EXCRETORY SYSTEM

I. Urinary system - General information

A. Kidneys - symmetrically paired organs that form the urine.
B. Ureters - carry urine to bladder, one from each kidney.
C. Bladder - site where urine is collected and stored until urination
D. Urethra - carries urine from bladder to external environment

II. Kidney

A. General external characteristics
1. Bean shaped => concave on one side, convex on the other
2. Kidney is surrounded by a dense connective tissue capsule.
3. An indentation in the concave side is called hilus where nerves, blood vessels and lymph vessels enter and leave.
4. Renal pelvis - expanded end of the ureter that connects to the hilus. A region where urine from the kidney collects and drains into ureter.
B. The Kidney can be divided into a cortex and a medulla.
1. Renal cortex contains
   a. Upper portions of nephrons
   b. Upper portions of the collecting ducts
2. Renal medulla consists of
   a. Parts of nephrons called loops of Henle
   b. The major portions of the collecting ducts that transport urine to the calyces.
   c. The major calyces and minor calyces that carry the urine to the renal pelvis
3. Cortex and Medulla in humans
   a. The medulla can be subdivided into structures called the medullary or Malpighian pyramids (also called renal lobules).
   b. These pyramids of tissue have their vertex (pointed end) at a renal calyx and their base at the border of the cortex.
   c. The pyramid tissues consist of
      * Collecting ducts that transfer urine from the nephrons in the cortex to the minor calyces
      * Portions of the nephron's loops of Henle.
      * Each side of the pyramid that extends toward the cortex is bordered by an interlobular artery.
d. Where the medullary pyramid tissue meets the cortex their are large arched blood vessels called **arcuate vessels**.

e. Portions of the medullary tissues called **medullary rays** (=pars radiata) project into the cortical regions subdividing it into regions called **cortical labyrinths** (=pars convoluta).

f. The cortical labyrinths consist of many bowman's capsules, and proximal and distal convoluted tubules and have a "tortuous appearance.

g. Note that in addition to the cortical areas between the capsule and the bases of the pyramids, cortical tissue also extends between the pyramids. These areas are called the **renal columns of Bertin**.

C. The **nephron** - the nephron is the functional unit of the kidney. There are approximately one million nephrons in each human kidney - consists of 2 components
1. Renal corpuscle - 4 parts
   a. Bowman's capsule
Can be considered to be the expanded and invaginated end of the proximal convoluted tubule.

* Outer surface - parietal layer
* Inner surface - visceral layer

** Composed of cells called podocytes that have many processes
** The smallest processes (pedicels) intimately surround the capillaries of the glomerulus.
** These pedicel interdigitate with each other and attach to the basal lamina of the capillary.
** Spaces between the interdigitating pedicels are called slit diaphragms or filtration slits
** Filtrate that composes the urine enters Bowman's capsule through the filtration slits.
** The function of the podocytes is probably mechanical. They probably act to prevent the rupture of the glomerular capillaries due to blood pressure and at the same time allow filtration to proceed.

* space between the two layers called the subcapsular space
* parietal layer is composed of simple squamous epithelium
* Bowman's capsule intimately surrounds the glomerulus

b. Glomerulus
* Composed of a tuft of tortuous capillary loops that arise from the afferent arteriole and connect to the efferent arteriole.
* The capillary walls are highly fenestrated and completely encircled by a continuous basal lamina (formed from fusion of endothelial cell and podocyte basal lamina, see below).
* This arrangement acts to form a selective filter that will allow certain components of the blood plasma (including excretory wastes) to pass into Bowman's capsule.

c. **Afferent arteriole**
* Typical arteriole except for the portion close to the glomerulus
** In this area it loses its internal elastic lamina
** Smooth muscle cells of tunica media become enlarged and glandular
** These are the juxtaglomerular cells that secrete the enzyme renin that is involved in the control of blood pressure.
* Function of renin
** Converts plasma protein angiotensinogen into angiotensin I.
** The angiotensin I is carried to the lungs by the circulatory system and there is converted to angiotensin II by an enzyme in lung tissue.
** Angiotensin II is a powerful vasoconstrictor that causes contraction of smooth muscle in the tunica media of arteries and a resultant increase in systemic blood pressure.
** The angiotensin II also causes an increase in secretion of the hormone aldosterone by the adrenyl medulla.
** Aldosterone acts on cells of renal tubules causing increased reabsorption of sodium from the filtrate.
** This reabsorption of sodium and its increased concentration in the blood along with additional retention of fluid causes further increase in the systemic blood pressure.

d. **Efferent arteriole**
* Not called a venule because structure is like an arteriole
* Similar to afferent arteriole, but fewer juxtaglomerular cells
* Almost immediately breaks up into a capillary bed that surrounds the convoluted tubules.
* Since it extends between capillary beds, this may be considered a portal system

