an output of less than 500 mL/day, and **anuria**[21] is an output of 0 to 100 mL/day. Low output can result from kidney disease, dehydration, circulatory shock, prostate enlargement, and other causes. If urine output drops to less than 400 mL/day, the body cannot

[19] *poly* = many, much
[20] *oligo* = few, a little
[21] *an* = without

Chapter 23

Table 23.1 Hormones Affecting Renal Function

Hormone	Target	Effects
Aldosterone	Distal tubule, collecting duct	Promotes Na^+ reabsorption, K^+ secretion; reduces urine volume
Angiotensin II	Afferent and efferent arterioles	Constricts arterioles, reduces GFR; stimulates ADH and aldosterone secretion; stimulates thirst; promotes water intake and reduces urine volume
Antidiuretic hormone	Collecting duct	Promotes H_2O reabsorption; reduces urine volume, increases concentration
Atrial natriuretic peptide	Afferent and efferent arterioles, collecting duct	Dilates afferent arteriole, constricts efferent arteriole, increases GFR; inhibits secretion of renin, ADH, and aldosterone; inhibits NaCl reabsorption by collecting duct; increases urine volume
Epinephrine and norepinephrine	Juxtaglomerular apparatus, afferent arteriole	Induces renin secretion; constricts afferent arteriole; reduces GFR and urine volume
Parathyroid hormone	Proximal and distal tubules, nephron loop	Promotes Ca^{2+} reabsorption by loop and distal tubule and Mg^{2+} reabsorption by proximal tubule; inhibits phosphate reabsorption by proximal tubule; promotes calcitriol synthesis

Table 23.2 Properties and Composition of Urine

Physical Properties		
Specific gravity	1.001–1.028	
Osmolarity	50–1,200 mOsm/L	
pH	6.0 (range 4.5–8.2)	
Solute	**Concentration***	**Output (g/day)****
Inorganic ions		
Chloride	533 mg/dL	6.4 g/day
Sodium	333 mg/dL	4.0 g/day
Potassium	166 mg/dL	2.0 g/day
Phosphate	83 mg/dL	1 g/day
Ammonia	60 mg/dL	0.68 g/day
Calcium	17 mg/dL	0.2 g/day
Magnesium	13 mg/dL	0.16 g/day
Nitrogenous wastes		
Urea	1.8 g/dL	21 g/day
Creatinine	150 mg/dL	1.8 g/day
Uric acid	40 mg/dL	0.5 g/day
Urobilin	125 μg/dL	1.52 mg/day
Bilirubin	20 μg/dL	0.24 mg/day
Other organics		
Amino acids	288 μg/dL	3.5 mg/day
Ketones	17 μg/dL	0.21 mg/day
Carbohydrates	9 μg/dL	0.11 mg/day
Lipids	1.6 μg/dL	0.02 mg/day

*Typical values for a reference male
**Assuming a urine output of 1.2 L/day

maintain a safe, low concentration of wastes in the blood plasma. The result is azotemia.

Diabetes

Diabetes[22] is any metabolic disorder exhibiting chronic polyuria. There are at least five forms of diabetes: *diabetes mellitus type I* and *type II, gestational diabetes, renal diabetes,* and *diabetes insipidus.* In most cases, the polyuria results from a high concentration of glucose in the renal tubule. Glucose opposes the osmotic reabsorption of water, so more water is passed in the urine *(osmotic diuresis)* and a person may become severely dehydrated. In diabetes mellitus and gestational diabetes, the high glucose concentration in the tubule is a result of hyperglycemia, a high concentration of glucose in the blood. About 1% to 3% of pregnant women experience gestational diabetes, in which pregnancy reduces the mother's insulin sensitivity, resulting in hyperglycemia and glycosuria. In renal diabetes, blood glucose level is not elevated, but there is a hereditary deficiency of glucose transporters in the PCT, which causes glucose to remain in the tubular fluid. Diabetes insipidus results from ADH hyposecretion. Without ADH, the collecting duct does not reabsorb as much water as normal, so more water passes in the urine.

Diabetes mellitus, gestational diabetes, and renal diabetes are characterized by glycosuria. Before chemical tests for urine glucose were developed, physicians diagnosed diabetes mellitus by tasting the patient's urine for sweetness.[23] Tests for glycosuria are now as simple as dipping a chemical test strip into the urine specimen—an advance in medical technology for which urologists are no doubt grateful. In diabetes insipidus,[24] the urine contains no glucose and, by the old diagnostic method, does not taste sweet.

Diuretics

Diuretics are chemicals that increase urine volume. They are used for treating hypertension and congestive heart failure because they reduce the body's fluid volume and blood pressure. Diuretics work by one of two mechanisms—increasing glomerular filtration or reducing tubular reabsorption. For example, caffeine, in the former category, dilates the afferent arteriole and increases GFR. Alcohol, in the latter category, inhibits ADH secretion. Also in the latter category are many osmotic diuretics, which reduce water reabsorption by increasing the osmolarity of the tubular fluid. Many diuretic drugs, such as furosemide (Lasix), produce osmotic diuresis by inhibiting sodium reabsorption.

Renal Function Tests

There are several tests for diagnosing kidney diseases, evaluating their severity, and monitoring their progress. Here we examine two methods used to determine renal clearance and glomerular filtration rate.

Renal Clearance

Renal clearance is the volume of blood plasma from which a particular waste is completely removed in 1 minute. It represents the net effect of three processes:

Glomerular filtration of the waste
\+ Amount added by tubular secretion
− Amount reclaimed by tubular reabsorption
Renal clearance

[22] *diabetes* = passing through

[23] *melli* = honey, sweet
[24] *insipid* = tasteless

In principle, we could determine renal clearance by sampling blood entering and leaving the kidney and comparing their waste concentrations. In practice, it is not practical to draw blood samples from the renal vessels, but clearance can be assessed indirectly by collecting samples of blood and urine, measuring the waste concentration in each, and measuring the rate of urine output.

Suppose the following values were obtained for urea:

U (urea concentration in urine) = 6.0 mg/mL

V (rate of urine output) = 2 mL/min

P (urea concentration in plasma) = 0.2 mg/mL

Renal clearance (C) is

$$C = UV/P$$

$$= \frac{(6.0 \text{ mg/mL})(2 \text{ mL/min})}{0.2 \text{ mg/mL}}$$

$$= 60 \text{ mL/min}$$

This means the equivalent of 60 mL of blood plasma is completely cleared of urea per minute. If this person has a normal GFR of 125 mL/min, then the kidneys have cleared urea from only 60/125 = 48% of the glomerular filtrate. This is a normal rate of urea clearance, however, and is sufficient to maintain safe levels of urea in the blood.

