The Urinary System: Functional Anatomy and Urine Formation by the Kidneys

**MULTIPLE FUNCTIONS OF THE KIDNEYS**

Most people are familiar with one important function of the kidneys—to rid the body of waste materials that are ingested or produced by metabolism. A second function that is especially critical is to control the volume and electrolyte composition of the body fluids. For water and virtually all electrolytes in the body, the balance between intake (due to ingestion or metabolic production) and output (due to excretion or metabolic consumption) is maintained largely by the kidneys. This regulatory function of the kidneys maintains the stable internal environment necessary for the cells to perform their various activities.

The kidneys perform their most critical functions by filtering the plasma and removing substances from the filtrate at variable rates, depending on the needs of the body. Ultimately, the kidneys clear unwanted substances from the filtrate (and therefore from the blood) by excreting them in the urine while returning substances that are needed back to the blood.

Although this chapter and the next few chapters focus mainly on the control of renal excretion of water, electrolytes, and metabolic waste products, the kidneys serve many important homeostatic functions, including the following:

- Excretion of metabolic waste products and foreign chemicals
- Regulation of water and electrolyte balances
- Regulation of body fluid osmolality and electrolyte concentrations
- Regulation of arterial pressure
- Regulation of acid-base balance
- Regulation of erythrocyte production
- Secretion, metabolism, and excretion of hormones
- Gluconeogenesis

**Excretion of Metabolic Waste Products, Foreign Chemicals, Drugs, and Hormone Metabolites.** The kidneys are the primary means for eliminating most of the waste products of metabolism that are no longer needed by the body. These products include urea (from the metabolism of amino acids), creatinine (from muscle creatine), uric acid (from nucleic acids), end products of hemoglobin breakdown (e.g., bilirubin), and metabolites of various hormones. These waste products must be eliminated from the body as rapidly as they are produced. The kidneys also eliminate most toxins and other foreign substances that are produced by the body or ingested, such as pesticides, drugs, and food additives.

**Regulation of Water and Electrolyte Balances.** For maintenance of homeostasis, excretion of water and electrolytes must match intake precisely. If intake exceeds excretion, the amount of that substance in the body will increase. If intake is less than excretion, the amount of that substance in the body will decrease. Although temporary (or cyclic) imbalances of water and electrolytes may occur in various physiological and pathophysiological conditions associated with altered intake or renal excretion, the maintenance of life depends on restoration of water and electrolyte balance.

Intake of water and many electrolytes is usually governed by a person’s eating and drinking habits, requiring the kidneys to adjust their excretion rates to match the intakes of various substances. Figure 26-1 shows the response of the kidneys to a sudden 10-fold increase in sodium intake from a low level of 30 mEq/day to a high level of 300 mEq/day. Within 2 to 3 days after raising the sodium intake, renal excretion also increases to about 300 mEq/day so that the balance between intake and output is rapidly re-established. However, during the 2 to 3 days of renal adaptation to the high sodium intake, there is a modest accumulation of sodium that raises extracellular fluid volume slightly and triggers hormonal changes and other compensatory responses that signal the kidneys to increase their sodium excretion.

The capability of the kidneys to alter sodium excretion in response to changes in sodium intake is tremendous. Experimental studies have shown that in many people, sodium intake can be increased to 1500 mEq/day (more than 10 times normal) or decreased to 10 mEq/day (<0.1 of normal), with relatively small changes in extracellular fluid volume or plasma sodium concentration. This phenomenon is also true for water and for most
other electrolytes, such as chloride, potassium, calcium, hydrogen, magnesium, and phosphate ions. In the next few chapters, we discuss the specific mechanisms that permit the kidneys to perform these amazing feats of homeostasis.

Regulation of Arterial Pressure. As discussed in Chapter 19, the kidneys play a dominant role in long-term regulation of arterial pressure by excreting variable amounts of sodium and water. The kidneys also contribute to short-term arterial pressure regulation by secreting hormones and vasoactive factors or substances (e.g., renin) that lead to the formation of vasoactive products (e.g., angiotensin II).

Regulation of Acid–Base Balance. The kidneys contribute to acid–base regulation, along with the lungs and body fluid buffers, by excreting acids and by regulating the body fluid buffer stores. The kidneys are the only means of eliminating certain types of acids from the body, such as sulfuric acid and phosphoric acid, which are generated by the metabolism of proteins.

