# **THE EXCRETORY SYSTEM**

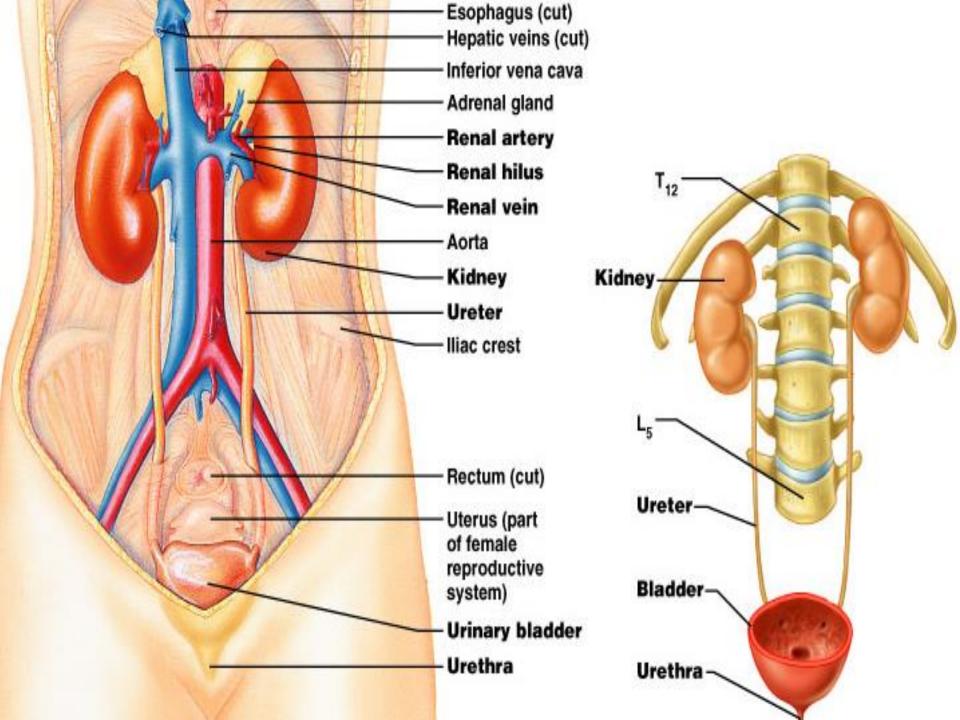
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2<sup>nd</sup> stage

PHYSIOLOGY #II University of Basra

## Urinary system <u>Overview</u>

- The urinary system consists of two kidneys, a single midline urinary bladder, two ureters which carry the urine from the kidney to the urinary bladder and a single urethra which carries the urine from the bladder to the outside of the body.
- The kidneys make up the main purification system of the body. They control the composition of the blood by removing the waste products and conserving the useful substances.
- The kidneys are the major excretory organ among other excretory organs of the body :skin ,liver, lungs and intestine.



# Functions of the kidneys Excretory functions

- Kidneys <u>filter</u> blood producing large volume of large molecules (proteins, RBCs)are retained in the blood, small molecules and ions enter the filtrate.(produce filtrate)
- Most of filtrate volume is <u>reabsorbed</u> back into the blood.
- Metabolic waste, toxic materials and excess ions remain in a small volume of filtrate.
- Additional waste products are <u>secreted</u> into the filtrate resulting <u>urine formation</u>.

