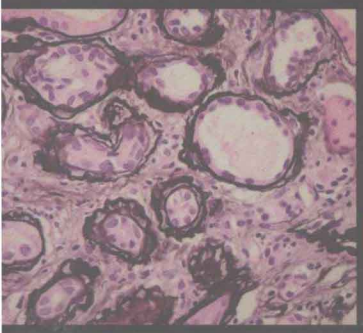
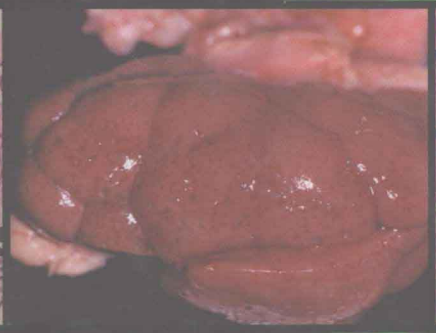
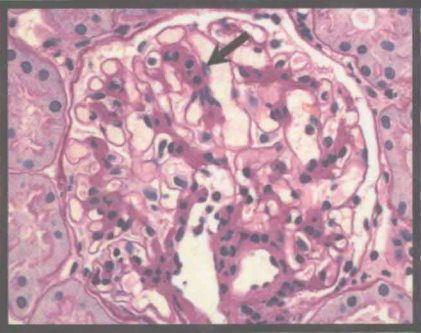
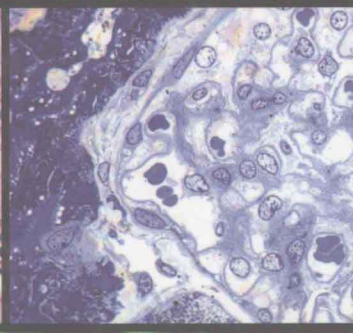
SILVA'S

Diagnostic Renal Pathology

Edited by

Xin J. Zhou • Zoltan Laszik • Tibor Nadasdy
Vivette D. D'Agati • Fred G. Silva

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Xin J. Zhou

University of Texas Southwestern Medical Center

Zoltan Laszik

University of California at San Francisco School of Medicine

Tibor Nadasdy

Ohio State University Medical Center

Vivette D. D'Agati

Columbia University, College of Physicians and Surgeons

Fred G. Silva

United States and Canadian Academy of Pathology

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SILVA'S DIAGNOSTIC RENAL PATHOLOGY

THE KIDNEYS perform many vital functions, but their primary role as a filter of plasma, receiving approximately 25% of the cardiac output, makes them extremely susceptible to disease. These diseases often can only be diagnosed by renal biopsy, a complicated diagnostic procedure requiring that the pathologist integrate the findings of light microscopy, immunofluorescence, and electron microscopy. Because of the expertise required to practice renal pathology, many academic centers maintain a separately designated, specialized renal pathology laboratory for interpretation of medical renal diseases. This book covers all approaches and technical methods used by renal pathologists to diagnose a wide range of kidney diseases. Unlike most textbooks in the field, this book's level of coverage is situated midway between encyclopedic and superficial, with the needs of the practicing ("signing-out") pathologist in mind. While focusing on medical diseases of the kidney, the book also covers a full spectrum of renal tumors (both pediatric and adult). Its numerous diagnostic algorithms provide a simplified road map that directs the reader to the major patterns of interest. The text is illustrated with more than 1,000 photomicrographs and diagrams. The accompanying CD-ROM includes a supplemental set of images.

Xin J. Zhou, MD, is Drs. George & Anne Race Distinguished Professor of Pathology, director of renal pathology, and professor of internal medicine at the University of Texas Southwestern Medical Center, Dallas. Dr. Zhou has published extensively in the areas of renal diseases and has served on the editorial boards of several prestigious renal journals. Dr. Zhou is past president of the Chinese American Society of Nephrology.

Zoltan Laszik, MD, is associate professor of clinical pathology at the University of California at San Francisco School of Medicine. Dr. Laszik, a renowned renal pathologist, has published nearly 100 original papers and book chapters.

Tibor Nadasdy, MD, is professor of pathology and director of renal pathology at Ohio State University School of Medicine, Columbus. Dr. Nadasdy, an experienced academic renal pathologist, has published numerous original papers and book chapters in the fields of renal pathology and renal transplantation.

