Urinary System
Homeostasis

Learning objectives

- Students should be able to distinguish the renal cortex and medulla in histological sections.
- Students should be able to identify capillaries, podoctyes, mesangial cells and parietal cells in the renal corpuscle.
- Students should be able to describe the properties of the structures that filter blood in the renal corpuscle
- Students should be able to distinguish proximal convoluted tubules, loop of Henle, distal convoluted tubule and collecting duct in histological sections and list the functional properties of each.
- Students should be able to identify components of the juxtaglomerular apparatus and describe how it regulates filtration rate of its corpuscle.
- Students should be able to describe the histological features of the ureter, bladder and urethra.

Pre-lab readings and videos and in-class material

http://medcell.org/tbl/histology_of_the_urinary_system

Introduction

The urinary system comprises the kidney, ureter, urinary bladder, and urethra. The kidney filters plasma to produce urine which allows the body to eliminate metabolic waste products, such as urea, and other harmful compounds. The kidney also uses urine also to maintain proper fluid and electrolyte levels and pH. Urine flows from the kidney through the ureter into the bladder where it is temporarily stored. The bladder is then emptied via the urethra.

This session will focus primarily on the kidney but will also cover briefly the other components of the urinary system.

Physiological Functions

The kidney performs several important functions:

- Maintenance of water and electrolyte homeostasis
- Regulation of acid-base balance in conjunction with the respiratory system
- Excretion of metabolic waste products, especially the toxic nitrogenous compounds
- Production of renin for blood pressure control and erythropoietin, which stimulates red blood cell production in the bone marrow
- Conversion of vitamin D into active form for the regulation of calcium balance

This session will describe the structures in the kidney that allow it to maintain water and electrolyte homeostasis, excrete waste products and maintain blood pressure.

Conceptually, the kidney can be thought of as a filter that allows water and small solutes in blood to flow into a separate space. Once in this space the fluid is called urine and it flows through a structure that recycles into the body all of the physiologically useful solutes while releasing harmful and waste solutes out of the body.

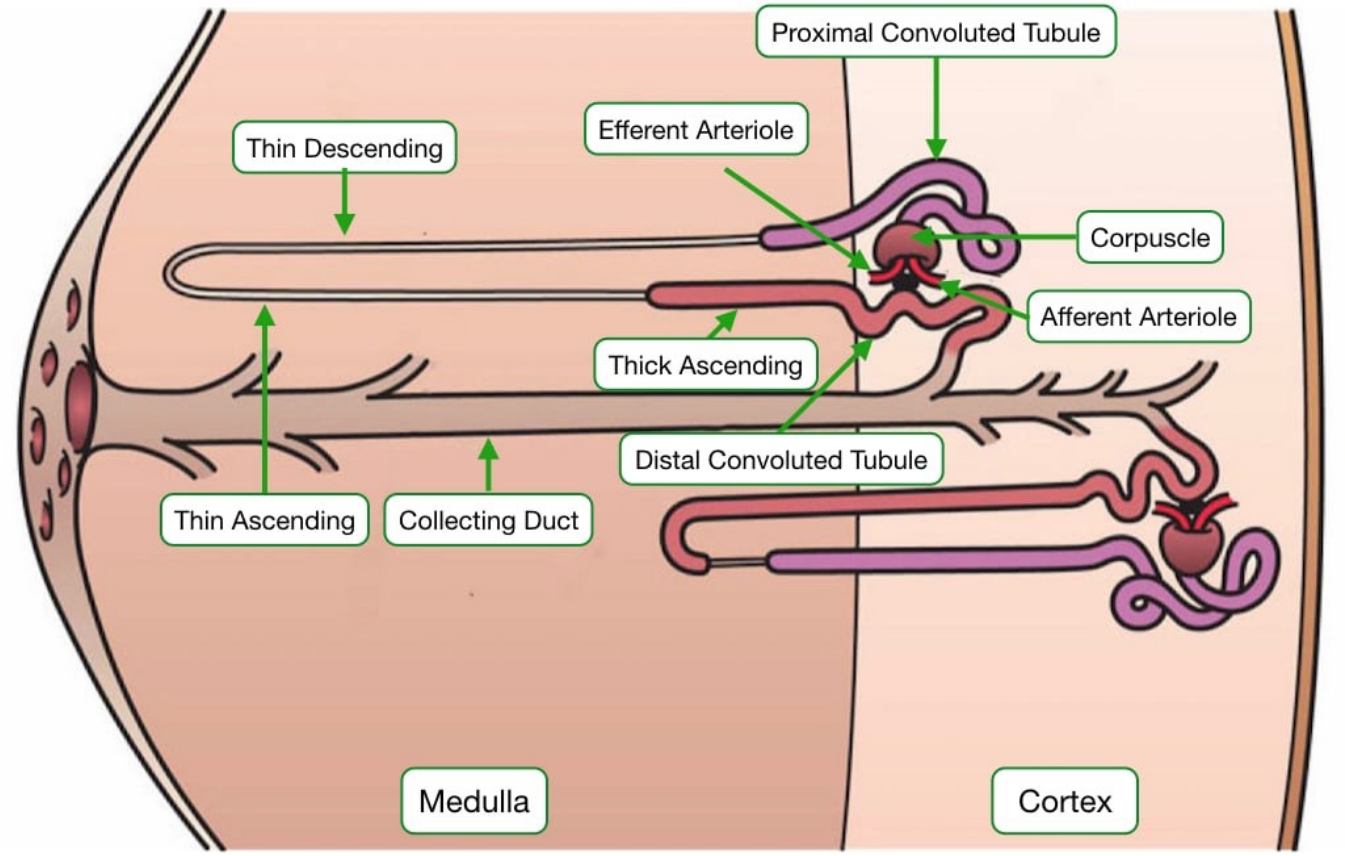
To efficiently remove metabolic waste produce by cells and other potentially harmful solutes, the kidneys filter about 180 liters of plasma every day (125 ml/min). This represents more than 10 times the volume of all of the extracellular fluid (ECF) in the body. Filtering fluid at that rate requires a large surface area. Similar to the lungs, the kidneys generate a large surface area through the contributions of many small units, but instead of alveoli, the kidneys use nephrons, roughly one million per kidney. Nephrons generate two structures with large surface areas. The first structure filters blood. The second structure absorbs 99% of the water and solutes that pass through the filter and provides opportunities to adjust the concentration of solutes in urine.

The filter in the nephron comprises a tuft of capillaries surrounded by a basement membrane and an epithelium that defines the space that collects the filtrate. Fluid in the capillaries is under high hydrostatic pressure which provides the driving force to push it and small solutes across the filter into the filtrate space.

The second structure in the nephron generates a large surface area that reabsorbs useful biological molecules that pass through the filter. The filter in the kidney is not selective for small solutes, so a lot of important biological molecules readily pass across the filter into the filtrate space. To reabsorb those molecules, the nephron passes urine through a long tube, part of which is coiled to increase its length. The tube is lined by an epithelium that is efficient at vectorial transport of specific solutes from filtrate into the interstitium. Other segments of the tube create an osmotic gradient between the fluid in the lumen of the tube and the interstitium. The kidney uses this osmotic gradient to absorb water from the lumen when needed.

Nephron

The cartoon below illustrates two different types of nephrons found in kidneys and their location within the kidney. Note that the kidney is histologically divided into an outer cortex and inner medulla. Both types of nephrons contain a structure called the renal corpuscle that filters plasma and a long tube that reabsorbs water and specific solutes. All nephrons have renal corpuscles in the cortex of the kidney, but some have their corpuscles closer to the outer region of the cortex whereas others have their renal corpuscles closer to the border with the medullary. The difference between the two types is that nephrons closer to the medullary have tubes that dip deep into the medullary and generate the osmotic gradient that will facilitate water absorption. Nephrons which reside in the outer cortex filter blood but do not contribute appreciably to the osmotic gradient for water absorption.



The kidney contains two types of nephrons to filter blood and regulate electrolyte concentration and pH.

The cartoon also illustrates the different segments of the nephron tube. Segments differ in their histological structure, ability to absorb solutes and permeability to water. The initial segment of the tube, which is connected to the renal corpuscle, is called the proximal convoluted tube (PCT) due to its vicinity to the renal corpuscle and coiled path. The majority of water and solute reabsorption occurs in the PCT. A short stretch of the proximal tubule is

more straight than coiled but has a similar function to the preceding coiled portion of the tube.

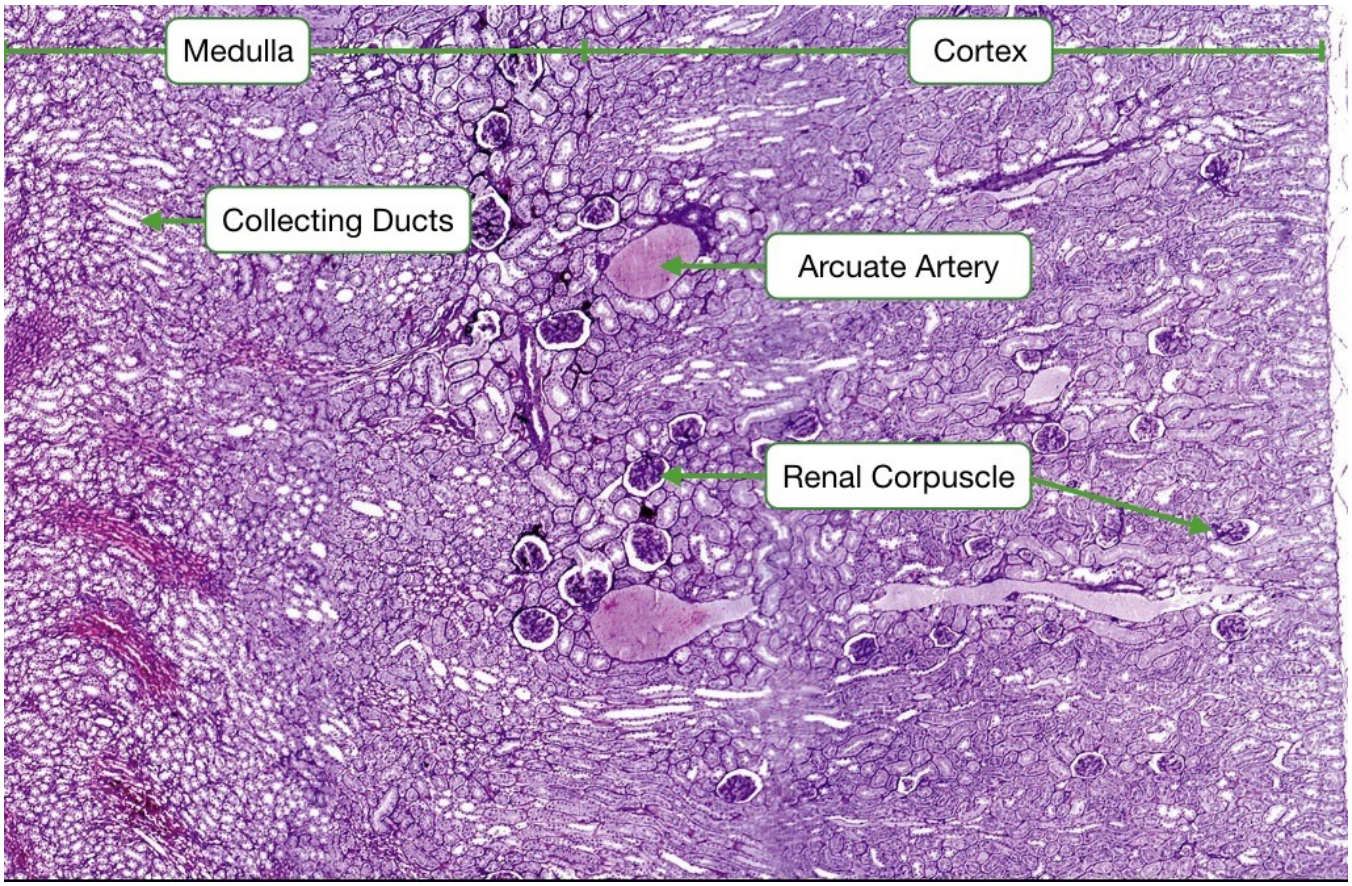
The segment after the PCT is called the loop of Henle. The loop of Henle is divided into the thin descending limb, a thin ascending limb and a thick ascending limb. Thin and thick refer to the shape of the epithelia that lines the tube (squamous and cuboidal). The loops of Henle differ between nephrons that reside in the cortical versus border region. Those nephrons whose corpuscles are closer to the medullary have a segment of the tube that dips deep into medullary, whereas those nephrons with corpuscles near the cortex have much shorter loops of Henle that barely reach into the medulla. The loops of Henle generate an osmotic gradient in the medulla that will facilitate water absorption from collecting ducts.