Think About It

What would you expect the value of renal clearance of glucose to be in a healthy individual? Why?

Glomerular Filtration Rate

Assessment of kidney disease often calls for a measurement of GFR. We cannot determine GFR from urea excretion for two reasons: (1) some of the urea in the urine is secreted by the renal tubule, not filtered by the glomerulus, and (2) much of the urea filtered by the glomerulus is reabsorbed by the tubule. To measure GFR ideally requires a substance that is not secreted or reabsorbed at all, so that all of it in the urine gets there by glomerular filtration.

There doesn't appear to be a single urine solute produced by the body that is not secreted or reabsorbed to some degree. However, several plants, including garlic and artichoke, produce a polysaccharide called inulin that is useful for GFR measurement. All inulin filtered by the glomerulus remains in the renal tubule and appears in the urine; none is reabsorbed, nor does the tubule secrete it. GFR can be measured by injecting inulin and subsequently measuring the rate of urine output and the concentrations of inulin in blood and urine.

For inulin, GFR is equal to the renal clearance. Suppose, for example, that a patient's plasma concentration of inulin is P = 0.5 mg/mL, the urine concentration is U = 30 mg/mL, and urine output is V = 2 mL/min. This person has a normal GFR:

$$GFR = UV/P$$

$$= \frac{(30 \text{ mg/mL})(2 \text{ mL/min})}{0.5 \text{ mg/mL}}$$

$$= 120 \text{ mL/min}$$

In clinical practice, GFR is more often estimated from creatinine excretion. This has a small but acceptable error of measurement, and is an easier procedure than injecting inulin and drawing blood to measure its concentration.

A solute that is reabsorbed by the renal tubules will have a renal clearance *less* than the GFR (provided its tubular secretion is less than its rate of reabsorption). This is why the renal clearance of urea is about 60 mL/min. A solute that is secreted by the renal tubules will have a renal clearance *greater* than the GFR (provided its reabsorption does not exceed its secretion). Creatinine, for example, has a renal clearance of 140 mL/min.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

17. Define *oliguria* and *polyuria*. Which of these is characteristic of diabetes?
18. Identify two causes of glycosuria other than diabetes mellitus.
19. How is the diuresis produced by furosemide like the diuresis produced by diabetes mellitus? How are they different?
20. Explain why GFR could not be determined from measurement of the amount of NaCl in the urine.

Urine Storage and Elimination

Objectives

When you have completed this section, you should be able to

- describe the functional anatomy of the ureters, urinary bladder, and male and female urethra; and
- explain how the nervous system and urethral sphincters control the voiding of urine.

Urine is produced continually, but fortunately it does not drain continually from the body. Urination is episodic—occurring when we allow it. This is made possible by an apparatus for storing urine and by neural controls for its timely release.

The Ureters

The renal pelvis funnels urine into the ureter, a retroperitoneal, muscular tube that extends to the urinary bladder. The ureter is about 25 cm long and reaches a maximum diameter of about 1.7 cm near the bladder. The ureters

pass dorsal to the bladder and enter it from below, passing obliquely through its muscular wall and opening onto its floor. As pressure builds in the bladder, it compresses the ureters and prevents urine from being forced back to the kidneys.

The ureter has three layers: an adventitia, muscularis, and mucosa. The adventitia is a connective tissue layer that binds it to the surrounding tissues. The muscularis consists of two layers of smooth muscle. When urine enters the ureter and stretches it, the muscularis contracts and initiates a peristaltic wave that "milks" the urine down to the bladder. These contractions occur every few seconds to few minutes, proportional to the rate at which urine enters the ureter. The mucosa has a transitional epithelium continuous with that of the renal pelvis above and urinary bladder below. The lumen of the ureter is very narrow and is easily obstructed or injured by kidney stones (see insight 23.2).

Insight 23.2 Clinical Application

Kidney Stones

A *renal calculus*[25] (kidney stone) is a hard granule of calcium, phosphate, uric acid, and protein. Renal calculi form in the renal pelvis and are usually small enough to pass unnoticed in the urine flow. Some, however, grow to several centimeters in size and block the renal pelvis or ureter, which can lead to the destruction of nephrons as pressure builds in the kidney. A large, jagged calculus passing down the ureter stimulates strong contractions that can be excruciatingly painful. It can also damage the ureter and cause hematuria. Causes of renal calculi include hypercalcemia, dehydration, pH imbalances, frequent urinary tract infections, or an enlarged prostate gland causing urine retention. Calculi are sometimes treated with stone-dissolving drugs, but often they require surgical removal. A nonsurgical technique called *lithotripsy*[26] uses ultrasound to pulverize the calculi into fine granules easily passed in the urine.

[25] *calc* = calcium, stone + *ul* = little
[26] *litho* = stone + *tripsy* = crushing

The Urinary Bladder

The urinary bladder (fig. 23.20) is a muscular sac on the floor of the pelvic cavity, inferior to the peritoneum and posterior to the pubic symphysis. It is covered by parietal peritoneum on its flattened superior surface and by a fibrous adventitia elsewhere. Its muscularis, called the **detrusor**[27] (deh-TROO-zur) **muscle,** consists of three layers of smooth muscle. The mucosa has a transitional epithelium, and in the relaxed bladder it has conspicuous wrinkles called **rugae**[28] (ROO-gee). The openings of the two ureters and the urethra mark a smooth-surfaced triangular area called the **trigone**[29] on the bladder floor. This is a common site of bladder infection (see insight 23.3). For photographs of the relationship of the bladder and urethra to other pelvic organs in both sexes, see figure A.22 (p. 51).

The bladder is highly distensible. As it fills, it expands superiorly, the rugae flatten, and the wall becomes quite thin. A moderately full bladder contains about 500 mL of urine and extends about 12.5 cm from top to bottom. The maximum capacity is 700 to 800 mL.

[27] *de* = down + *trus* = push

The Urethra

The urethra conveys urine out of the body. In the female, it is a tube 3 to 4 cm long bound to the anterior wall of the vagina by connective tissue. Its opening, the **external urethral orifice,** lies between the vaginal orifice and clitoris. The male urethra is about 18 cm long and has three regions: (1) The **prostatic urethra** begins at the urinary bladder and passes for about 2.5 cm through the prostate gland. During orgasm, it receives semen from the reproductive glands. (2) The **membranous urethra** is a short (0.5 cm), thin-walled portion where the urethra passes through the muscular floor of the pelvic cavity. (3) The **spongy (penile) urethra** is about 15 cm long and passes through the penis to the external urethral orifice. It is named for the *corpus spongiosum* of the penis, through which it passes. The male urethra assumes an S shape: it passes downward from the bladder, turns anteriorly as it enters the root of the penis, and then turns about 90° downward again as it enters the external, pendant part of the penis. The mucosa has a transitional epithelium near the bladder, a pseudostratified columnar epithelium for most of its length, and finally stratified squamous near the external urethral orifice. There are mucous **urethral glands** in its wall.

