The Urinary System

INTRODUCTION

The kidneys, in concert with hormonal and neural inputs that control their function, are the organs primarily responsible for maintaining the stability of ECF volume, electrolyte composition, and osmolarity (solute concentration). By adjusting the quantity of water and various plasma constituents that are either conserved for the body or eliminated in the urine, the kidneys can maintain water and electrolyte balance within the very narrow range compatible with life, despite a wide range of intake and losses of these constituents through other avenues. The kidneys not only adjust for wide variations in ingestion of water (H_2O), salt, and other electrolytes, but they also adjust urinary output of these ECF constituents to compensate for abnormal losses through heavy sweating, vomiting, diarrhea, or hemorrhage. Thus as the kidneys do what they can to maintain homeostasis. urine composition varies widely.

When the ECF has a surplus of water or a particular electrolyte such as salt (NaCl), the kidney can eliminate the excess in urine. If there is a deficit, the kidneys cannot provide additional quantities of the depleted constituent, but they can limit urinary losses of the material in short supply and thus conserve it until the person can take in more of the depleted substance. Accordingly, the kidneys can compensate more efficiently for excesses than for deficits. In fact, in some instances the kidneys cannot completely halt the loss of a valuable substance in urine, even though the substance may be in short supply. A prime example is the case of a H_2O deficit. Even if a person is not consuming any H_2O, the kidneys must put out about half a liter of H_2O in the urine each day to fill another major role as the body's cleaners.

In addition to the kidneys' important regulatory role in maintaining fluid and electrolyte balance, they are the main route for eliminating potentially toxic metabolic wastes and foreign compounds from the body. These wastes cannot be eliminated as solids; they must be excreted in solution, thus obligating the kidneys to produce a minimum volume of around 500 ml of waste-filled urine per day.

OVERVIEW OF KIDNEY FUNCTIONS

The kidneys perform the following specific functions, most of which help preserve the constancy of the internal fluid environment:

1. *Maintaining H_20 balance in the body.*
2. *Maintaining the proper osmolarity of body fluids, primarily through regulating H_2O balance.* This function is important to prevent osmotic fluxes into or out of the cells, which could lead to detrimental swelling or shrinking of the cells, respectively.
3. *Regulating the quantity and concentration of most ECF ions,* including sodium (Na^+),

chloride (Cl^-), potassium (K^+), calcium (Ca^{2+}), hydrogen ion (H^+), bicarbonate (HCO_3^-), phosphate (PO_4^{3-}), sulfate (SO_4^-), and magnesium (Mg^{2+}). Even minor fluctuations in the ECF concentrations of some of these electrolytes can have profound influences. For example, changes in the ECF concentration of K^+ can potentially lead to fatal cardiac dysfunction.

4. *Maintaining proper plasma volume,* which is important in the long-term regulation of arterial blood pressure. This function is accomplished through the kidneys' regulatory role in salt (Na^+ and Cl^-) and H_2O balance.
5. *Helping maintain the proper acid-base balance* of the body by adjusting urinary output of H^+ and HCO_3^-.
6. *Excreting (eliminating) the end products (wastes) of bodily metabolism* such as urea, uric acid, and creatinine. If allowed to accumulate, these wastes are toxic, especially to the brain.
7. *Excreting many foreign compounds* such as drugs, food additives, pesticides, and other exogenous nonnutritive materials that have entered the body.
8. *Producing erythropoietin, a hormone that produces red blood cell production.*
9. *Producing renin, an enzymatic hormone that triggers a chain reaction important in salt conservation by the kidneys.*
10. *Converting vitamin* D *into its active form.*

The kidneys form the urine; the rest of the urinary system carries the urine to the outside

The urinary system consists of the urine-forming organs -the kidneys- and the structures that carry the urine from the kidneys to the outside for elimination from the body **(**Figure 13-1a). The kidneys are a pair of bean-shaped organs that lie in the back of the abdominal cavity, one on each side of the vertebral column, slightly above the waistline. Each kidney is supplied by a renal artery and a renal vein, which, respectively, enters and leaves the kidney at the medial indentation that gives this organ its beanlike form. The kidney acts on the plasma flowing through it to produce urine, conserving materials to be retained in the body and eliminating unwanted materials into the urine.

After urine is formed, it drains into a central collecting cavity, the renal pelvis, located at the medial inner core of each kidney **(**Figure 13-lb). From there urine is channeled into the ureter, a smooth muscle-walled duct that exits at the medial border in close proximity to the renal artery and vein. There are two ureters, each one carrying urine from each kidney to the single urinary bladder.

