

Unit 2 Lecture 6

THE EXCRETORY SYSTEM

The renal system includes the **kidneys, ureters, bladder, and urethra**. The primary function of the urinary system is to help maintain homeostasis by controlling the composition, volume and pressure of blood. The threat to life in renal failure often comes not from the accumulation of metabolic wastes, but from loss of the body's ability to balance the daily intake of salts and water with the appropriate rate of excretion.

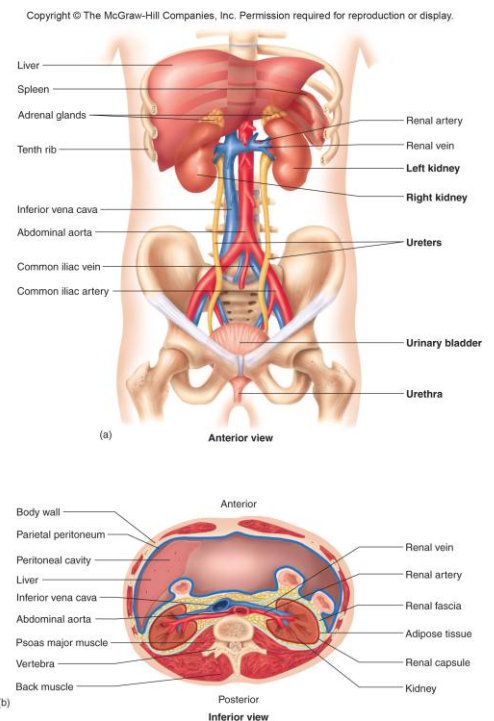
Functions of the Kidney

1. Regulation of blood volume and it's composition
2. Regulation of blood pressure
3. Maintenance of blood osmolarity
4. Production of hormones: release erythropoietin and renin
5. Homeostatic regulation of pH: Conserve or secrete H^+ or HCO_3^- to maintain pH
6. Synthesize glucose and participate in vitamin D synthesis
7. Excretion of wastes and foreign substances: products of metabolism such as urea and substances like drugs and toxins

Anatomy of the Kidneys

The kidneys are shaped like a pair of large kidney beans weighing @125-250 gm each and are located just above the waist on the back wall of the abdominal cavity. A hilum, a notch in center of one of the sides, allows blood and lymph vessels and the ureter to enter and/or leave the kidney. External to the kidney are a series of layers. The renal capsule is the innermost layer followed by the adipose capsule and renal fascia. Their function is to protect the kidney against trauma and to anchor the kidney to the abdominal wall.

The [kidney](#) can be divided into an outer region, the cortex, and an inner region, the medulla. There are 8-18 renal pyramids found in the medulla. Their bases face the cortex and their apices are called renal papillae. Renal columns are portions of the cortex that extend between the renal pyramids. The renal pelvis is a cavity into which urine drains. Each kidney contains 2-3 major calyces along with the 8-18 minor calyces. Urine drains from the pyramids into the minor calyces, which drain into the major calyces to the renal pelvis and out via the ureter.



