The Urinary System

Objectives

1. Specify the glomerular components that produce the urinary filtrate, outlining the role of each component.
2. Name the major segments of the nephron and summarize the chief functions of each segment.
3. Recognize proximal and distal convoluted tubules and thin-walled segments of loops of HenIe in sections.
4. State where juxtaglomerular cells are situated and discuss their functional importance.
5. Specify the lining epithelium and arrangement of smooch muscle in the urinary passages and bladder.

Introduction

The urinary system is composed of two kidneys, two ureters, the bladder, and the urethra.

The urinary system functions to

1. Filter blood and reabsorb nutrients.
2. Control the water, ion, and salt balance of the body.
3. Maintain the acid-base balance of the blood.
4. Excrete metabolic wastes (urea and uric acid), toxins, and drug components.
5. Secrete hormones, such as Renin and Erythropoietin.
6. Produce Calcitriol (an active form of vitamin D).

KIDNEYS

Bilaterally attacked to posterior abdominal wall, kidneys lie retroperitoneally on each side of the vertebral column, each measure (12 x 6 x 3) cm.

The associated ureter, renal artery, renal vein, major lymphatic vessels, and surrounding nerve plexus emerge through adipose tissue at the Hilum.

Besides having a tough fibrous capsule made of irregular dense C.T, the kidneys are protected by large quantities of associated perirenal fat tissue.

Their outer region, the renal cortex, has a granular appearance when cut, the inner region, known as the renal medulla, has a more striated appearance.

The kidney is multilobar, develops from a number of lobes (8–15) each consists of a conical mass (pyramid) of medullary tissue capped with cortex.

Individual lobes (pyramids) are delineated by renal columns (of Bertin), which represent partitions of interlobar cortical tissue that penetrate deep into the medulla.

The rounded-off apex of each pyramid, termed its papilla, projects into the renal pelvis.

Facilitating urine collection from the many papilIae, the expanded proximal end of the associated ureter is subdvided into major and then minor calyces, small funnel-like structures that cap the renal papillae. The simple columnar epithelial covering of each papilla is continuous with the transitional epithelial lining of its associated calyx.

Each lobe is made up of several lobules that are less distinct than lobes.

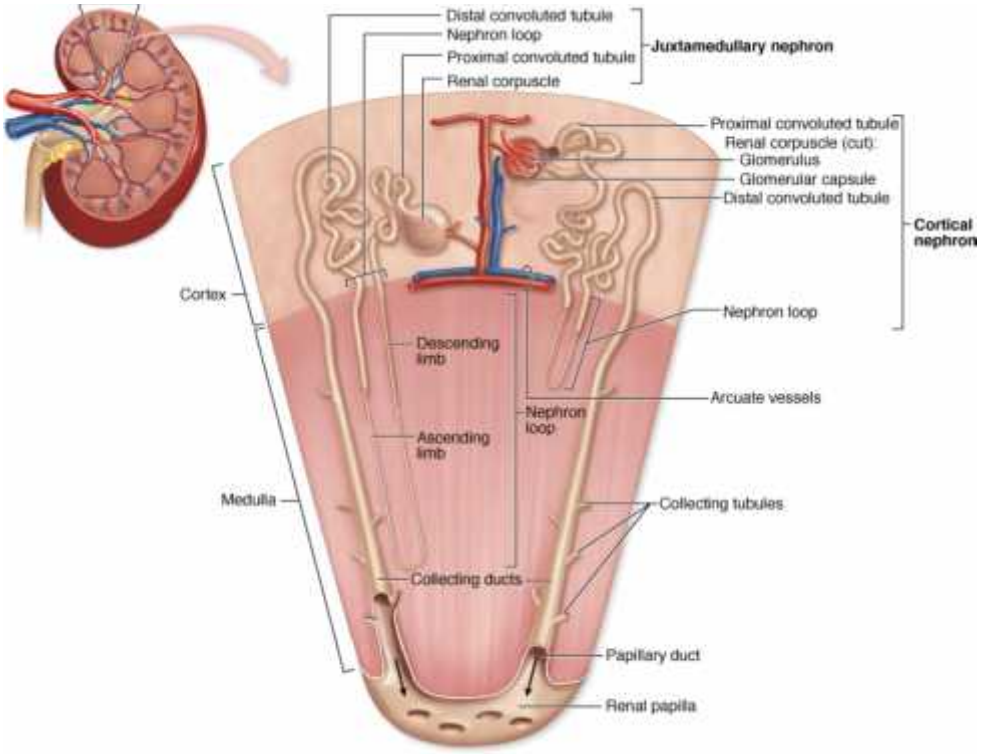
Histology of the Urinary System

Functional and histological unit of the kidney

I. Nephron	II. Collecting system
A. Renal corpuscle B. Proximal convoluted tubule (PCT) C. Loop of Henle (LOH) 1. Descending limb a. Thick descending limb b. Thin descending limb 2. Ascending limb a. Thin ascending limb b. Thick ascending limb **D.** Distal convoluted tubules (DCT)	**A.** Cortical collecting tubule **B.** Collecting ducts (CD) **C.** Papillary ducts (PD)

Approximately one-seventh of all nephrons are located near the corticomedullary junction and are therefore called **juxtamedullary nephrons.** The other nephrons are called **cortical nephrons.**