Vivette D. D'Agati, MD, is professor of pathology and director of renal pathology at Columbia University, College of Physicians and Surgeons, in New York. Dr. D'Agati has published more than 300 original articles and book chapters and coedited several renal pathology texts. She serves on the editorial boards of the major nephrology journals and has directed the Columbia University Renal Biopsy Course for more than two decades. She is past president of the Renal Pathology Society.

Fred G. Silva, MD, is executive vice-president/secretary-treasurer of the United States and Canadian Academy of Pathology, Augusta, Georgia. Dr. Silva is adjunct professor of pathology at Emory University and the Medical College of Georgia. He is formerly the Lloyd Rader Professor and chair of the department of pathology at the University of Oklahoma Health Sciences Center. Dr. Silva, a preeminent expert in renal pathology, has published hundreds of articles on subjects spanning the entire spectrum of renal pathology and coedited several renal pathology books.

ZHOU

To my loving wife, Jian Wang, and our wonderful children, Jason and Jaclyn

LASZIK

To my beautiful wife, Erika, and our wonderful children, Nandi, Laura, and Aron

NADASDY

To my wife, Gyongyi, and my daughters, Krisztina and Orsolya

D'AGATI

To my devoted husband, Edward Imperatore, and my loving children,

Edward and Paul, without whose constant support and encouragement

my academic career would not be possible

SILVA

To my lovely wife, Jean, and wonderful daughter, Lindsay

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Contributors

MAHUL B. AMIN, MD
Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, Los Angeles, California

PEDRAM ARGANI, MD
Department of Pathology, Johns Hopkins University Medical Center, Baltimore, Maryland

STEVEN A. BIGLER, MD
Department of Pathology, University of Mississippi Medical Center, Jackson, Mississippi

WILLIAM L. CLAPP, MD
Department of Pathology, University of Florida College of Medicine, Gainesville, Florida

VIVETTE D. D'AGATI, MD
Department of Pathology, Columbia University, College of Physicians and Surgeons, New York, New York

LUKAS HARAGSIM, MD
Department of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma

RANDOLPH A. HENNIGAR, MD, PhD
Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta, Georgia

GUILLERMO A. HERRERA, MD
Nephrocor, Bostwick Laboratories, Tempe, Arizona

MICHAEL D. HUGHSON, MD
Department of Pathology, University of Mississippi Medical Center, Jackson, Mississippi

ZOLTAN G. LASZIK, MD, PhD
Department of Pathology, University of California at San Francisco School of Medicine, San Francisco, California

GLEN S. MARKOWITZ, MD
Department of Pathology, Columbia University, College of Physicians and Surgeons, New York, New York

SHANE M. MEEHAN, MD
Department of Pathology, University of Chicago, Chicago, Illinois

GYONGYI NADASDY, MD
Department of Pathology, Ohio State University Medical Center, Columbus, Ohio

TIBOR NADASDY, MD, PhD
Department of Pathology, Ohio State University Medical Center, Columbus, Ohio

SAMIH H. NASR, MD
Department of Pathology, Columbia University, College of Physicians and Surgeons, New York, New York

DINESH RAKHEJA, MD
Department of Pathology, University of Texas Southwestern Medical Center, Dallas, Texas

THOMAS E. ROGERS, MD
Department of Pathology, University of Texas Southwestern Medical Center, Dallas, Texas

ANJALI SATOSKAR, MD
Department of Pathology, Ohio State University Medical Center, Columbus, Ohio

FRED G. SILVA, MD
United States and Canadian Academy of Pathology, Augusta, Georgia

MICHAEL B. STOKES, MD
Department of Pathology, Columbia University, College of Physicians and Surgeons, New York, New York

SATISH K. TICKOO, MD
Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, New York

ROBERT D. TOTO, MD
Department of Medicine, University of Texas Southwestern Medical Center, Dallas, Texas

JAMES A. TUMLIN, MD
Clinical Research Division, Southeast Renal Associates, Charlotte, North Carolina

ARTHUR G. WEINBERG, MD
Department of Pathology, University of Texas Southwestern Medical Center, Dallas, Texas

XIN J. ZHOU, MD
Department of Pathology, University of Texas Southwestern Medical Center, Dallas, Texas

Preface

> "If you do not know the names of things, the knowledge of them is lost, too."
>
> – Carl Linnaeus

