Histology of the Kidney

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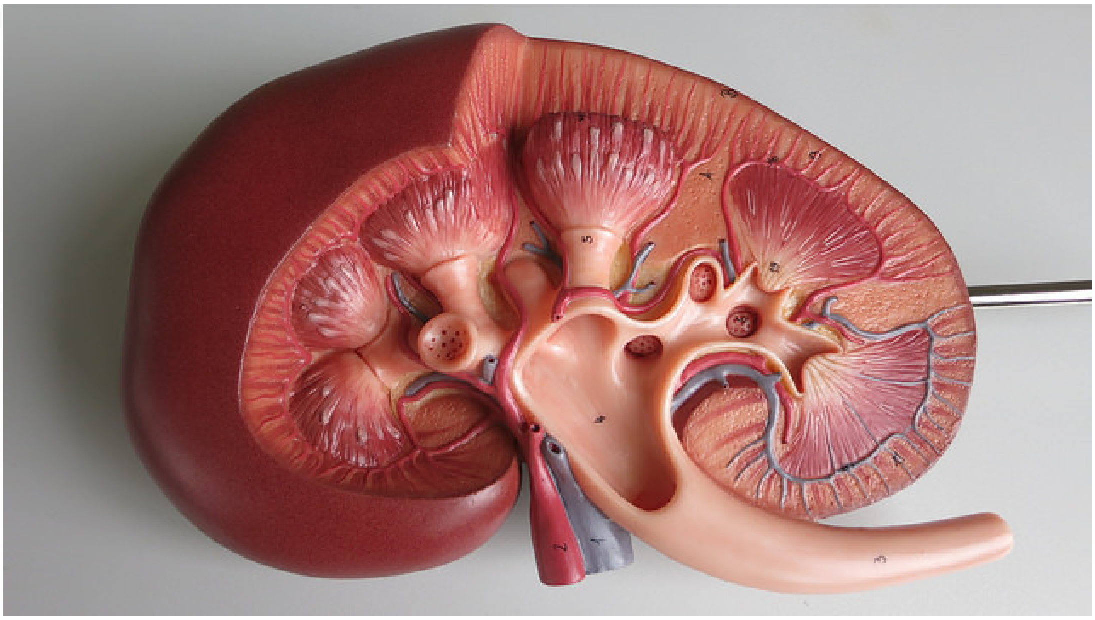
Only a few organs are essential enough that the body owns two of their kind. The kidney, which filters metabolic products, toxins, and drugs, is one of them. Modern medicine can replace it but the price dialysis patients have to pay is high. By contrast, the body is able to accomplish this complicated task within the smallest space. Every tissue of the kidney is specially structured depending on its task and the demanding function already manifests in its histology.



The Kidney

The kidneys are 2 retroperitoneal organs weighing about 150 grams each. They are lined and protected by a fibrous capsule. The kidneys play a key role in the ultrafiltration and excretion of metabolic waste products, maintenance of electrolyte and water balance, secretion of hormones, and in ensuring acid-base homeostasis.

Nephron—The Functional Unit of Kidney

The nephron is the smallest functional unit of the kidney, which filters urine from the blood. A kidney contains about **1.4 x 10^6 nephrons**. Structurally, the nephron consists of a bundle of capillaries **(glomerulus)** and a **Bowman's** capsule forming the **renal corpuscle,** which passes into the **renal canaliculi** comprising proximal, intermediate and distal tubules.

The renal corpuscle

Any unfiltered blood passes through the **arterioles/afferent vessels** into **glomerulus** and leaves after filtration through the efferent vessels at the same spot. The glomerular capillaries are connected to the mesangium and extend into the **Bowman's capsule**. Glomerulus and Bowman's capsules form the filtration barrier.

The Bowman's capsule can be imagined as a bubble containing the glomerulus. It is lined by a **visceral layer,** which is in contact with the glomerulus and a **parietal layer,** which forms the wall of the 'ball'. A tubule leaves the capsular space (**urinary pole**) at the opposite end of the entry and exit of the capillaries (**vascular pole**). It drains the primary urine from the capsular space.

Note: The renal corpuscle is only a part of the nephron.

The filtration barrier

The filtrate overcomes 3 barriers to reach the capsular space: the endothelium, the glomerular basement membrane, and the slit membrane of the podocytes.