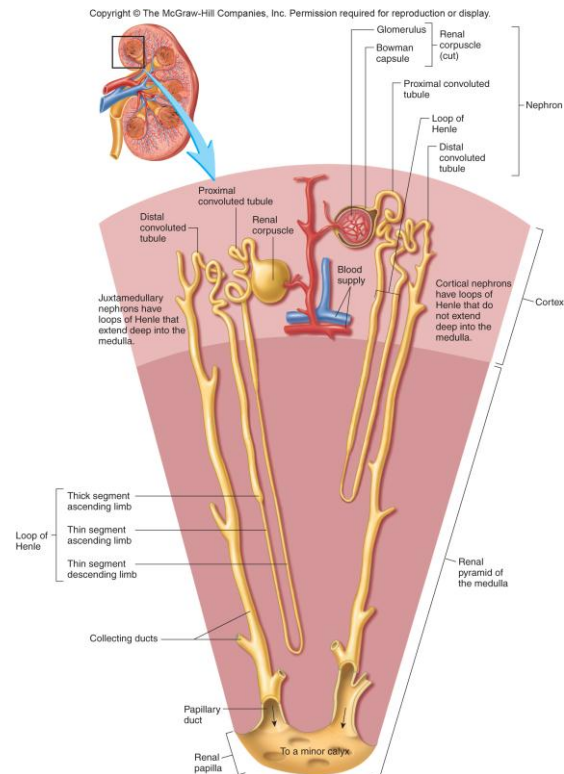
Blood Supply of the Kidneys

Blood flows to the kidneys through the **renal artery**. This large artery branches into **segmental arteries** that branch into **interlobar arteries** that, in turn, branch into **arcuate arteries**. The blood in the arcuate arteries flows through the **interlobular arteries** to supply the nephron. Blood from the interlobular **artery** drains into the **afferent arteriole**. The afferent arteriole gives rise to the **glomerulus** (where filtration takes place). The blood from the glomerulus enters the **efferent arteriole**. Blood then enters the **peritubular capillaries** (a dense network of capillaries surrounding the tubes of the nephron), which then drains into the **interlobular vein**, the **arcuate vein**, the **interlobar vein**, and then into the **renal vein** where it joins the Inferior Vena Cava.

The Nephron

The nephron is the functional unit of the kidneys. There are over 1 million nephrons in each kidney. Their function is to filter the blood, reabsorb essential substances, and excrete nonessential molecules and waste. Each nephron is composed of a highly coiled hollow tube surrounded by a complex blood supply.

The **glomerular capsule** surrounds a very small, highly permeable capillary bed called the **glomerulus**. Together these structures are called the **renal corpuscle**. This is the site where the blood is filtered in a process called glomerular filtration. The fluid that is filtered from the blood that enters the glomerular capsule (or capsular space) is called the filtrate. Glomerular filtration is facilitated by a highly permeable capillary endothelium that is surrounded by podocytes. The larger diameter afferent arteriole and smaller diameter efferent arteriole also enhance glomerular filtration by regulating the flow of blood through the kidney. The tubular portion of the nephron consists of the following structures in order: the **proximal convoluted tubule**, the **descending and ascending limb of the loop of Henle**, the **distal convoluted tubule**, and the **collecting duct**. It is in the renal tubule that reabsorption and secretion occur. Several distal convoluted tubules are linked to form a single collecting duct. Several collecting ducts merge to form papillary ducts which drain into a minor calyx. There are about 30 papillary ducts per renal papillae. The renal capsule and convoluted tubules lie in the cortex whereas the nephron loop is found in the medulla.



Cortical and [juxtamedullary nephrons](#) are the two types of nephrons. The cortical nephron has its glomerulus located in the outer and mid regions of the cortex of the kidney; its short nephron loop just penetrates the medulla. The glomerulus of the juxtamedullary nephron is placed in the inner region of the cortex and the long nephron loop that almost reaches the renal papillae is in the medulla: 15-20% of the nephrons have the long loop. The Juxtaglomerular apparatus (JGA) consists of juxtaglomerular cells of the afferent arteriole and the macula densa (tall epithelial cells) of the distal convoluted tubule. The JGA helps regulate blood pressure and the rate of filtration in the kidneys by release of the hormone renin from cells located in the afferent arteriole.

Processes along the Nephron

- **Filtration** is the movement of fluid through the glomerular capillary due to hydrostatic pressures. The **filtrate** is the solution created by filtration. The filtrate is generally composed of water plus all the dissolved solutes in the blood (except for large proteins that are too big to be filtered).
- **Reabsorption** is defined as the movement of a substance from the lumen of the nephron back into the blood.
- **Secretion** is the movement of a substance from the blood into the lumen of the nephron.

$$\text{Excretion} = \text{filtration} + \text{secretion} - \text{reabsorption}$$

GLOMERULAR FILTRATION

Glomerular filtration is the bulk flow of fluid from the blood into the glomerular capsule. This fluid, called the filtrate, contains the same substances as plasma with the exception of large proteins and red blood cells. Glomerular filtration is affected by the extremely permeable capillaries, which make up the glomerulus, and Starling Forces. Starling Forces cause the bulk movement of fluid across capillaries due to a combination of hydrostatic and colloid osmotic forces. The glomerular capillary is similar, although the pressure of each force will be different.