The distal convoluted tubule follows the thick ascending limb and similar to PCT has a coiled path. The distal convoluted tubule transitions into a connecting tubule and then an initial collecting tubule. Initial collecting tubules from different nephrons coalesce into a common tube called a collecting duct. Collecting ducts penetrate deep into the medulla and are sites where the kidney can regulate the amount of water it reabsorbs.

The cartoon also illustrates the blood supply to each nephron. An afferent arteriole brings blood into the renal corpuscle. The arteriole ramifies into a capillary bed where blood is filtered. The capillaries coalesce into a second arteriole called the efferent arteriole that leaves the renal corpuscle and delivers blood to capillaries that lay adjacent to tubules deeper in the cortex and medulla.

Arrangement of Corpuscles and Tubules

This is a low power view of a cross section of the kidney illustrates the difference between cortex and medulla. The cortex contains corpuscles, proximal and distal convoluted tubules, and blood vessels, whereas the medullary primarily contains loops of Henle, collecting ducts and blood vessels. Note that some renal corpuscles reside close to the medulla. The tubule from these corpuscles will form a loop of Henle in the medulla. The tubules from the renal corpuscles near the outer cortex lack a loop of Henle and dip only just a little beyond the border into the medulla. The large blood vessels called arcuate arteries roughly define the border of the cortex and medulla.



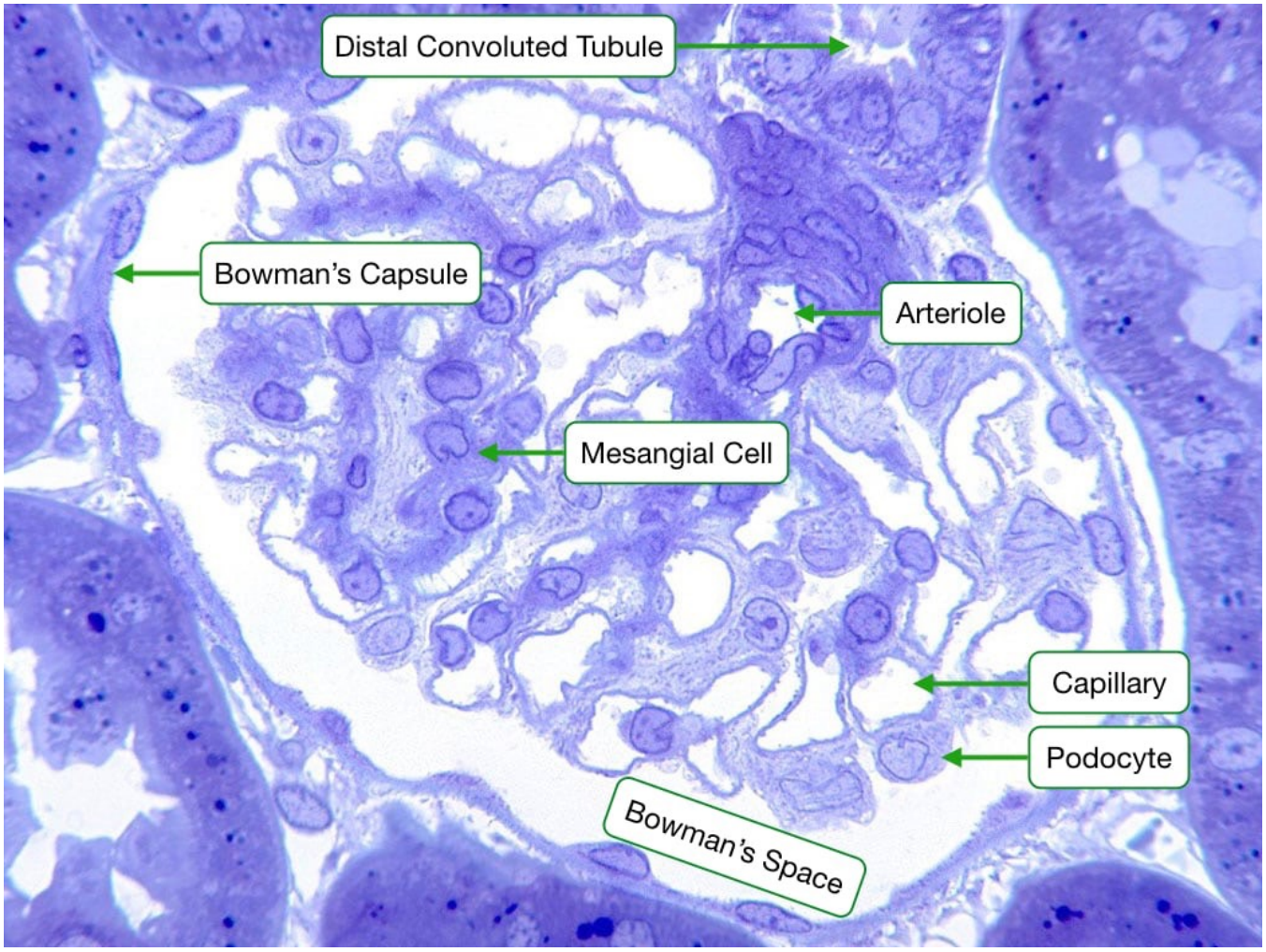
Arcuate arteries define the border between cortex and medulla in the kidney.

Filtering Unit - Renal Corpuscle

The renal corpuscle is responsible for the filtration of plasma. It contains two structures: the glomerulus and Bowman's capsule. The glomerulus is the site of filtration and contains a cluster of capillaries surrounded by a thick basement membrane and a layer of epithelial cells called podocytes. Blood flows into the capillaries from an afferent arteriole and leaves the corpuscle via an efferent arteriole. Blood in the efferent arteriole enters a second capillary bed that perfuses the region of the kidney that house the nephron tubules.

Bowman’s capsule surround the glomerular capillaries and is composed of a layer of epithelial cells. The space between the capillaries and capsule is called Bowman’s space and contains the filtered blood called glomerular filtrate or urine.

One other cell found in the renal corpuscle is the mesangial cell. Mesangial cells secrete proteins and glycoproteins that compose the extracellular matrix, called mesangium. Mesangium supports the endothelial cells and podocytes. Mesangial cells are distributed throughout the corpuscle between the endothelial cells and podocytes.



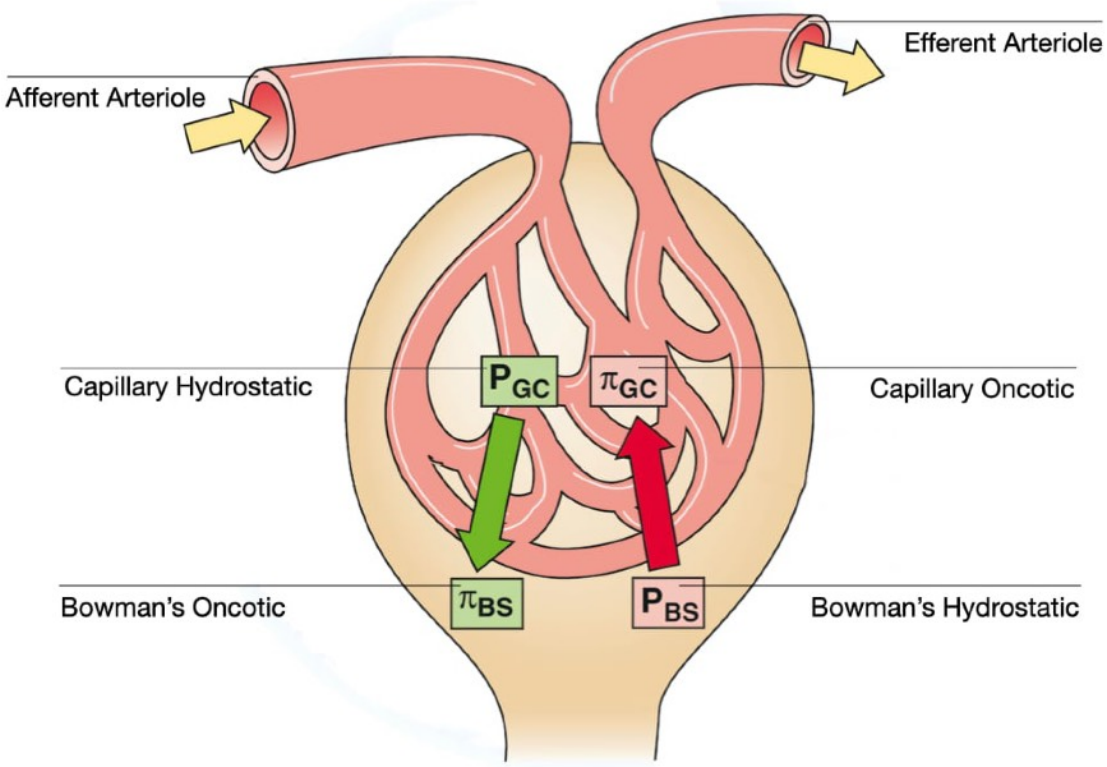
Renal corpuscles filter blood from a tuft of capillaries into Bowman's space.

Starling forces determine the flow of blood out of the glomerular capillaries. Hydrostatic pressure in the capillaries and oncotic pressure in Bowman's space push fluid out of the capillaries into Bowman's space. Hydrostatic pressure in Bowman's space and oncotic pressure in the capillaries draws fluid from Bowman's space into the capillaries. Hydrostatic pressure and oncotic pressure in Bowman's space are significantly lower than their counterparts in the capillaries, so the direction of fluid flow is largely determined by hydrostatic and oncotic pressure in the capillaries.

As blood enter the glomerular capillaries, the hydrostatic pressure is significantly higher than oncotic pressure which pushes fluid out of the capillaries into Bowman's space and the rest of the nephron. As blood flows through the capillaries, the hydrostatic pressure decreases until it roughly equals oncotic pressure at roughly the halfway point of the capillaries. The extra length of capillary allows the nephron to filter a larger amount of blood when needed.

The hydrostatic pressure in the capillaries is regulated by the afferent and efferent arterioles. Hydrostatic pressure is increased when the afferent arteriole is dilated and the efferent arteriole is constricted. Hydrostatic pressure is decreased when the afferent arteriole

is constricted and the efferent arteriole is dilated. Later, we'll discuss how feedback in nephrons regulates hydrostatic pressure in the glomerular capillaries.



Starling forces determine the direction of fluid flow in the glomerular capillaries.