2. **Renal tubule** - extends from Bowman's capsule, through cortex, into medulla, back into cortex where it connects with a papillary collecting duct - 3 parts
a. **Proximal convoluted tubule**
* Filtrate exits Bowman's capsule through proximal convoluted tubule.
* The tubule wall is composed of a simple cuboidal epithelium with a microvillar brush border along the lumen of the tubule.
* Cells have many mitochondria located basally, a central, spherical nucleus, and a well developed basement membrane.
* Lateral walls of these cells interdigitate with each other.
* The apical plasmelemma shows very active pinocytosis between microvilli. This is because these cells are responsible for reabsorption of proteineceous molecules from the filtrate.
* These cells also reabsorb 75 - 80% of the water and sodium ions in the filtrate, as well as certain sugars and amino acids.

b. Loop of Henle
* Composed of the decending and ascending components.
* Each of these has a thick and thin segment.
** Each thick segment is a transition zone: decending thick segment goes from a simple cuboidal to simple squamous epithelium, ascending thick segment goes from a simple squamous to a simple cuboidal epithelium.
** Thin segment resembles a blood capillary with somewhat thicker walls than normal.
* The loop of Henle further concentrates the urine by the removal of aditional water by a osmotic diffusion.

c. Distal convoluted tubule
* Lined by simple cuboidal epithelium in most regions (but see below).
* On your lab slides these cells will look similar to those that line the proximal tubule, however they lack a microvillar brush boarder.
* At the point where the distal tubule is adjacent to the afferent and efferent arterioles of it’s own renal corpuscle, the structure of its epithelium changes (called the juxtaglomerular region).
* Cells become more columnar and take on a darker stain.
* This region is called the macula densa.
* Function of the macula densa is not certain, but it's close association with the juxtgglomerular cells suggests that it may provide "information" to these cells that regulates the secretion of renin.

D. Collecting tubules and ducts
1. The distal convoluted tubules of the nephrons empty into the collecting tubules.
2. The collecting tubules extend into the renal medulla and merge to form the large papillary ducts of Bellini that empty into the calyces.
3. The smaller tubules are lined with simple cuboidal epithelium. As they penetrate deeper into the medulla and approach the papillary ducts, the lining becomes columnar.

4. The collecting tubules and papillary ducts are not areas of reabsorption, but simply act to transfer the urine to the calyces.

E. Cardiovascular circulation to the kidney
1. The kidneys receive blood from renal arteries.
2. These enter the kidney through the connective tissue of the hilus.
3. Within the hilus these arteries branch to form the interlobar arteries which extend between the medullary pyramids.
4. As the interlobular arteries reach the medullary - cortical boundary, they branch to form the arcuate arteries that run parallel to the connective tissue capsule surrounding the kidney at the level of the cortical-medullary junction.
5. Branches from the arcuate arteries extend perpendicular into the cortex and give rise to the afferent arterioles of the glomeruli.
6. The capillaries of the glomerulus recoalesce to form the efferent arteriole that leaves the glomerulus and then rebranches to form two capillary networks, a. one surrounding the proximal and distal convoluted tubules and b. the other extending into the medullary tissue to form a capillary net around the loop of Henle.
7. In the case of the juxtamedullary (next to the medulla) nephrons, one arteriole branch of the efferent arteriole follows a path into the medulla were it breaks up into linear capillaries that run parallel to the linear portions of the loops Henle and the collecting ducts. These linear capillaries then loop back toward the cortex where they form venules that will join the arcuate vein. These linear capillaries are called the vasa recta and provide oxygen and nutrients to the tissues of the medulla.
8. The interlobular veins receive blood from the capillaries and carry it to the arcuate veins which connect to interlobar veins that extend parallel to their corresponding interlobar arteries.
9. The interlobar veins connect to the renal vein that carries blood out of the kidney.
10. There are also the stellate veins in the peripheral cortex of the kidney that result from the convergence of capillaries in this area.
E. The calyces, pelvis, ureter, bladder and urethral structure is relatively simple.
### URINE FORMATION

**Step 1** in urine formation, **Filtration** - Fluid pressure forces water and dissolved substances out of the blood into Bowman's capsule. Filtration averages 125 ml/min for your two kidneys. This amounts to about 180 Liters per day. Since we urinate an average of 1500 ml per day, more than 99% must be returned to the blood. Filtration involves the small molecules: water, electrolytes, urea, glucose, amino acids. It does not involve the blood proteins or cells. The large amount of filtration is the result of the porous glomerular membrane and filtration slits in the visceral layer of Bowman's capsule.

