MD Program
UNIVERSITY OF TORONTO

Histology

The Urinary System

eMODULE TUTORIAL

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H16 The Urinary System

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Recommended online resources:

Western University Virtual Slide Box

University of Michigan Virtual Microscopy

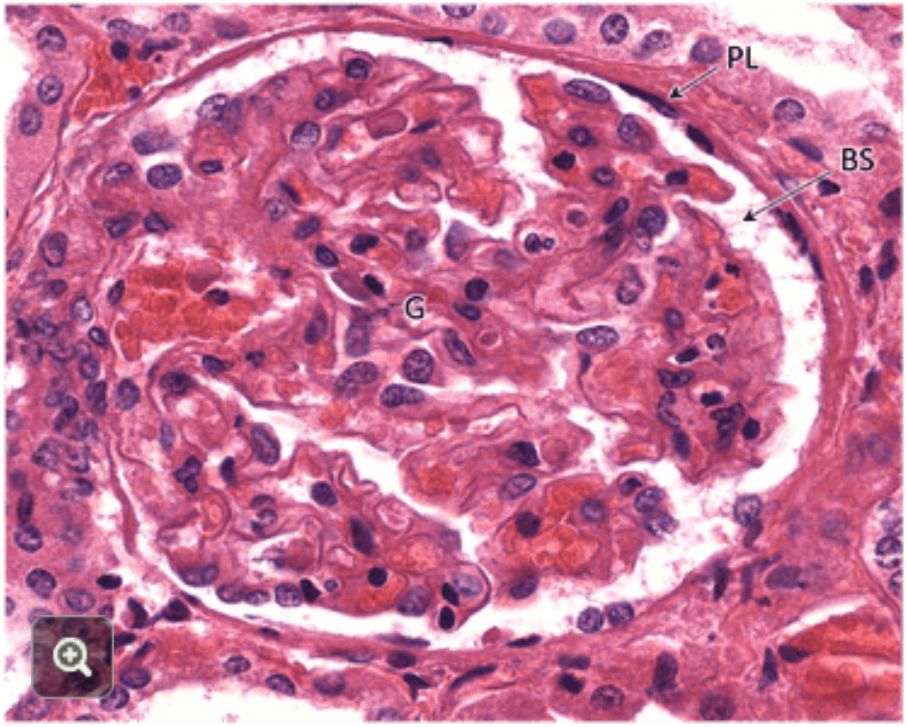
University of Minnesota Histology Guide

University of Leeds Histology Guide

University of Illinois Cell and Tissue Biology

When you have learned the material presented here, you will be able to describe the:

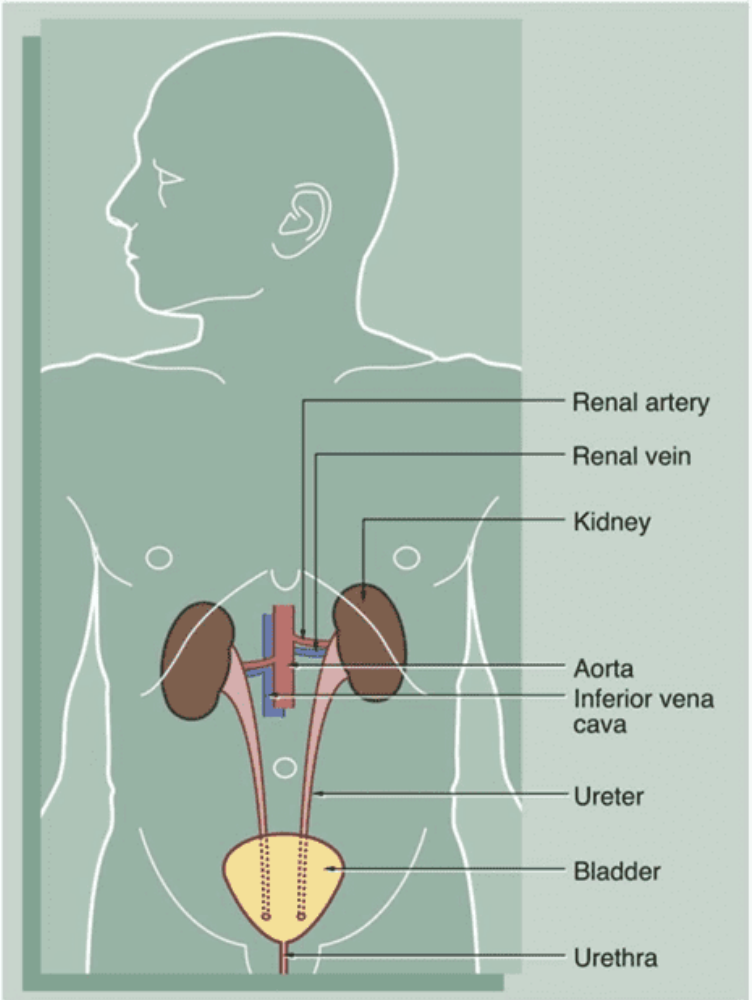
- structure and function of the nephron, including the renal corpuscle, renal tubule and juxtaglomerular apparatus
- structure and function of the renal collecting system
- structure and function of the ureter, bladder and urethra



The components of the urinary system are the paired **kidneys** and **ureters**, the **bladder** and **urethra**. The urinary system primarily functions to **monitor and control various properties of blood, and therefore, body fluids**.

To this end, the kidneys carry out a variety of functions, including the:

- regulation of **water and electrolyte**, and **acid-base balance**
- **excretion** of metabolic wastes, excess water and electrolytes, and drugs
- production and secretion of **renin**, an enzyme that functions in the regulation of blood pressure
- production and secretion of **erythropoietin**, a hormone that promotes the production of erythrocytes in bone marrow
- conversion of vitamin D to its active form, **1,25-dihydroxyvitamin D_3** or calcitriol



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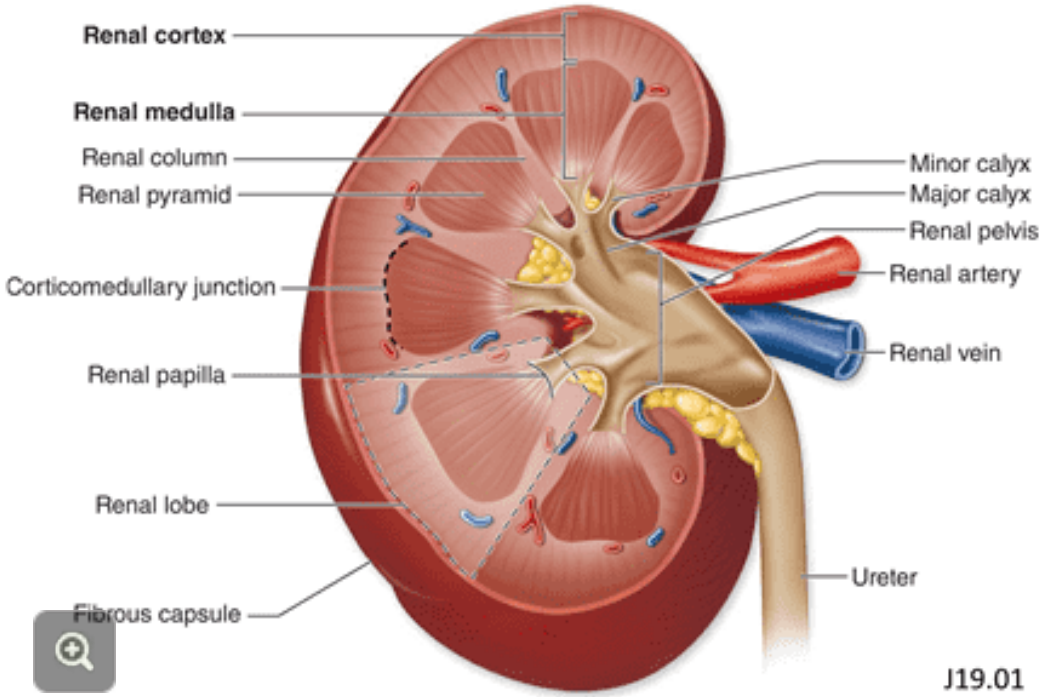
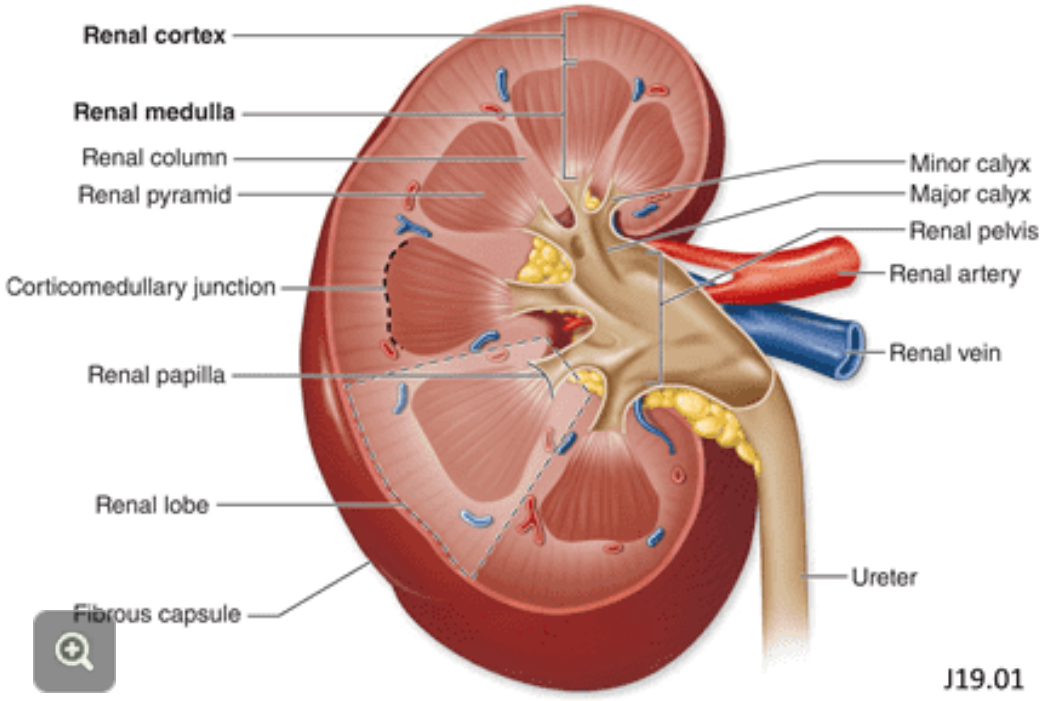
The size of the kidney is variable, but, in adults, it is generally 12-cm long, 6-cm wide, and 2.5-cm thick. The kidney is **convex laterally** and **concave medially**, where its **hilum** is located. The kidney is enclosed in a **fibrous CT capsule** which extends into its hilum. Like many organs you've studied, the hilum of the kidney contains **blood vessels, nerves and lymphatics**.

In the case of the kidney, the hilum also contains the **renal pelvis**, the first part of the **ureter**. The ureter transports urine, formed in the kidney, to the urinary bladder where it is stored until it is eliminated. The renal pelvis is formed by the union of several **major calyces** (**singular, calyx**), which are formed, in turn, by the union of several **minor calyces**. The region within the renal hilum, surrounding the renal pelvis calyces and blood vessels, is called the **renal sinus**. It is filled with **adipose tissue**.



Like other organs you've studied (adrenal glands, ovaries), the parenchyma of the kidney is subdivided into a superficial region, the **renal cortex**, and a deeper region, the **renal medulla**, each with a distinct histological structure and function. The transition from cortex to medulla is abrupt, and occurs at the **corticomedullary junction**.

Medullary tissue is organized into **renal pyramids**, with the **bases** of the pyramids facing the surface of the kidney and their **apices** pointed toward the hilum. The apex of each medullary pyramid, its **renal papilla**, inserts into a **minor calyx**. As urine is produced, it drips from the renal papilla into the minor calyx, where it is collected for transport to the bladder. The medullary pyramids are separated by **renal columns**, extensions of cortical tissue between adjacent pyramids. A single medullary pyramid and its surrounding cortical tissue is called a **renal lobe**.



At the microscopic level, parallel arrays of ducts and tubules extend from the medulla into the cortex. These are **medullary rays**, and with their associated cortical tissue they comprise **renal lobules**.

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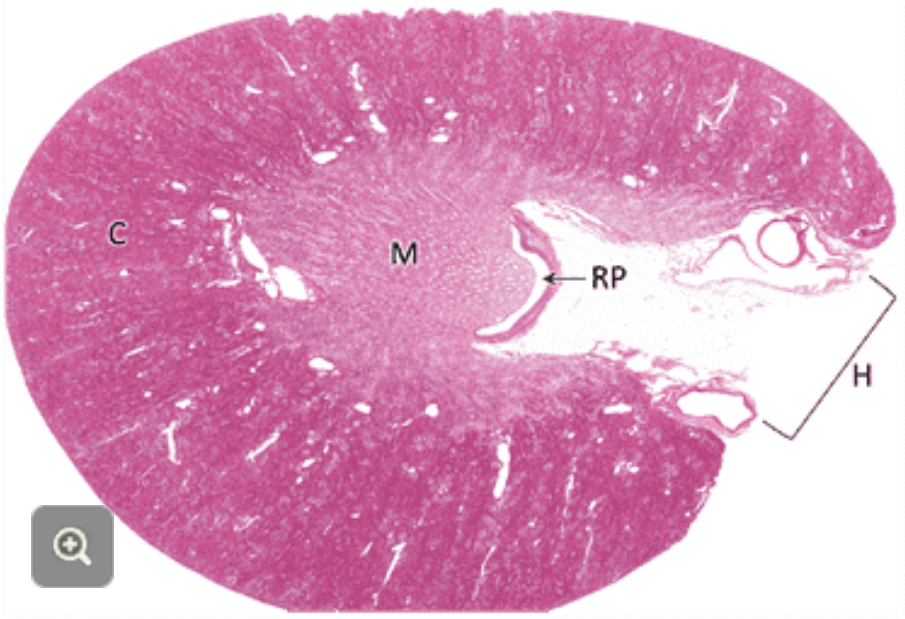

C - **Cortex**, darker outer region
M - **Medulla**, lighter inner region
RP – **Renal pelvis**, funnel-shaped origin of the ureter
H - **Hilum**, concave region where vessels enter/exit kidney

At the microscopic level, parallel arrays of ducts and tubules extend from the medulla into the cortex. These are **medullary rays**, and with their associated cortical tissue they comprise **renal lobules**.

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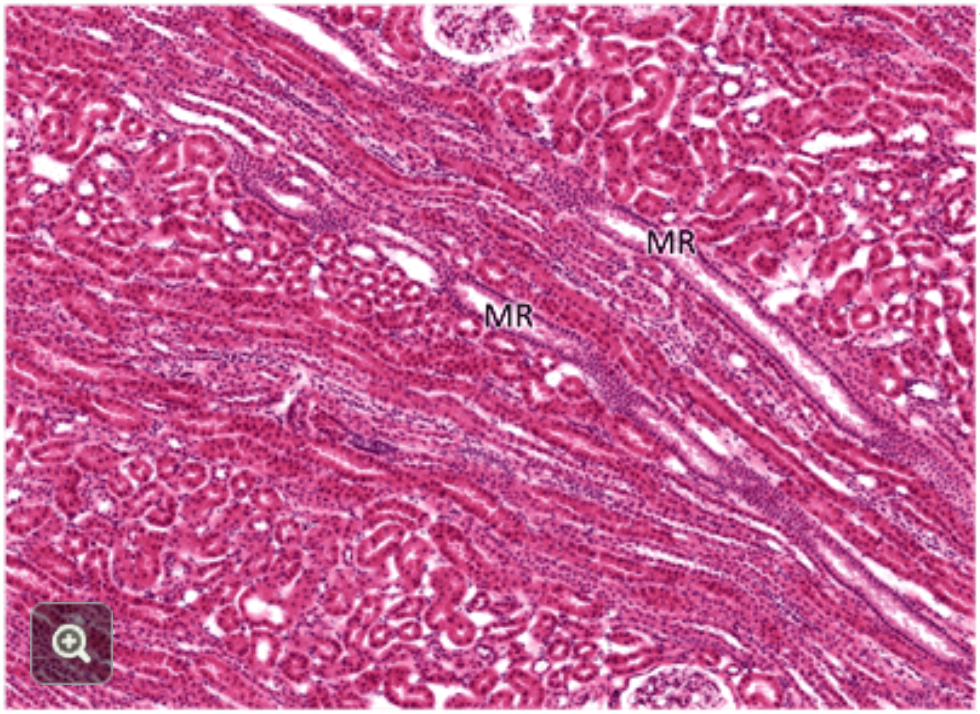
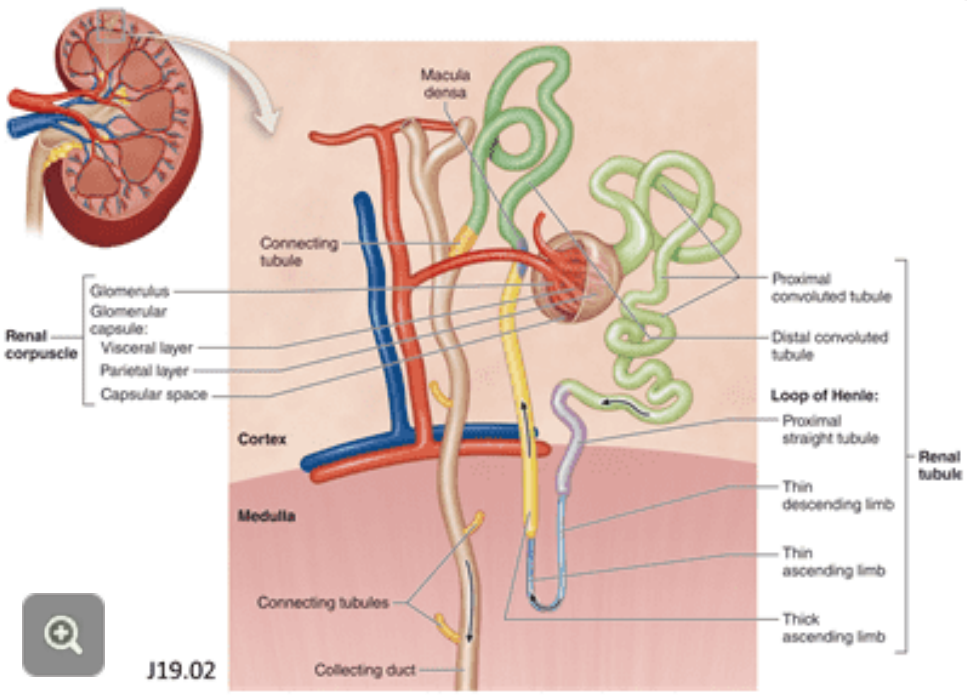


MR – **Medullary rays**, parallel arrays of tubules between the cortex and medulla that contain straight tubules and collecting ducts

At the microscopic level, parallel arrays of ducts and tubules extend from the medulla into the cortex. These are **medullary rays**, and with their associated cortical tissue they comprise **renal lobules**.

Each kidney contains 1-4 million microscopic structures called **nephrons**. Each nephron consists of two parts: a **renal corpuscle** and a **renal tubule**. In the accompanying diagram, identify the parts of a nephron:

The **renal corpuscle** is the globular, initial portion of the nephron, and is always located in the renal cortex. It is composed of a **glomerular (Bowman's) capsule** which contains within it a tuft of capillaries called the **glomerulus (G)**. The glomerular capsule is composed of a **visceral layer**, which is applied to the glomerulus, and a **parietal layer (PL)**, which forms the outer wall of the capsule. The space between the parietal and visceral layers of the glomerular capsule is the **capsular (Bowman's) space (BS)**.



The **renal tubule** is a single, long, unbranched tubule that extends from the corpuscle in the cortex into the renal medulla; it then bends to return to the cortex. The wall of the renal tubule is composed of a **simple epithelium,** although **the height of the epithelium varies** along its length. Its walls are a **continuation of the parietal layer of the glomerular capsule** and **its lumen is a continuation of the capsular space**.

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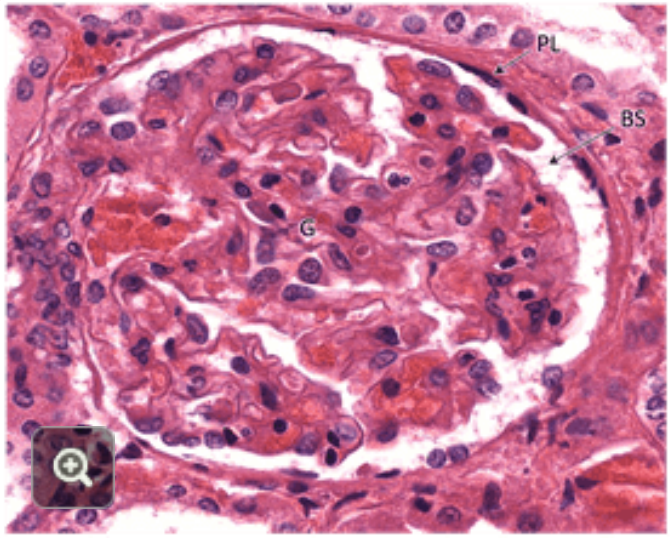

Histological image of a renal corpuscle.

G - **Glomerulus**, tuft of capillaries.
BS – **Bowman's space**, space between the parietal and visceral layers of Bowman's capsule.
PL – **Parietal layer of Bowman's capsule**, composed of simple squamous epithelium. The visceral layer of the Bowman's capsule is composed of podocytes covering the glomerular capillaries but is not discernable.