In both sexes, the detrusor muscle is thickened near the urethra to form an **internal urethral sphincter,** which compresses the urethra and retains urine in the bladder. Since this sphincter is composed of smooth muscle, it is under involuntary control. Where the urethra passes through the pelvic floor, it is encircled by an **external urethral sphincter** of skeletal muscle, which provides voluntary control over the voiding of urine.

[28] *ruga* = fold, wrinkle
[29] *tri* = three + *gon* = angle

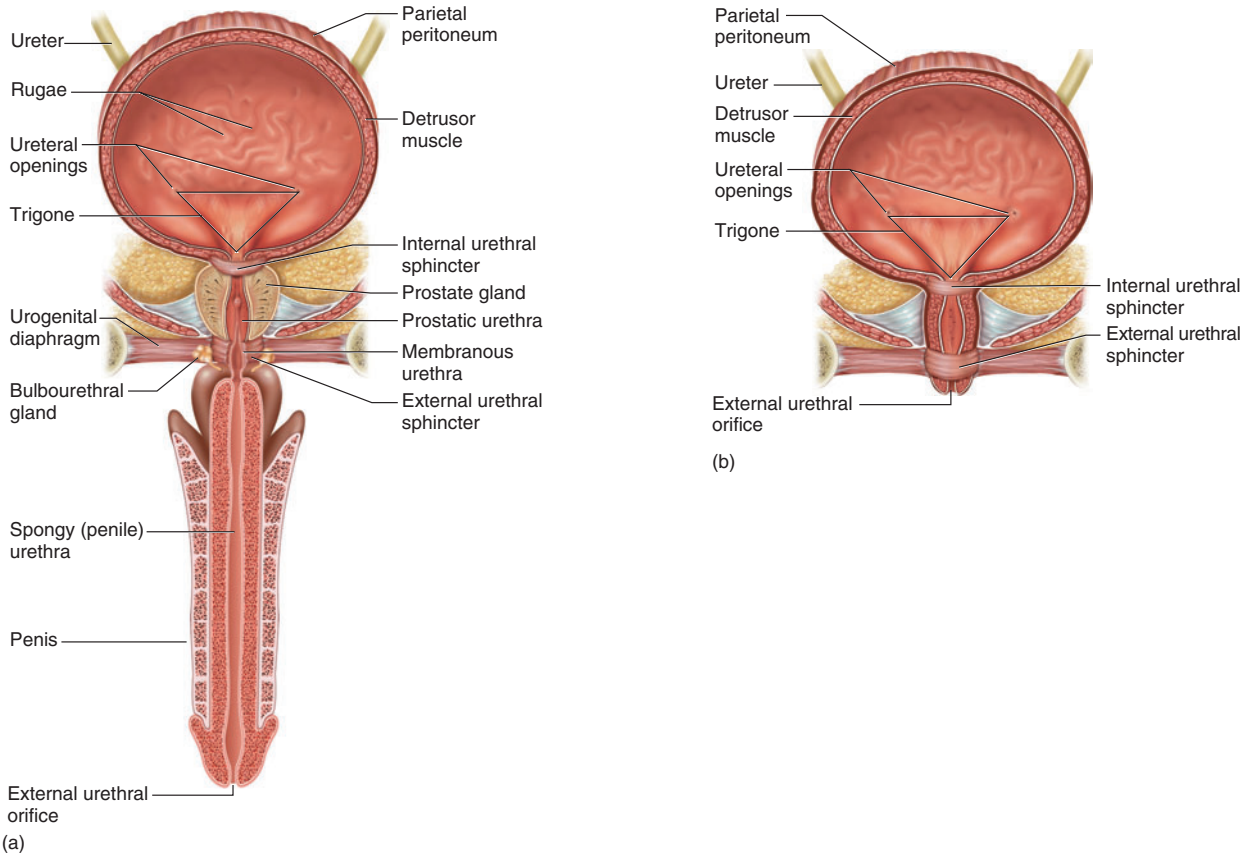


Figure 23.20 Anatomy of the Urinary Bladder and Urethra. (*a*) Male; (*b*) female.
Why are women more susceptible to bladder infections than men are?

Insight 23.3 Clinical Application

Urinary Tract Infections

Infection of the urinary bladder is called *cystitis.*[30] It is especially common in females because bacteria such as *Escherichia coli* can travel easily from the perineum up the short urethra. Because of this risk, young girls should be taught never to wipe the anus in a forward direction. If cystitis is untreated, bacteria can spread up the ureters and cause *pyelitis,*[31] infection of the renal pelvis. If it reaches the renal cortex and nephrons, it is called *pyelonephritis.* Kidney infections can also result from invasion by blood-borne bacteria. Urine stagnation due to renal calculi or prostate enlargement increases the risk of infection.

[30] *cyst* = bladder + *itis* = inflammation
[31] *pyel* = pelvis

Voiding Urine

Urination, or emptying of the bladder, is also called **micturition**[32] (MIC-too-RISH-un). It is controlled in part by the **micturition reflex** shown in figure 23.21, which is numbered to correspond to the following description:

(1) When the bladder contains about 200 mL of urine, stretch receptors in the wall send afferent nerve impulses to the spinal cord by way of the pelvic nerves. **(2)** By way of a parasympathetic reflex arc through segments S2 to S3 of the cord, signals return to the bladder and stimulate contraction of the detrusor muscle **(3)** and relaxation of the internal urethral sphincter **(4).** This reflex is the predominant mechanism that voids the bladder in infants and young children.

