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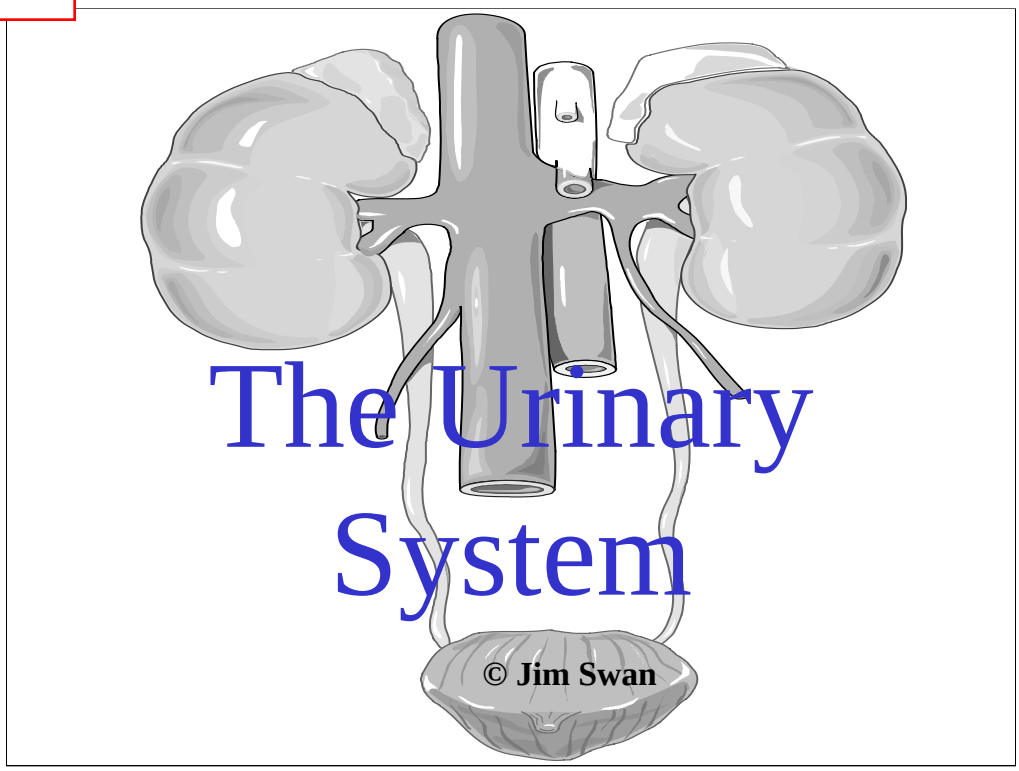


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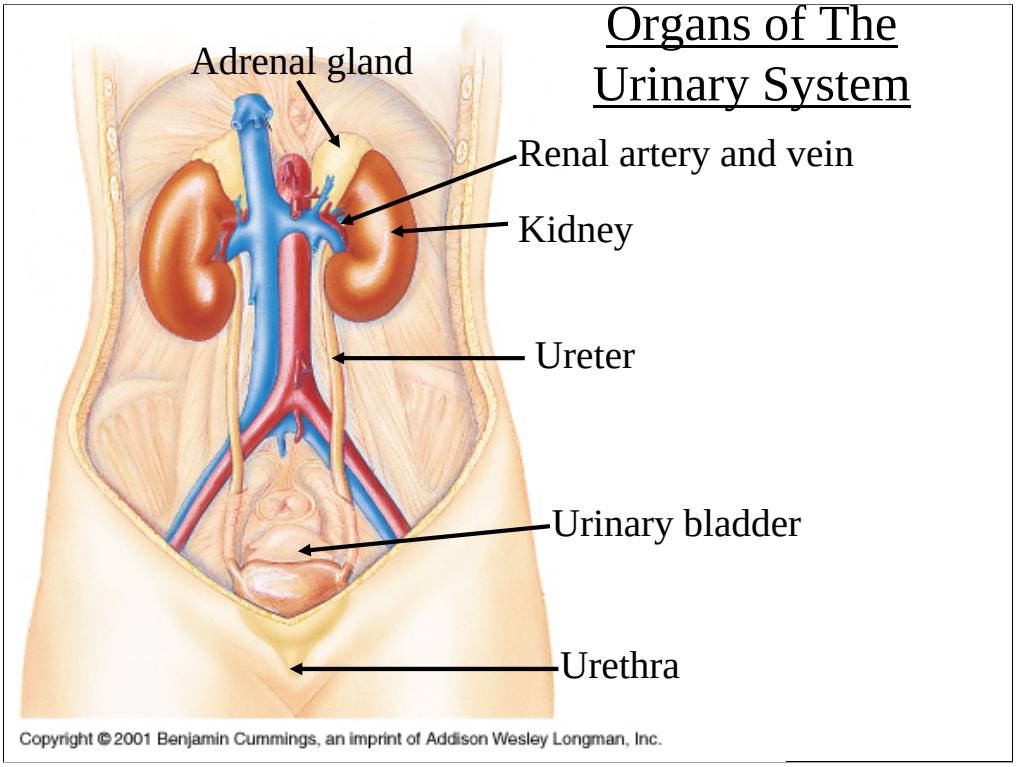
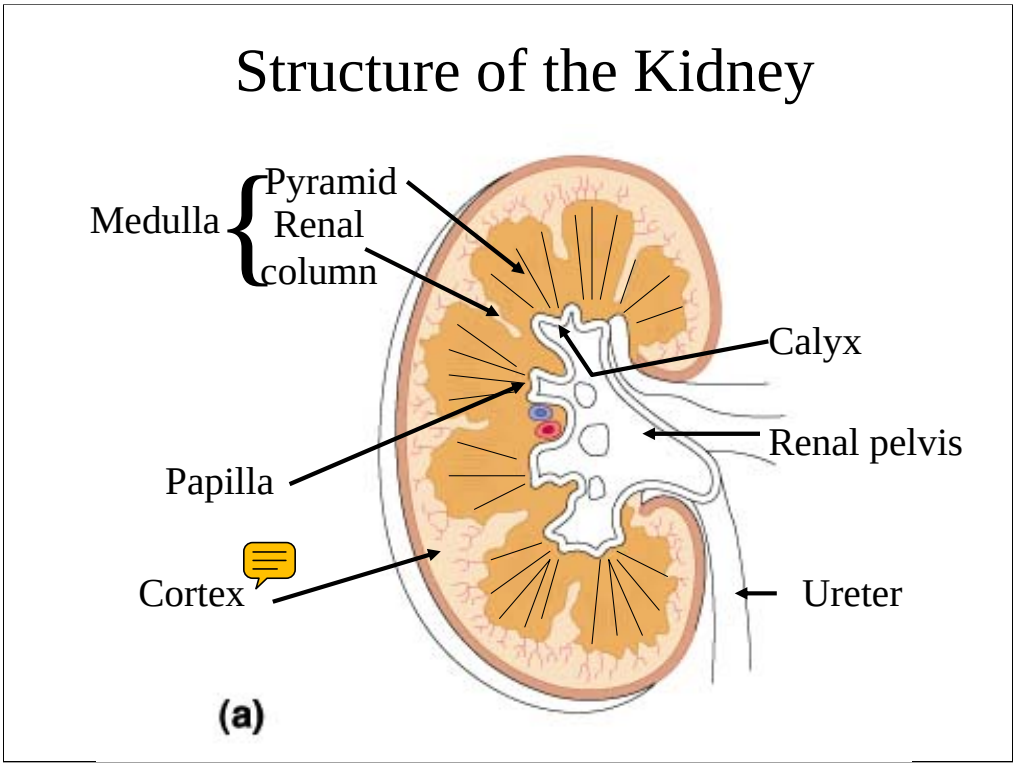


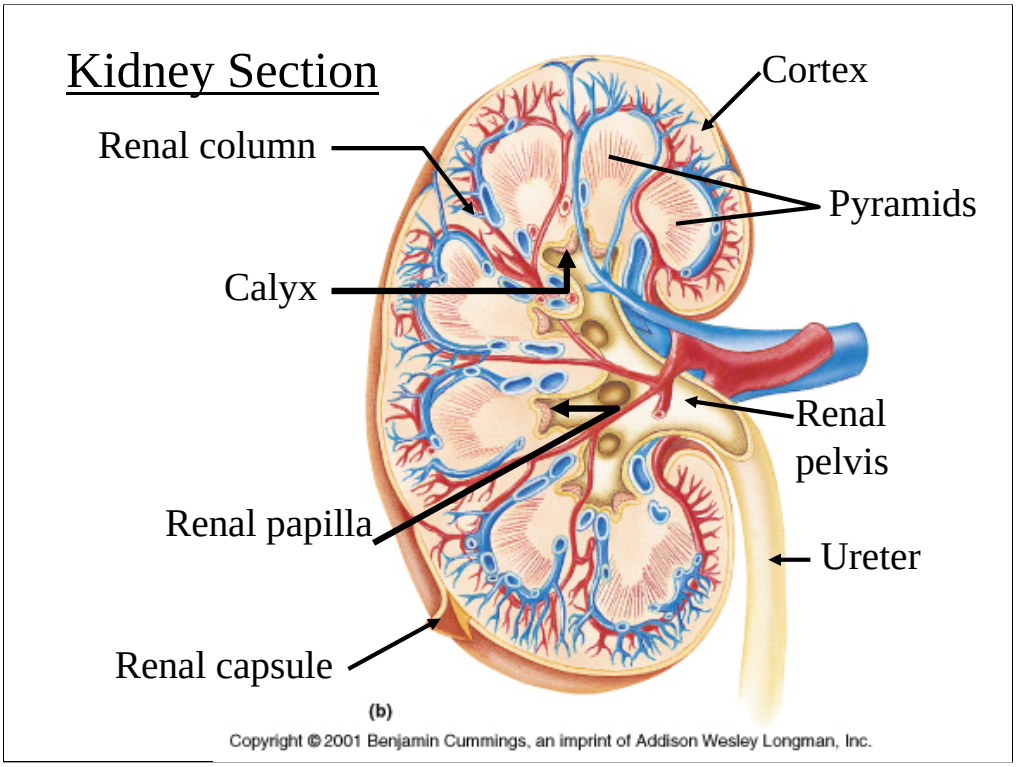

The urinary bladder stores urine prior to micturition, the urethra expels urine from the bladder, the ureters bring

urine to the bladder. But the function of the kidneys is NOT to make urine, it is to maintain homeostasis of the

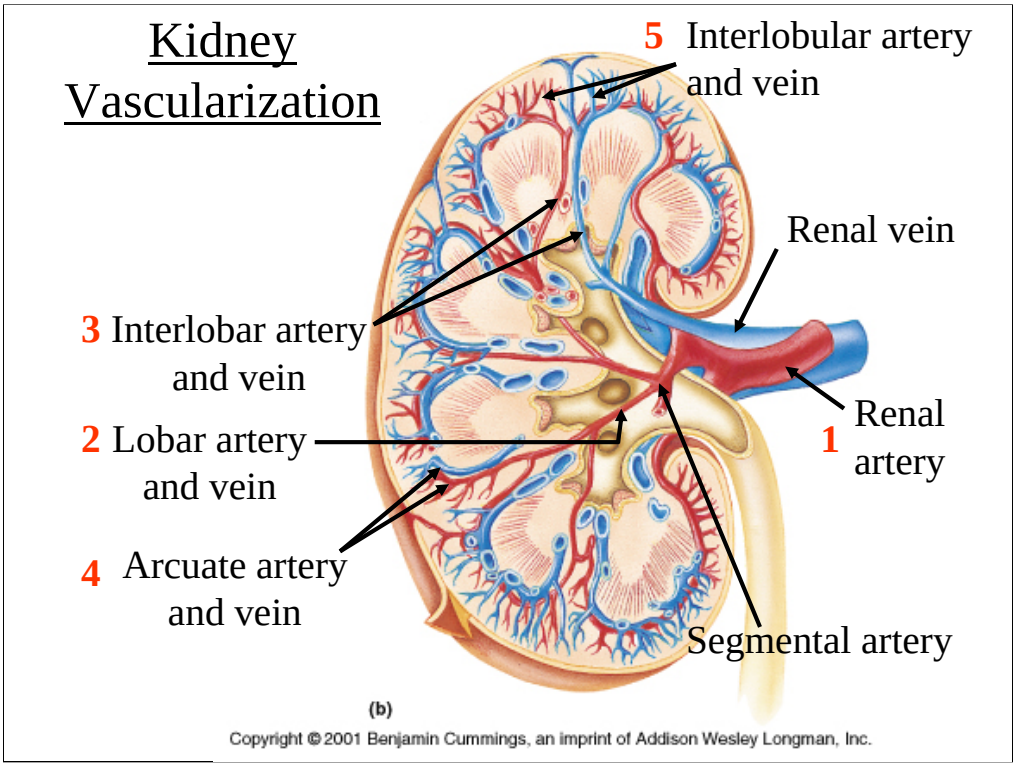
blood: excreting wastes, keeping nutrients, maintaining electrolytes, acid base balance, and other things.