Regulation of Erythrocyte Production. The kidneys secrete erythropoietin, which stimulates production of red blood cells by hematopoietic stem cells in the bone marrow, as discussed in Chapter 33. One important stimulus for erythropoietin secretion by the kidneys is hypoxia. The kidneys normally account for almost all the erythropoietin secreted into the circulation. In people with severe kidney disease or who have had their kidneys removed and have been placed on hemodialysis, severe anemia develops as a result of decreased erythropoietin production.

Regulation of 1,25-Dihydroxyvitamin D₃ Production. The kidneys produce 1,25-dihydroxyvitamin D₃ (calcitriol), the active form of vitamin D, by hydroxylating this vitamin at the “number 1” position. Calcitriol is essential for normal calcium deposition in bone and calcium re-absorption by the gastrointestinal tract. As discussed in Chapter 80, calcitriol plays an important role in calcium and phosphate regulation.

Glucose Synthesis. The kidneys synthesize glucose from amino acids and other precursors during prolonged fasting, a process referred to as gluconeogenesis. The kidneys’ capacity to add glucose to the blood during prolonged periods of fasting rivals that of the liver.

With chronic kidney disease or acute failure of the kidneys, these homeostatic functions are disrupted, and severe abnormalities of body fluid volumes and composition rapidly occur. With complete renal failure, enough potassium, acids, fluid, and other substances accumulate in the body to cause death within a few days unless clinical interventions such as hemodialysis are initiated to restore, at least partially, the body fluid and electrolyte balances.

**PHYSIOLOGIC ANATOMY OF THE KIDNEYS**

**GENERAL ORGANIZATION OF THE KIDNEYS AND URINARY TRACT**

The two kidneys lie on the posterior wall of the abdomen, outside the peritoneal cavity (Figure 26-2). Each kidney of the adult human weighs about 150 grams and is about the size of a clenched fist. The medial side of each kidney contains an indented region called the hilum through which pass the renal artery and vein, lymphatics, nerve supply, and ureter, which carries the final urine from the kidney to the bladder, where it is stored until the bladder is emptied. The kidney is surrounded by a tough fibrous capsule that protects its delicate inner structures.

If the kidney is bisected from top to bottom, the two major regions that can be visualized are the outer cortex and the inner medulla regions. The medulla is divided into 8 to 10 cone-shaped masses of tissue called renal pyramids. The base of each pyramid originates at the border between the cortex and medulla and terminates in the papilla, which projects into the space of the renal pelvis, a funnel-shaped continuation of the upper end of the ureter. The outer border of the pelvis is divided into open-ended pouches called major calyces that extend downward and divide into minor calyces, which collect urine from the tubules of each papilla. The walls of the calyces, pelvis, and ureter contain contractile elements that propel the urine toward the bladder, where urine is stored until it is emptied by micturition, discussed later in this chapter.
RENAL BLOOD SUPPLY

Blood flow to the two kidneys is normally about 22% of the cardiac output, or 1100 ml/min. The renal artery enters the kidney through the hilum and then branches progressively to form the interlobar arteries, arcuate arteries, interlobular arteries (also called radial arteries), and afferent arterioles, which lead to the glomerular capillaries, where large amounts of fluid and solutes (except the plasma proteins) are filtered to begin urine formation (Figure 26-3). The distal ends of the capillaries of each glomerulus coalesce to form the efferent arteriole, which leads to a second capillary network, the peritubular capillaries, that surrounds the renal tubules.

The renal circulation is unique in having two capillary beds, the glomerular and peritubular capillaries, which are arranged in series and are separated by the efferent arterioles. These arterioles help regulate the hydrostatic pressure in both sets of capillaries. High hydrostatic pressure in the glomerular capillaries (≈60 mm Hg) causes rapid fluid filtration, whereas a much lower hydrostatic pressure in the peritubular capillaries (≈13 mm Hg) permits rapid fluid reabsorption. By adjusting the resistance of the afferent and efferent arterioles, the kidneys can regulate the hydrostatic pressure in the glomerular and the peritubular capillaries, thereby changing the rate of glomerular filtration, tubular reabsorption, or both in response to the body’s homeostatic demands.

The peritubular capillaries empty into the vessels of the venous system, which run parallel to the arteriolar vessels. The blood vessels of the venous system progressively form the interlobular vein, arcuate vein, interlobar vein, and renal vein, which leaves the kidney beside the renal artery and ureter.

