CHAPTER 1

Renal Anatomy

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Knowledge of the elaborate structure of the kidney provides insight into its functions and facilitates an understanding of renal diseases. One cannot recognize what is abnormal in the kidney if one does not know what is normal. The following sections consider the macroanatomy, functional units, architectural organization, microanatomy, and basic functions of the kidney. Unless otherwise stated, the illustrations will emphasize the human kidney. For additional information, readers are referred to several detailed reviews [1–4].

GROSS ANATOMY

Location, Size, and Shape

The retroperitoneum is divided into fascia-enclosed compartments, including the anterior pararenal, perirenal, and posterior pararenal spaces. The kidneys lie within the perirenal space, which contains abundant fat and is enclosed by the anterior and posterior layers of renal fascia, known as Gerota's fascia.The kidneys extend from the twelfth thoracic to the third lumbar vertebrae with the

right kidney slightly lower. Their position may be 2.5 cm lower in the erect than in the supine position and their craniocaudal movement during respiration may be up to 4 cm. The renal upper poles slant slightly toward the midline and the posterior. The hilar aspect of each kidney has an anteromedial orientation.

Each adult kidney weighs 125 to 170 g in men and 115 to 155 g in women. However, kidney weight correlates best with body surface area. Each kidney averages about 11 to 12 cm in length, 5 to 7.5 cm in width, and 2.5 to 3 cm in thickness. The left kidney is slightly larger than the right. As measured by magnetic resonance imaging (MRI), individual kidney volume averages 202 ± 36 ml for men and 154 ± 33 ml for women [5]. The estimated renal volume may vary with changes in blood pressure and intravascular volume. Known as bean-shaped organs, the posterior surface of each kidney is flatter whereas the anterior surface is more convex. The left kidney may have focal bulging of the lateral contour due to compression by the spleen. Located on the concave medial surface of each kidney is an aperture called the hilum through which pass branches of the renal artery and vein, lymphatics, nerves, and ureter. The hilum continues into a fat-filled cavity, the renal sinus, which contains the expanded portion of the ureter, the renal pelvis, and the calyces. A thin fibrous capsule surrounds the kidney. Within the renal sinus, the capsule does not enclose the columns of Bertin, allowing access between the cortical parenchyma and the sinus [6]. This continuity provides a route for tumor dissemination.

Blood Supply

After entering the hilar region, the main renal artery usually divides to form anterior and posterior divisions, which in turn, branch into segmental arteries that supply segmental regions of the parenchyma (Figure 1.1) [7]. The majority of the segmental arteries arise from the anterior division. No collateral circulation exists between the segmental arteries and their subsequent branches. Thus, they are considered end-arteries. Some so-called accessory arteries represent segmental arteries with an early origin from the main renal artery or aorta. Ligation of such a segmental artery in the belief that it is an accessory vessel will result in infarction of the corresponding parenchymal segment. Although the major intrarenal veins accompany the corresponding arteries, unlike the arteries, the veins form abundant anastomoses.

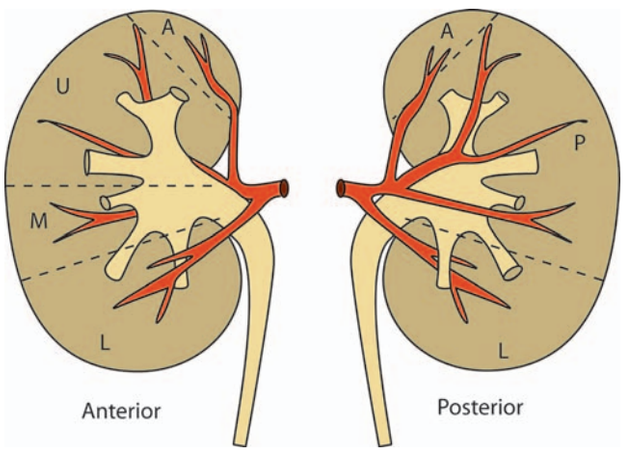

***FIGURE 1.1:** Diagram of arterial supply of the kidney. The anterior division of the renal artery divides into segmental branches that supply the upper (U), middle (M), and lower (L) segments of the anterior surface. The apical (A) segment is usually supplied by a branch from the anterior division. The posterior division of the renal artery branches into segmental vessels that supply the posterior (P) and lower (L) segments of the posterior surface. (Modified from Graves FT. The anatomy of the intrarenal arteries and its application to segmental resection of the kidney.* Br J Surg *1954;42:132–9).*

Form of Kidney

On the cut surface of a bisected kidney, the cortex (an outer region) and the medulla (an inner region) are revealed (Figure 1.2). The cortex has a more granular appearance due to the presence of glomeruli and convoluted tubules. The human kidney is a multipapillary type of mammalian kidney with the medulla containing striated conical structures called pyramids. The striated appearance reflects the parallel linear orientation of straight tubules (loops of Henle and collecting ducts). Each pyramid has a base situated at the corticomedullary junction and an apex extending into the renal sinus, forming a papilla. On the tip of each papilla, the area cribrosa, are twenty to seventy small openings that represent the distal ends of the collecting ducts (of Bellini). The cortex forms a 1 cm outer layer, covers the base of each pyramid, and extends down between pyramids forming the columns (septa) of Bertin. An enlarged column of Bertin may rarely be clinically mistaken for a renal tumor. Longitudinal light-colored striations, termed medullary rays, extend from the bases of the pyramids out into the cortex. Despite their name, the medullary rays are part of the cortex and formed by straight tubule segments (proximal straight tubules, thick ascending limbs, and collecting ducts).

A single pyramid with its surrounding cortex represents a renal lobe [8]. One lobe from a multipapillary kidney may be generally considered as equivalent to an entire unipapillary kidney, such as

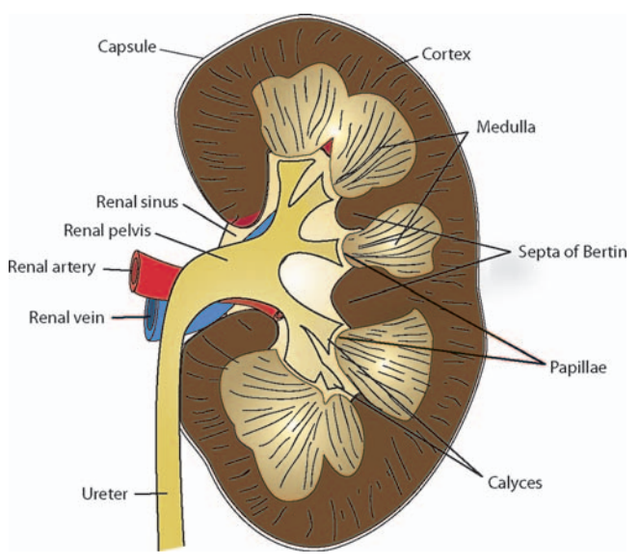

***FIGURE 1.2:** Diagram of a bisected kidney showing major macroanatomic features. (Modified from Clapp WL, Croker BP. Kidney In: Mills SE, ed.* Histology for Pathologists. *3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2007: 839–907.)*

those in a mouse or rat. The human kidney has an average of fourteen lobes, which are established by the twenty-eighth week of gestation. At this stage, deep surface clefts separate the lobes and fourteen calyces correspond with the same number of lobes. A process of lobar fusion during the embryologic development leads to coalescence of some pyramids and their papillae and remodeling of the corresponding calyces, reducing the number of papillae and calyces to between nine and eleven. Although the mature kidney eventually develops a smooth outer surface, a degree of persistent lobation is observed in some adult kidneys.