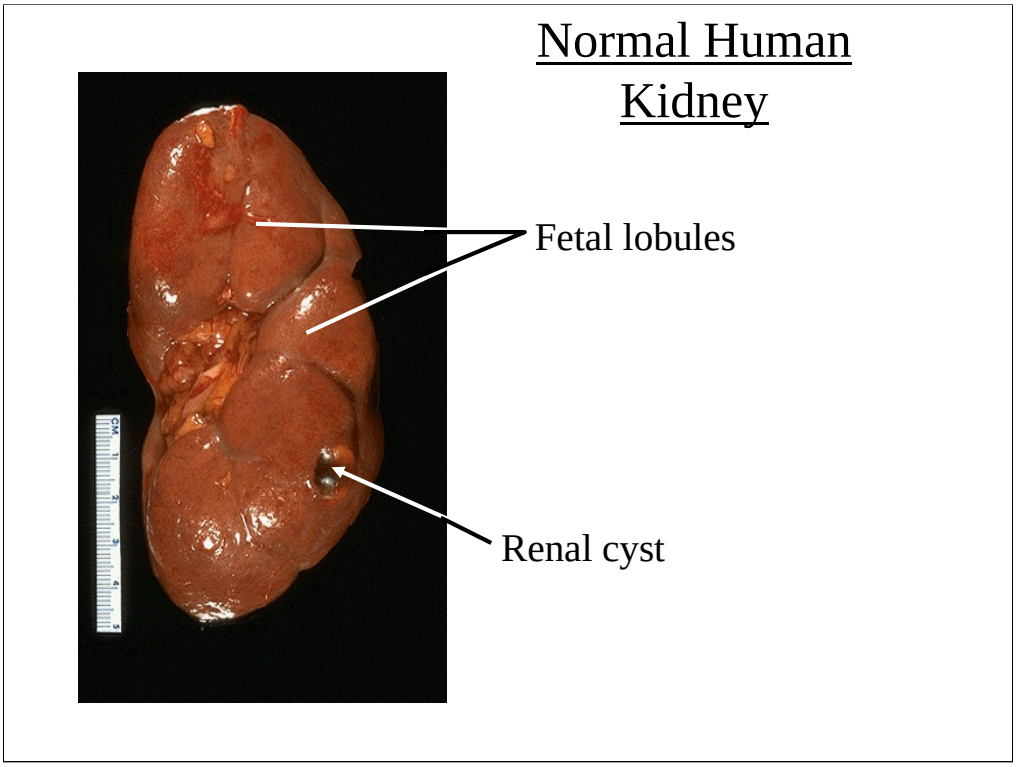

The kidney is composed of several layers and is covered with a fibrous capsule, the **renal capsule**. The outer layer of the kidney is the **cortex**. It contains the major (upper) portion of the **nephrons.** The middle layer of the kidney is the medulla. It is composed of the triangular shaped pyramids and the renal columns. The pyramids contain the collecting tubules and loops of Henle, the lower portion of the nephrons. These tubules run nearly parallel to one another and give the pyramids a grain which leads to their points or papillae. The renal columns are regions between the pyramids in which blood vessels run to and from the cortex. The papilla of each pyramid projects into a funnel-shaped area known as the calyx. The calyces (plural of calyx) collect the urine released from the papillae and allow it to drain into a large area known as the renal pelvis and then into the ureter.




This view of the kidney shows not only the regions mentioned previously but also the manner in which blood vessels supply these regions.

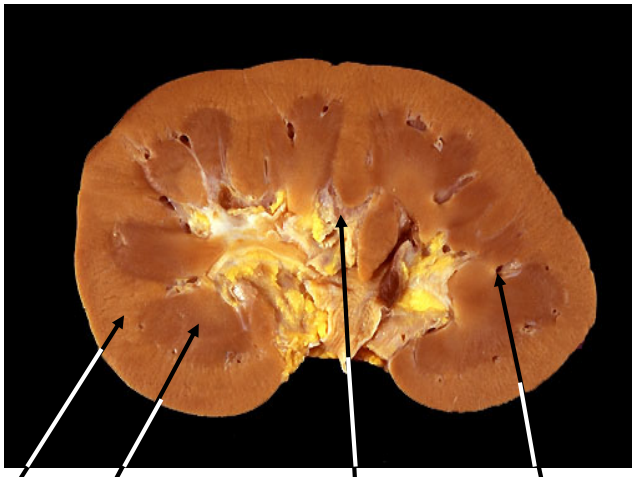



The blood supply of the kidney is paramount in its function. The two kidneys receive between 15 and 20% of the body's systemic blood flow at rest. The **renal artery** branches into **lobar** and then interlobar arteries. These pass through the renal columns toward the cortex. **Arcuate** arteries branch into the cortex and lead to interlobular arteries which distribute the blood evenly throughout the cortex to the **afferent arterioles** which serve the **nephrons**. Blood flow leaving the nephrons returns by veins of the corresponding names.

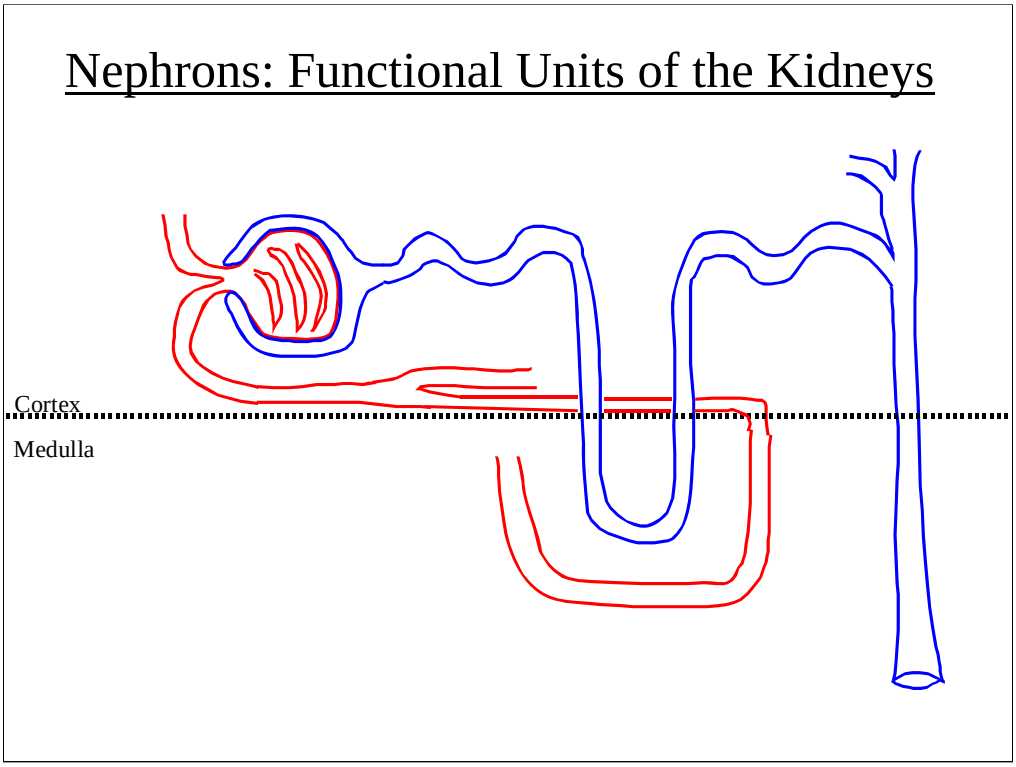



Here is a normal adult kidney. The capsule has been removed and a pattern of fetal lobules still persists, as it sometimes does. The hilus at the mid left contains some adipose tissue. At the lower right is a smooth-surfaced, small, clear fluid-filled simple renal cyst. Such cysts occur either singly or scattered around the renal parenchyma and are not uncommon in adults. Only when cysts are large and extensive do they have the potential to interfere with kidney structure and function.

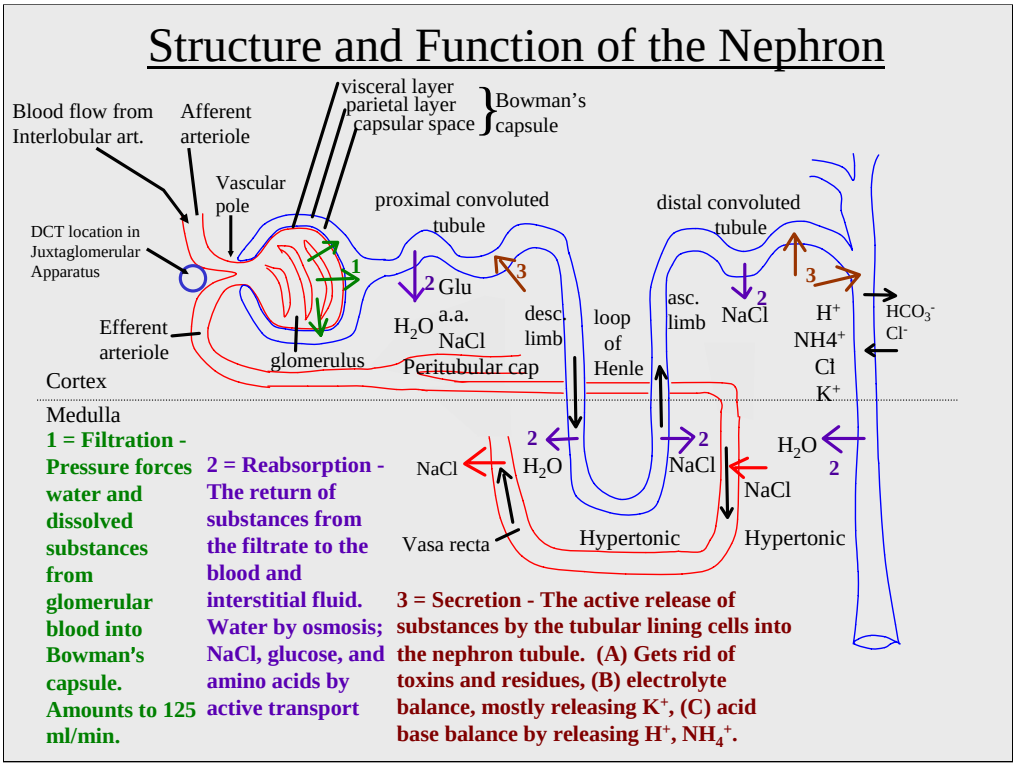
## Kidney Section




In a sectioned human kidney can easily be seen the regions shown in previous slides. Much of the **hilus** (notch) of the kidney is filled with the fat, the yellowish tissue.




**The Nephron**: - The nephrons are the functional units of the kidney, i.e. individually and collectively they perform the functions of the kidney. Use this unlabeled nephron diagram to label and describe its various functions.