THE NEPHRON IS THE FUNCTIONAL UNIT OF THE KIDNEY

Each human kidney contains about 800,000 to 1,000,000 nephrons, each of which is capable of forming urine. The kidney cannot regenerate new nephrons. Therefore, with renal injury, disease, or normal aging, the number of nephrons gradually decreases. After age 40 years, the number of functioning nephrons usually decreases about 10% every 10 years; thus, at age 80 years, many people have 40% fewer functioning nephrons than they did at age 40 years. This loss is not life-threatening because adaptive changes in the remaining nephrons allow them to excrete the proper amounts of water, electrolytes, and waste products, as discussed in Chapter 32.

Each nephron contains (1) a tuft of glomerular capillaries called the glomerulus, through which large amounts of fluid are filtered from the blood, and (2) a long tubule in which the filtered fluid is converted into urine on its way to the pelvis of the kidney (see Figure 26-3). The glomerulus contains a network of branching and anastomosing glomerular capillaries that, compared with other capillaries, have high hydrostatic pressure (≈60 mm Hg). The glomerular capillaries are covered by epithelial cells, and the total glomerulus is encased in Bowman’s capsule.

Fluid filtered from the glomerular capillaries flows into Bowman’s capsule and then into the proximal tubule, which lies in the cortex of the kidney (Figure 26-4). From the proximal tubule, fluid flows into the loop of Henle, which dips into the renal medulla. Each loop consists of a descending and an ascending limb. The walls of the descending limb and lower end of the ascending limb are very thin and therefore are called the thin segment of the loop of Henle. After the ascending limb of the loop returns partway back to the cortex, its wall becomes much thicker; this segment is referred to as the thick segment of the ascending limb.

At the end of the thick ascending limb is a short segment that has in its wall a plaque of specialized epithelial cells, known as the macula densa. As discussed later, the macula densa plays an important role...
in controlling nephron function. Beyond the macula densa, fluid enters the distal tubule, which, like the proximal tubule, lies in the renal cortex. The distal tubule is followed by the connecting tubule and cortical collecting tubule, which lead to the cortical collecting duct. The initial parts of 8 to 10 cortical collecting ducts join to form a single, larger collecting duct that runs downward into the medulla and becomes the medullary collecting duct. The collecting ducts merge to form progressively larger ducts that eventually empty into the renal pelvis through the tips of the renal papillae. In each kidney, there are about 250 of these very large collecting ducts, each of which collects urine from about 4000 nephrons.

Regional Differences in Nephron Structure: Cortical and Juxtamedullary Nephrons. Although each nephron has all the components described earlier, there are some differences, depending on how deep the nephron lies within the kidney mass. The nephrons that have glomeruli located in the outer cortex are called cortical nephrons; they have short loops of Henle that penetrate only a short distance into the medulla (Figure 26-5).

About 20% to 30% of the nephrons have glomeruli that lie deep in the renal cortex near the medulla and are called juxtamedullary nephrons. These nephrons have long loops of Henle that dip deeply into the medulla, in some cases all the way to the tips of the renal papillae.

The vascular structures supplying the juxtamedullary nephrons also differ from those supplying the cortical nephrons. For the cortical nephrons, the entire tubular system is surrounded by an extensive network of peritubular capillaries. For the juxtamedullary nephrons, long efferent arterioles extend from the glomeruli down into the outer medulla and then divide into specialized peritubular capillaries called vasa recta, which extend downward into the medulla, lying side by side with the loops of Henle. Like the loops of Henle, the vasa recta return toward the cortex and empty into the cortical veins. This specialized network of capillaries in the medulla plays an essential role in the formation of a concentrated urine, discussed in Chapter 29.

Micturition

Micturition is the process whereby the urinary bladder empties when it becomes filled. This process involves two main steps. First, the bladder fills progressively until the tension in its walls rises above a threshold level. This tension elicits the second step, which is a nervous reflex called the micturition reflex that empties the bladder or,
if this fails, at least causes a conscious desire to urinate. Although the micturition reflex is an autonomic spinal cord reflex, it can also be inhibited or facilitated by centers in the cerebral cortex or brain stem.