Throughout our many combined years of teaching renal pathology, we have been impressed by the challenges to students learning the subject for the first time. There are many reasons why the study of renal pathology is considered difficult. First, there is insufficient knowledge of the normal histology/structure of the kidney. Second, one disease can manifest many different morphologic patterns, while a particular morphologic pattern can be produced by different diseases or etiologic factors. And finally, several different names (synonyms) have been applied to particular patterns or diseases. Yet, the many years of teaching have convinced us that there can be a systematic and orderly approach to the study of renal pathology. Therefore, a new book emphasizing an algorithmic, deductive approach to the interpretation of renal pathology seemed timely. This book organizes the various renal patterns and diseases in a standardized fashion, with emphasis on clinical–pathologic correlations. We have limited our inclusion of renal morphologic patterns to comparatively stable taxonomic groups covering the major diagnostic entities accepted by the published literature.

Standardized names and terminology are essential for communication among renal experts, whether they are clinicians or pathologists. The terminology used in this book is generally consistent with that used by most North American renal pathologists. Wherever possible, we have applied the widely recognized International Nomenclature of Disease (IND), a joint project of the Council for International Organization of Medical Sciences and the World Health Organization. The purpose is to ease communications and facilitate the storage and retrieval of medical information. As noted by the IND, a "few diseases have a single recognized name; most have several different…names. The principle objective of the IND is to provide…a single recommended name" (specific, unambiguous, self-descriptive, simple, and based on cause whenever feasible). It is meant to be a truly international language of disease. The importance of precise terminology and diagnostic criteria cannot be overstated.

The approach and classification used in this book are neither unique nor original. They are based on the "capture" of ideas from the many members of the Renal Pathology Society, Inc., and from major courses in the field, such as Medical Diseases of the Kidney, a postgraduate course held annually for more than 30 years by the Columbia University College of Physicians and Surgeons in New York City, under the direction of Dr. Vivette D'Agati. The approach to renal biopsy has been influenced enormously by Dr. Conrad L. Pirani, and it should come as no surprise that the editors of this book have either studied directly under him (V.D., F.G.S.) or been mentored directly by Dr. Pirani's student, Dr. Silva (X.J.Z., Z.L., and T.N.).

A useful classification (and the subsequent approach to diagnosis) should be based on the following requirements:

1. The classification should be clinically relevant and provide useful information to the clinician (about diagnosis, prognosis, identification of clinical subsets, optimal choice of therapy, evaluation of response to therapy, and future management).
2. It should be based on facts (reflecting the ideals of evidence-based medicine), be scientifically correct, and incorporate our current level of biologic understanding.
3. It should be relatively easy to use by pathologists throughout the world and be reproducible between observers.

The approach of *Silva's Diagnostic Renal Pathology*, which incorporates these principles, is morphologically based and designed for practicing anatomic (and renal) pathologists. By maintaining a high level of expertise in renal pathology, pathologists can ensure that the current trend of increasing use of renal biopsy for diagnosis and patient management will continue.

Many algorithms that collectively detail the clinical, laboratory, and pathologic patterns of renal disease have been included. These algorithms, based upon clinical and morphologic findings, will allow one to find the correct diagnosis. The algorithms provide a simplified road map that directs the reader to the major patterns of interest. To this end, we have adopted a combined "clinical and pathologic" classification scheme in this

book. We have always found it ironic that most dictionaries, atlases, and textbooks require a priori that one knows what something is (e.g., what the diagnosis is and how to spell a particular word) in order to look it up and find the relevant entry. We hope that this book will eliminate that problem.

We believe that the approach in this book, neither final nor perfect, will allow the student to discover and categorize the type of renal involvement, correlate it with the clinical and laboratory findings, and determine the renal prognosis and optimal therapy. Of course, there are always "varieties" or "cross-overs" or "dual diseases," which render exact classification difficult. Nonetheless, a good description is always reliable. More atypical or unusual cases are likely to be referred for renal biopsy, because the clinically obvious cases (e.g., minimal change nephrotic syndrome in children, acute postinfectious glomerulonephritis, diabetic nephropathy with retinopathy) often are not biopsied unless they exhibit atypical features. In the end, it is the renal morphology interpreted in an informed clinical context that leads pathologists to an accurate diagnosis. Although this book is intended as a practical guide for the diagnostic pathologist with primary responsibility for renal biopsy interpretation, as "clinical biologists," we should not lose sight of the pathogenetic factors behind the morphology. Thus, we have included a short section on "Pathogenesis" in each of the chapters.