The urinary bladder, which temporarily stores urine, is a hollow, distensible, smooth muscle-walled sac. Periodically, urine is emptied from the bladder to the outside through another tube, the urethra, as a result of bladder contraction. The urethra in females is straight and short, passing directly from the neck of the bladder to the outside. In males the urethra is much longer and follows a curving course from the bladder to the outside, passing through both the prostate gland and the penis (Figure 13-1a). The male urethra serves the dual function of providing both a route for eliminating urine from the bladder and a passageway for semen from the reproductive organs. The prostate gland lies below the neck of the bladder and completely encircles the urethra. Prostatic enlargement, which often occurs during middle to older age, can partially or completely occlude the urethra, impeding the flow of urine. The parts of the urinary system beyond the kidneys merely serve as ductwork to transport urine to the outside. Once formed by the kidneys, urine is not altered in composition or volume as it moves downstream through the rest of the tract.

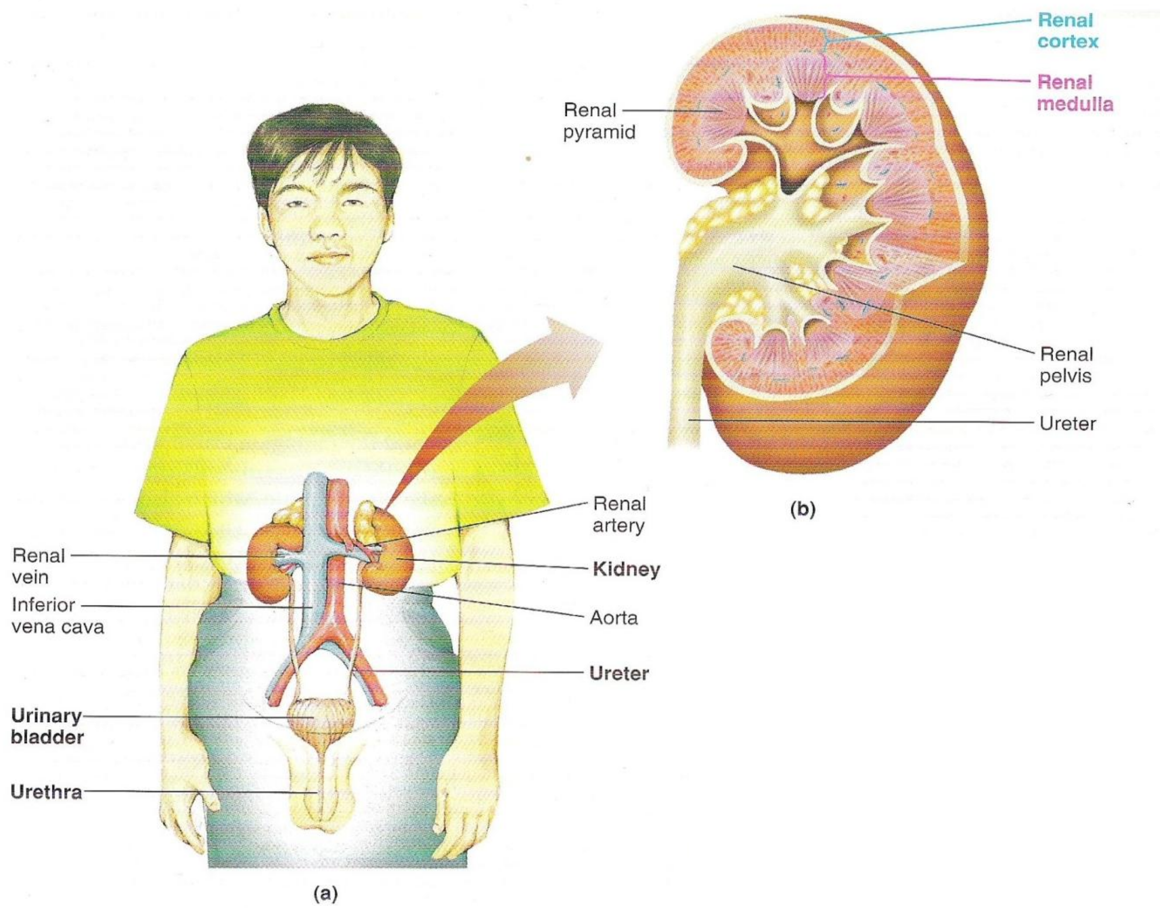


FIGURE 13-1

The urinary system. (a) *The components of the urinary system.* The pair of kidneys form the urine, which the ureters carry to the urinary bladder. Urine is stored in the bladder and periodically emptied to the exterior through the urethra. (b) *Longitudinal section of a kidney.* The kidney consists of an outer, granular-appearing renal cortex and an inner, striated-appearing renal medulla. The renal pelvis at the medial inner core of the kidney collects urine after it is formed.