[32] *mictur* = to urinate

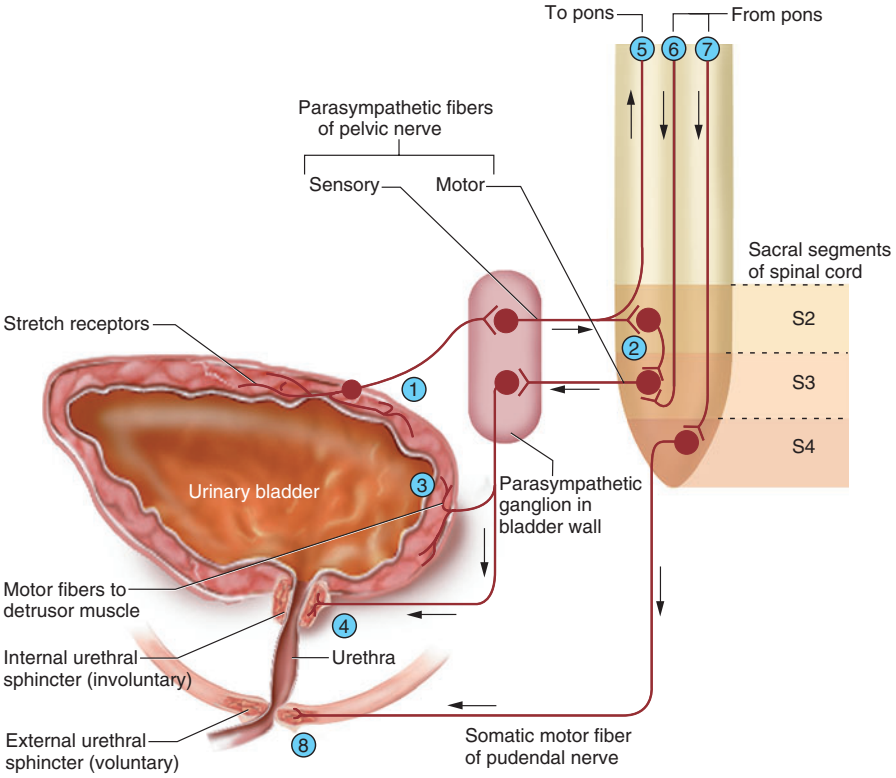


Figure 23.21 **Neural Control of Micturition.** Circled numbers correspond to text description.

As the brain and spinal cord mature, however, we acquire voluntary control over the external urethral sphincter, and emptying of the bladder is controlled predominantly by a **micturition center** in the pons. This center receives signals from the stretch receptors **(5)** and integrates this information with cortical input concerning the appropriateness of urinating at the moment. It sends back impulses **(6)** that excite the detrusor and relax the internal urethral sphincter. **(7)** At times when it is inappropriate to urinate, a steady train of nerve impulses travel from the brainstem through the pudendal nerve to the external urethral sphincter, thus keeping it contracted. When you wish to urinate, these impulses are inhibited, the external sphincter relaxes **(8),** and contractions of the detrusor muscle expel the urine. The Valsalva maneuver (p. 855) also aids in expulsion of urine by increasing pressure on the bladder. Males voluntarily contract the bulbocavernosus muscle encircling the base of the penis to expel the last few milliliters of urine.

When it is desirable to urinate (for example, before a long trip) but the urge does not yet exist because the bladder is not full enough, the Valsalva maneuver can activate the micturition reflex. Contraction of the abdominal muscles compresses the bladder and may excite the stretch receptors even if there is less than 200 mL of urine in the bladder.

The effects of aging on the urinary system are discussed on pages 1111 to 1112. Some disorders of this system are briefly described in table 23.3.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

21. Describe the location and function of the detrusor muscle.
22. Compare and contrast the functions of the internal and external urethral sphincters.
23. How would micturition be affected by a spinal cord lesion that prevented voluntary nerve impulses from reaching the sacral part of the cord?

Table 23.3 Some Disorders of the Urinary System

Acute glomerulonephritis	An autoimmune inflammation of the glomeruli, often following a streptococcus infection. Results in destruction of glomeruli leading to hematuria, proteinuria, edema, reduced glomerular filtration, and hypertension. Can progress to chronic glomerulonephritis and renal failure, but most individuals recover from acute glomerulonephritis without lasting effect.
Acute renal failure	An abrupt decline in renal function, often due to traumatic damage to the nephrons or a loss of blood flow stemming from hemorrhage or thrombosis.
Chronic renal failure	Long-term, progressive, irreversible loss of nephrons; see insight 23.4 for a variety of causes. Requires a kidney transplant or hemodialysis.
Hydronephrosis[33]	Increase in fluid pressure in the renal pelvis and calices owing to obstruction of the ureter by kidney stones, nephroptosis, or other causes. Can progress to complete cessation of glomerular filtration and atrophy of nephrons.
Nephroptosis[34] *(NEFF-rop-TOE-sis)*	Slippage of the kidney to an abnormally low position *(floating kidney)*. Occurs in people with too little body fat to hold the kidney in place and in people who subject the kidneys to prolonged vibration, such as truck drivers, equestrians, and motorcyclists. Can twist or kink the ureter, which causes pain, obstructs urine flow, and potentially leads to hydronephrosis.
Nephrotic syndrome	Excretion of large amounts of protein in the urine (≥ 3.5 g/day) due to glomerular injury. Can result from trauma, drugs, infections, cancer, diabetes mellitus, lupus erythematosus, and other diseases. Loss of plasma protein leads to edema, ascites, hypotension, and susceptibility to infection (because of immunoglobulin loss).
Urinary incontinence	Inability to hold the urine; involuntary leakage from the bladder. Can result from incompetence of the urinary sphincters; bladder irritation; pressure on the bladder in pregnancy; an obstructed urinary outlet so that the bladder is constantly full and dribbles urine *(overflow incontinence);* uncontrollable urination due to brief surges in bladder pressure, as in laughing or coughing *(stress incontinence);* and neurological disorders such as spinal cord injuries.

Disorders described elsewhere

Azotemia 881	Oliguria 901	Renal diabetes 902
Hematuria 887	Proteinuria 887	Uremia 881
Kidney stones 904	Pyuria 900	Urinary tract infection 904
Nephrosclerosis 889		

[33] *hydro* = water + *nephr* = kidney + *osis* = medical condition
[34] *nephro* = kidney + *ptosis* = sagging, falling

Insight 23.4 Clinical Application

Renal Insufficiency and Hemodialysis

Renal insufficiency is a state in which the kidneys cannot maintain homeostasis due to extensive destruction of their nephrons. Some causes of nephron destruction include:

- Chronic or repetitive kidney infections.
- Trauma from such causes as blows to the lower back or continual vibration from machinery.
- Prolonged ischemia and hypoxia, as in some long-distance runners and swimmers.
- Poisoning by heavy metals such as mercury and lead and solvents such as carbon tetrachloride, acetone, and paint thinners. These are absorbed into the blood from inhaled fumes or by skin contact and then filtered by the glomeruli. They kill renal tubule cells.
- Blockage of renal tubules with proteins small enough to be filtered by the glomerulus—for example, myoglobin released by skeletal muscle damage and hemoglobin released by a transfusion reaction.
- Atherosclerosis, which reduces blood flow to the kidney.
- Glomerulonephritis, an autoimmune disease of the glomerular capillaries.