More lobar fusion occurs in the polar regions than in the midregion of the kidney, generating two types of pyramids (or papillae) (see Figure 1.2). Simple papillae occur mainly in the midregions, drain only one lobe, and have convex tips containing small, slit-like openings of the ducts of Bellini. Compound papillae are situated primarily in the polar regions, drain two or more adjacent fused lobes, and have flattened or concave tips with round, often gaping orifices of the ducts of Bellini. It is believed that the more open orifices of compound papillae are less capable of preventing intrarenal reflux, which may be associated with an increase in intrapelvic pressure and/or vesicoureteral reflux. This concept is supported by the observation that pyelonephritic scars associated with intrarenal reflux are found more commonly in the renal poles, where the compound papillae predominantly occur.

The renal pelvis is the saclike expansion of the upper ureter [9]. Outpouchings, the major calyces, extend from the pelvis and divide into the minor calyces, into which the papillae protrude. Elaborate extensions, termed fornices, extend from the minor calyces into the medulla. The smooth muscle within the walls of the calyces, pelvis, and ureter provides peristaltic contractions that facilitate urine movement toward the bladder.

NEPHRONS

The functional unit of the kidney is the nephron, which consists of the renal corpuscle (glomerulus and Bowman's capsule) connected to an elongated tubular component (proximal tubule, thin limbs, distal tubule), all of which are derived from the metanephric blastema. A transitional segment, the connecting tubule, joins the nephron components to a draining collecting duct, which is ureteric-bud derived. Although the collecting duct is not, strictly speaking, considered part of the nephron embryologically, practically the term nephron is used to include the nephron components and the collecting duct.

Nephron Number

Classically, it is stated there are 1 million nephrons per kidney. More recent stereological studies have revealed lower average nephron numbers, ranging from 600,000 to 800,000 per kidney. Moreover, such studies have shown that a large variation in nephron number per kidney exists among adults, from less than 500,000 to over 1,500,000 nephrons per kidney [10]. These studies have used glomerular number as a surrogate for nephron number. Nephron numbers are lower in individuals with a low birth weight, which may reflect intrauterine growth retardation or premature birth. A leading hypothesis is that a congenital deficit of nephrons associated with low birth weight predisposes individuals to acquired renal disease, including hypertension [11]. In fact, it has been reported that adults with a history of hypertension have fewer nephrons than matched normotensive controls [12].

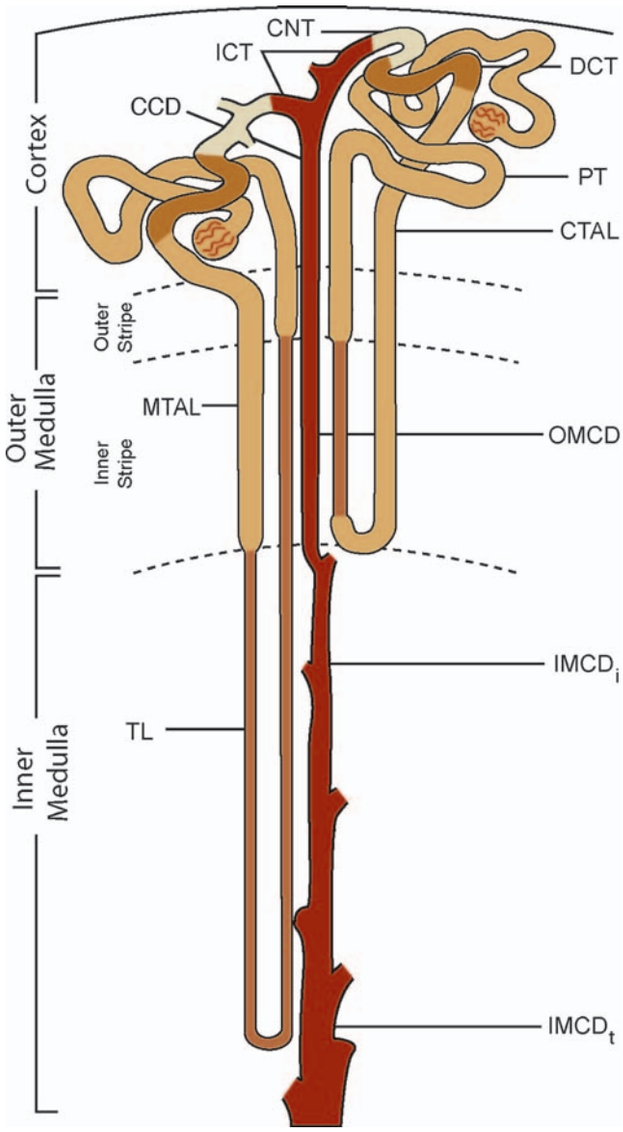

***FIGURE 1.3:** Diagram depicting the segments of the nephron and the regions (zones) of the kidney. PT, proximal tubule; TL, thin limb; MTAL, medullary thick ascending limb; CTAL, cortical thick ascending limb; DCT, distal convoluted tubule; CNT, connecting tubule; ICT, initial collecting tubule; CCD, cortical collecting duct; OMCD, outer medullary collecting duct; IMCD$_i$, initial inner medullary collecting duct; IMCD$_t$, terminal inner medullary collecting duct. (Modified from Madsen KM, Tisher CC. Structural-functional relationships along the distal nephron.* **Am J Physiol** *1986;250:F1–F15.)*

Nephron Types

Nephrons are also classified by the length of their loop of Henle (Figure 1.3). Short-looped nephrons arise from superficial and midcortical glomeruli and form their bend within the outer

medulla. Long-looped nephrons begin from juxtamedullary glomeruli and make their bend within the inner medulla. The short-looped nephrons are seven times more numerous than long-looped nephrons in the human kidney.

Nephrons are also classified as superficial, midcortical, or juxtamedullary, based on the position of their glomeruli in the cortex. Superficial nephrons have glomeruli located in the outer cortex, and they drain singly into a collecting duct. Juxtamedullary nephrons have glomeruli situated above the corticomedullary junction, and they empty into an arched arrangement of connecting segments called an arcade. Midcortical nephrons are located between the other two nephron types and most drain individually into a collecting duct.