The nephron is the functional unit of the kidney

Each kidney consists of about 1 million microscopic functional units known as nephrons, which are bound together by connective tissue. Recall that a functional unit is the smallest unit within an organ capable of performing all of that organ's functions. Because the main function of the kidneys is to produce urine and, in so doing, maintain constancy in the ECF composition, a nephron is the smallest unit capable of forming urine.

The arrangement of nephrons within the kidneys gives rise to two distinct regions-an outer region called the renal cortex, which looks granular, and an inner region, the renal medulla, which is made up of striated triangles, the renal pyramids (Figure 13-1b). Each nephron consists of a *vascular component* and a *tubular component,* both of which are intimately related structurally and functionally (Figure 13-2).

VASCULAR COMPONENT OF THE NEPHRON

The dominant part of the nephron's vascular component is the glomerulus, a ball-like tuft of capillaries through which part of the water and solutes is filtered from blood passing through. This filtered fluid, which is almost identical in composition to plasma, then passes through the nephron's tubular component, where various transport processes convert it into urine.

On entering the kidney; the renal artery subdivides to ultimately form many small vessels known as afferent arterioles, one of which supplies each nephron. The afferent arteriole delivers blood to the glomerulus. The glomerular capillaries rejoin to form another arteriole, the efferent arteriole, through which blood that was not filtered into the tubular component leaves the glomerulus. The efferent arterioles are the only arterioles in the body that drain from capillaries. Typically; arterioles break up into capillaries that rejoin to form venules. At the glomerular capillaries, no O_2 or nutrients are extracted from the blood for use by the kidney tissues nor are waste products picked up from the surrounding tissue. Thus arterial blood enters the glomerular capillaries through the afferent arteriole, and arterial blood leaves the glomerulus through the efferent arteriole.

The efferent arteriole quickly subdivides into a second set of capillaries, the peritubular capillaries, which supply the renal tissue with blood and are important in exchanges between the tubular 'System and blood during conversion of the filtered fluid into urine. These peritubular capillaries, as their name implies, are intertwined around the tubular system *(peri* means "around"). The peritubular capillaries rejoin to form venules that ultimately drain into the renal vein, by which blood leaves the kidney.