Nephrons can regenerate and restore kidney function after short-term injuries. Even when some of the nephrons are irreversibly destroyed, others hypertrophy and compensate for their lost function. Indeed, a person can survive on as little as one-third of one kidney. When 75% of the nephrons are lost, however, urine output may be as low as 30 mL/hr compared with the normal rate of 50 to 60 mL/hr. This is insufficient to maintain homeostasis and is accompanied by azotemia and acidosis. Uremia develops when there is 90% loss of renal function. Renal insufficiency also tends to cause anemia because the diseased kidney produces too little erythropoietin (EPO), the hormone that stimulates red blood cell formation.

Hemodialysis is a procedure for artificially clearing wastes from the blood when the kidneys are not adequately doing so (fig. 23.22). Blood is pumped from the radial artery to a *dialysis machine* (artificial kidney) and returned to the patient by way of a vein. In the dialysis machine, the blood flows through a semipermeable cellophane tube surrounded by dialysis fluid. Urea, potassium, and other solutes that are more concentrated in the blood than in the dialysis fluid diffuse through the membrane into the fluid, which is discarded. Glucose, electrolytes, and drugs can be administered by adding them to the dialysis fluid so they will diffuse through the membrane into the blood. People with renal insufficiency also accumulate substantial amounts of body water between treatments, and dialysis serves also to remove this excess water. Patients are typically given erythropoietin (EPO) to compensate for the lack of EPO from the failing kidneys.

Hemodialysis patients typically have three sessions per week for 4 to 8 hours per session. In addition to inconvenience, hemodialysis carries risks of infection and thrombosis. Blood tends to clot when exposed to foreign surfaces, so an anticoagulant such as heparin is added during dialysis. Unfortunately, this inhibits clotting in the patient's body as well, and dialysis patients sometimes suffer internal bleeding.

A procedure called *continuous ambulatory peritoneal dialysis (CAPD)* is more convenient. It can be carried out at home by the patient, who is provided with plastic bags of dialysis fluid. Fluid is introduced into the abdominal cavity through an indwelling catheter. Here, the peritoneum provides over 2 m^2 of blood-rich semipermeable membrane. The fluid is left in the body cavity for 15 to 60 minutes to allow the blood to equilibrate with it; then it is drained, discarded, and replaced with fresh dialysis fluid. The patient is not limited by a stationary dialysis machine and can go about most normal activities. CAPD is less expensive and promotes better morale than conventional hemodialysis, but it is less efficient in removing wastes and it is more often complicated by infection.

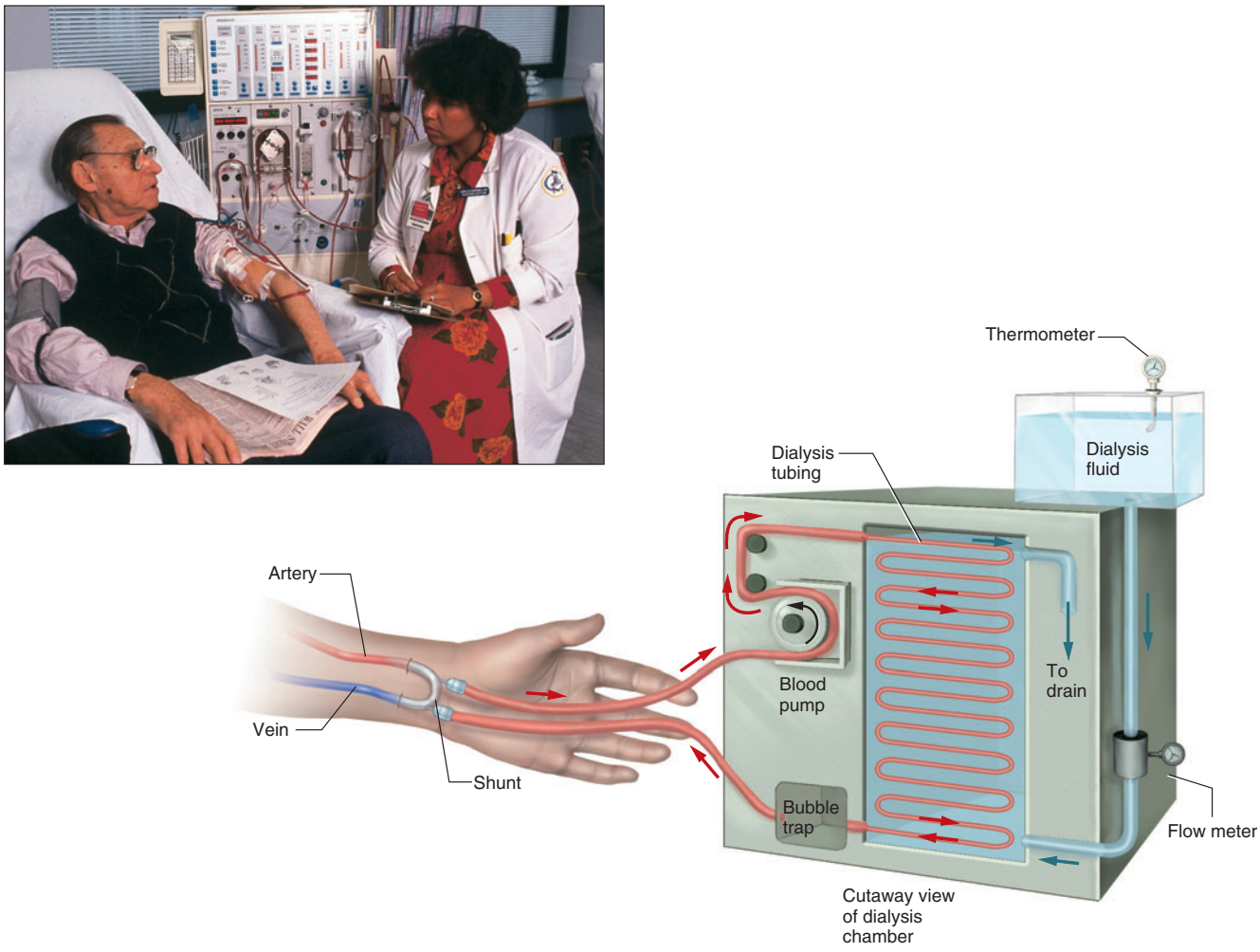


Figure 23.22 Hemodialysis. Blood is pumped into a dialysis chamber, where it flows through selectively permeable dialysis tubing surrounded by dialysis fluid. Blood leaving the chamber passes through a bubble trap to remove air before it is returned to the patient's body. The dialysis fluid picks up excess water and metabolic wastes from the patient's blood and may contain medications that diffuse into the blood.

