University of Anbar
College of science
Department of biotechnology

Lectures of human physiology

Lec. 10

Physiology of the Kidneys

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STRUCTURE AND FUNCTION OF THE KIDNEYS

Each kidney contains many tiny tubules that empty into a cavity drained by the ureter. Each of the tubules receives a blood filtrate from a capillary bed called the glomerulus. The filtrate is modified as it passes through different regions of the tubule and is thereby changed into urine.

The primary function of the kidneys is regulation of the extracellular fluid (plasma and interstitial fluid) environment in the body. This is accomplished through the formation of urine, which is a modified filtrate of plasma. In the process of urine formation, the kidneys regulate:

1. the volume of blood plasma (and thus contribute significantly to the regulation of blood pressure);

2. the concentration of waste products in the plasma;

3. the concentration of electrolytes (Na^+, K^+, HCO_3^- and other ions) in the plasma; and

4. the pH of plasma.

Gross Structure of the Urinary System

The paired **kidneys** lie on either side of the vertebral column below the diaphragm and liver. Each adult kidney weighs about 160 g and is about 11 cm (4 in.) long and 5 to 7 cm (2 to 3 in.) wide—about the size of a fist. Urine produced in the kidneys is drained into a cavity known as the *renal pelvis* and then is channeled from each kidney via long ducts—the **ureters**—to the **urinary bladder** (fig. 1).

A coronal section of the kidney shows two distinct regions (fig. 2). The outer cortex is reddish brown and granular in appearance because of its many capillaries. The deeper region, or medulla, is striped in appearance due to the presence of microscopic tubules and blood vessels. The medulla is composed of 8 to 15 conical renal pyramids separated by renal columns.

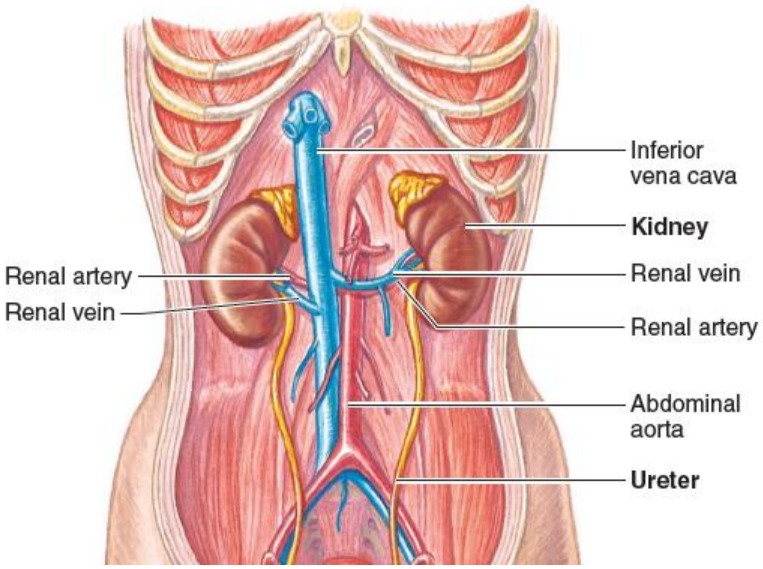

Figure 1 **The organs of the urinary system**

The cavity of the kidney is divided into several portions. Each pyramid projects into a small depression called a minor calyx (the plural form is calyces). Several minor calyces unite to form a major calyx. The major calyces then join to form the funnel-shaped renal pelvis. The renal pelvis collects urine from the calyces and transports it to the ureters and urinary bladder.