The authors each bring their own unique personal insights to their individual chapters. However, we have attempted to bind them together through a unanimity of purpose, as reflected in their similar styles and analytic approaches.

At each step, the renal pathologist is integrating knowledge about the light microscopy, fluorescence microscopy, electron microscopy, renal functional studies, urinalysis, systemic findings, medication history, serologies, and radiologic studies. It is this multidisciplinary approach that constitutes the most rewarding aspect of renal pathology. Despite the complexity of the subject material, we hope that the approach outlined in this book will provide a user-friendly guide into this fascinating field.

As our mentor, Dr. Conrad Pirani, often said, it is important that clinical nephrologists and pathologists work closely together for the good of the patient. The pathologist cannot function in isolation. The most difficult diagnostic dilemmas can usually be solved by combining the knowledge of clinician and pathologist on an individual case. As Dr. Pirani has stated in a renal biopsy textbook, "[s]tructure and function have finally met at the microscope." The pathologist and nephrologist can learn a great deal from each other by reviewing cases together over the multiheaded microscope.

Lastly, we would like to thank the renal patients, physicians, and pathologists without whom we would not have had the opportunity to collect these biopsy materials for teaching purposes. We thank them for providing us with such valuable illustrative cases. We, pathologists, strive to understand what we see and place it in a diagnostic context that guides the nephrologist toward more specific therapies. As better and more targeted therapies are developed, an accurate biopsy interpretation will become even more important. It is highly likely that the renal biopsy will continue to be cost-effective for all those we serve – our patients and our clinicians.

Contents

CHAPTER 1

Renal Anatomy

William L. Clapp, MD

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

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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.

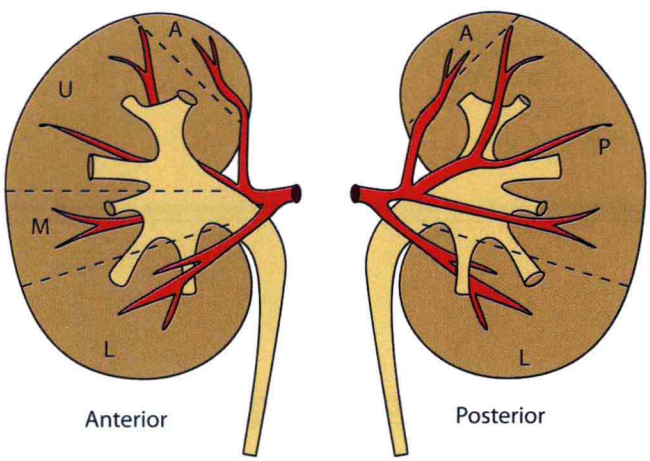

***FIGURE 1.1:** Diagram of arterial supply of the kidney. The anterior division of the renal artery divides into segmental branches that supply the upper (U), middle (M), and lower (L) segments of the anterior surface. The apical (A) segment is usually supplied by a branch from the anterior division. 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

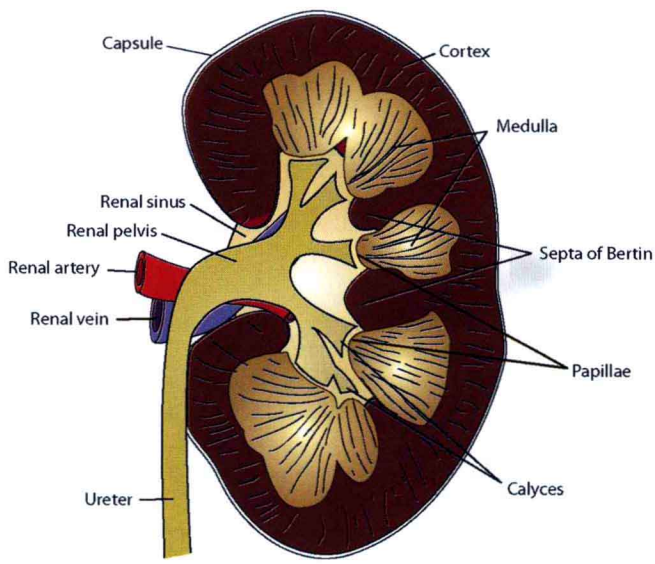

***FIGURE 1.2:** Diagram of a bisected kidney showing major macroanatomic features. (Modified from Clapp WL, Croker BP. Kidney In: Mills SE, ed.* Histology for Pathologists. *3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2007: 839–907.)*

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].