Connective Issues

Interactions Between the URINARY SYSTEM and Other Organ Systems

← indicates ways in which this system affects other systems
→ indicates ways in which other systems affect this one

All Systems

The urinary system serves all other systems by eliminating metabolic wastes and maintaining fluid, electrolyte, and acid-base balance

Integumentary System

← Renal control of fluid balance essential for sweat secretion

→ Epidermis is normally a barrier to fluid loss; profuse sweating can lead to oliguria; skin and kidneys collaborate in calcitriol synthesis

Skeletal System

← Renal control of calcium and phosphate balance and role in calcitriol synthesis are essential for bone deposition

→ Lower ribs and pelvis protect some urinary system organs

Muscular System

← Renal control of Na^+, K^+, and Ca^{2+} balance important for muscle contraction

→ Some skeletal muscles aid or regulate micturition (external urethral sphincter, male bulbocavernosus muscle, abdominal muscles used in Valsalva maneuver); muscles of pelvic floor support bladder

Nervous System

← Nervous system is very sensitive to fluid, electrolyte, and acid-base imbalances that may result from renal dysfunction

→ Regulates glomerular filtration and micturition

Endocrine System

← Renin secretion by kidneys leads to angiotensin synthesis and aldosterone secretion; kidneys produce erythropoietin

→ Regulates renal function through angiotensin II, aldosterone, atrial natriuretic factor, and antidiuretic hormone

Circulatory System

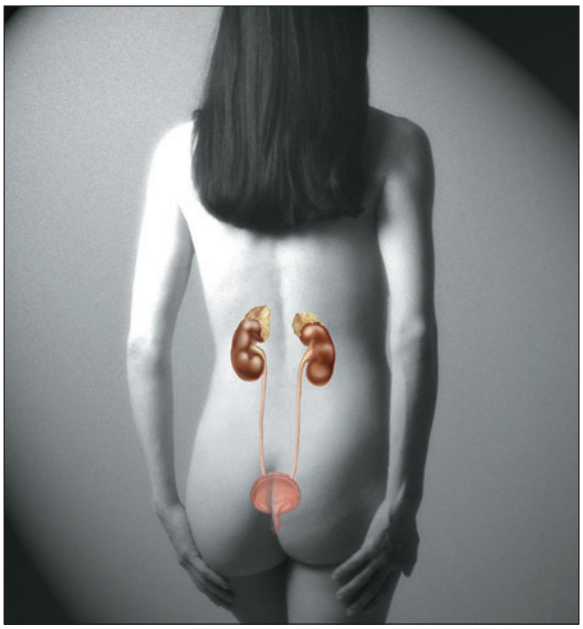
← Kidneys control blood pressure more than any other organ; erythropoietin from kidneys regulates hematocrit; kidneys regulate plasma composition; cardiac rhythm is very sensitive to electrolyte imbalances that may result from renal dysfunction

→ Perfuses kidneys so wastes can be filtered from blood; blood pressure influences glomerular filtration rate; blood reabsorbs water and solutes from renal tubules

Lymphatic/Immune Systems

← Acidity of urine provides nonspecific defense against infection

→ Return of fluid to bloodstream maintains blood pressure and fluid balance essential for renal function; immune system protects kidneys from infection



Respiratory System

← Rate of acid secretion by kidneys affects pH of blood and may therefore affect respiratory rhythm

→ Provides O_2 to meet high metabolic demand of kidneys; dysfunctions of pulmonary ventilation may require compensation by kidneys to maintain acid-base balance; inhaled toxic fumes can damage kidneys

Digestive System

← Kidneys excrete toxins absorbed by digestive tract; kidneys excrete hormones and metabolites after liver deactivates them; calcitriol synthesized by kidneys regulates Ca^{2+} absorption by small intestine

→ Liver synthesizes urea, the main nitrogenous waste eliminated by kidneys; urea contributes to osmotic gradient of renal medulla; liver and kidneys collaborate to synthesize calcitriol

Reproductive System

← Urethra serves as common passageway for urine and sperm in males; urinary system of a pregnant woman eliminates metabolic wastes of fetus

→ Enlarged prostate can cause urine retention and kidney damage in males; pregnant uterus compresses bladder and reduces its capacity in females

Chapter Review

Review of Key Concepts

Functions of the Urinary System (p. 880)

1. The kidneys filter blood plasma, separate wastes from useful chemicals, regulate blood volume and pressure, secrete renin and erythropoietin, regulate blood pH, synthesize calcitriol, detoxify free radicals and drugs, and generate glucose in times of starvation.
2. Metabolic wastes are wastes produced by the body, such as CO_2 and nitrogenous wastes. The main human nitrogenous wastes are *urea, uric acid,* and *creatinine.*
3. The level of nitrogenous wastes in the blood is often expressed as blood urea nitrogen (BUN). An elevated BUN is called *azotemia,* and may progress to a serious syndrome called *uremia.*
4. *Excretion* is the process of separating wastes from the body fluids and eliminating them from the body. It is carried out by the respiratory, integumentary, digestive, and urinary systems.

Anatomy of the Kidney (p. 881)

1. The kidney has a slit called the *hilum* on its concave side, where it receives renal nerves, blood and lymphatic vessels, and the ureter.
2. From superficial to deep, the kidney is enclosed by the renal fascia, adipose capsule, and renal capsule.
3. The renal parenchyma is a C-shaped tissue enclosing a space called the renal sinus. The parenchyma is divided into an outer *renal cortex* and inner *renal medulla.* The medulla consists of 6 to 10 *renal pyramids.*
4. The apex, or papilla, of each pyramid projects into a receptacle called a minor calyx, which collects the urine from that pyramid. Minor calices converge to form major calices, and these converge on the renal pelvis, where the ureter arises.
5. Each kidney contains about 1.2 million functional units called *nephrons.*
6. A nephron begins with a capillary ball, the *glomerulus,* enclosed in a double-walled glomerular capsule. A *renal tubule* leads away from the capsule and consists of a highly coiled *proximal convoluted tubule (PCT),* a U-shaped *nephron loop,* and a coiled *distal convoluted tubule (DCT).* The DCTs of several nephrons then drain into a *collecting duct,* which leads to the papilla of a medullary pyramid.
7. The kidney is supplied by a *renal artery,* which branches and gives rise to *arcuate arteries* above the pyramids and then *interlobular arteries,* which penetrate into the cortex. For each nephron, an *afferent arteriole* arises from the interlobular artery and supplies the glomerulus. An *efferent arteriole* leaves the glomerulus and usually gives rise to a bed of *peritubular capillaries* around the PCT and DCT. Blood then flows through a series of veins to leave the kidney by way of the *renal vein.*
8. Juxtamedullary nephrons give rise to blood vessels called the *vasa recta,* which supply the tissue of the renal medulla.