**Step 2, Reabsorption** - The return of substances from the filtrate to the blood and interstitial fluid. The major substances reabsorbed are water, NaCl, glucose, and amino acids. Some of the urea, together with other salts are also reabsorbed.

**Water** is reabsorbed by osmosis. Entering the proximal convoluted tubule the filtrate is very dilute compared to the blood. 65% of water reabsorption occurs from the PCT as a result of this osmotic gradient. As the filtrate enters the descending limb of the loop of Henle, especially in juxtamедullary nephrons with long loops, it is exposed to increasingly hypertonic medulla. This pulls at least another 20% of absorbable water out of the filtrate. Reabsorption in this area is termed **obligatory** because it must occur due to the osmolarity of the surrounding interstitial fluid. As the filtrate enters the ascending limb the tubule becomes impermeable to water. Otherwise it might actually diffuse back into the tubule as the osmotic gradient reverses. When the filtrate, now nearly urine, passes through the medulla again in the collecting tubule it is once again exposed to the hypertonicity of the deep medulla. This has the potential to pull more water out by osmosis. But reabsorption of water from the collecting tubule is **facultative** because it is under control of the hormone ADH (See below).

The **Countercurrent Mechanisms** to increase water reabsorption:

1) The **Countercurrent Multiplier** - This mechanism works in the loop of Henle to increase water reabsorbed from the descending limb as a result of salt reabsorbed from the ascending limb. The term countercurrent comes from the fact that fluid is moving in opposite directions in the two limbs of the loop. This magnifies the effect of transport from one limb on transport from the other limb. The same principle is at work in heat exchangers used in industry.

2) The **countercurrent exchange of salt** in the vasa recta. The vasa recta has descending and ascending limbs too. Blood flowing into the medulla in the descending limb picks up salt from the hypertonic medulla. As the surrounding medullary fluid becomes more and more salty toward the papilla the gradient increases and more and more salt is picked up by the descending vasa recta limb. But as the blood heads back up to the cortex in the ascending limb of the vasa recta, the interstitial fluid becomes less and less salty. This causes the gradient to reverse and salt diffuses back out of the vasa recta into the medulla. This helps to conserve salt and keep the medulla hypertonic.

3) Urea is also reabsorbed, passively, from the nephron and this too helps to keep the surrounding fluid hypertonic, pulling water. This same urea will be filtered later and may in fact be reabsorbed again. Overall though, urea experiences a net loss from the body.
because more is filtered and released in the urine than is reabsorbed.

**Step 3. Secretion**

Secretion is the release by active transport of substances into the filtrate. It is accomplished by the tubular lining cells. The substances released are usually derived from the blood in the peritubular capillaries. Actually secretion has already been going on but it is the third process we consider. It begins in the proximal convoluted tubule and continues in the distal convoluted tubule and the collecting tube. It is done for three purposes:

1) to release any residues from **toxins and drugs** which haven't been filtered;

2) to establish **electrolyte balance**. Since positive ions, namely sodium, are reabsorbed, positive ions must be secreted in exchange. The first choice is potassium, $K^+$. In addition negative ions will be managed. This usually means chloride, $Cl^-$, will either be secreted or will diffuse down its electrochemical gradient. Other anions may be available for release such as sulfate, but certain ions will never be secreted. For example, bicarbonate will always be retained to help manage the buffering capacity of blood.

3) **acid - base balance**. Usually this means getting rid of acid. The first choice for this is $H^+$. Hydrogen ions are derived from the reaction of carbon dioxide and water, just as they are in the rbc and in stomach lining cells. The reaction yields carbonic acid which dissociates into $H^+$ and $HCO_3^-$ as you've already learned. The bicarbonate produced is retained for the buffer (as mentioned above) and exchanged for chloride, called the chloride shift. Hydrogen ions can be secreted during moderately acidic conditions, but when you have more severe acidity they reach their limit, called the tubular maximum. At that point they neutralize some of the $H^+$ with $NH_2$ and $NH_3$ groups derived from certain amino acids. The result is ammonium ions, $NH_4^+$, which are secreted during these more severely acidic conditions. During extreme acidity they can also secrete phosphoric acid.

Since the hydrogen ions and ammonium ions are also cations, less potassium is secreted during acidic conditions as well. Since conserving potassium may be important for many people, consuming liquids which are acidic as well as contain potassium are important in supplying the needed potassium and encouraging it to be retained by the body. Citrus juice, although containing potassium, does not acidify the blood greatly, but cranberry juice, grape juice, watermelon etc. work well. Cranberry juice also acidifies the urine which can help discourage bacteria and some types of kidney stones. Cranberry juice also reduces the adherence of bacteria onto the walls of the urinary tract thus reducing urinary tract infections.

