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Introduction and Key Concepts for the Urinary System

The urinary system is composed of two kidneys, two ureters, the bladder, and the urethra. The kidneys produce urine, the ureters transport urine to the bladder, and the bladder temporarily stores and empties urine through the urethra to outside of the body. The urinary system functions to (1) filter blood and reabsorb nutrients; (2) control the water, ion, and salt balance of the body; (3) maintain the acid-base balance of the blood; (4) excrete metabolic wastes (urea and uric acid), toxins, and drug components; (5) secrete hormones, such as renin and erythropoietin; and (6) produce calcitriol (an active form of vitamin D) to help the body absorb dietary calcium into the blood.

Kidneys

The kidneys are bean-shaped organs located in the posterior abdominal region on each side of the vertebral column. The kidney can be divided into the renal cortex, the renal medulla, and the hilum. The renal cortex is composed of renal corpuscles and various cortical tubules, which include the proximal convoluted tubules, the distal convoluted tubules, and the cortical collecting tubules. The renal medulla is located deep to the cortex, and its tubules extend as medullary rays into the cortex region. The medulla comprises 10 to 18 renal pyramids; each pyramid contains the loops of Henle, collecting ducts, and papillary ducts. The apical projection of a renal pyramid is called the renal papilla. The papillary ducts empty urine at the tip of a renal papilla onto its surface, which is called the area cibrosa (perforated area). Each renal papilla is surrounded by a space, the minor calyx; several minor calices unite to form a major calyx. There are two or three major calyces for each kidney. The major calices unite to form the renal pelvis, which funnels urine into the ureter. The hilum is the region in the medial portion of the kidney where the renal artery, the renal vein, and the ureter enter and exit the kidney (Fig. 12-2). Functionally and structurally, the kidney can be divided into the nephron and the collecting system (Fig. 12-8B). The nephron produces urine. The collecting system adjusts the composition of urine and transports urine to the calyces.

THE NEPHRON comprises a renal corpuscle, a proximal convoluted tubule, a loop of Henle, and a distal convoluted tubule.

A renal corpuscle is composed of a glomerulus and a Bowman capsule. (1) A glomerulus consists of a spherical knot of capillaries, which is fed by an afferent arteriole and drained by an efferent arteriole at the vascular pole. (2) A Bowman capsule consists of a visceral layer and a parietal layer. The visceral layer is composed of podocytes, which cover the capillaries of a glomerulus. These cells have long, interdigitating cellular processes and play an important role in blood filtration. The interstitial tissues surrounding the glomerular capillaries contain cells called intraglomerular mesangial cells. The parietal layer of the Bowman capsule is a hollow spherical structure lined by simple squamous epithelium. The space between the visceral and the parietal layers of the Bowman capsule is called the Bowman space. Blood flows through the glomerular capillaries, and its plasma passes through the glomerular filtration barrier (the fused basal laminae of the endothelial cells and the podocytes); the filtrate is collected in the Bowman space (Fig. 12-6A,B). Thus, the renal corpuscle, as a whole, forms a blood-filtering unit, which allows water, metabolic wastes, ions, and small molecules to pass through the capillary wall but prevents circulating cells and large plasma proteins from leaving the blood.

Proximal Convoluted Tubules are long tubes that follow a serpentine course as they drain the filtrate from the renal corpuscles into the loop of Henle. Each is lined by a simple cuboidal epithelium with abundant long microvilli (brush border) bordering the lumen. Each proximal convoluted tubule connects to a renal corpuscle at its urinary pole. The relatively large epithelial cells of the proximal convoluted tubule contain many mitochondria, which render their cytoplasm brightly acidophilic (pink). The lateral boundaries between the cells interdigitate, so that the boundaries between adjacent cells are unclear in light microscopy. Their long microvilli appear to fill much of the space within the lumen (Fig. 12-9A,B). The combined structural features of the proximal convoluted tubules contribute to their functions of actively transporting ions and reabsorbing water, glucose, amino acids, proteins, and vitamins from the filtrate.

The Loop of Henle is a continuation of the proximal convoluted tubule. It is a U-shaped structure that includes a descending limb and an ascending limb (Fig. 12-8B). The descending limb consists of a thick descending limb (proximal straight tubule) and a thin descending limb (descending thin segment). The ascending limb contains a thin ascending limb (ascending thin segment) and a thick ascending limb (distal straight tubule). The loop of Henle plays a crucial role in generating a high sodium concentration gradient in the interstitium of the renal medulla. This permits water to move passively
from collecting ducts into the interstitium. Some physiology textbooks do not include the thick descending limb (proximal straight tubule) as a part of the loop of Henle proper because it does not significantly contribute to its physiological function. The proximal straight tubules are similar in structure to the proximal convoluted tubules. The descending and ascending thin segment tubules are lined by squamous cells and are structurally similar to each other. The descending limb is permeable to water, Cl⁻, and Na⁺. The tubules of the descending limb reabsorb water and salts and reduce the volume of the filtrate that has passed through the proximal convoluted tubules. The ascending limb is very active physiologically. It is impermeable to water, and it actively pumps Cl⁻ and Na⁺ from the lumen into the medullary interstitium.