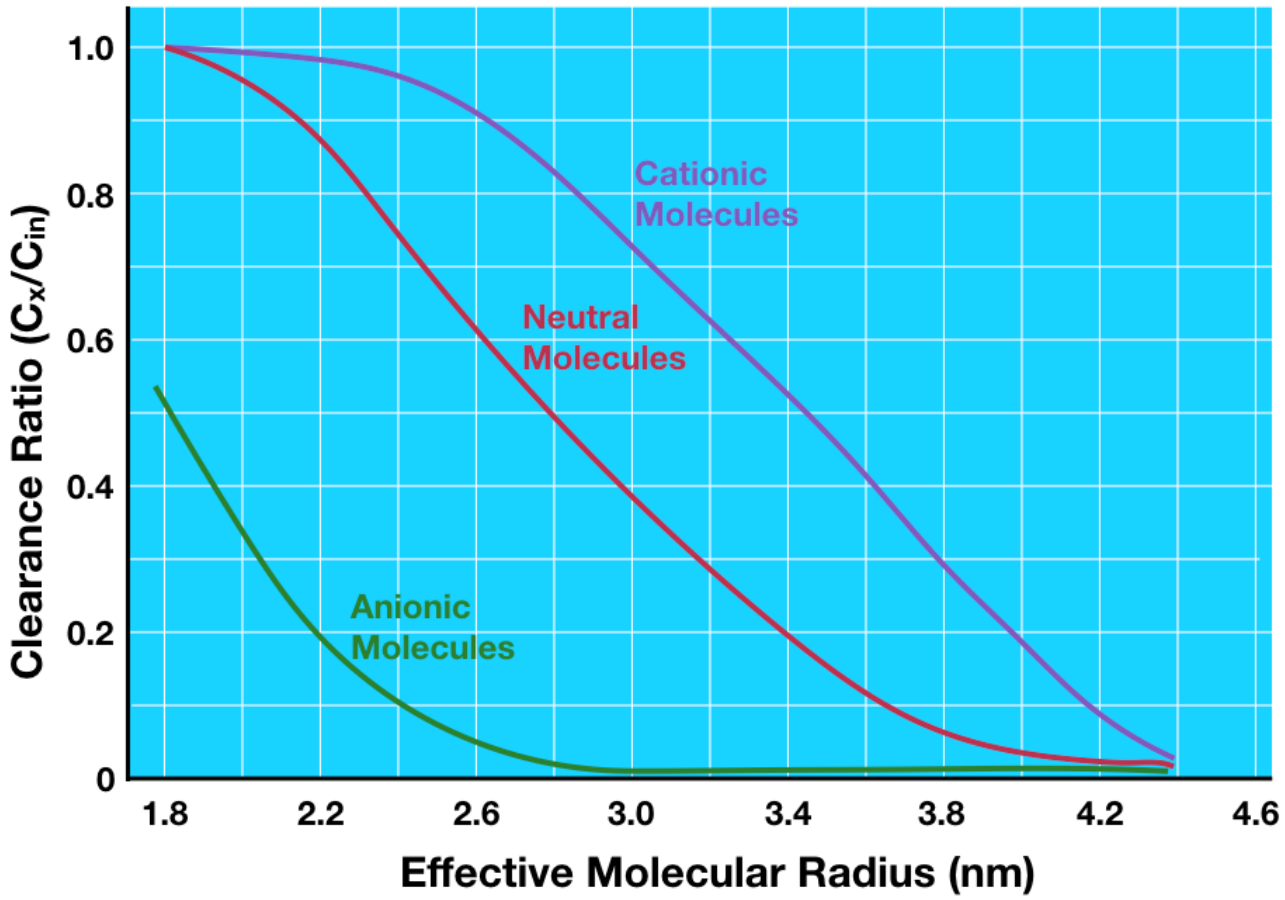
Filtration Barrier

To pass from the capillary into Bowman's space, the components of blood must penetrate an elaborate filtration barrier that comprises the endothelial cells of the capillaries, a thick basement membrane and a layer of epithelial cells called podocytes. Podocytes form a continuous layer of epithelium with the cells of Bowman's capsule.

Experimental evidence indicates that the filtration barrier of the glomerulus is a size and charge selective barrier. The graph below summarizes the permeability of the filtration barrier to molecules of different sizes and charges. The y-axis shows the clearance ratio which is a measure of how much of a specific molecule passes through the filtration barrier compared to a molecule which freely passes across the barrier. A clearance ratio of 1.0 means the barrier does not restrict passage of the molecule whereas a low clearance ratio indicates the barrier restricts passage of the molecule.

The graph shows that the filtration barrier allows uncharged molecules with a radius of 2 nm or smaller to freely pass from blood into Bowman's space but uncharged molecules with

radii between 2 nm and 4 nm show a linear decrease in passage across the barrier. Molecules larger than 4 - 5 nm are prevented from passing across the barrier.



Renal corpuscles filter solutes based on size and charge.

Particles of the same size but different net charges cross the barrier at different rates. Positively charge particles move more readily across the barrier compared to neutral particles of the same size, whereas negatively charged particles move less readily across the barrier.

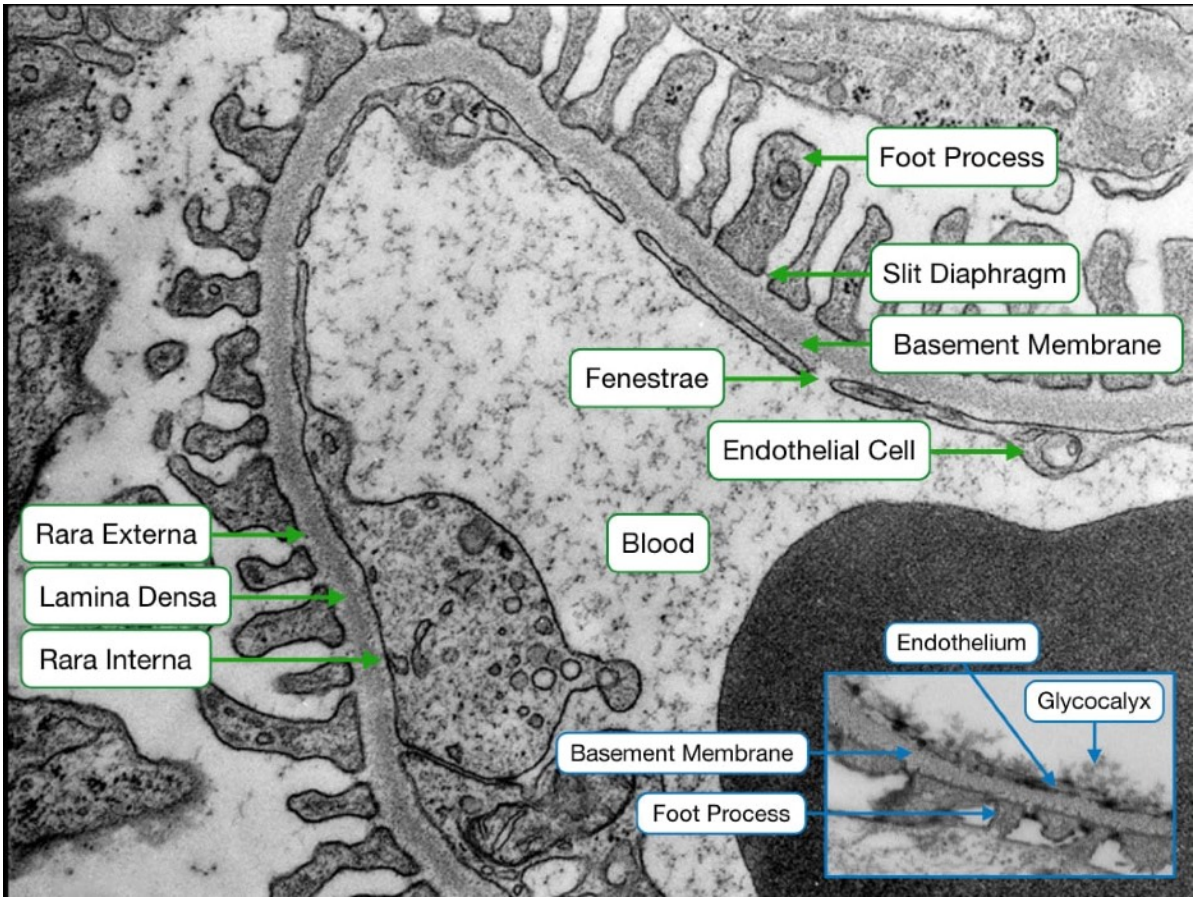
In practical terms, the barrier prevents the passage of cells and large proteins (greater than 5 nm in diameter) while allowing ions and small molecules, such as glucose and amino acids, to freely pass. In between these two classes are small to medium size proteins. The most important of these proteins is albumin due to its high concentration in plasma and its critical role in generating oncotic pressure. Albumin has a molecular radius of about 3.5 nm and has a net negative charge and therefore, is deterred from passing the barrier due to the size and charge restrictive properties of the barrier. If albumin were neutral about 10% of it pass through the barrier into filtrate.

Because the filtration barrier comprises the endothelium, basement membrane and podocytes, we'll explore in more detail what we know about how these components contribute to the properties of the filtration barrier.

Fenestrated Endothelium

The glomerular capillaries contain a fenestrated endothelium which is more permeable than fenestrated endothelium in other parts of the body due to the larger number of fenestrae and larger size of each fenestra (about 60 nm). Thus, the fenestrae mostly deter passage of cells.

The apical surface of the endothelium contains a structure called glycocalyx which is composed of numerous proteoglycans and glycosaminoglycans. Recall that these structures contain a strong negative charge. There is some experimental evidence that glycocalyx inhibits passage of albumin. Removing glycocalyx with digestive enzymes increases by about two-fold the permeability of glomerulus to albumin. Special preparation is required to preserve glycocalyx during electron microscopy so it is not always seen in images. The inset in the image below shows a small section of glomerulus where glycocalyx has been preserved.



The filtration barrier consists of fenestrated endothelium, basement membrane and podocytes.

Basement Membrane

Beneath the endothelium is a thick basement membrane (~350 nm) which is produced by both endothelia cells and podocytes. The primary components of the basement membrane are type IV collagen, laminin and a collection of glycoproteins, proteoglycans and glycosaminoglycans. Similar to other basement membranes, collagens and laminin form mesh-like networks.

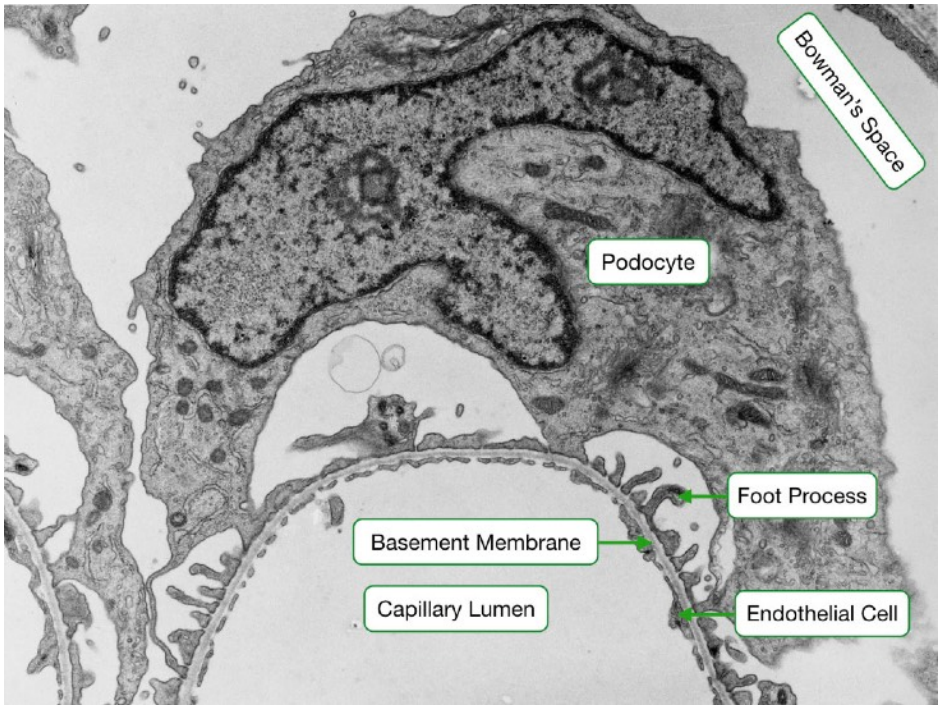
The glomerular basement membrane can be divided into three structural layers.

- Lamina rara externa sits adjacent to the podocytes and contains a high concentration of negatively charged molecules, such as heparan sulfate. These negatively charged molecules are thought to inhibit the diffusion of negatively charged protein such as albumin. Laminin and other proteins mediate attachment of podocytes to the basement membrane.
- In the middle resides the lamina dense that contains a type IV collagen network that provides structural support to the basement membrane and also functions as a sized-based filter.
- The lamina rara interna resides adjacent to the endothelial cells of the capillaries and has similar components as the lamina rara externa.