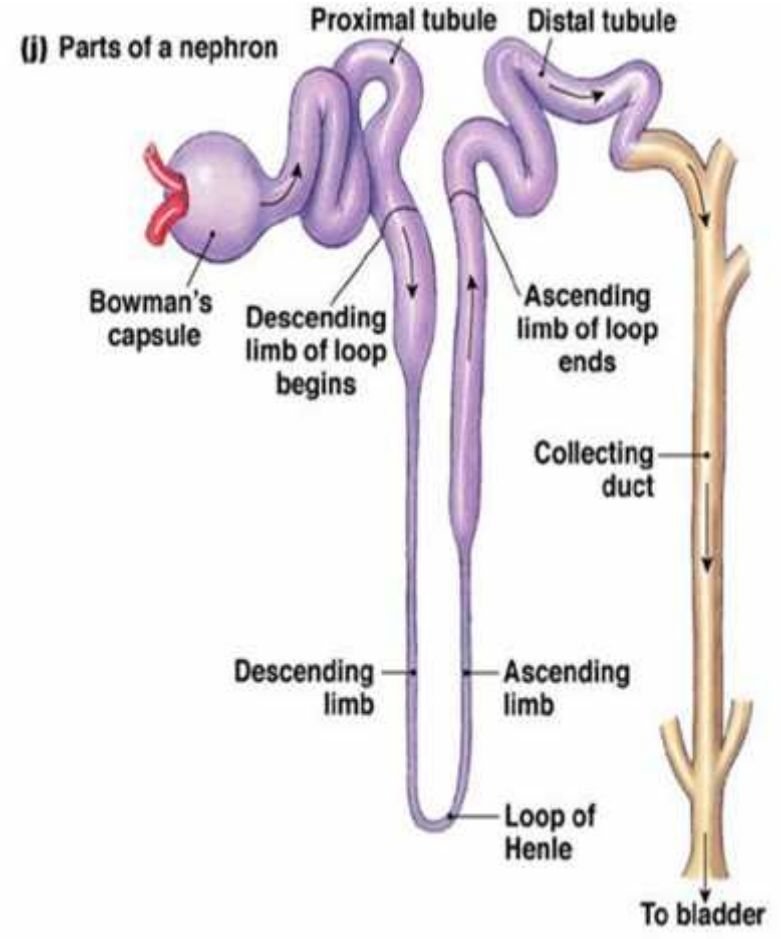
All nephrons participate in the processes of filtration, absorption, and secretion. Juxtamedullary nephrons, however, are of prime importance in establishing the gradient of hypertonicity in the medullary interstitium, the basis of the kidneys' ability to produce hypertonic urine. Juxtamedullary nephrons have very long Henle's loops, extending deep into the medulla. These loops consist of a short thick descending limb, long thin descending and ascending limbs, and a thick ascending limb. Cortical nephrons, on the other hand, have very short thin descending limbs and no thin ascending limbs.



Pathway of Nephron in Kidney lobule

Each kidney is made up of more than a million nephrons

The proximal end of each nephron is expanded into an ovoid to spherical filtration unit termed a renal corpuscle.



The renal corpuscle and PCT both lie in the renal cortex.

At the end of its tortuous course through the cortex in the vicinity of the renal corpuscle, the PCT extends down into the renal medulla as the straight descending portion of the LOH. Proximally, this looped segment is thick walled like the PCT, but deeper in the medulla the loop is thin-walled.

The thin-walled part of the loop descends farther into the medulla before making a U-turn and ascending to the cortex as the ascending portion of the LOH. The ascending portion is thin-walled deep in the medulla but becomes thick-walled before it re-enters the cortex and continues as the tortuous DCT.

The DCT then winds through the cortex, usually following along beside the PCT, and joins a small tributary of a main collecting duct (papillary duct or duct of Bellini) that passes down through the medulla and opens at the tip of a renal papilla onto its surface, in an area called the area cribrosa (perforated area).

Thus, the granular appearance of the renal cortex reflects its content of renal corpuscles and convoluted tubules, and the striated appearance of the renal medulla reflects its content of LOH and collecting tubules, which pursue a more or less straight course through this region.

However, much as interlobar extensions of the renal cortex project down into the medulla as renal columns, minor extensions of the renal medulla project up into the cortex as ray-like groups called medullary rays.

In the kidney, the term lobule means a group of nephrons that open into branches of the same main collecting duct. Kidney lobules are not easy to discern, but their lateral margins are sometimes recognizable by the presence of arteries or veins that course between the lobules (interlobular vessels). These lobules may also be recognized by the fact that their central cores are medullary ray.

