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HISTOLOGY OF MAMMALIAN KIDNEY

The kidneys are paired retroperitoneal organs of the urinary system. Its main function is to filter blood and produce urine. Each kidney consists of a cortex, medulla and calyces. Nephrons are the main functional units of the kidney that removes metabolic wastes and excess water from the blood and adjust water, salt and pH to maintain the homeostatic balance of tissue fluids. It is central organs or homeostasis in the organisms. In human, around 180 liters of blood are filtered per day by the kidneys, accounting for around 20% of cardiac output. It is also known to regulate blood pressure through the renin-angiotensin-aldosterone system, erythrocyte production through production of erythropoietin, and circulating calcium and phosphate levels, in part through the activation of vitamin D.

Structure of kidneys

The kidney is usually a bean shaped organ with a convex lateral surface, concave medial surface and superior and inferior poles. The medial surface features the hilum of the kidney, which is the passageway for the renal vessels and the ureter. A connective tissue capsule, called as renal capsule and a layer of perinephric (perirenal) fat protect and cushion the kidney. The capsule contains a layer of contractile cells called myofibroblasts, which make the capsule able to adapt to the constant pressure changes within the kidney. The suprarenal, which is also called as adrenal gland, sits on the kidney's superior pole, separated from it by the perinephric fat. Both the kidney and the suprarenal gland are covered by a layer of renal fascia.

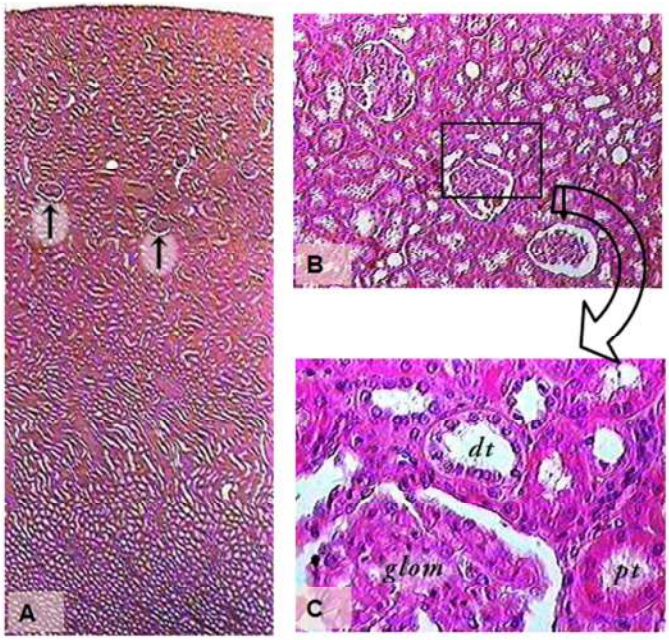
A bat kideny | A porcine kidney (right with capsule) | Human kidneys | Sagittal section of a lamb kidney

Images are not in scale, these are presented to show the external morphology of kidneys in different mammalian species.

The kidney parenchyma consists of two layers; an outer cortex and inner medulla. There are about one million nephrons ensheathed in the renal capsule. Urine is collected into a system of renal calyces, which is a series of distinctive chambers within a kidney. Calyces gradually increase in size, starting with the minor calyces, which open into larger major calyces that empty into the renal pelvis. From the renal pelvis, the urine passes into the ureter. The portion of the kidney which contains the calyces, renal pelvis, ureter and renal vessels is called the renal sinus.

Usually, renal cortex is darker than its underlying renal medulla due to high supply of blood. It receives over 90% of the total kidney blood supply. The cortex has a grainy appearance, as it mostly contains ovoid and coiled parts of the nephrons (renal corpuscles and convoluted tubules). On the other hand, the renal medulla is lighter and appears striped, as it contains vertical nephron structures (tubules, collecting ducts). It consists of renal (medullary) pyramids separated by projections of the renal cortex (renal columns). The apices of the pyramids project towards the renal pelvis and open into the minor calyces via perforated plates on their surfaces (area

cribrosa). Each renal pyramid, with its surrounding cortical tissue, forms a renal lobe. Renal lobes are further divided into renal lobules. Each lobule consists of a group of nephrons emptying into one collecting duct. These structures can be observed in a coronal section of the kidney.