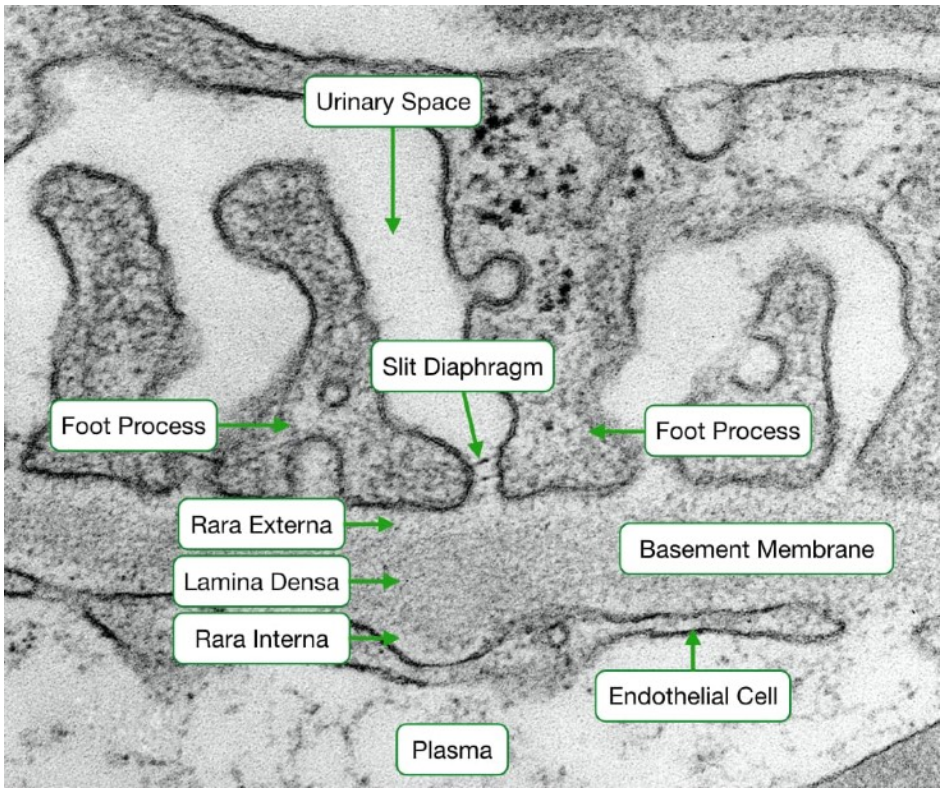
Genetic mutations which eliminate or compromise the function of specific components of the basement membrane demonstrate a direct role for these components in restricting passage of albumin. For example, Alport Syndrome is caused by mutations in Type IV collagen and leads to proteinuria (protein in urine). Mutations in genes encoding laminin also cause proteinuria.

Podocytes

Podocytes are specialized epithelial cells that separate the network of capillaries in the glomerulus from Bowman's space. Podocytes extend processes that surround the capillaries. These processes form secondary processes called foot processes. The foot processes associate with the basement membrane opposite from the endothelial cells of the capillaries. Foot processes from different podocytes interdigitate to form filtration slits. A protein-based structure, called a slit diaphragm, spans the filtration slits. Slit diaphragms create pores of 4 to 14 nm through which plasma must pass to gain entry to Bowman's space.



Podocytes form foot processes that attach to the basement membrane.

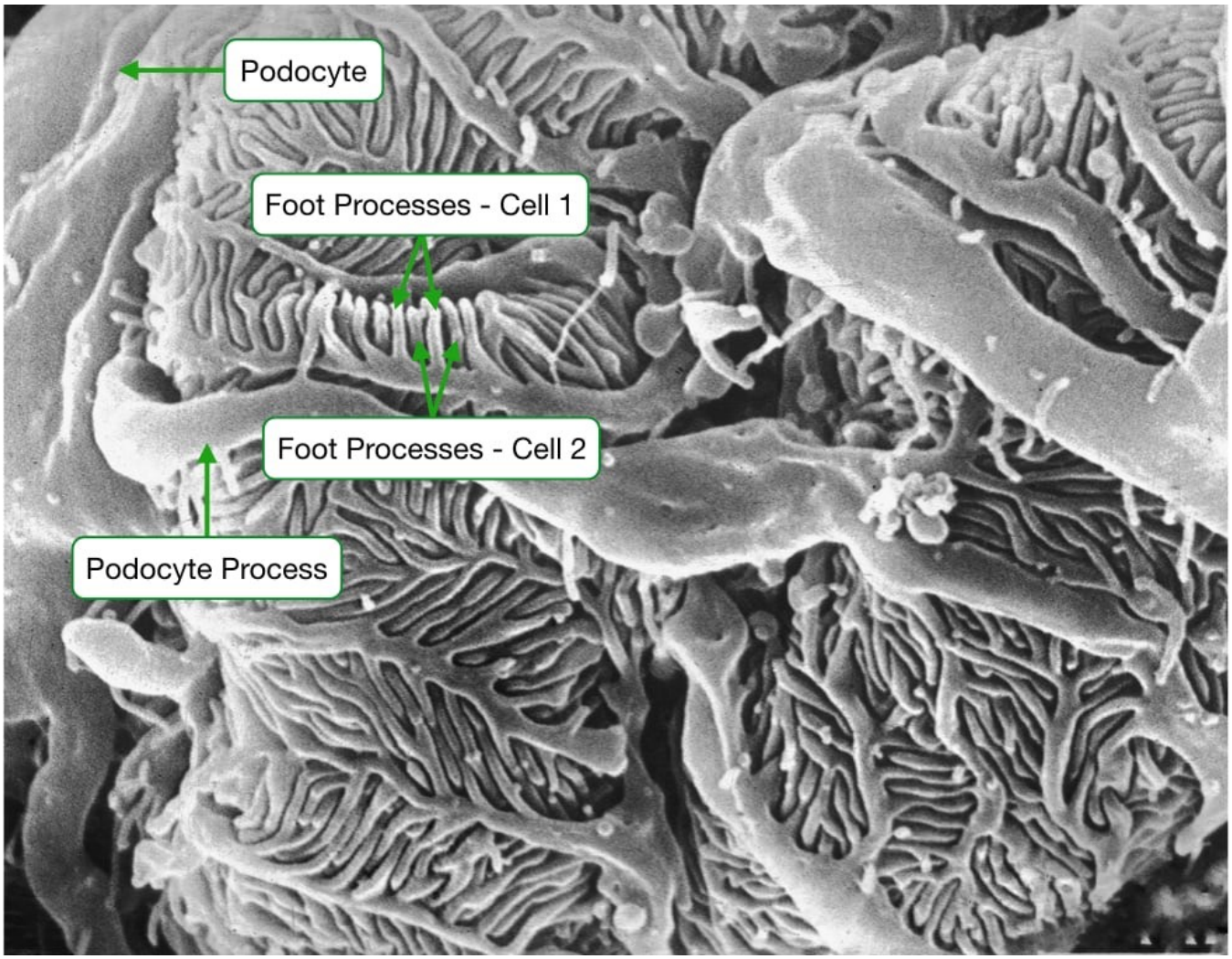


Slit diaphragms span the distance between foot processes and contribute to the filtration barrier.

Nephrin is the primary protein component of slit diaphragms. Similar to other adhesion proteins, nephrin is a transmembrane protein in the cell membrane of foot processes. Nephrin proteins in adjacent foot processes interact to create the slit diaphragm. Because

foot adjacent foot processes arise from different cells, nephrin is similar to a cell adhesion molecule, such as cadherin. Mutations in the genes that encode nephrin can lead to proteinuira.

The scanning electron micrograph below shows more clearly the interdigitation of foot processes from different podocytes. Note the small gaps between foot processes though which filtrate flows to enter Bowman's space. Also, adjacent foot processes come from different cells so the connections between foot processes are intercellular.

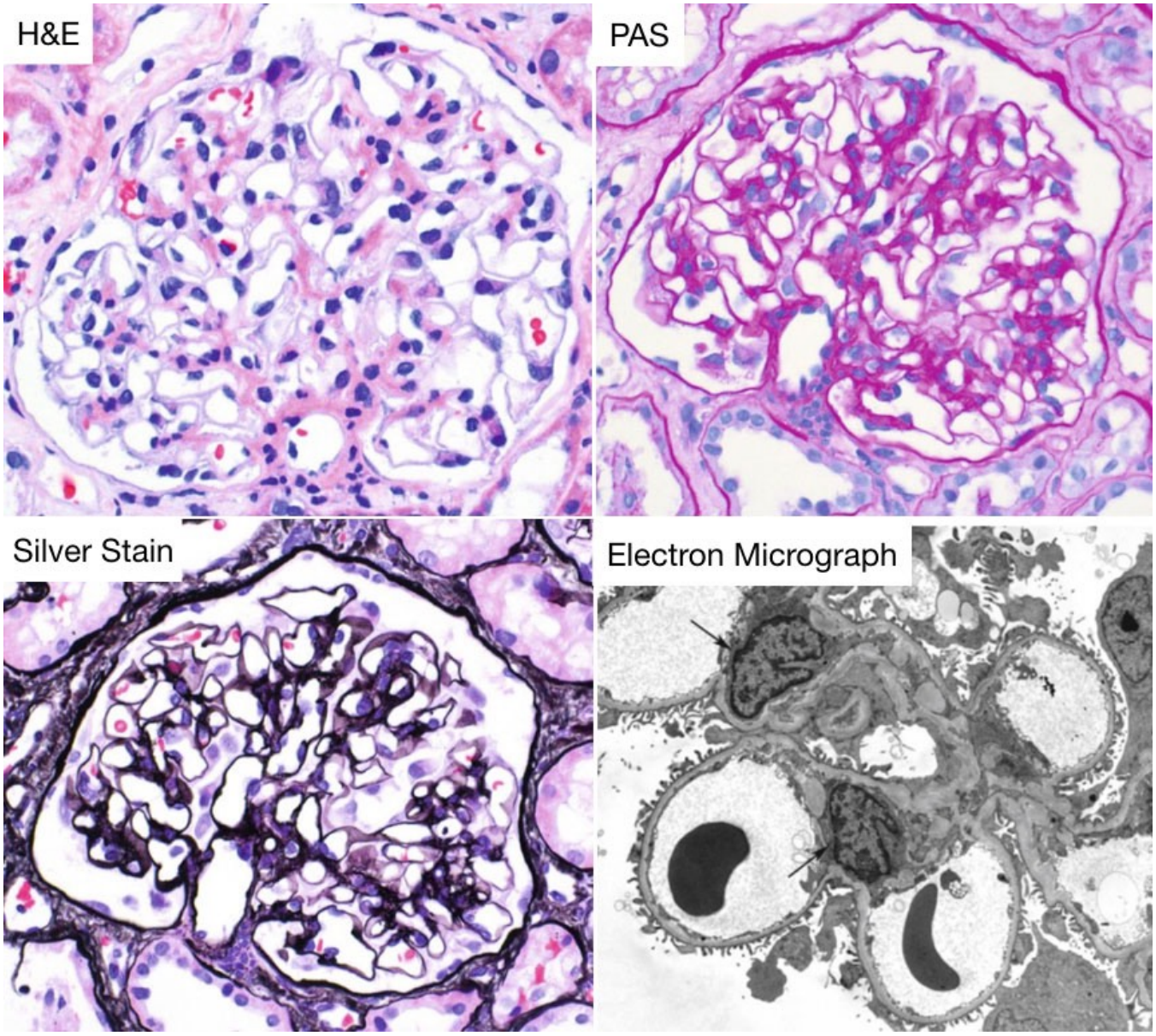


Foot processes from adjacent podocytes interdigitate and surround capillaries.