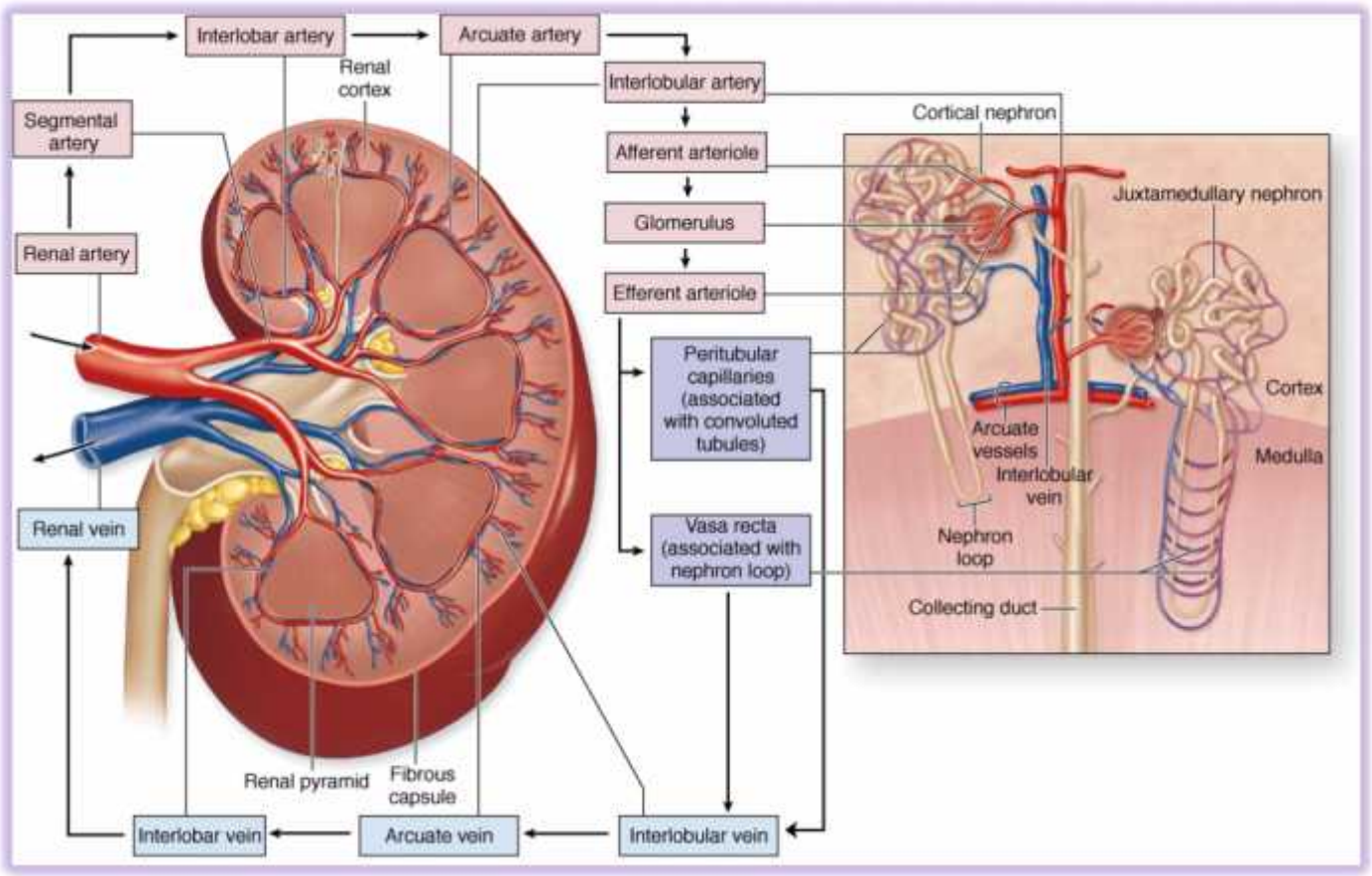
Renal Blood Supply

In the hilar region of the kidney, the *renal artery* branches into a number of *segmental arteries* from which *interlobar arteries* extend, between lobes, to the corticomedullary border. Here, the interlobar arteries give rise to *arcuate arteries*, so called because they arch over, radiating from the tip of an interlobar artery like ribs of an umbrella. From the arcuate arteries, *interlobular arteries* ascend between lobules and give off lateral intralobular arteries, which lie within lobules and give rise to *afferent arterioles* supplying *glomeruli*.

Terminal branches of the interlobular arteries supply capsular capillaries.

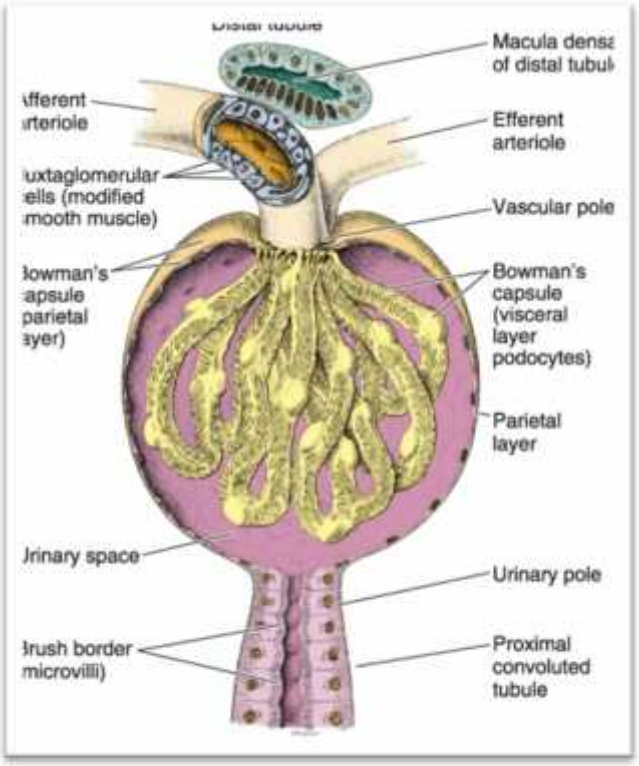
Blood reaches the *cortical capillaries* from efferent arterioles of more superficially situated glomeruli, whereas *medullary capillaries* (*vasa recta*) are supplied by efferent arterioles of deeper and juxtamedullary glomeruli.

Blood leaves the kidneys by way of a roughly comparable distribution of veins and enters the renal veins.



Renal Corpuscle

At the beginning of each nephron is a renal corpuscle, containing a loose knot of capillaries, the glomerulus, surrounded by a double walled epithelial capsule called the glomerular (Bowman's) capsule. The internal layer (visceral layer) of the capsule closely envelops the glomerular capillaries. The external parietal layer forms the outer surface of the capsule.

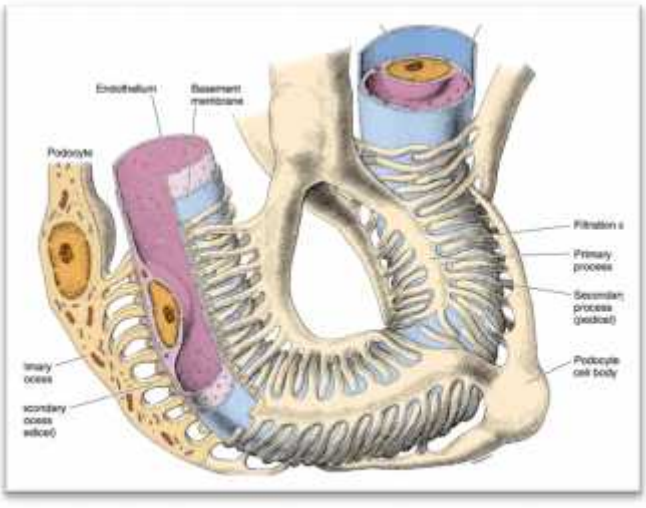


Between the two capsular layers is the urinary or capsular space, which receives the fluid filtered through the capillary wall and the visceral layer.