**PHYSIOLOGIC ANATOMY OF THE BLADDER**

The urinary bladder, shown in Figure 26-6, is a smooth muscle chamber composed of two main parts: (1) the body, which is the major part of the bladder in which urine collects; and (2) the neck, which is a funnel-shaped extension of the body, passing inferiorly and anteriorly into the urogenital triangle and connecting with the urethra. The lower part of the bladder neck is also called the posterior urethra because of its relationship to the urethra.

The smooth muscle of the bladder is called the detrusor muscle. Its muscle fibers extend in all directions and, when contracted, can increase the pressure in the bladder to 40 to 60 mm Hg. Thus, contraction of the detrusor muscle is a major step in emptying the bladder. Smooth muscle cells of the detrusor muscle fuse with one another so that low-resistance electrical pathways exist from one muscle cell to the other. Therefore, an action potential can spread throughout the detrusor muscle, from one muscle cell to the next, to cause contraction of the entire bladder at once.

On the posterior wall of the bladder, lying immediately above the bladder neck, is a small triangular area called the trigone. At the lowermost apex of the trigone, the bladder neck opens into the posterior urethra, and the two ureters enter the bladder at the uppermost angles of the trigone. The trigone can be identified by the fact that its mucosa, the inner lining of the bladder, is smooth, in contrast to the remaining bladder mucosa, which is folded to form rugae.

Each ureter, as it enters the bladder, courses obliquely through the detrusor muscle and then passes another 1 to 2 centimeters beneath the bladder mucosa before emptying into the bladder.

The bladder neck (posterior urethra) is 2 to 3 centimeters long, and its wall is composed of detrusor muscle interlaced with a large amount of elastic tissue. The muscle in this area is called the internal sphincter. Its natural tone normally keeps the bladder neck and posterior urethra empty of urine and, therefore, prevents emptying of the bladder until the pressure in the main part of the bladder rises above a critical threshold.

Beyond the posterior urethra, the urethra passes through the urogenital diaphragm, which contains a layer of muscle called the external sphincter of the bladder. This muscle is a voluntary skeletal muscle, in contrast to the muscle of the bladder body and bladder neck, which is entirely smooth muscle. The external sphincter muscle is
under voluntary control of the nervous system and can be used to consciously prevent urination, even when involuntary controls are attempting to empty the bladder.

**Innervation of the Bladder.** The principal nerve supply of the bladder is via the *pelvic nerves*, which connect with the spinal cord through the *sacral plexus*, mainly connecting with cord segments S2 and S3 (Figure 26-7). Coursing through the pelvic nerves are both *sensory nerve fibers* and *motor nerve fibers*. The sensory fibers detect the degree of stretch in the bladder wall. Stretch signals from the posterior urethra are especially strong and are mainly responsible for initiating the reflexes that cause bladder emptying.

The motor nerves transmitted in the pelvic nerves are *parasympathetic fibers*. These fibers terminate on ganglion cells located in the wall of the bladder. Short postganglionic nerves then innervate the detrusor muscle.

In addition to the pelvic nerves, two other types of innervation are important in bladder function. Most important are the *skeletal motor fibers* transmitted through the *pudendal nerve* to the external bladder sphincter. These fibers are *somatic nerve fibers* that innervate and control the voluntary skeletal muscle of the
sphincter. Also, the bladder receives sympathetic innervation from the sympathetic chain through the hypogastric nerves, connecting mainly with the L2 segment of the spinal cord. These sympathetic fibers stimulate mainly the blood vessels and have little to do with bladder contraction. Some sensory nerve fibers also pass via the sympathetic nerves and may be important in the sensation of fullness and, in some cases, pain.

URINE TRANSPORT FROM THE KIDNEYS THROUGH THE URETERS AND INTO THE BLADDER

Urine that is expelled from the bladder has essentially the same composition as fluid flowing out of the collecting ducts. There are no significant changes in the composition of urine as it flows through the renal calyces and ureters to the bladder.

Urine flowing from the collecting ducts into the renal calyces stretches the calyces and increases their inherent pacemaker activity, which in turn initiates peristaltic contractions that spread to the renal pelvis and then downward along the length of the ureter, thereby forcing urine from the renal pelvis toward the bladder. In adults, the ureters are normally 25 to 35 centimeters (10–14 inches) long.