ARCHITECTURE

The kidney has an intricate architecture that underlies its complex functions. The arrangement of nephron segments, vasculature, and interstitium provides for coordination (axial) of complex functions along the cortical–medullary axis, as well as integration (regional) of functions in a specific region of cortex or medulla.

Cortex

Cortical Labyrinth and Medullary Rays

In the cortex, the tubules are packed closely together with little interstitial space (Figure 1.4). Two architectural regions of the cortex – the cortical labyrinth and the medullary rays – can be distinguished (Figure 1.5) [13]. The cortical labyrinth is a continuous parenchymal zone that surrounds the regularly distributed medullary rays. The cortical labyrinth contains glomeruli, proximal and distal convoluted tubules, interlobular vessels and their branches, capillaries, and lymphatics. (Figure 1.6). The proximal convoluted tubules are the predominant component of the labyrinth.

The medullary rays contain the proximal and distal straight tubules and collecting ducts, all of which enter the medulla

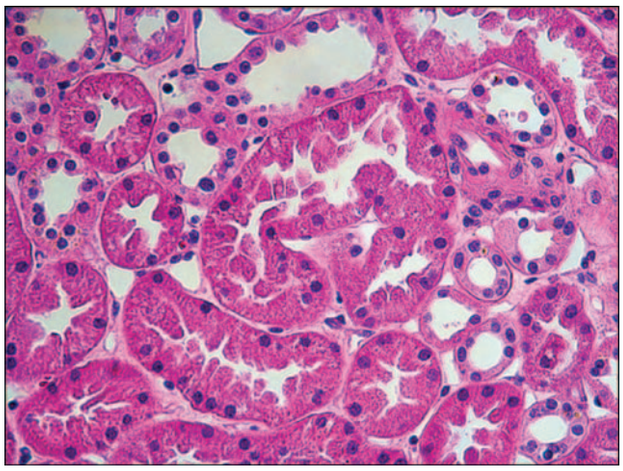

FIGURE 1.4: *Light micrograph of cortex showing compact back-to-back arrangement of tubules with minimal intervening interstitium. A few peritubular capillaries are evident. (H&E, × 400.)*

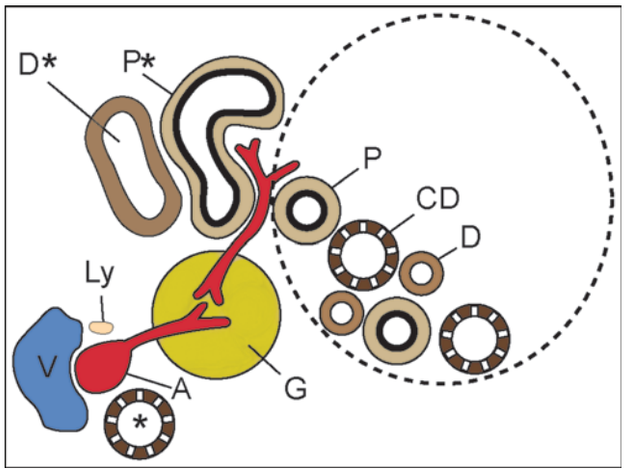

FIGURE 1.5: *Schematic drawing of architectural regions of the cortex. The cross section depicts a medullary ray (encircled by a dotted line), and the cortical labyrinth as a continuous zone (outside the dotted line). The medullary ray includes the proximal straight (P) and distal straight (D) tubules and collecting ducts (CD). The cortical labyrinth includes the glomeruli (G), proximal (P*) and distal (D*) convoluted tubules, arcades (*) of connecting tubules, arteries (A), veins (V), and lymphatics (Ly). (Modified from Kriz W, Kaissling B. Structural organization of the mammalian kidney. In: Seldin DW, Giebisch G, eds.* **The Kidney: Physiology and Pathophysiology.** *3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2000:587–654.)*

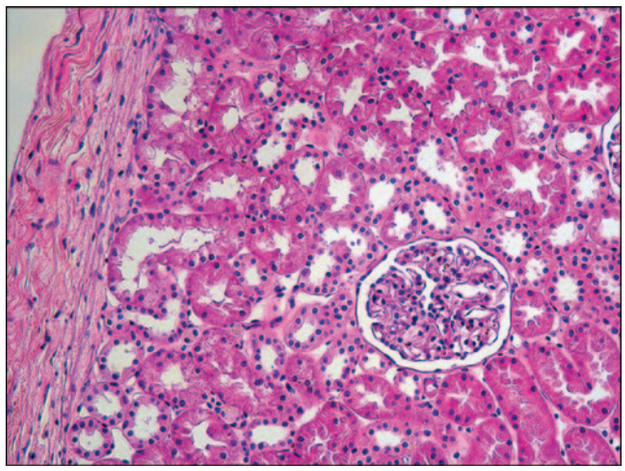

FIGURE 1.6: *Micrograph of outer cortex illustrating the cortical labyrinth. Proximal convoluted tubules are predominant. The renal capsule (left) is evident. (H&E, × 200.)*

(Figure 1.7). The distal straight tubules are the thick ascending limbs of Henle. Because of their perpendicular orientation to the corticomedullary junction, they are best identified in optimal longitudinal or cross-sections.

Renal Lobule

The renal cortex also can be partitioned into lobules. Most commonly, a renal lobule is considered as all the nephrons that

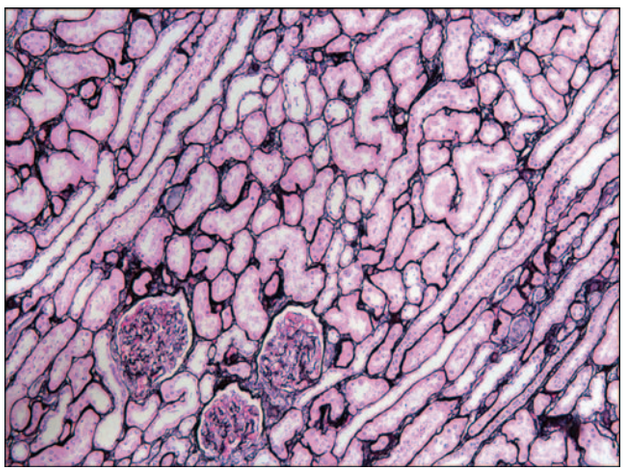

FIGURE 1.7: ***Longitudinal section of cortex illustrating two linear arrangements of tubules representing medullary rays. The cortical labyrinth containing glomeruli and convoluted tubules is between the two medullary rays. (Methenamine silver, × 100.)***

surround and drain into the collecting ducts of a central positioned medullary ray. Another version proposes that the lobule consists of all the nephrons supplied by a central positioned interlobular artery. Adjacent renal lobules lack separating connective tissue septa and are difficult to demarcate histologically. Moreover, because there is no apparent structural–functional significance, the concept of the renal lobule is not favored.