The glomerular capillary has many fenestrations (holes). Special epithelial cells called podocytes surround the capillaries. The podocytes have large filtration slits that are formed between pedicles. These structural features increase filtration at the glomerulus. The glomerular capillaries are long, providing a large surface area for filtration and the endothelial-capsular membrane is thin allowing for a greater filtration rate. The blood hydrostatic pressure is around 60 mmHg which is about twice that in a regular capillary, causing filtration of fluid into the glomerular capsule. This pressure is mainly due to the difference in diameter between the afferent (larger) and efferent (smaller) arterioles. The colloid osmotic pressure due to plasma proteins is 32 mmHg, causing reabsorption of fluid into the plasma. The capsular hydrostatic pressure is 18 mmHg, causing the reabsorption of fluid. There is

no colloid osmotic force in the glomerular capsule since very few proteins are filtered. Therefore, the resulting net filtration pressure is 10 mmHg ($60 - (32 + 18)$) out of the glomerulus into the capsular space.

Net filtration pressure (NFP): $NFP = GCHP - (CHP + GCOP)$

The filtration of blood depends on three mechanisms; glomerular capillary hydrostatic pressure (GCHP) minus the capsular hydrostatic pressure (CHP) and the glomerular capillary osmotic pressure (GCOP). CHP & GCOP oppose GCHP and push blood back into capillary.

Glomerular Filtration Rate (GFR) and Filtered Load

The **GFR** is the volume of fluid that is filtered by the glomerulus during a certain time period. Usually the kidneys filter about 180 L/day (48 gallons/day). GFR must be controlled. If GFR is too high, the filtrate flows through the tubules too quickly to reabsorb the normal amount of water and solutes. If GFR is too low, too much waste is reabsorbed. GFR tends to decrease with age and in renal disease due to a decrease in the number of functioning glomeruli. Measurement of GFR is an important index of renal function and progression or amelioration of renal disease. A decrease in GFR is associated with renal dysfunction or potential disease. Most regulation is autoregulation by the kidneys themselves.

Regulation of GFR

Glomerular blood flow depends on autoregulation, hormonal regulation and neural regulation. GFR remains relatively constant due to autoregulation but can decrease by strong stimuli from renal nerves. Autoregulation enables the kidneys to maintain a constant blood pressure and GFR and occurs within the kidneys.

Hormonal regulation is due to angiotensin II, atrial natriuretic peptide (ANP), and aldosterone. When blood pressure drops, the sympathetic nerves stimulate the JGA to secrete renin which acts on a plasma protein, angiotensinogen. In the lungs and kidneys this protein is further converted to angiotensin II. Angiotensin II stimulates widespread vasoconstriction which raises the mean arterial pressure. It also constricts the afferent and efferent arterioles reducing GFR and water loss. Angiotensin II also stimulates the release of ADH, which promotes water retention, and aldosterone, which promotes sodium and water retention. Finally, it stimulates the thirst center to encourage water intake. I

If blood pressure is too high, Atrial Natriuretic Peptide (ANP) is secreted by the heart. This hormone does just the opposite of ADH. It dilates the afferent arteriole and constricts the efferent arteriole which causes an increase in the GFR. It inhibits the adrenal cortex from releasing aldosterone, the kidney

from secreting renin, and the anterior pituitary gland from secreting ADH. All of this promotes water and NaCl loss.

Since the kidneys filter many other substances, it is important to be able to calculate *the amount of these substances filtered by the kidneys per day*; this is called the **filtered load**. The filtered load can be calculated using the following equation:

$$\text{Filtered Load} = \text{GFR} \times \text{Plasma Concentration of the Substance}$$

It is often important to be able to calculate not only the GFR and filtered load of a substance but also its urine concentration and the amount of solute excreted. These values also tell the physician important information concerning the health and functioning of the kidneys. Urine concentration is the amount of the solute that is excreted per unit volume of urine (g/L). The amount of solute excreted is the actual amount (in grams) of solute that is excreted in the urine and can be calculated using the following equation.

$$\text{Amount Excreted} = \text{Urine Concentration} \times \text{Amount of water excreted per day} \\ (@1.8\text{L/day})$$

The amount reabsorbed is the amount of filtered substance that is taken back up (reabsorbed) by the kidneys and can be calculated using the first of the two equations. The fraction excreted is calculated using second equation.

$$\text{Amount reabsorbed} = \text{Filtered Load} - \text{Amount Excreted}$$

$$\text{Fraction excreted} = (\text{Filtered Load}/\text{Amount Excreted}) \times 100\%$$