The walls of the ureters contain smooth muscle and are innervated by sympathetic and parasympathetic nerves, as well as by an intramural plexus of neurons and nerve fibers that extends along the entire length of the ureters. As with other visceral smooth muscle, peristaltic contractions in the ureter are enhanced by parasympathetic stimulation and inhibited by sympathetic stimulation.

The ureters enter the bladder through the detrusor muscle in the trigone region of the bladder, as shown in Figure 26-6. Normally, the ureters course obliquely for several centimeters through the bladder wall. The normal tone of the detrusor muscle in the bladder wall tends to compress the ureter, thereby preventing backflow (reflux) of urine from the bladder when pressure builds up in the bladder during micturition or bladder compression. Each peristaltic wave along the ureter increases the pressure within the ureter so that the region passing through the bladder wall opens and allows urine to flow into the bladder.

In some people, the distance that the ureter courses through the bladder wall is less than normal, and thus contraction of the bladder during micturition does not always lead to complete occlusion of the ureter. As a result, some of the urine in the bladder is propelled backward into the ureter, a condition called vesicoureteral reflux. Such reflux can lead to enlargement of the ureters and, if severe, can increase the pressure in the renal calyces and structures of the renal medulla, causing damage to these regions.

Pain Sensation in the Ureters and the Ureterorenal Reflex. The ureters are extensively supplied with pain nerve fibers. When a ureter becomes blocked (e.g., by a ureteral stone), intense reflex constriction occurs, which is associated with severe pain. Also, the pain impulses cause a sympathetic reflex back to the kidney to constrict the renal arterioles, thereby decreasing urine output from the kidney. This effect is called the ureterorenal reflex and is important for attenuating flow of fluid into the pelvis of a kidney with a blocked ureter.

Filling of the Bladder and Bladder Wall Tone—the Cystometrogram

Figure 26-8 shows the approximate changes in intravesical pressure as the bladder fills with urine. When there is no urine in the bladder, the intravesical pressure is about 0, but by the time 30 to 50 milliliters of urine have collected, the pressure rises to 5 to 10 centimeters of water. Additional urine—200 to 300 milliliters—can collect with only a small additional rise in pressure; this constant level of pressure is caused by intrinsic tone of the bladder wall. Beyond 300 to 400 milliliters, collection of more urine in the bladder causes the pressure to rise rapidly.

Superimposed on the tonic pressure changes during filling of the bladder are periodic acute increases in pressure that last from a few seconds to more than 1 minute. The pressure peaks may rise only a few centimeters of water or may rise to more than 100 centimeters of water. These pressure peaks are called micturition waves in the cystogram and are caused by the micturition reflex.

MICTURITION REFLEX

Referring again to Figure 26-8, one can see that as the bladder fills, many superimposed micturition contractions begin to appear, as shown by the dashed spikes. These are the result of a stretch reflex initiated by sensory stretch receptors in the bladder wall, especially by the receptors in the posterior urethra when this area begins to fill with
Urinary at the higher bladder pressures. Sensory signals from the bladder stretch receptors are conducted to the sacral segments of the cord through the pelvic nerves and then reflexively back again to the bladder through the parasympathetic nerve fibers by way of these same nerves.

When the bladder is only partially filled, these micturition contractions usually relax spontaneously after a fraction of a minute, the detrusor muscles stop contracting, and pressure falls back to the baseline. As the bladder continues to fill, the micturition reflexes become more frequent and cause greater contractions of the detrusor muscle.

Once a micturition reflex begins, it is self-regenerative. That is, initial contraction of the bladder activates the stretch receptors to cause a greater increase in sensory impulses from the bladder and posterior urethra, which causes a further increase in reflex contraction of the bladder; thus, the cycle is repeated again and again until the bladder has reached a strong degree of contraction. Then, after a few seconds to more than a minute, the self-regenerative reflex begins to fatigue, and the regenerative cycle of the micturition reflex ceases, permitting the bladder to relax.

Thus, the micturition reflex is a single complete cycle of the following: (1) progressive and rapid increase of pressure; (2) a period of sustained pressure; and (3) return of the pressure to the basal tone of the bladder. Once a micturition reflex has occurred but has not succeeded in emptying the bladder, the nervous elements of this reflex usually remain in an inhibited state for a few minutes to 1 hour or more before another micturition reflex occurs. As the bladder becomes filled more and more, micturition reflexes occur more and more often and powerfully.