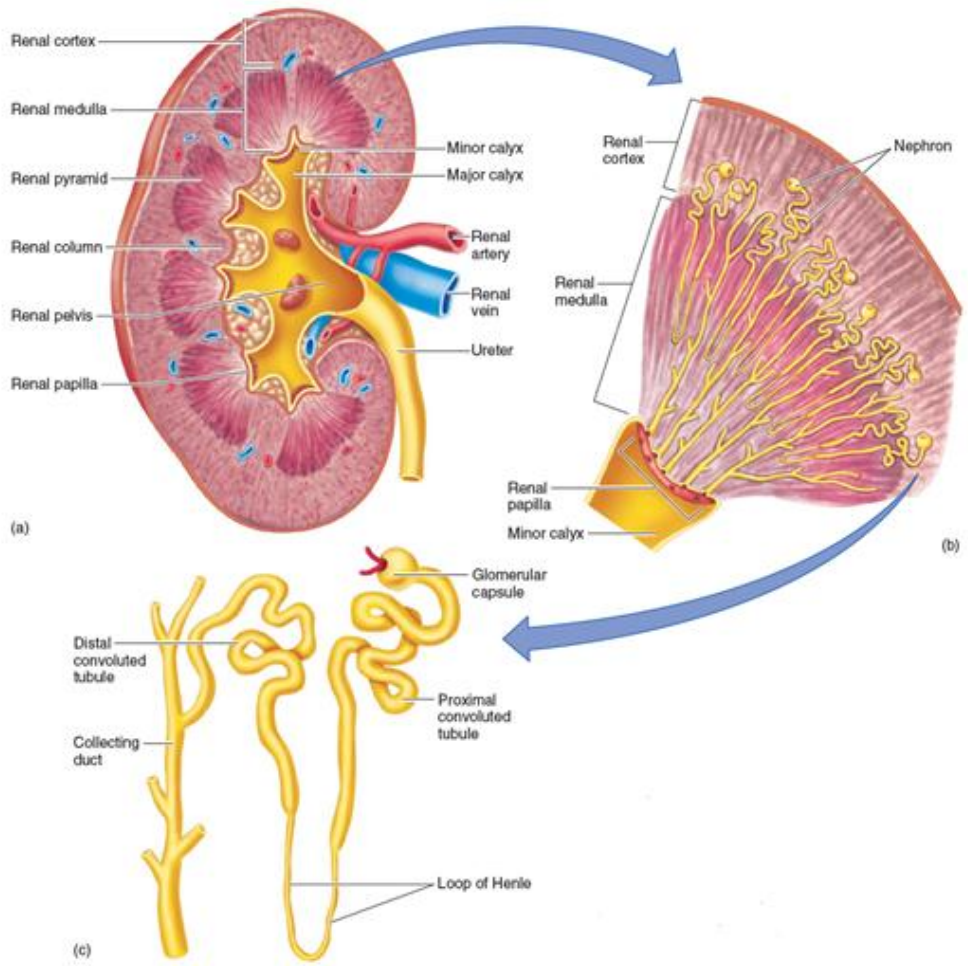

Figure 2 **The structure of a kidney.** The figure depicts (*a*) a coronal section of a kidney and (*b*) a magnified view of the contents of a renal pyramid. (*c*) A single nephron tubule, microscopic in actual size, is shown isolated.

The ureter undergoes peristalsis, wavelike contractions similar to those that occur in the digestive tract. (This results in intense pain when a person passes a kidney stone.) Interestingly, the pacemaker of these peristaltic waves is located in the renal calyces and pelvis, which contain smooth muscle. The calyces and pelvis also undergo rhythmic contractions, which may aid the emptying of urine from the kidney.

The urinary bladder is a storage sac for urine, and its shape is determined by the amount of urine it contains. An empty urinary bladder is pyramidal; as it fills, it becomes ovoid and bulges upward into the abdominal cavity.

Microscopic Structure of the Kidney

The nephron (see fig. 2) is the functional unit of the kidney responsible for the formation of urine. Each kidney contains more than a million nephrons. A nephron consists of small tubes, or tubules, and associated small blood vessels. Fluid formed by capillary filtration enters the tubules and is subsequently modified by transport processes; the resulting fluid that leaves the tubules is urine.

Nephron Tubules

The tubular portion of a nephron consists of a glomerular capsule, a proximal convoluted tubule, a descending limb of the loop of Henle, an ascending limb of the loop of Henle, and a distal convoluted tubule (fig. 17.5). **The glomerular (Bowman's) capsule** surrounds the glomerulus. The glomerular capsule and its associated glomerulus are located in the cortex of the kidney and together constitute the renal corpuscle. The glomerular capsule contains an inner visceral layer of epithelium around the glomerular capillaries and an outer parietal layer. The space between these two layers is continuous with the lumen of the tubule and receives the glomerular filtrate, as will be described in the next section.