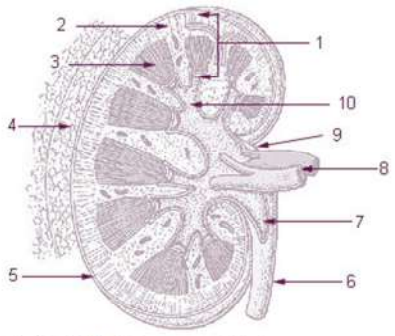
A. This image represents almost the entire thickness of the kidney. The outer layer of the kidney--the cortex--is on the top. The round structures in this part of the kidney are called renal corpuscles (rc). Each renal corpuscle consists of a glomerular capsule (part of the nephron) surrounding a clump of capillaries called the glomerulus. The other structures that are seen sections of various parts of the nephrons: proximal convoluted tubules, loops of Henle, and distal convoluted tubules (dt), and collecting tubules or collecting ducts.

B. This image shows part of the kidney cortex and includes three examples of renal corpuscles. The arrow points to one of them. Most of the other things in this image are cross sections of proximal or distal convoluted tubules. The area in the box is enlarged in the image below.

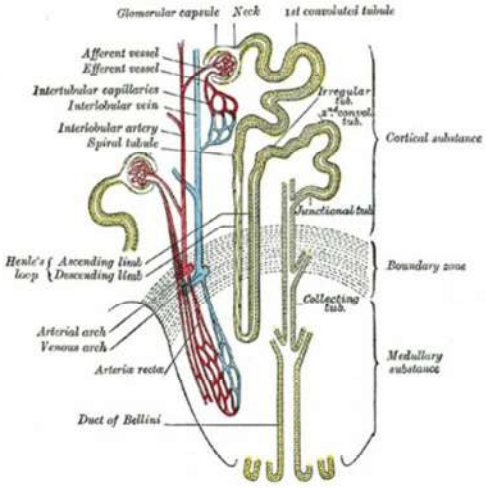
C. This image shows the enlarged view of the section in **B.** In this image, the glomerulus is easy to identify due to the presence of white space of the glomerular capsule around it. The proximal (pt) and distal (dt) convoluted tubules can be differentiated by looking at the cells that make up the walls of the tubules and the diameter of the lumen.

Source: *https://www.austincc.edu/histologyhelp/organs/ow_kidney.html*

Histology of a mammalian kidney



1. Parenchyma
2. Cortex
3. Medulla
4. Perirenal fat
5. Capsule
6. Ureter
7. Pelvis of kidney
8. Renal vessels
9. Hilum
10. Calyx



Schematic of a mammalian kidney

Nephron

- Functional unit of kidney
- Humans up to 1 million
- Filtration of waste from blood
- Endocrine
- Blood pressure regulation

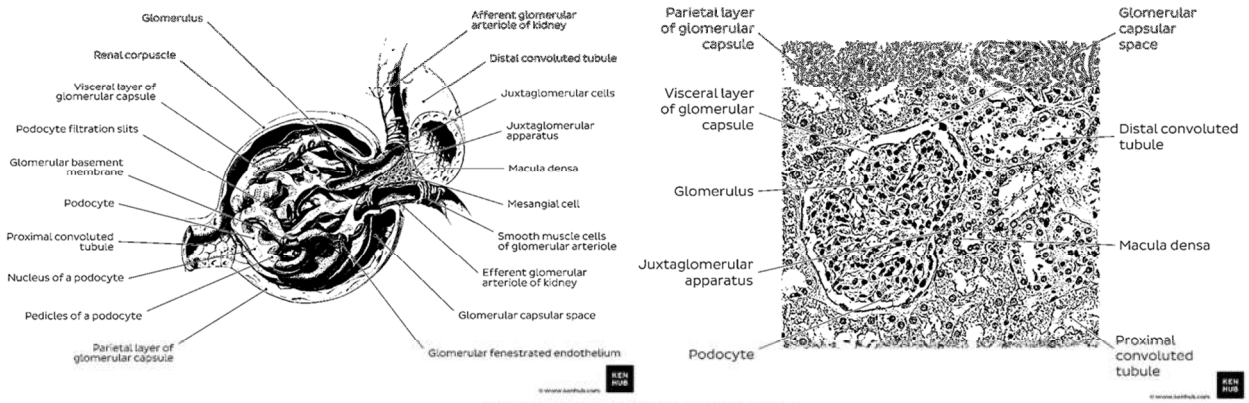
Nephron

The nephron is the functional unit of the kidney. It produces concentrated urine by creating an ultrafiltrate from blood. A nephron consists of two main parts: a renal corpuscle and its associated renal tubule system. Renal corpuscles are located in the renal cortex, while their tubular systems extend into the medulla. Depending on their distribution and morphology, there are two main types of nephrons in the kidney; cortical and juxtamedullary. Cortical nephrons have their corpuscles close to the kidney capsule. Their tubules are very short, extending only into the upper medulla and