Distal Convoluted Tubules are lined by small, simple cuboidal epithelial cells, which have no brush border. They may show a few short, irregular microvilli on their apical surfaces and plasma membrane infoldings on their basal region at the EM level (Fig. 12-10A,B). Their lumens appear clear and wider than those of proximal tubules. The distal convoluted tubules are located in the cortex of the kidney and are closely associated with the renal corpuscles. At the junction between the distal straight and the convoluted tubules, there is an important specialized sensory structure, the macula densa, which senses and monitors ionic content and water volume of the filtrate. The macula densa is composed of cells that are taller and more tightly packed than other cells of the distal tubule (see Fig. 12-5A,B). This portion of the distal tubule is positioned between afferent and efferent arterioles at the vascular pole of the renal corpuscle. The distal convoluted tubules remove Na⁺ and add K⁺ to the filtrate if aldosterone stimulation is present; they also reabsorb bicarbonate ions and secrete ammonium to adjust the pH balance. The distal convoluted tubules connect distal straight tubules (thick ascending limb of the loop of Henle) to the collecting tubules. The distal convoluted and straight tubules are structurally similar to each other, differing mainly in their locations and courses.

THE COLLECTING SYSTEM consists of cortical collecting tubules, collecting ducts, and papillary ducts. The collecting tubules are small and lined by cuboidal cells. They are located in the renal cortex, so they are also called cortical collecting tubules. They drain the filtrate from distal convoluted tubules into the collecting ducts of the medullary rays, which, in turn, drain into larger collecting ducts in the medulla. Collecting ducts have larger lumens than collecting tubules, and they are lined by taller cuboidal or columnar cells. Both collecting tubules and ducts have clear cytoplasm and distinct cell-to-cell boundaries. These tubules become highly permeable to water under the influence of antidiuretic hormone (ADH). Depending on ADH levels, the tubules passively diffuse a variable volume of water from their lumens into the medullary interstitium, thus increasing the concentration of urine. The collecting ducts are the last components of the kidney that process and determine the final urine composition. Papillary ducts, also called ducts of Bellini, are continuations of the collecting ducts. They are located in the papilla of the renal medulla. Several collecting ducts merge into a single papillary duct, which empties urine into the minor calyx at the tip of the renal papilla.

THE VASCULAR SUPPLY TO THE KIDNEY comes from the renal artery, which enters the kidney at the hilum; segmental branches of the renal artery give rise to the interlobar arteries. These pass through the renal columns between the renal pyramids and give rise to arcuate arteries. The arcuate arteries run along the junction between the cortex and the medulla of the kidney and give rise to the interlobular arteries, which extend into the medulla to supply the afferent arterioles of renal corpuscles. Each afferent arteriole supplies a glomerulus of capillaries from which blood is drained by an efferent arteriole at the vascular pole. The efferent arterioles of corpuscles in the outer cortex feed into the peritubular capillary network, which supplies the cortical tissue surrounding the cortical tubules. These peritubular capillaries provide for gas and material exchange and also receive renal interstitial fluid, which is reabsorbed out of the tubules and goes back into the vascular bed. Venues carry blood to the interlobular veins and to the arcuate veins in the renal corticomedullary junction. The efferent arterioles of deeper (juxtamedullary) corpuscles extend into the medulla where they give rise to capillaries called vasa recta, which receive interstitial fluid (reabsorbed from filtrate) in the medulla and send it back to the circulation. The vasa recta take a hairpin course in the medulla following the loop of Henle. They return to the corticomedullary junction to join the interlobular veins and then drain into the arcuate veins. The arcuate veins drain blood into the interlobar veins, which then merge to form the branches of the segmental renal veins, which in turn finally merge into the renal vein (see Fig. 11-2).

Ureters

The two ureters lie in the extraperitoneal connective tissue, laterally positioned on each side of the vertebral column. The ureters are long, relatively small tubules lined by transitional epithelium and surrounded by a thin layer of smooth muscle and connective tissue. Superiorly, they drain the funnel-shaped renal pelvis, and inferiorly, they empty into the bladder by penetrating its posterior wall. The ureters have a much thinner wall than the bladder. Like most tubular organs, the wall of the ureter is composed of several layers of tissues: mucosa, muscularis, and adventitia (Fig. 12-13A,B).

Urinary Bladder

The urinary bladder, a distensible sac-shaped organ located in the pelvic cavity, temporarily stores urine. The wall of the bladder has three openings, two of them for ureters to enter and one for emptying urine into the urethra. Like the ureter, the urinary bladder wall consists of mucosal, muscularis, and adventitial layers, but the bladder wall is much thicker, having three substantial layers of smooth muscle in the muscularis. (1) The mucosa consists of a transitional epithelium lining and a layer of connective tissue (lamina propria) containing blood vessels and nerve fibers. (2) The muscularis contains the three layers of smooth muscle: inner longitudinal smooth muscle, middle circular smooth muscle, and outer longitudinal smooth muscle. The muscularis contracts in different directions to enable the urinary bladder to empty urine. (3) The outer portion of the bladder is protected by both a serosa and an adventitia depending on whether it projects into the peritoneal cavity. The superior surface of the bladder is covered by serosa, which is a layer of connective tissue covered by mesothelium; the inferior
surface of the bladder is covered by adventitia, which is a layer of connective tissue without a mesothelial covering.

**Urethra**

The *urethra* is structurally different in the male and female. The proximal end of the *male urethra* is surrounded by an internal urethral sphincter (smooth muscle) that functions mainly to prevent seminal fluids from entering the bladder during ejaculation. The male urethra is about 20 cm long, and it is composed of three segments: prostatic, membranous, and penile (spongy) urethra. The *prostatic portion* is surrounded by the prostate gland and is lined by transitional epithelium. The *membranous portion* is a short segment surrounded by the skeletal muscle of the external sphincter (urogenital diaphragm) and is lined by pseudostratified columnar epithelium. The *penile (spongy) urethra* (also called the cavernous urethra) is surrounded by the corpus spongiosum of the penis, and its epithelial lining changes from pseudostratified columnar to stratified squamous. In this region, there are many small mucous glands called the glands of Littré, which secrete mucus to coat and protect the lining of the urethra.