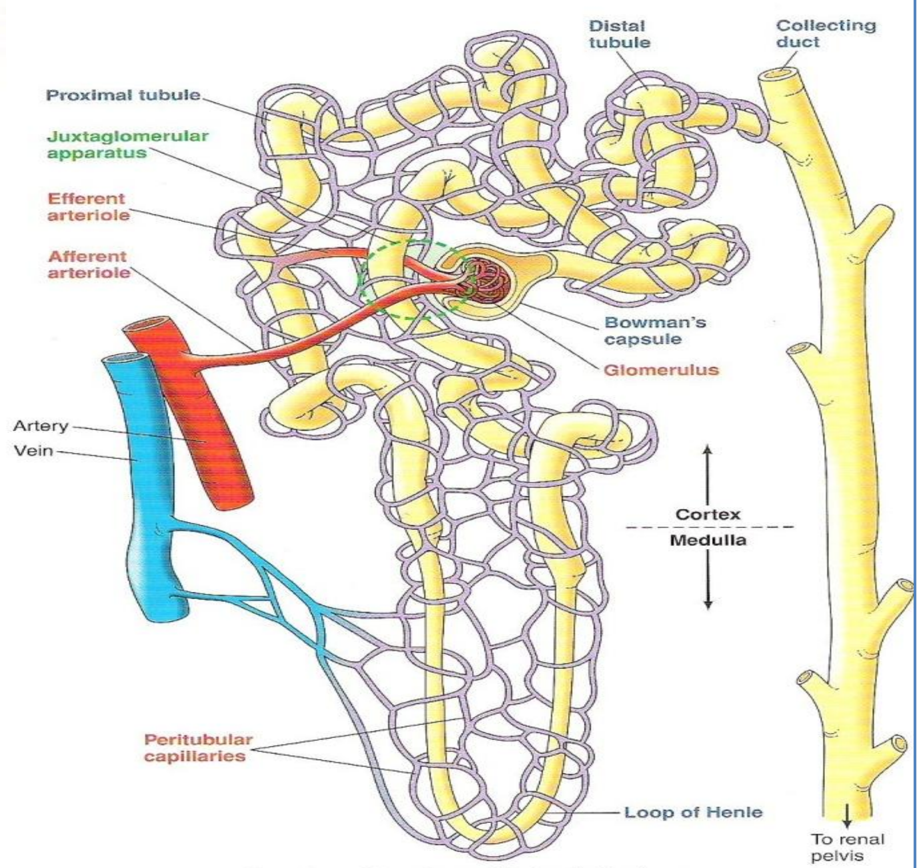


FIGURE 13-2
A nephron

Overview of Functions of Parts of a Nephron

Vascular component
- Afferent arteriole—carries blood to the glomerulus
- Glomerulus—a tuft of capillaries that filters a protein-free plasma into the tubular component
- Efferent arteriole—carries blood from the glomerulus
- Peritubular capillaries—supply the renal tissue; involved in exchanges with the fluid in the tubular lumen

Combined vascular/tubular component
- Juxtaglomerular apparatus—produces substances involved in the control of kidney function

Tubular component
- Bowman's capsule—collects the glomerular filtrate
- Proximal tubule—uncontrolled reabsorption and secretion of selected substances occur here
- Loop of Henle—establishes an osmotic gradient in the renal medulla that is important in the kidney's ability to produce urine of varying concentration
- Distal tubule and collecting duct—variable, controlled reabsorption of Na^+ and H_2O and secretion of K^+ and H^+ occur here; fluid leaving the collecting duct is urine, which enters the renal pelvis

TUBULAR COMPONENT OF THE NEPHRON

The nephron's tubular component is a hollow, fluid-filled tube formed by a single layer of epithelial cells. Even though the tubule is continuous from its beginning near the glomerulus to its ending at the renal pelvis, it is arbitrarily divided into various segments based on differences in structure and function along its length (Figure 13-2). The tubular component begins with Bowman's capsule, an expanded, double-walled invagination that cups around the glomerulus to collect fluid filtered from the glomerular capillaries. The presence of all glomeruli and associated Bowman's capsules in the cortex produces this region's granular appearance.

From Bowman's capsule, the filtered fluid passes into the proximal tubule, which lies entirely within the cortex and is highly coiled or convoluted throughout much of its course. The next segment, the loop of Henle, forms a sharp U-shaped or hairpin loop that dips into the renal medulla. The *descending limb* of Henle's loop plunges from the cortex into the medulla; the *ascending limb* traverses back up into the cortex. The ascending limb returns to the glomerular region of its own nephron, where it passes through the fork formed by the afferent and efferent arterioles. Both the tubular and vascular cells at this point are specialized to form the juxtaglomerular apparatus, a structure that lies next to the glomerulus (*juxta* means "next to"). This specialized region plays an important role in regulating kidney function. Beyond the juxtaglomerular apparatus, the tubule once again coils tightly to form the distal tubule, which also lies entirely within the cortex. The distal tubule empties into a collecting duct or tubule, with each collecting duct draining fluid from up to eight separate nephrons. Each collecting duct plunges down through the medulla to empty its fluid contents (now converted into mine) into the renal pelvis.

Glomerular filtration, tubular reabsorption, and tubular secretion

Three basic processes are involved in forming urine: *glomerular filtration, tubular reabsorption, and tubular secretion* (Figure 13-4).

GLOMERULAR FILTRATION

As blood flows through the glomerulus, protein-free plasma filters through the glomerular capillaries into Bowman's capsule. Normally, about 20% of the plasma that enters the glomerulus is filtered. This process, known as glomerular filtration, is the first step in urine formation. On average, 125 ml of glomerular filtrate (filtered fluid) are formed collectively through all the glomeruli each minute. This amounts to 180 liters each day. This means that the kidneys filter the entire plasma volume about 65 times per day.