Urine Formation I: Glomerular Filtration (p. 886)

1. The first step in urine production is to filter the blood plasma, which occurs at the glomerulus.
2. In passing from the blood capillaries into the capsular space, fluid must pass through the fenestrations of the capillary endothelium, the basement membrane, and filtration slits of the podocytes. These barriers hold back blood cells and most protein, but allow water and small solutes to pass.
3. Glomerular filtration is driven mainly by the high blood pressure in the glomerular capillaries.
4. Glomerular filtration rate (GFR), an important measure of renal health, is typically about 125 mL/min in men and 105 mL/min in women.
5. Renal autoregulation is the ability of the kidneys to maintain a stable GFR without nervous or hormonal control. There are a myogenic mechanism and a tubuloglomerular feedback mechanism of renal autoregulation.
6. The sympathetic nervous system also regulates GFR by controlling vasomotion of the afferent arterioles.
7. GFR is also controlled by hormones. A drop in blood pressure causes the kidneys to secrete renin. Renin and angiotensin-converting enzyme convert a plasma protein, angiotensinogen, into angiotensin II.
8. Angiotensin II helps to raise blood pressure by constricting the blood vessels, reducing GFR, promoting secretion of antidiuretic hormone (ADH) and aldosterone, and stimulating the sense of thirst.
9. ADH promotes water retention by the kidneys. Aldosterone promotes sodium retention, which in turn leads to water retention.

Urine Formation II: Tubular Reabsorption and Secretion (p. 891)

1. The GFR is far in excess of the rate of urine output. Ninety-eight to 99% of the filtrate is reabsorbed by the renal tubules and only 1% to 2% is excreted as urine.
2. About 65% of the glomerular filtrate is reabsorbed by the PCT.
3. PCT cells absorb Na^+ from the tubular fluid through the apical cell surface and pump it out the basolateral cell surfaces by active transport. The reabsorption of other solutes—water, Cl^-, HCO_3^-, K^+, Mg^{2+}, phosphate, glucose, amino acids, lactate, urea, and uric acid—is linked in various ways to Na^+ reabsorption.
4. The peritubular capillaries pick up the reabsorbed water by osmosis, and other solutes follow by *solvent drag.*
5. The *transport maximum (T_m)* is the fastest rate at which the PCT can reabsorb a given solute. If a solute such as glucose is filtered by the glomerulus faster than the PCT can reabsorb it, the excess will pass in the urine (as in diabetes mellitus).

6. The PCT also carries out *tubular secretion,* removing solutes from the blood and secreting them into the tubular fluid. Secreted solutes include urea, uric acid, bile salts, ammonia, catecholamines, creatinine, H^+, HCO_3^-, and drugs such as aspirin and penicillin.
7. The nephron loop serves mainly to generate an osmotic gradient in the renal medulla, which is necessary for collecting duct function; but it also reabsorbs a significant amount of water, Na^+, K^+, and Cl^-.
8. The DCT reabsorbs salt and water, and is subject to hormonal control. Aldosterone stimulates the DCT to reabsorb Na^+ and secrete K^+.
9. Atrial natriuretic peptide increases salt and water excretion by increasing GFR, antagonizing aldosterone and ADH, and inhibiting NaCl reabsorption by the collecting duct.
10. Parathyroid hormone acts on the nephron loop and DCT to promote Ca^{2+} reabsorption, and acts on the PCT to promote phosphate excretion.

Urine Formation III: Water Conservation (p. 897)

1. The collecting duct (CD) reabsorbs varying amounts of water to leave the urine as dilute as 50 mOsm/L or as concentrated as 1,200 mOsm/L.
2. The CD is permeable to water but not to NaCl. As it passes down the increasingly salty renal medulla, it loses water to the tissue fluid and the urine in the duct becomes more concentrated.
3. The rate of water loss from the CD is controlled by antidiuretic hormone (ADH). ADH stimulates the installation of aquaporins in the CD cells, increasing permeability of the CD to water. At high ADH concentrations, the urine is scanty and highly concentrated; at low ADH concentrations, the urine is dilute.
4. The salinity gradient of the renal medulla, which is essential to the ability of the CD to concentrate the urine, is maintained by the countercurrent multiplier mechanism of the nephron loop.
5. The vasa recta supply a blood flow to the renal medulla and employ a countercurrent exchange system to prevent them from removing salt from the medulla.

Urine and Renal Function Tests (p. 899)

1. Urine normally has a yellow color due to *urochromes* derived from hemoglobin breakdown products.
2. Urine normally has a specific gravity from 1.001 to 1.028, an osmolarity from 50 to 1,200 mOsm/L, and a pH from 4.5 to 8.2.
3. A foul odor to the urine is abnormal and may result from bacterial degradation, some foods, urinary tract infection, or metabolic diseases such as diabetes mellitus or phenylketonuria.
4. The most abundant solutes in urine are urea, NaCl, and KCl. Urine normally contains little or no glucose, hemoglobin, albumin, ketones, or bile pigments, but may do so in some diseases.
5. Most adults produce 1 to 2 L of urine per day. Abnormally low urine output is *anuria* or *oliguria;* abnormally high output is *polyuria.*
6. *Diabetes* is any chronic polyuria of metabolic origin. Forms of diabetes include diabetes mellitus types I and II, gestational diabetes, renal diabetes, and diabetes insipidus.
7. *Diuretics* are chemicals that increase urine output by increasing GFR or reducing tubular reabsorption. Caffeine and alcohol are diuretics, as are certain drugs used to reduce blood pressure.
8. Renal function can be assessed by making clinical measurements of GFR or *renal clearance.* The latter is the amount of blood completely freed of a given solute in 1 minute.