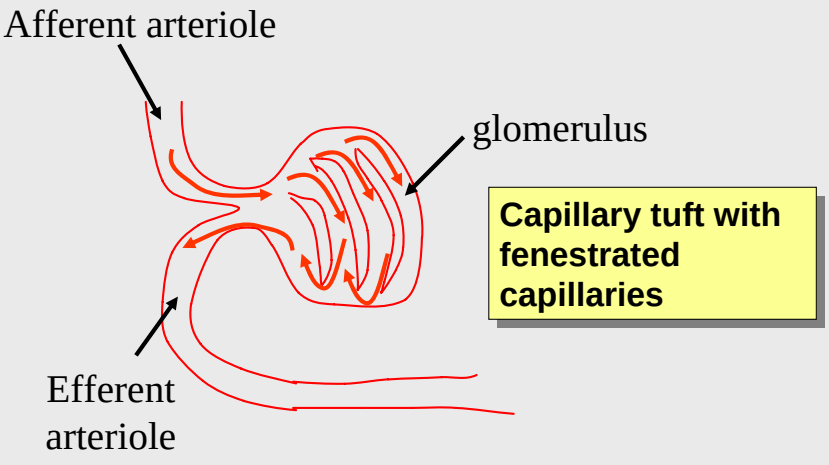

The nephrons are the functional units of the kidney. They consist of a number of specific parts which we will

discuss. Nephrons are microscopic, and there are up to a million in your two kidneys. This diagram

summarizes the parts and functions of the nephrons. We will elucidate each. See also [Nephron Diagram]

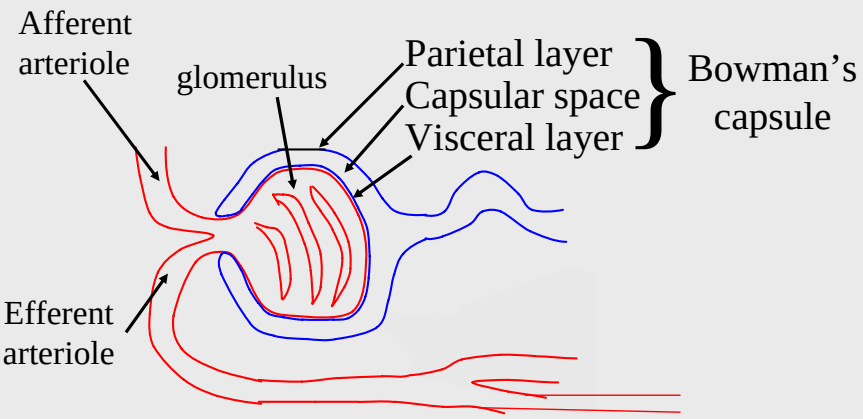
[Bare Nephron] [Functional Nephron] [Test Nephron]

## Structure of the Nephron: the Glomerulus

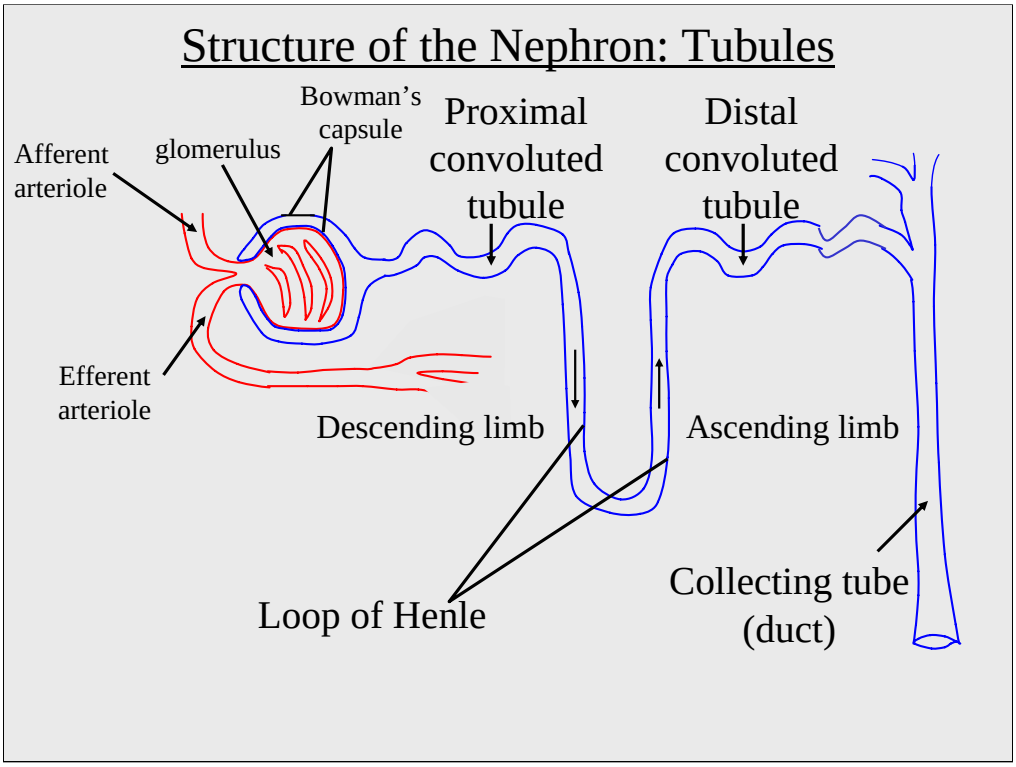



Each nephron is served with blood by the **afferent arteriole**. This vessel brings blood into a capillary tuft called the **glomerulus**. Blood leaving the glomerulus flows into the **efferent arteriole**.

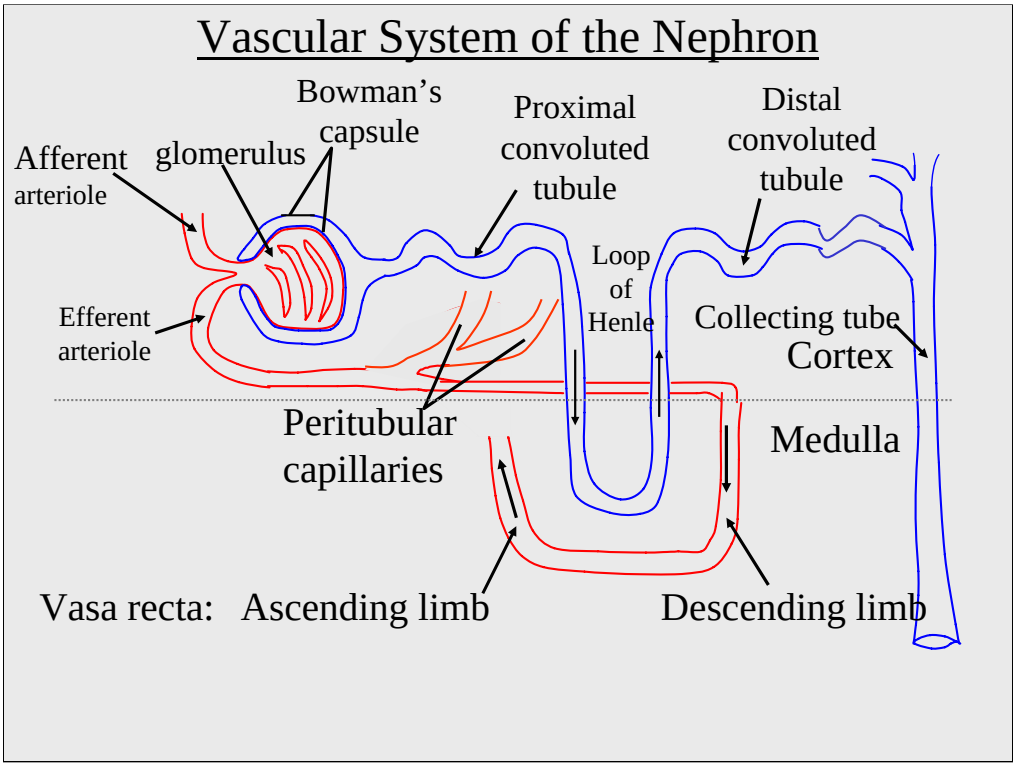
## Structure of the Nephron: Bowman's Capsule



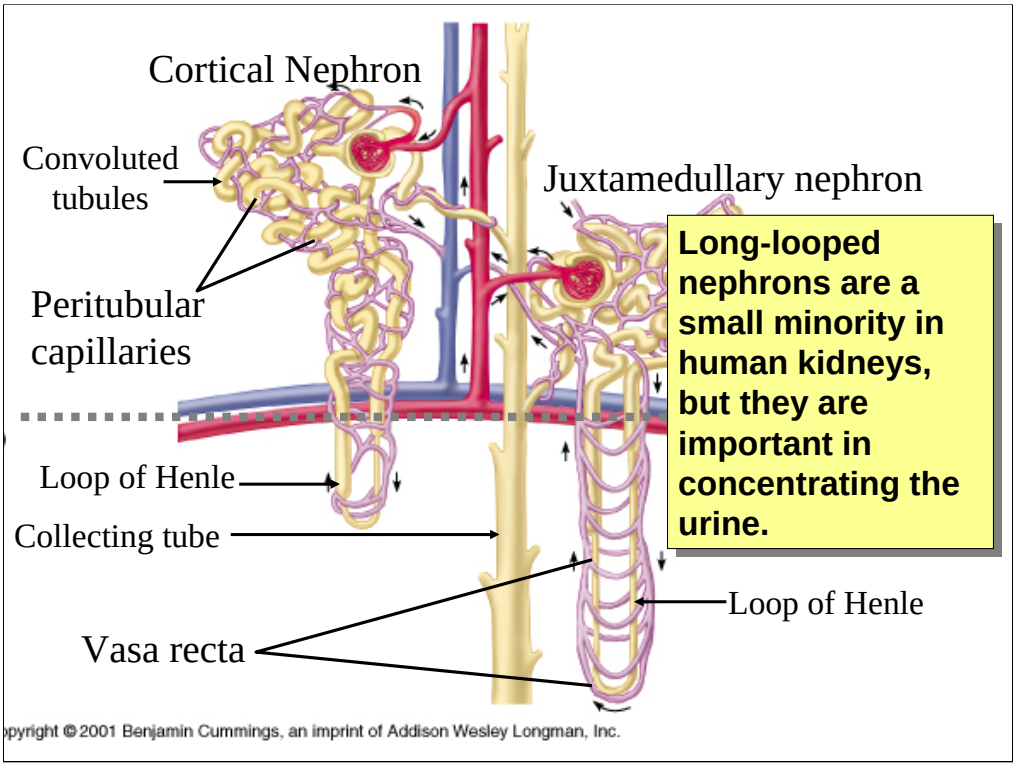

A capillary tuft differs from a capillary bed in that it does not perfuse a tissue like a capillary bed does. Instead this capillary tuft is a condensed mass of capillaries which allows substances to escape by filtration. The capillaries of this tuft are surrounded by specialized cells which form the inner (visceral) layer of Bowman's capsule. The parietal layer is composed of simple squamous cells with tight junctions that form an outer wall which contains the filtrate.



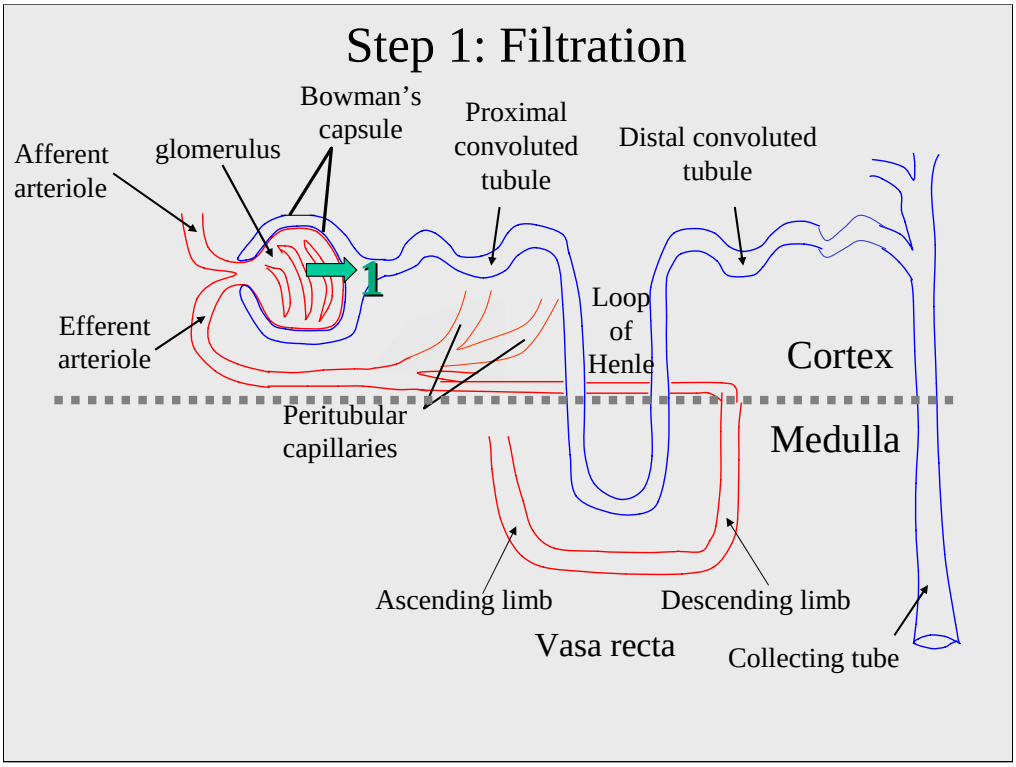

The Bowman's capsule opens into the **proximal convoluted tubule** which leads to the **loop of Henle**. The loop of Henle has a **descending limb** which passes into the medulla, recurves, and becomes the **ascending limb** which leads back up to the **distal convoluted tubule** in the cortex. Most human nephrons are termed **cortical** nephrons because their corpuscles are located in the mid to outer cortex and their loops of Henle are very short and pass only into the outer medulla. But a small portion are called **juxtamedullary nephrons** and their loops travel deep into the inner medulla. These nephrons are important in concentrating the urine by increasing the amount of water reabsorbed. Distal convoluted tubules lead into collecting tubules and ducts which pass through the medullary pyramids to the papillae. See [**Orientation of the Nephron**] diagram.