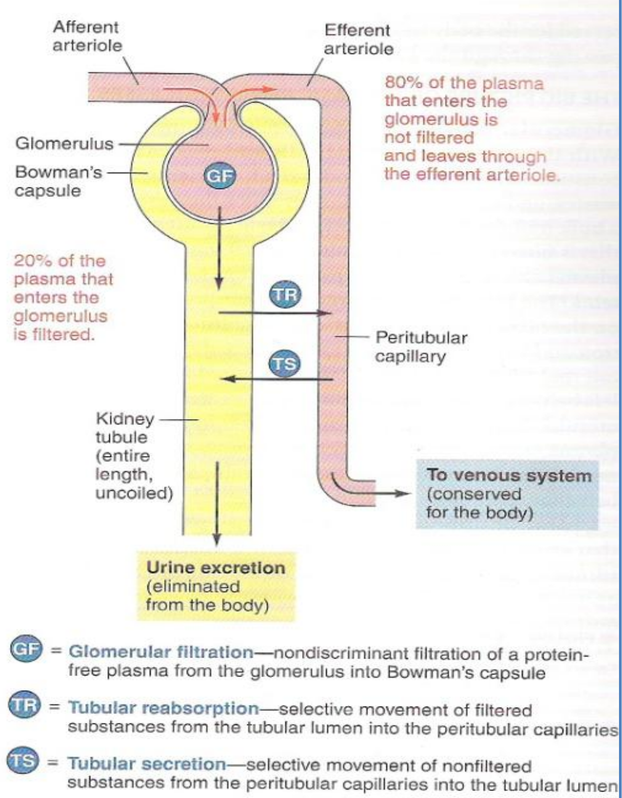


FIGURE 13-4

Basic renal processes. Anything filtered or secreted but not reabsorbed is excreted in the urine and lost from the body. Anything filtered and subsequently reabsorbed, or not filtered at all, enters the venous blood and is saved for the body.

TUBULAR REABSORPTION

As the filtrate flows through the tubules, substances of value to the body are returned to the peritubular capillary plasma. This selective movement of substances from inside the tubule (the tubular lumen) into the blood is called tubular reabsorption. Reabsorbed substances are not lost from the body in the urine but instead are carried by the peritubular capillaries to the venous system and then to the heart to be recirculated. Of the 180 liters of plasma filtered per day, 178.5 liters on average are reabsorbed. The remaining 1.5 liters left in the tubules passes into the renal pelvis to be eliminated as urine. In general, substances the body needs to conserve are selectively reabsorbed, whereas unwanted substances that must be eliminated stay in the urine.

TUBULAR SECRETION

The third renal process, tubular secretion, is the selective transfer of substances from the peritubular capillary blood into the tubular lumen. It provides a second route for substances to enter the renal tubules from the blood, the first being by glomerular filtration. Only about 20% of the plasma flowing through the glomerular capillaries is filtered into Bowman's capsule; the remaining 80% flows on through the efferent arteriole into the peritubular capillaries. A few substances may be discriminatingly transferred by tubular secretion from the plasma in the peritubular capillaries into the tubular lumen.

URINE EXCRETION

Urine excretion is the elimination of substances from the body in the urine. It is not really a separate process but rather is the result of the first three processes. All plasma constituents that are filtered or secreted but are not reabsorbed remain in the tubules and pass into the renal pelvis to be excreted as urine and eliminated from the body (Figure 13-4). Note that anything filtered and subsequently reabsorbed, or not filtered at all, enters the venous blood from the peri tubular capillaries and thus is conserved for the body instead of being excreted in urine, despite passing through the kidneys.