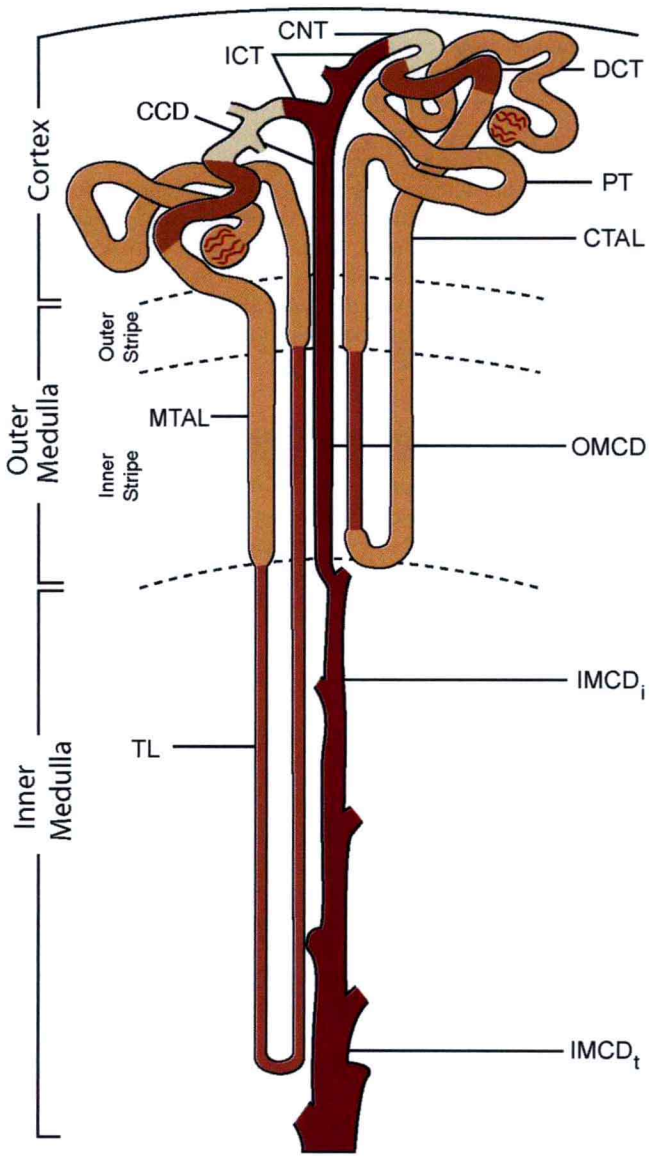

***FIGURE 1.3:** Diagram depicting the segments of the nephron and the regions (zones) of the kidney. PT, proximal tubule; TL, thin limb; MTAL, medullary thick ascending limb; CTAL, cortical thick ascending limb; DCT, distal convoluted tubule; CNT, connecting tubule; ICT, initial collecting tubule; CCD, 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

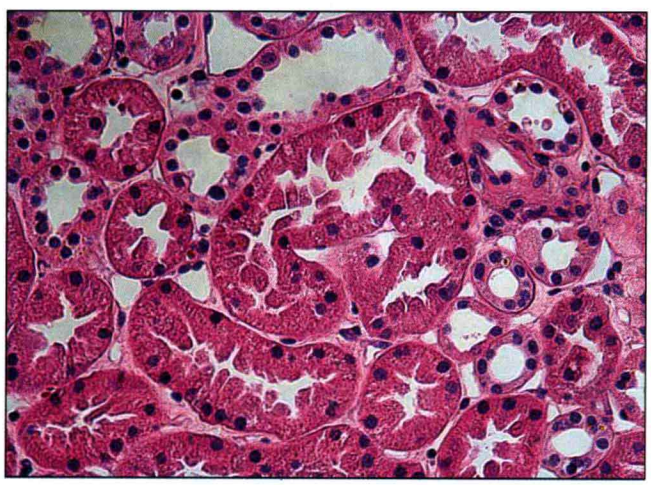

FIGURE 1.4: Light micrograph of cortex showing compact back-to-back arrangement of tubules with minimal intervening interstitium. A few peritubular capillaries are evident. (H&E, × 400.)