Usually an arteriole flows into a venule. But in this case the efferent arteriole flows into more capillaries, the **peritubular capillaries**, and, in juxtamedullary neurons, the **vasa recta**. The peritubular capillaries and vasa recta then lead to venules and the venous drainage of the kidney.




Cortical nephrons have short loops of Henle which barely enter the medulla. Longer loops which dip much further into the medulla belong to juxtamedullary nephrons. These nephrons are important for concentrating the urine by absorbing extra water.




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.

# 1. Filtration

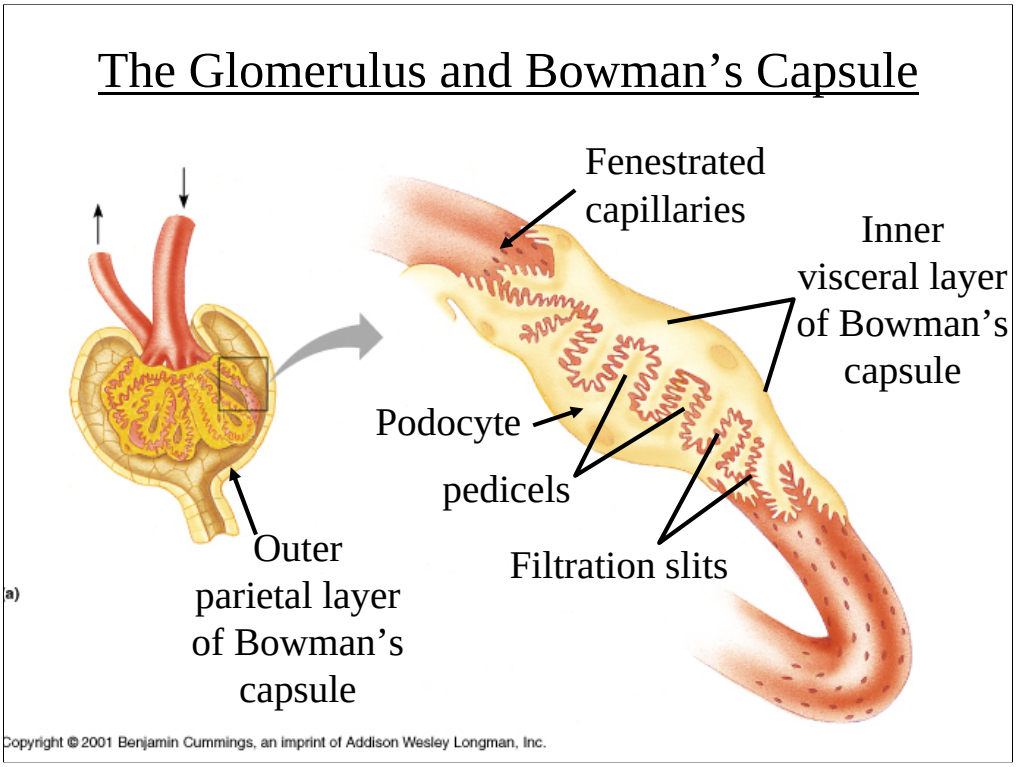
Filtration – Hydrostatic pressure (blood pressure) forces water and dissolved substances out of the glomerular blood into Bowman's capsule.

$H_2O$, glucose, amino acids, electrolytes, wastes

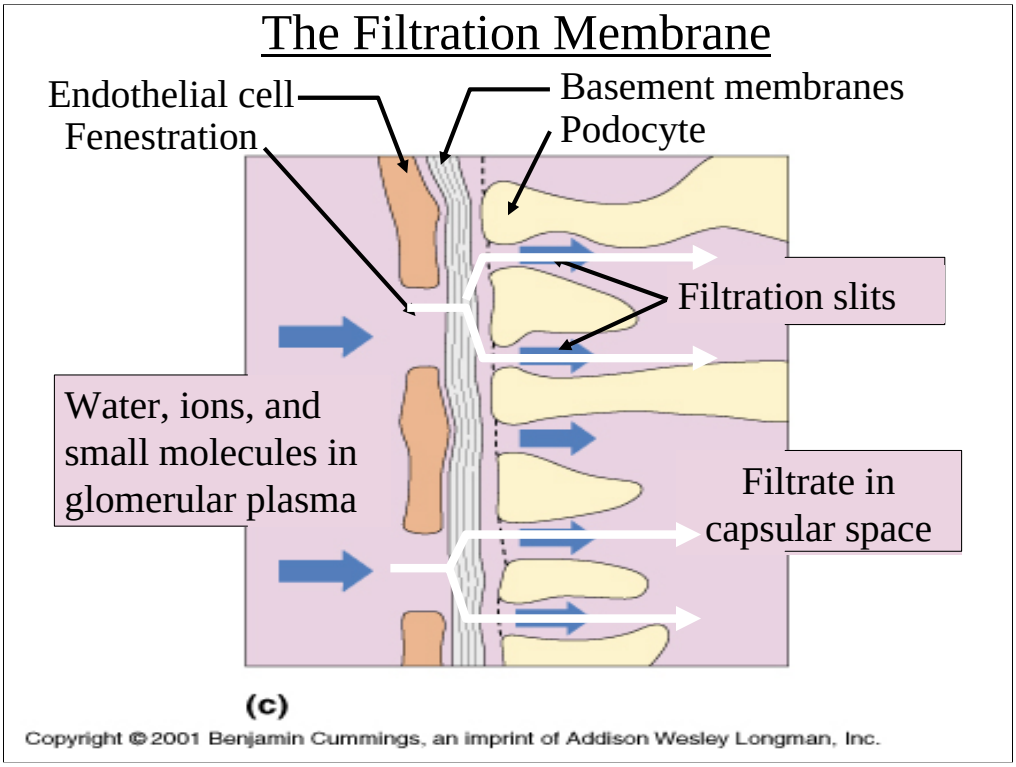
Averages 125 ml/min for both kidneys → 180 liters/day

The vast majority of the filtrate must be taken back!

Filtration is a product of the blood pressure and the nature of the fenestrated capillaries which make up the **glomerulus**.




The capillaries of the glomerulus are surrounded by specialized cells which form the inner (visceral) layer of Bowman's capsule. (See Figures 26.7 and 26.8)These specialized cells are called **podocytes** (foot cells) because they have processes called **pedicels** which interdigitate or interlace producing openings called **filtration slits**. The capillaries are fenestrated in order to allow a large amount of filtration. The outer (parietal) layer of Bowman's capsule consists of epithelial cells with tight junctions and serves to contain the filtrate in the **capsular space**.




The filtration membrane is a double layered membrane composed of the endothelial cells of the capillary wall juxtaposed with the podocytes of the visceral layer of Bowman's capsule. Substances make their way through the capillary fenestrations, then through the combined basement membranes of capillary and podocyte cells, and through the filtration slits into the capsular space.

## Step 2: Reabsorption

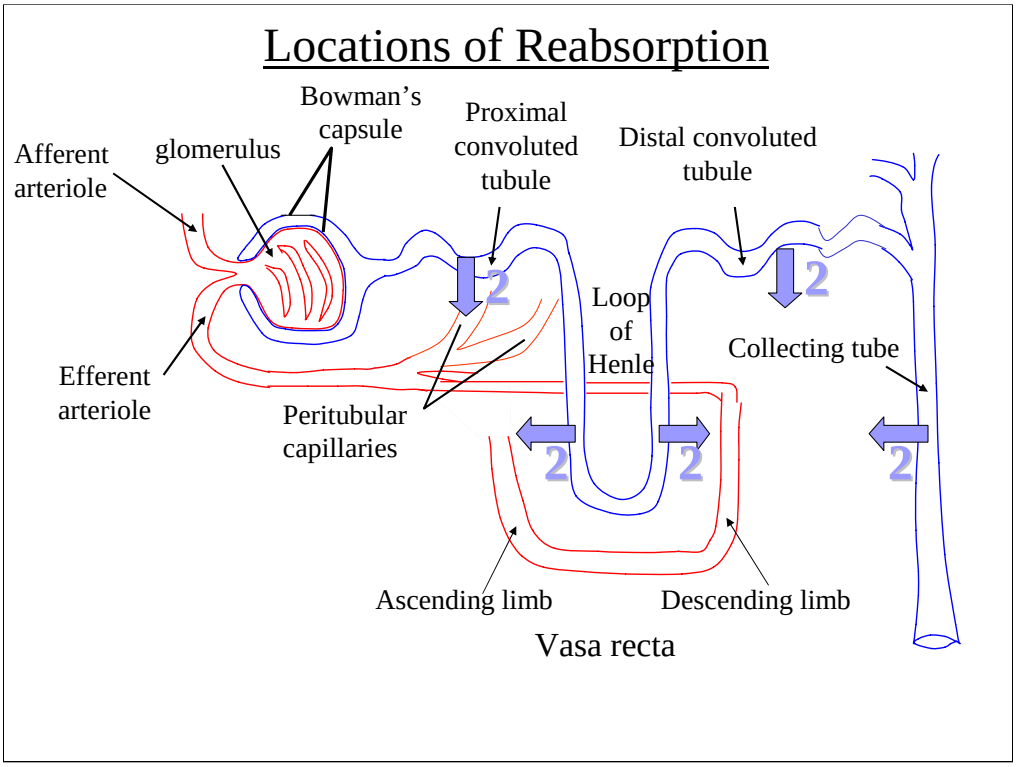
Reabsorption – the return of substances from filtrate in the nephron tubule to the blood or interstitial fluid.

$H_2O$ - osmosis

NaCl - active transport

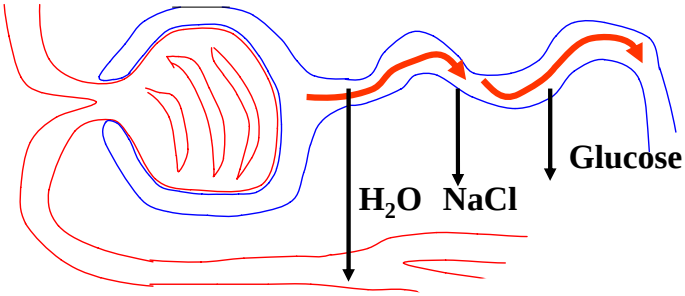
Glucose, amino acids - active co-transport

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.




Reabsorption occurs in each of these areas for various substances and to various degrees: Most reabsorption occurs in the **PCT** (**Proximal Convoluted Tubule**), but reabsorption of water also occurs from the **descending limb** of the **Loop of Henle**, reabsorption of salt from the **ascending limb** and the **DCT** (**Distal Convoluted Tubule**), and more water from the **Collecting Duct**.