Each renal corpuscle has a vascular pole, where the afferent arteriole enters and the efferent arteriole leaves, and a urinary or tubular pole, where the proximal convoluted tubule begins.

The parietal layer of a glomerular capsule consists of a simple squamous epithelium supported externally by a basal lamina and a thin layer of reticular fibers. At the tubular pole, this epithelium changes to the simple cuboidal epithelium characteristic of the proximal tubule.

During embryonic development, the simple epithelium of the parietal layer remains relatively unchanged, whereas the visceral layer is greatly modified.



The cells of this layer, the podocytes, have a cell body from which arise several primary processes. Each primary process gives rise to numerous secondary (foot) processes or pedicels that embrace a portion of one glomerular capillary. The cell bodies of podocytes do not contact the basement membrane of the capillary, but each pedicel is in direct contact with this structure.

The pedicels interdigitate, defining elongated spaces 30–40 nm wide (the filtration slits).

Spanning adjacent processes (and thus bridging the filtration slits) is a thin semipermeable diaphragm of uniform thickness. These slit diaphragms are a highly specialized type of intercellular junction in which the large transmembrane protein nephrin is important both structurally and functionally.

Projecting from the cell membrane on each side of the slit, nephrin molecules interact to form a porous structure within the diaphragm.

Glomerular Filtration Barrier

Every molecule that enters the capsular space from a glomerular capillary has to pass through three layers:

First, it must traverse the fenestrated endothelium that lines the capillary. This layer is provided with large open fenestrae, however, so it does not restrict passage of plasma and it behaves only as a pre-filter that excludes blood cells and platelets.

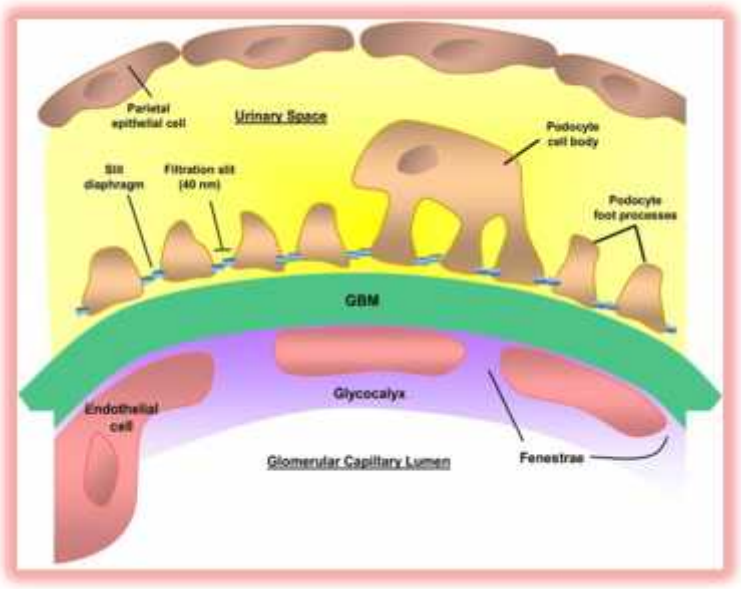
The next layer, the glomerular basement membrane (GBM), is considered the main filtration barrier of the kidney. It is thicker than other basement membranes because essentially it is a fused basement membrane representing both an epithelial and an endothelial basement membrane. It has a three layered appearance in the EM. The electron-lucent layer bordering on the endothelium is termed the lamina lucida (or rara) interna. The comparatively electron dense middle layer is the lamina densa. The electron lucent layer adjacent to the glomerular epithelium is the lamina lucida (or rara) externa.

The third component is the glomerular epithelium itself.

Extending along each filtration slit between adjacent podocyte feet is a thin shelf-like filtration slit diaphragm with an axial supporting rib and somewhat zipper-like appearance. Glomerular filtrate has to pass through this diaphragm to enter the capsular space.

Glomerular capillaries are uniquely situated between two arterioles—afferent and efferent—the muscle of which allows increased hydrostatic pressure in these vessels, favoring movement of plasma across the glomerular filter. The glomerular filtration rate (GFR) is constantly regulated by neural and hormonal inputs affecting the degree of constriction in each of these arterioles.

The total glomerular filtration area of an average adult has been estimated at 500 cm^2 and the average GFR at 125mL per minute or 180 liters per day. Because the total amount of circulating plasma averages 3 L, it follows that the kidneys typically filter the entire blood volume 60 times every day.



Mesangial Cells

In addition to endothelial cells and podocytes, the glomerular capillaries have mesangial cells adhering to their walls.