Medulla

The location of the nephron segments at various levels in the medulla account for the division of the medulla into an outer and inner medulla. The relative tissue volumes for the cortex, outer medulla, and inner medulla are 70, 27, and 3 percent, respectively.

Outer Medulla

The outer medulla is subdivided into an outer and an inner stripe (see Figure 1.3). The outer stripe is relatively thin. It contains the terminal portion of the proximal straight tubules, the thick ascending limbs of Henle, and the collecting ducts. The thin limbs of Henle are not present in the outer stripe. Compared to the outer stripe, the inner stripe of the outer medulla is thicker. It contains thin descending limbs, thick ascending limbs, and collecting ducts. Proximal straight tubules do not enter the inner stripe.

Inner Medulla

The inner medulla tapers to form the papilla. The thin descending and the thin ascending limbs of Henle, and the collecting ducts are situated in the inner medulla (see Figure 1.3). Thick ascending limbs are absent in the inner medulla.

Algorithm for Architecture

Knowledge of the above architectural features allows one to determine the specific region or zone in sections of a kidney biopsy (Figure 1.8). The presence of glomeruli confirms the presence of cortex and more specifically, the cortical labyrinth. Proximal convoluted tubules are also a prominent marker of cortex and its labyrinth. A distinctive feature of proximal tubules, both convoluted and straight portions, is their periodic acid-Schiff (PAS)-positive luminal brush border. Profiles of proximal convoluted tubules are larger with more irregular or coiled (convoluted) contours than those of proximal straight tubules. The absence of convoluted portions but the presence of straight segments of

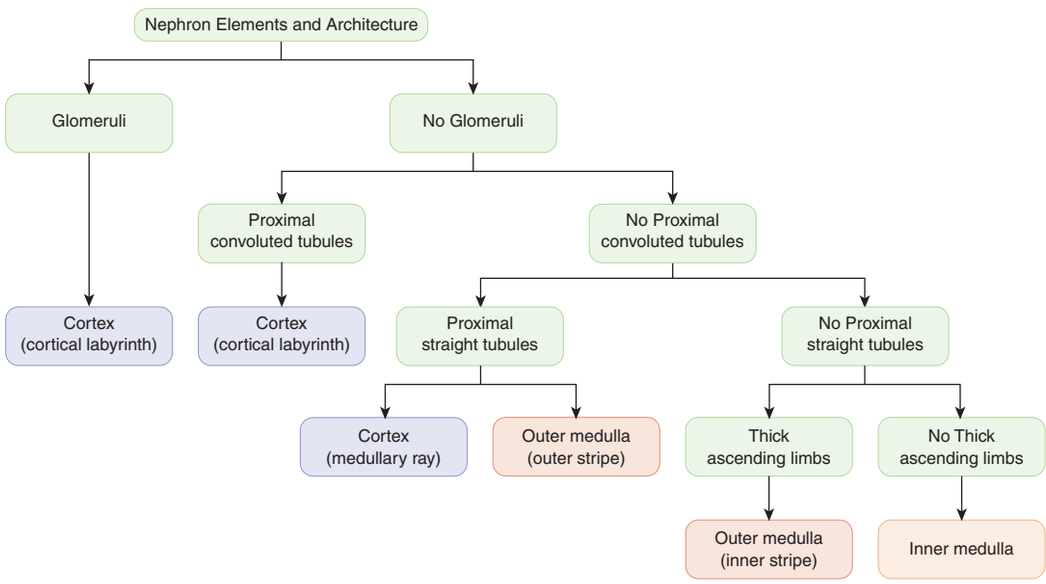

FIGURE 1.8: ***Algorithm for determination of the architectural region or particular zone of the kidney based on the presence and/or absence of specific nephron components or segments.***

proximal tubules characterizes both the medullary rays of cortex and the outer stripe of the outer medulla. Although these two adjacent regions, cortex and outer stripe of outer medulla, can usually be differentiated by other tissue elements in the same section, it may be difficult near their transition. Proximal straight tubules are absent in both the inner stripe of the outer medulla and the inner medulla. However, the two regions can be distinguished by the presence of thick ascending limbs in the inner stripe of the outer medulla and their absence in the inner medulla. For example, a biopsy showing no glomeruli and no tubules with a brush border likely represents the medulla, and the presence of thick ascending limbs likely indicates the inner stripe of the outer medulla. Not uncommonly, different regions or zones are observed in a single renal biopsy.

PARENCHYMA

Knowledge of the four main components of the renal parenchyma – the vasculature, glomeruli, tubules, and interstitium – facilitates the morphologic evaluation of the kidney and an understanding of its diseases. Normal morphologic aspects and structural–functional relationships of these components are considered in the following sections. A standard nomenclature for these components exists [14].

Vasculature

Macrovasculature

The segmental arteries, branching from the anterior and posterior divisions of the main renal artery, divide to form the interlobar arteries. The interlobar arteries penetrate the parenchyma between the columns of Bertin and the pyramids. At the corticomedullary junction, the interlobar arteries give rise to the arcuate arteries, which curve along the base of the pyramids parallel to the kidney surface. From the arcuate arteries, the interlobular arteries arise and ascend within the cortical labyrinth between medullary rays. Similar to vessels elsewhere in the body, the arteries have three layers: an inner endothelial cell-lined intima, a media consisting of smooth muscle cells, and an outer collagenous adventitia. The media is separated from the intima by an internal elastic lamina. Some larger arteries have a thin external elastic lamina between the media and the adventitia. In all blood vessels, immunohistochemical studies for Factor VIII-related antigen, CD34 and CD31 stain endothelium, whereas the smooth muscle media stains with smooth muscle actin and vimentin antibodies.