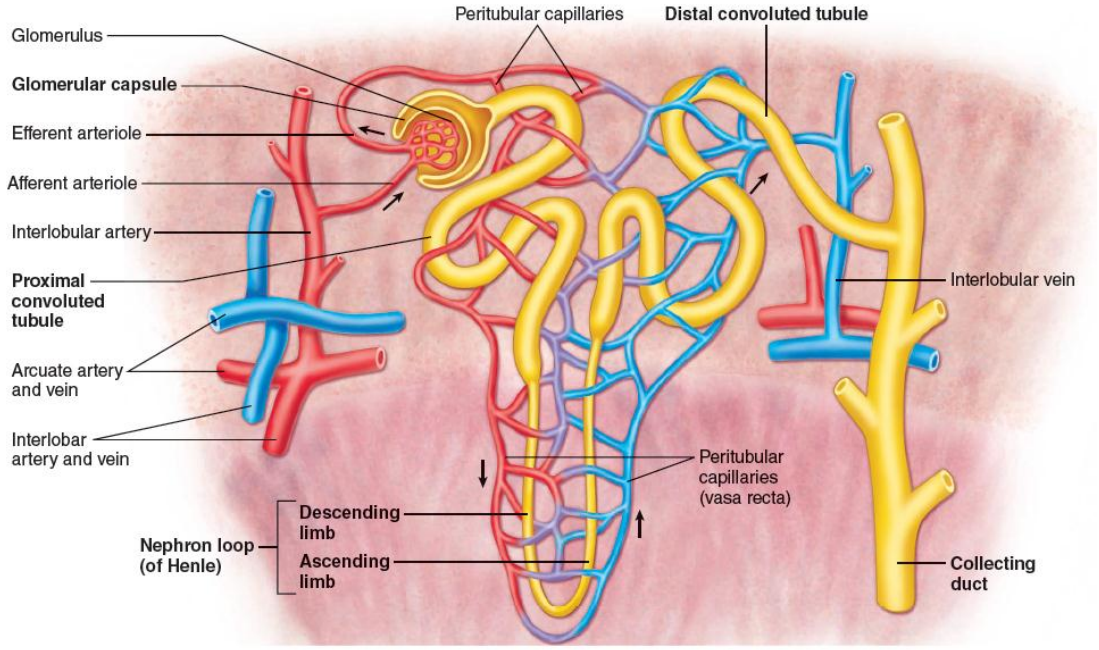

Figure 3 **The nephron tubules and associated blood vessels.**

The tubular portion of a nephron consists of a glomerular capsule, a proximal convoluted tubule, a descending limb of the loop of Henle, an ascending limb of the loop of Henle, and a distal convoluted tubule (fig. 3). The glomerular (Bowman's) capsule surrounds the glomerulus. The glomerular capsule and its associated glomerulus are located in the cortex of the kidney and together constitute the renal corpuscle. The glomerular capsule contains an inner visceral layer of epithelium around the glomerular capillaries and an outer parietal layer. The space between these two layers is continuous with the lumen of the tubule and receives the glomerular filtrate, as will be described in the next section.

Filtrate that enters the glomerular capsule passes into the lumen of the **proximal convoluted tubule**. The wall of the proximal convoluted tubule consists of a single layer of cuboidal cells containing millions of microvilli; these microvilli increase the surface area for reabsorption. In the process of reabsorption, salt, water, and other molecules needed by the body are transported from the lumen, through the tubular cells and into the surrounding peritubular capillaries. The glomerulus, glomerular

capsule, and convoluted tubule are located in the renal cortex. Fluid passes from the proximal convoluted tubule to the nephron loop, or **loop of Henle**. This fluid is carried into the medulla in the **descending limb** of the loop and returns to the cortex in the **ascending limb** of the loop. Back in the cortex, the tubule again becomes coiled and is called the **distal convoluted tubule**. The distal convoluted tubule is shorter than the proximal tubule and has relatively few microvilli. The distal convoluted tubule terminates as it empties into a collecting duct. The two principal types of nephrons are classified according to their position in the kidney and the lengths of their loops of Henle. Nephrons that originate in the inner one-third of the cortex—called juxtamedullary nephrons because they are next to the medulla—have longer nephron loops than the more numerous cortical nephrons, which originate in the outer two thirds of the cortex (fig. 4). The juxtamedullary nephrons play an important role in the ability of the kidney to produce a concentrated urine.