## Reabsorption from Proximal Convoluted Tubule

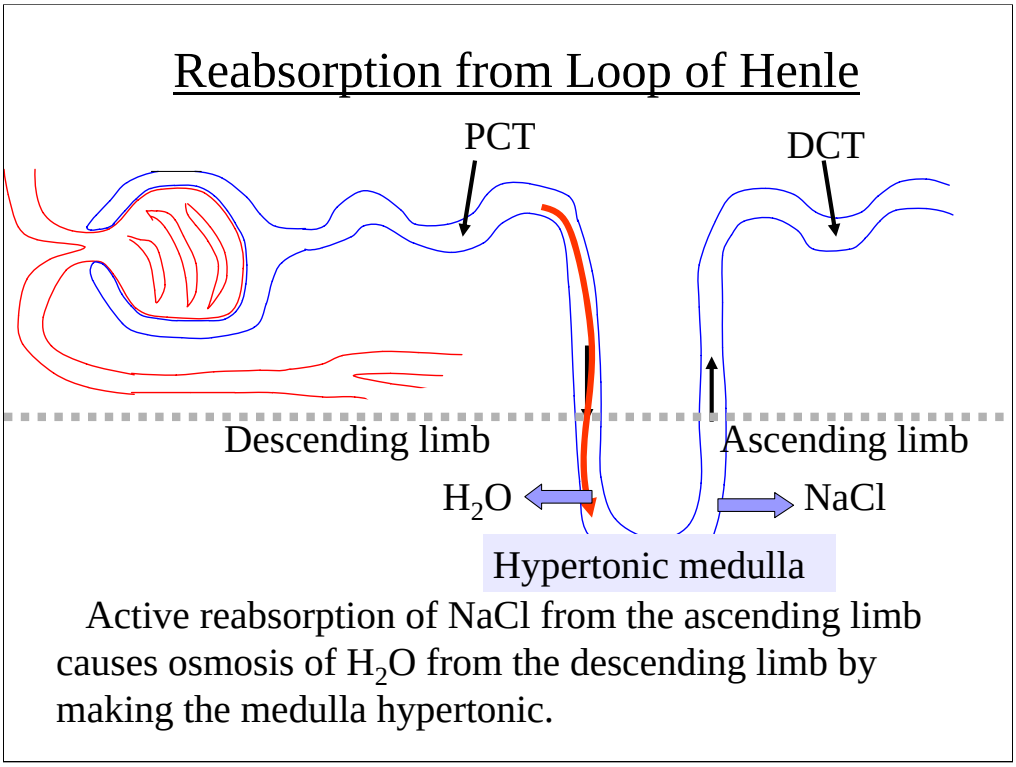



A) $H_20$ – pulled by osmosis into hypertonic blood. 65% occurs in PCT

B) NaCl – active transport of either Na+ or Cl-, pulls water along.

C) 100% of glucose and amino acid transported - occurs in PCT by active co-transport.

**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.

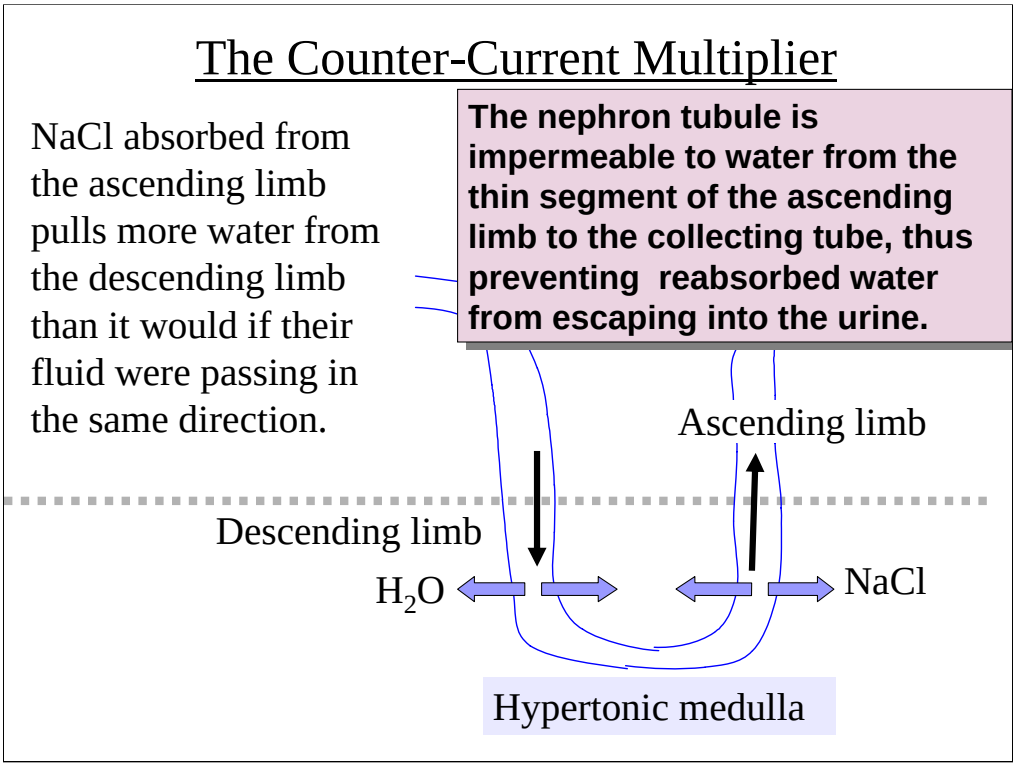



As the filtrate enters the descending limb of the loop of Henle, especially in juxtamedullary nephrons with long loops, it is exposed to increasingly hypertonic medulla. This pulls at least another 20% of absorbable water out of the filtrate. Reabsorption in this area is termed **obligatory** because it must occur due to the osmolarity of the surrounding interstitial fluid.

## The Counter-Current Mechanisms

1) The **counter-current multiplier** – increases the amount of $H_2O$ reabsorbed because of opposite movement in the two limbs of the loop of Henle.

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.



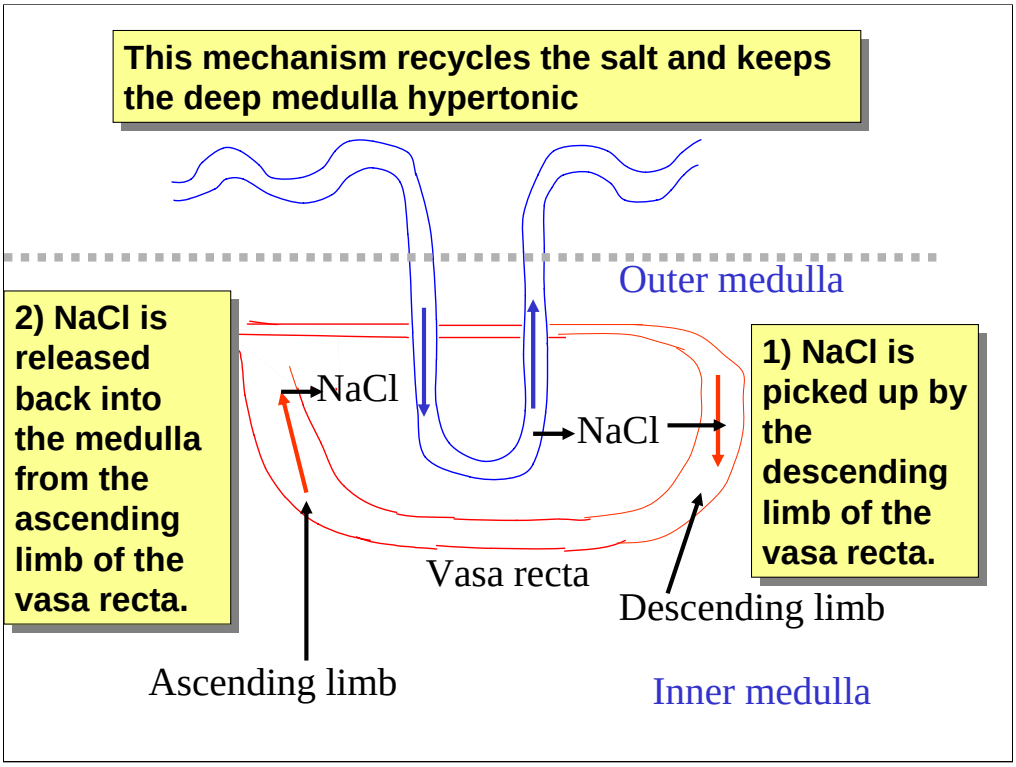

As the filtrate enters the thin segment of the ascending limb the tubule becomes impermeable to water. Otherwise it might actually diffuse back into the tubule as the osmotic gradient reverses

## The Counter-Current Mechanisms

1) The counter-current multiplier – increases the amount of $H_2O$ reabsorbed because of opposite movement in the two limbs of the loop of Henle.

2) The countercurrent exchange of salt – increases the reabsorption of $H_2O$ by retaining NaCl in the medulla.

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.

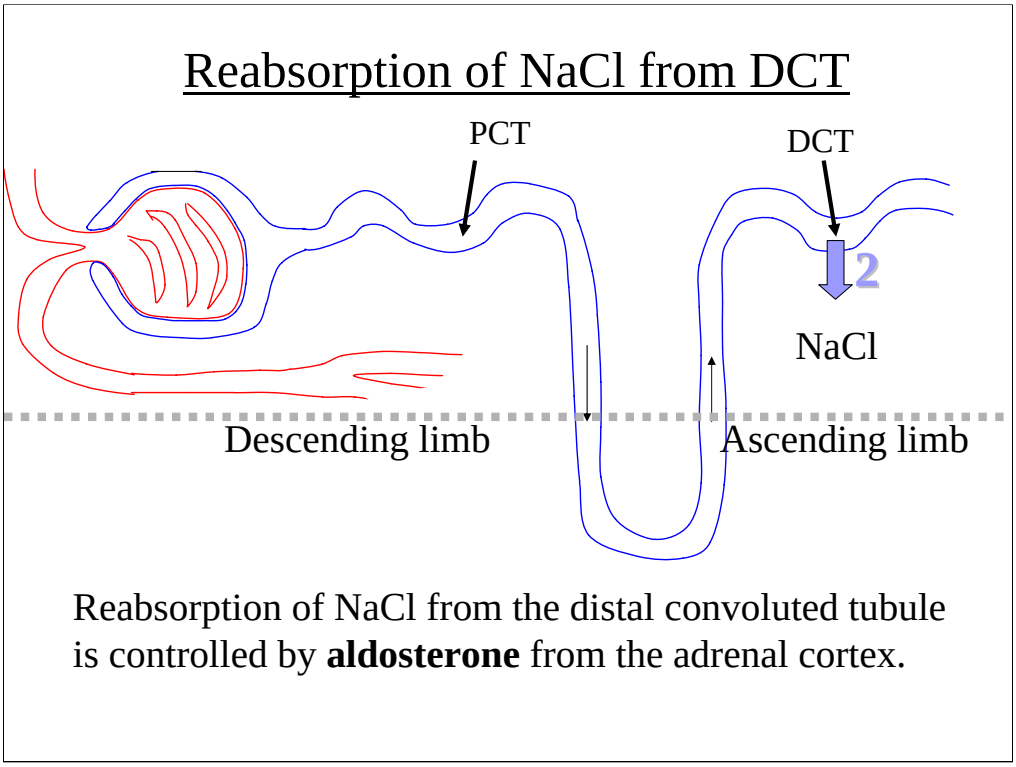



1) NaCl is picked up by the descending limb of the vasa recta. 2) NaCl is released into the medulla by the

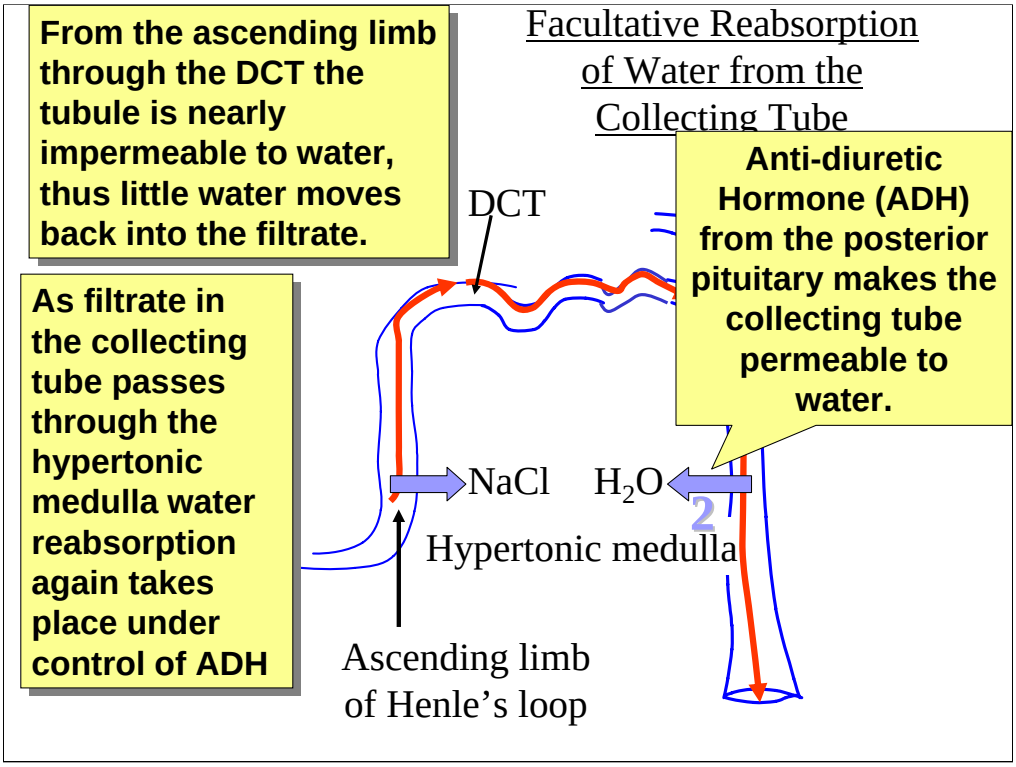
ascending limb of the vasa recta. This mechanism recycles the salt and keeps the deep medulla hypertonic.