1. The **endothelium** is fenestrated (window size, 70–100 nm) without the diaphragm. At its inner side, a negatively charged **glycocalyx** blocks the filtration of larger, negative molecules.
2. The **glomerular basement membrane** consists of lamina rara interna, lamina densa, and lamina rara externa. The collagen IV content of the lamina densa stabilizes the structures and sustains the blood pressure within the capillaries. In both laminae rarae, many molecules and proteins contribute to the negative charge of the basement membrane.
3. The **slit membrane** is formed by branches of the **podocytes,** which form the visceral layer of the Bowman's capsule. The foot processes of the podocytes are interlocked. Little interstices are spanned by the slit diaphragm, which is formed by the membranous protein **nephrin**. Molecules that measure up to 4.4 nm in diameter are filtered through the pores in the slit diaphragm.

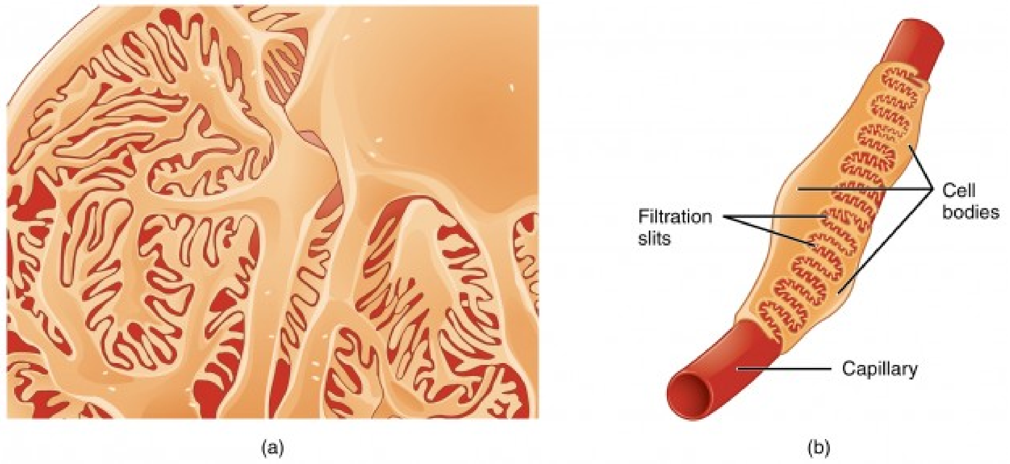


Image: Podocytes. By philschatz, License: CC BY 4.0

The nephron tubules

The nephron tubule **converts the primary urine into the final urine** via reabsorption of about 99% of the filtered water, glucose, and electrolytes. The epithelium is connected via **tight junctions** in every section. It contains a distinct **basal labyrinth** (folding of the basement membrane) and multiple **mitochondria** to meet the high energy demand.

The nephron tubule appears as a dark basal striation of the cells under a light microscope. Further, the segments differ in terms of structure and function. The segments of the tubule starting from the urinary pole of the renal corpuscle, and their main functions are listed below. The specific epithelia are discussed in detail, later.

<table>
<tr><th></th><th>Segment</th><th>Localization</th><th>Function</th></tr>
<tr><td></td><td>Proximal convoluted tubule</td><td>Cortex</td><td rowspan="2">Resorption of glucose, amino acids and 70–80% of the filtered H_2O and sodium, secretion of organic acids and cations</td></tr>
<tr><td rowspan="3">Loop of Henle</td><td>Proximal straight tubule</td><td>Outer medulla</td></tr>
<tr><td>Intermediate tubule</td><td>Outer + Inner medulla</td><td>Urinary concentration</td></tr>
<tr><td>Distal straight tubule</td><td>Outer medulla</td><td rowspan="2">Active transport of ions and concentration of the urine</td></tr>
<tr><td></td><td>Distal convoluted tubule</td><td>Cortex</td></tr>
<tr><td></td><td>Connecting tubule</td><td>Cortex</td><td></td></tr>
<tr><td></td><td>Collecting duct</td><td>Cortex + Medulla</td><td>ADH-dependent transport of water; aldosterone-dependent resorption of sodium</td></tr>
</table>

Note: The collecting duct is not a developmental biological and anatomical component of the nephron. It is listed in the table above due to its role in urine production.

The proximal tubule

The cubic epithelial cells are interlocked and carry a distinct basal labyrinth as well as a high brush border. The **basolateral Na-K-ATPase** is the driving force for reabsorption of amino acids, sodium, and glucose. Water osmotically diffuses through the zonulae occludentes (tight junctions) of the epithelium.