are known as proximal tubule. The corpuscles of the juxtamedullary nephrons are located close to the corticomedullary border. Their tubular systems are much longer making the lumen smaller, have long microvilli, extending deep into the medulla with a fuzzy appearance, known as distal tubule. Each nephron is surrounded by a network of capillaries. Branches from the renal interlobular arteries enter a nephron as the afferent arteriole, form a capillary tuft (glomerulus) then exit the nephron as the efferent arteriole. The capillary network then continues to surround the nephrons renal tubule system as peritubular capillaries, forming the vasa recta around the nephron loop. *These peritubular capillaries secrete erythropoietin (EPO), a hormone that regulates red blood cell production.*

Renal corpuscles

The renal corpuscle is the filtration apparatus of the nephron. Each corpuscle consists of two main elements; the glomerulus and glomerular (Bowman's) capsule. The glomerulus is a network of capillaries formed by branches of the renal artery (afferent and efferent arterioles). *The glomerulus shrinks during tissue processing, leaving a thin white space between it and the outer wall of the capsule. This white space makes the renal corpuscles easy to find. They make good landmarks for identifying renal cortex; because that is the only place they are found.*

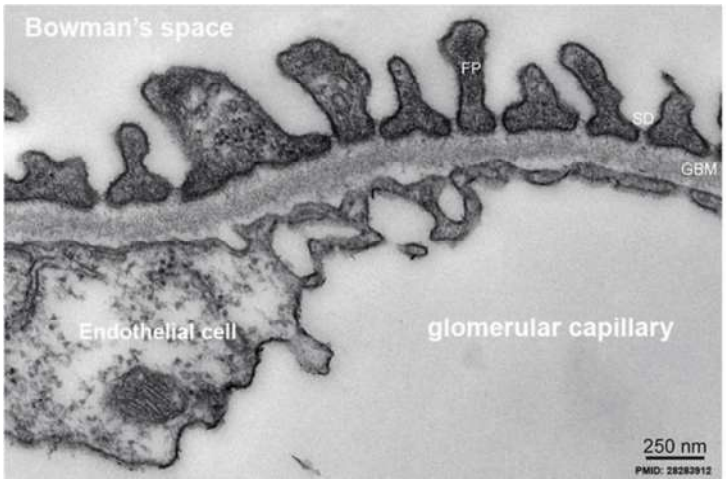


Renal corpuscle and juxtaglomerular apparatus

It surrounds the glomerulus and hence also known as glomerular capsule. It consists of two layers (parietal and visceral), which bound a cavity called the glomerular capsular space (Bowman's / urinary space). The inner visceral layer is made of special cells called podocytes. Podocytes cover the walls of glomerular capillaries, interdigitating with each other and forming narrow slits between their projections. The outer parietal layer is made of simple squamous epithelium and is continuous with the nephron tubules. The afferent and efferent arterioles enter the renal corpuscle at the vascular pole, while the site where the glomerular capsule narrows and continues as the proximal thick segment of the nephron is called the urinary pole.

Renal tubular system

The tubule system is the part of the nephron which processes glomerular ultrafiltrate into urine by reabsorbing necessary molecules and secreting the unnecessary and waste substances. It consists of three parts; proximal tubule, nephron loop, and distal tubule.