Microvasculature

(Cortex). The regulation of hemodynamics in the kidney occurs, in large part, because of its intricate microvasculature (Figure 1.9) [15]. Arterioles have three layers, albeit thinner than arteries, but generally lack the internal and external elastic lamina. Arteries and arterioles have a nonfenestrated or continuous endothelium. The afferent arterioles branch off the interlobular arteries and supply the glomeruli. The angle of origin of the afferent arterioles from the interlobular arteries varies according to the area of the cortex. Afferent arterioles

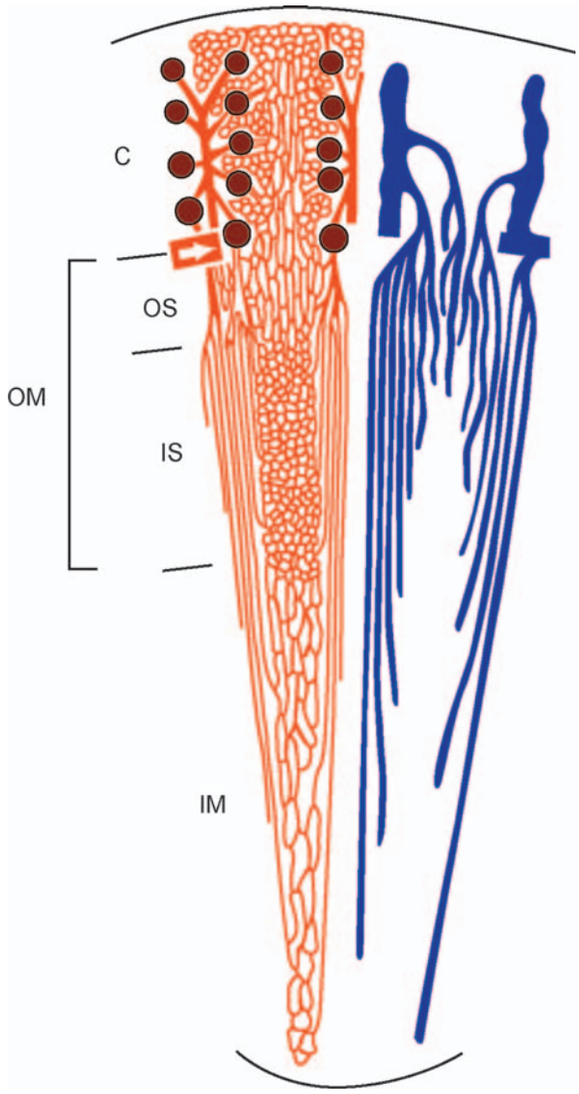

FIGURE 1.9: *Schematic of renal microvasculature. The arterial vessels, glomeruli, and capillaries are represented on the left side (red). An arcuate artery gives rise to an interlobular artery which ascends in the cortex and branches to form afferent arterioles which supply the glomeruli. The efferent arterioles of the superficial and midcortical glomeruli divide to form the peritubular capillaries of the cortical labyrinth and the medullary rays. The efferent arterioles of the juxtamedullary glomeruli descend into the medulla and form the descending vasa recta (DVR) which supply the adjacent capillary plexuses. The DVR traverse the inner stripe of the outer medulla within vascular bundles (shown as straight vessels). Note the prominent capillary network in the inner stripe of the outer medulla. The right side (blue) depicts the venous system. It may be superimposed on the arterial system (left). The ascending vasa recta (AVR) drain the medulla and empty into the interlobular and arcuate veins, which drain the cortex. The AVR from the inner medulla travel within the vascular bundles, whereas most AVR from the inner stripe travel between the bundles. (Modified from Kriz W, Kaissling B. Structural organization of the mammalian kidney. In: Seldin DW, Giebisch G, eds.* **The Kidney: Physiology and Pathophysiology.** *3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2000: 587–654.)*

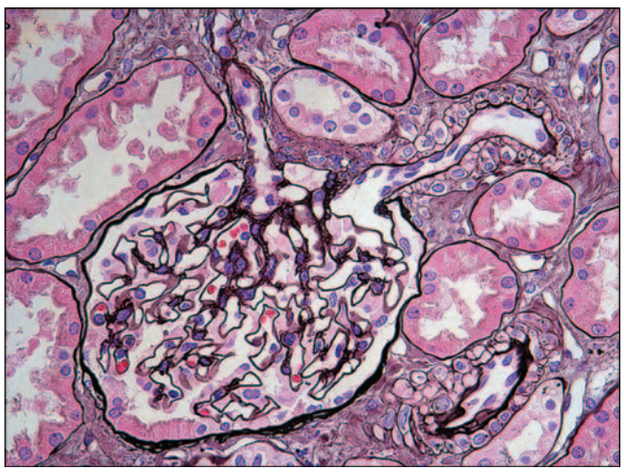

FIGURE 1.10: *Light micrograph of glomerulus depicting both afferent and efferent arterioles. The afferent arteriole (right) has a more prominent media of smooth muscle cells. (Methenamine silver, × 400.)*

supplying the superficial glomeruli arise at an acute angle; afferent arterioles to midcortical glomeruli travel transversely for the most part and those to juxtamedullary glomeruli tend to originate at a recurrent angle. The efferent arterioles drain the glomeruli, may loop partially around the glomerular tuft, and branch to form complex capillary networks that supply the cortical and medullary parenchyma. Thus, the blood supply to the renal parenchyma is postglomerular. At the vascular pole of the glomerulus, the afferent arteriole enters and the efferent arteriole exits (Figure 1.10) [16]. The afferent arteriole has a larger diameter than the efferent arteriole because of a larger lumen and thicker media. Within the media, the nuclei of smooth muscle cells are larger in the afferent arteriole. In contrast to the afferent arteriole, the efferent arteriole has a more continuous intraglomerular segment. At the glomerular tuft-exit, endothelial cells may bulge into the lumen of the efferent arteriole, reducing its diameter. These differences may be difficult to recognize since both the afferent and efferent arterioles of a glomerulus are seen only in fortuitous planes of section. However, the afferent arteriole may be identified by an observed connection to an interlobular artery or the presence of hyalinosis, which only involves the afferent arteriole in nondiabetics. The afferent arteriole can also be distinguished by the presence of intramural granular cells containing renin. In addition, the myosin heavy chain B isoform (MHC-B) is expressed in afferent, but not efferent arterioles [17]. The afferent and efferent arterioles regulate glomerular inflow and outflow resistance, respectively. For example, an increased afferent arteriolar tone prevents an elevated perfusion pressure being transmitted to the glomerular capillaries, preserving the glomerular filtration rate (GFR). In contrast, an increased efferent arteriolar tone maintains the GFR when the perfusion pressure is reduced.