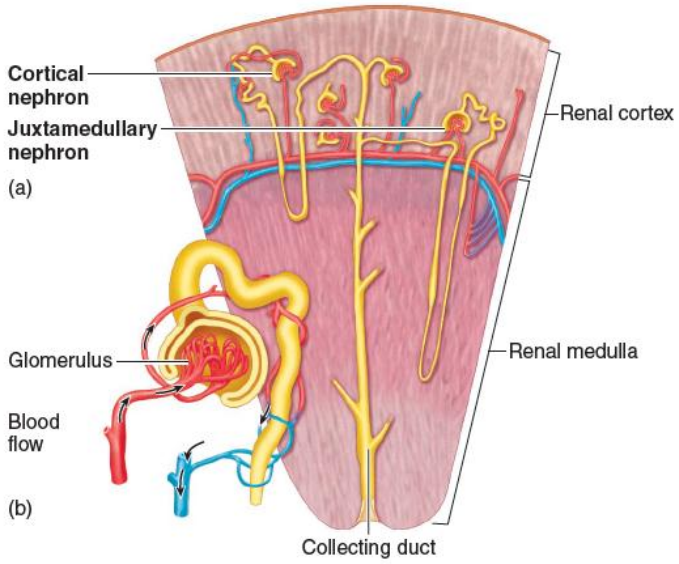

Figure 4 **The contents of a renal pyramid.** (*a*) The position of cortical and juxtamedullary nephrons is shown within the renal pyramid of the kidney. (*b*) The direction of blood flow in the vessels of the nephron is indicated with arrows.

GLOMERULAR FILTRATION

The glomerular capillaries have large pores in their walls, and the layer of Bowman's capsule in contact with the glomerulus has filtration slits.

Water, together with dissolved solutes, can thus pass from the blood plasma to the inside of the capsule and the nephron tubules.

Endothelial cells of the glomerular capillaries have large pores (200 to 500 Å in diameter) called fenestrae; thus, the glomerular endothelium is said to be fenestrated. As a result of these large pores, glomerular capillaries are 100 to 400 times more permeable to plasma water and dissolved solutes than are the capillaries of skeletal muscles. Although the pores of glomerular capillaries are large, they are still small enough to prevent the passage of red blood cells, white blood cells, and platelets into the filtrate.

Before the fluid in blood plasma can enter the interior of the glomerular capsule, it must pass through three layers that could serve as selective filters. The fluid entering the glomerular capsule is thus referred to as a filtrate. This is the fluid that will become modified as it passes through the different segments of the nephron tubules to become the urine. The first potential filtration barrier is the capillary fenestrae, which are large enough to allow proteins to pass but are surrounded by charges that may present some barrier to plasma proteins. The second potential barrier is the glomerular basement membrane, a layer of collagen IV and proteoglycans. The second potential barrier is the glomerular basement membrane, a layer of collagen IV and proteoglycans lying immediately outside the capillary endothelium. The glomerular basement membrane is more than five times as thick as the basement membrane of other vessels, and is the structure that most restricts the rate of fluid flow into the capsule lumen.

The filtrate must then pass through the inner (visceral) layer of the glomerular capsule, where the third potential filtration barrier is located. This layer is composed of podocytes, which are unique epithelial cells with a bulbous cell body, primary processes extending from the cell body, and thousands of foot processes that branch from the primary processes. The podocyte processes are attached to the glomerular basement

membrane, while their cell bodies float in the fluid within the glomerular capsules. The foot processes of neighboring podocytes interdigitate and surround the basement membrane of the glomerular capillaries. The narrow slits (30 to 50 nm wide) between adjacent foot processes provide passageways for molecules entering the interior of the glomerular capsule as glomerular filtrate (fig. 5).