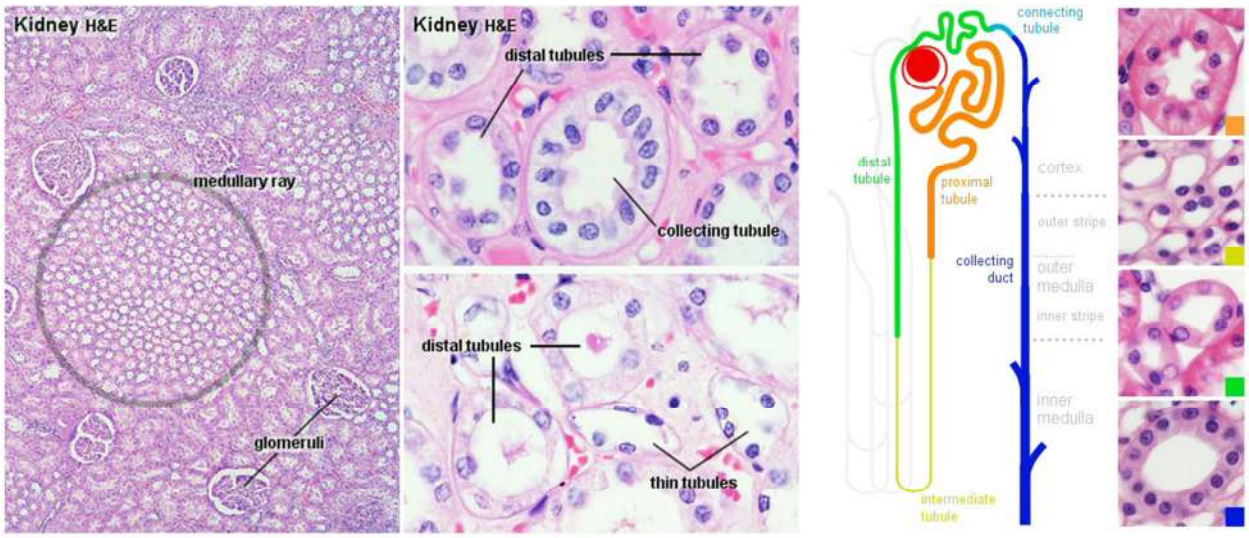


Transmission electron micrscopy of a mouse glomerular capillary revealing the structural composition of the glomerulus. Here, the primary filtrate drains into Bowman's space (BS) and, via the urinary pole, reaches the proximal tubule.

Ultrastructure of glomerular capillary reveals that there is the foot processes (**FP**) on the outside of the capillary., which cover a major part of the glomerular basement membrane (**GBM**) circumference. The slit-diaphram can be discerned in between the foot processs.es. he endothelial cell coats the inner surface of the capillary wall and is followed by the three layers of the glomerular basement membrane (**GBM**).

Proximal tubule: The proximal tubule is the first part of the tubular system. It consists of *convoluted* and *straight segments*. The proximal convoluted tubule is located within the renal cortex and is continuous with the capsular space. The straight proximal tubule (or thick descending limb) extends down into the medulla. Both parts are composed of simple cuboidal epithelium, rich in mitochondria and microvilli (brush border). This morphology is adapted to the proximal tubule function of absorption and secretion. More than half of the previously filtered water and molecules are returned to the blood (reabsorption) by the proximal tubules.

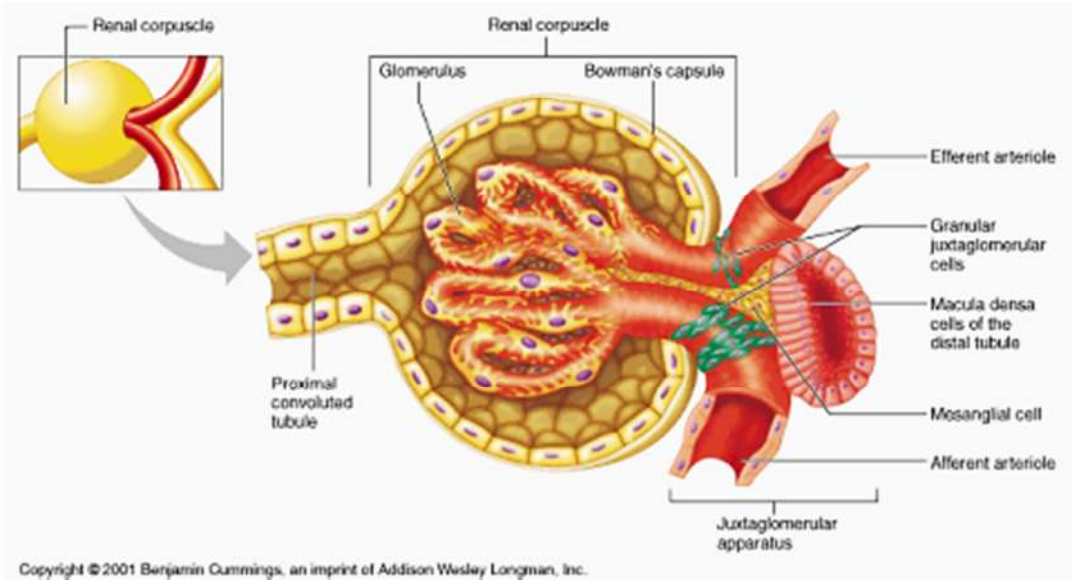
Medullary loop or nephron loop: The nephron loop is the U-shaped bend of a nephron which extends through the medulla of the kidney. Histologically, it consists of two parts; *thin descending* and *thin ascending limbs*. Both limbs are composed of simple squamous epithelium. The cells have few organelles, little to no microvilli and low secretion abilities. The two limbs work in parallel, with the surrounding vasa recta capillaries, to adjust the filtrate's salt (e.g. sodium, chloride, potassium) and water levels. More specifically, the descending limb is highly permeable to water, less permeable to solutes, while the ascending limb is the opposite.