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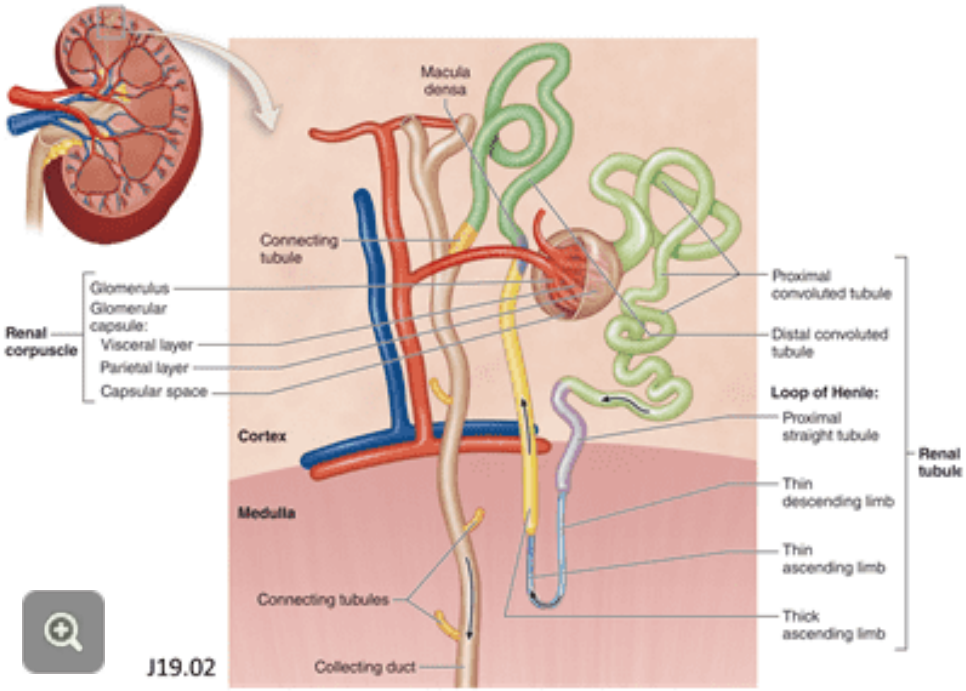
The renal tubule has structural and functional subdivisions. The **proximal convoluted tubule, PCT,** is the first part of the renal tubule. Within the cortex, the PCT is very tortuous. It then dives into the medulla to form the **loop of Henle**. The first parts of the loop of Henle are the **proximal straight tubule** and the **thin descending limb**. The thin descending limb makes a hairpin turn to become the **thin ascending limb**, which continues as the **thick ascending limb**. The tubule re-enters the cortex and passes between the arterioles that feed into and out of the glomerulus. There the cells lining the tubular wall are specialized as the **macula densa**. Beyond the macula densa, the tubule again becomes tortuous as the **distal convoluted tubule, DCT**. The last part of the renal tubule is the short **connecting tubule**.

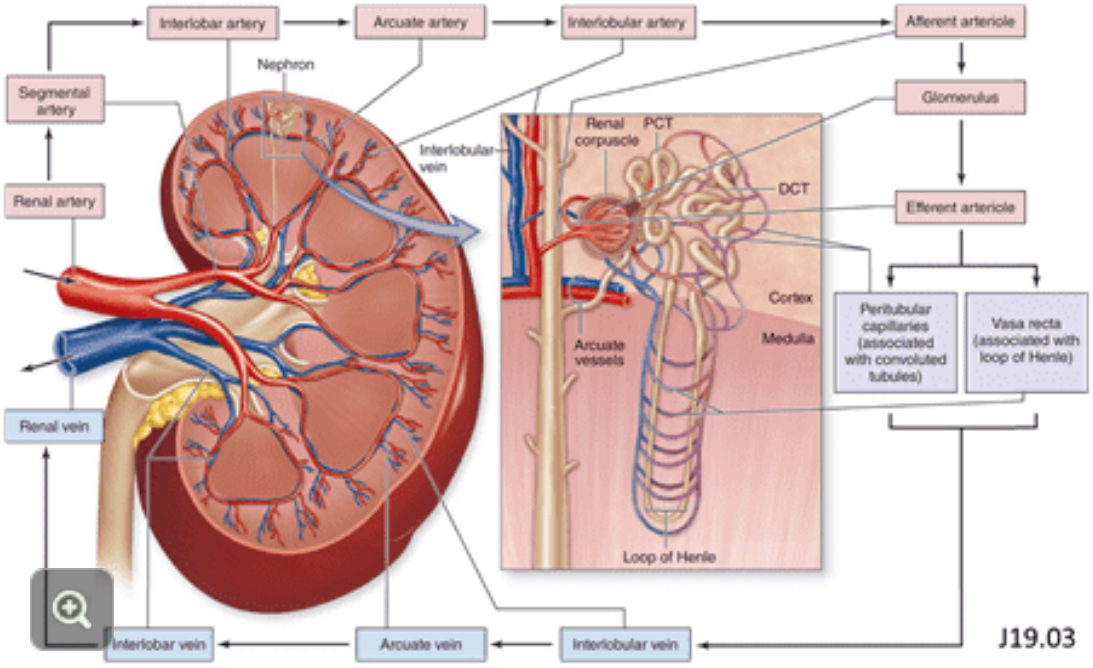


Connecting tubules from many nephrons empty into **collecting ducts**. Collecting ducts pass through the medulla toward the apex of the renal pyramid, where they **open at the renal papilla**. Formed urine drips from the openings at the renal papilla and collect in a **minor calyx**.

Most nephrons, located almost wholly in the cortex, are called **cortical nephrons**. About one-seventh of nephrons have **renal corpuscles** located at **the corticomedullary junction** and have **long loops of Henle that extend deep within the medulla**. These are called **juxtamedullary nephrons**.

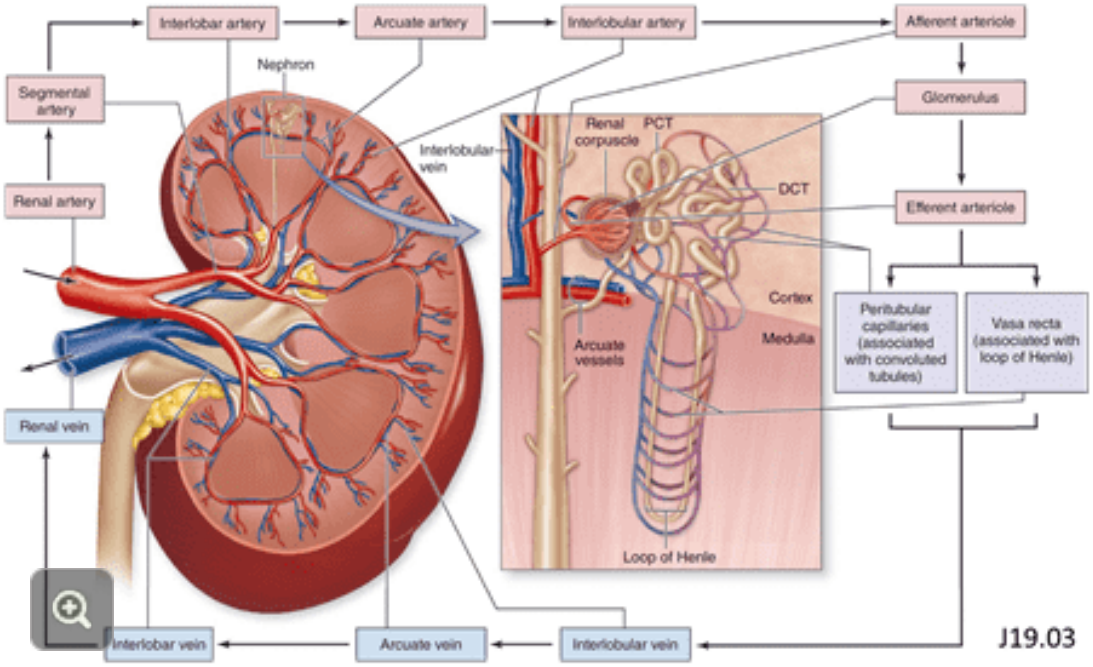
An understanding of renal blood supply is critical for the comprehension of renal function. Renal blood supply is dense and highly ordered. The names of renal blood vessels are descriptive, and therefore can easily be learned; they describe the location of the vessel or its shape.

The right and left **renal arteries** are branches of the abdominal aorta. At the hilum of the kidney, each renal artery forms two or more **segmental arteries**, which themselves branch to form **interlobar arteries**.



At the **corticomedullary junction**, interlobar arteries divide to form **arcuate arteries**, which arch along the base of the renal pyramid. Arcuate arteries give off branches called **interlobular arteries** (or cortical radiate arteries) which radiate through the renal cortex toward its surface

INSET: Interlobular arteries give rise to **afferent arterioles**. Each afferent arteriole enters a renal corpuscle to form a **glomerulus** within its renal capsule. Glomerular capillaries coalesce to form an **efferent arteriole**, which leaves the renal corpuscle. The efferent arteriole branches as the **peritubular capillaries** which surround and supply the convoluted tubules of the **renal cortex**. In the case of juxtaglomerular nephrons near the corticomedullary junction, the peritubular capillaries give rise to capillary loops called the **vasa recta** which dive deep into the medulla in conjunction with the loops of Henle and collecting ducts, and then return to the cortex.



Veins draining the different regions of the kidney take the same names as their companion arteries.

Glomerular filtrate, formed within the renal corpuscle, is modified as it passes through the renal tubule and collecting ducts to ultimately drip, as urine, from the renal papilla into the minor calyx. The processes responsible for the modification of this fluid are the function of the epithelium that lines these tubules.

In **Filtration**, which occurs in the renal corpuscle, components of plasma pass from the lumen of the glomerulus into the capsular space.

In **Secretion**, substances are added to the filtrate by the epithelial cells that form the walls of the renal tubule. The secreted substances are derived from the tissue fluid surrounding the tubules, and in turn from the capillaries within the interstitium.

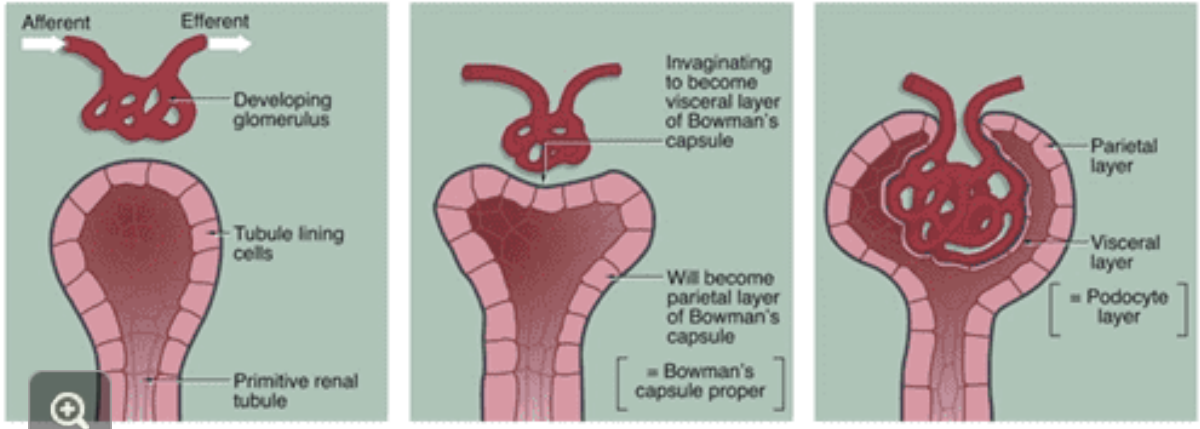
In **Absorption**, components of the glomerular filtrate move from the tubular lumen across its epithelial wall into the surrounding tissue fluid, and from there into the capillaries within the interstitium.

Once the filtrate has passed through the renal tubule and the processes of secretion and absorption have modified its composition, it enters the minor calyx and is conducted from there through the major calyx, renal pelvis and ureter to the urinary bladder for storage. Ultimately it passes through the urethra for **excretion**.

The structure of the renal corpuscle, in particular the relationship between the glomerulus and the glomerular (Bowman's) capsule, is better understood by consideration of its **development**.

The renal tubules develop as **blind-ended tubes** consisting of a simple cuboidal epithelium supported by a basement membrane. The glomerulus develops from mesoderm that **invaginates into the end of the developing renal tubule**, and becomes enveloped by it. This forms the **glomerular capsule**.

The capsular cells that become adhered to the glomerulus differentiate into **podocytes**, which form the **visceral layer** of the glomerular capsule. Most tissue interposed between the podocytes and the endothelial cells of the glomerulus disappears, and their basement membranes fuse, thus forming the **glomerular basement membrane, GBM**. The small amount of intervening tissue that remains to support the capillary loops of the glomerulus differentiates to form the **mesangium**.



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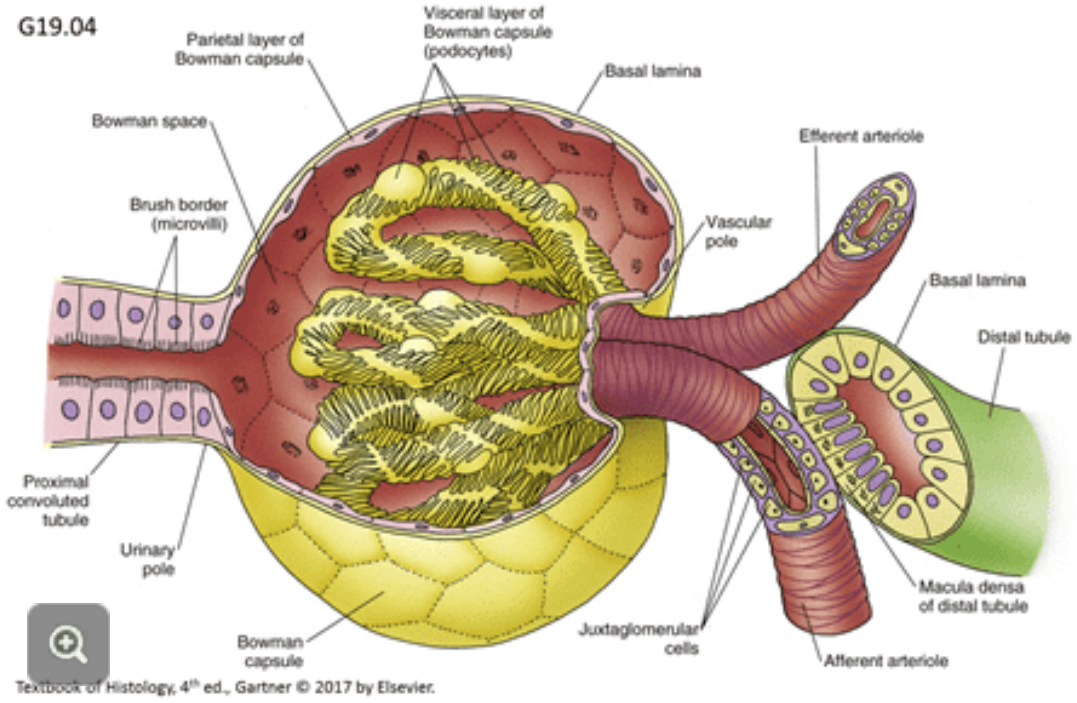
The **parietal layer** of the glomerular capsule is separated from the visceral layer of the glomerular capsule by the **capsular (Bowman's, urinary) space**, which is continuous with the lumen of the renal tubule.

As illustrated, the renal corpuscle has a **vascular pole**, at which the **afferent and efferent arterioles** feed into and out of the **glomerulus**, respectively. At the vascular pole, the **distal tubule** of the nephron passes between the afferent and efferent arterioles, where it is modified to form the **macula densa**, one component of a more elaborate structure called the **juxtaglomerular apparatus, JGA**. Blood entering the corpuscle via the afferent arteriole is filtered across i) the glomerular endothelium, ii) its enveloping podocyte layer, and iii) the intervening, shared, glomerular basement membrane, GBM. These three components form the **glomerular filter.**



The **filtrate** thus produced fills the **capsular (Bowman's, urinary) space**, and enters the **lumen of the PCT** at the **urinary pole** of the renal corpuscle. Notice, at the urinary pole, the abrupt transition from the **simple squamous epithelium** of the parietal layer of the renal corpuscle to the **simple cuboidal epithelium** of the PCT. The components of the **blood** that are unable to pass through the glomerular filter, either due to their size or charge, leave the glomerulus via the **efferent arteriole.**

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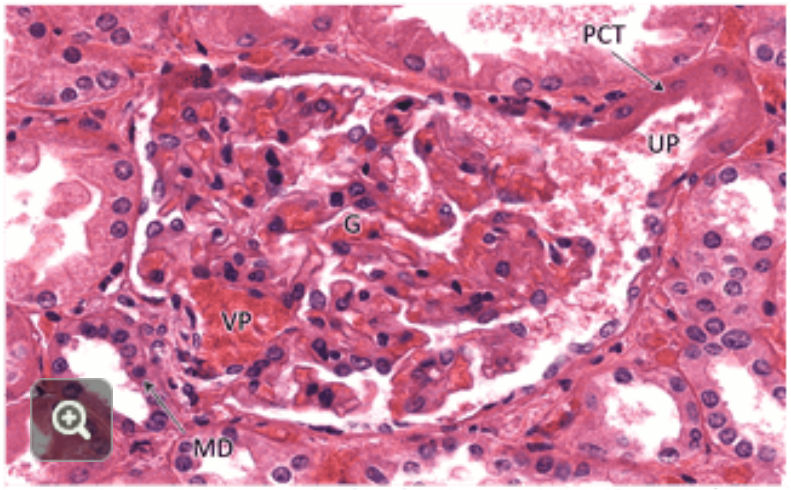

A Renal Corpuscle.

Note the **vascular pole (VP)** where the afferent/efferent arteriole enter/exit the **glomerulus (G)**. The **urinary pole (UP)** is where the ultrafiltrate exits Bowman's space and enters the **PCT** (simple cuboidal epithelium). **Macula densa (MD)**, tightly packed columnar cells where the distal tubule contacts the afferent arteriole at the vascular pole.

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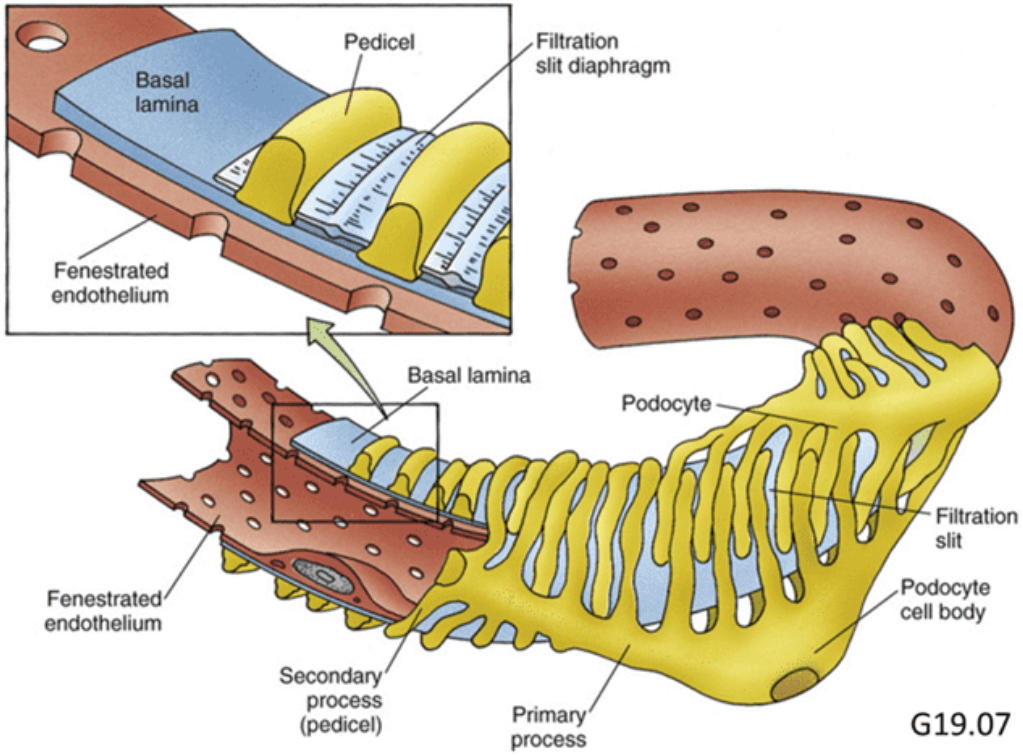
A closer look at the components of the glomerular filter shows that the endothelium of the glomerulus is **fenestrated**. Podocytes extend **1° cell processes** that wrap around the glomerulus and themselves give off numerous, smaller, 2° cell processes, called **pedicels**. The pedicels of adjacent podocytes 1° cell processes **interdigitate** with each other. The narrow spaces that remain between the pedicels are called **filtration slits**. Filtration slits are not open, but are closed over by macromolecular complexes called **filtration slit diaphragms**.



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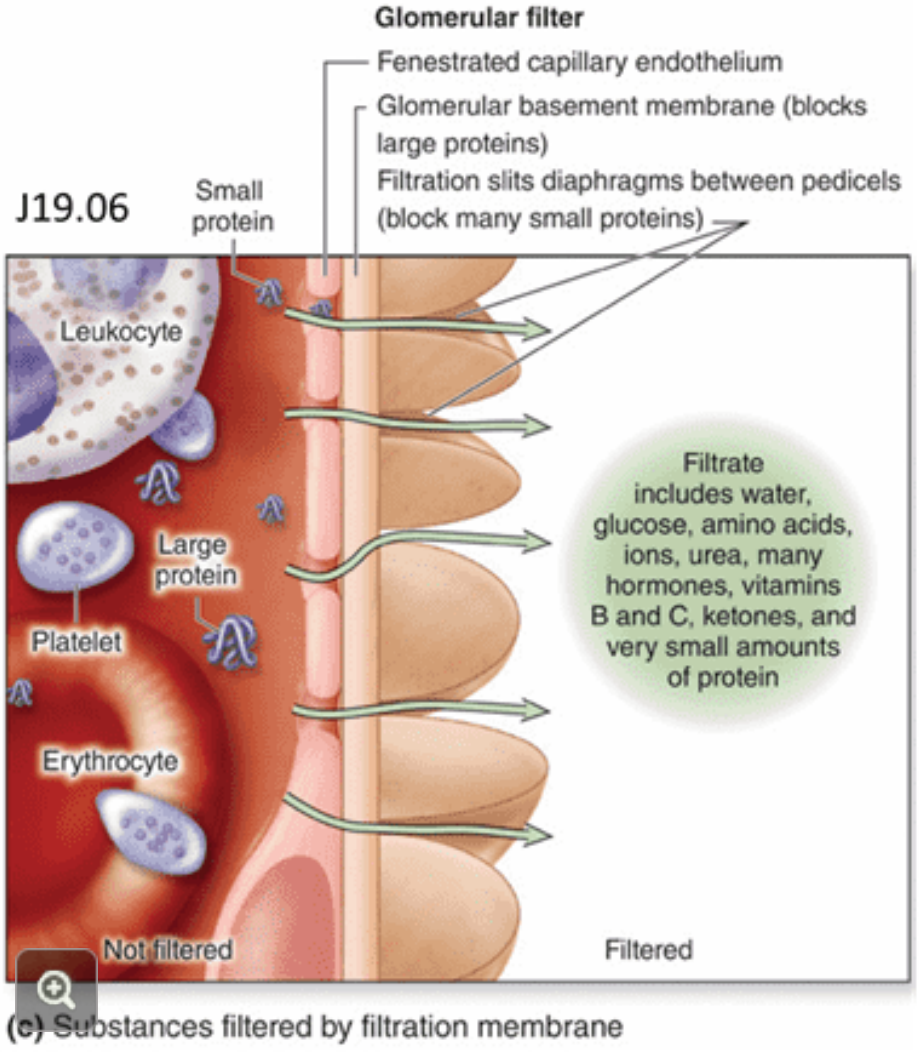
The **glomerular filter** is composed of the i) fenestrated capillary **endothelium**, ii) glomerular **basement membrane** (GBM), and ii) **filtration slit diaphragms**.