From the ascending limb of Henle's loop through the distal convoluted tubule the nephron is impermeable to

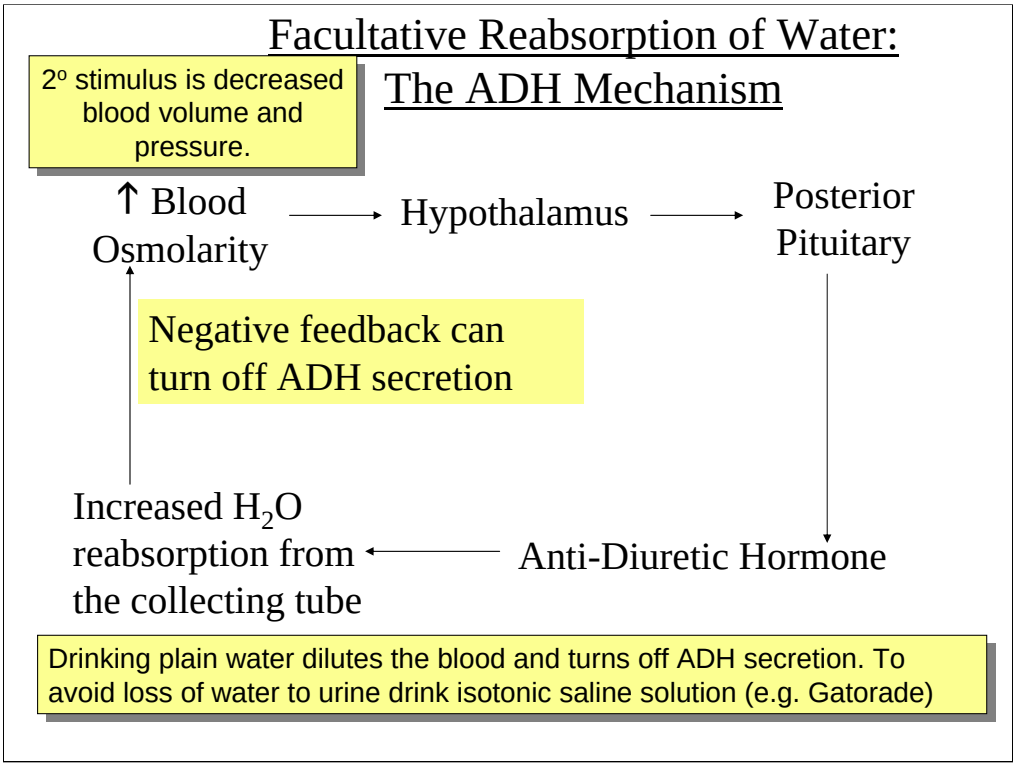
water. This prevents the reabsorbed water from being lost to the urine.




Reabsorption of salt continues into the DCT under the control of the hormone aldosterone. Aldosterone is one of a group of hormones from the adrenal cortex called mineralcorticoids which regulate salt levels in the body.




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.




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**.**

## Step 3: Secretion

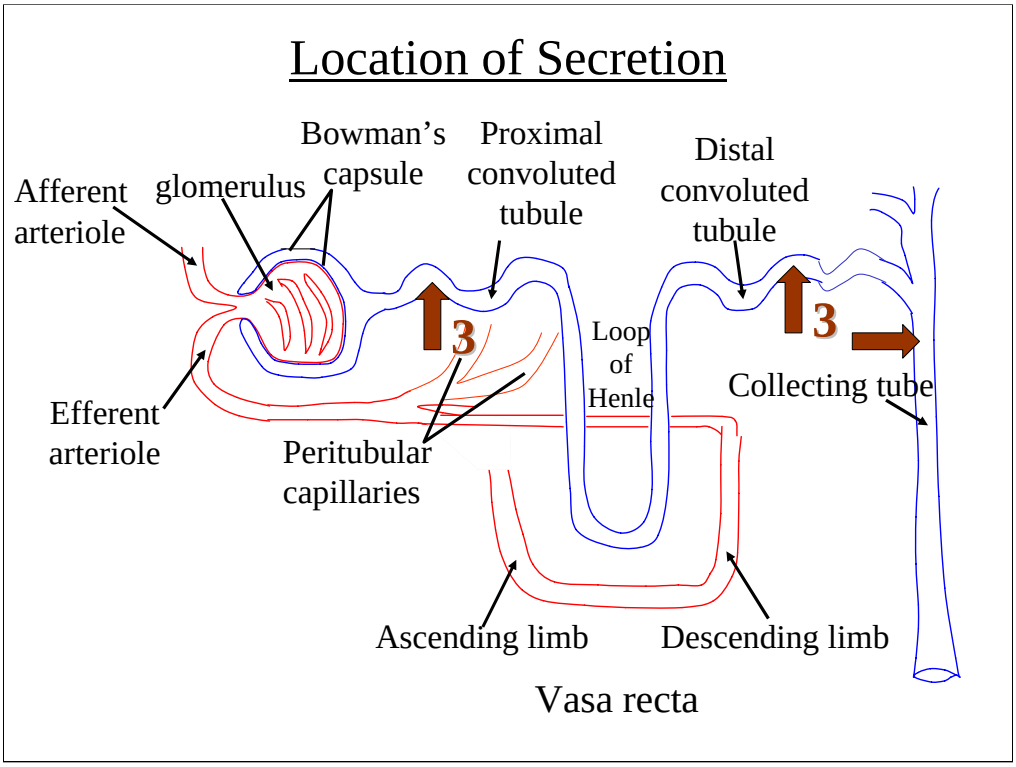
Secretion is the active release of substances into the nephron tubule by the tubular lining cells.

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 bee 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.




Secretion occurs as an active transport by the cells of the nephron tubule in which they transport substances

obtained from the peritubular blood or interstitial fluid into the nephron tubule. It occurs in the proximal

convoluted tubule, distal convoluted tubule, and collecting tubule.

## Secreted Substances

Secretion is the active release of substances into the nephron tubule by the tubular lining cells.

Toxins and drug residues.

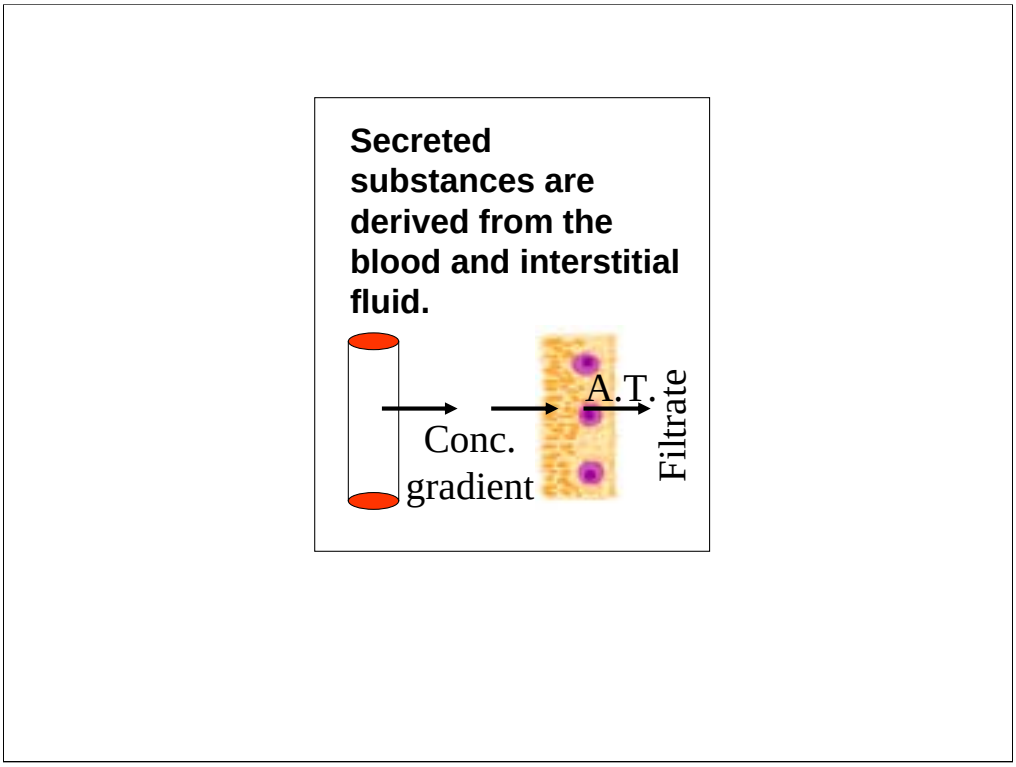
Electrolyte balance: $K^+$ exchanged for $Na^+$

Acid-base balance: $H^+$ , $NH_4^+$
$Cl^-$ exchanged for $HCO_3^-$

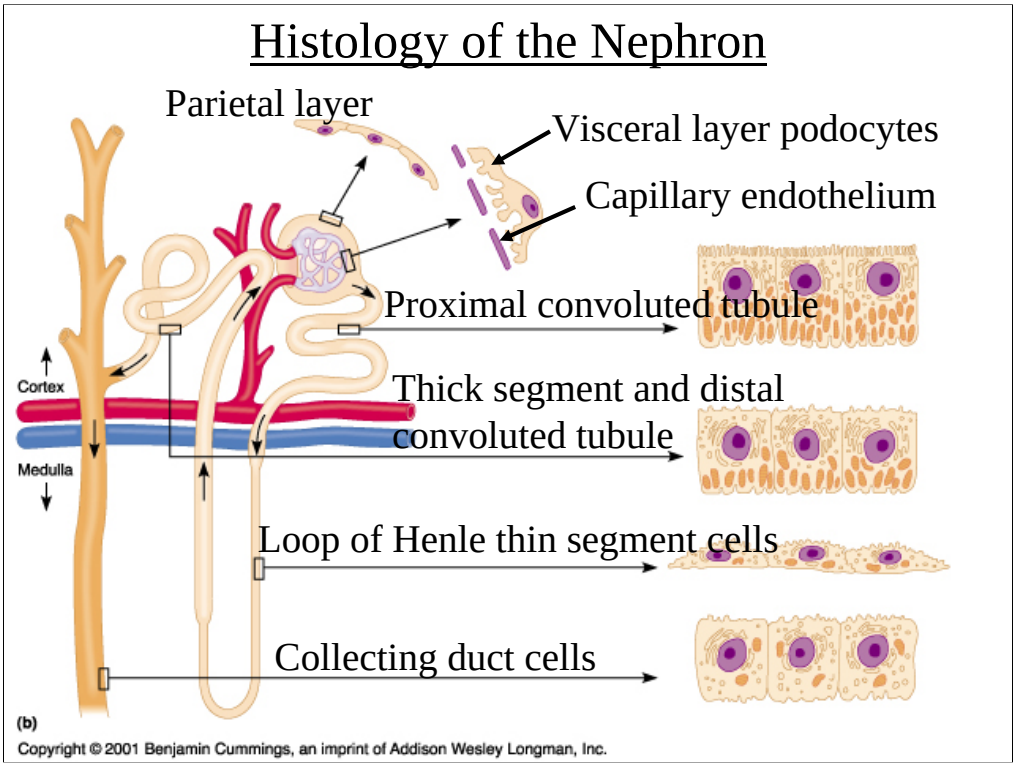
**$H^+$ are obtained from reaction of $CO_2$ and water. Bicarbonate ions are always kept in exchange for chloride.**

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 strongly 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.