Visualizing Glomeruli

There are several different methods for examining the structure of glomeruli. A traditional H&E stain reveals the main structures of the glomerulus. Periodic acid-Schiff stain (PAS) is used to label the connective tissue portions of the glomerulus, including mesangium and basement membrane. A methenamine sliver stain can be used to label the basement membrane, which is particularly effective for outlining the capillaries. Lastly, an electron

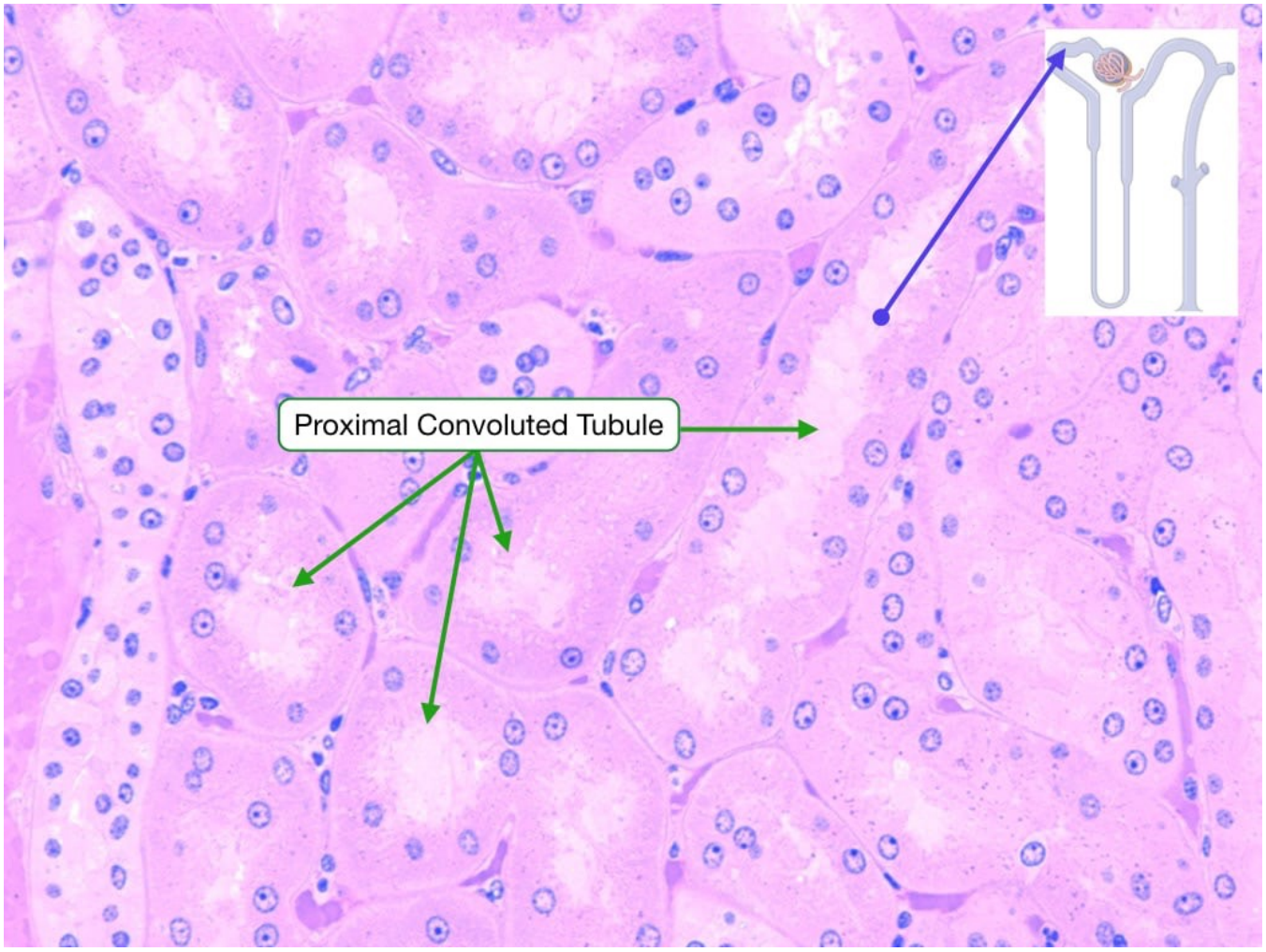
microscope can be used to visualize the finer details of the glomerulus that are not resolvable by light microscopy.



Different stains and microscopy methods are used to visualize features of renal corpuscles.

Proximal Convoluted Tubule

The proximal convoluted tubule begins at the urinary pole of the glomerulus. The proximal convoluted tubule is the site where the majority of glucose, amino acids, ions and water is reabsorbed from the filtrate. Also, most of the protein that has crossed the filtration barrier is reabsorbed here, too. The epithelia cells of the proximal convoluted tubule are large and cuboidal with a deeply stained, eosinophilic cytoplasm. The cells are so large that in cross section to the tubule not every nucleus will be visible, making it appear that the proximal convoluted tubule has fewer nuclei than other tubules.



The proximal convoluted tubule absorbs most of the water and important biological solutes.

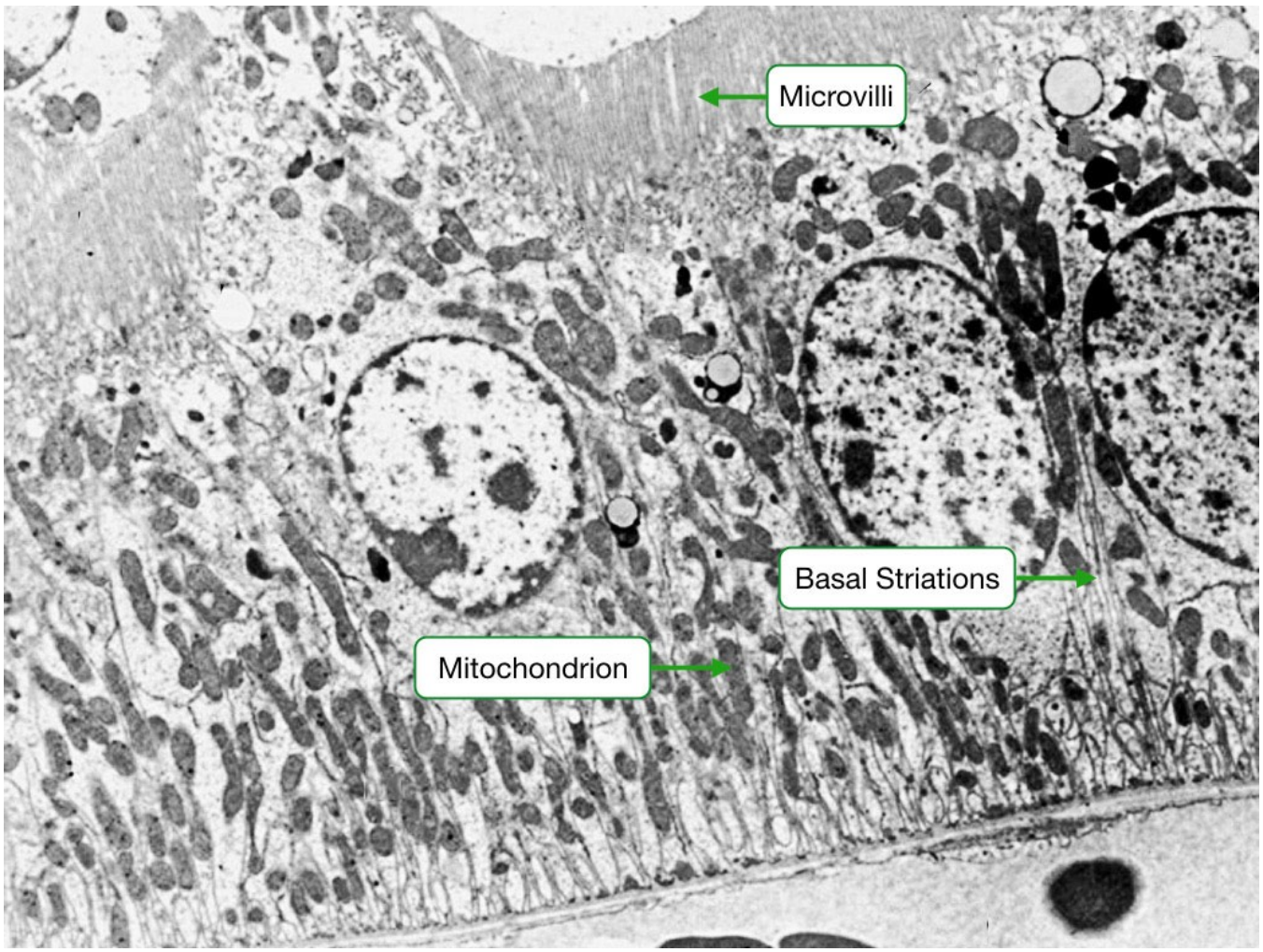
The proximal convoluted tubule is the longest section of a nephron tubule, giving it more opportunity to absorb ions and molecules from the lumen. To accommodate its length within a small space, the tubule is extensive coiled, hence the name convoluted. Consequently, in a section of kidney one sees numerous cross-sections of the same proximal convoluted tubule.

To reabsorb physiologically important molecules, the cells of the proximal convoluted tubule contain several different types of co-transporters (e.g. sodium-glucose co-transporters - SGLT1 and SGLT2) that use the strong sodium electrochemical potential across the apical membrane to import specific molecules from the lumen into epithelial cells. These molecules then diffuse down their concentration gradient to exit cells through channels along the basolateral surface into the interstitium and then the peritubular capillaries. This arrangement allows the cells of the proximal convoluted tubules to absorb almost all of the glucose from the filtrate.

The proximal convoluted tubule also reabsorbs about 67% of the filtered sodium. The numerous sodium-based co-transporters and exchangers in the apical membrane and sodium-potassium pumps in the basolateral membrane drive sodium from the lumen of the

proximal convoluted tubule into the interstitium. Chloride and water follow the flow of sodium from lumen to interstitium with most of the chloride and water taking the paracellular route across the epithelium.

An electron micrograph of the proximal convoluted tubule reveals several important structures that facilitate the absorptive capacity of its epithelial cells. Note the microvilli forming the brush border on the apical surface to increase the surface area of the cell membrane that lines the lumen of the proximal convoluted tubule. The basal surface of the epithelial cells appears striated due to infolding of the basal cell membrane which increases its surface area. Adjacent to the cell membrane in the cytosol are numerous mitochondria. These mitochondria produce ATP to support active transport by sodium-potassium pumps on the basal plasma membrane. The sodium-potassium pump maintains the strong sodium electrochemical gradient across the apical membrane that drives uptake of important small molecules.



Microvilli on the apical surface and basal striations increase the surface area of epithelial cells.

Loop of Henle

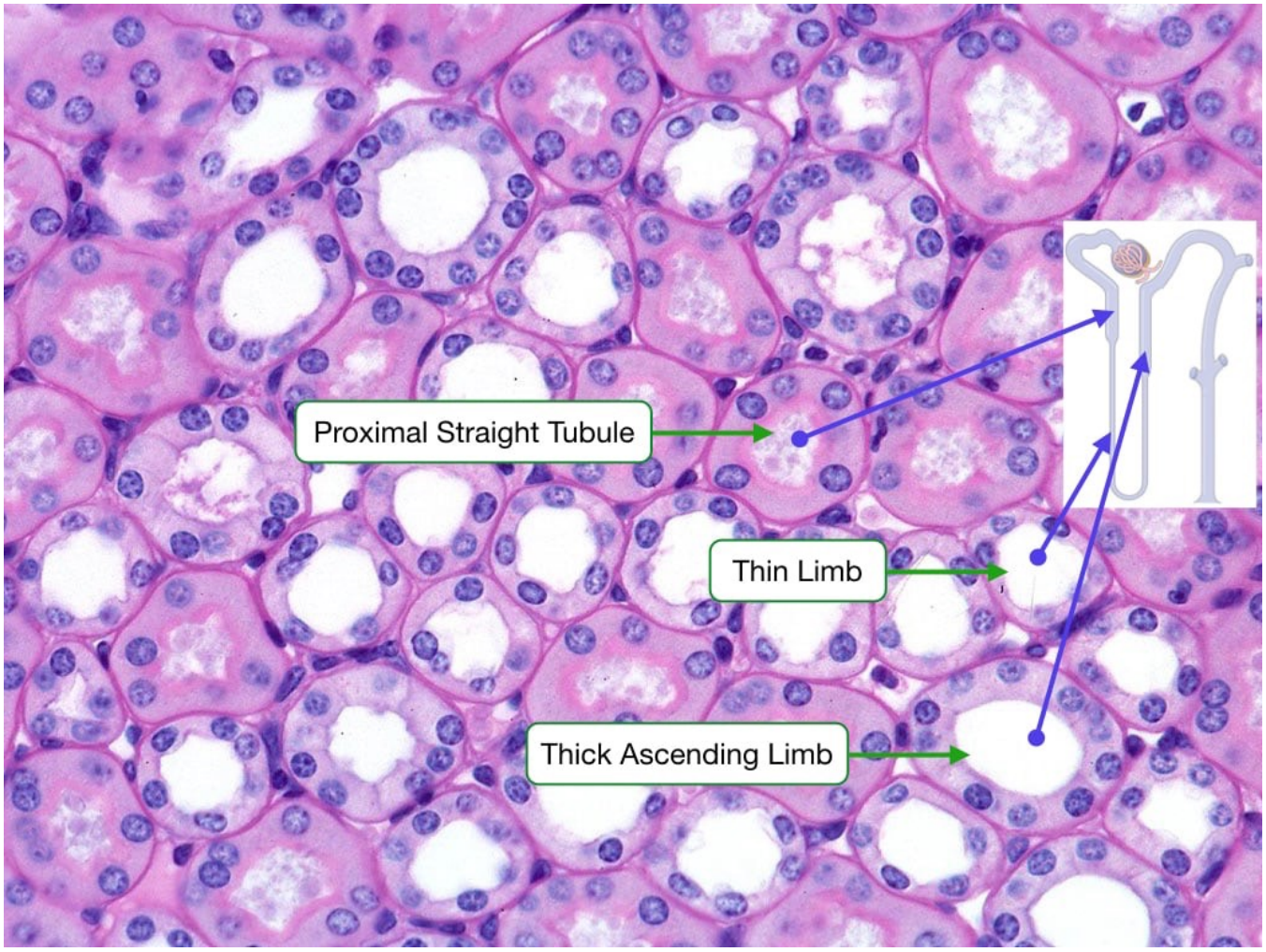
The loop of Henle extends from the proximal convoluted tubule and consists of thin descending limb, the thin ascending limb, and the thick ascending limb. The functions of the loop of Henle are to dilute the urine and increase the osmolality of the interstitium by primarily removing sodium chloride from the urine and releasing it into the interstitium. The elevated interstitial osmolality will be used by the kidney to draw water out of collecting ducts (see below). At the end of the loop of Henle, the tubule fluid will be hypo-osmotic compared to plasma.