The fenestrated capillary **endothelium** retains the formed elements of blood, i.e. the cells and platelets.

The **GBM** provides **adherence** for both the glomerular endothelial cells and the podocytes. It includes an interwoven network of cross-linked collagen type IV molecules and large, anionic proteoglycans. The GBM **limits the passage of proteins** larger than 69 kDa, thus excluding **albumin** from glomerular filtrate. Small proteins that do pass through the glomerular filter are **degraded** and their constituent **amino acids absorbed** by the epithelium lining the **PCT**.



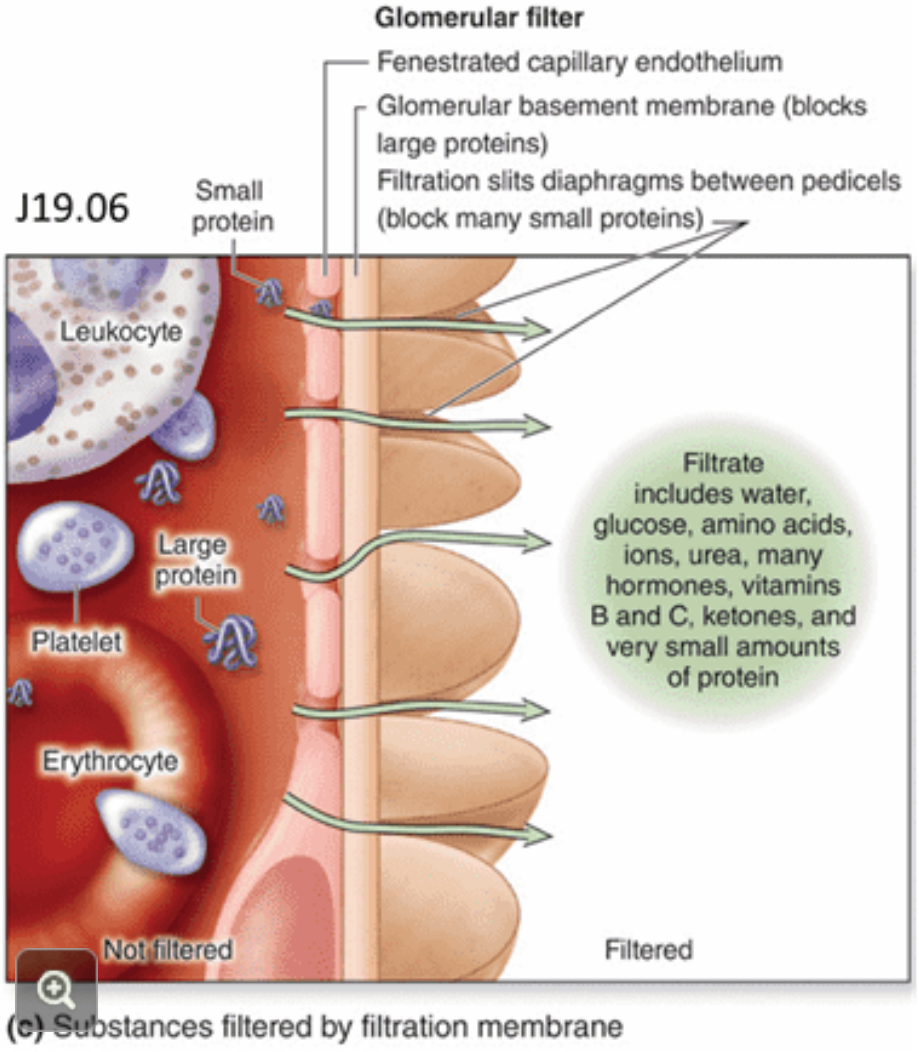
(c) Substances filtered by filtration membrane

The filtration slits between adjacent pedicels are spanned by **slit diaphragms**, which are described as **elaborate tight junctions**. They include specialized proteins called **nephrins**, amongst other proteins, proteoglycans and glycoproteins, which **together create a polyanionic layer** with a series of small openings in it that **restricts the passage of many smaller proteins and organic anions**.

Glomerular filtrate, therefore, is chemically **similar to plasma**, except that it contains **very little protein**.

INFO: Proteinuria

The glomerular filter is altered in certain disease states (diabetes mellitus, glomerulonephritis), as evidenced by **elevated levels of protein in the urine**, known as **proteinuria**.



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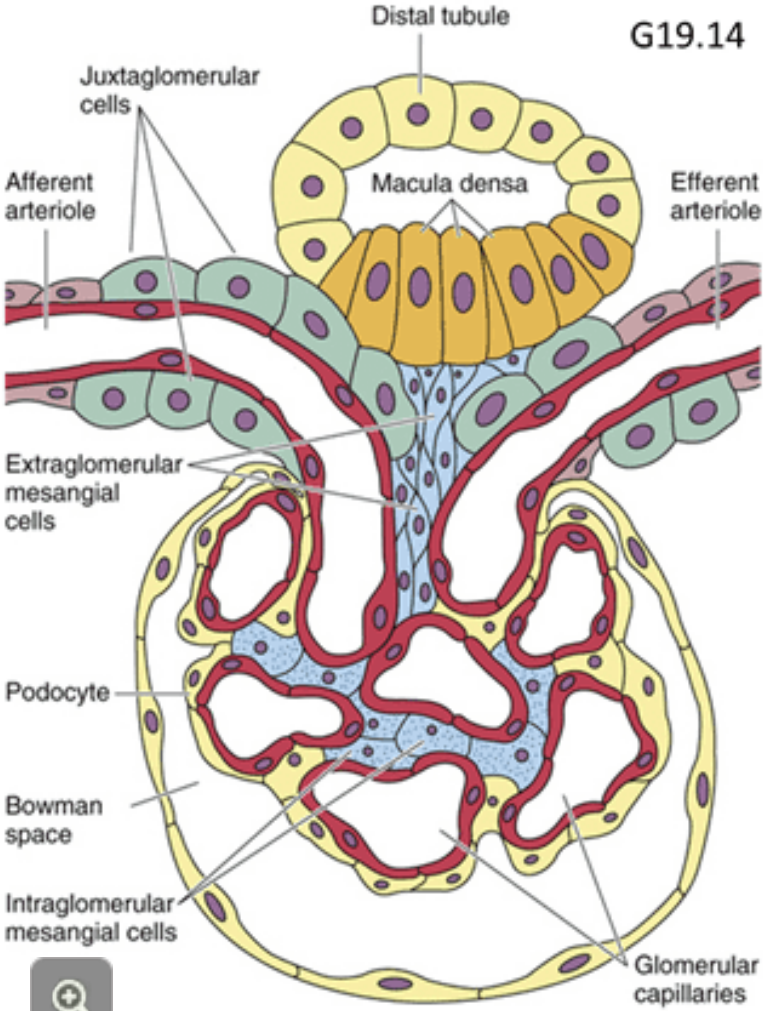

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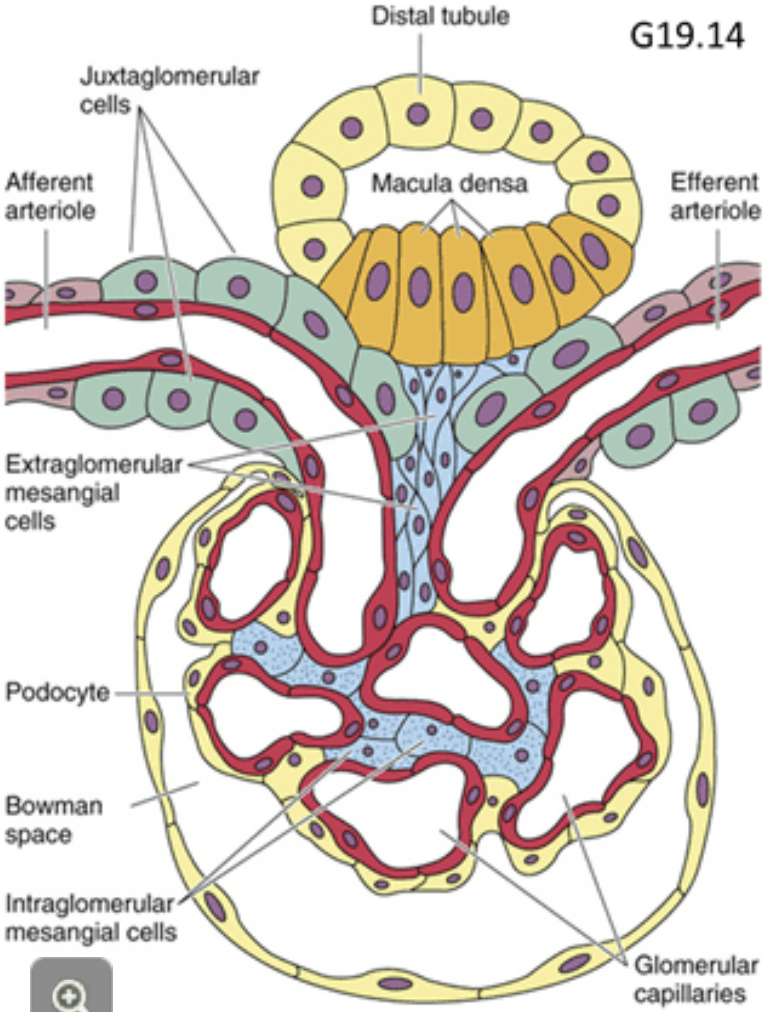
Note that the afferent and efferent arterioles are just that: arterioles. It is unusual that a capillary bed, such as the glomerulus, is situated between two arterioles, each with its smooth muscle **tunica media**. The **relative resistance in the afferent and efferent arterioles determines the hydrostatic pressure in the glomerulus**, which is directly proportional the amount of glomerular filtrate produced per unit time, i.e. the **glomerular filtration rate, GFR**.

The vascular resistance in the afferent and efferent arterioles, and therefore GFR, is **under hormonal and neural control**. The average GFR in an adult is estimated to be 125 mL/min or 180 L/d.



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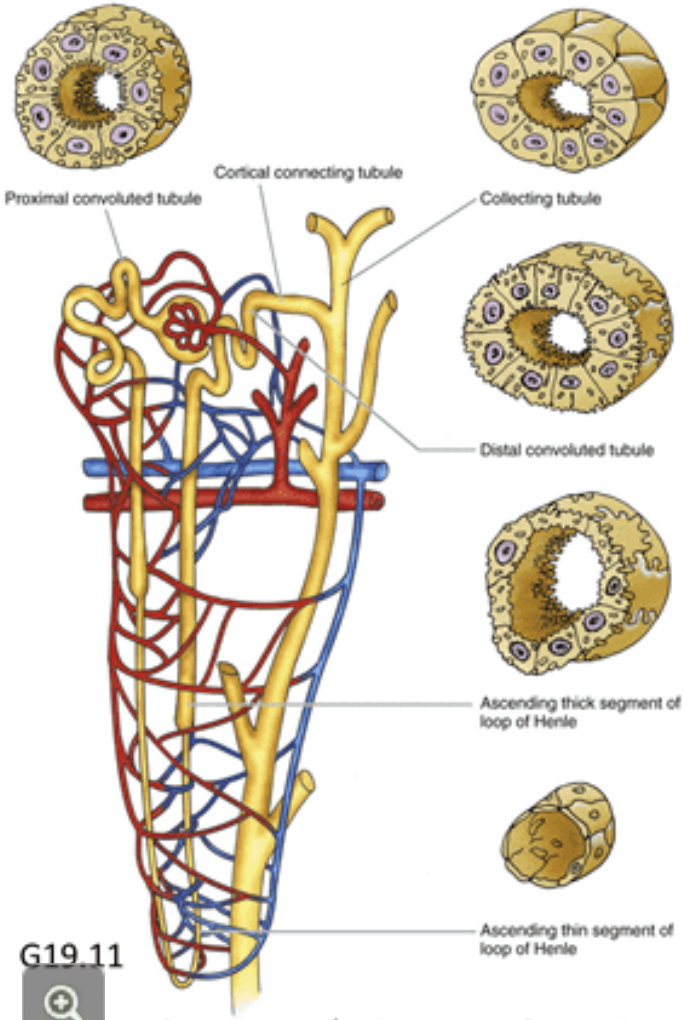
As introduced earlier, the **mesangium** is the tissue between the glomerular endothelial cells and the podocytes. This tissue includes **mesangial cells**, which are **phagocytic, contractile and secretory**. They perform a variety of functions, including i) **physical support** of the glomerulus; ii) cleaning the glomerular filter by **phagocytosis** of accumulated protein, including the antigen-antibody complexes that accrue in many disease states; iii) adjustment of the GFR by **contracting** in response to changes in blood pressure; iv) **secretion** of the acellular components of the mesangium as well as cytokines that function in maintenance and repair of the glomerulus.



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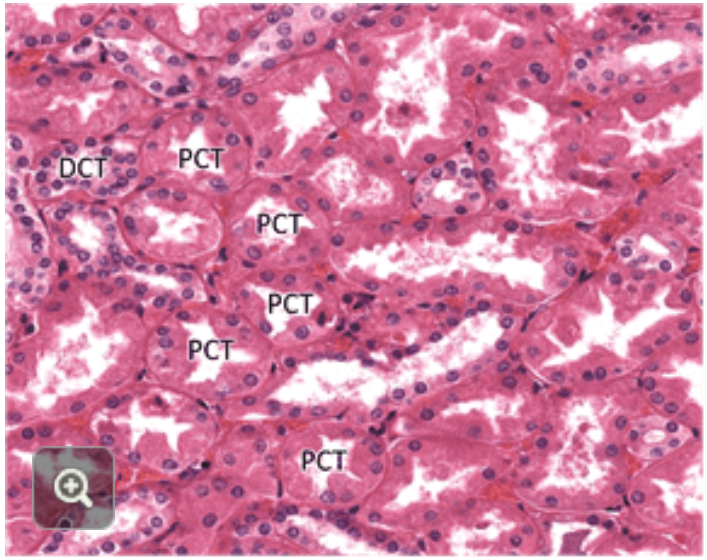
At the urinary pole of the renal corpuscle, there is an **abrupt transition** from the **simple squamous** epithelium of the parietal layer of the renal corpuscle to the **simple cuboidal** epithelium of the PCT. In any given nephron, **the PCT is longer than the DCT**, so if follows that PCTs dominate in the renal cortex.

As glomerular filtrate passes through the PCT, most of the **water and electrolytes**, and all **organic molecules** (glucose, amino acids, vitamins), are absorbed across its wall into the **surrounding interstitium**, and from there into the **peritubular capillaries**. These components of the glomerular filtrate are, therefore, reclaimed. **Absorption** of these components of the glomerular filtrate in the PCT occurs by both **active and passive means**. Epithelial cells of the PCT have an assortment of pumps, channels, transporters, membrane-bound enzymes and carrier proteins. Passive absorption, in particular of water and Cl^-, occurs through the paracellular route, down osmotic and concentration gradients, respectively



Cross-section showing many **proximal convoluted tubules (PCT)**.

Simple cuboidal epithelium lines the **PCT**. Its numerous microvilli clump with fixation forming a **stellate-shaped lumen**. Cells of the PCT are generally **larger** and **more eosinophilic** compared to those of the **distal convoluted tubule (DCT)**. Because cells are larger, there are **fewer nuclei in section**.

At the urinary pole of the renal corpuscle, there is an **abrupt transition** from the **simple squamous** epithelium of the parietal layer of the renal corpuscle to the **simple cuboidal** epithelium of the PCT. In any given nephron, **the PCT is longer than the DCT**, so if follows that PCTs dominate in the renal cortex.

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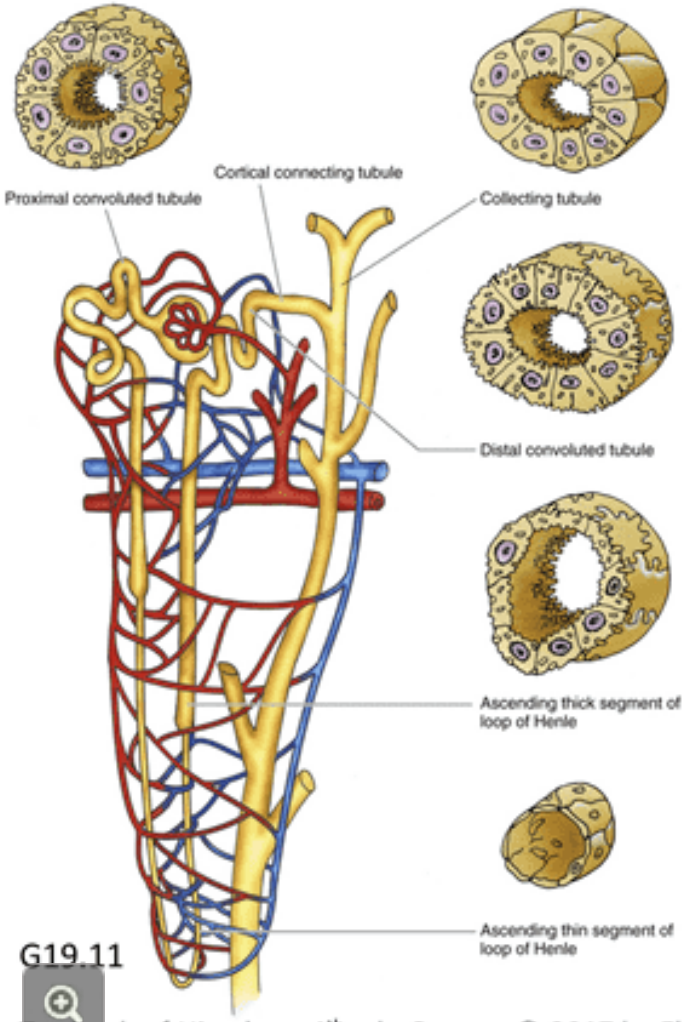

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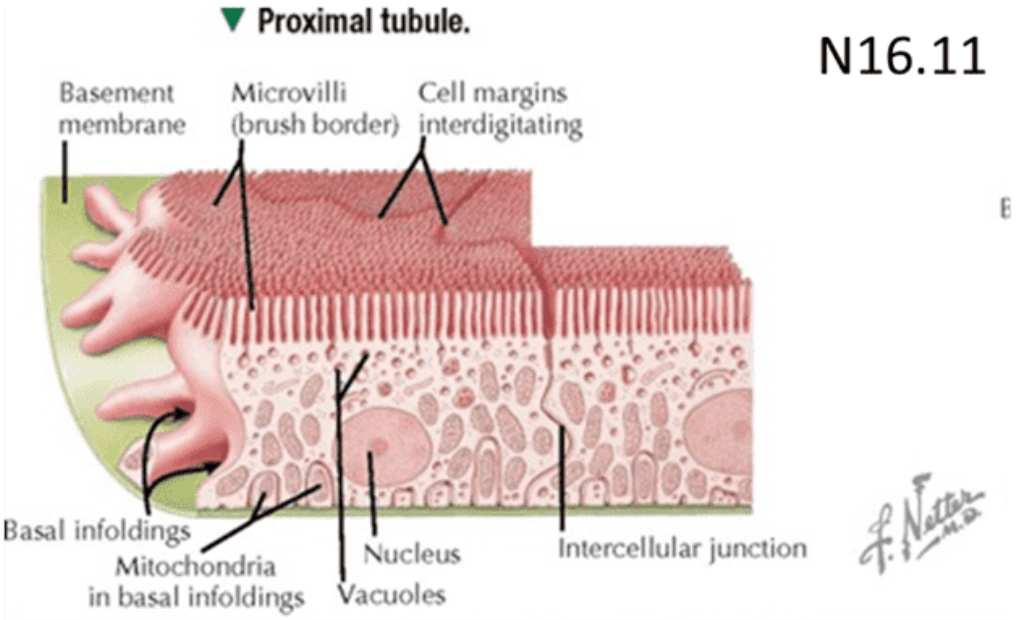
While these solutes are reclaimed by the PCT, others are added to the glomerular filtrate by **tubular secretion**. These include **cations unable to pass through the glomerular filter** and **organic anions**. Such solutes pass from the peritubular capillaries into the interstitium of the renal cortex, from there are taken up across the basolateral surface of the epithelial cells of the PCT, and then transferred across their apical surface into the tubular fluid. The **organic anion and cation transporters** involved act on physiological substances, such as **bile salts** and **creatinine**, but also transfer many **antibiotics** and other **drugs**, making tubular secretion **important in drug clearance**.

The epithelial lining of the PCT is **abundantly suited to its role in molecular transfer**. The apical surfaces of these cuboidal cells are densely packed with long **microvilli**, which accounts for the prominent brush border seen with the light microscope. The basolateral surface area is increased by elaborate **invaginations**. The invaginations of the lateral surfaces of adjacent cells interdigitate with each other, resulting in their characteristic indistinct lateral borders under the light microscope. Long **mitochondria** pack the basal invaginations and supply the ATP required for active molecular transport. With the electron microscope, numerous **endocytotic pits and vesicles**, as well as **lysosomes** are seen at the bases of the microvilli. These illustrate the intake of **proteins** by both **endocytosis and pinocytosis**, and its **lysosomal degradation**. Transport of the resulting **amino acids** across the basolateral membrane into the subadjacent interstitium completes the **reclamation** of protein that managed to pass through the glomerular filter. Also seen under the electron microscope are the **tight junctions** that control paracellular molecular movement, largely limiting it to water and Cl^-.