Tubular lining cells obtain substances for secretion which have diffused into interstitial fluid from blood in the peritubular capillaries. Secretion is an active process requiring ATP use by the tubular cells.




Proximal tubule cells have abundant mitochondria and microvilli for extensive reabsorption and secretion. Thin

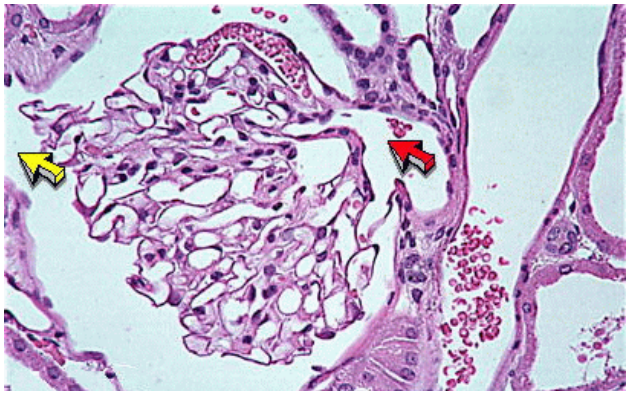
segment cells in descending limb are modified simple squamous epithelium for reabsorption of water by

osmosis. Thick segment ascending limb and DCT cells are similar to PCT but have fewer microvilli and

mitocondria - they also allow secretion and reabsorption but not as much as in PCT. Collecting duct cells are

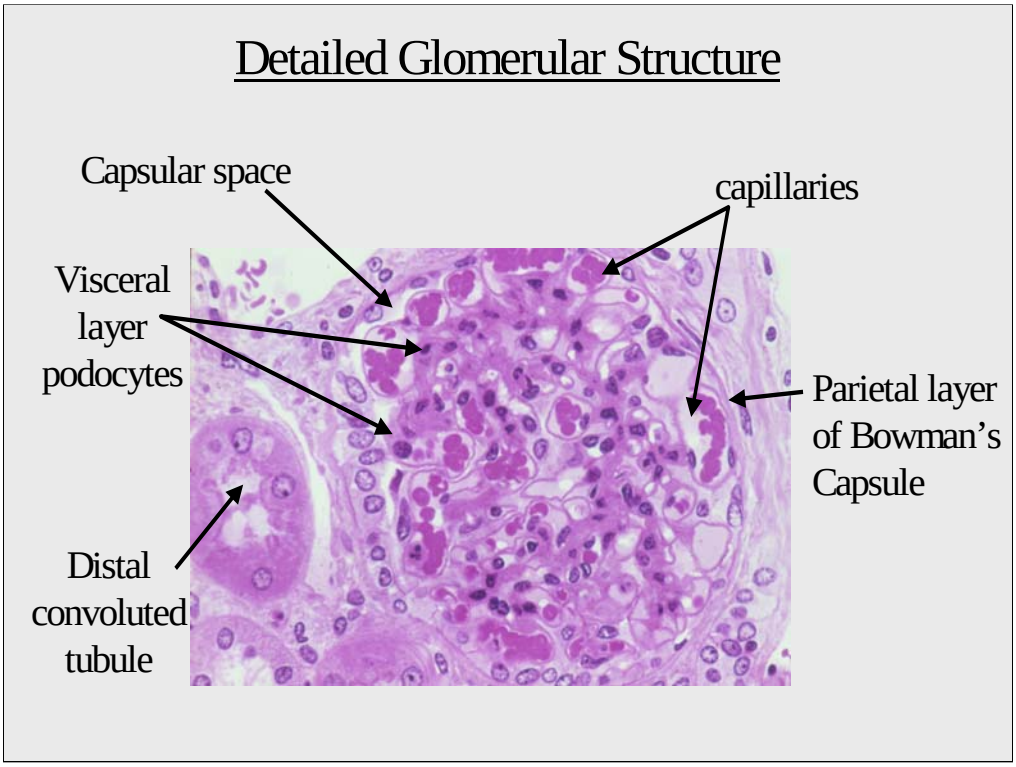
cuboidal and allow minor amounts of secretion and absorption.

## Glomerular Structures



Red indicates the afferent arteriole where it enters the glomerulus at the **vascular pole**. Yellow arrow indicates the opening of the Bowman's capsule into the proximal convoluted tubule.

This is an unusual view of the glomerulus in which the actual **afferent arteriole** can be seen. On the other side of the **glomerulus** is the opening into the **Proximal Convoluted Tubule** (**PCT**). Also a small section of the **macula densa cells**, mentioned in a later slide, is visible.

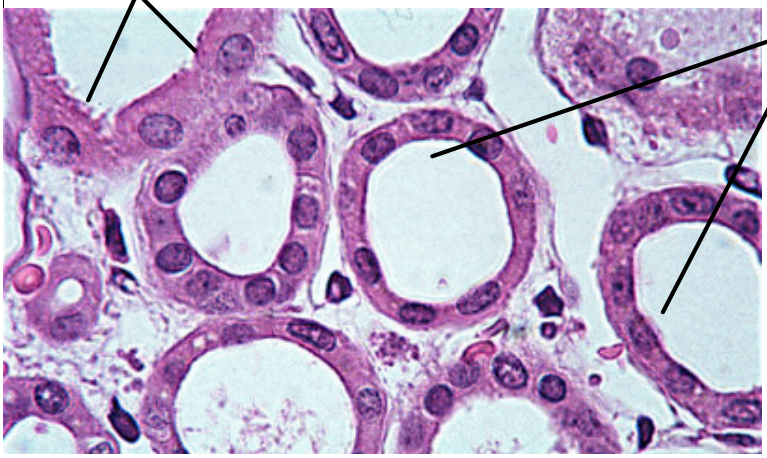



A detailed view of the glomerulus reveals the detailed structure of the capillaries, Bowman's capsule, podocytes, distal tubule and macula densa cells.

## Convoluted Tubules

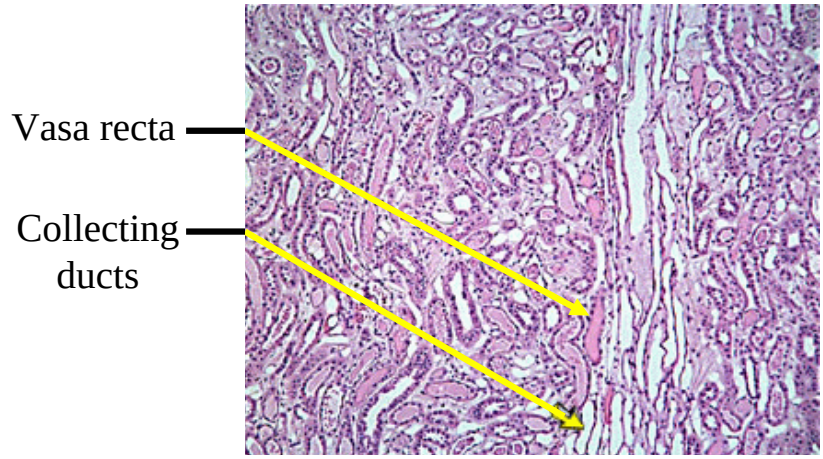
proximal convoluted tubule with brush border

distal convoluted tubule



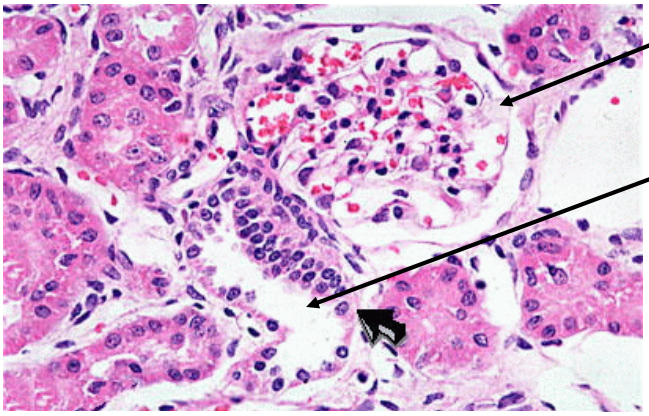
Note the structural difference between the cells of the proximal and distal tubules. Proximal tubule cells are much more active in reabsorption and secretion and are thicker and with brush border (microvilli) for surface area. Distal cells are less active and are therefore thinner.

## Renal Medulla




In the medulla, the collecting tubes (ducts) and loops of Henle run parallel with one another as they travel through the pyramids. Therefore these tubules appear elongated when compared with those in the cortex. Also seen in the medulla are the blood vessels of the vasa recta which surround the long loops of Henle from the juxtamedullary nephrons.

## The Macula Densa




The macula densa (black) monitors the distal tubular fluid salt concentration so that the juxtaglomerular apparatus can control the filtration rate (via tubuloglomerular feedback).

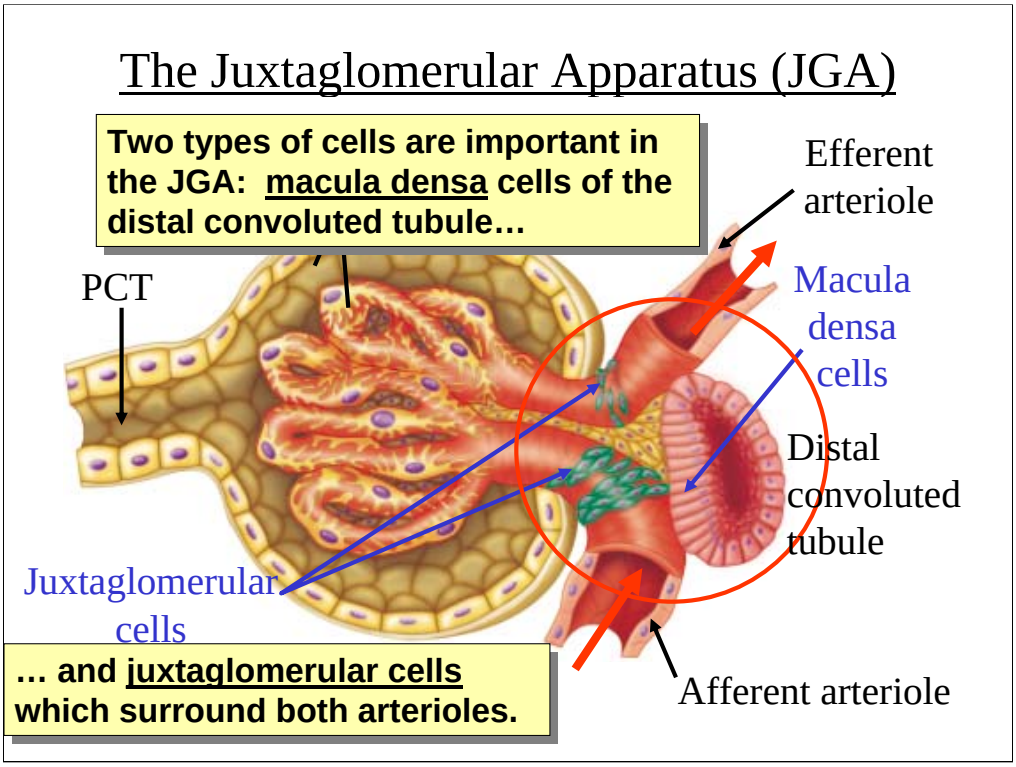
The **macula densa** is a group of cells which are part of the distal convoluted tubule where it comes into contact with the glomerulus at the **juxta-glomerular apparatus**.