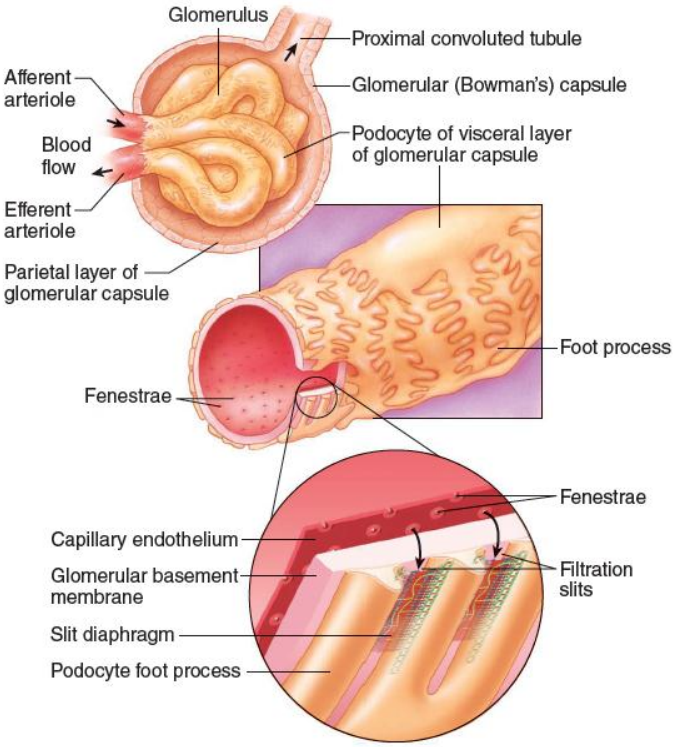

Figure 5 **The structure of the glomerulus and capsule.** An illustration of the relationship between the glomerular capillaries and the inner layer of the glomerular (Bowman's) capsule. Notice that filtered molecules pass out of the fenestrae of the capillaries and through the filtration slits to enter the cavity of the capsule. Plasma proteins are excluded from the filtrate by the glomerular basement membrane and the slit diaphragm

However, a slit diaphragm (fig. 6), analogous in composition to an adherens junction, links the interdigitating foot processes and presents the last potential filtration barrier.

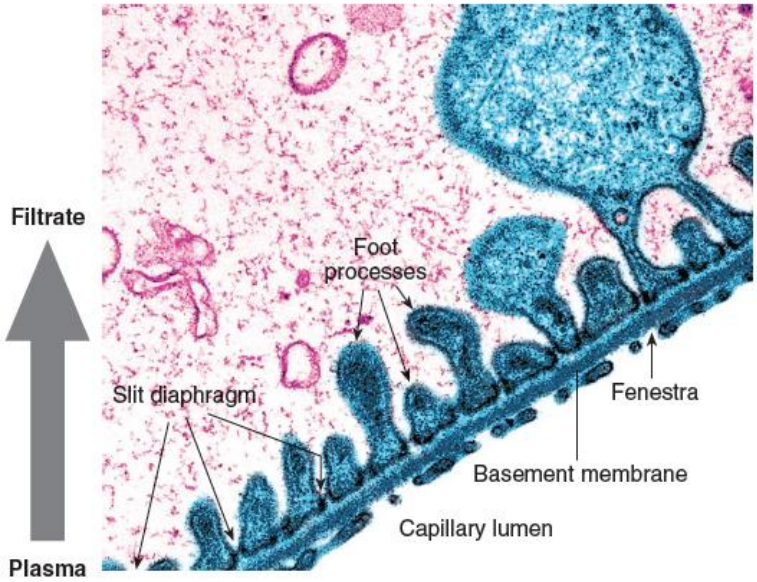

Figure 6 **An electron micrograph of the filtration barrier.** This electron micrograph shows the barrier separating the capillary lumen from the cavity of the glomerular (Bowman's) capsule.

Glomerular Ultrafiltrate

The fluid that enters the glomerular capsule is called filtrate, or ultrafiltrate (fig. 7) because it is formed under pressure—the hydrostatic pressure of the blood. The force favoring filtration is opposed by a counterforce developed by the hydrostatic pressure of fluid in the glomerular capsule. Also, since the protein concentration of the tubular fluid is low (less than 2 to 5 mg per 100 ml) compared to that of plasma (6 to 8 g per 100 ml), the greater colloid osmotic pressure of plasma promotes the osmotic return of filtered water. When these opposing forces are subtracted from the hydrostatic pressure of the glomerular capillaries, a net filtration pressure of only about 10 mmHg is obtained.

Because glomerular capillaries are extremely permeable and have an extensive surface area, this modest net filtration pressure produces an extraordinarily large volume of filtrate. The **glomerular filtration rate (GFR)** is the volume of filtrate produced by both kidneys per minute. The GFR averages 115 ml per minute in women and 125 ml per minute in men. This is equivalent to 7.5 L per hour or 180 L per day (about 45 gallons). Since the total blood volume averages about 5.5 L, this means that the total blood volume is filtered into the urinary tubules every 40 minutes. Most of the filtered water must obviously be returned

immediately to the vascular system or a person would literally urinate to death within minutes.