TUBULAR TRANSPORT MECHANISMS: REABSORPTION

Tubular Reabsorption is the movement of filtrate back into peritubular capillaries or vasa recta. About 99% of the filtrate is reabsorbed as it passes through the tubules. There are microvilli present on the apical surfaces of cells lining the lumen that function in reabsorption. Reabsorption and secretion involve a variety of transport mechanisms that include **diffusion**, **osmosis**, and **active transport**. Some substances can diffuse between the tubular cells by a process called paracellular transport, which is not regulated. Other substances diffuse across the tubular cells from the lumen into the cell then into the interstitial fluid. This form of reabsorption is called transcellular or transepithelial transport and can be either regulated by hormones or not regulated at all.

Regulated forms of transcellular transport include the Na⁺/K⁺ pump. This transport mechanism requires adenosine triphosphate (ATP) and moves 3 Na⁺ out of the cell and 2 K⁺ into the cell. Many simple Na⁺ channels that

are found in the cell membrane can be regulated by hormones (directly by aldosterone and indirectly by angiotensin II). These hormone-regulated channels are generally found on the luminal side of the tubule cell.

Nonregulated forms of transcellular transport include the Na⁺/Glucose symporter and the Na⁺/H⁺ exchanger. These transporters are powered by the Na⁺ concentration gradient established by the Na⁺/K⁺ pump. Since the Na⁺/K⁺ pump is an active transport system and since they indirectly rely on the Na⁺/K⁺ pump, these transporters are considered secondary active transport mechanisms.

The Na⁺/Glucose symporter is located on the luminal side of tubule cells and transports one Na⁺ and one glucose molecule into the cell during each cycle. It is driven by the Na⁺ concentration gradient. The Na⁺/H⁺ exchanger also relies on the Na⁺ concentration gradient that is established by the Na⁺/K⁺ pump. This exchanger moves one Na⁺ into the cell for every H⁺ that it pumps out. It is also located on the luminal side of the cells.

Glucose, amino acids, ions, water and nutrients are reabsorbed. Reabsorption of sodium occurs in the proximal convoluted tubule (PCT). The amount of sodium reabsorbed is second only to amount of H₂O reabsorbed and is done by active transport. When sodium is actively transported, it promotes the passive diffusion of other solutes and water that travel with the sodium. ATP is used as energy source. Almost 100% of filtered glucose, amino acids, lactic acid and other metabolites are reabsorbed in the PCT. This is done by a method called secondary active transport and uses cellular structures called symporters. There is a transport maximum; a limited amount of a substance that can be absorbed. At the renal threshold, if the plasma concentration of the substance is exceeded and the excess nutrients spill into the urine.

Diabetes mellitus is a disease that affects the pancreas' ability to produce the hormone **insulin**. Insulin is essential for cells to take up and store **glucose** after a meal. Therefore, without insulin, glucose concentrations build up in the blood. Large quantities of glucose are filtered by the glomerulus, and as a result, the Na⁺/glucose symporters cannot reabsorb all of it. Consequently, some is excreted in the urine because the concentration of glucose crosses the threshold and spills over into the urine. One of the important symptoms of diabetes mellitus is glucose in the urine (glucosuria).

Eighty to ninety percent of HCO₃⁻, 65% of sodium and H₂O, 50% of Cl⁻ and K⁺ are absorbed in the PCT. After reabsorbing Na⁺, glucose, and water, the concentration of the filtrate leaving the proximal tubule will not have changed significantly from what it was at the beginning of the tubule. It is still roughly 290–300 mOsm/kg water. Essentially, this means that the same proportion of solute and water is being reabsorbed in the proximal tubule.

Reabsorption in Nephron Loop

The loop of Henle consists of a **descending** section that extends deep into the medulla of the kidneys and an **ascending** section that loops back into the cortex. About 15% of the filtered water and roughly 20% of the filtered sodium is reabsorbed in these regions.

There is a dramatic change in the concentration of the interstitial fluid within the medulla. At the junction between the cortex and the medulla, the concentration of the interstitial fluid is 300 mOsm/kg water. As the nephron descends into the medulla, the concentration progressively increases to 1200 mOsm/kg water. The higher this number is, the more solutes in the solution. This is important for the reabsorption of water in the loop of Henle.