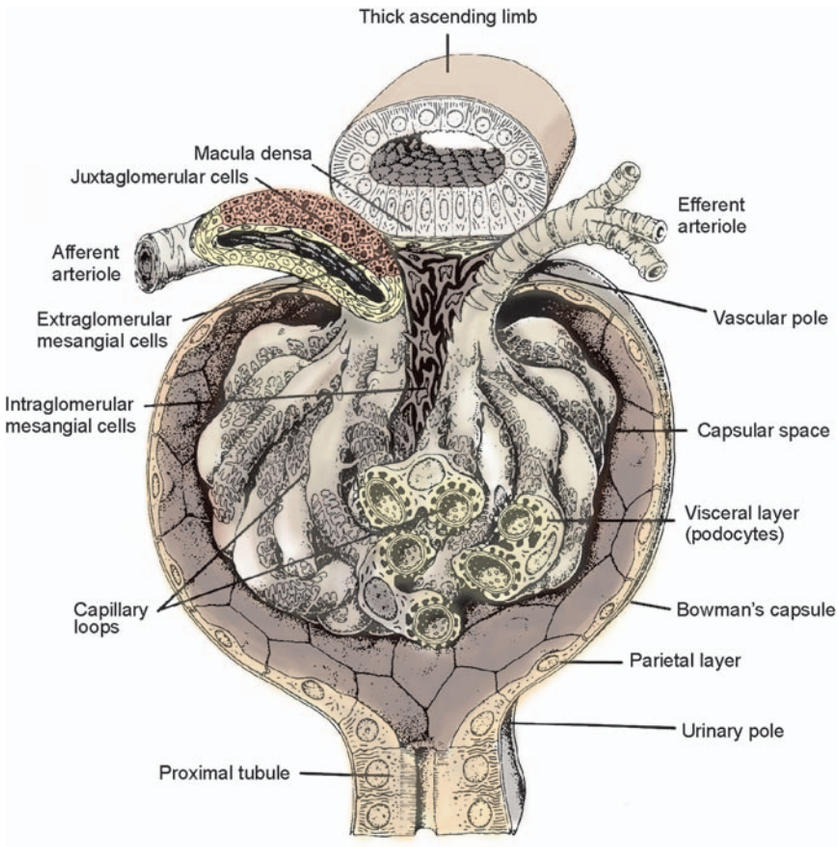

FIGURE 1.11: *Three-dimensional schematic drawing of the glomerulus. (Modified from Geneser F. Textbook of Histology. Philadelphia: Lea & Febiger; 1986.)*

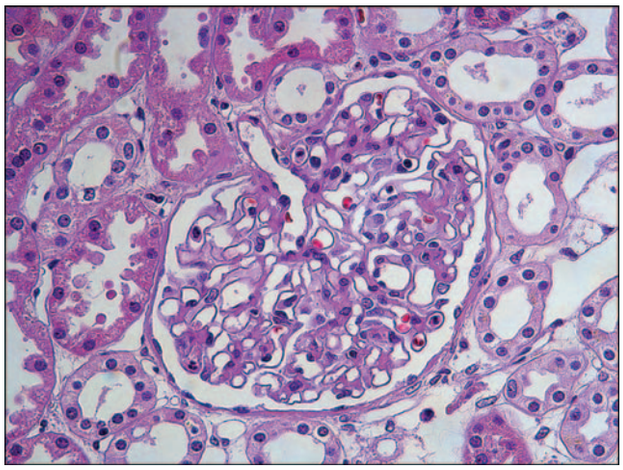

FIGURE 1.12: Light micrograph of a glomerulus exhibiting a round configuration and filling Bowman's space. It shows normal cellularity and patent capillary lumens. (H&E, × 400).

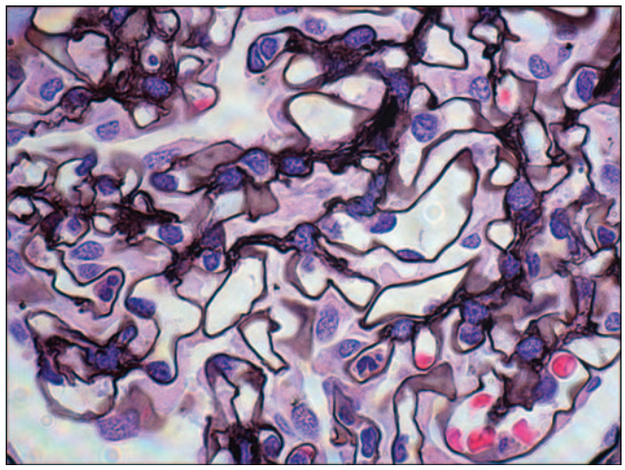

FIGURE 1.14: Higher magnification light micrograph demonstrating thin glomerular basement membranes and narrow profiles of mesangial matrix. The glomerular cell types can be distinguished. (Methenamine silver, × 1,000).

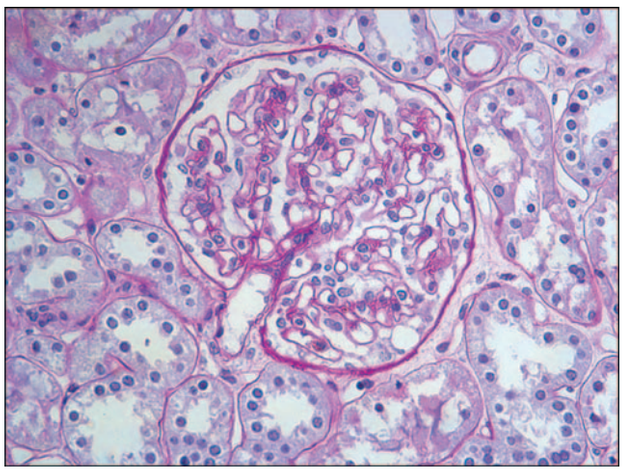

FIGURE 1.13: Glomerulus showing delicate capillary loops and inconspicuous mesangium. (PAS, × 400.)

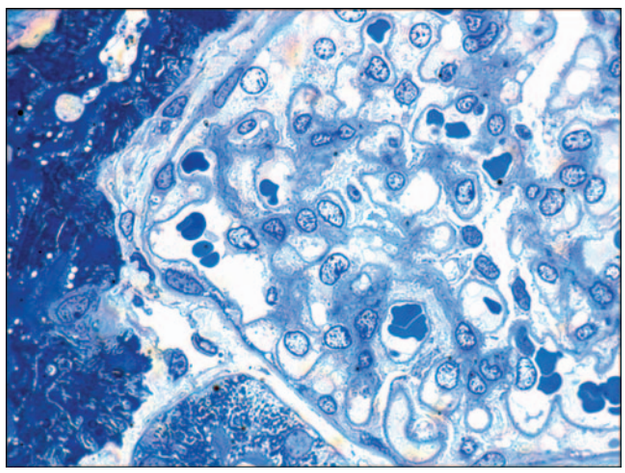

FIGURE 1.15: Light micrograph of a glomerulus illustrating the intrinsic cell types: endothelial cells, mesangial cells, podocytes, and parietal epithelial cells. (1- um toluidine blue-stained Epon section, × 1,000.)

The efferent arterioles give rise to a complex postglomerular microcirculation (see Figure 1.9). Although gradations exist, three types of efferent arterioles may be distinguished. The superficial efferent arterioles branch into capillary networks that supply convoluted tubules of the outer cortical labyrinth. Efferent arterioles of midcortical glomeruli generate capillaries that supply the adjacent cortical labyrinths as well as the medullary rays in that region. Efferent arterioles from juxtamedullary glomeruli descend and supply the medulla. When compared to the efferent arterioles of superficial and midcortical glomeruli, those from juxtamedullary glomeruli have a larger diameter with thicker smooth muscle layers on cross section.