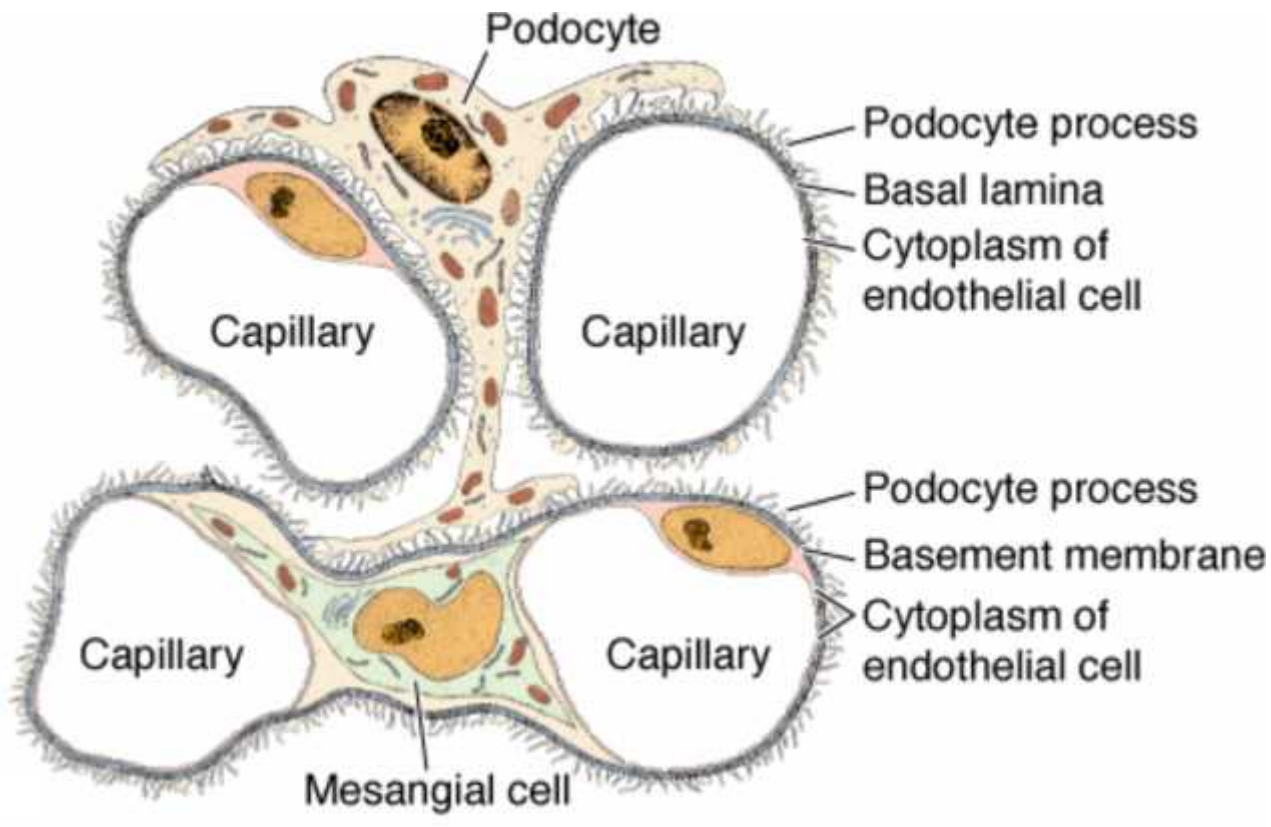
Mesangial cells are contractile and have receptors for angiotensin II. When these receptors are activated, the glomerular flow is reduced.

Mesangial cells also have receptors for the natriuretic factor produced by cardiac atria cells. This factor is a vasodilator and relaxes the mesangial cells, probably increasing the blood flow and the effective surface area available for filtration.

Mesangial cells also have several other functions:

1. They give structural support to the glomerulus,
2. Synthesize extracellular matrix,
3. Endocytose and dispose of normal and pathological (immune complex) molecules trapped by the glomerular basement membrane, and
4. Probably produce chemical mediators such as cytokines and prostaglandins.

- In the vascular pole but outside the glomerulus, there are the so-called extraglomerular mesangial cells (Lacis cells) that form part of the juxtaglomerular apparatus.



CLINICAL CORRELATION

❖ **Depletion of plasma protein resulting from glomerular damage**

The GBM loses its highly selective permeability properties when it deteriorates or become damaged. Certain kinds of antigen-antibody complexes formed when humoral antibodies combine with antigen are notorious for causing this kind of glomerular damage. Such complexes can become lodged in the GBM, where upon they may elicit an acute inflammatory response. In severe cases, damage to the GBM may lead to massive and potentially fatal loss of plasma proteins in urine (a complication in the **nephritic syndrome**).

Juxtaglomerular Complex

From the renal cortex, the kidney tubule extends into the renal medulla as the LOH and then returns (as the DCT) to the vascular pole of the same renal corpuscle, where it fits into the notch lying between the afferent and efferent arterioles. Here, the side of the tubular wall that is nearest to the glomerulus is characterized by a densely nucleated spot called the macula densa, where the lining epithelial cells of the tubule are narrower and as a result their nuclei lie closer together. This heavily nucleated region is generally regarded as indicating the site where the DCT begins.

The most significant specialization at the vascular pole, however, is found in the wall of the afferent arteriole. Here, smooth muscle cells of the media are highly modified as special secretory cells called juxtaglomerular (JG) cells. These cells have large PAS-positive secretory granules that contain the proteolytic enzyme *renin.*

The internal elastic membrane of the afferent arteriole disappears in the area of the JG cells.

Small numbers of JG cells may be present in the efferent arteriole as well.

Basic function of the JGA is the autoregulation of the glomerular filtration rate (GFR) and controlling blood pressure.

At the tubular pole of the renal corpuscle, the squamous epithelium of the capsule's parietal layer is continuous with the cuboidal epithelium of the PCT. This very tortuous tubule is longer than the DCT and is therefore more frequently seen in sections of renal cortex.