Because Na^+ and glucose have been reabsorbed, the filtrate will have a lower solute concentration (and higher water concentration) compared to the cell and interstitial fluid. Therefore, water will move down its concentration gradient by **osmosis** into the cell. The descending loop of Henle is **very permeable to water** and **not very permeable to Na^+** . With this and the presence of a large concentration gradient in the interstitial area in mind, water will move out of the filtrate by osmosis into the interstitial space. Very few Na^+ will diffuse into the lumen down their concentration gradient because of the impermeable nature of the descending limb. The end result will be loss of water and a very small gain of solute. This will increase the concentration of the filtrate to almost 1200 mOsm/kg water (the same as the interstitial space) by the time it reaches the ascending limb at the bottom of the loop.

The **ascending limb of the loop of Henle** is **not permeable to water** at all but is very **permeable to Na^+** . The transport of Na^+ out of the filtrate is the same as in the proximal tubule. The Na^+/K^+ pump will create a concentration gradient for Na^+ , which, as a result, will diffuse into the cell only to be pumped out into the interstitial space. The end result of reabsorbing so much Na^+ will be a filtrate with a concentration of roughly 100 mOsm/kg water.

What is happening in the nephron loop is described as the **Countercurrent Exchange System**. This system allows for the concentration of solutes in urine. Blood in the vasa recta exchanges water for salt. It works as follows in the nephron loop. More salt is continually added to the filtrate in the proximal convoluted tubule. As the extracellular fluid (ECF) increases in osmolarity, more water leaves the descending limb of the loop of Henle. The more water that leaves the descending limb, the saltier the fluid that remains in the loop becomes. The saltier the fluid in the ascending limb, the more salt the tubule pumps into the ECF. The more salt that is pumped out, the more salty the ECF in the renal medulla becomes.

Reabsorption in the DCT and Collecting Tubules

The **distal convoluted tubule** is a short section of the nephron between the loop of Henle and the collecting duct. About 95% of the filtrate has already been reabsorbed by the time it gets to the DCT. Aldosterone and ADH act on principle cells in DCT to regulate final concentrations that have to be reabsorbed. If ADH is absent about 20 liters of dilute urine is excreted/day. If ADH is at maximum levels, then only 400-500 ml/day are excreted. Normally is 1-2 liters of urine is excreted per day. About 90% of water has already been reclaimed. The last 10% occurs in collecting tubules due to ADH. Renal clearance refers to the ability of kidneys to remove (clear) substance from filtrate.

Tubular Transport Mechanisms: Secretion

Secretion is the process by which the kidneys remove unwanted substances from the blood into the lumen of the nephron and control pH. Secretion is a hormonally regulated process that requires transport mechanisms found in the membrane of the tubule cells. Most substances that are secreted are eventually excreted in the urine. Secretion enables the nephron to enhance the excretion of a molecule. Secretion is an active process because the movement of molecules is against the concentration gradient. It therefore, requires energy.

Secretion of K^+ is important, because if K^+ is not secreted, cardiac arrhythmia may develop which can lead to death. It is controlled by aldosterone, the K^+ concentration in the plasma and the Na^+ concentration in the DCT. The secretion of H^+ requires a high energy active transport process. Blood pH can be maintained in three ways: secrete H^+ ions into the filtrate, reabsorbing filtered HCO_3^- , and by processing new HCO_3^- . This takes place in the epithelial cells of the PCT where antiporters (counter transporters are used) and in the collecting ducts. Most HCO_3^- combines with H^+ to form H_2CO_3 which disassociates into CO_2 and water. Secretion of urea and ammonia is necessary because ammonia is toxic to the body. Antiporters are used to secrete and the amount secreted is dependent on blood pH.

Collecting Duct

The collecting duct collects the filtrate from many nephrons and is the final area for processing the filtrate into urine. As a result, the collecting duct plays an important role in determining the final concentration of the urine. Only **10%** of all of the filtered Na^+ and water is reabsorbed in this region but always under the control of hormones. Na^+ reabsorption is controlled by the hormone **aldosterone**, while water reabsorption depends on the presence of **antidiuretic hormone (ADH)**. An increase in aldosterone or ADH will increase the reabsorption of Na^+ or water respectively. The collecting duct can produce urine as dilute as 50 mOsm/L, (when you drink a lot of fluids is

a short period of time), or as concentrated as 1200 mOsm/L depending on the body's need to retain water.