Once the micturition reflex becomes powerful enough, it causes another reflex, which passes through the pudendal nerves to the external sphincter to inhibit it. If this inhibition is more potent in the brain than the voluntary constrictor signals to the external sphincter, urination will occur. If not, urination will not occur until the bladder fills still further, and the micturition reflex becomes more powerful.

Facilitation or Inhibition of Micturition by the Brain.
The micturition reflex is an autonomic spinal cord reflex, but it can be inhibited or facilitated by centers in the brain. These centers include the following: (1) strong facilitative and inhibitory centers in the brain stem, located mainly in thepons; and (2) several centers located in the cerebral cortex that are mainly inhibitory but can become excitatory.

The micturition reflex is the basic cause of micturition, but the higher centers normally exert final control of micturition, as follows:

1. The higher centers keep the micturition reflex partially inhibited, except when micturition is desired.
2. The higher centers can prevent micturition, even if the micturition reflex occurs, by tonic contraction of the external bladder sphincter until a convenient time presents itself.

3. When it is time to urinate, the cortical centers can facilitate the sacral micturition centers to help initiate a micturition reflex and, at the same time, inhibit the external urinary sphincter so that urination can occur.

Voluntary urination is usually initiated in the following way. First, a person voluntarily contracts the abdominal muscles, which increases pressure in the bladder and allows extra urine to enter the bladder neck and posterior urethra under pressure, thus stretching their walls. This action stimulates the stretch receptors, which excites the micturition reflex and simultaneously inhibits the external urethral sphincter. Ordinarily, all the urine will be emptied, with rarely more than 5 to 10 milliliters left in the bladder.

Abnormalities of Micturition

**Atonic Bladder and Incontinence Caused by Destruction of Sensory Nerve Fibers.** Micturition reflex contraction cannot occur if the sensory nerve fibers from the bladder to the spinal cord are destroyed, thereby preventing transmission of stretch signals from the bladder. When this happens, a person loses bladder control, despite intact efferent fibers from the cord to the bladder and despite intact neurogenic connections within the brain. Instead of emptying periodically, the bladder fills to capacity and overflows a few drops at a time through the urethra. This occurrence is called overflow incontinence.

A common cause of atonic bladder is crush injury to the sacral region of the spinal cord. Certain diseases can also cause damage to the dorsal root nerve fibers that enter the spinal cord. For example, syphilis can cause constrictive fibrosis around the dorsal root nerve fibers, destroying them. This condition is called tabes dorsalis, and the resulting bladder condition is called tabetic bladder.

**Automatic Bladder Caused by Spinal Cord Damage Above the Sacral Region.** If the spinal cord is damaged above the sacral region but the sacral cord segments are still intact, typical micturition reflexes can still occur. However, they are no longer controlled by the brain. During the first few days to several weeks after the damage to the cord has occurred, the micturition reflexes are suppressed because of the state of spinal shock caused by the sudden loss of facilitative impulses from the brain stem and cerebrum. However, if the bladder is emptied periodically by catheterization to prevent bladder injury caused by overstretching of the bladder, the excitability of the micturition reflex gradually increases until typical micturition reflexes return; then, periodic (but unannounced) bladder emptying occurs.

**Uninhibited Neurogenic Bladder Caused by Lack of Inhibitory Signals From the Brain.** Another abnormality of micturition is the so-called uninhibited neurogenic bladder, which results in frequent and relatively uncontrolled micturition. This condition derives from partial damage in the spinal cord or the brain stem that interrupts most of the inhibitory signals. Therefore, facilitative impulses passing continually down the cord keep the sacral centers so excitatory that even a small quantity of urine elicits an uncontrollable micturition reflex, thereby promoting frequent urination.
Urine formation results from glomerular filtration, tubular reabsorption, and tubular secretion

The rates at which different substances are excreted in the urine represent the sum of three renal processes, shown in Figure 26-9: (1) glomerular filtration of substances in the blood; (2) reabsorption of substances from the renal tubules into the blood; and (3) secretion of substances from the blood into the renal tubules as follows:

\[
\text{Urinary excretion rate} = \text{Filtration rate} - \text{Reabsorption rate} + \text{Secretion rate}
\]

Urine formation begins when a large amount of fluid that is virtually free of protein is filtered from the glomerular capillaries into Bowman’s capsule. Most substances in the plasma, except for proteins, are freely filtered, so their concentration in the glomerular filtrate in Bowman’s capsule is almost the same as in the plasma. As filtered fluid leaves Bowman’s capsule and passes through the tubules, it is modified by reabsorption of water and specific solutes back into the blood or by secretion of other substances from the peritubular capillaries into the tubules.