The structure and function of the epithelium changes along the length of the loop of Henle.

- The thin descending limb consists of a squamous epithelium which is permeable to water but mostly impermeable to sodium.
- The thin ascending limb is also composed of a squamous epithelium which, in contrast to the descending limb, is permeable to sodium and impermeable to water.
- The thick ascending limb is a cuboidal epithelium which is impermeable to water but actively absorbs sodium.

As mentioned above, loops of Henle are mostly found in nephrons whose corpuscles are located close to the medulla. The loops of Henle in these nephrons extend deep into the medulla where they increase the osmolality of the interstitium. Collecting ducts also run through the medulla and will use the increased osmolality of the interstitium to absorb water from urine (see below).

At its end, the loop of Henle transitions into the distal convoluted tubule.

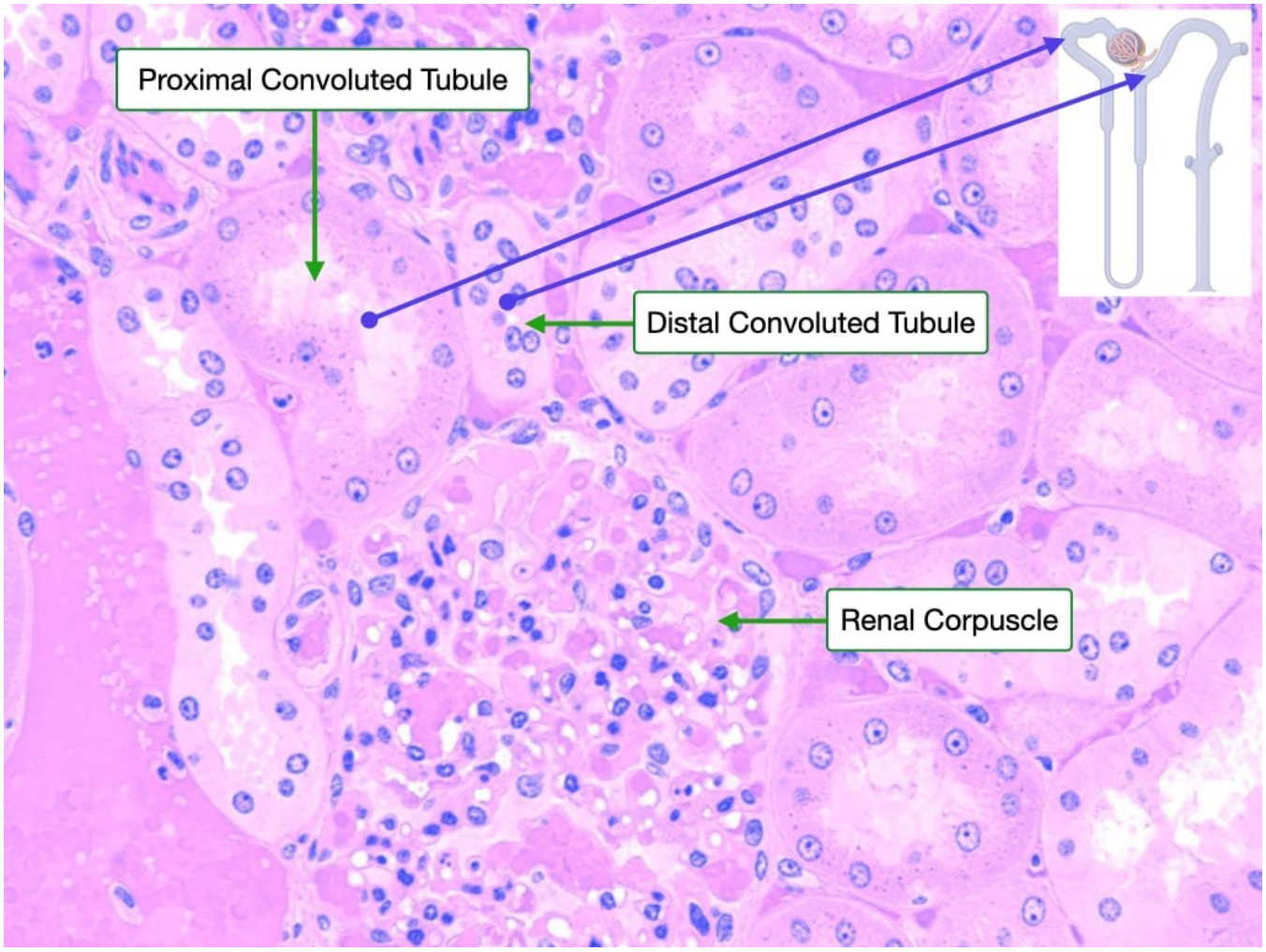


The loop of Henle in juxtamedullary nephrons increases the osmolality of the interstitium.

A cross section reveals several segments of the loop of Henle. First note the proximal straight tubule which extend from the proximal convoluted tubule. The epithelial cells here show a similar structure to the proximal convoluted tubule: cuboidal cells with brush border. The thin descending and ascending limbs look similar to each other and both contain a squamous epithelium. The thick ascending limbs are composed of cuboidal cells, but unlike the proximal convoluted tubule, they do not have apical brush borders. The cells of the thick ascending limbs absorb sodium via Na/K/Cl (NKCC2) co-transporter on their apical surface and Na-K pumps and Cl- channels on their basolateral surfaces.

Distal Convoluted Tubule

The distal convoluted tubule follows the loop of Henle. Further reabsorption of sodium occurs in this segment. The initial segment of the distal convoluted tubule lies right next to the corpuscle and forms the juxtaglomerular apparatus.



The distal convoluted tubule reabsorbs sodium and resides near the renal corpuscle.

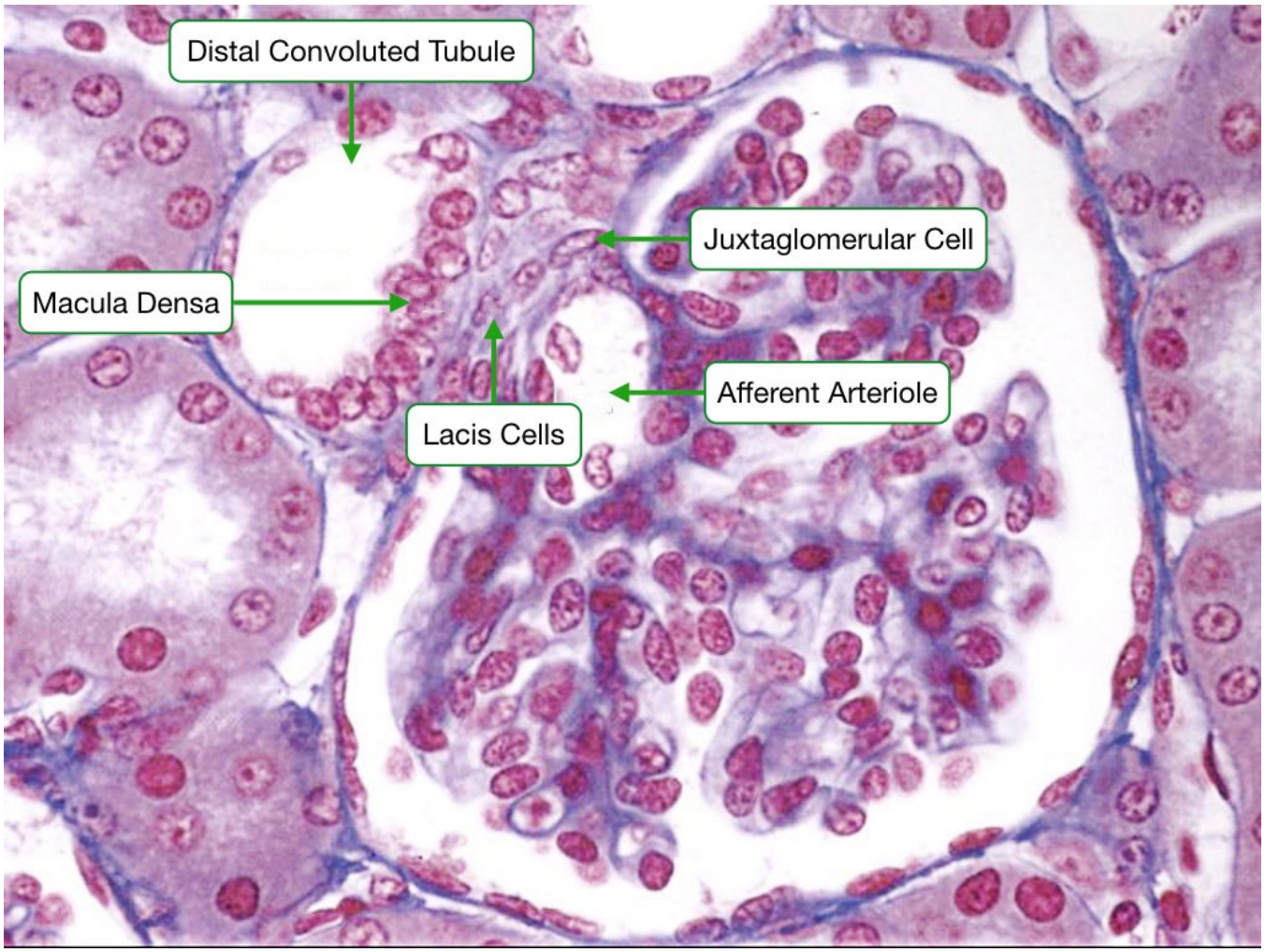
The cells of the distal convoluted tubule are smaller and more lightly stained than those of the proximal convoluted tubule. Consequently, more nuclei are apparent in a cross section of distal convoluted tubule compared to proximal convoluted tubule. Distal convoluted tubules also lack a brush border on their apical surface. Note that in any given section of the kidney cortex, much less space is occupied by distal convoluted tubules as compared to proximal convoluted tubules. This is simply because the distal convoluted tubule is shorter and less convoluted.