## **Regulatory function**

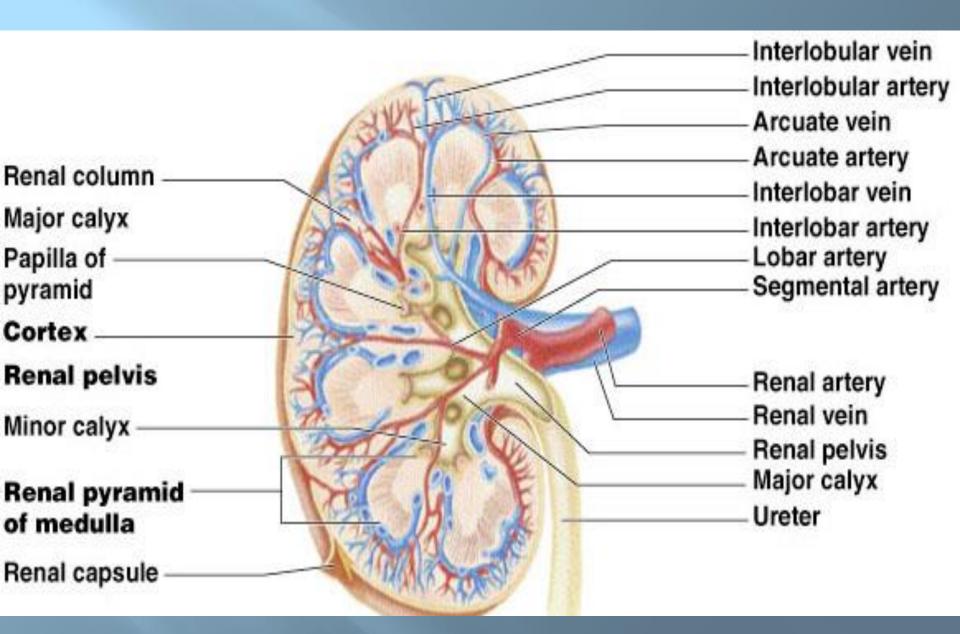
- Regulation of blood volume and pressure by controlling the extracellular fluid volume (ECF) in the body by producing either a large volume of diluted urine or a small volume of concentrated urine.
- Regulation of concentration of solutes in the blood by regulation of concentration of major ions (Na<sup>+</sup>,Cl<sup>-</sup>,HCO3<sup>-</sup>,HPO4<sup>2-</sup>).
- Regulation of PH of ECF by secreting variable amounts of H<sup>+</sup>.
- Regulation the synthesis of RBCs by secreting of erythropoietin hormone.
- Vitamin D synthesis, therefore regulates Ca2+ blood level.

### **Structural considerations**

- The kidneys are paired of bean shaped organs that lie behind peritoneal lining of the abdominal cavity.
- Each kidney is surrounded by a thin capsule to resist stretch and limit the swelling.
- \* The renal artery ,renal vein ,renal lymphatics and ureter enter and leave the kidney through a **helium** on the midline concave surface of the kidney.

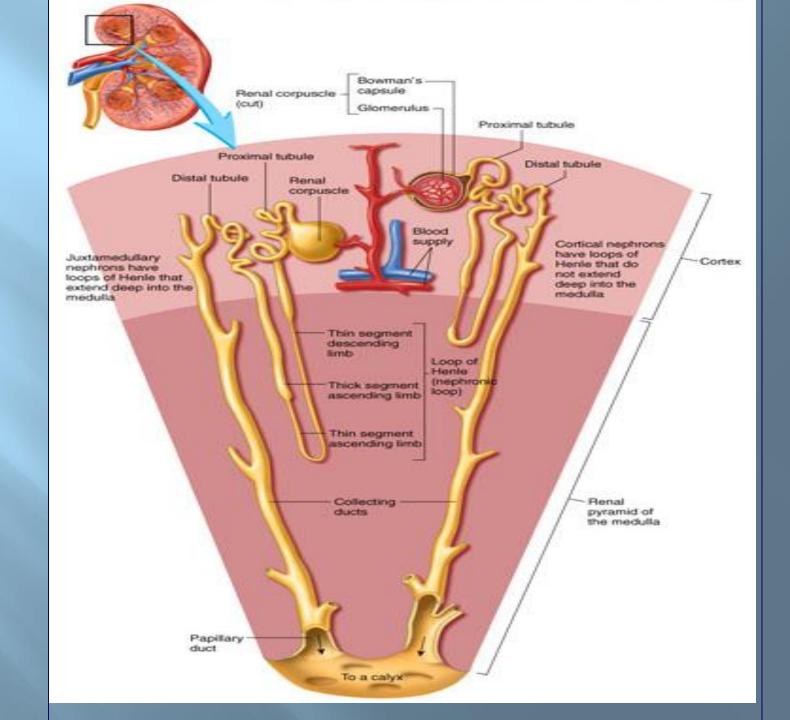
### **Internal structure of the kidneys**

- \* There are two distinguished layers inside the longitudinal section of the kidney .The outer layer the **cortex** and the inner layer the **medulla**.
- \* The medulla is made up of series of cone shape **pyramids** which project to the **minor calyces**.
- Minor calyces open into major calyces which open into renal pelvis.
- \* The renal pelvis leads to the ureter which drains into the bladder.