THE BIG PICTURE OF THE BASIC RENAL PROCESSES

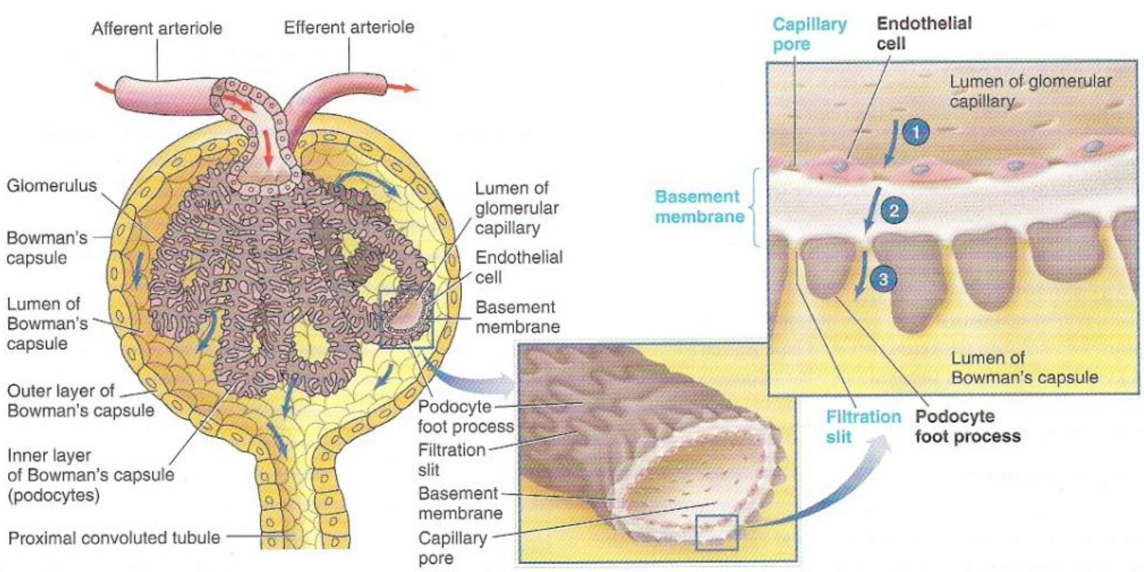
Glomerular filtration is largely an indiscriminate process. With the exception of blood cells and plasma proteins, all constituents within the blood -H_2O, nutrients, electrolytes, wastes, and so on –nonselectively enter the tubular lumen as a bulk unit during filtration. The highly discriminating tubular processes then work on the filtrate to return to the blood a fluid of the composition and volume necessary to maintain the constancy of the internal fluid environment. The unwanted filtered material is left behind in the tubular fluid to be excreted as urine. It is up to the tubular system to salvage by reabsorption the filtered materials that need to be preserved for the body, while leaving behind substances that must be excreted. In addition, some substances are not only filtered but are also secreted, so that the amounts of these substances excreted in the urine are greater than the amounts that were filtered. For many substances, these renal processes are subject to physiologic control. Thus the kidneys handle each constituent in the plasma in a characteristic manner by a particular combination of filtration, reabsorption, and secretion.

GLOMERULAR FILTRATION

Fluid filtered from the glomerulus into Bowman's capsule must pass through the following three layers that make up the glomerular membrane **(**Figure 13-5):

● FIGURE 13-5

Layers of the glomerular membrane



To be filtered, a substance must pass through

1. the pores between the endothelial cells of the glomerular capillary
2. an acellular basement membrane
3. the filtration slits between the foot processes of the podocytes of the inner layer of Bowman's capsule

1. The *wall of the glomerular capillaries,* which is a single layer of flattened endothelial cells. It is perforated by many large pores that make it over 100 times more permeable to H_2O and solutes than capillaries elsewhere in the body.

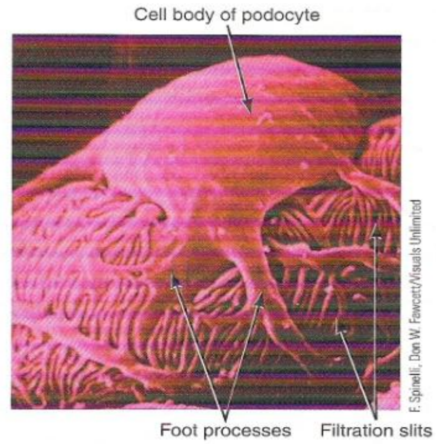
2. The *basement membrane,* which is an acellular (lacking cells) gelatinous layer.

3. The *inner layer of Bowman's capsule,* which consists of podocytes, octopus-like cells that encircle the glomerular tuft. Each podocyte bears many elongated foot processes *(podo* means "foot"; a *process* is a projection or appendage) that interdigitate with foot processes of adjacent podocytes, much as you interlace your fingers between each other when you cup your hands around a ball **(**Figure 13-6). The narrow slits between adjacent foot processes, known as filtration slits, provide a pathway through which fluid leaving the glomerular capillaries can enter the lumen of Bowman's capsule.

Collectively, these layers function as a fine molecular sieve that retains the blood cells and plasma proteins but permits H_2O and solutes of small molecular dimension to filter through. Thus the route that filtered substances take across the glomerular membrane is completely extracellular-first through capillary pores, then through the acellular basement membrane and finally through capsular filtration slits (Figure 13-5).

FIGURE 13-6

Bowman's capsule podocytes with foot processes and filtration slits. Note the filtration slits between adjacent foot processes on this scanning electron micrograph. The podocytes and their foot processes encircle the glomerular capillaries.