Netter's Essential Histology, 2nd ed., by Ovalle, and Nahirney,

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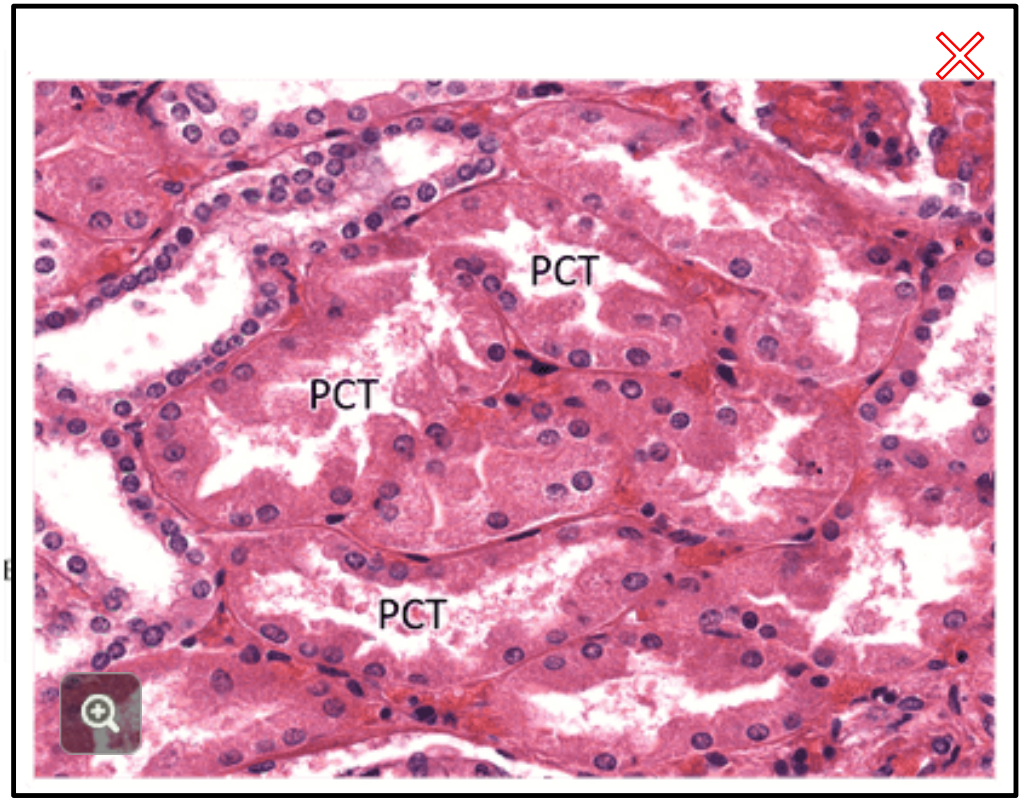

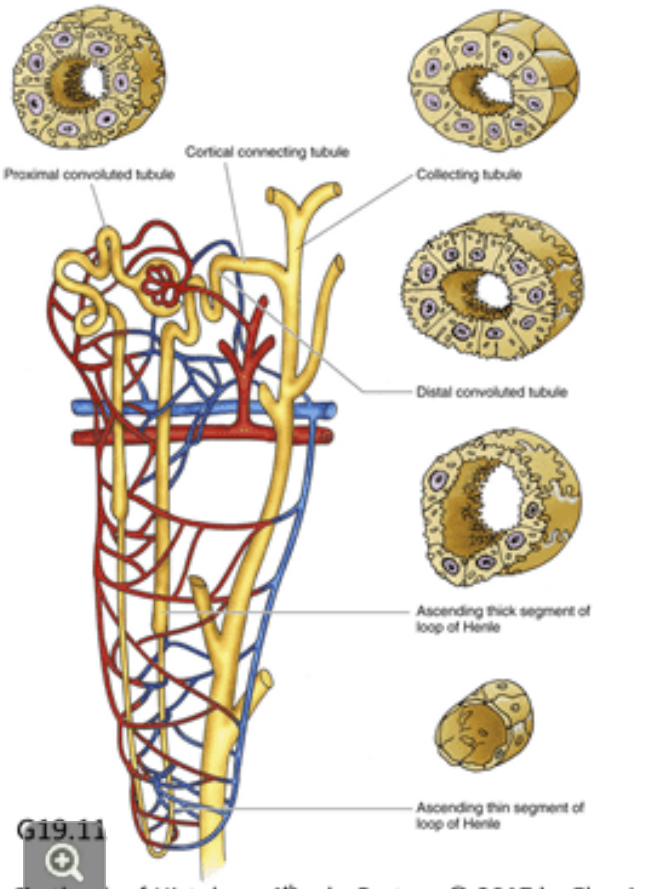

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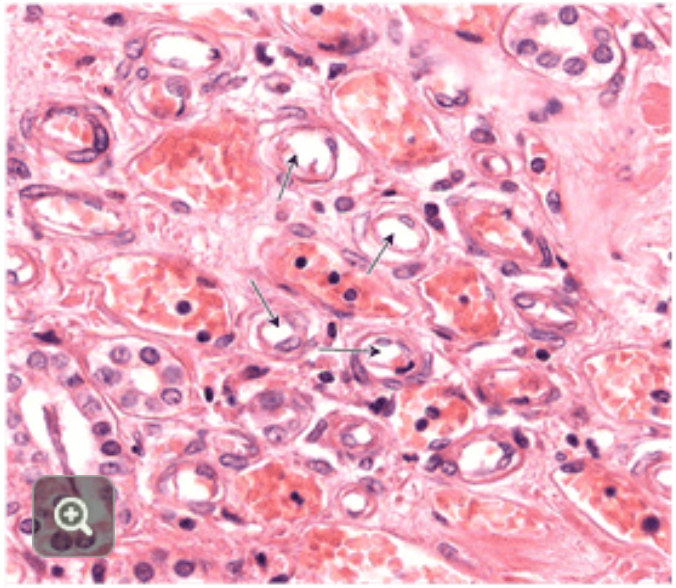
The next part of the renal tubule is the **loop of Henle**, which leaves the cortex to enter the medulla, and then turns back on itself to re-enter the cortex. The length of the loop of Henle varies; **cortical nephrons** have **short loops** that dip only a small distance into the renal medulla before returning to the cortex. **Juxtamedullary** nephrons have **long loops** of Henle that penetrate deep into the medulla, approaching the apex of the medullary pyramid, before turning back to re-enter the cortex.

The first part of the loop of Henle is variably called the **proximal straight tubule** or the **thick descending limb** of the loop of Henle. The outer diameter of the thick limb decreases abruptly, reflecting a sudden change in the tubular wall **from a simple cuboidal to a simple squamous epithelium**, which denotes the beginning of the **thin descending limb** of the loop of Henle. The thin descending limb turns back toward the cortex as the **thin ascending limb** of the loop of Henle. The structure of these portions of the renal tubule reflect their functions; the **squamous epithelium** lining the thin segments of the loop of Henle are largely involved in **passive transport functions**, and the epithelium lining the thin segments **respond passively to their surrounding interstitium**.



Cross-section showing many **thin descending and ascending limbs of the Loop of Henle.**

The thin descending limb of the Loop of Henle is a continuation of the proximal straight tubule. It is lined by simple squamous epithelium (arrows).

The next part of the renal tubule is the **loop of Henle**, which leaves the cortex to enter the medulla, and then turns back on itself to re-enter the cortex. The length of the loop of Henle varies; **cortical nephrons** have **short loops** that dip only a small distance into the renal medulla before returning to the cortex. **Juxtamedullary** nephrons have **long loops** of Henle that penetrate deep into the medulla, approaching the apex of the medullary pyramid, before turning back to re-enter the cortex.

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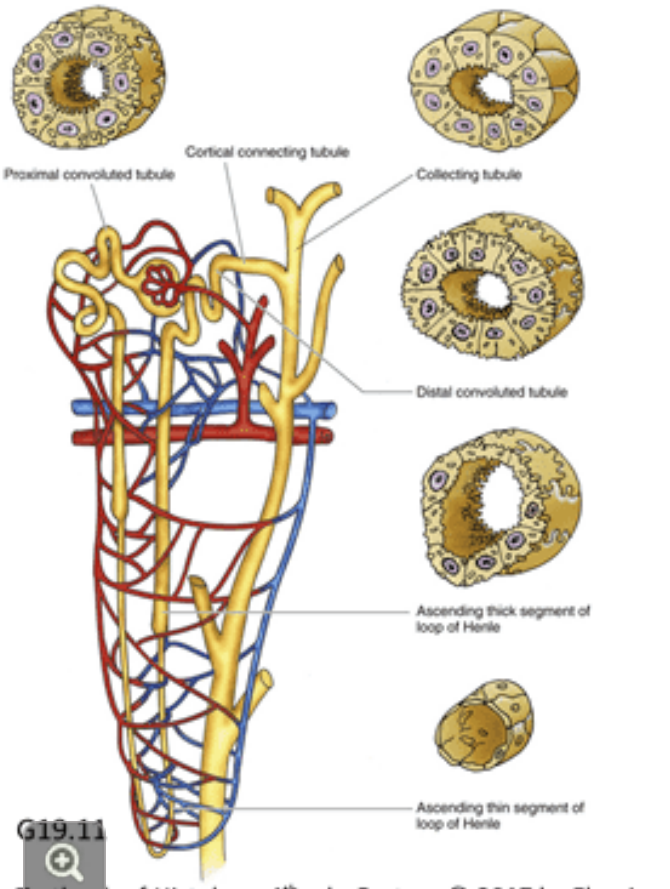

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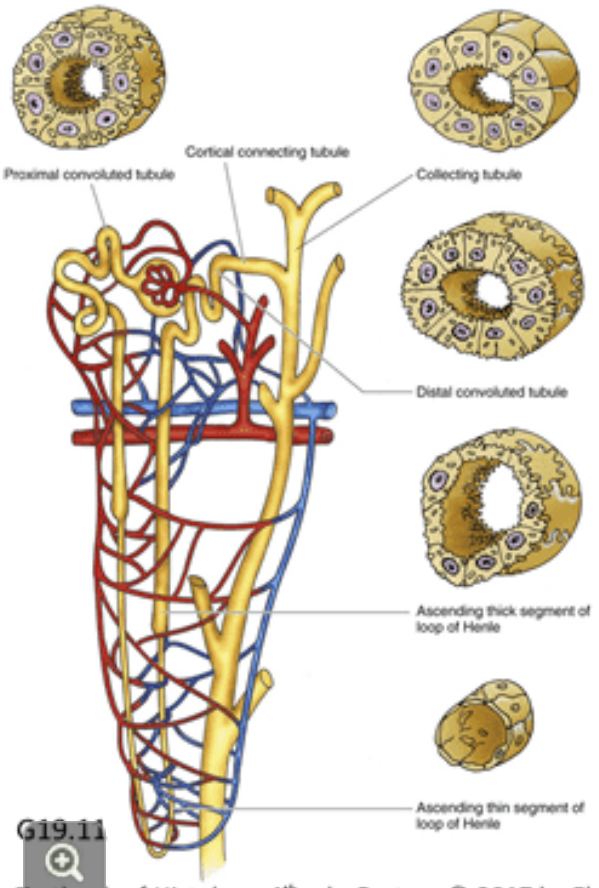
A similarly abrupt transition occurs in the structure of the ascending limb as it changes back **from a squamous to a cuboidal epithelium**, and is now called the **thick ascending limb**. The cuboidal epithelium of the thick ascending limb reflects its **function in active ion transport**. Its apical surface has some short microvilli and its lateral surfaces have some interdigitations, but these features are much more highly developed in the PCT. The basal surfaces of these epithelial cells are remarkable in the **elaborate infoldings of its basal membrane** and the **numerous mitochondria** associated with them. Very functionally important are the **highly-developed tight junctions** between adjacent cells in this tubular segment. The functional significance of these features will be explained. The thick ascending limb returns to the cortex, and passes between the afferent and efferent arterioles of the nephron, where its lining cells are modified to form the **macula densa**.



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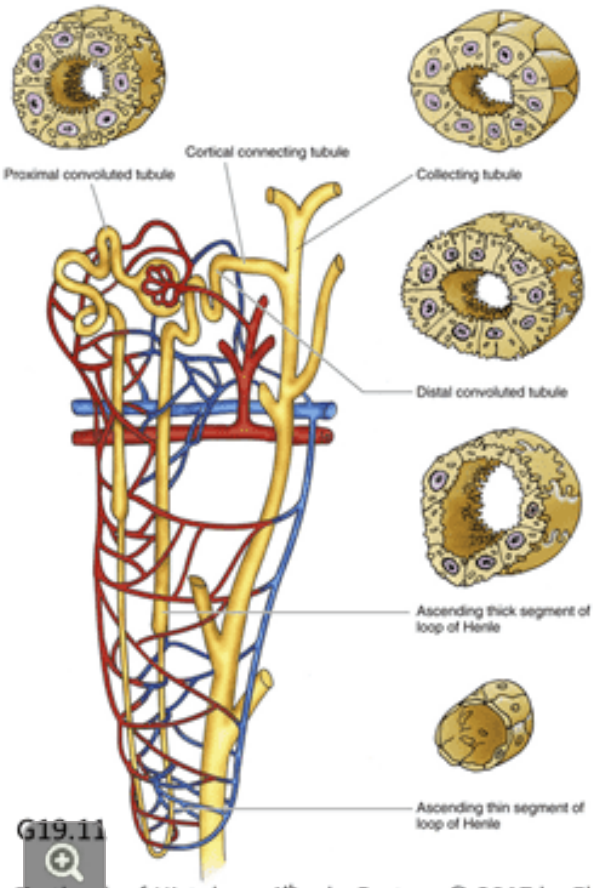
Recall that the peritubular capillaries of the juxtaglomerular nephrons give rise to the **vasa recta**. The course of the vasa recta parallels that of the loops of Henle: they enter the medulla from the cortex, make a hairpin turn and return to the cortex to **empty into the arcuate veins**. Between them, **the loops of Henle and the vasa recta function to generate a high osmotic pressure in the interstitial fluid of the renal medulla**. This is achieved by the different permeability characteristics of the regions of the loops in a process known as the **counter-current exchange mechanism**. As you will see, the functional significance of the high osmotic pressure in the renal medullary interstitium is that it acts as a force **capable of drawing water out of the renal filtrate passing through the renal collecting ducts, thus conserving water and concentrating urine**.



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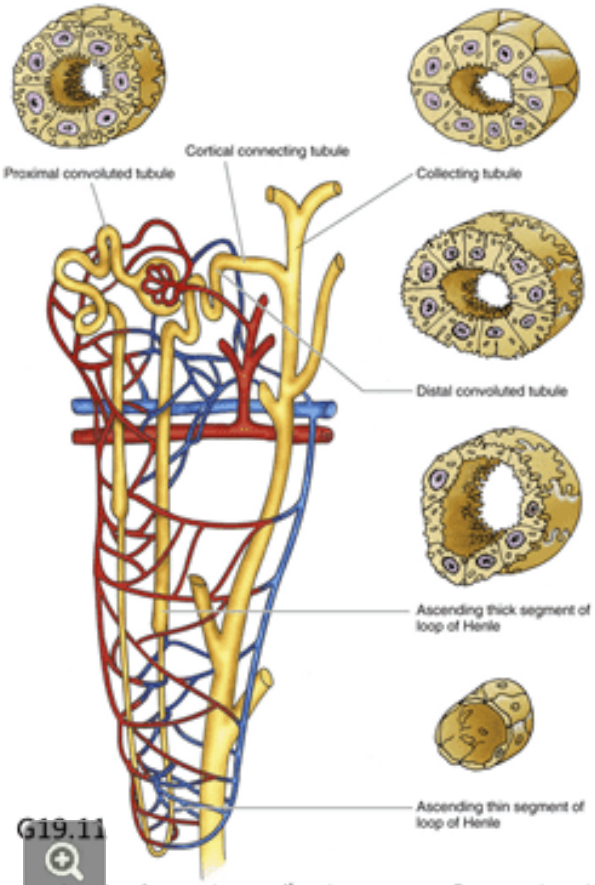
The countercurrent exchange mechanism is best explained by **starting at the thick ascending limb** of the loop of Henle.

As the tubular fluid in this segment flows toward the renal cortex, the epithelium lining the thick ascending limb **actively transports Na^+, K^+ and Cl^-** out of the tubular filtrate and **into the renal medullary interstitium**. The thick ascending limb is, however, **impermeable to water**. This has two effects: **the renal interstitium becomes hyperosmotic**, and the **tubular fluid becomes hypo-osmotic**.

The amount of salt transferred to the interstitium decreases with the salt content of the tubular fluid as it ascends through the ascending thick limb, and thus **an osmotic gradient is established in the renal medulla**, such that the osmolality of the interstitial fluid is **4x plasma at the apex of the medullary pyramid** and **iso-osmotic with plasma at the cortico-medullary junction**.



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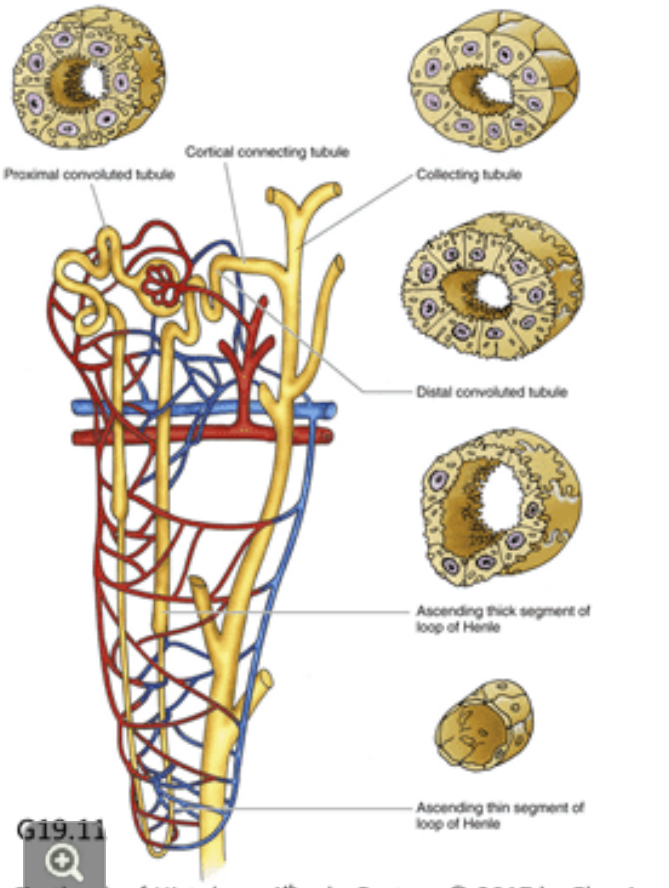
Meanwhile, back at the renal corpuscle, glomerular filtrate is iso-osmotic to plasma. In the PCT, equal amounts of solute and water are absorbed, and therefore, the tubular fluid entering the loop of Henle is also iso-osmotic to plasma. Because the **descending thin limb is freely permeable to water**, water is absorbed from the filtrate as it passes through this segment, and the absorbed water is reclaimed by the vasae rectae carrying blood back toward the cortex. The tubular filtrate equilibrates with the renal interstitium and its osmolality, too, becomes 4x plasma at the apex of the renal medulla.

Because the **ascending thin limb is impermeable to water, but freely permeable to salts**, salts move from the filtrate into the interstitium in response to the osmotic gradient as the fluid moves through the thin ascending limb. **Now we're back at the thick ascending limb**, where salts are actively removed from the filtrate, but water cannot follow. **This creates in the hypo-osmotic tubular fluid that enters the distal convoluted tubule (DCT).**



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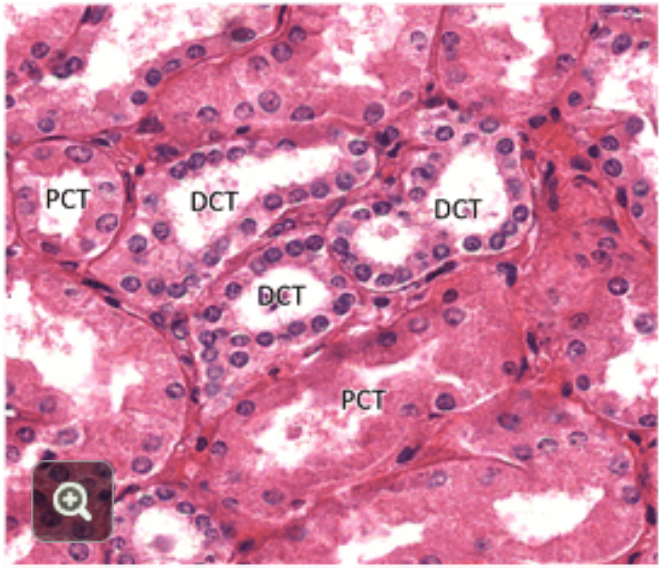
The DCT is short, as compared to the PCT, and much less absorption takes place here. Like the thick ascending limb of the loop of Henle, the cells lining the DCT are **cuboidal** and bear a **few, blunt microvilli**. However, here the **basal interdigitations are less well-developed and the mitochondria less numerous**. DCTs empty, via their connecting tubule, to collecting tubules, which coalesce to form the collecting ducts.

Like the thick ascending limb of the loop of Henle, the DCT is **impermeable to water**. In response to the hormone **aldosterone**, these cells are **capable of absorbing almost all remaining Na^+ (with Cl^- following), and secreting K^+ and H^+ into the tubular lumen**. The filtrate that leaves the DCT, and therefore the nephron, to enter the renal collecting system, is thus **hypotonic**.



Cross-section showing **distal convoluted tubules (DCT)**.

Cells lining the DCT are cuboidal with few microvilli, so their lumena are circular, as compared to the stellate-shaped lumena of the PCT. The cells in the DCT are smaller, more tightly-packed and more neutral-staining as compared to cells of the PCT.