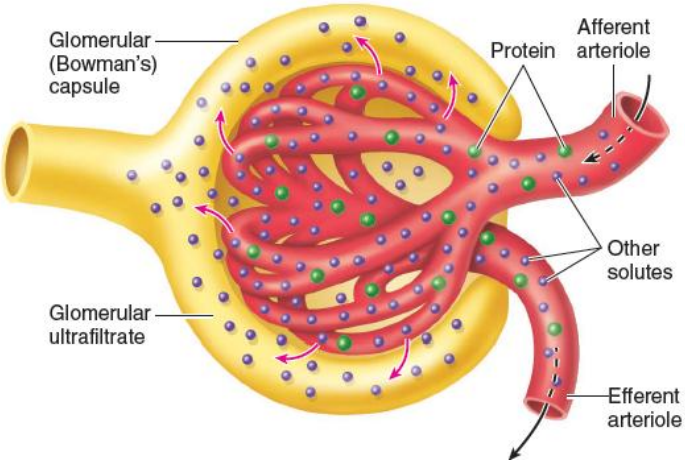

Figure 7 **The formation of glomerular ultrafiltrate.** Only a very small proportion of plasma proteins (green *spheres)* are filtered, but smaller plasma solutes (purple *spheres)* easily enter the glomerular ultrafiltrate. Arrows indicate the direction of filtration.

REABSORPTION OF SALT AND WATER

Regardless of the body's state of hydration, it is clear that most of the filtered water must be returned to the vascular system to maintain blood volume and pressure. The return of filtered molecules from the tubules to the blood is called reabsorption (fig. 8). About 85% of the 180 L of glomerular filtrate formed per day is reabsorbed in a constant, unregulated fashion by the proximal tubules and descending limbs of the nephron loops. This reabsorption, as well as the regulated reabsorption of the remaining volume of filtrate, occurs by osmosis. A concentration gradient must thus be created between tubular filtrate and the plasma in the surrounding capillaries that promotes the osmosis of water back into the vascular system from which it originated.

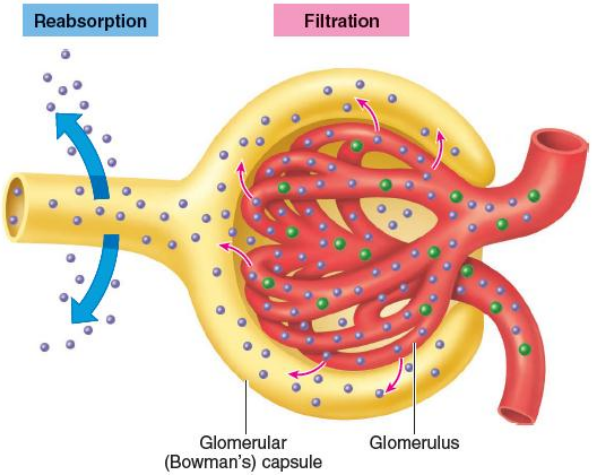

Figure 8 **Filtration and reabsorption**

Reabsorption in the Proximal Tubule

Because all plasma solutes, with the exception of proteins, are able to enter the glomerular ultrafiltrate freely, the total solute concentration (osmolality) of the filtrate is essentially the same as that of plasma. Reabsorption by osmosis cannot occur unless the solute concentrations of plasma in the peritubular capillaries and the filtrate are altered by active transport processes. This is achieved by the active transport of Na^+ from the filtrate to the peritubular blood.

Active and Passive Transport

The epithelial cells that compose the wall of the proximal tubule are joined together by tight junctions only toward their apical sides—that is, the sides of each cell that are closest to the lumen of the tubule. Each cell has four exposed surfaces: the apical side facing the lumen, which contains microvilli; the basal side facing the peritubular capillaries; and the lateral sides facing the narrow clefts between adjacent epithelial cells.

The concentration of Na^+ in the glomerular ultrafiltrate— and thus in the fluid entering the proximal tubule—is the same as in plasma. The cytoplasm in epithelial cells of the tubule, however, has a much lower Na^+

concentration. This lower Na^+ concentration is partially due to the low permeability of the plasma membrane to Na^+ and partially due to the active transport of Na^+ out of the cells by Na^+/K^+ pumps. In the cells of the proximal tubule, the Na^+ / K^+ pumps are located in the basal and lateral sides of the plasma membrane but not in the apical membrane. As a result of the action of these active transport pumps, a concentration gradient is created that favors the diffusion of Na^+ from the tubular fluid across the apical plasma membranes and into the epithelial cells of the proximal tubule. The Na^+ is then extruded into the surrounding interstitial (tissue) fluid by the Na^+ / K^+ pumps. The transport of Na^+ from the tubular fluid to the interstitial fluid surrounding the proximal tubule creates a potential difference across the wall of the tubule, with the lumen as the negative pole. This electrical gradient favors the passive transport of Cl^- toward the higher Na^+ concentration in the interstitial fluid. In the early proximal tubule, reabsorption of Cl^- occurs mainly by transcellular transport (through the epithelial cells) fig. 9.