The epithelial cells of the distal convoluted tubules actively reabsorb sodium from urine. Their apical surfaces contain either the Na-Cl co-transporter (NCC) or NCC along with the epithelial sodium channel (ENaC). Their basolateral surfaces contain a large number of Na-K pumps. The combination of apical sodium channels and basolateral Na-K pumps always epithelial cells to transport sodium from urine into the interstitium.

Juxtaglomerular Apparatus

The juxtaglomerular apparatus is a specialized structure formed by the distal convoluted tubule and the glomerular afferent arteriole near the vascular pole of the glomerulus. The complex has two main functions. First, it regulates systemic blood pressure by secreting renin as part of the renin-angiotensin-aldosterone system. Second, it controls the filtration rate of the glomerulus to which it is associated by controlling the amount of blood that flows through the afferent arteriole.

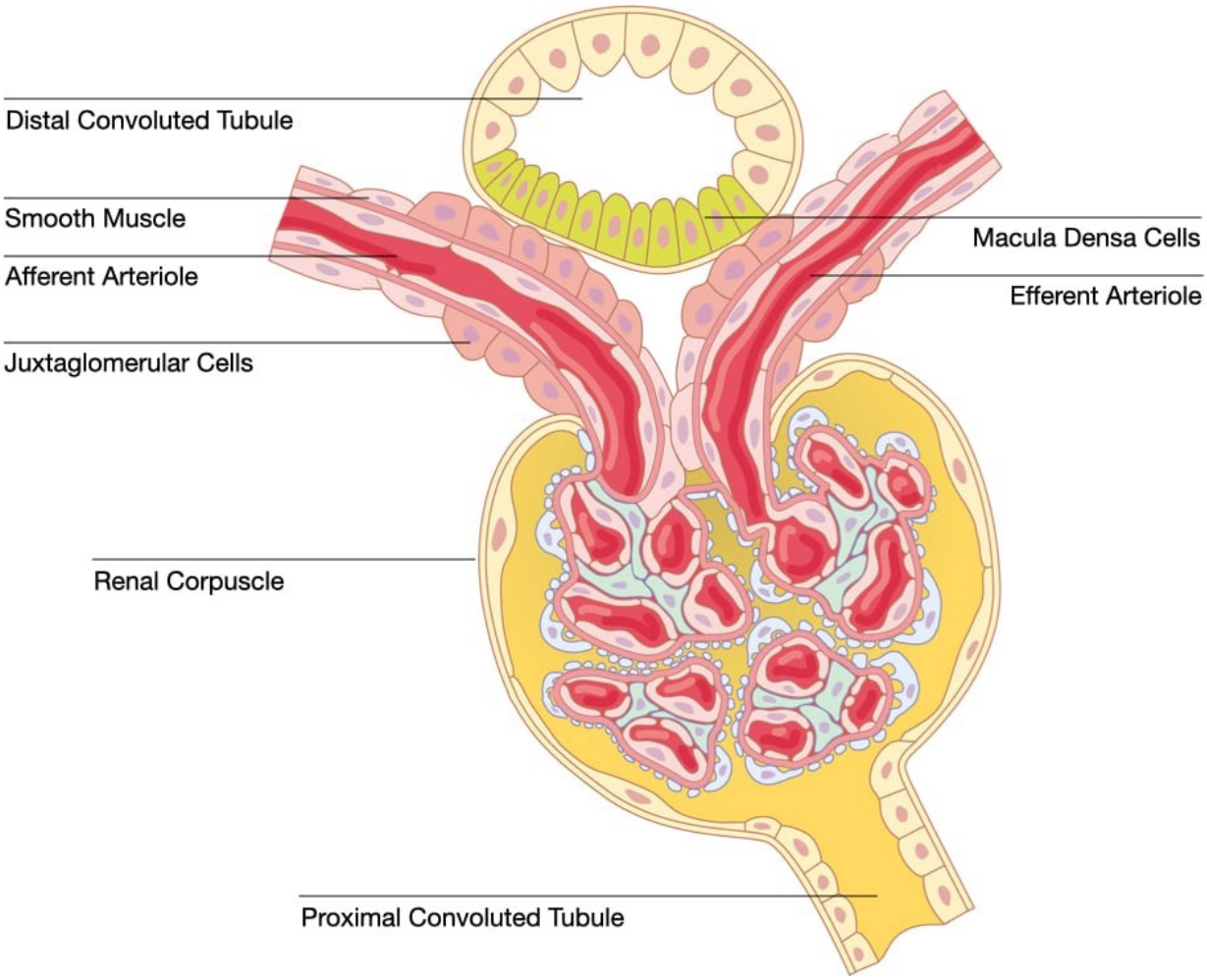
The juxtaglomerular apparatus consists of the macula densa, juxtaglomerular cells and Lacis cells.



Cells of the distal convoluted tubule and afferent arteriole form the juxtamedullary complex.

The macula densa is a collection of specialized epithelial cells lining the distal convoluted tubule. These cells are slightly taller than the other cells in the epithelium of distal convoluted tubule. The cells of the macula densa sense sodium chloride concentration in the tubule which is an indicator of glomerular filtration rate in the nephron. If GFR is too high, the amount of filtrate in the nephron will exceed the capacity of its tubule epithelial

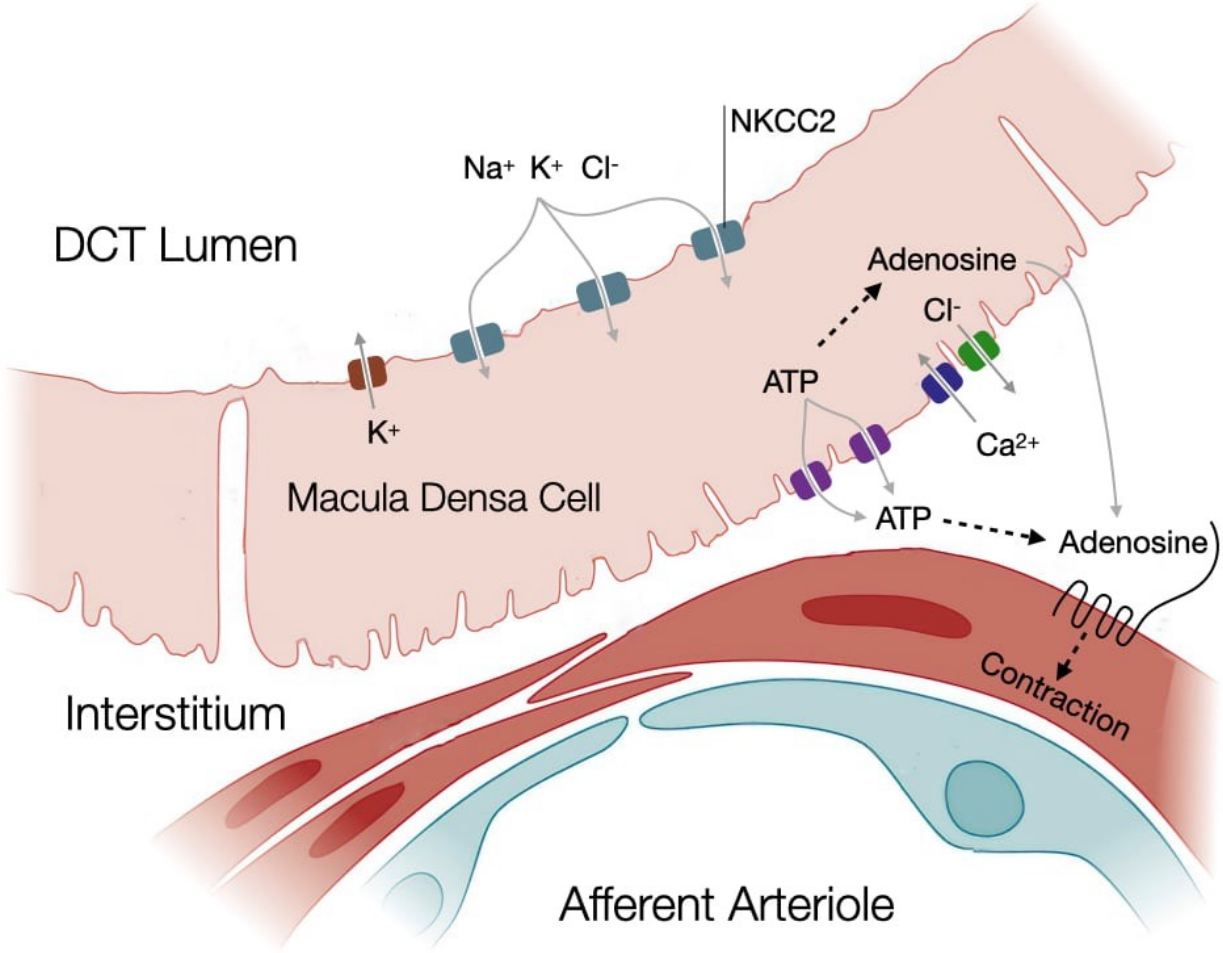
cells to absorb sodium. Consequently, the filtrate reaching the distal convoluted tubule will have a higher sodium concentration. The macula densa cells respond to higher sodium by stimulating the smooth muscle around the afferent arteriole to constrict decreasing the flow of blood into the glomerular capillaries. Decreasing the hydrostatic pressure in glomerular capillaries generates less filtrate.



Macula densa cells sense sodium to regulate the glomerular filtration rate.

Macula densa cells communicate with the afferent arteriole via a paracrine signaling pathway. Macula densa cells sense sodium and chloride concentration in fluid in the distal convoluted tubule via the sodium-potassium-chloride co-transporter (NKCC2) in their apical membranes. As sodium and chloride concentration rises in the filtrate, more sodium, chloride and potassium enter macula densa cells through NKCC2. Potassium is recycled across the apical membrane, whereas chloride diffuses across the basolateral membrane through chloride channels, which depolarizers the basolateral membrane. Depolarization opens calcium channels to increase cytosolic calcium. Cytosolic calcium opens channels in the basolateral membrane that allow ATP to diffuse into the interstitium. Enzymes in the interstitium convert ATP to adenosine. Cytosolic calcium also activates enzymes in macula

densa cells that convert ATP to adenosine which can diffuse across the basolateral membrane into the interstitium. Adenosine binds receptors on smooth muscle cells that surround the afferent arteriole. Adenosine causes the smooth muscle cells to constrict which decreases the diameter of the afferent arteriole lowering blood flow into the glomerulus.



Sodium chloride uptake triggers release of ATP and adenosine which constricts the afferent arteriole.

The juxtaglomerular cells are part of the afferent arterioles, which secrete renin when blood pressure falls. Renin increases blood pressure via the renin-angiotensin-aldosterone system. Juxtaglomerular cells reside just beneath the endothelial cells that line the afferent arteriole.

Three mechanisms trigger juxtaglomerular cells to release renin. First, juxtaglomerular cells respond directly to changes in blood pressure in the afferent arteriole. Elevated blood pressure stretches juxtaglomerular cells which inhibits renin release, whereas a fall in blood pressure relaxes juxtaglomerular cells, triggering renin release.