The *female urethra* is short, about 4 to 5 cm. It is lined chiefly by stratified squamous epithelium and, in a few places, may have patches of pseudostratified columnar epithelium. Glands of Littré are also present in the female urethra. The proximal end of female urethra is surrounded by skeletal muscle (external sphincter) where it penetrates the urogenital diaphragm. The external sphincter muscle in both male and female is innervated by the pudendal nerves; it functions to control retention or release of the urine from the urinary bladder through the urethra and helps maintain urinary continence. A female does not have an internal sphincter.
The urinary system plays an important role in eliminating the body’s metabolic wastes and toxins; controlling water and ion balance and regulating blood pressure; maintaining the acid-base (pH) balance of the blood; and in reabsorbing and conserving nutrients. The urinary system achieves these goals by filtering the blood and producing urine. The complex tubule system in the kidney helps to reabsorb and readjust water and ion content and to excrete urine. The urinary system consists of two kidneys, two ureters, the urinary bladder, and the urethra. The kidneys are the organs that produce urine and accomplish the essential functions listed above. After urine is produced, it passes through the ureters to the bladder for temporary storage, finally exiting the body through the urethra.

**Structures of the Kidney**

**General structure of the kidney:**

I. **Renal cortex**
   A. Renal corpuscles
   B. Proximal convoluted tubules
   C. Distal convoluted tubules
   D. Cortical collecting tubules

II. **Renal medulla (renal pyramids)**
   A. Outer medulla
   B. Inner medulla
   C. Renal papillae

III. **Renal hilum**
   A. Minor calyx
   B. Major calyx
   C. Renal pelvis

**Functional and histological unit of the kidney:**

I. **Nephron**
   A. Renal corpuscle
   B. Proximal convoluted tubule
   C. Loop of Henle
      1. Descending limb
         a. Thick descending limb (proximal straight tubule)
         b. Thin descending limb (descending thin segment)
      2. Ascending limb
         a. Thin ascending limb (ascending thin segment)
         b. Thick ascending limb (distal straight tubule)
   D. Distal convoluted tubules

II. **Collecting system**
   A. Cortical collecting tubule
   B. Collecting ducts
   C. Papillary ducts
The kidney can be divided into three regions: the renal cortex, the renal medulla, and the hilum. The renal cortex is composed of renal corpuscles, proximal and distal convoluted tubules, cortical collecting tubules, and the blood vessels supplying the renal cortex. The renal medulla is made up of renal pyramids. The renal pyramids can be divided into three zones: the outer medulla, the inner medulla, and the renal papillae. The renal medulla is composed of several types of tubules oriented parallel to one another: the descending limb of the loop of Henle (thin descending and thin descending limbs), the ascending limb of the loop of Henle (thin ascending and thick ascending limbs), the cortical collecting tubules, the collecting ducts, and the papillary ducts (see Fig. 12-8B). The papillary ducts drain urine into the minor calices and then to the major calices; the major calices merge into the renal pelvis, which drains urine into the renal ureter. The blood vessels supplying the kidneys include the renal artery and vein, branches of the renal artery and vein (segmental arteries and veins), interlobar arteries and veins, arcuate arteries and veins, interlobular arteries and veins, and afferent and efferent arteries. The microvasculature consists of the glomeruli of the renal corpuscle, the peritubular capillaries, and the vasa recta.

### Vascular Supply of the Kidney

![Diagram of renal vasculature](Image)

- **Renal artery**
  - Branches of renal arteries (segmental arteries)
  - Interlobar arteries
  - Arcuate arteries

- **Renal vein**
  - Branches of renal veins (segmental veins)
  - Interlobar veins
  - Arcuate veins

- **Glomerulus**
  - Afferent arterioles
  - Interlobular arteries
  - Interlobular veins
  - Peritubular capillary network to venules
  - Efferent arterioles
  - Vasa recta

- **Renal corpuscle**
- **Renal cortex**
- **Renal medulla and hilum**
Figure 12-3. Orientation of detailed urinary system illustrations.

Structures of the Urinary System with Figure Numbers

**Kidney**
- Renal cortex and medulla
  - Figure 12-4A
  - Figure 12-4B
  - Figure 12-4C
- Renal corpuscles
  - Figure 12-5A
  - Figure 12-5B
- Glomerulus and filtration barrier
  - Figure 12-6A
  - Figure 12-6B
  - Figure 12-7
- Medullary ray and urinary tubules
  - Figure 12-8A
  - Figure 12-8B
- Proximal tubules
  - Figure 12-9A
  - Figure 12-9B
- Distal tubules
  - Figure 12-10A
  - Figure 12-10B

**Medullary tubules**
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- Figure 12-11B
- Figure 12-11C
- Figure 12-11D
- Figure 12-12A

**Ureter**
- Figure 12-13A
- Figure 12-13B
- Figure 12-13C

**Urinary bladder**
- Figure 12-14A
- Figure 12-14B
- Figure 12-14C
- Figure 12-15A
- Figure 12-15B

**Male and female urethrae**
- Figure 12-16A
- Figure 12-16B
- Figure 12-16C
Kidneys

This section shows the renal cortex and the medulla. The dashed white line indicates the junction between the cortex and the medulla. The difference in appearance between the cortex and the medulla is due to the arrangement of the uninniferous tubules (nephrons and collecting ducts). The renal cortex is stained darker than the renal medulla. There are numerous renal corpuscles and various convoluted tubules in the cortex region. Both the cortex and the medulla have a rich blood supply. The arcuate vessels (arteries and veins) are visible at the border of the corticomedullary junction. The interlobular vessels (arteries and veins) arise from arcuate vessels and course upward (arteries) or downward (veins) in the renal cortex. The renal medulla is composed of 10 to 18 renal pyramids. Each pyramid contains numerous medullary tubules (loops of Henle, collecting ducts, and papillary ducts). Each papillary duct opens at the surface of the renal papilla (called the area cribriforma) where it empties urine into the minor calyx. The renal medulla can be divided into inner and outer zones based on differences in the types of tubules residing in the two regions (Fig. 12-11A–C).