Of the total renal blood flow, 85 to 90 percent goes to the cortex. Convoluted tubules in the superficial cortex are perfused by capillaries arising from the efferent arterioles of their parent glomeruli. However, in the midcortex and inner cortex are perfused by capillaries from efferent arterioles of other glomeruli. In other words, the peritubular capillaries supplying a given nephron in the mid- or inner cortex are derived from several different efferent arterioles. As a result of glomerular filtration, the blood leaving the glomerulus in the efferent arterioles and entering the peritubular capillaries has a relatively high protein concentration, and thus an elevated oncotic pressure. Also, the flow of blood through two resistance vessels in series (afferent and efferent arterioles) leads to a decreased hydrostatic pressure within the peritubular capillaries. These physiologic factors favor the uptake of fluid reabsorbed from the proximal tubules into the peritubular capillaries.

(Medulla). The efferent arterioles of juxtamedullary glomeruli are the major source of blood supply to the medulla, which

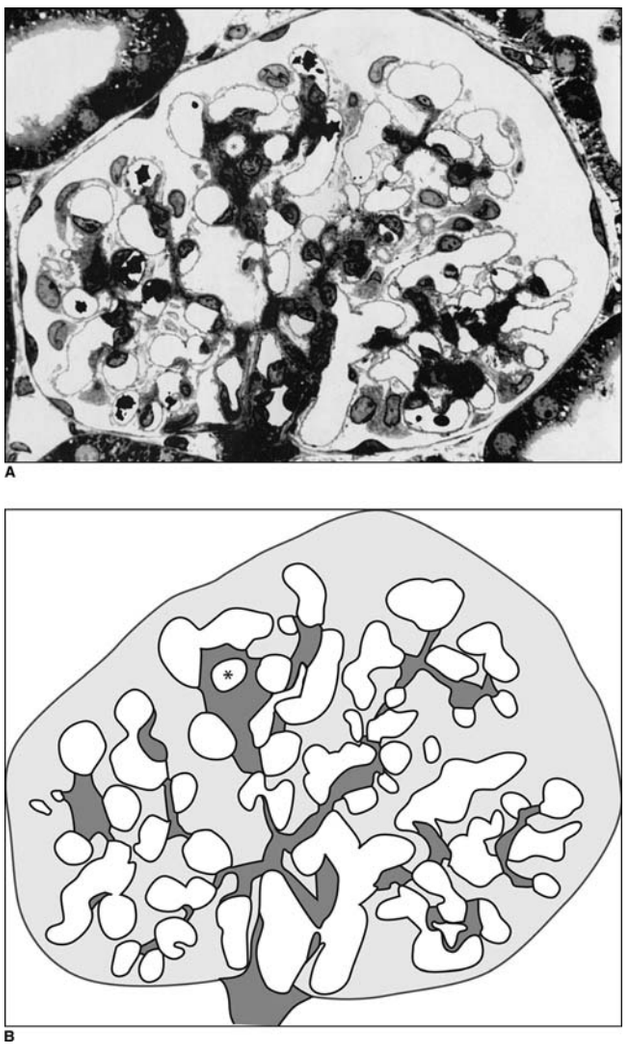

FIGURE 1.16: *Mesangial structure. A. Light micrograph of a rat glomerulus in a 0.5 um Epon section through the vascular pole. In the periphery, a "mesangial loop" (*), representing the complete enclosure of a capillary by mesangium, is observed. (× 960) B. Tracing of the glomerulus in A. showing the outline of the GBM around the capillaries and the mesangium (gray). Although on sections the mesangium may appear as islets separate from the main mesangial stalk at the vascular pole, three-dimensional studies have revealed there is continuity of the entire mesangium within a glomerulus. (× 430) (From Inkyo-Hayasaka K, Sakai T, Kobayashi N, et al. Three-dimensional analysis of the whole mesangium in the rat.* **Kidney Int** *1996;50:672–83.)*

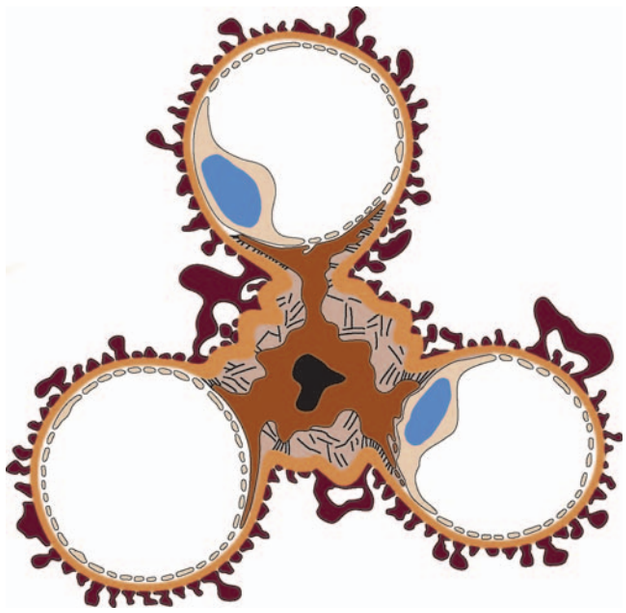

FIGURE 1.17: *Schematic illustrating the relationship between the glomerular capillaries, mesangium and GBM. The surrounding podocyte foot processes (dark brown) and the lining endothelium (light cytoplasm with blue nuclei) are illustrated. The mesangium consists of the central mesangial cell (medium brown cytoplasm and black nucleus) surrounded by the mesangial matrix (gray fibrillar texture). Note that the GBM encloses the mesangium and its attached capillaries. Two areas of the mesangium are shown: the juxtacapillary region adjacent to the capillary endothelium and the central axial region surrounded by the perimesangial GBM. Cytoplasmic processes of mesangial cells are connected to the GBM, directly or indirectly by microfibrils in the mesangial matrix. (Modified from Kriz W, Elger M, Lemley L, Sakai T. Structure of the glomerular mesangium: a biomechanical interpretation.* **Kidney Int. Suppl.** *1990;30:S2–S9.)*

receives 10 to 15 percent of the total renal blood flow (see Figure 1.9). They extend downward and some early branches form a capillary network supplying tubules in the outer stripe of the outer medulla. However, most of the branches continue as the descending vasa recta organized into vascular bundles as they descend through the inner stripe of the outer medulla. At intervals, branches exit the bundles to form capillary plexuses supplying tubules between the bundles in the inner stripe. Descending vasa recta enter the inner medulla and their branches form capillary networks, which converge to form the ascending vasa recta. Draining the inner medulla at various levels, the ascending vasa recta traverse the inner stripe within the vascular bundles. Some ascending venous recta, draining the inner stripe, ascend between the vascular bundles to the outer stripe. All the ascending vasa recta traverse the outer stripe as individual vessels, and finally empty into the interlobular or arcuate veins.