Nephron tubule

Distal tubule: The distal tubule also consists of *straight* and *convoluted* segments. The straight distal tubule (thick ascending limb) continues on from the thin ascending limb of the nephron loop at the level between the inner and outer medulla. The convoluted distal tubule projects into the cortex. Both parts of the distal tubule are composed of simple cuboidal epithelium, similar in morphology to the proximal tubule. A key difference between them is that the epithelium of the distal tubule has less well-developed microvilli. Reabsorption and secretion occurs here, albeit to a lesser degree than in the proximal tubule. By having lots of mitochondria the straight distal tubules can reabsorb any useful substances (electrolytes), and secrete any remaining waste products using active transport. It absorbs sodium under the regulation of aldosterone.

Juxtaglomerular apparatus (JGA): It is a collection of cells that lies into the vascular pole of the nephron. It is formed by 3 types of cells; macula densa, juxtaglomerular granular (JG) cells and extraglomerular mesangial (Lacis) cells. It regulates glomerular blood flow and filtration rate, and systemic blood pressure.



Macula densa: The macula densa are found in the wall of the distal tubule, at the point where the tubule comes in contact with the glomerulus. Here the regular cuboidal epithelium of the distal tubule crowd together and become columnar in shape.

Juxtaglomerular granular (JG) cells: These are modified smooth muscle cells found surrounding the afferent, and sometimes efferent, arteriole.

Extraglomerular mesangial (Lacis) cells: These are located in the triangular space between the afferent and efferent arterioles.

All these cells are involved in the regulation of various functions as described above. Glomerular blood flow is regulated by a feedback mechanism, whereby the macula densa responds to high sodium chloride levels in the filtrate by releasing vasoconstrictor chemicals. These chemicals cause the afferent arteriole to vasoconstrict, thus lowering glomerular pressure and, in turn, filtration rate.

This system maintains a mostly constant pressure within the nephrons. *Systemic blood pressure is regulated through the renin-angiotensin-aldosterone system. Low systemic blood pressure, recognised by baroreceptors, triggers the juxtaglomerular granular cells to secrete an enzyme called renin. Renin, in turn, activates the renin-angiotensin-aldosterone system, raising systemic blood pressure through the actions of angiotensin and aldosterone*.

Collecting system or collecting tubules

The collecting system of the kidney is a series of tubes that moves urine from the nephrons into the minor calyces. Several distal convoluted tubules from neighbouring nephrons drain into a collecting duct via connecting/collecting tubules. Collecting ducts then travel through the kidney medulla, converging at the apex of each renal pyramid. Here, several ducts merge to form a single large **papillary duct (of Bellini)**, which opens into the minor calyx through the **area cribrosa**. They are made of epithelial cells, which get progressively taller as the ducts get larger and progressively increase the diameter towards the medullar region. Type of collecting ducts depends on the part of the kidney parenchyma that part of the duct is located, which are as follows;

- ***Cortical collecting ducts:*** simple cuboidal epithelium
- ***Medullary collecting ducts:*** simple columnar epithelium
- ***Papillary ducts:*** simple columnar epithelium