# Autoregulation:

(a.k.a. tubuloglomerular feedback)

Autoregulation of Glomerular Pressure and GFR – mechanisms centered in the juxtaglomerular apparatus which act to maintain normal glomerular filtration rate and glomerular blood pressure.

The juxtaglomerular apparatus is a site where the distal convoluted tubule, afferent arteriole, and efferent arteriole of the nephron contact one another.



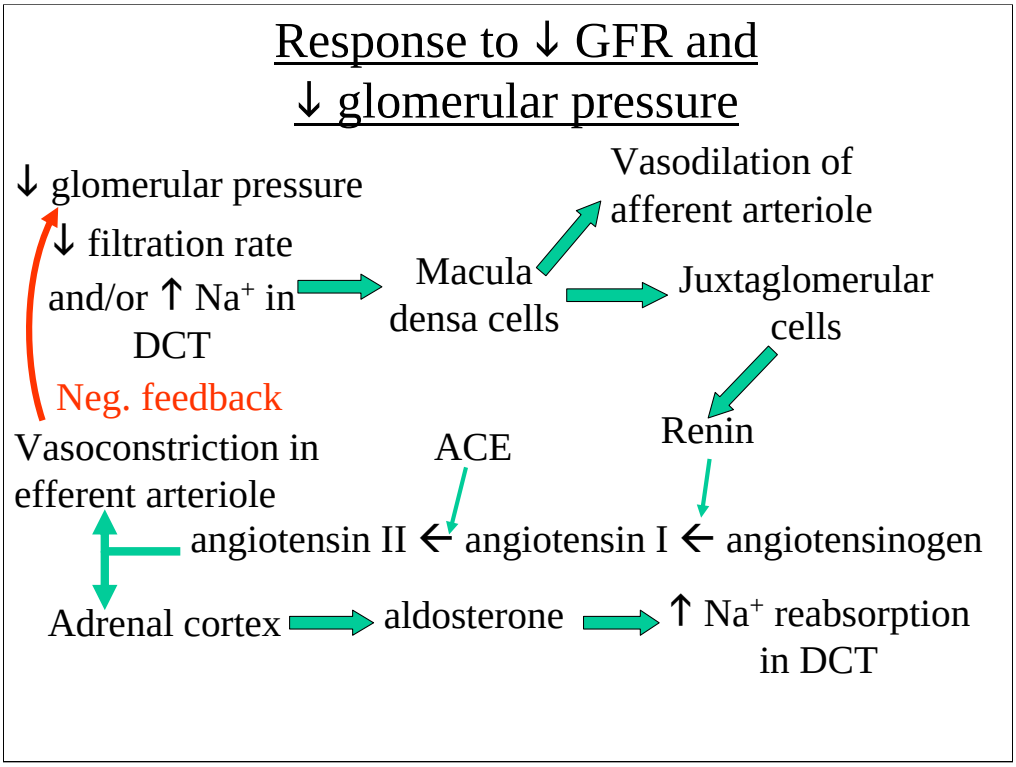

The juxtaglomerular apparatus is a place where the distal convoluted tubule lies close to the glomerulus and to the afferent and efferent arterioles. Within the JGA is a group of cells lining the distal tubule called the **macula densa** cells. These cells monitor the rate of filtrate flow in the distal tubule, which is directly related to the glomerular filtration rate (GFR) and the glomerular pressure.

# Functions of the JGA Cells:

Macula densa cells sense the glomerular filtration rate via the salt ($Na^+$) concentration in the distal tubule.

Juxtaglomerular cells secrete renin into the blood of the arterioles. They are modified smooth muscle cells which can also vasoconstrict or vasodilate.

Macula densa cells basically sense the salt ($Na^+$) levels in the DCT. Increased salt levels can mean the body is losing excess sodium. They can also reflect reduced glomerular filtration rate.




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 and 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.

ACE = angiotensin converting enzyme. Some antihypertensive drugs use ACE inhibitors to block production of

angiotensin II. Angiotensin II causes general peripheral vasoconstriction, increasing overall blood pressure.

Reabsorption counteracts the original stimulus and increases overall blood pressure due to water

reabsorption.

## Response to ↑ Glomerular Pressure

Myogenic response: high glomerular pressure in the afferent arteriole causes the juxtaglomerular cells, which are modified smooth muscle cells, to constrict, reducing blood flow into the glomerulus.

**General vasoconstriction raises peripheral blood pressure, but local vasoconstriction reduces blood flow and pressure to the tissue.**

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.

## Effect of Sympathetic N.S. on the Kidney

Sympathetic stimulation causes vasoconstriction in arteries leading into the kidneys and in afferent arterioles, reducing glomerular pressure and reducing kidney function.

The sympathetic nervous system reduces blood flow to the kidney and GI tract during exercise. This significantly shuts down blood flow, and over time can result in significant build up of wastes in the plasma.

## Renal Connection to the Heart and Circulation

Rt. Atrium and other stretch receptors:

↑↑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 excessively 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.

We discussed the importance of pressoreceptors in the right atrium in cardiac control. But these receptors also respond to excessive high or low pressure and act through the kidneys to help regulate it.

# Normal Constituents of Urine

Water (sp. Gravity 1.001 to 1.035),

urea, **Nitrogenous waste from deamination.**

uric acid, **Waste from purine metabolism**

creatinine, **Released during anaerobic muscle activity.**

$Na^{+}$, $K^{+}$, $PO_4^{-3}$, $SO_4^{-2}$, $Ca^{+2}$, $Mg^{+2}$

Urine has a specific gravity slightly higher than pure water due to the solutes. Urea and uric acid are nitrogenous wastes which have been put into the blood by the liver. Creatinine is a combination of two creatine molecules, released from skeletal muscle during exercise. The other electrolytes are normal and vary in amount.

## Abnormal Constituents of Urine

Glucose - Recent intake of sugary foods, diabetes m.

Protein - Physical exertion, high protein;
hypertension, glomerulonephritis.

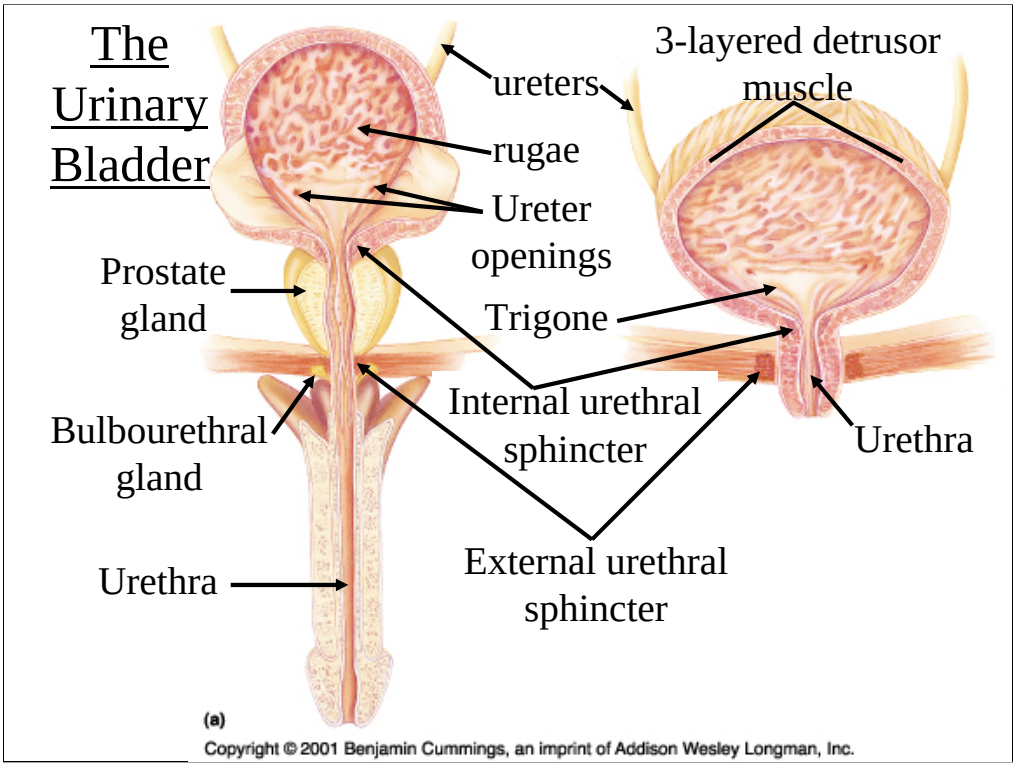
Ketone bodies - Starvation, untreated diabetes mellitus

Hemoglobin - Hemolytic anemia, severe burns

Bile pigments - Hepatitis, cirrhosis, bile obstruction

Erythrocytes - Bleeding due to trauma, kidney stones, infection, cancer.

Leucocytes - Urinary tract infection




The **bladder** and the **ureters** are lined by **transitional epithelium** in order to stretch. The bladder stretches to accommodate an increase in volume, the ureters stretch of absorb any back pressure created when the **detrusor** muscle contracts. The detrusor muscle is a 3-layered muscle, whose layers are in reverse order to those of the stomach. This muscle contracts to produce bladder compression during **micturition**.

Two urethral sphincters regulate urine flow into the urethra: the **internal urethral sphincter** is **involuntary**, and relaxes when fullness is experienced. The **external urethral sphincter** is **voluntary**, and relaxes with voluntary stimuli from the cerebral cortex.

The **trigone** funnels urine out through the **urethra**, and partially closes the ureteral openings into the bladder.

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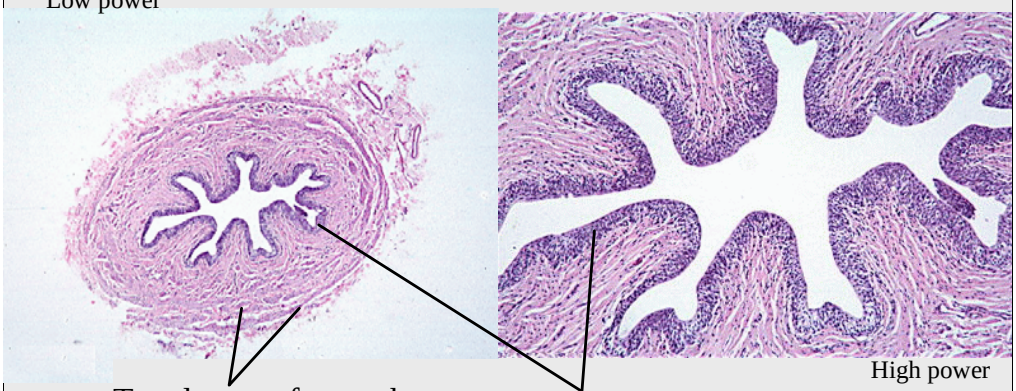
# The Ureters

Low power



High power

Two layers of smooth muscle (three near the bladder) move urine by peristalsis.

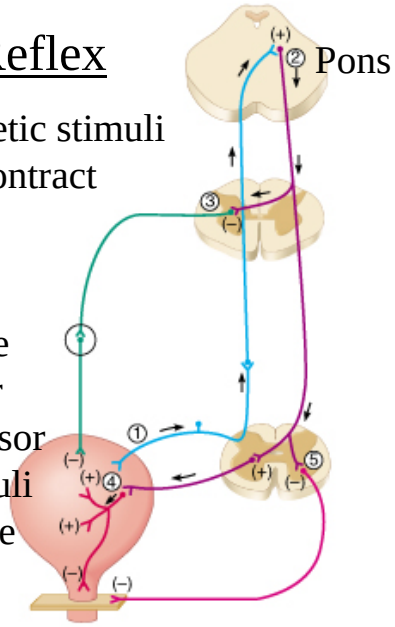
Mucosa of transitional epithelium allows expansion and damping of pressure.

Transitional epithelial lining allows both the bladder and ureter to stretch.

## Micturition Reflex

When not urinating, sympathetic stimuli inhibit detrusor muscle and contract sphincters.

When pressure ↑ in bladder sensory stimuli cause reflexive inhibition of internal sphincter and mild contractions of detrusor muscle. Parasympathetic stimuli inhibit sphincters and stimulate detrusor muscle.




(b)



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.