Glomerular capillary blood pressure is the major force that induces glomerular filtration

No active transport mechanisms or local energy expenditures are involved in moving fluid from the plasma across the glomerular membrane into Bowman's capsule. Passive physical forces similar to those acting across capillaries elsewhere accomplish glomerular filtration.

FORCES INVOLVED IN GLOMERULAR FILTRATION

Three physical forces are involved in glomerular filtration (Table 13-1): glomerular capillary blood pressure, plasma-colloid osmotic pressure, and Bowman's capsule hydrostatic pressure. Let's examine the role of each.

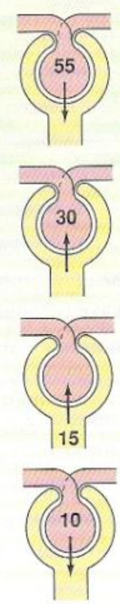
1. *Glomerular capillary blood pressure* is the fluid pressure exerted by the blood within the glomerular capillaries. It ultimately depends on contraction of the heart (the source of energy that produces glomerular filtration) and the resistance to blood flow offered by the afferent and efferent arterioles. Glomerular capillary blood pressure, at an estimated average value of 55 mm Hg, is higher than capillary blood pressure elsewhere. The reason for the higher pressure in the glomerular capillaries is the larger diameter of the afferent arteriole compared to the efferent arteriole. Because blood can more readily enter the glomerulus through the wide afferent arteriole than it can leave through the narrower efferent arteriole, glomerular capillary blood pressure is maintained high as a result of blood damming up in the glomerular capillaries. Furthermore, because of the high resistance offered by the efferent arterioles, blood pressure does not have the same tendency to fall along the length of the glomerular capillaries as it does along other capillaries. This raised, nondecremental glomerular blood pressure tends to push fluid out of the glomerulus

into Bowman's capsule along the glomerular capillaries' entire length and it is the major force producing glomerular filtration. Whereas glomerular capillary blood pressure *favors* filtration, the two other forces acting across the glomerular membrane (plasma-colloid osmotic pressure and Bowman's capsule hydrostatic pressure) *oppose* filtration.

2. *Plasma-colloid osmotic pressure* is caused by the unequal distribution of plasma proteins across the glomerular membrane. Because plasma proteins cannot be filtered, they are in the glomerular capillaries but not in Bowman's capsule. Accordingly, the concentration of H_2O is higher in Bowman's capsule than in the glomerular capillaries. The resulting tendency for H_2O to move by osmosis down its own concentration gradient from Bowman's capsule into the glomerulus opposes glomerular filtration. This opposing osmotic force averages 30 mm Hg, which is slightly higher than across other capillaries. It is higher because much more H_2O is filtered out of the glomerular blood, so the concentration of plasma proteins is higher than elsewhere.

TABLE 13-1
Forces Involved in Glomerular Filtration

FORCE	EFFECT	MAGNITUDE (mm Hg)
Glomerular Capillary Blood Pressure	Favors filtration	55
Plasma-Colloid Osmotic Pressure	Opposes filtration	30
Bowman's Capsule Hydrostatic Pressure	Opposes filtration	15
Net Filtration Pressure (difference between force favoring filtration and forces opposing filtration)	Favors filtration	10



55 − (30 + 15) = 10

3. *Bowman's capsule hydrostatic pressure*, the pressure exerted by the fluid in this initial part of the tubule, is estimated to be about 15 mm Hg. This pressure, which tends to push fluid out of Bowman's capsule, opposes the filtration of fluid from the glomerulus into Bowman's capsule.

GLOMERULAR FILTRATION RATE

As can be seen in Table 13-1, the forces acting across the glomerular membrane are not in balance. The total force favoring filtration is attributable to the glomerular capillary blood pressure at 55 mm Hg. The total of the two forces opposing filtration is 45 mm Hg. The net difference favoring filtration (10 mm Hg of pressure) is called the net filtration pressure. This modest pressure forces large volumes of fluid from the blood through the highly permeable glomerular membrane.

Normally, about 20% of the plasma that enters the glomerulus is filtered at the net filtration pressure of 10 mm Hg, producing collectively through all glomeruli 180 liters of glomerular filtrate each day for an average glomerular filtration rate (GFR) of 125 ml/min.

Changes in the GFR primarily result from changes in glomerular capillary blood pressure

Because the net filtration pressure that accomplishes glomerular filtration is simply due to an imbalance of opposing physical forces between the glomerular capillary plasma and Bowman's capsule fluid, alterations in any of these physical forces can affect the GFR. We will examine the effect that changes in each of these physical forces have on the GFR.