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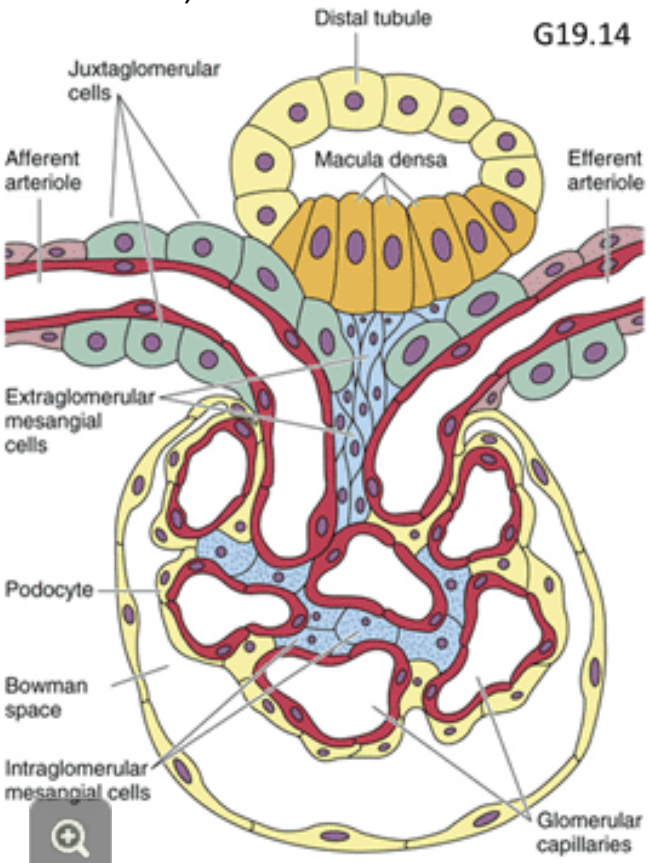
The juxtaglomerular apparatus (JGA) is a specialization of the afferent arteriole and distal tubule of the same nephron. It consists of the **macula densa of the distal tubule**, the **juxtaglomerular cells** (JG cells) **of the afferent arteriole** and the **extraglomerular mesangial cells**. The JGA functions to regulate glomerular blood flow, and therefore GFR.



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The **macula densa** consists of **modified epithelial cells of the distal tubule** in the region where it contacts the vascular pole of the renal corpuscle. Cells of the macula densa are tightly-packed columnar cells and their darkly-staining nuclei give it a dense appearance under the light microscope.

Adjacent to the macula densa, the smooth muscle cells in the tunica media of the afferent arteriole are modified as **JG cells**, which are richly innervated by the **sympathetic nervous system** and bear the appearance of **secretory cells**. Their **granules contain the protease renin**.

The third component of the JG apparatus are the **extraglomerular mesangial cells**., which **surround and support** the structures of the vascular pole of the renal corpuscle, the **afferent and efferent arteriole and the macula densa** of the distal tubule. The extraglomerular mesangial cells are likely continuous with the intraglomerular mesangial cells, and have many of the same supportive and contractile functions.

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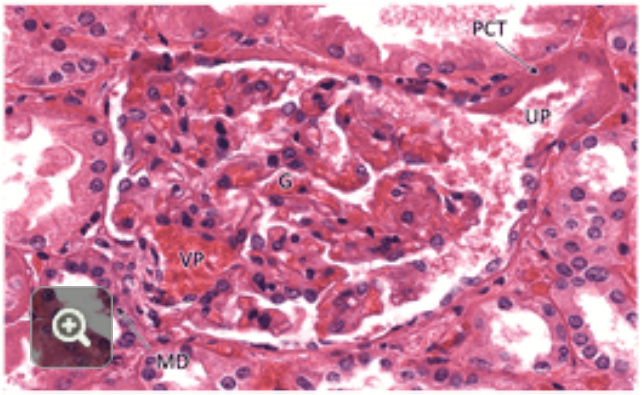

Histological image of a renal corpuscle.

Macula densa (MD), tightly-packed columnar cells lining the distal tubule where it contacts the afferent arteriole at the vascular pole.

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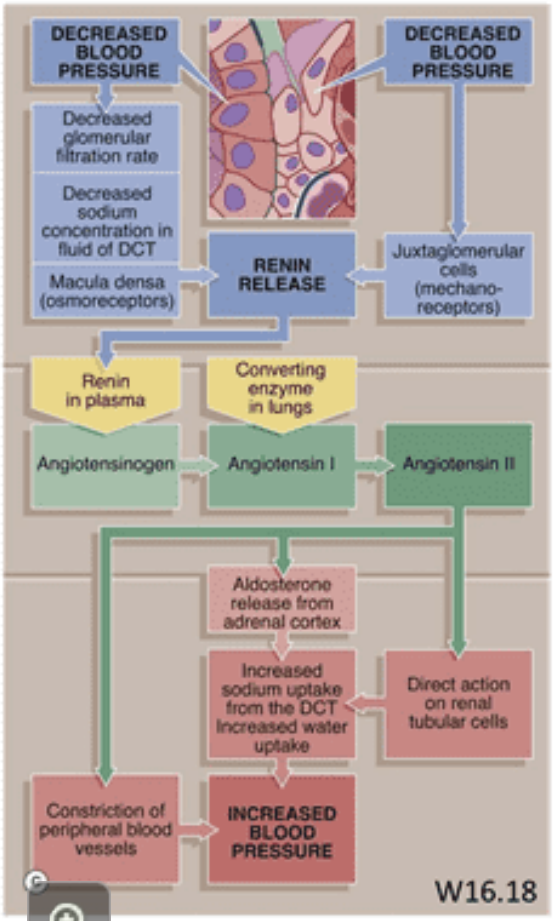


Wheater's Functional Histology, 6th ed., Young, O'Dowd, and Woodford, ©2014 by Elsevier (Churchill Livingstone).

Renin is an enzyme that catalyzes the first step in a hormonal cascade that elevates blood pressure (BP). Renin release from the JG cells is controlled by three main mechanisms.

Baroreceptors in the **afferent arteriole** monitor BP. A drop in BP triggers the release of renin from JG cells.

The cells of the **macula densa** are **chemosensors** that monitor the Na^+ concentration of the fluid in the distal tubule. Decreased BP decreases GFR, which decreases the Na^+ ion concentration of the distal tubular fluid. This is detected by the macula densa which triggers the release of renin from the JG cells.

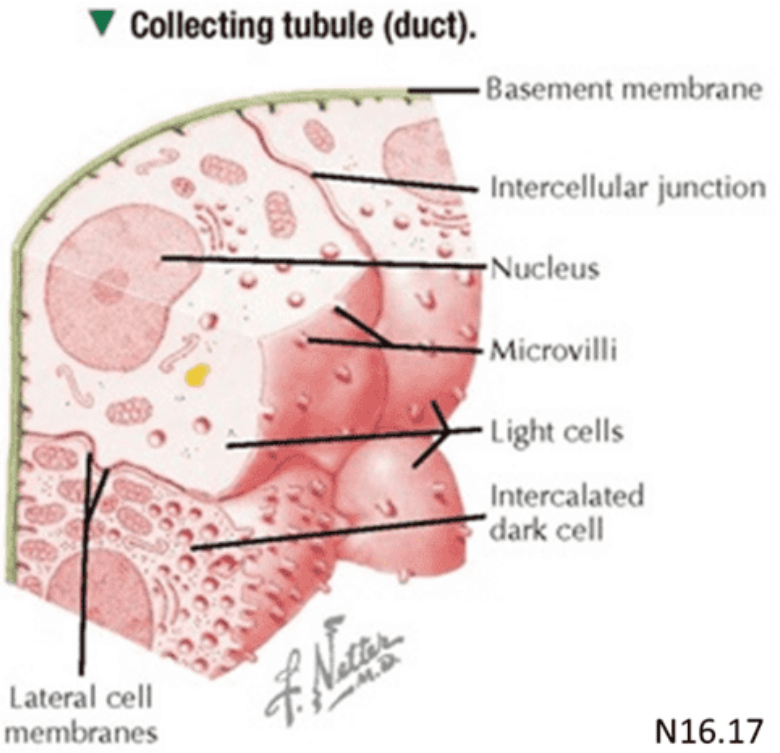
Sympathetic input to the kidneys increases with a drop in BP, which again stimulates the release of renin from the JG cells.

Renin catalyzes the conversion of **angiotensinogen**, produced in the liver, to **angiotensin I (A I)**. **Angiotensin converting enzyme (ACE)**, present on endothelial cells, particularly in the lungs, converts AI to **angiotensin II (A II)**.

A II is a **potent vasoconstrictor**. It also stimulates the release of **aldosterone** from the adrenal cortex, which promotes the adsorption of Na^+ and Cl^- in the DCT. Lastly, A II stimulates the release of **antidiuretic hormone, ADH**, from the posterior pituitary, which, as will be described next, **increases the permeability of the renal collecting ducts to water**, thereby promoting its retention. All of these actions **elevate BP**.

The nephron ends with a short segment called the **connecting tubule**, into which the hypotonic fluid of the DCT flows. The connecting tubules of many nephrons join to form a **collecting duct**. Many collecting ducts group together to form the **medullary rays** of the **renal lobule**. The collecting ducts pass from the **renal cortex** through the **renal medulla** and coalesce to form **papillary ducts**, which open at the **renal papilla** to **empty into a minor calyx**. Because the tubes of the renal collecting system run parallel to the loops of Henle and vasa recta, **the tubular fluid in the collecting system is exposed to the hyperosmotic interstitium of the renal medulla**.

The epithelial cells lining the collecting ducts include pale-staining **principal cells** which have short microvilli and few mitochondria. These cells have numerous basal, but not lateral, membrane infoldings and are joined by elaborate tight junctions. Principle cells express **aquaporin channels**, which they store intracellularly in membranous vesicles. In the **presence of ADH**, they **insert the aquaporin-containing vesicles into their apical membranes**, a process that is **reversed in the absence of ADH**. Aquaporin channels are constitutively present in their basal domains.



Netter's Essential Histology, 2nd ed., by Ovalle, and Nahirney, Copyright © 2013, 2008 by Elsevier (Saunders.

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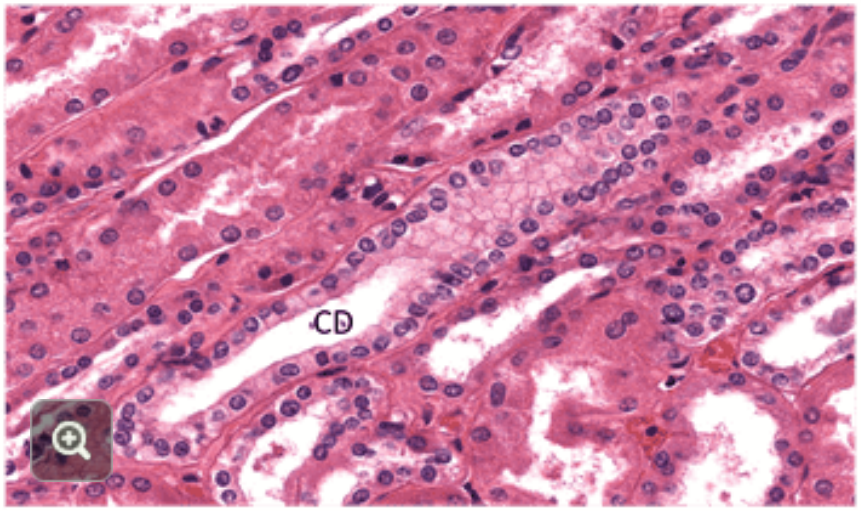
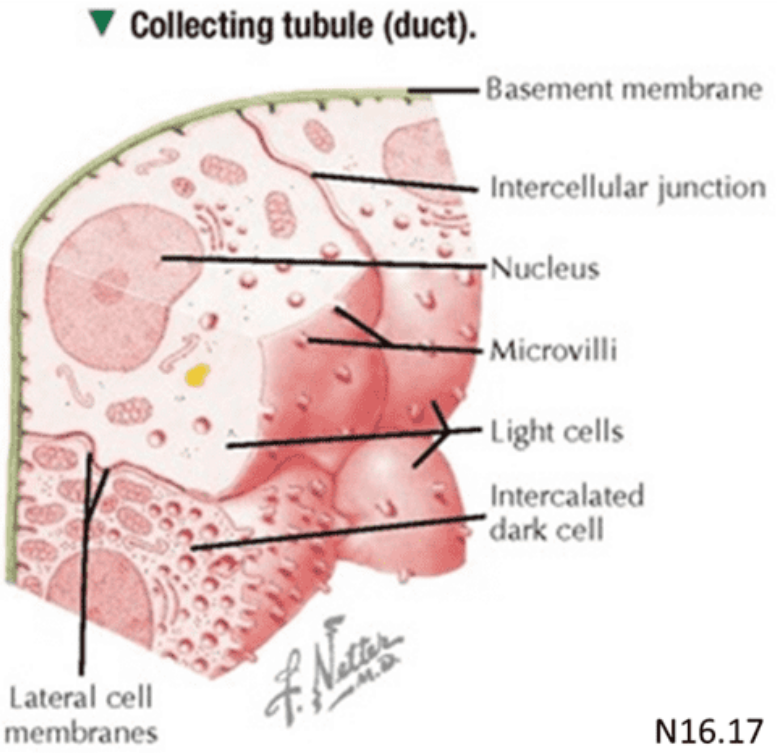


Histological image of a **collecting duct (CD)**.

The epithelial lining of the CD is simple cuboidal to simple columnar with **well-defined borders** between cells. These borders are **not visible in the PCT or DCT**. Cells of the CD also stain lightly as seen in this image.

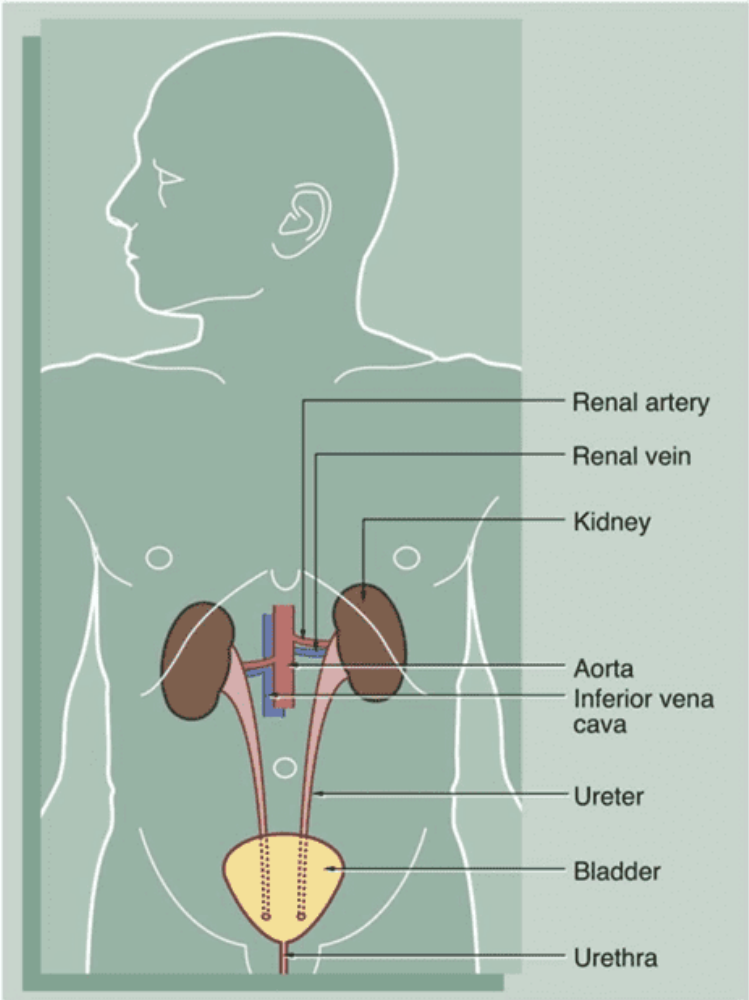
In the **absence of ADH**, the collecting ducts are **impermeable to water**, and a **large volume of dilute urine** is excreted. In the **presence of ADH**, the collecting ducts become **permeable to water**. The hypertonic renal interstitium is now able to **absorb water** from the hypotonic fluid that enters the collecting ducts from the DCT, and deliver it to the vasae rectae. This results in **water retention** and the excretion of a **smaller volume of concentrated urine**.

In addition to the principle cells, the renal collecting ducts include dark-staining **intercalated cells**, with abundant mitochondria and apical infoldings, which function in acid-base homeostasis. Type A (or α-intercalated) cells acidify urine through the secretion of H^+, while type B (or β-intercalated) cells decrease the acidity of urine through the secretion of HCO_3^-.

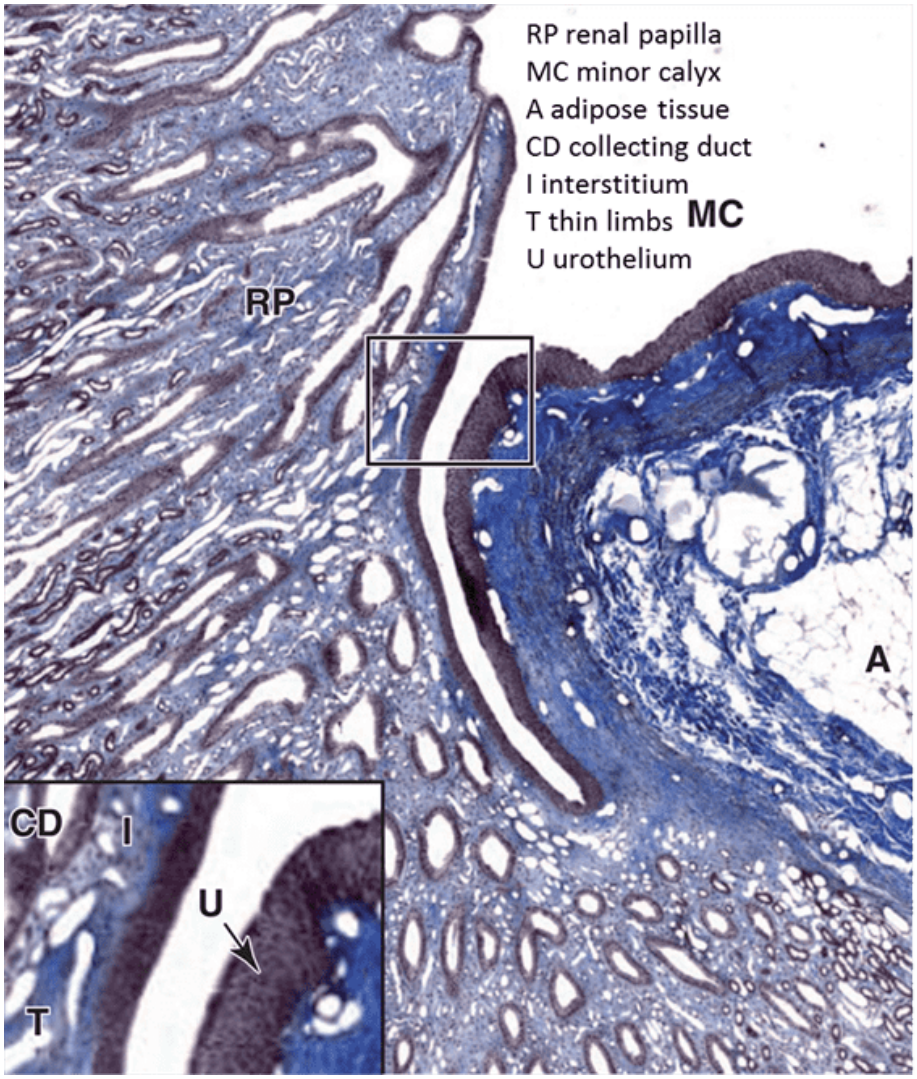


As no modification of urine occurs after it drips from the renal papilla into the minor calyx, the lower urinary tract simply functions to **conduct and store urine**. It starts with the minor calyx, and continues with the major calyx, renal pelvis, ureter, urinary bladder and urethra.

The components of the lower urinary tract are hollow structures with **muscular walls**. With the exception of the distal urethra, the lower urinary tract is lined by a mucosa that includes a **transitional epithelium** which, you will recall, is specialized for its ability to **stretch and recoil** in response to pressure. It is also **protective**, shielding the underlying tissues from exposure to the contained urine. The thickness of the transitional epithelium varies in different regions of the lower urinary tract. Appropriately, the **fibroelastic lamina propria** that supports this epithelium also stretches to accommodate luminal filling.



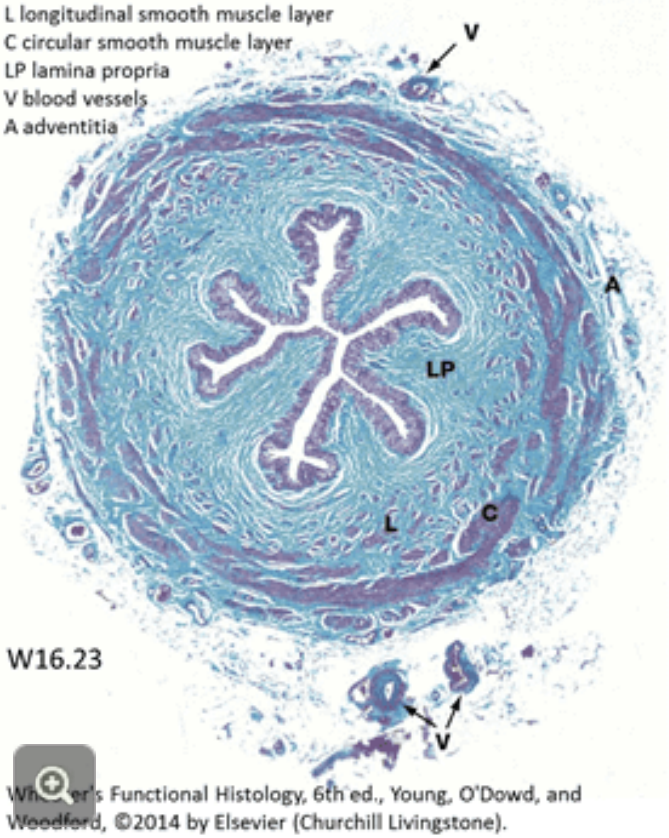
Wheater's Functional Histology, 6th ed., Young, O'Dowd, and Woodford, ©2014 by Elsevier (Churchill Livingstone).