Figure 26-10 shows the renal handling of four hypothetical substances. The substance shown in panel A is freely filtered by the glomerular capillaries but is neither reabsorbed nor secreted. Therefore, its excretion rate is equal to the rate at which it was filtered. Certain waste products in the body, such as creatinine, are handled by the kidneys in this manner, allowing excretion of essentially all that is filtered.

In panel B, the substance is freely filtered but is also partly reabsorbed from the tubules back into the blood. Therefore, the rate of urinary excretion is less than the rate of filtration at the glomerular capillaries. In this case, the excretion rate is calculated as the filtration rate minus the reabsorption rate. This pattern is typical for many of the electrolytes of the body, such as sodium and chloride ions.

In panel C, the substance is freely filtered at the glomerular capillaries but is not excreted in the urine because all the filtered substance is reabsorbed from the tubules into the blood. This pattern occurs for some of the nutritional substances in the blood, such as amino acids and glucose, allowing them to be conserved in the body fluids.

The substance in panel D is freely filtered at the glomerular capillaries and is not reabsorbed, but additional quantities of this substance are secreted from the peritubular
capillary blood into the renal tubules. This pattern often occurs for organic acids and bases, permitting them to be cleared from the blood rapidly and excreted in large amounts in the urine. The excretion rate in this case is calculated as filtration rate plus tubular secretion rate.

For each substance in the plasma, a particular combination of filtration, reabsorption, and secretion occurs. The rate at which the substance is excreted in the urine depends on the relative rates of these three basic renal processes.

**Filtration, Reabsorption, and Secretion of Different Substances**

In general, tubular reabsorption is quantitatively more important than tubular secretion in the formation of urine, but secretion plays an important role in determining the amounts of potassium and hydrogen ions and a few other substances that are excreted in the urine. Most substances that must be cleared from the blood, especially the end products of metabolism, such as urea, creatinine, uric acid, and urates, are poorly reabsorbed and are therefore excreted in large amounts in the urine. Certain foreign substances and drugs are also poorly reabsorbed but, in addition, are secreted from the blood into the tubules, so their excretion rates are high. Conversely, electrolytes, such as sodium ions, chloride ions, and bicarbonate ions, are highly reabsorbed, so only small amounts appear in the urine. Certain nutritional substances, such as amino acids and glucose, are completely reabsorbed from the tubules and do not appear in the urine, even though large amounts are filtered by the glomerular capillaries.

Each of the processes—glomerular filtration, tubular reabsorption, and tubular secretion—is regulated according to the needs of the body. For example, when there is excess sodium in the body, the rate at which sodium is filtered usually increases slightly, and a smaller fraction of the filtered sodium is reabsorbed, causing increased urinary excretion of sodium.

For most substances, the rates of filtration and reabsorption are extremely large relative to the rates of excretion. Therefore, even slight changes of filtration or reabsorption can lead to relatively large changes in renal excretion. For example, an increase in the glomerular filtration rate (GFR) of only 10% (from 180 to 198 L/day) would raise the urine volume by 13-fold (from 1.5 to 19.5 L/day) if tubular reabsorption remained constant. In reality, changes in glomerular filtration and tubular reabsorption usually act in a coordinated manner to produce the necessary changes in renal excretion.

**Why Are Large Amounts of Solutes Filtered and Then Reabsorbed by the Kidneys?** One might question the wisdom of filtering such large amounts of water and solutes and then reabsorbing most of these substances. One advantage of a high GFR is that it allows the kidneys to remove waste products rapidly from the body that depend mainly on glomerular filtration for their excretion. Most waste products are poorly reabsorbed by the tubules and, therefore, depend on a high GFR for effective removal from the body.

A second advantage of a high GFR is that it allows all the body fluids to be filtered and processed by the kidneys many times each day. Because the entire plasma volume is only about 3 liters, whereas the GFR is about 180 L/day, the entire plasma can be filtered and processed about 60 times each day. This high GFR allows the kidneys to control the volume and composition of the body fluids precisely and rapidly.

**Bibliography**

See the bibliography for Chapters 27 to 32.