Diabetic nephropathy, a complication of both type 1 and type 2 diabetes mellitus, may result in chronic renal failure and is the leading cause of end-stage renal disease in the United States and other Western countries. Major histologic changes in the glomeruli in diabetic nephropathy include thickening of the glomerular basement membrane, diffuse glomerulosclerosis, and nodular glomerulosclerosis, also called Kimmelstiel-Wilson disease. As the disease progresses, edema (swelling), hypertension, foamy urine, fatigue, headache, and nausea and vomiting may occur. Tight control of blood glucose levels tends to delay the onset of development. Treatment includes dialysis and renal transplantation. Shown here is a renal glomerulus with nodular glomerulosclerosis, or Kimmelstiel-Wilson disease.
**Figure 12-5A. Renal corpuscle, renal cortex.**

The **renal corpuscle** is the site of blood filtration and initial production of urine. The main components of a renal corpuscle are a tuft of capillaries called the **glomerulus** and a surrounding sac, the **Bowman capsule**. The area of the renal corpuscle through which the arterioles pass into and out of the glomerulus is called the **vascular pole**. The surfaces of the capillaries of the glomerulus are covered by podocytes, which make up the **visceral layer** of the Bowman capsule. The outer wall of the renal corpuscle is a simple squamous epithelium called the **parietal layer** of the Bowman capsule. Fluid is filtered from the blood in glomerular capillaries into the space between the two layers, the **Bowman space**. Fluid exits through the **urinary pole** to enter the **proximal convoluted tubule**. There are phagocytic cells called **mesangial cells** (or **intraglomerular mesangial cells**) in the interstitial tissue between the glomerular capillaries. Similar cells are called **extraglomerular mesangial cells** when located at the vascular pole of the corpuscle. **Juxtaglomerular cells** in the walls of afferent arteriole are modified smooth muscle cells that secrete renin in order to regulate blood pressure. The **macula densa** of the distal tubule is located between the afferent and the efferent arteries.

**Figure 12-5B. Renal corpuscle, glomerulus and Bowman capsule. H&E, ×402; insets (left) ×921; insets (lower right) ×183**

A **glomerulus** housed within the **Bowman capsule** is shown here. The lighter space between these two structures is the **Bowman space**. The **upper left small inset** shows the **macula densa**, a row of columnar cells that are densely packed together. This is a special sensory structure of the distal tubule as it passes close to the afferent and efferent arterioles at the vascular pole (Fig. 12-5A). The macula densa plays a role in monitoring ionic content and volume of the filtrate. The **lower left small inset** shows the Bowman space between the glomerulus and the parietal layer of the Bowman capsule. The **lower right inset** shows the **urinary pole**.
The endothelial cells of the fenestrated glomerular capillaries coproduce and share a common basal lamina with the terminal cells and the glomerulus. In addition to the endothelial cells of the capillaries are two other cell types, intraglomerular mesangial podocytes, and the cells and structures associated with the glomerulus. The central part of a renal corpuscle is composed of a bed of capillaries, the glomerulus, renal cortex. H&E, ×310; insets ×841.

Each glomerulus is formed by a tuft of capillaries that is fed by the afferent arteriole and drains into the efferent arteriole. Pressure in the glomerulus due to resistance of the efferent artery provides the force for filtration into the Bowman space. The glomerular capillaries are fenestrated capillaries lined by endothelial cells with gaps (fenestrae) that lack the usual diaphragms (see Fig. 9-13A). These capillaries are covered by processes of podocytes. The endothelial cells, basal lamina, and podocytes combine to form a glomerular filtration barrier. Intraglomerular mesangial cells within the glomerulus provide structural support as well as phagocytosis of debris and large molecules, thereby preventing material from accumulating on the filtration barrier. They also have a contractile capability, which may function in regulating glomerular blood flow.

The central part of a renal corpuscle is composed of a bed of capillaries, the glomerulus, and the cells and structures associated with the glomerulus. In addition to the endothelial cells of the capillaries are two other cell types, podocytes and the intraglomerular mesangial cells. The endothelial cells of the fenestrated glomerular capillaries coproduce and share a common basal lamina with the terminal podocyte processes (pediciles, foot processes) that cover them. As blood flows through the capillaries, a filtrate of plasma is formed as it passes through several layers (fenestrations of the capillary, trilayered basal lamina, and filtration slits between podocytes) to enter the Bowman space (urinary space). Intraglomerular mesangial cells, lodged among the podocytes and endothelial cells, serve an incompletely understood maintenance function. The upper left inset shows the basement membrane of the glomerulus, pediciles (small podocyte processes), and cytoplasm of the endothelial cell, which together form a filtration barrier that selectively allows water, ions, and small molecules to pass through but not large molecules and blood cells. The lower left inset shows foot processes of the podocyte resting on the basement membrane of the glomerulus. The upper right color inset indicates the afferent and efferent arterioles.
This scanning electron microscopy (SEM) image shows that the surface of the glomerulus is entirely covered by podocytes and their processes. Each podocyte is composed of a cell body (with nucleus) and several branching processes. The small terminal branches that cover the capillaries are called foot processes or pedicles. The pedicles from two podocytes interdigitate with each other. The gaps between adjacent pedicles are referred to as filtration slits, which are bridged by filtration slit diaphragms. The inner core of the pedicles is supported by actin filaments. The inner core of the primary processes is supported mainly by microtubules and intermediate filaments. The podocytes and their unique arrangement are important components in establishing the glomerular filtration barrier.