Proximal Convoluted Tubule

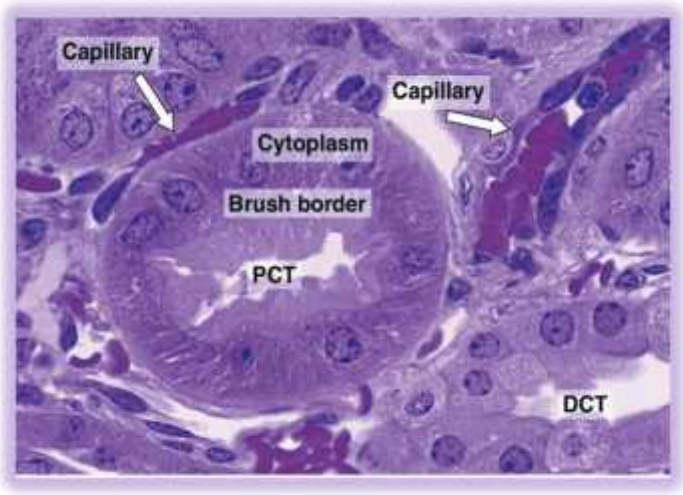
Histological Features

The cells are large, so each transverse section of a PCT has only 3-5 nuclei.

They have acidophilic cytoplasm due to presence of numerous mitochondria.

The cell apex has abundant long microvilli which form a prominent **brush border** for reabsorption,

In routine histologic preparations, the brush border may be disorganized and give the lumens a fuzz-filled appearance.



Ultrastructurally the apical cytoplasm of these cells has numerous pits and vesicles near the bases of the microvilli, indicating active pinocytosis. Pinocytotic vesicles contain small plasma proteins that passed through the glomerular filter. The vesicles fuse with lysosomes for proteolysis and amino acids are released to the circulation.

The cells also have many long basal membrane invaginations and lateral interdigitations with neighboring cells.

The Na+/K+-ATPase (sodium pump) responsible for actively transporting sodium ions out of the cells is localized in these basolateral membranes.

Long mitochondria are concentrated along the basal invaginations characteristically for cells engaged in active ion transport.

Because of the extensive interdigitations of the lateral membranes, discrete limits between cells of the PCT are difficult to see in the light microscope.

Physiological Functions:

1. **Tubular Reabsorption** : active transport of substances from the tubular lumen into the peritubular capillaries
   - 2/3 of the water
   - 85 % of the NaCl.
   - Almost all of the glucose, amino acids, nutrients, ions, vitamins, and small plasma proteins.
2. **Tubular Secretion** : active transport of substances from the peritubular capillaries into the tubular lumen

   (Choline, creatinine and many foreign compounds such as penicillin) are excreted in this manner, which allows kidneys to dispose of such substances at a higher rate than by glomerular filtration alone.
3. **Vitamin D hydroxylation**.

The Loop of Henle (Nephron Loop)

It is a U-shaped structure that includes:

1) **Descending Limb** consists of:

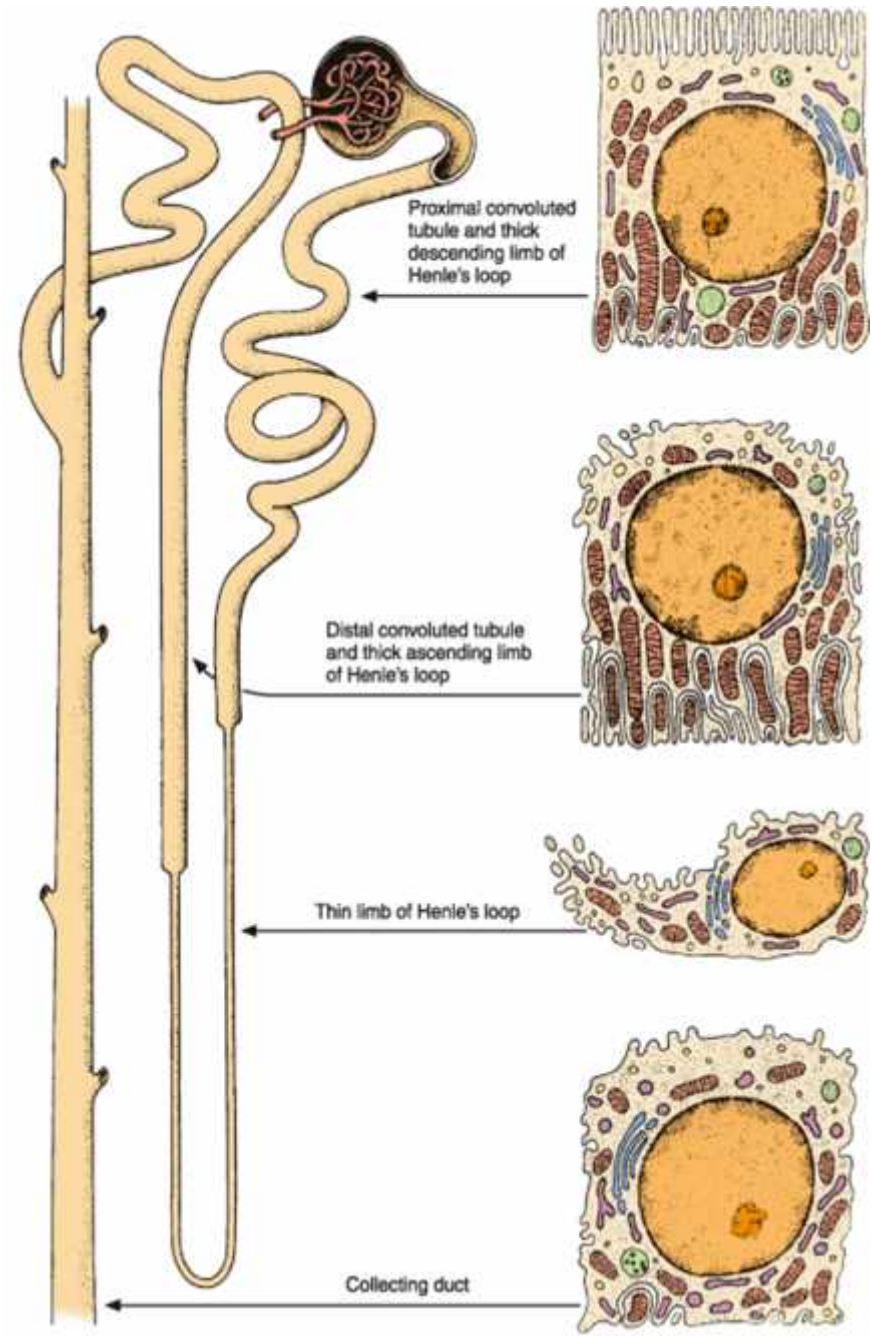
a) A thick descending limb (proximal straight tubule - pars recta)

b) A thin descending limb (descending thin segment).