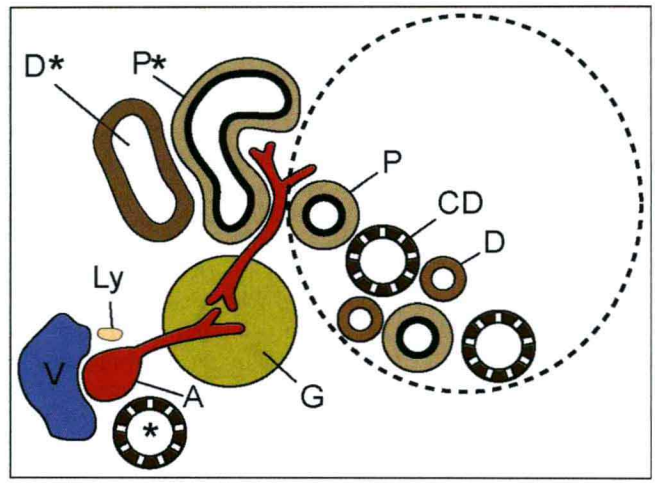

FIGURE 1.5: Schematic drawing of architectural regions of the cortex. The cross section depicts a medullary ray (encircled by a dotted line), and the cortical labyrinth as a continuous zone (outside the dotted line). The medullary ray includes the proximal straight (P) and distal straight (D) tubules 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.)

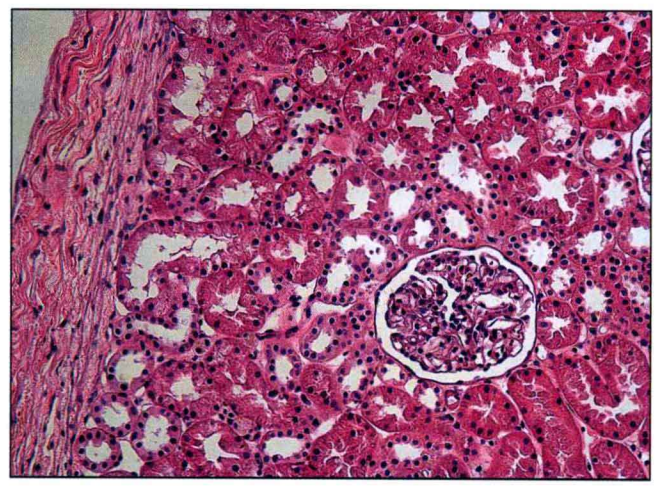

FIGURE 1.6: Micrograph of outer cortex illustrating the cortical labyrinth. Proximal convoluted tubules are predominant. The renal capsule (left) is evident. (H&E, × 200.)

(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

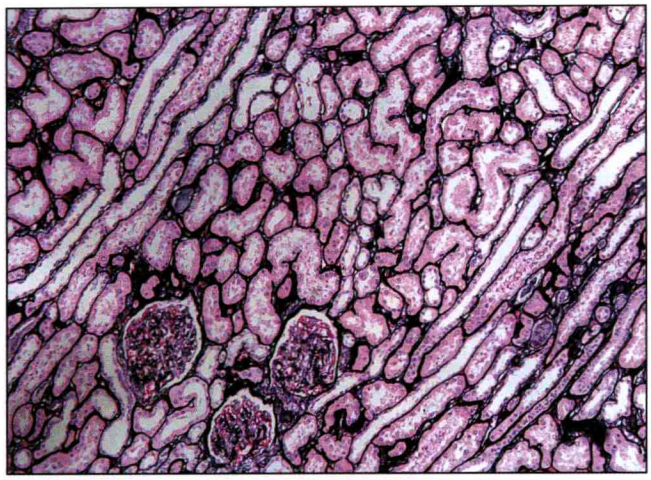

FIGURE 1.7: Longitudinal section of cortex illustrating two linear arrangements of tubules representing medullary rays. The cortical labyrinth containing glomeruli and convoluted tubules is between the two medullary rays. (Methenamine silver, × 100.)