UNREGULATED INFLUENCES ON THE GFR

Plasma-colloid osmotic pressure and Bowman's capsule hydrostatic pressure are not subject to regulation and under normal conditions do not vary much, However, they can change pathologically and thus inadvertently affect the GFR. Because plasma-colloid osmotic pressure opposes filtration, a decrease in plasma protein concentration, by reducing this pressure, leads to an increase in the GFR. An uncontrollable reduction in plasma protein concentration might occur, for example, in severely burned patients who lose a large quantity of protein-rich, plasma-derived fluid through the exposed burned surface of their skin.

Bowman's capsule hydrostatic pressure can become uncontrollably elevated, and filtration subsequently can decrease, given a urinary tract obstruction, such as a kidney stone or prostatic enlargement. The damming up of fluid behind the obstruction elevates capsular hydrostatic pressure.

CONTROLLED ADJUSTMENTS IN THE GFR

Unlike plasma-colloid osmotic pressure and Bowman's capsule hydrostatic pressure-which may be uncontrollably altered in various disease states and, thereby inappropriately alter the GFR-glomerular capillary blood pressure can be controlled to adjust the GFR to suit the body's needs. Controlled changes in the GFR are brought about by the sympathetic nervous system, which adjusts glomerular blood flow by regulating the caliber of the afferent arterioles. The parasympathetic nervous system does not have any influence on the kidneys. Sympathetic control of the GFR is aimed at long-term regulation of arterial blood pressure. If plasma volume is decreased-for example, by hemorrhage-the resulting fall in arterial blood pressure is detected by the arterial carotid sinus and aortic arch baroreceptors, which initiate neural reflexes to raise blood pressure toward normal. These reflex responses are coordinated by the cardiovascular control center in the brain stem and are mediated primarily through increased sympathetic activity to the heart and blood vessels. Although the resulting increase in both cardiac output and total peripheral resistance helps raise blood pressure toward normal, plasma volume is still reduced. In the long term, plasma volume must be restored to normal. One compensation for a depleted plasma volume is reduced urine output so that more fluid than normal is conserved for the body, Urine output is reduced in part by reducing the GFR; if less fluid is filtered, less is available to excrete.

No new mechanism is needed to decrease the GFR. It is reduced by the baroreceptor reflex response to a fall in blood pressure (Figure 13-7). During this reflex, sympathetically induced vasoconstriction occurs in most arterioles throughout the body (including the afferent arterioles) as a compensatory mechanism to increase total peripheral resistance. When the afferent arterioles carrying blood to the glomeruli constrict from increased sympathetic activity, less blood flows into the glomeruli than normal, lowering glomerular capillary blood pressure (Figure 13-8a). The resulting decrease in GFR in turn reduces urine volume. In this way, some of the H_2O and salt that would otherwise have been lost in urine are saved for the body, helping in the long term to restore plasma volume to normal so that short-term cardiovascular adjustments that have been made are no longer necessary.

Conversely, if blood pressure is elevated (for example, because of an expansion of plasma volume following ingestion of excessive fluid), the opposite responses occur. When the baroreceptors detect a rise in blood pressure, sympathetic vasoconstrictor activity to the arterioles, including the renal afferent arterioles, is reflexly reduced, allowing afferent arteriolar vasodilation to occur. As more blood enters the glomeruli through the dilated afferent arterioles, glomerular capillary blood pressure rises, increasing the GFR **(**Figure 13-8b). As more fluid is filtered, more fluid is available to be eliminated in urine. Contributing to the increase in urine volume is a hormonally adjusted reduction in the tubular reabsorption of H_2O and salt. These two renal mechanisms-increased glomerular filtration and decreased tubular reabsorption of H_2O and salt- increase urine volume and eliminate the excess fluid from the body. Reduced thirst and fluid intake also help restore an elevated blood pressure to normal.

TUBULAR REABSORPTION

All plasma constituents except the proteins are indiscriminately filtered together through the glomerular capillaries. In addition to waste products and excess materials that the body must eliminate, the filtered fluid also contains nutrients, electrolytes, and other substances that the body cannot afford to lose in the urine. Indeed, through ongoing glomerular filtration greater quantities of these materials are filtered per day than are even present in the entire body. It is important that the essential materials that are filtered be returned to the blood by *tubular reabsorption,* the discrete transfer of substances from the tubular lumen into the peritubular capillaries.