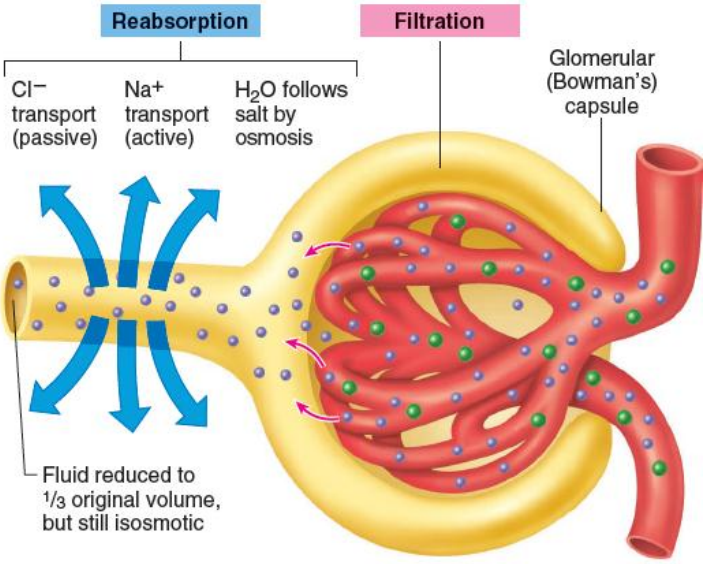

Figure 9 **Salt and water reabsorption in the proximal tubule.** Sodium is actively transported out of the filtrate and chloride follows passively by electrical attraction. Water follows the salt out of the tubular filtrate into the peritubular capillaries by osmosis.

The Countercurrent Multiplier System

Water cannot be actively transported across the tubule wall, and osmosis of water cannot occur if the tubular fluid and surrounding interstitial fluid are isotonic to each other. In order for water to be reabsorbed by osmosis, the surrounding interstitial fluid must be hypertonic. The osmotic pressure of the interstitial fluid in the renal medulla is raised to more than four times that of plasma by juxtamedullary nephrons. This is partly due to the geometry of the nephron loops, which bend sharply so that descending and ascending limbs are in close enough proximity to interact. Because the ascending limb is the active partner in this interaction, its properties will be described before those of the descending limb.

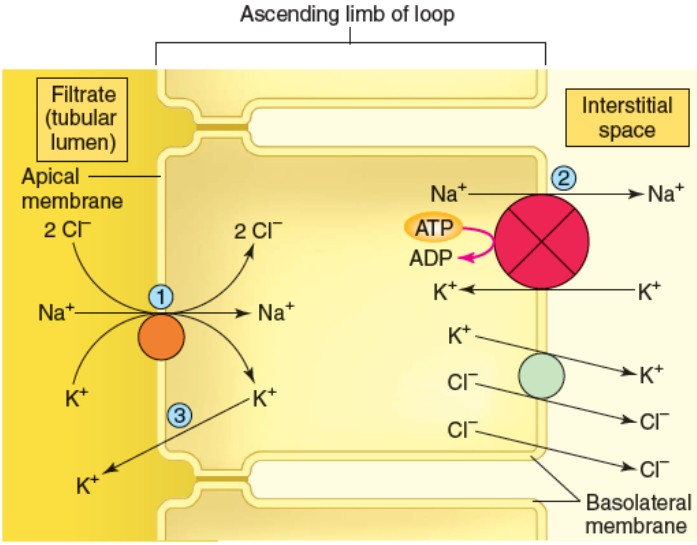

Figure 10 **The transport of ions in the ascending limb.** (1) In the thick segment of the ascending limb of the loop, Na^+ and K 1 together with two Cl^- enter the tubule cells. (2) Na^+ **is** then actively transported out into the interstitial space and Cl^- **follows** passively. (3) The K^+ diffuses back into the filtrate, and some also enters the interstitial space.