Urine Storage and Elimination (p. 903)

1. Peristalsis of the ureters causes urine to flow from the kidneys to the urinary bladder.
2. The urinary bladder has a smooth muscle layer called the *detrusor muscle* with a thickened ring, the *internal urethral sphincter,* around the origin of the urethra.
3. The urethra is 3 to 4 cm long in the female, but in the male it is 18 cm long and divided into *prostatic, membranous,* and *spongy (penile)* segments. An *external urethral sphincter* of skeletal muscle encircles the urethra in both sexes where it passes through the pelvic floor.
4. Emptying of the bladder is controlled in part by a spinal *micturition reflex* initiated by stretch receptors in the bladder wall. Parasympathetic nerve fibers relax the internal urethral sphincter and contract the detrusor muscle.
5. Micturition can be voluntarily controlled through the *micturition center* of the pons. This center keeps the external urethral sphincter constricted when it is inappropriate to urinate. When urination is desired, it allows this sphincter to relax so that the involuntary micturition reflex can empty the bladder.

Selected Vocabulary

nitrogenous waste 881
urea 881
azotemia 881
uremia 881
renal cortex 882
renal medulla 882
nephron 882
glomerulus 882
glomerular capsule 882
proximal convoluted tubule 883
nephron loop 883
distal convoluted tubule 883
collecting duct 883
afferent arteriole 885
efferent arteriole 885
peritubular capillary 885
glomerular filtration 886
angiotensin II 891
tubular reabsorption 892
glycosuria 895
tubular secretion 895
polyuria 901
oliguria 901
diuretic 902
micturition 905

Testing Your Recall

1. Micturition occurs when the _____ contracts.
   a. detrusor muscle
   b. internal urethral sphincter
   c. external urethral sphincter
   d. muscularis of the ureter
   e. all of the above
2. The compact ball of capillaries in a nephron is called
   a. the nephron loop.
   b. the peritubular plexus.
   c. the renal corpuscle.
   d. the glomerulus.
   e. the vasa recta.
3. Which of these is the most abundant nitrogenous waste in the blood?
   a. uric acid
   b. urea
   c. ammonia
   d. creatinine
   e. albumin
4. Which of these lies closest to the renal cortex?
   a. the parietal peritoneum
   b. the renal fascia
   c. the renal capsule
   d. the adipose capsule
   e. the renal pelvis
5. Most sodium is reabsorbed from the glomerular filtrate by
   a. the vasa recta.
   b. the proximal convoluted tubule.
   c. the distal convoluted tubule.
   d. the nephron loop.
   e. the collecting duct.
6. A glomerulus and glomerular capsule make up one
   a. renal capsule.
   b. renal corpuscle.
   c. kidney lobule.
   d. kidney lobe.
   e. nephron.
7. The kidney has more _____ than any of the other structures listed.
   a. arcuate arteries
   b. minor calices
   c. medullary pyramids
   d. afferent arterioles
   e. collecting ducts
8. The renal clearance of _____ is normally zero.
   a. sodium
   b. potassium
   c. uric acid
   d. urea
   e. amino acids
9. Beavers have relatively little need to conserve water and could therefore be expected to have _____ than humans do.
   a. fewer nephrons
   b. longer nephron loops
   c. shorter nephron loops
   d. longer collecting ducts
   e. longer convoluted tubules
10. Increased ADH secretion should cause the urine to have
    a. a higher specific gravity.
    b. a lighter color.
    c. a higher pH.
    d. a lower urea concentration.
    e. a lower potassium concentration.
11. The _____ reflex is an autonomic reflex activated by pressure in the urinary bladder.
12. _____ is the ability of a nephron to adjust its GFR independently of external nervous or hormonal influences.
13. The two ureters and the urethra form the boundaries of a smooth area called the _____ on the floor of the urinary bladder.
14. The _____ is a group of epithelial cells of the distal convoluted tubule that monitors the flow or composition of the tubular fluid.
15. To enter the capsular space, filtrate must pass between foot process of the _____, cells that form the visceral layer of the glomerular capsule.
16. Glycosuria occurs if the rate of glomerular filtration of glucose exceeds the _____ of the proximal convoluted tubule.
17. _____ is a hormone that regulates the amount of water reabsorbed by the collecting duct.
18. The _____ sphincter is under involuntary control and relaxes during the micturition reflex.
19. Very little _____ is found in the glomerular filtrate because it is negatively charged and is repelled by the basement membrane of the glomerulus.
20. Blood flows through the _____ arteries just before entering the interlobular arteries.

Answers in Appendix B

True or False

Determine which five of the following statements are false, and briefly explain why.

1. The proximal convoluted tubule is not subject to hormonal influence.
2. Sodium is the most abundant solute in the urine.
3. The kidney has more distal convoluted tubules than collecting ducts.
4. Tight junctions prevent material from leaking between the epithelial cells of the renal tubule.
5. All forms of diabetes are characterized by glucose in the urine.
6. If all other conditions remain the same, constriction of the afferent arteriole reduces the glomerular filtration rate.
7. Angiotensin II reduces urine output.
8. The minimum osmolarity of urine is 300 mOsm/L, equal to the osmolarity of the blood.
9. A sodium deficiency (hyponatremia) could cause glycosuria.
10. Micturition depends on contraction of the detrusor muscle.

Answers in Appendix B

Testing Your Comprehension

1. How would glomerular filtration rate be affected by kwashiorkor (see p. 683)?
2. A patient produces 55 mL of urine per hour. Urea concentration is 0.25 mg/mL in her blood plasma and 8.6 mg/mL in her urine. (a) What is her rate of renal clearance for urea? (b) About 95% of adults excrete urea at a rate of 12.6 to 28.6 g/day. Is this patient above, within, or below this range? Show how you calculated your answers.
3. A patient with poor renal perfusion is treated with an ACE inhibitor and goes into renal failure. Explain the reason for the renal failure.
4. Drugs called *renin inhibitors* are used to treat hypertension. Explain how they would have this effect.
5. Discuss how the unity of form and function is exemplified by differences between the thin and thick segments of the nephron loop, between the proximal and distal convoluted tubules, and between the afferent and efferent arterioles.

Answers at the Online Learning Center

Answers to Figure Legend Questions

23.2 Ammonia is produced by the deamination of amino acids; urea is produced from ammonia and carbon dioxide; uric acid from nucleic acids; and creatinine from creatine phosphate.

23.3 The kidney lies between the peritoneum and body wall rather than in the peritoneal cavity. The pancreas, aorta, inferior vena cava, and renal artery and vein are also retroperitoneal.

23.9 The afferent arteriole is bigger. The relatively large inlet to the glomerulus and its small outlet results in high blood pressure in the glomerulus. This is the force that drives glomerular filtration.

23.14 It lowers the urine pH because of the Na^+-H^+ antiport (see the second cell from the bottom). The more Na^+ that is reabsorbed, the more H^+ is secreted into the tubular fluid.

23.20 The relatively short female urethra is less of an obstacle for bacteria traveling from the perineum to the urinary bladder.

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