2) **Ascending Limb** contains:

a) A thin ascending limb (ascending thin segment)

b) A thick ascending limb (distal straight tubule- pars recta).



Histological Features:

The thick limbs are very similar in structure to the PCT& DCT near to it.

The lumen of thin limbs is wide because the wall consists of squamous epithelial cells whose nuclei protrude only slightly into the lumen. Excepts for the absence of blood cells from its lumen, however, there is little to distinguish this part of the nephron from the numerous straight blood capillaries (vasa recta) that surround it.

The ascending portion of the loop lies beside the descending portion which extends for a variable distance into the renal medulla.

Juxtamedullary nephron has a relatively long LOH that extends deep into the medulla. In contrast, most of the LOH of a superficial cortical nephron is generally situated in a medullary ray.

Physiological Functions:

The nephron loop and surrounding tissue are involved in making urine hypertonic and conserving water.

- Cuboidal cells of the loops' thick ascending limbs actively transport NaCl out of the tubule against a concentration gradient into the hyaluronate-rich interstitial connective tissue, making that compartment hyperosmotic.
- Squamous cells of the loops' thin descending limbs are freely permeable to water but not salts, while the thin ascending limbs are permeable to NaCl but impermeable to water.
- Flow of the filtrate in opposite directions (countercurrent flow) in the two parallel limbs of nephron loops establishes a gradient of osmolarity in the interstitium of the medullary pyramids and countercurrent blood flow in the loops of the vasa recta help maintain this gradient.
- The interstitial osmolarity at the pyramid tips is about four times that of the blood. The high interstitial osmolarity draws water passively from the collecting ducts in the medullary pyramids, concentrating the urine.
- Water permeability of these ducts is increased by antidiuretic hormone (ADH), which is released from the pituitary when body water is low. The water thus saved immediately enters the blood in the adjacent capillaries of the vasa recta.
- The role of the nephron loop and vasa recta in establishing the conditions for urine concentration is called the **countercurrent multiplier effect**.

Distal Convoluted Tubule

The thick ascending limb of the nephron loop is straight as it enters the cortex, and then becomes tortuous as the **distal convoluted tubule.**

The simple cuboidal cells of these tubules differ from those of the PCT in being smaller and having no brush border, Because distal tubule cells are flatter and smaller than those of the proximal tubule, more nuclei are typically seen in sections of distal tubules than in those of proximal tubules.

Cells of the DCT do have basal membrane invaginations and associated mitochondria similar to PCT, indicating their similar ion-transporting function.

The DCT connect distal straight tubules (thick ascending limb of LOH) to the collecting tubules. The distal convoluted and straight tubules are structurally similar to each other, differing mainly in their locations and courses.

Physiological Functions:

1) Reabsorbs Na+ and secretes K+, if aldosterone stimulation is present;
2) Reabsorbs bicarbonate and secretes ammonium to adjust PH
3) Important component of the juxtaglomerular apparatus.

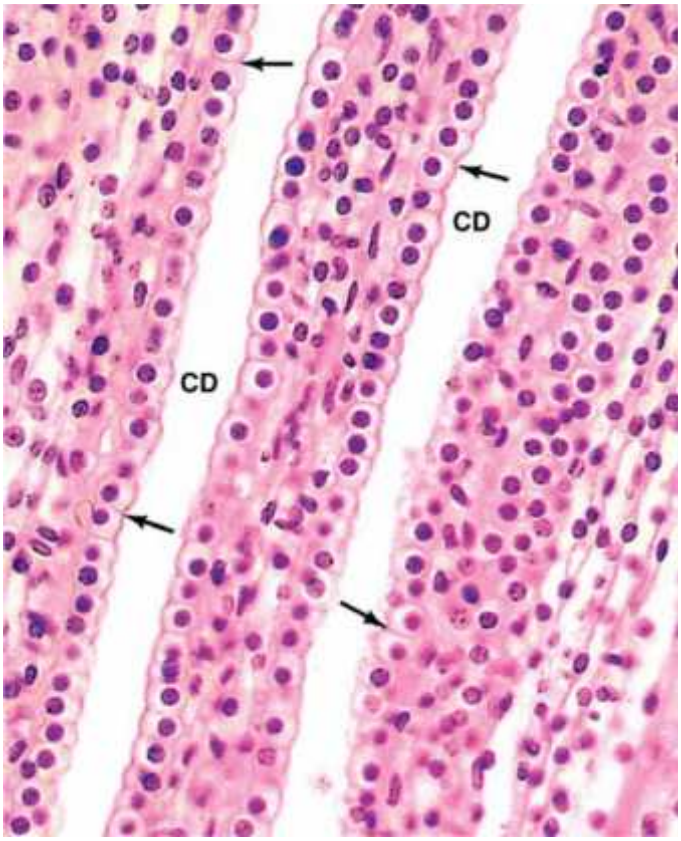
Collecting Tubules & Ducts

Urine passes from the DCT to collecting tubules, which join each other to form larger, straight collecting ducts that run to the tips of the medullary pyramids and empty into the minor calyces.