The intermediate tubule

The cells of the intermediate tubule are rather flat, and the lumen of the tubule is the smallest (12–15 µm). The nuclei often curve into the lumen. The cytoplasm is thicker than the cytoplasm inside the blood capillaries. In the descending portion of the loop of Henle, the epithelium is permeable to water, while it is impermeable in the ascending segment, thus contributing to the concentration of the final urine.

The distal tubule

The epithelium is cubic with a round nucleus and has a distinct basal labyrinth as well as single microvilli inside the tubule lumen. The tight junctions are particularly distinct here and the epithelium is absolutely impermeable to water.

The Collecting Duct—Fine Adjustment of the Final Urine

The collecting duct is not related to nephron either biologically or functionally. Urine from about 11 nephrons in the cortex proceeds through the outer and inner medullary collecting ducts along with the medullary rays to the renal medulla and papilla.

En route, the collecting ducts repeatedly merge and the lumen widens up to 200 µm. The epithelium changes from **cubic to prismatic shape,** and a rarely distinct basal labyrinth. The two types of cells include:

- **Chief cells**
    - Microvilli surrounding the kinocilia appear **lighter** under a light microscope
    - Seat of the **ADH-dependent integration of aquaporins** and, therefore, reabsorption of water: In the collecting duct, about 20–30% of the water reabsorption occurs (70–80% in the proximal tubule). The reabsorption is matched with the physiological needs of the body by **ADH** secretion.
    - Regulation of **sodium resorption and potassium secretion** by aldosterone
- **Switch cells**
    - Rich in mitochondria; appear **darker** under a light microscope
    - **Type A switch cells:** secretion of **protons**, resorption of bicarbonate
    - **Type B switch cells:** secretion of **bicarbonate** in alkaline metabolism