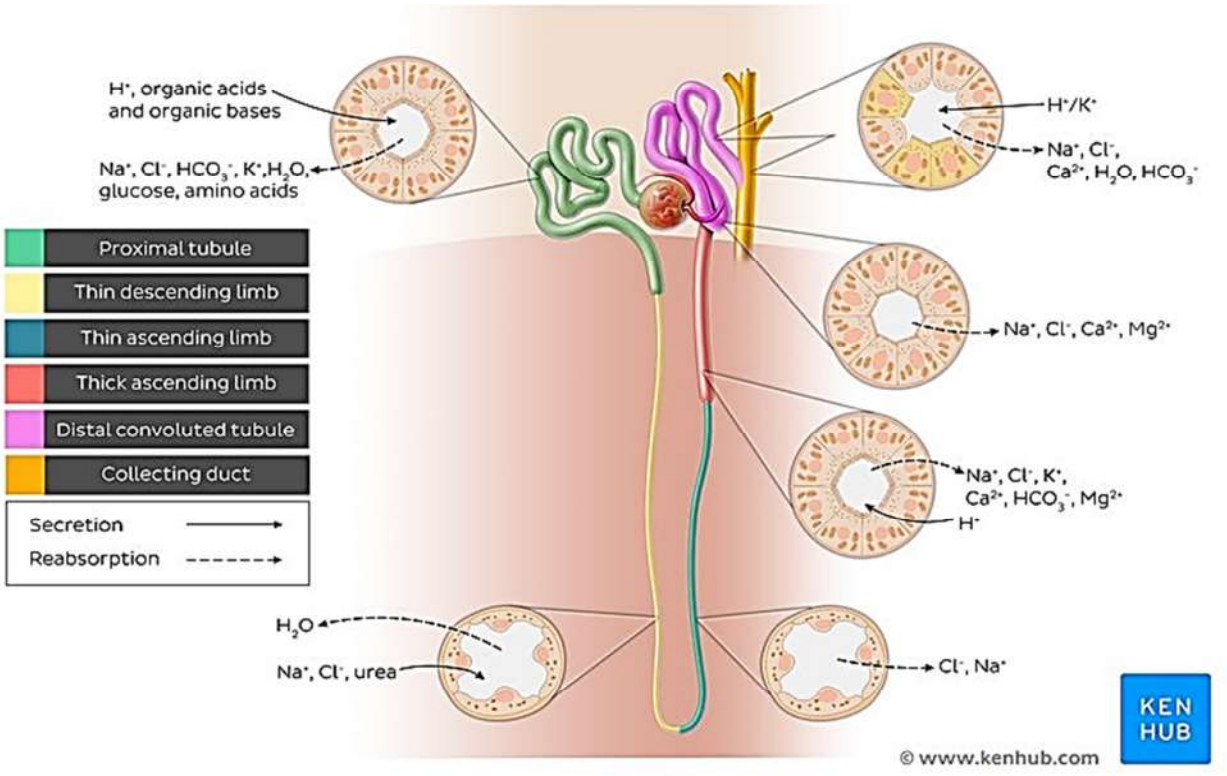
In addition to the epithelial cells, two more different types of cells are present in these ducts, which are known as principal cells and intercalated cells. The principal cells, which are pale staining, play a role in ion transport, while intercalated cells are darker and scattered amongst the principal cells and are responsible for acid-base balance. Collecting ducts are the last chance site for water and electrolyte reabsorption from the filtrate further concentrating the urine, particularly under the influence of antidiuretic hormone (ADH). No more reabsorption takes place past the medullary collecting ducts.

Secretion and reabsorption

As discussed elsewhere in this chapter, the function of nephron is to maintain homeostasis of the body fluids, by excreting unwanted products in urine. Therefore, nephron anatomy is specialized to create urine from the blood through four key activities i.e. filtration, reabsorption, secretion and excretion.

Filtration: Filtration is the process by which nephron filters unwanted substances from the blood and forms filtrate as a byproduct in this process that forms urine after reabsorption of some useful substances and water. It occurs in the renal corpuscle of the nephron.

Reabsorption and secretion: Reabsorption and secretion are activities that occur in the nephrons renal tubular system. These processes fine tune what substances are excreted and what are kept, by the body. **Reabsorption** is the process by which water and molecules, lost from the blood during filtration, are reabsorbed back into the capillaries surrounding the nephron. **Secretion** is where water and molecules leave the peritubular capillaries and enter (or re-enter) the urine filtrate. The remaining product, urine, is then excreted from the kidney via the ureters.



Reabsorption and secretion are finely controlled processes, whereby the epithelial cells of each segment of the tubular system reabsorbs and secretes different substances in order to achieve maximum control over the urine concentration. Regulation of these processes includes; passive (countercurrent exchange system), nervous (sympathetic nervous system) and hormonal (angiotensin, aldosterone and antidiuretic hormone) mechanisms. The result of this process is urine, a fluid highly concentrated with body metabolic waste and excess substances. In healthy individuals, urine normally contains ions, urea, creatinine and variable amounts of water. Healthy urine is free of microorganisms, glucose, blood cells and blood proteins.

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