Along their entire extent, collecting tubules and ducts are composed mainly of weakly staining principal cells with few organelles and scanty microvilli.

The intercellular limits of the cells are clearly visible in the light microscope. Ultrastructurally the principal cells can be seen to have basal membrane infoldings, consistent with their role in ion transport.

Scattered among the principal cells are variably darker intercalated cells with more abundant mitochondria which help regulate the acid-base balance by secreting H+ and absorbing HCO3.



Physiological Functions:

In the medulla, collecting ducts are a major component of the urine-concentrating mechanism. Cells of collecting ducts are particularly rich in **aquaporins**, integral proteins found in most cell membranes that function as selective pores for passage of water molecules. Here aquaporins are sequestered in membranous cytoplasmic vesicles. ADH (arginine vasopressin) makes collecting ducts more permeable to water, increasing the rate at which water molecules are pulled osmotically from their lumens and transferred to the vasa recta, and thus retained in the body. This effect is produced when activated ADH receptors on the basolateral cell membrane stimulate the movement of vesicles with specific aquaporins and their insertion into either the apical or basolateral membranes, increasing the number of membrane channels for water movement through the cells.

URETERS, BLADDER, & URETHRA

The calyces, renal pelvis, ureter, and bladder have the same basic histologic structure, with the walls becoming gradually thicker closer to the bladder.

The mucosa of these organs is lined by unique stratified **transitional epithelium** or urothelium, This is surrounded by a folded lamina propria and submucosa, followed by a dense sheath of interwoven smooth muscle layers and adventitia.

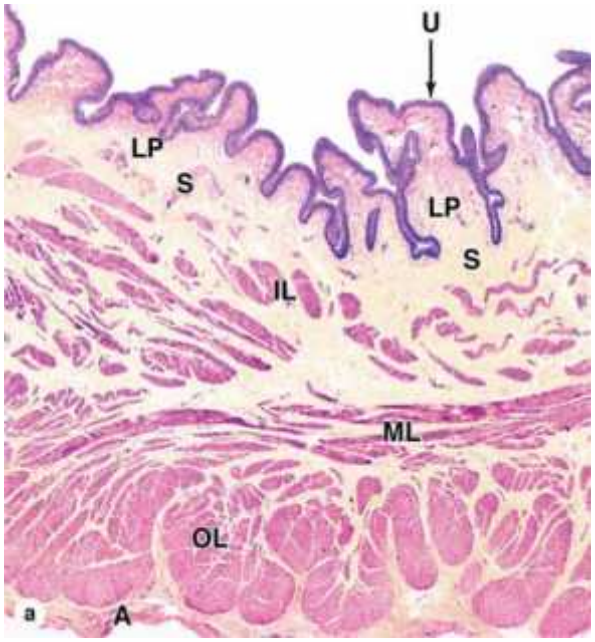
Urine moves from the renal pelvises to the bladder by peristaltic contractions.

The urothelium is composed of the following three layers:

(1) A single layer of small basal cells resting on a very thin basement membrane,
(2) An intermediate region containing from one to several layers of more columnar cells,
(3) A superficial layer of very large, polyhedral or bulbous cells called **umbrella cells** which are occasionally bi- or multinucleated and are highly differentiated to protect underlying cells against the cytotoxic effects of hypertonic urine.

Umbrella cells are especially well developed in the bladder where contact with urine is the greatest. These cells have extensive intercellular junctional complexes surrounding unique apical membranes. Most of the apical surface consists of asymmetric unit membranes, in which regions of the outer lipid layer appear twice as thick as the inner leaflet. These regions are lipid rafts containing mostly integral membrane proteins called **uroplakins** which assemble into paracrystalline arrays of stiffened plaques 16 nm in diameter. Urine contacts primarily these membranous plaques, which are impermeable and protect cytoplasm and underlying cells from its hyperosmotic effects. Plaques are hinged together by more narrow regions of typical membrane.

When the bladder is emptied, not only does the mucosa fold extensively, but individual umbrella cells decrease their apical surface area by folding the membrane at its hinge domains and internalizing the folded plaques in discoidal vesicles. As the bladder fills again the discoidal vesicles rejoin the apical membrane, increasing its surface area as the cell shape changes from round to flat. The urothelium becomes thinner, apparently the result of the intermediate cells being pushed and pulled laterally to accommodate the increased volume of urine.



The bladder's lamina propria and dense irregular connective tissue of the submucosa are highly vascularized.

The muscularis consists of three poorly delineated layers, collectively called the detrusor muscle, which contract to empty the bladder

Three muscular layers are seen most distinctly at the neck of the bladder near the urethra.

The ureters pass through the wall of the bladder obliquely, forming a ***valve*** that prevents the backflow of urine into the ureters.

All the urinary passages are covered externally by an adventitial layer, except for the upper part of the bladder which is covered by serous peritoneum.

The **urethra** is a tube that carries the urine from the bladder to the exterior.

The urethral mucosa has large longitudinal folds, giving it a distinctive appearance in cross section.

The male urethra is longer and consists of three segments:

(1) The prostatic urethra, 3–4 cm long, extends through the prostate gland and is lined by urothelium

(2) The membranous urethra, a short segment, passes through an external sphincter of striated muscle and is lined by stratified columnar and pseudostratified epithelium

(3) The spongy urethra, 15 cm in length, is enclosed within erectile tissue of the penis and is lined by stratified columnar and pseudostratified columnar epithelium, with stratified squamous distally.

The female urethra is a tube 4 to 5 cm long, lined initially with transitional epithelium, then by stratified squamous epithelium and some areas of pseudostratified columnar epithelium. The middle part of the female urethra is surrounded by the external striated muscle sphincter.