Production and Drainage of Urine

[Diagram showing the pathways of glomerulus, Bowman space, collecting duct, renal corpuscle, renal pelvis, ureter, and urethra]
Each medullary ray is composed of proximal straight tubules, distal straight tubules, and collecting ducts. These tubes run parallel to each other within a medullary ray, which separates the glomeruli into groups. Although medullary rays are located in the renal cortex region, they are an extension of the renal medulla. The proximal straight tubules are lined by cuboidal cells with acidophilic cytoplasm and long microvilli. The distal straight tubules and collecting ducts are lined by cuboidal cells with clear cytoplasm. However, the collecting ducts have a larger lumen and more distinct cell-to-cell borders than do distal straight tubules. The proximal straight tubules convey filtrate from the proximal convoluted tubules into the thin segment tubules. The distal straight tubules convey the filtrate into the distal convoluted tubules, from which it drains into the collecting tubules and ducts (see below).

The kidney is composed of nephrons and a collecting system. Each nephron comprises a renal corpuscle, a proximal convoluted tubule, a loop of Henle, and a distal convoluted tubule. The U-shaped loop of Henle connects the proximal convoluted tubules to the distal convoluted tubules. The loop of Henle creates a high concentration of solutes in the interstitium of the medulla, which is essential in controlling the concentration of urine. The collecting system (yellow) includes cortical collecting tubules, collecting ducts, and papillary ducts. The collecting system (yellow) includes cortical collecting tubules, collecting ducts, and papillary ducts. Most glucose and amino acids and a large volume of water and salt are reabsorbed by the proximal convoluted and straight tubules before the filtrate enters the descending thin segment of the loop of Henle. The thin descending segment is highly permeable to water and less permeable to salt, so water passes from the lumen to the interstitium of the medulla and returns back to the blood circulation via the vasa recta. The thin ascending limb is impermeable to water but permeable to salt, and the thick ascending segment, which is also impermeable to water, actively pumps salt into the interstitium. As a result, the concentration of solutes increases to about four times the normal amount in the interstitium of the deep medulla. This hypertonic environment drives the movement of water from the lumens of the collecting ducts, therefore increasing the concentration of the urine. The permeability to water in the cortical collecting tubules and collecting ducts (and, therefore, the final concentration of urine) is controlled by the level of ADH released by pituitary glands. The reabsorption of various ions by the distal convoluted tubule is controlled by hormones, primarily aldosterone. The final urine is collected by papillary ducts and emptied at the area cribrosa into the minor calyx.
Both proximal convoluted and straight tubules have a similar structure and function. They are lined by large acidophilic cuboidal cells with brush borders formed by numerous long microvilli. The brush border extends into the lumen, which, in conjunction with postmortem changes, makes the lumen appear smaller and filled with acidophilic material (brush border and glycocalyx). The proximal tubules have a substantial reabsorption function. About 65% of the water and sodium and more than 90% of glucose, amino acids, and bicarbonate are reabsorbed by the proximal convoluted tubules. The proximal convoluted tubules are located in the cortical labyrinth and are connected to the renal corpuscle at the urinary pole. The proximal straight tubules are part of the loop of Henle (Fig. 12-8B).

This is a cross section of a proximal tubule. It is lined by cuboidal and low columnar cells with apical microvilli, which form a brush border, a feature that is associated with reabsorption function. The numerous mitochondria are more concentrated at the basolateral surface where they support the energy requirements of sodium pumps located in the expanded plasmalemma. The apical regions of the cells contain pinocytotic vesicles, which reflect the uptake of proteins that evaded the filtration barrier in the renal corpuscle and entered the filtrate. The inset shows long microvilli and pinocytotic vesicles in the apical surface of the cells.
The distal tubules are lined by small cuboidal cells with faintly eosinophilic or clear cytoplasm. The lateral boundaries between cells are not as distinguishable as those of the collecting duct. The distal convoluted and straight tubules are similar in structure. The distal straight tubule exits the medullary ray and approaches the vascular pole of the renal corpuscle of the same nephron to which the distal tubule belongs. As the distal tubule passes adjacent to the afferent and efferent arterioles, part of its wall becomes modified as a sensory structure, macula densa, which monitors ionic content and water volume of the filtrate (Fig. 12-5A,B). The macula densa is considered to mark the transition from the distal straight to the distal convoluted tubule. This figure shows the distal convoluted tubules in the renal cortex. Distal tubules function mainly to remove sodium and add potassium ions to the filtrate when stimulated by aldosterone, a hormone produced by the adrenal gland.