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

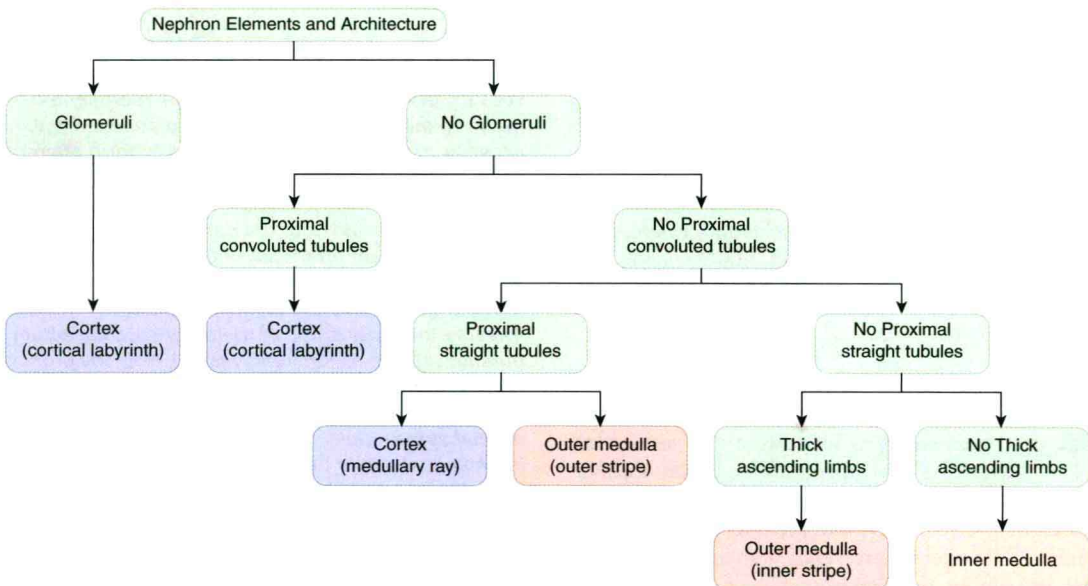

FIGURE 1.8: Algorithm for determination of the architectural region or particular zone of the kidney based on the presence and/or absence of specific nephron components or segments.

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

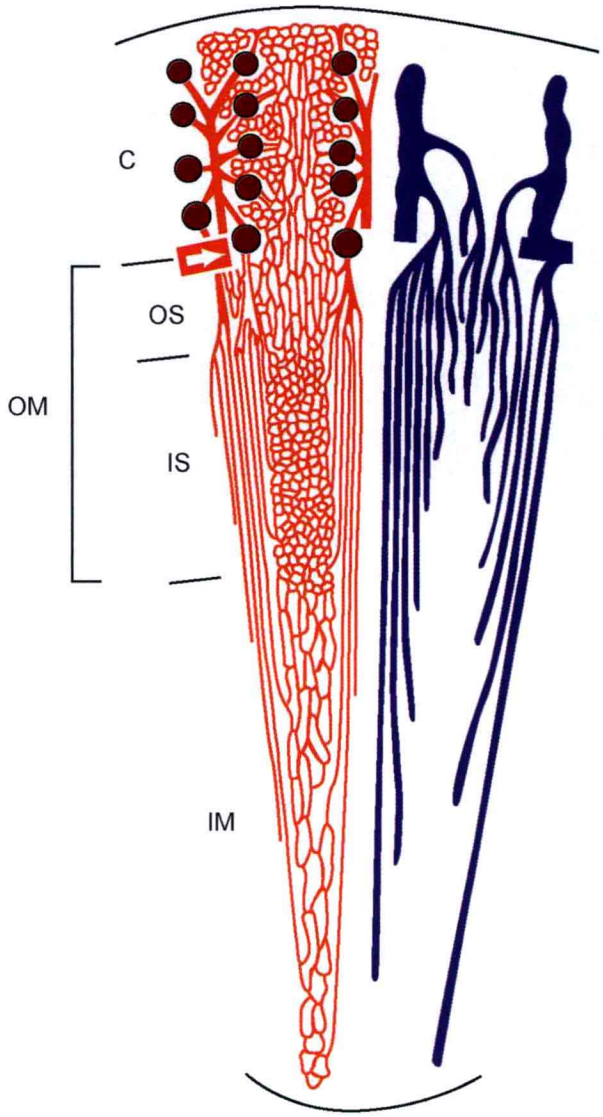

FIGURE 1.9: ***Schematic of renal microvasculature. The arterial vessels, glomeruli, and capillaries are represented on the left side (red). An arcuate artery gives rise to an interlobular artery which ascends in the cortex and branches to form afferent arterioles which supply the glomeruli. The efferent 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.)***