**The ADH Mechanism** for controlling **facultative reabsorption**.

Reabsorption in the collecting tubule is controlled by a hormone from the posterior pituitary gland known as **ADH, anti-diuretic hormone**. Actually this hormone is released by nerve fibers coming from the hypothalamus and stored in the pituitary. ADH is then released into the blood on command of the hypothalamus. The hypothalamus responds to high blood osmolarity. Increased osmolarity results from water loss and dehydration from sweating, vomiting and the like, and from simply not taking in enough replacement water.
ADH allows water to be reabsorbed from the collecting tubule and not leave the body with the urine. The water is reabsorbed by osmosis due to medullary hypertonicity. Lack of ADH causes the production of a large amount of dilute urine, a condition called diabetes insipidus.

**Juxtaglomerular Apparatus** (JGA) and the tubuloglomerular mechanism in autoregulation.

The juxtaglomerular apparatus is a place where the distal convoluted tubule lies close to the glomerulus and to the afferent and efferent arterioles. Within the JGA is a group of cells lining the distal tubule called the macula densa cells. These cells monitor the rate of filtrate flow in the distal tubule, which is directly related to the glomerular filtration rate (GFR) and the glomerular pressure. It also monitors the salt levels. In response to rising salt levels and reduced GFR the macula densa cells do two things:

1) The macula densa causes the juxtaglomerular cells lining the arterioles to secrete renin. **Renin** acts as an enzyme to cause a substance already in the blood, angiotensinogen, to undergo a structural change to become angiotensin I, which is then converted to angiotensin II by angiotensin converting enzyme. See [Angiotensin Converting Enzyme, ACE]. Angiotensin II acts as a vasoconstrictor, first causing vasoconstriction in the efferent arteriole. Since the efferent arteriole is the outflow from the glomerulus, constricting it rapidly raises glomerular pressure. Angiotensin II also causes the adrenal cortex to release aldosterone. Aldosterone acts on the distal convoluted tubule to increase Na+ reabsorption. More sodium reabsorption means more water reabsorption, and more water reabsorption means an increase in blood pressure.

2) The macula densa also acts directly on the afferent arteriole and cause it to vasodilate. So at the same time the efferent arteriole is constricting, the afferent arteriole is dilating bringing in more blood and the combination dramatically raises glomerular pressure and GFR.

**Other Autoregulation:**

The only mechanism responsive to high blood pressure is the direct myogenic autoregulation of the afferent arteriole. This vessel, like others in the body, responds to high pressure with vasoconstriction. This reduces blood flow into the glomerulus and brings GFR back down to normal levels. This mechanism works only for transitory pressure increases and is not effective against sustained hypertension.

**The heart-renal connection:**

Several mechanisms are at work to respond to excessively high or excessively low blood volume. These mechanisms are based on pressoreceptors located in the heart, primarily the right atrium, and in other regions such as the aortic and carotid sinuses. These receptors are constantly monitoring blood volume and pressure by responding to physical stretch.

When blood volume and pressure rises excessively, stretch acts to inhibit ADH secretion and release ANF (atrial natriuretic factor) which dilates the afferent arteriole and reduces Na+ reabsorption. These actions effectively release fluid into the urine thus reducing the blood volume.
Absence of stretch due to low blood volume acts to release significant amounts of ADH (vasopressin) which acts to generally vasoconstrict arterioles throughout the body. These actions increase blood pressure and blood volume.

**Normal and Abnormal Constituents of Urine:**

**The Ureter, Bladder, and the Micturition Reflex -**

Urine travels to the urinary bladder through the ureter by peristalsis. The ureter has two layers of smooth muscle which work like smooth muscle in the intestine, except they are in reversed position (longitudinal toward the inside, circular toward the outside). The ureter is lined with **transitional epithelium** to allow for stretch and reduce back pressure on the kidney.

The bladder is also lined with transitional epithelium and has many rugae for expansion. The bladder's **detrusor muscle** consists of three layers like the stomach's and also serves for compression. At the lower end of the bladder the ureteral openings form a triangle with the urethra which is called the trigone. The trigone has longitudinal folds which funnel the urine toward the urethra. These folds help squeeze the ureteral openings closed when micturition occurs.

The urethra varies from a short tubule in females to a longer tubule in males with several sections (see diagram). Near the bladder the urethra is lined with transitional epithelium and near the external os it is stratified squamous, while in the middle it is pseudostratified columnar epithelium.

When urine pressure stimulates presso-receptors in the bladder wall it triggers a parasympathetic reflex which stimulates mild detrusor contractions and relaxation of the internal urethral sphincter. Pathways to the brain stimulate the sense of a need to urinate. Then, when conditions are appropriate, additional parasympathetic stimuli result in micturition and voluntary stimuli relax the external sphincter.