Producing dilute and concentrated urine is dependent on ADH. In the mechanism of urine dilution, urine must contain more water than that found in blood. It must be hypotonic to plasma. This is due to renal tubules absorbing more solutes than water. In the mechanism of urine concentration, more water is reabsorbed in the tubules (done to conserve water, yet eliminate wastes). Urine must be hypertonic to plasma. The mechanisms involve differences in solute and water reabsorption in different sections of the nephron loop and the collecting ducts. Urea recycling is affected by presence of ADH. Water absorbed in collecting duct causes urea to buildup in interstitial fluid. Urea passes into the filtrate and is passed in the urine.

Excretion

Urine output is the result of filtration, reabsorption, and secretion in the nephron. The average adult will pass one to two liters of urine per day. Volume can be influenced by diuretic and antidiuretic drugs. What comes into the body must go out. Urine is made up of mostly of water (95%) and solutes (5%). The most abundant solute is urea. It is unusual to find glucose, free hemoglobin, albumin, or ketones in urine. Their presence may indicate disease. Urochrome gives urine a pale to yellow pigment. The darker the color the more concentrated it is. Urine can also be red, green, blue, brown, or black due to diet or disease. Usually urine is clear but can be cloudy due to the presence of mucous, cells, or salts (phosphates, urates). Urine develops an ammonia smell upon standing and the urine of diabetics has a sweet odor due to ketone bodies. The range of pH is 4.6 - 8.0, usually about 6.0 and the specific gravity is 1.001 - 1.035.

Abnormal constituents in urine can include:

- Albumin (albuminuria): most common protein found in urine
- Glucose (glucosuria): indicates diabetes
- RBC (hematuria): indicates disease of some type
- WBC (pyuria): indicates infection in the kidneys or urinary organs
- Ketone bodies (ketosis): indicates diabetes
- Bilirubin (bilirubinuria) and urobilinogen (urobilinogenuria): indicates breakdown of RBC and hemoglobin
- Casts: tiny masses of material in the shape of lumen (WBC, RBC, epithelial casts)
- Microbes: bacteria, yeast, protozoa

Evaluation of Kidney Function

Laboratory tests used include BUN (Blood Urea Nitrogen) which measures the nitrogen that is part of urea. When GFR decreases due to renal disease or obstruction, BUN increases. The plasma creatinine measures how efficiently a substance is removed. The renal plasma clearance test is the most beneficial

in determining kidney function. High renal clearance equals efficient removal. The renal plasma clearance test depends on filtration, reabsorption and secretion.

Other Urinary Tract Structures

Two **ureters**, one from each kidney, connect each kidney from the renal pelvis to the bladder. There are three layers in the walls of the ureters. A muscularis layer functions in moving urine from kidney to bladder by peristalsis. It is in the ureters that renal calculi (kidney stones) most often will lodge. If the obstruction is not removed, the kidney will fail. Lithotripsy or surgery is used to remove it.

The **urinary bladder** is a hollow organ used to store urine. It is located anterior to rectum in the male and anterior to the vagina and inferior to the uterus in the female which causes it to be smaller. The trigone is a triangular area in the base of the bladder bounded by two ureteral openings and the internal urethral orifice (an opening leading to the urethra). An involuntary urethral sphincter controls the urethral opening. Rugae allow the bladder to stretch as it fills. The detrusor muscle is three layers of muscle in the walls of the bladder. An internal urethral sphincter is a muscle found around the opening to the urethra. The external urethra sphincter is used for voluntary control of urination.

The **urethra** is a tube leading from bladder to the exterior urethral orifice. Its function is to carry urine out of the body. Urination or micturition allows urine to leave the bladder. The urge to urinate impulses is sent when the bladder is 1/4 to 1/2 full. An automatic bladder refers to cases where there are no sensory stimuli from higher nervous center (spinal cord injuries) the bladder can fill and empty spontaneously. Initially there is a reflex due to stimuli but the reflex can be controlled through the external urethral sphincter. Problems with urination range from incontinence or the lack of voluntary control to retention (incomplete voiding) and are often due to an obstruction in the urethra.