There are generally **10-15 renal lobes** per kidney, each of which is served by a **minor calyx**. Minor calyces unite, forming the 3-4 **major calyces** that are characteristic of each kidney. These major calyces coalesce to form the **renal pelvis**, which narrows to form the **ureter**.

The transitional epithelium lining the minor calyces is thin, consisting of only 2-3 cell layers. Underlying its fibroelastic lamina propria is a **smooth muscle layer** that contracts to propel urine from the minor calyx to a major calyx. The wall of the minor calyx is enclosed in an adventitia. The structure of the major calyx and renal pelvis is similar, but the layers increase in thickness as the passages unite.

J19.16

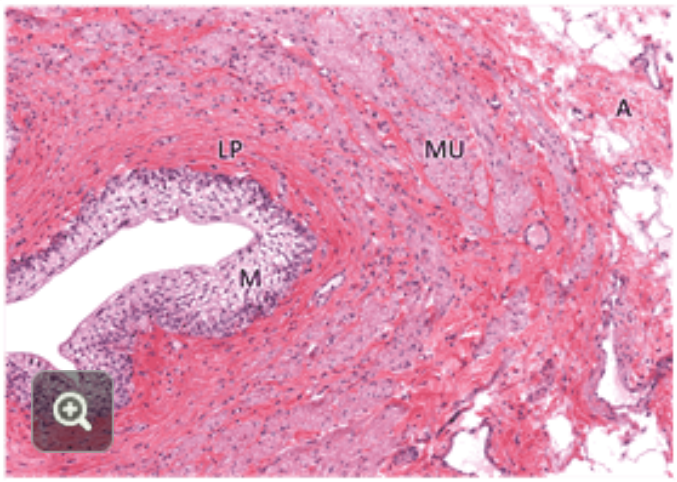


The ureters extend from the hilum of the kidney to the base of the urinary bladder. Each is 3 - 4 mm in diameter and about 30 cm long. Ureters are hollow tubes consisting of three layers; from the lumen outward, these are the mucosa, muscularis and an adventitia.

As illustrated in the accompanying micrograph, the **mucosa (M)** of the ureter is thrown into **longitudinal folds** when its lumen is empty; it unfolds as required to accommodate the passage of urine. The **transitional epithelial lining (urothelium)** is thicker than that of the calyces, consisting of 3-5 layers of cells, as is its underlying **fibroelastic lamina propria (LP).**

The **muscularis (MU)** of the proximal ureter consists of two layers of smooth muscle, but as it approaches the bladder, the ureter acquires a third layer of muscle. Urine is conducted from the kidneys to the bladder **by peristalsis**.

The **adventitia (A)** of the ureter blends with the kidney capsule proximally and with the adventitia surrounding the bladder distally. The ureters pass through the bladder wall **obliquely**. Because the muscular wall of the bladder is under constant tone, it **compresses the intramural portions of the ureters** and **prevents the backflow of urine**. When the bladder wall contracts during micturition, even greater pressure is applied to the intramural portion of the ureters, ensuring the one-way flow of urine into the urethra.



Remember, the epithelial component of the **mucosa (M)** of the ureter is composed of **transitional epithelium**!

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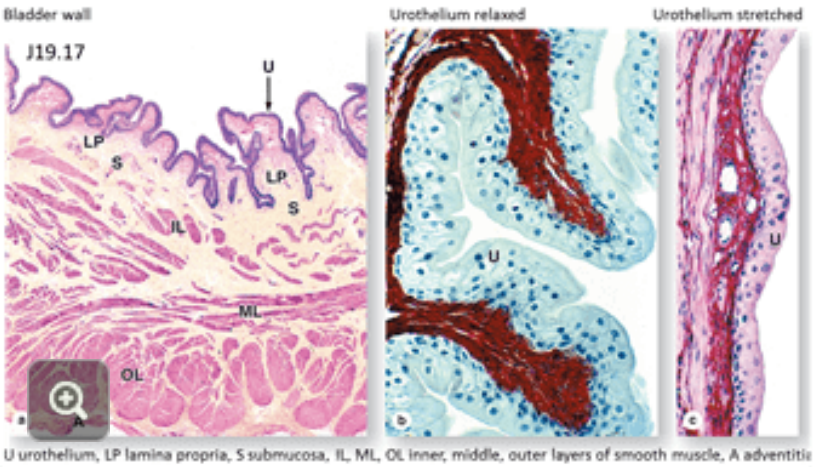
The urinary bladder stores urine until a convenient time and place presents itself for excretion.

The mucosal (M) surface of the bladder is long exposed to formed urine. Its **transitional epithelium** is therefore particularly **well developed**, consisting of 6 to 8 layers of cells. The epithelium lining the bladder must prevent the osmotic movement of water from underlying tissues into hypertonic urine. An osmotic barrier is created by the presence of well-developed **tight junctions** between adjacent cells and the presence of unusual integral membrane proteins in their apical surfaces that thicken the cell membrane.

The **muscularis (MU)** of the urinary bladder consists of three poorly-organized layers of muscle collectively called the **detrusor muscle**. Only at the neck of the bladder are the layers of smooth muscle organized into distinct layers. Here, the muscle fibres are organized into an innermost longitudinal layer, an intermediate circular layer, and an outermost longitudinal layer. The middle layer surrounds the first part of the urethra and forms the involuntary **internal urethral sphincter**.



U urothelium, LP lamina propria, S submucosa, IL, ML, OL inner, middle, outer layers of smooth muscle, A adventitia

While its superior surface faces the peritoneal cavity and is covered by a serosa, the bulk of the bladder is covered by an **adventitia**.

In the micturition reflex, sensory fibres detect stretch of the bladder wall and **parasympathetics** stimulate **contraction of the detrusor muscle** and **relaxation of the internal urethral sphincter**, which permits bladder emptying. The **sympathetic** nervous system controls vascular tone in bladder tissues. It also stimulates contraction of the internal urethral sphincter during emission to prevent semen from entering the bladder.

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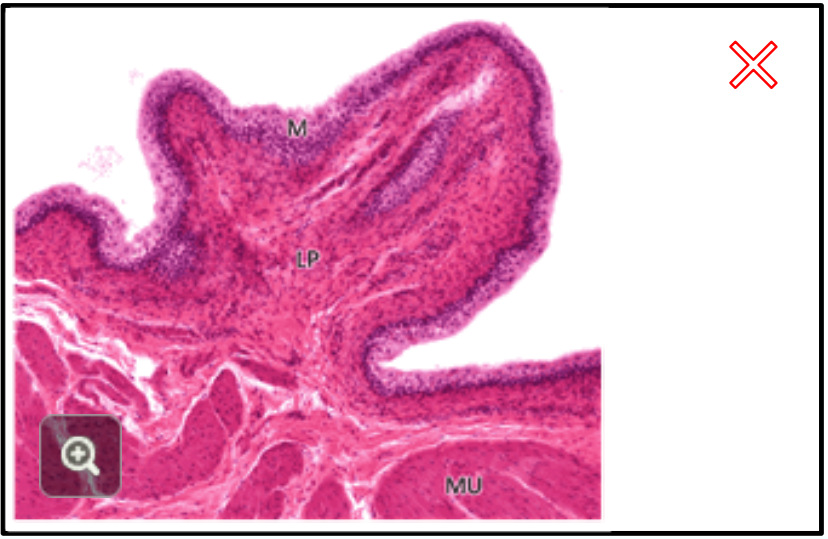

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During the **micturition reflex**, the urethra conducts urine from the urinary bladder to the exterior to the body at the **external urethral orifice.** Numerous **mucous-secreting glands** along its length provide a protective coat of mucous to its epithelial surface. It has a **fibroelastic lamina propria** and a **thin muscularis**. The details of its structure differs in men and women.

In **women**, the urethra is about **5 cm long**, and its inner lining of transitional epithelium quickly changes to stratified squamous epithelium. Just superior to the perineal membrane, the urethra is surrounded by a **skeletal muscle sphincter** which is **under voluntary control**. This is the **external urethral sphincter**.

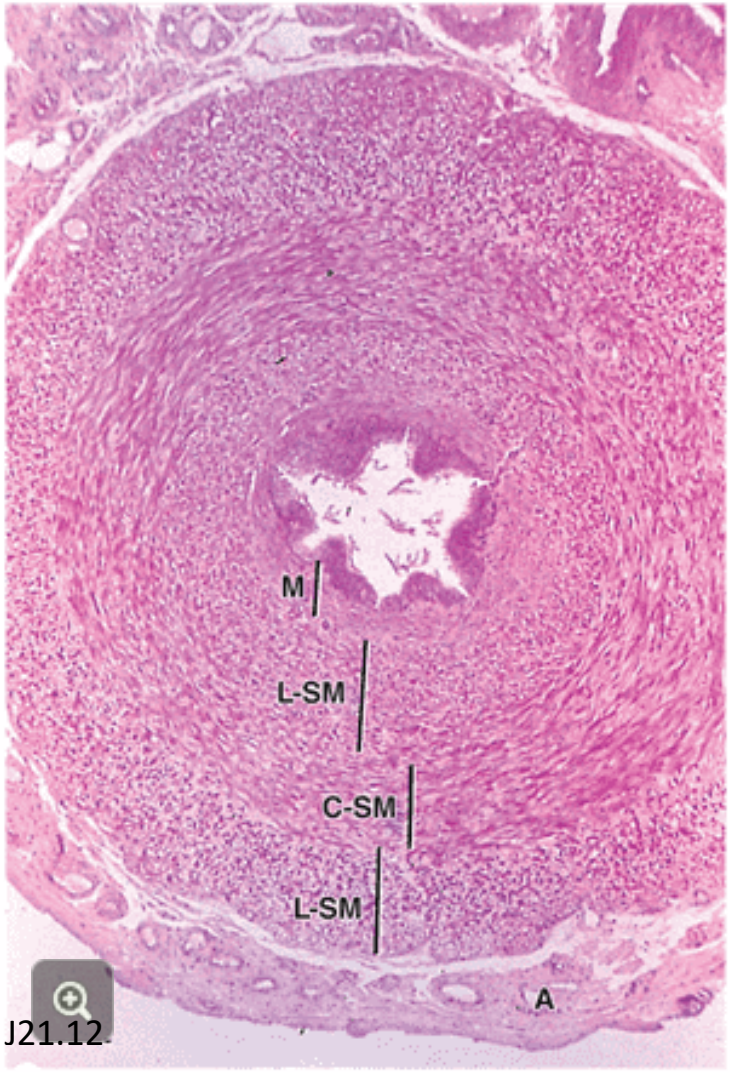
In **men**, the urethra is approximately **20 cm long**, and is divided into the:

i) **prostatic urethra**, 3-4 cm long, and entirely surrounded by the prostate gland. It receives the numerous openings of the ducts of the prostate gland, as well as the paired ejaculatory ducts from the male reproductive tract.

ii) **membranous urethra**, 1-2 com long, which passes through the perineal membrane. As in females, just superior to the perineal membrane the urethra is surrounded by the **external urethral sphincter**, composed of skeletal muscle and under voluntary control.

iii) **spongy urethra**, 15 cm long, which passes through the length of the corpus spongiosum of the penis.

The male urethra is initially lined by a transitional epithelium, which changes first to a stratified columnar and then a stratified squamous epithelium as it approaches the external urethral orifice.

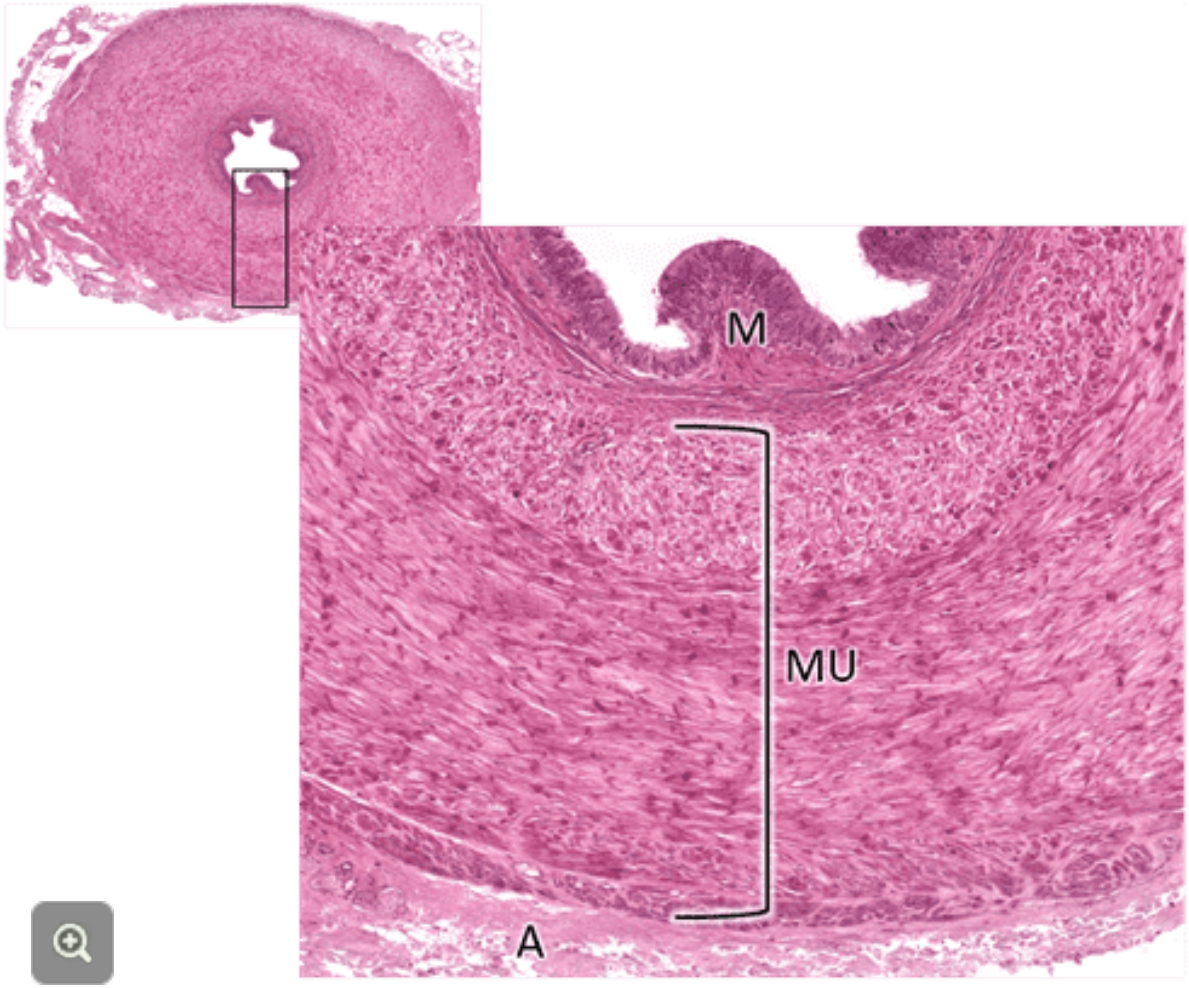


J21.12

From the tail of the epididymis, the **ductus (vas) deferens** ascends posterior to the testis, and leaves the scrotum as a component of the spermatic cord, along with the testicular BVs, Ns and Ls. These structures pass through the inguinal canal, and at the deep inguinal ring, the vas diverges from the other components of the spermatic cord, which pass retroperitoneally to the posterior body wall, along the path taken by the testis during its descent. The vas **arches over the bladder to its base**, where it widens as the **ampulla**. It merges with the **duct of the seminal vesicle**, to form the short **ejaculatory duct**, which opens into the **prostatic urethra**.

Histologically, the vas deferens consists of a mucosa, a muscularis and an adventitia. The **mucosa (M)** includes a pseudostratified epithelium and an elastic LP. It is thrown into folds when empty, which allow expansion with the passage of fluid during emission. The **muscularis (MU) is extraordinarily thick**, and consists of three layers: outer and inner longitudinal layers with a circular layer intervening. It is capable of very strong **peristaltic contractions during emission**.

M mucosa
L-SM longitudinal layer, smooth muscle
C-SM circular layer, smooth muscle
A adventitia

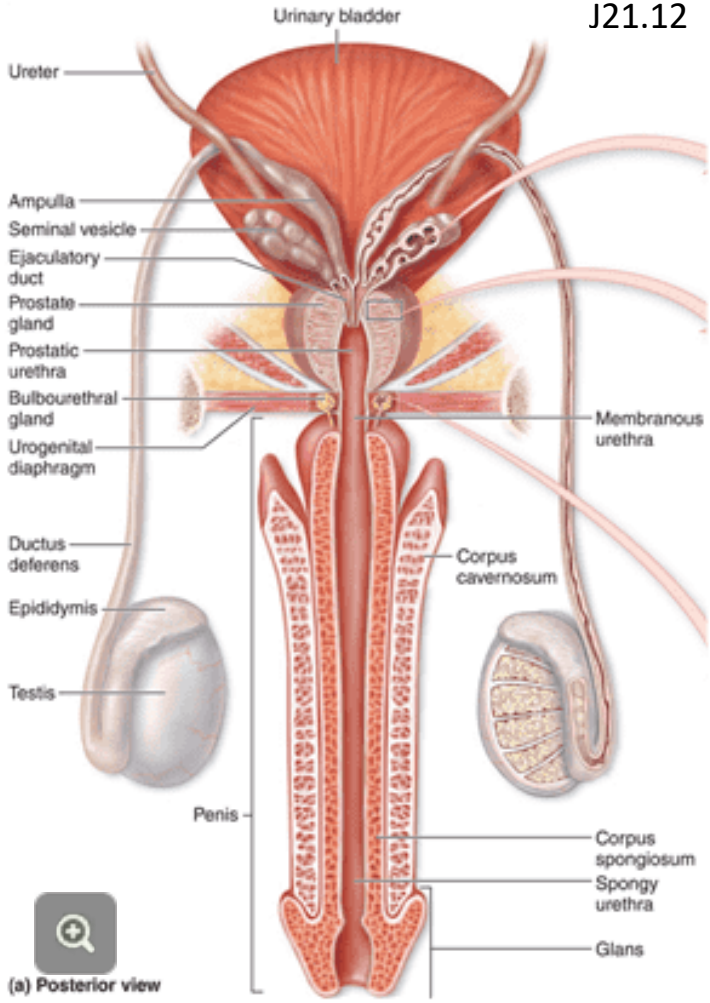


Histological image of the **Vas Deferens**.

Mucosa (M) lined by pseudostratified columnar epithelium.

Thick **muscularis (MU)** composed of three layers; inner longitudinal, middle circular and outer longitudinal – allows for strong peristaltic contractions during ejaculation.

Adventitia (A) composed of loose CT.



The **accessory glands** of the male reproductive system are the prostate, the seminal vesicles and the bulbourethral glands. At emission, their secretions mix with sperm to form **semen**.

The histological structure and activity level of these glands is **testosterone-dependent**. The height of their epithelial lining increases with circulating testosterone levels, as does the manufacturing of their secretory products.

All include abundant **smooth muscle** that contracts during **emission** to expel their secretions into the reproductive tract.

The **seminal vesicles** are paired tubular glands posterior to the bladder, inferior to the ureters. Each is 15 cm in length, coiled into a compact structure ~3 cm long, enclosed in a dense CT capsule. Their ducts merge with the ampullae of the vas to form the **ejaculatory ducts**, which open into the prostatic urethra.

The seminal vesicles are lined with a **mucosa** that includes a simple to pseudostratified epithelium and an elastic LP. Their secretory product contributes **70%** of the volume of ejaculate. It is rich in **fructose**, which is a major energy source for sperm, **prostaglandins**, which stimulate the female reproductive tract, and **fibrinogen**, which promotes the coagulation of sperm following ejaculation.

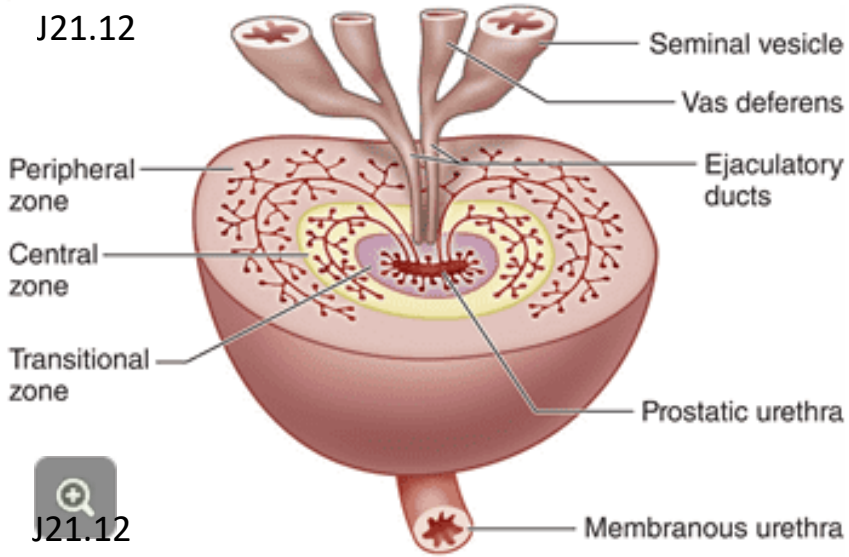
The **prostate gland** surrounds the neck of the bladder and the initial portion of the urethra, the prostatic urethra. It is 2 cm x 3 cm x 4 cm, and is often described as being the size of a walnut.

It consists of **30-50 tubuloacinar glands** embedded in a dense **fibromuscular stroma** that **contracts** to expel its secretory products **at emission**. The prostatic urethra passes through the middle of the gland, the ducts of which open into its lumen. The prostate is divided into **three concentric histological zones**.

The **transitional zone** surrounds the initial portion of the prostatic urethra and comprises 5% of its volume. It includes the periurethral mucosal glands, which are commonly implicated in **benign prostatic hypertrophy**, a common condition in older males that causes compression of the urethra and difficulty with urination.

The **central zone** comprises 25% of the gland and includes the periurethral submucosal glands.