A cross section of a distal tubule, which is lined by cuboidal and columnar cells, is shown. In contrast to the extravagant brush border of cells lining the proximal tubule, these cells have just a few, short microvilli. These cells have basally located nuclei and tightly interdigitated lateral walls. In distal tubules, there are many mitochondria in the cytoplasm as there are in the proximal tubules. The upper left inset shows short and irregular microvilli bulging into the lumen and many mitochondria beneath them. The lower left inset shows a nucleus and basal enfolding (basal plasma membrane enfolding) of the cell. The basal enfolding is due to corrugation of the cell membrane in the basal region of the cell. This increases the surface area of the cell and is closely associated with mitochondria, which produce adenosine triphosphate for active transport of ions.
The renal medulla is composed of the loop of Henle, the collecting ducts, and the papillary ducts (ducts of Bellini). It can be divided into an outer zone and an inner zone. The thin segment tubules and distal straight tubules of the loop of Henle and collecting ducts of the outer zone are shown here. The inner zone contains only thin segments and collecting ducts, along with the vasa recta. Blood vessels (vasa recta) are found throughout the medulla.

Renal cell carcinoma, which arises from the renal tubular epithelium, is the most common renal cancer in adults. Risk factors for development of renal cell carcinoma include smoking, exposure to toxic substances, chronic renal failure, and acquired cystic disease of the kidney as well as genetic predisposition in various familial syndromes. Renal carcinoma presents clinically with hematuria, abdominal mass, or flank pain. Renal cell carcinoma tends to metastasize early, especially to the lungs and bones. On gross examination, renal cell carcinoma is well circumscribed, lobulated, and yellow, with areas of hemorrhage and necrosis. The most common renal cell carcinoma is the clear cell type, the cells of which may be arranged in cords, nests, or tubules. The cells are large and polygonal with clear or granular cytoplasm. Other types of renal cell carcinoma include papillary carcinoma, chromophobe carcinoma, and collecting duct carcinoma. Treatment is primarily surgical removal, with lesser roles for immunotherapy and chemotherapy.

**CLINICAL CORRELATION**

Renal cell carcinoma, which arises from the renal tubular epithelium, is the most common renal cancer in adults. Risk factors for development of renal cell carcinoma include smoking, exposure to toxic substances, chronic renal failure, and acquired cystic disease of the kidney as well as genetic predisposition in various familial syndromes. Renal carcinoma presents clinically with hematuria, abdominal mass, or flank pain. Renal cell carcinoma tends to metastasize early, especially to the lungs and bones. On gross examination, renal cell carcinoma is well circumscribed, lobulated, and yellow, with areas of hemorrhage and necrosis. The most common renal cell carcinoma is the clear cell type, the cells of which may be arranged in cords, nests, or tubules. The cells are large and polygonal with clear or granular cytoplasm. Other types of renal cell carcinoma include papillary carcinoma, chromophobe carcinoma, and collecting duct carcinoma. Treatment is primarily surgical removal, with lesser roles for immunotherapy and chemotherapy.
Renal oncocytoma is a benign and less common neoplasm of the kidney and originates from the epithelium of the proximal tubules. It is typically a solid, encapsulated mass with homogeneous enhancement in radiographic imaging. Gross examination shows a spherical mass with a mahogany cut surface and a tan, fleshy central scar. Histologically, the tumor cells are large with abundant eosinophilic cytoplasm due to the presence of numerous mitochondria. The cells are arranged in sheets or in a tubulocystic pattern. It is usually asymptomatic and detected as an incidental renal mass on imaging. Treatment options include surgical excision of the kidney (nephrectomy) or removal of a portion of the kidney (partial nephrectomy).

Hemodialysis is a common treatment for end-stage kidney disease. The dialyzer is a canister containing thousands of small fibers through which blood is passed. The fibers are made up of semipermeable membranes with small pores allowing wastes and extra fluids to pass from the blood into a solution. A cleansing fluid called dialysate is pumped around the fibers. Solute and extra fluids are cleared from the blood compartment by either diffusion or ultrafiltration, depending on the concentration gradient and pressure difference between the blood and the dialysate. The cleansed blood is returned via the circuit back to the body. Hemodialysis is usually given three times a week and can be done in a dialysis center or at home. The model illustrated here is commonly used in critical care units.