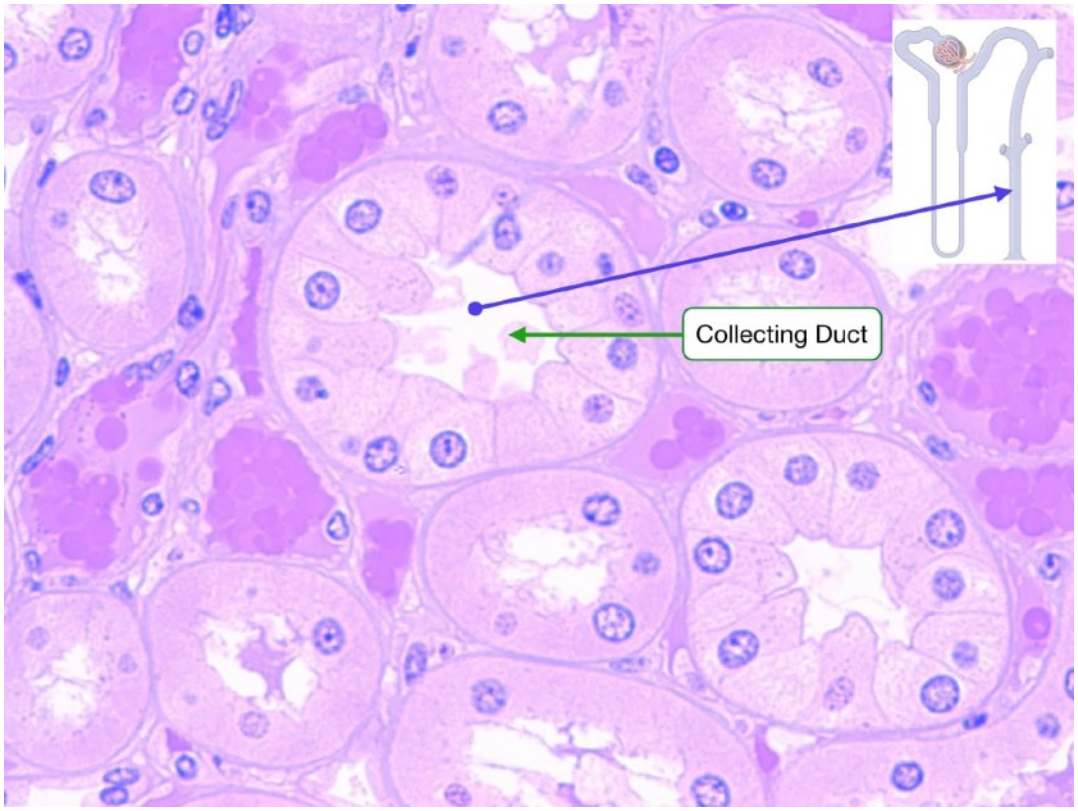
A second mechanism involves macula dense cells. When blood pressure falls, GFR is reduced and the concentration of sodium and chloride in the filtrate that reaches the macula

densa is lower than normal. Reduced movement of sodium and chloride through the NKCC2 channel activates a signaling pathway that leads to production of prostagladin E2 (PGE2). PGE2 diffuses to juxtaglomerular cells where it binds a receptor to trigger renin release.

Lastly, the sympathetic nervous system can trigger release of renin from juxtaglomerular cells primarily through β-adrenergic receptors.

Collecting Ducts

The terminal portion of the distal tubule transitions into a connecting tubule and then initial collecting tubule. Collecting tubules from different nephrons empty into a straight collecting duct. The epithelium of collecting ducts contains two different types of cells: intercalated cells and principles cells. Intercalated cells regulate pH by secreting either H+ or HCO3-. Principle cells regulate the solute concentration of urine through regulated absorption of water. Principle cells are under the control of antidiuretic hormone (ADH). When ADH is present, principle cells become more permeable to water. The high osmotic pressure in the intersitium surrounding collecting ducts (generated by loops of Henle) draws water from the renal tubule into epithelial cells of the collecting duct and then into the surrounding interstitium.



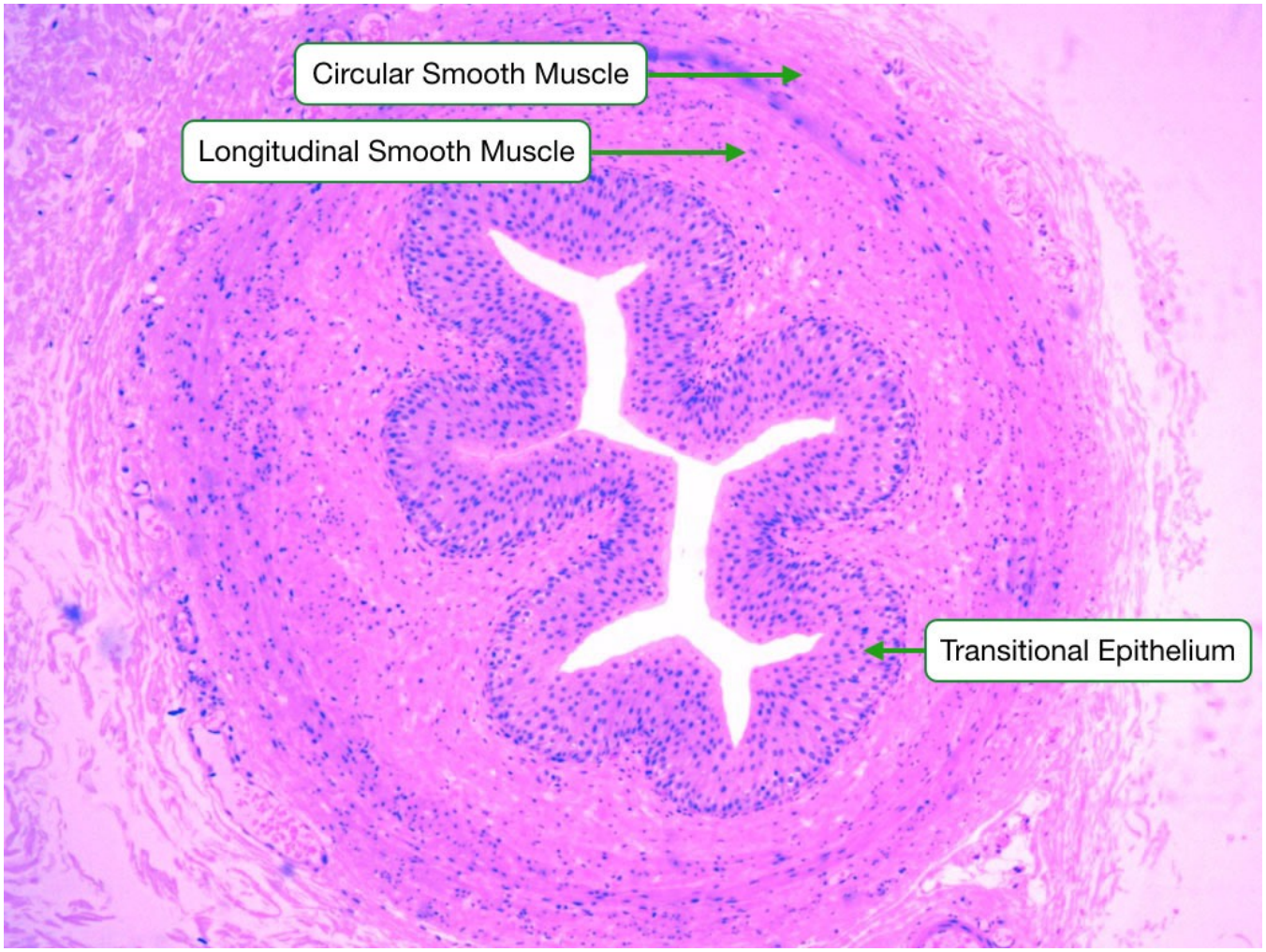
Collecting ducts contain intercalated cells and principle cells to regulate pH and water absorption.

To increase the flow of water from tubule fluid into epithelial cells, ADH increases the number of aquaporin 2 channels in their apical membrane of epithelial cells. Aquaporins allow the diffusion of water across membranes. In the absence of ADH, epithelial cells of the collecting duct store aquaporin 2 in cytoplasmic vesicles. ADH stimulates the transport of these vesicles to the cell membrane where fusion of the vesicle releases aquaporin 2 into the cell membrane.

Collecting ducts can be differentiated from other tubules by their prominent lateral borders between epithelial cells.

Renal Pelvis and Ureter

Numerous collecting ducts merge into the renal pelvis, which then becomes the ureter. The ureter connects the kidney and the urinary bladder.



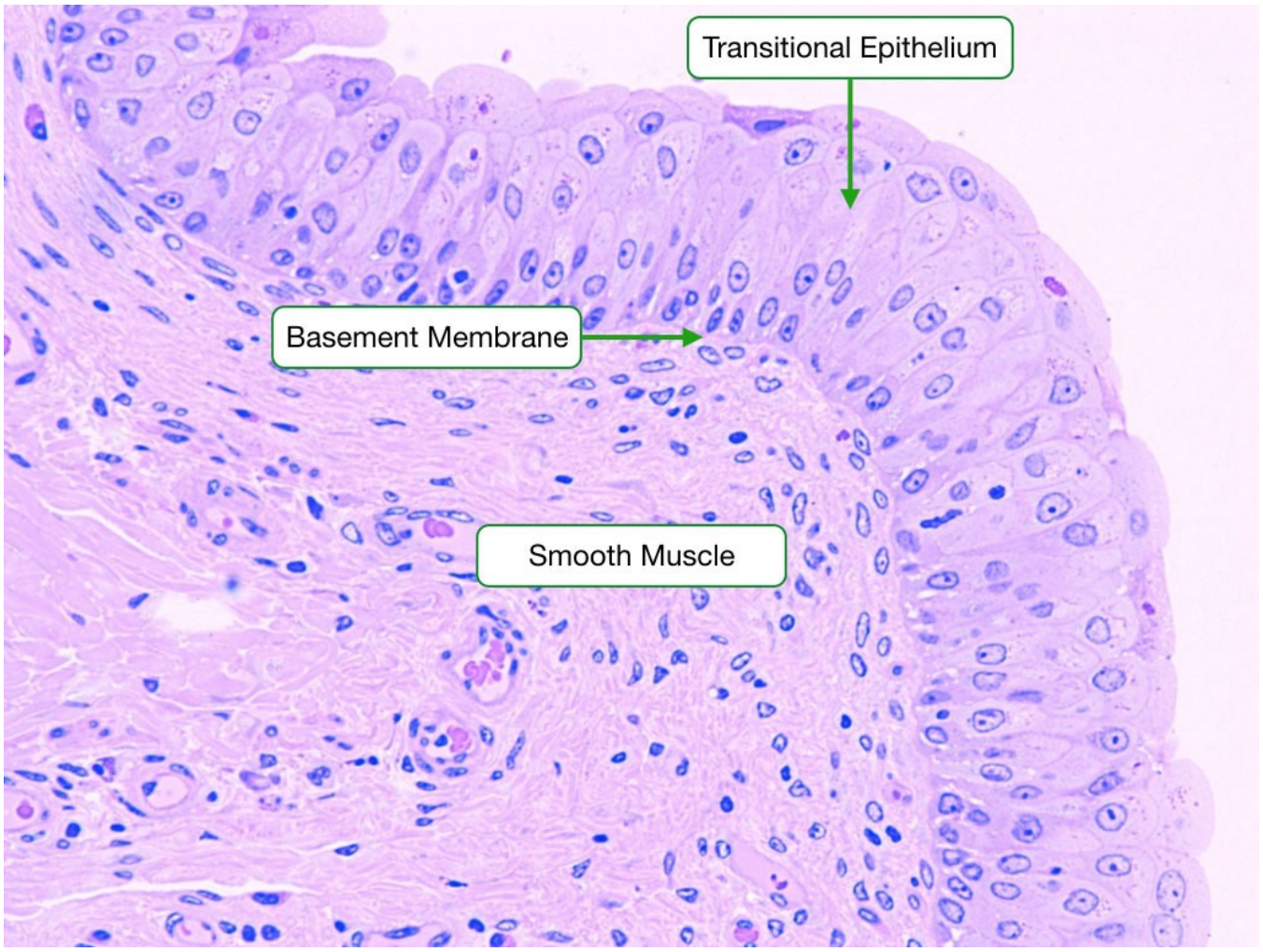
The ureter is a muscular tube that connects the kidney to the urinary bladder.

The ureter is a muscular tube, composed of an inner longitudinal layer and an outer circular layer of smooth muscle. The lumen of the ureter is covered by transitional epithelium (also

called urothelium). Recall that the transitional epithelium is unique to the conducting passages of the urinary system. Its ability to stretch allows the dilation of the conducting passages when necessary.

Urinary Bladder

The ureter empties the urine into the bladder. The transitional epithelium continues over the surface of this organ. The thickened muscular layers become interwoven and cannot be clearly identified at this point. This image shows a relaxed bladder where the epithelial cells appear cuboidal. In a distended bladder the epithelial cells are stretched and become more squamous.



The urinary bladder is lined by a transitional epithelium that stretches as urine fills the bladder.

Urethra

The urethra carries the urine away from the bladder to the outside of the body. In the male, it is joined by the genital system. The epithelium changes from transitional to stratified or pseudostratified columnar in the urethra, and to stratified squamous in the distal end of the urethra.