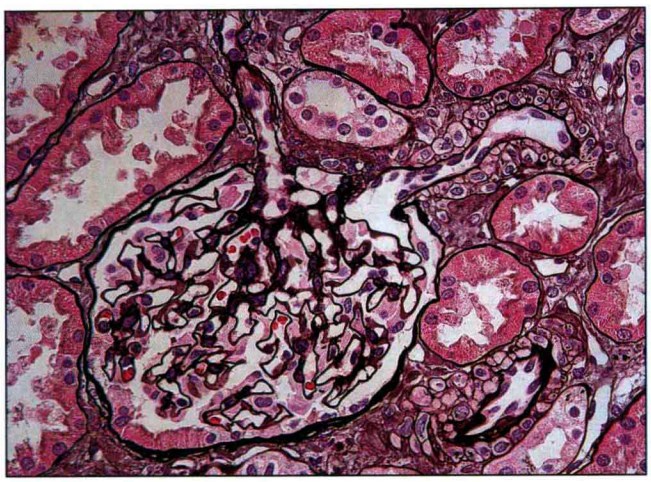

FIGURE 1.10: Light micrograph of glomerulus depicting both afferent and efferent arterioles. The afferent arteriole (right) has a more prominent media of smooth muscle cells. (Methenamine silver, × 400.)

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.

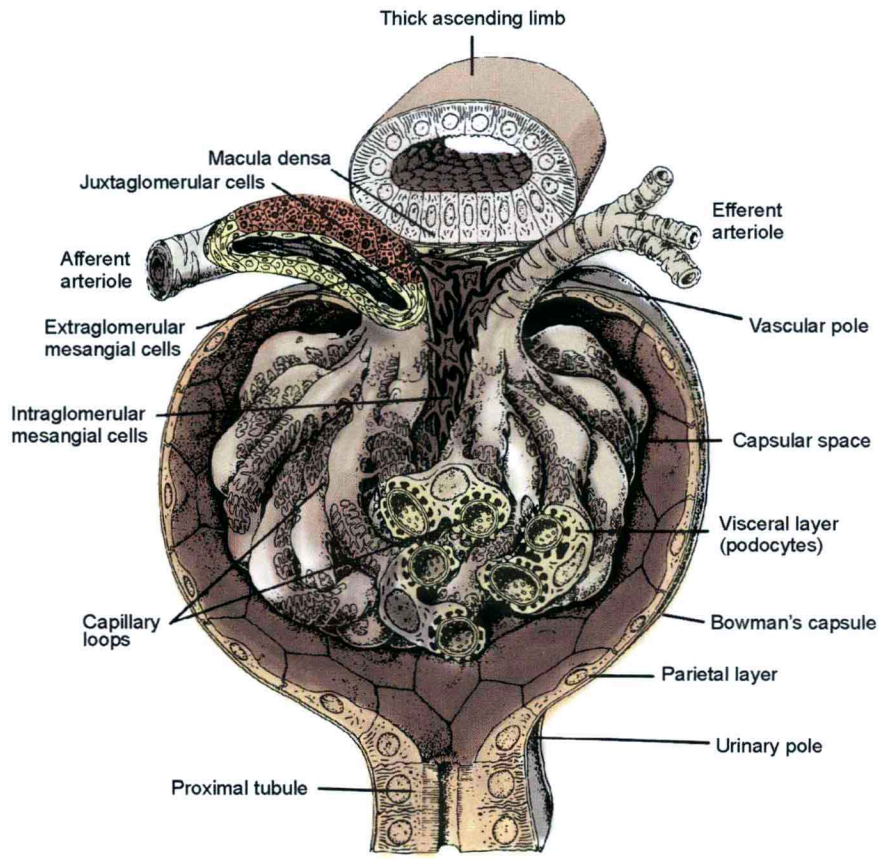

FIGURE 1.11: Three-dimensional schematic drawing of the glomerulus. (Modified from Geneser F. Textbook of Histology. Philadelphia: Lea & Febiger; 1986.)

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