**SYNOPSIS 12-1  Clinical and Pathological Terms for the Urinary System**

- **Glomerulonephritis**: Refers to primary glomerular disease not related to infection of the kidneys themselves. The causes of glomerulonephritis are heterogeneous, such as viral or bacterial infection; drugs; and malignancy, resulting in many distinct clinical entities including focal and segmental glomerulonephritis and membranous nephropathy. The causes are often not identified (idiopathic glomerulonephritis).
- **Glomerulopathy**: Refers to secondary glomerular injury as a result of systemic diseases, such as diabetes mellitus and systemic lupus erythematosus.
- **Glomerulosclerosis**: Scarring or sclerosis of the renal glomeruli in diseases such as diabetic nephropathy and focal segmental glomerulosclerosis.
- **Dysuria**: Pain or burning upon urination, most often caused by a urinary tract infection affecting the bladder (cystitis) or urethra (urethritis).
- **Frequency**: The need to urinate more often than normal without an increase in total urine output; common causes include lower urinary tract infection and benign prostatic hyperplasia; other less common causes include tumors and extrinsic bladder compression.
- **Hematuria**: The presence of blood in the urine, causes of which include trauma, infection, tumors of the urinary system, kidney stones, and hyperplasia of the prostate gland; hematuria may be microscopic or “macroscopic,” meaning visible to the unaided eye.
- **Lithotripsy**: Extracorporeal shock wave lithotripsy is a procedure for treating kidney and ureteral stones using focused high-energy shock waves that pass through the body and break stones into small pieces that can then pass into the urine and be eliminated.
- **Urgency**: A strong urge to urinate, most often caused by a lower urinary tract infection or other causes of bladder irritation such as interstitial cystitis, which mainly affects females.
<table>
<thead>
<tr>
<th>Structure</th>
<th>Epithelial Lining of the Tubules</th>
<th>Characteristics of the Tubules</th>
<th>Main Locations</th>
<th>Main Functions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nephron</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal corpuscle</td>
<td>Simple squamous epithelium</td>
<td>Composed of glomerulus (blood vessels covered by podocytes) and Bowman capsule</td>
<td>Renal cortex</td>
<td>Filters blood and forms urine</td>
</tr>
<tr>
<td>Proximal convoluted tubule</td>
<td>Simple cuboidal epithelium with long microvilli (brush border)</td>
<td>Long and highly convoluted tubule; relatively small lumen and acidophilic cytoplasm; abundant basolateral plasma membrane enfoldings</td>
<td>Renal cortex</td>
<td>Drains fluid from the renal corpuscle to the loop of Henle; reabsorbs 70%–80% Na⁺ and Cl⁻ and water; also reabsorbs glucose, amino acids, and proteins and produces calcitriol (active form vitamin D)</td>
</tr>
<tr>
<td>Thick descending limb (proximal straight tubule)</td>
<td>Simple cuboidal epithelium with long microvilli (brush border)</td>
<td>Similar to proximal convoluted tubule but shorter and straight; small mitochondria; no basolateral plasma membrane enfoldings</td>
<td>Medullary ray and outer zone of the renal medulla</td>
<td>Absorptive function is similar to proximal convoluted tubule but less significant</td>
</tr>
<tr>
<td>Thin descending limb (descending thin segment)</td>
<td>Simple squamous epithelium</td>
<td>Thin, small tubule; epithelial cells may reveal basolateral enfoldings and small microvilli</td>
<td>Partial outer zone and most of the inner zone of the renal medulla</td>
<td>Highly permeable to water (loss of water from lumen to interstitium); less permeable to salt (keeps or may gain some Na⁺ and Cl⁻ in the lumen)</td>
</tr>
<tr>
<td>Thin ascending limb (ascending thin segment)</td>
<td>Simple squamous epithelium</td>
<td>Similar to descending thin segment; may have basolateral enfoldings and small microvilli</td>
<td>Inner zone of the renal medulla</td>
<td>Impermeable to water (retains water); highly permeable to salt (loss of Na⁺ and Cl⁻ from the lumen to the interstitium)</td>
</tr>
<tr>
<td>Thick ascending limb (distal straight tubule)</td>
<td>Simple cuboidal epithelium with short microvilli</td>
<td>Straight tubule; numerous mitochondria; less acidophilic cytoplasm; many basolateral plasma membrane enfoldings</td>
<td>Medullary ray and outer zone of the renal medulla</td>
<td>Impermeable to water (retains water); highly permeable to salt (loss of Na⁺ and Cl⁻ from the lumen to the interstitium)</td>
</tr>
<tr>
<td>Distal convoluted tubule</td>
<td>Simple cuboidal epithelium with short microvilli</td>
<td>Numerous mitochondria; basolateral plasma membrane enfoldings; less acidophilic cytoplasm; highly convoluted tubule</td>
<td>Renal cortex</td>
<td>Reabsorbs Na⁺ and secretes K⁺, if aldosterone stimulation is present; reabsorbs bicarbonate ions and secretes ammonium to adjust pH</td>
</tr>
<tr>
<td><strong>Collecting System</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Collecting tubule</td>
<td>Simple cuboidal epithelium with few microvilli</td>
<td>Straight tubule; much less acidophilic cytoplasm; more than one cell type</td>
<td>Renal cortex</td>
<td>Highly permeable to water; loss of water from the lumen to the interstitium when ADH is present</td>
</tr>
<tr>
<td>Collecting duct</td>
<td>Simple columnar</td>
<td>Large straight tubule; clear cytoplasm and distinct boundaries between cells; well-developed basal enfoldings</td>
<td>Medullary ray and renal medulla</td>
<td>Highly permeable to water; loss of water from the lumen to the interstitium when ADH is present</td>
</tr>
<tr>
<td>Papillary duct</td>
<td>Simple columnar epithelium</td>
<td>Short duct; links collecting duct to the minor calyx</td>
<td>Bottom tip of the pyramid of the medulla</td>
<td>Conducts urine</td>
</tr>
</tbody>
</table>
The ureter is a small muscular tubule lined with transitional epithelium. It carries urine from the renal pelvis to the urinary bladder. The wall of the ureter is composed of mucosa, muscularis, and adventitia. The mucosa consists of transitional epithelium and loose connective tissue (lamina propria). The middle layer, the muscularis, is relatively thick and contains inner longitudinal and outer circular smooth muscle layers. These two muscle layers are often difficult to distinguish. The wall of the ureter becomes thicker as it nears the bladder. As it approaches the urinary bladder, the ureter may also contain a third layer of smooth muscle. The adventitia layer is composed of connective tissues, nerve fibers, and blood vessels. It provides protection, blood supply, and nervous innervation to the ureter.

Transitional epithelium lines the urinary tract from the urinary calyces to the bladder. This type of epithelium can change shape as it is stretched to accommodate a change in volume. Cells on the surface layer appear round and dome shaped when the bladder is in a relaxed state. These cells become flattened and the layers of cells are reduced in number when the epithelium is stretched. The transitional epithelium lining the urinary tract is also called urothelium; it has tight junctions and thick cytoplasm (Figs. 12-14B and 12-15A,B). The lumen of the ureter appears as a white space here.