Descending Limb of the Loop of Henle

The descending limb does not actively transport salt, and indeed is impermeable to the passive diffusion of salt. It is, however, permeable to water. Because the surrounding interstitial fluid is hypertonic to the filtrate in the descending limb, water is drawn

out of the descending limb by osmosis and enters blood capillaries. The concentration of tubular fluid is thus increased, and its volume is decreased, as it descends toward the tips of the loops. As a result of these passive transport processes in the descending limb, the fluid that "rounds the bend" at the tip of the loop has the same osmolality as that of the surrounding interstitial fluid (1,200 mOsm). There is, therefore, a higher salt concentration arriving in the ascending limb than there would be if the descending limb simply delivered isotonic fluid. Salt transport by the ascending limb is increased accordingly, so that the "saltiness" (NaCl concentration) of the interstitial fluid is multiplied. Fig.11 .

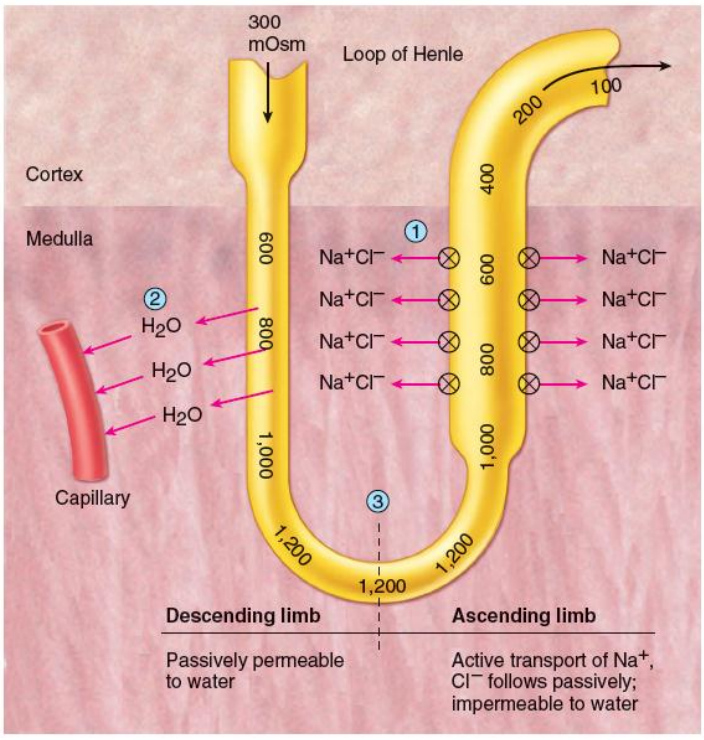

Figure 11 **The countercurrent multiplier system.**

Countercurrent Multiplication

Countercurrent flow (flow in opposite directions) in the ascending and descending limbs and the close proximity of the

two limbs allow for interaction between them. Because the concentration of the tubular fluid in the descending limb reflects the concentration of surrounding interstitial fluid, and the concentration of this fluid is raised by the active extrusion of salt from the ascending limb, a positive feedback mechanism is created. The more salt the ascending limb extrudes, the more concentrated will be the fluid that is delivered to it from the descending limb. This positive feedback mechanism, which multiplies the concentration of interstitial fluid and descending limb fluid, is called the countercurrent multiplier system.

RENAL CONTROL OF ELECTROLYTE AND ACID-BASE BALANCE

The kidneys regulate the blood concentrations of Na^+, K^+, HCO_3^+ and H^+ and thereby are responsible for maintaining the homeostasis of plasma electrolytes and the acid-base balance. Renal reabsorption of Na^+ and secretion of K^+ and H^+ are stimulated by aldosterone.

The kidneys help regulate the concentrations of plasma electrolytes—sodium, potassium, chloride, bicarbonate, sulfate, and phosphate—by matching the urinary excretion of these compounds to the amounts ingested. For example, the reabsorption of sulfate and phosphate ions across the walls of the proximal tubules is the primary determinant of their plasma concentrations. Parathyroid hormone (PTH) secretion, stimulated by a fall in plasma Ca^{2+}, acts on the kidneys to decrease the reabsorption of phosphate. The control of plasma Na^+ is important in the regulation of blood volume and pressure; the control of plasma K^+ is required to maintain proper function of cardiac and skeletal muscles.

-Reference

Fox, S. I. (2014). Fox Human Physiology.