The decending vasa recta (DVR) display a continuous endothelium and are surrounded by pericytes that are immunoreactive for smooth muscle actin. The aquaporin-1 (AQP1) water channel and the facilitative urea transporter, UT-B, are expressed in the DVR. In contrast, the ascending vasa recta (AVR) have a highly fenestrated endothelium that is immunoreactive for the fenestrae protein PV-1. The counterflow arrangement of the DVR and AVR provides a countercurrent exchange of solutes and water in the medulla [18]. Solutes diffuse from the medulla into the DVR and as blood returns in the AVR, solutes diffuse into the interstitium. Water loss from the DVR, via AQP1, is shunted to the AVR. As a result, effective blood flow through the medulla is lowered and medullary hypertonicity is preserved, factors that facilitate urinary concentration.

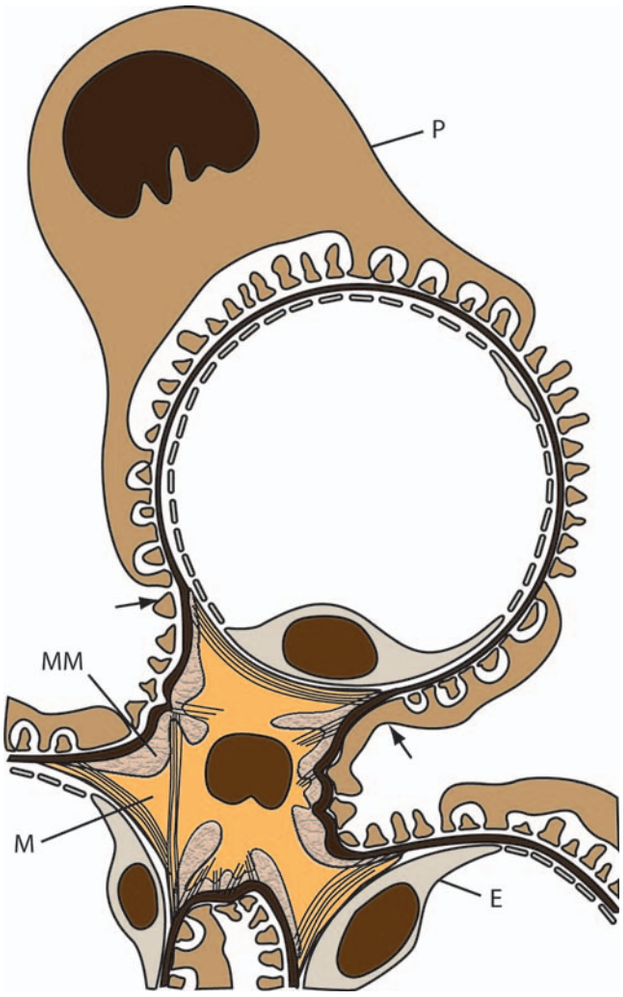

FIGURE 1.18: *Drawing of a glomerular capillary and the mesangium. In the center, a mesangial cell (M, yellow cytoplasm), is surrounded by mesangial matrix (MM, tan). Mesangial cell processes, containing microfilament bundles, extend to the GBM (black). The mesangial matrix is rich in microfibrils, which participate in connecting the mesangial cell processes to the GBM. The GBM surrounds the peripheral portion of the capillary, and at the "mesangial angles" (arrows), begins to cover the mesangium. The capillary endothelium (E) is fenestrated. The podocyte (P) foot processes overlie the entire GBM. (Modified from Reilly Jr RF, Bulger RE, Kriz W. Structural-functional relationships in the kidney. In: Schrier EW, ed.* **Diseases of the Kidney & Urinary Tract.** *8th ed. Philadelphia: Lippincott Williams & Wilkins;2007:2–53.)*

Lymphatics

Two lymphatic networks exist in the kidney: a deeper cortical system and a less extensive capsular network. Lymphatics originate as small vessels around the interlobular arteries and empty into arcuate and interlobar lymphatics, which drain into larger lymph vessels at the renal hilus. Valves are present in the interlobar and hilar lymphatics. Lymphatics are sparse to absent in the medulla. The less prominent lymphatics within the renal capsule drain into subcapsular lymphatic channels that appear to communicate with the major lymphatics in the cortex.

The lymphatics are situated in the periarterial loose connective tissue but they are not prominent on routine histologic sections. Lymphatic vessels have a thin endothelial layer without an underlying basement membrane. The identification of lymphatics has been facilitated by the availability of markers of lymphatic endothelium including VEGFR-3, LYVE-1, Prox-1, and podoplanin. The lymphatics may serve as a route for the intrarenal distribution of hormones and inflammatory cells.

Nerves

The nerve supply to the kidney derives largely from the celiac plexus [19]. Nerve fibers, immunoreactive for neurofilament and S-100, accompany the arteries and arterioles in the cortex and outer medulla. There is prominent innervation of the juxtaglomerular apparatus. Nerve fibers escort the efferent arterioles and descending vasa recta until they lose their surrounding smooth muscle layer. Although the direct relationship of nerve terminals to tubules has been somewhat controversial, autoradiographic studies have provided evidence for the innervation of both proximal and distal convoluted tubules, and especially the thick ascending limb.

Glomerulus

General Features

The renal glomerulus (or corpuscle) is a tuft of interconnected capillaries, matrix, and specialized cells enclosed within Bowman's capsule (Figure 1.11). Rather than simply representing a cluster of capillaries, the glomerulus is one of the most intricate structures in the body. The capillaries are attached to a central supporting region termed the mesangium, which contains cells and surrounding matrix material. The capillaries are lined by a thin layer of endothelial cells contain an underlying basement membrane, and are covered by podocytes (epithelial cells) that form the visceral layer of Bowman's capsule. At the vascular pole where the afferent arteriole enters the glomerulus and the efferent arteriole exits, the visceral epithelium is continuous with the parietal epithelium lining Bowman's capsule. The glomerular tuft projects into Bowman's space, the cavity between the visceral and parietal epithelial layers. At the urinary pole, this space and the parietal epithelium continue into the lumen and epithelium of the proximal tubule. Thus, the glomerulus resembles a blind-pouched extension (Bowman's capsule) of the proximal tubule invaginated by a tuft of capillaries. Upon entering the tuft, the afferent arteriole divides into branches, which are arranged as lobules. Anastomoses exist between individual capillaries within a lobule as well as between lobules. This lobular arrangement is often inconspicuous in light microscopic sections. The efferent arteriole, formed by rejoined capillaries, is separated from the afferent arteriole only by the mesangium, and leaves the glomerulus at the vascular pole. In contrast to the afferent arteriole, the efferent arteriole has a more continuous intraglomerular segment.

The human glomerulus is round to oval with an average diameter of 200 μm. However, a significant degree of variation in