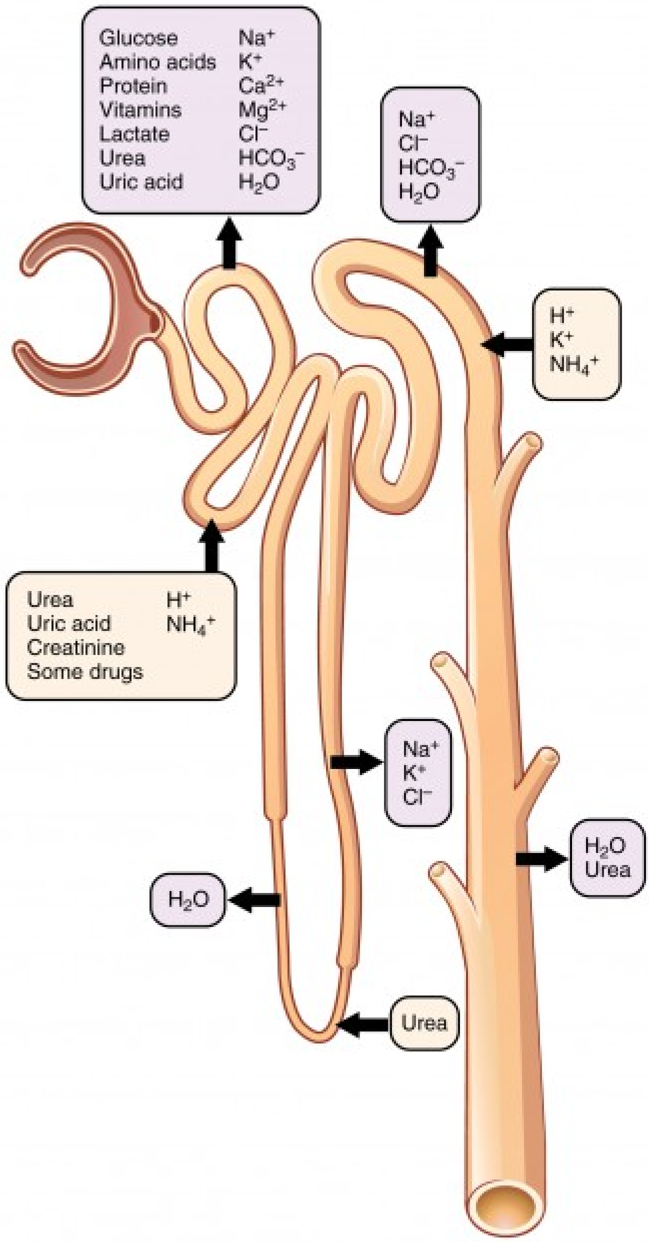


Image: Reabsorption nephron. By philschatz, License: CC BY 4.0

The Juxtaglomerular Apparatus

The distal straight tubule of every nephron directly crosses the afferent arteriole of its glomerulus at one junction, where the glomerular filtration is regulated. The juxtaglomerular apparatus includes the tubular epithelium (columnar and dark = **macula densa**), the **juxtaglomerular smooth muscle cells** as well as the **extraglomerular mesangial cells**.

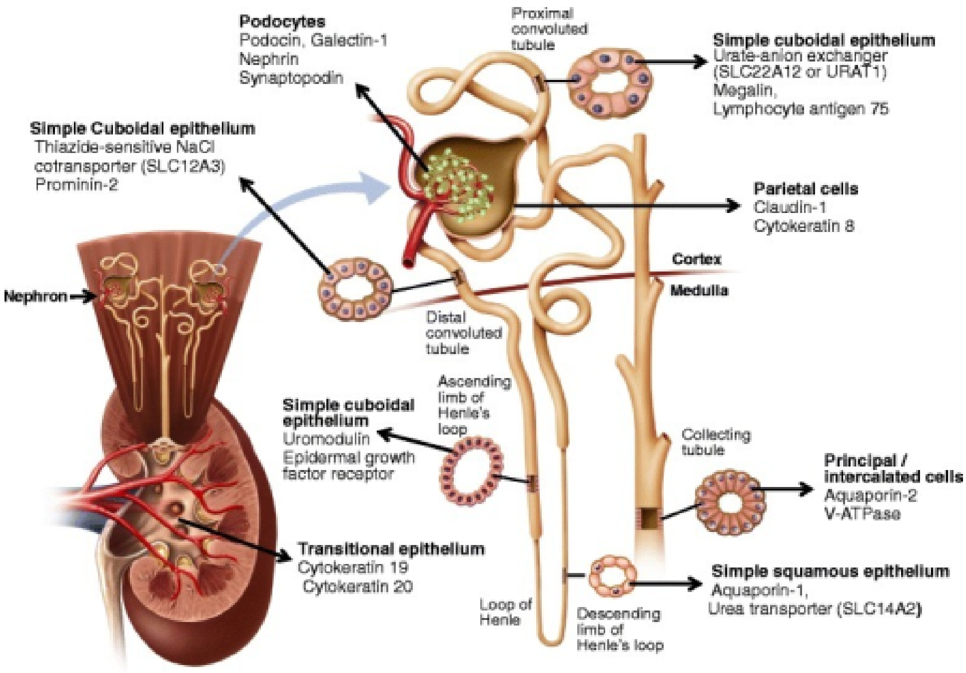
The distal epithelium contributes to the actual ion concentration of the urine. The baroreceptors of the juxtaglomerular cells record the blood pressure in the afferent vessel. Both factors trigger the release of renin from the juxtaglomerular cells.

[Image](): The juxtaglomerular apparatus. By philschatz, License: [CC BY 4.0]()

Topography of the Nephron

All nephrons and the corresponding collecting ducts are arranged similarly. The transition between different tubular segments of the nephrons is similar. Due to the parallel structure of all nephrons, the histological transitions between the cortex and medulla are macroscopically visible.

The nephrons and convoluted parts of the proximal and distal tubules lie in the cortex. The transition to the straight segment marks the cortex-medulla-line. Collecting ducts and loops of Henle that belong to the superior nephrons appear as collimated medullary streaks in the cortex. These functionally belong to the medulla but reach the cortex. The other collecting ducts and loops of Henle are found within the medulla.



[Image](): Specific markers were used to identify EVs derived from cells of different segments of the nephron and renal pelvis. By Openi, License: [CC BY 4.0]()

The Renal Interstitium

The renal interstitium is made up of extravascular intertubular spaces or renal parenchyma, cellular elements, and extracellular substances.

Only a small connective tissue is found inside the peritubular interstitium. However, several macrophages and fibroblasts can be found. The fibroblasts are responsible for erythropoietin production. Erythropoietin stimulates the formation of red blood cells within the bone marrow. Furthermore, many interstitial cells secrete prostaglandins.

References

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Notes