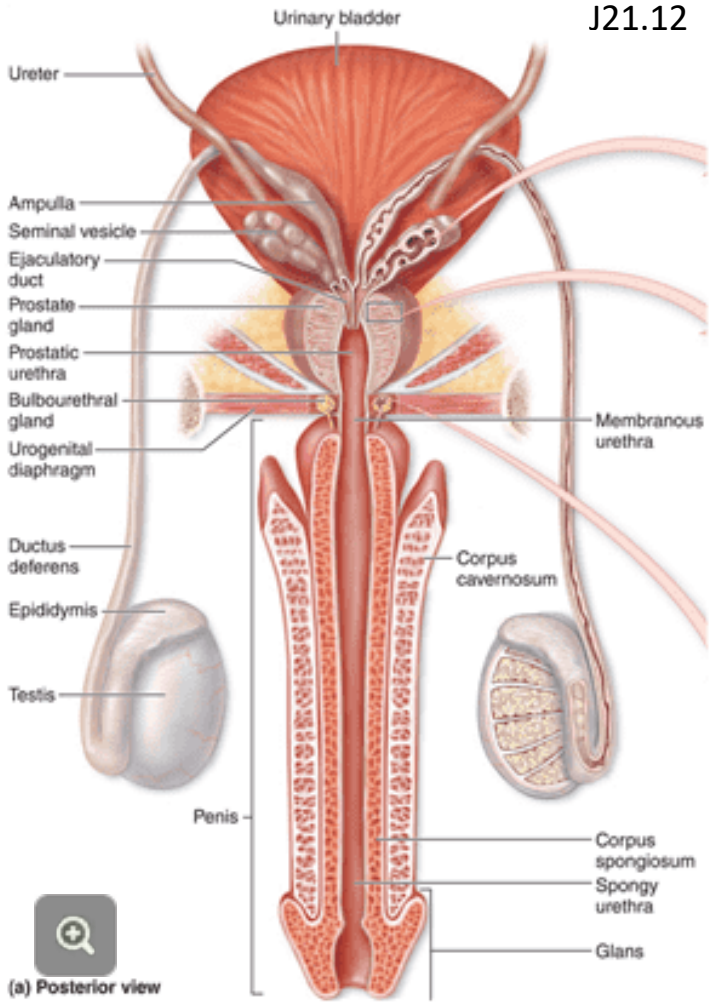
J21.12



J21.12

The **peripheral zone** comprises 70% of the prostate and includes the main glands. Glands of this zone are **most commonly implicated in prostate cancer**.

The products of the simple or pseudostratified epithelium of the prostate gland include **prostate-specific antigen (PSA)**, a serine protease that disassociates coagulated semen after ejaculation. Some PSA enters the prostatic vasculature and is thus **normally present in blood**. Elevated levels of serum PSA are suggestive of abnormal glandular mucosa, commonly due to inflammation or carcinoma.



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The **bulbourethral (Cowper's) glands** are paired, pea-sized glands located in the deep perineal pouch. Their ducts extend to open into the proximal portion of the penile urethra. Each gland is composed of many lobules containing tubuloacinar secretory units. The mucosa of the secretory units includes a simple columnar epithelium which **secretes a mucous product**. The height and activity level of the epithelium is, again, testosterone-dependent.

The bulbourethral glands produce a clear mucous secretion **during erection** that lubricates the wall of the urethra. This ensures the smooth passage of semen during emission.

Which vessels run parallel to the base of the renal pyramid?

- [ ] afferent arterioles
- [ ] interlobar arteries
- [ ] arcuate arteries
- [ ] peritubular capillaries

SUBMIT

Which type of epithelium lines the thick ascending limb of the loop of Henle?

- [ ] pseudostratified columnar
- [ ] simple cuboidal
- [ ] simple columnar
- [ ] stratified squamous
- [ ] transitional

SUBMIT

From what vessels do the afferent arterioles arise?

- [ ] the interlobar arteries
- [ ] the arcuate arteries
- [ ] the interlobular arteries
- [ ] the efferent arteries

SUBMIT

Which of the following is a functionally important feature of the light cells of the renal collecting ducts?

- [ ] a high level of aquaporin expression
- [ ] tall, dense microvilli
- [ ] elaborate infoldings of the basal plasmalemma
- [ ] abundant mitochondria

SUBMIT

Which of the following is NOT a component of the juxtaglomerular apparatus?

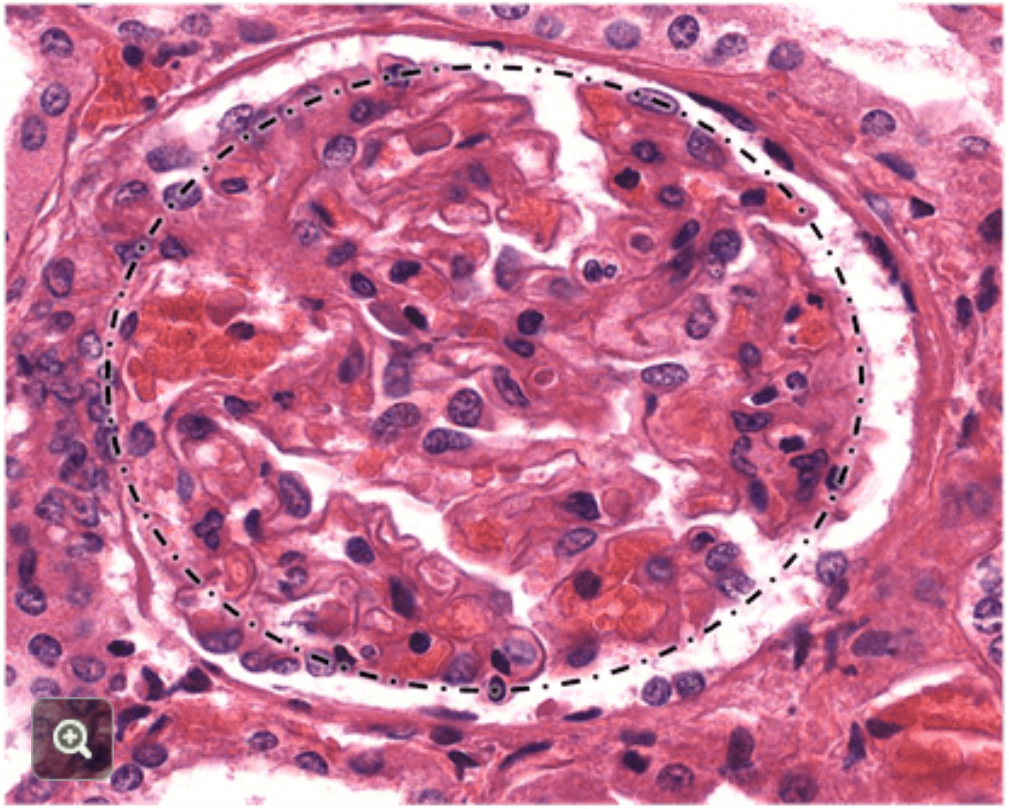
- [ ] modified smooth muscle cells of the afferent arteriole
- [ ] extraglomerular mesangial cells
- [ ] intraglomerular mesangial cells
- [ ] modified cells of the distal tubule

SUBMIT

H16 Question 6

Identify the structure outlined. Be specific.

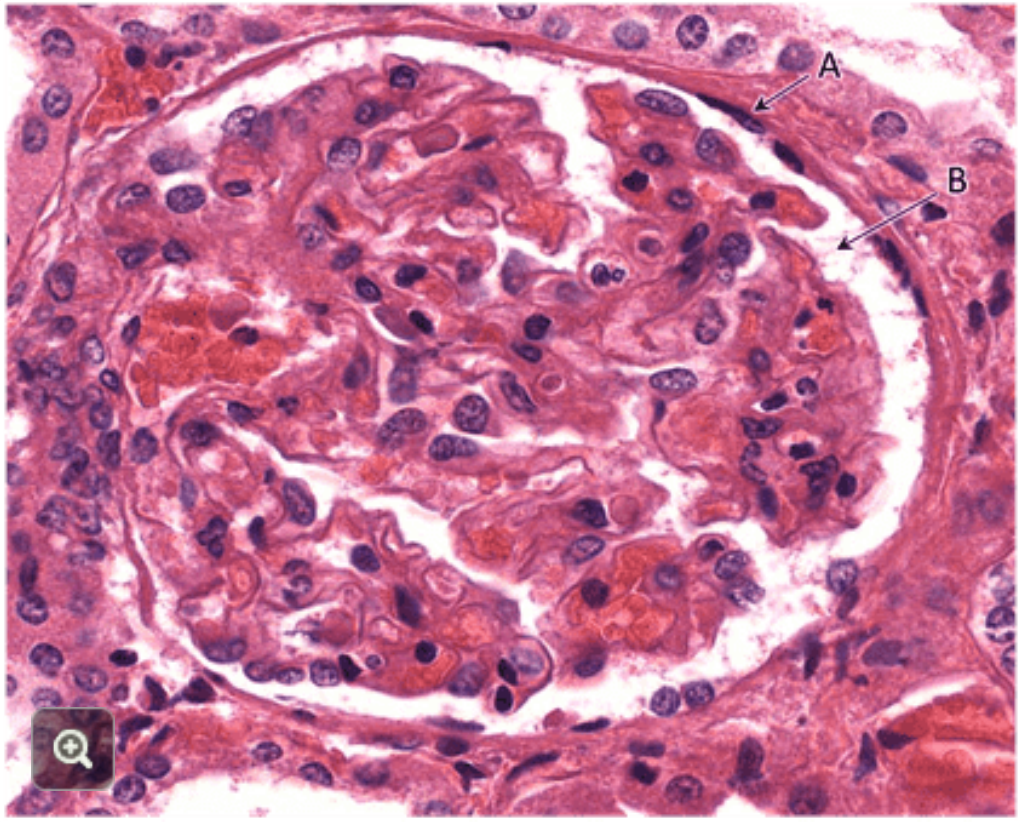
type your text here



SUBMIT

Identify A.

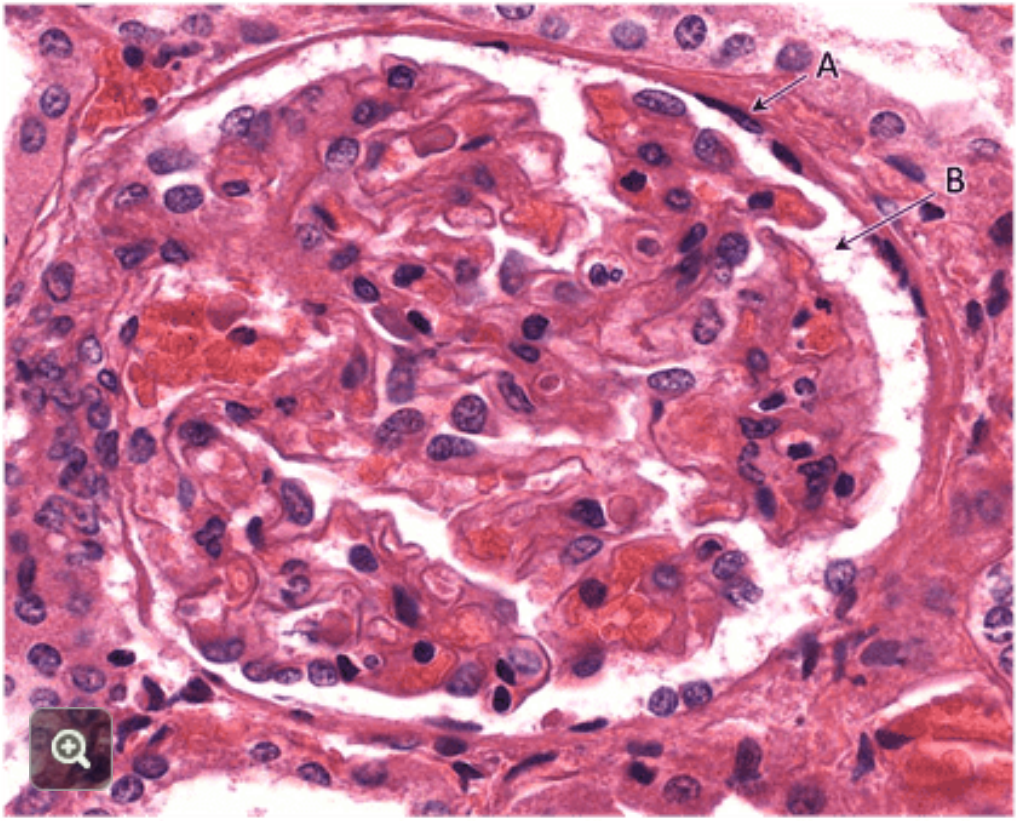
type your text here



SUBMIT

Identify B.

type your text here

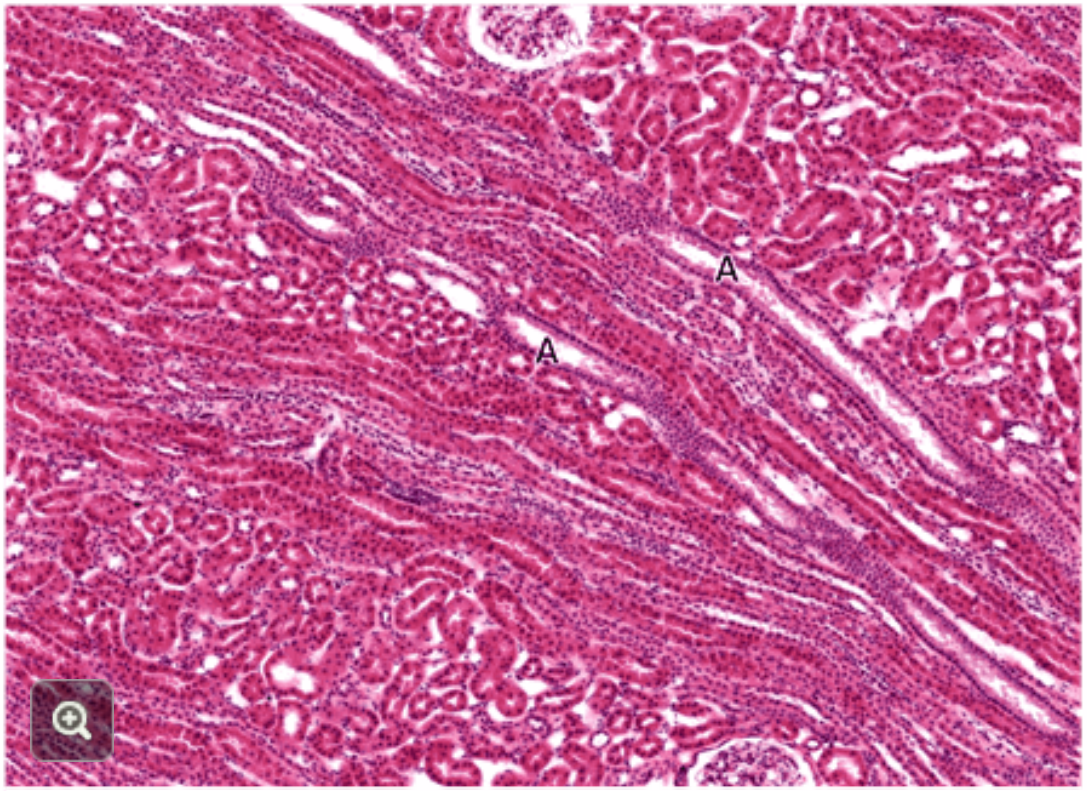


SUBMIT

H16 Question 9

Identify the structures outlined. Be specific.

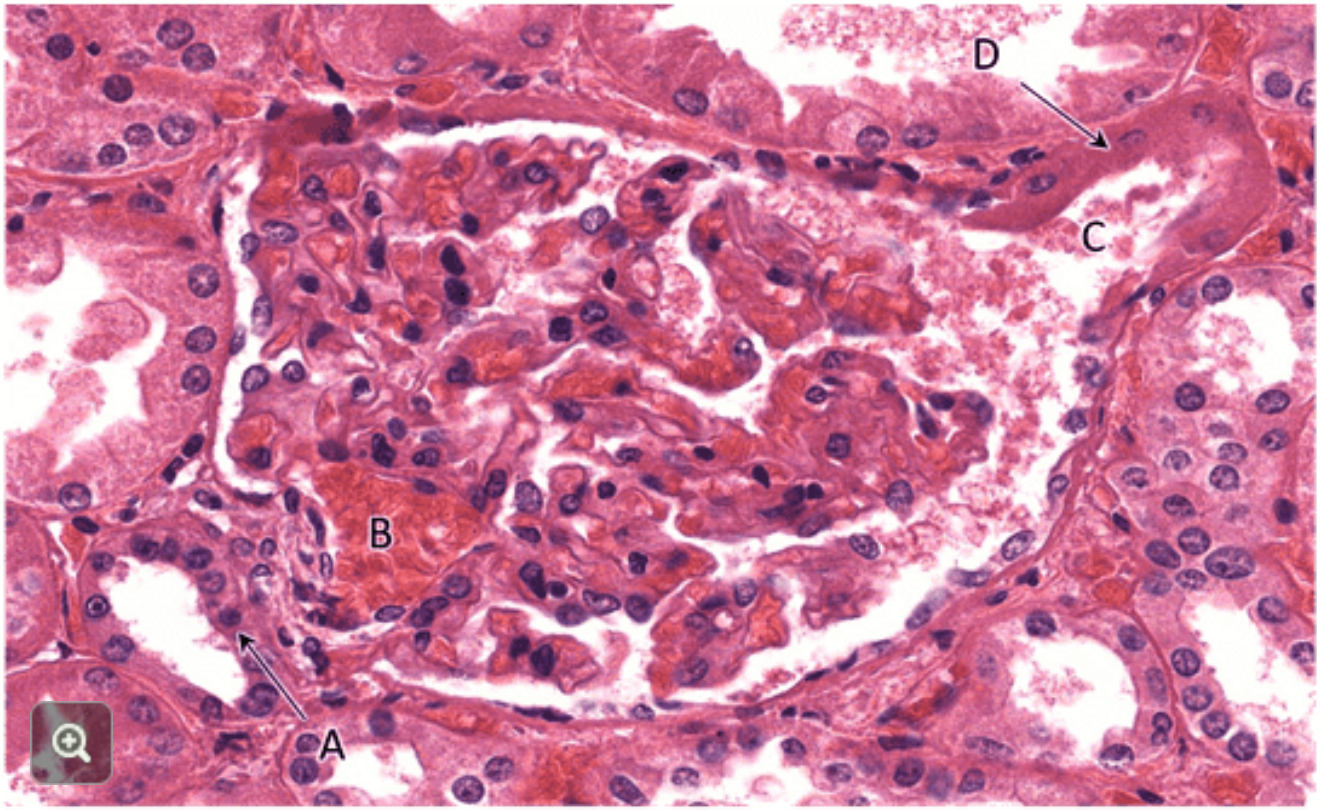
type your text here



SUBMIT

Identify A. Be specific.

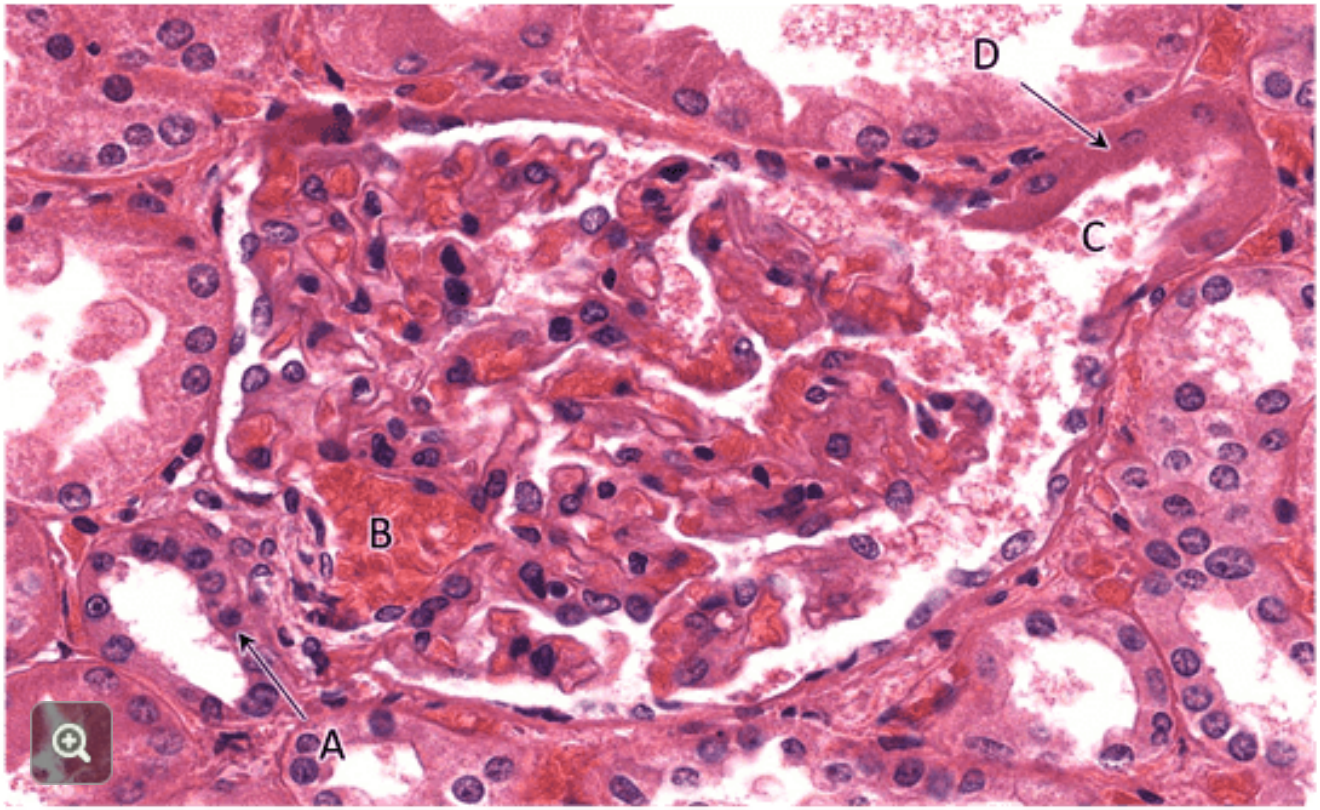
type your text here



SUBMIT

Identify region B.