Nephrolithiasis (renal stones) is common in clinical practice. Symptoms range from vague abdominal pain to renal colic and hematuria when stones pass from the renal pelvis into the narrow portion of the ureter. Most renal stones are composed of the calcium salts, calcium oxalate, or calcium phosphate. Other less common forms include uric acid, magnesium ammonium phosphate (struvite), and cystine stones. Risk factors for the development of kidney stones include dietary factors, metabolic abnormalities, abnormal urine pH, family history of renal stones, frequent upper urinary tract infections, and low fluid intake. Struvite stones are associated with urinary tract infection with urea-splitting bacteria such as Proteus species. Treatment varies based upon the location and size of the stones and includes analgesics, shock wave lithotripsy, ureteroscopy, and surgery.
Urinary Bladder

The **urinary bladder** has three layers (mucosa, muscularis, and adventitia/serosa), similar to those in the ureter, but its wall is much thicker. Thick mucosa and muscularis layers make up the wall of the urinary bladder. The mucosa is composed of extensively folded transitional epithelium and lamina propria. This arrangement gives the bladder the distensibility needed to store urine. The muscularis consists of three smooth muscle layers: the inner longitudinal, middle circular, and outer longitudinal smooth muscle. These three smooth muscle layers are arranged in two different orientations to help the urinary bladder contract to empty urine efficiently. The outer layer of the bladder is mainly covered by adventitia (connective tissue); its superior (free) surface is covered by serosa, which is a layer of connective tissue with a lining of mesothelium.

**CLINICAL CORRELATION**

**Urothelial (Transitional) Carcinoma.** H&E, ×108

Urothelial carcinoma may arise in the urinary bladder, ureters, or renal pelvis and is the most common urinary bladder carcinoma. More than 90% of bladder cancers originate from the transitional epithelium (urothelium) in the urinary system. Urothelial carcinoma is most prevalent in older men but may occur at any age. Risk factors include cigarette smoking, exposure to arylamines and radiation, long-term use of cyclophosphamide, and infection by the parasite *Schistosoma haematobium*. Infection with *S. haematobium* is also a risk factor for the development of squamous cell carcinoma of the urinary bladder. Symptoms include painless gross hematuria, frequency, urgency, and dysuria. Urothelial carcinomas typically display a papillary morphology and are subdivided into low and high grade depending on cytologic features and the amount of architectural disorder present. Treatment includes transurethral resection, chemotherapy, immunotherapy, and radical cystectomy. Tumors have a high recurrence rate after local excision.
This figure shows the surface of transitional epithelium and the border between the cells of the top layer and the underlying layer. There are many flattened vesicles (membrane vesicles) in the cytoplasm of these cells. The vesicles are more numerous close to the apical region of the cytoplasm. These vesicles are formed from the surface membrane when the bladder is in a relaxed state. It is important to recall that the surface of the transitional epithelium of the bladder is highly convoluted when the bladder is empty (relaxed). This may create many “pseudovesicles”; most of the vesicles disappear when the surface of the epithelium is stretched and flattened in the distended state. The boxed area indicates Figure 12-15B at higher magnification.

A higher power view of the surface of the top layer cells in the transitional epithelium is shown. The junction complex indicates the border of neighboring cells. Tight junctions (zonula occludens) and desmosomes (macula adherens) can be observed here. The cells are filled with flattened vesicles and tonofilaments.
Urethra

The urethra provides for the passage of urine from the bladder to the outside of the body. The male urethra is significantly different from that of the female. It is a long tube (18–20 cm), which passes through the prostate and penis. The male urethra can be divided into three parts: prostatic, membranous, and penile (spongy) based on its anatomical location. This figure shows a cross section of the prostatic urethra connecting to two ejaculatory ducts, surrounded by the prostate. The prostatic urethra is a short segment (3–4 cm), usually lined by transitional epithelium. This portion of the urethra is surrounded by prostatic glands. The membranous urethra is narrow and short (1–2 cm) and passes through the deep perineal pouch. It is lined by pseudostratified columnar epithelium and surrounded by an inner longitudinal smooth muscle and an outer skeletal muscle of the external urethral sphincter. The penile (spongy) urethra is the longest segment (12–14 cm).

The penile urethra is also called the spongy urethra because it passes through the penis and is surrounded by erectile tissue (corpus spongiosum). The terms “cavernous” or “bulbous” urethra may also be used to refer to the penile urethra. The penile urethra is lined by pseudostratified columnar epithelium. Close to the tip of the penis, the lining becomes stratified squamous epithelium. This view shows the urethra in the corpus spongiosum, surrounded by spongy erectile tissue. Within the lining of pseudostratified columnar epithelium are clusters of mucus-secreting cells, the glands of Littré. The glands of Littré located in the epithelium are called intraepithelial glands of Littré; similar glands found in the submucosa are termed submucosal or extrapithelial glands of Littré. The secretions of the mucous cells of these glands protect the urethra from the effects of the urine. The upper left inset shows the urethra associated with the corpus spongiosum and corpora cavernosa in the penis.

The female urethra is 4 to 5 cm long, much shorter than the male urethra. It conveys urine from the urinary bladder, passing inferiorly through the pelvic floor and exiting anterior/superior to the vaginal opening in the vestibule. The female urethra is initially lined by pseudostratified columnar epithelium, which changes to stratified squamous epithelium as it approaches the external opening of the urethra. It has a thick lamina propria with many elastic fibers and venous plexi. The glands of Littré are also present in the female urethra. Its wall is surrounded by longitudinal smooth muscle. The middle portion of the wall of the urethra is surrounded by the outer layer of the external urethral sphincter, which has the same function as in the male urethra.