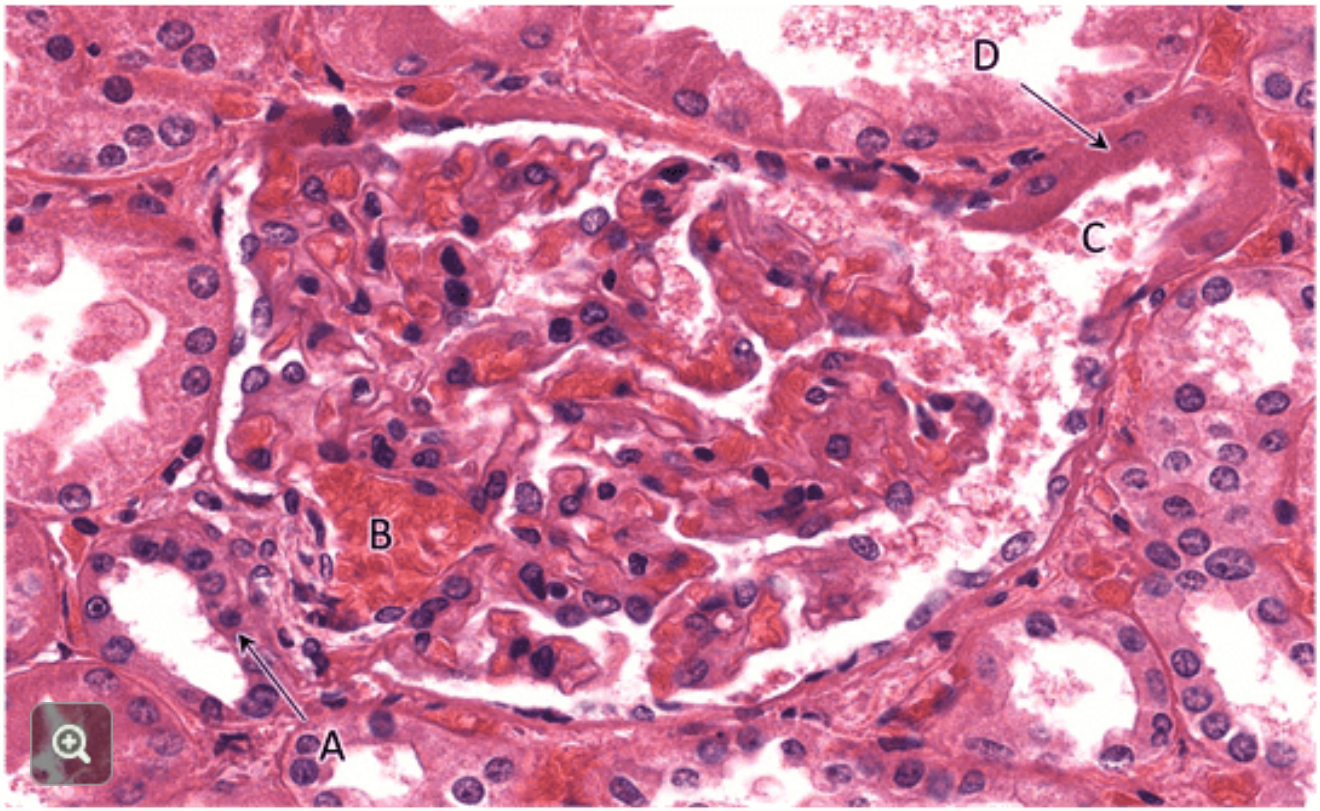
type your text here



SUBMIT

Identify region C.

type your text here

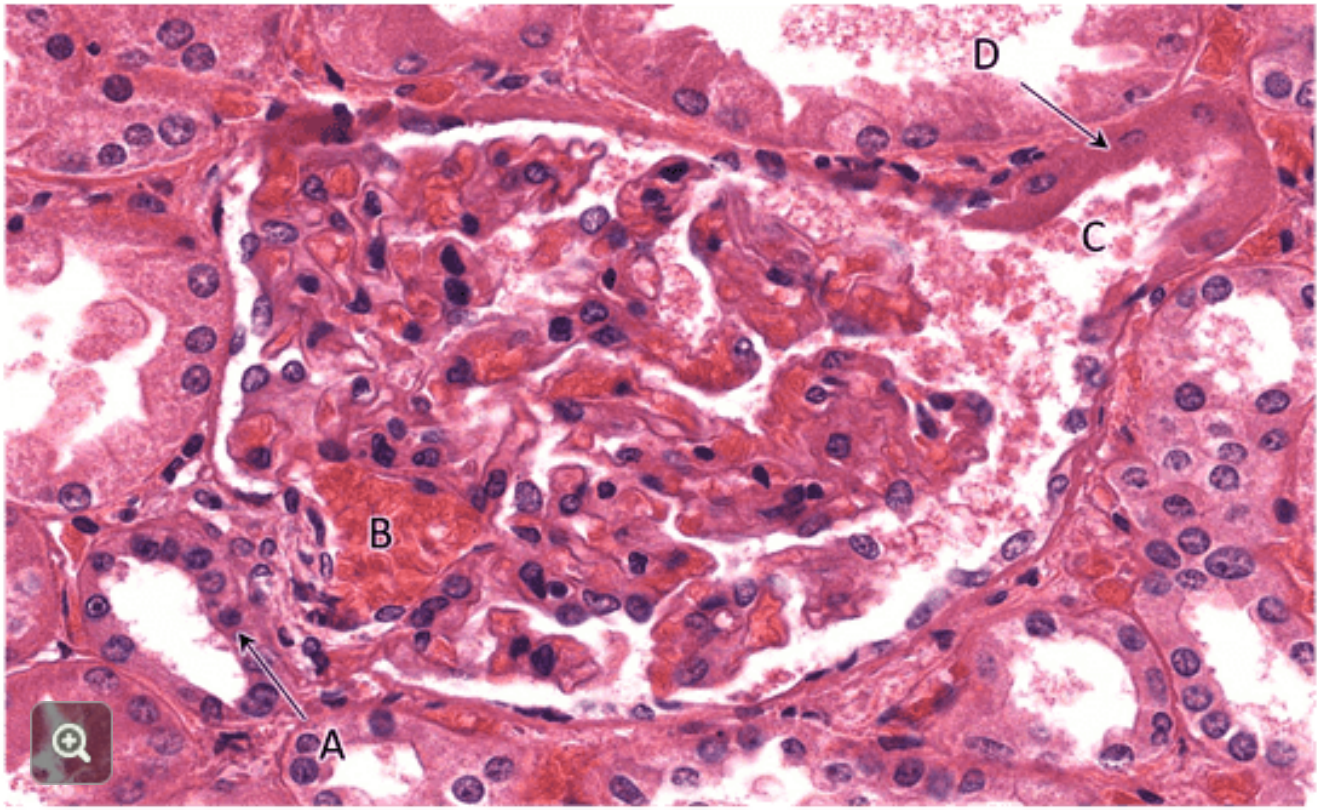


SUBMIT

H16 Question 13

Identify D.

type your text here

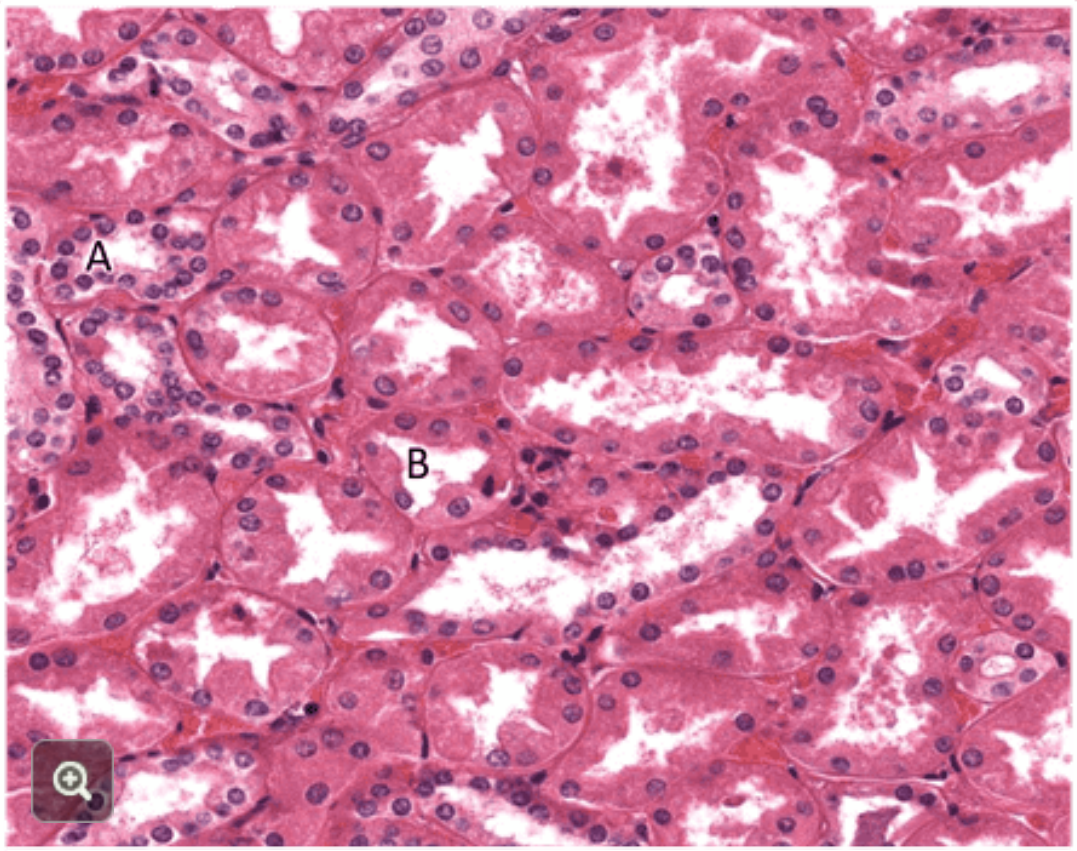


SUBMIT

H16 Question 14

Identify A.

type your text here



SUBMIT

Identify B.

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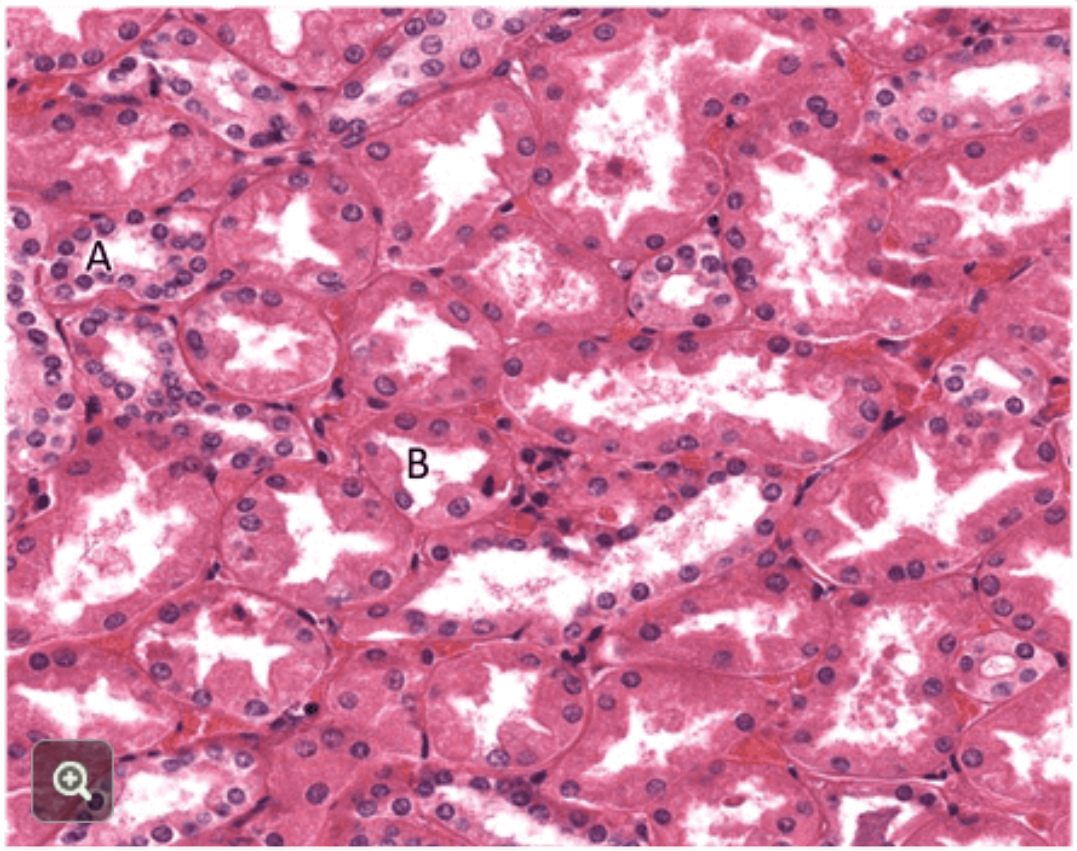
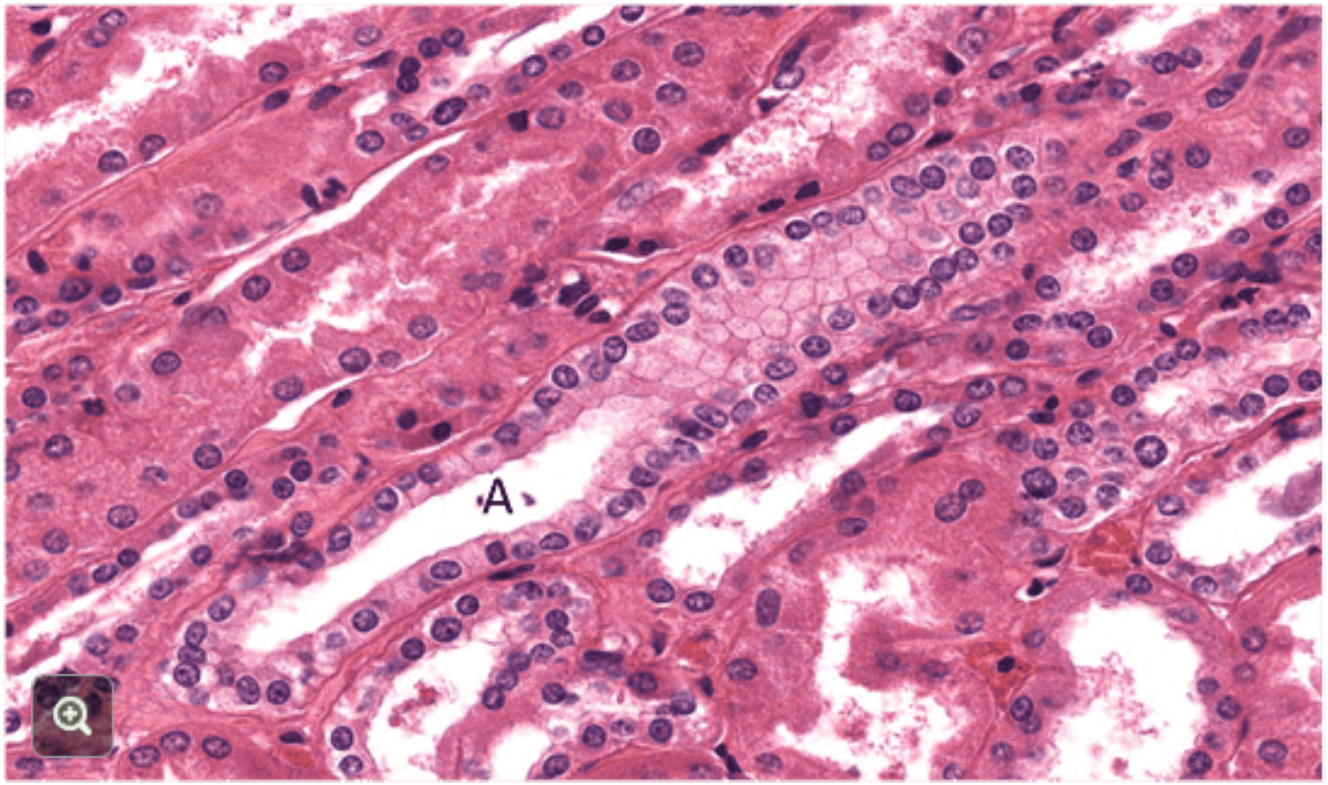


SUBMIT

Identify the structure indicated by A. Be specific.

type your text here

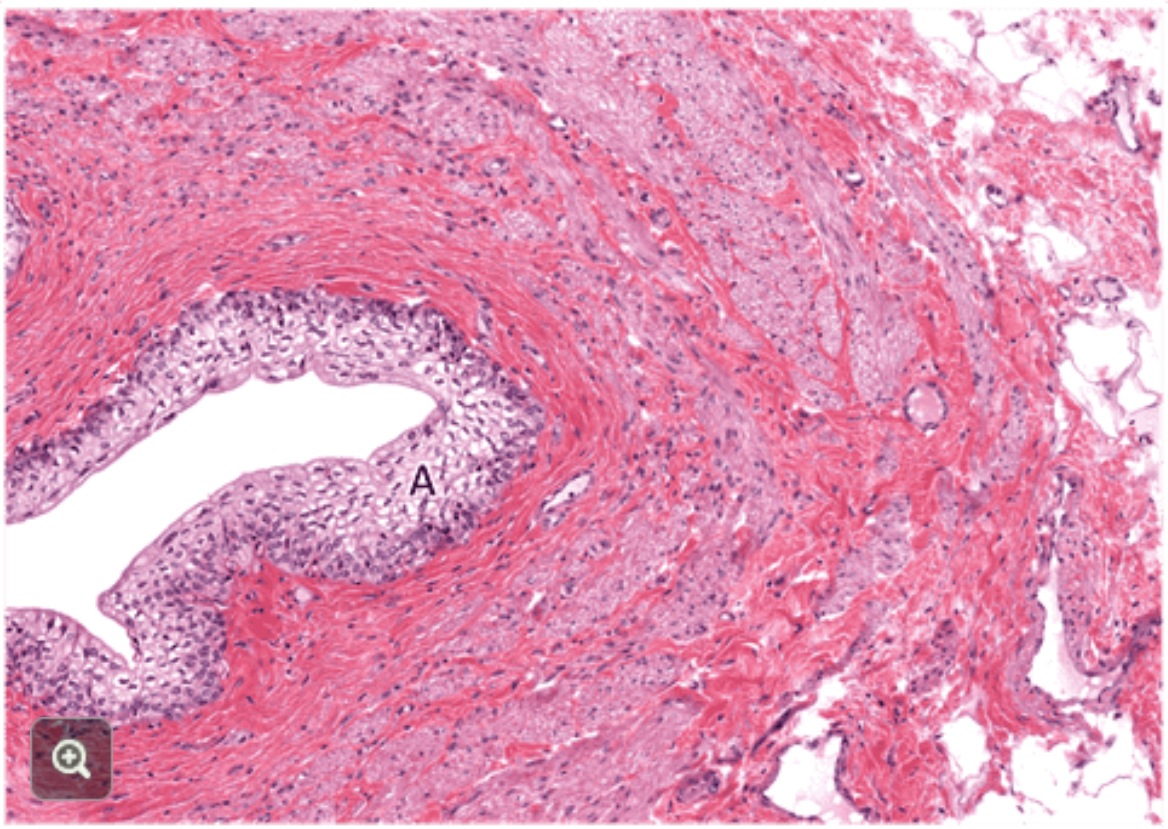


SUBMIT

H16 Question 17

Identify A. Be specific.

type your text here

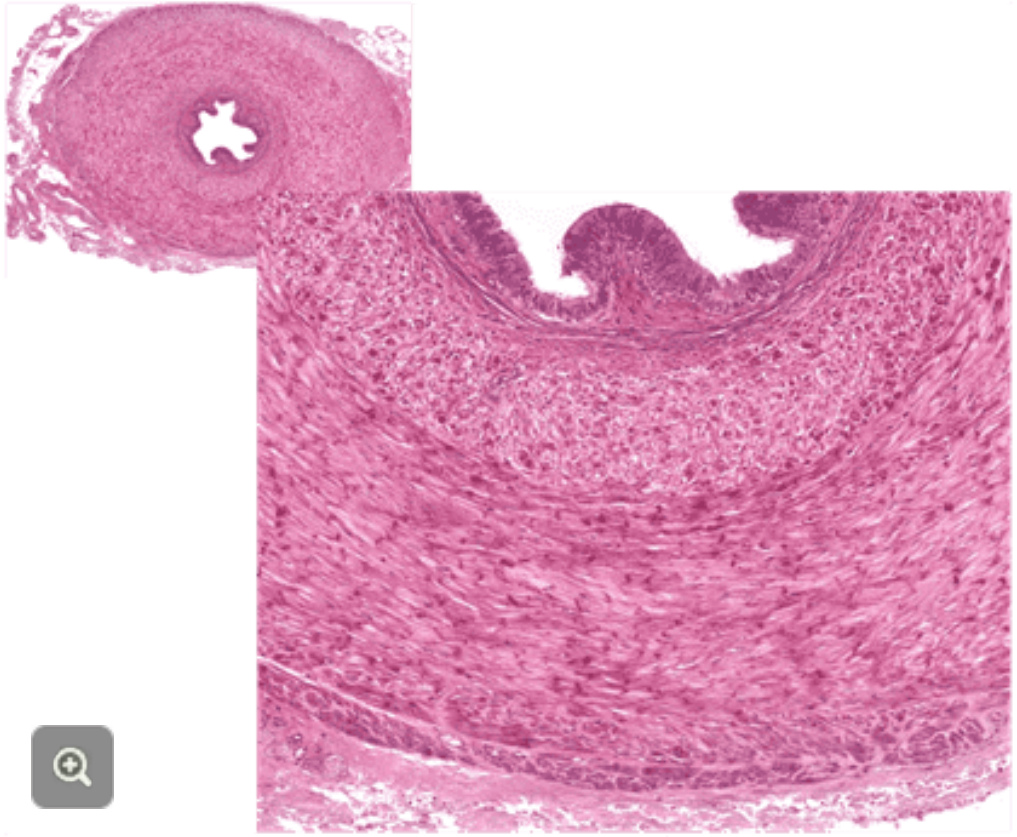


SUBMIT

H16 Question 18

From what tissue was this cross-section obtained from?

type your text here



SUBMIT