## **Structure of the nephron**

- The functional unit of the kidney is the **nephron** (where the blood is filtrated)
- Nepheron is blind end tubules running from the Bowman's capsule into the renal pelvis.
- There are about one million nephron in each kidney .
- The nephron begins at the glomerulus (comprises a tuft of glomerular capillaries with the Bowman's capsule
- The capillaries are derived from the **afferent arterioles** and drain into the **efferent arterioles**.
- Many branches of capillaries form cluster that invaginates into the Bowman's capsule
- \* The glomerulus and the Bowman's capsule form the **renal corpuscle.**



- The materials leave the blood in the glomerulus and enter the Bowman,s capsule through the filtration membrane.
- Fluids from Bowman,s capsule flows into the coiled segment (proximal convoluted tubule), then into loop of Henle, down into the medulla.

# There are two types of nephrons:

## **1-Cortical nephrons :**

- The glomeruli are in the two thirds of the cortex.
- Short loop of Henle ,that dip into the outer medulla.
- **2-Juxtamedullary nephrons**
- **Glomeruli in the inner cortex.**
- Long loop of Henle extends deeply into the medulla
- Proximal convoluted tubule is about 14 mm long ,60 µm in diameter .It is composed of simple cuboidal epithelial cells ,made up the wall.

- Loops of Henle are continuous of proximal convoluted tubule .Each loop has two limbs : descending and ascending.
  - The ascending limb of loop of Henle leads into a second coil section: **the distal convoluted tubule.**
- **Distal convoluted tubule** begins at a special structure: the **juxtaglomerular apparatus**.
- **Collecting duct: The** cells of collecting duct have some microvilli and numerous mitochondria. The absorb Na<sup>+</sup> , K<sup>+</sup> and Cl<sup>-</sup> actively.

## Juxtaglomerular apparatus.

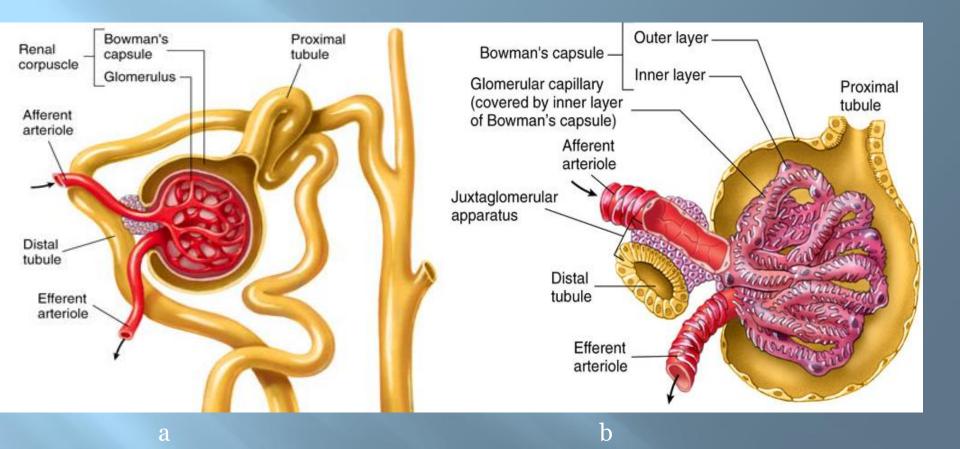
- The tubule passes between the afferent arteriole that supplies blood to the glomerulus and the efferent arteriole that drains it. This short section of the tubular cells is known as macula densa
- Juxtaglomeruler apparatus secretes enzyme rennin, and play an important role in the regulation of filtrate formation and blood pressure.
- The distal tubules of several nephrons join to form a **collecting duct** that passes through the medulla to the **papilla**.

#### Juxtaglomerular (JG) cells

- They are modified smooth muscle cells in afferent arteriole wall detect changes in blood pressure (a stretch reflex),
- Secrete enzyme renin to trigger Renin-Angiotensin system if blood pressure falls
- Distal tubule contacts afferent arteriole at renal corpuscle
  Macula Densa (MD) cells
- Special cells in the wall of the distal tubule in this area monitor the osmotic potential in the filtrate in the distal tubule
- They stimulate JG cells to release renin if filtrate is too dilute, indicating insufficient filtration and/or low blood pressure/low blood volume
- Both JG and MD cells work together to regulate blood pressure and blood volume

# **Renin-Angiotensin System**

- Hepatocytes secrete inactive precursor Angiotensinogen into the bloodstream
- Juxtaglomerular (JG) cells secrete the enzyme renin to convert Angiotensinogen to Angiotensin I in the bloodstream
- Angiotensin I is transported to the lungs where Angiotensin Converting Enzyme (ACE) converts Angiotensin I to Angiotensin II
- Both Angiotensin I and Angiotensin II act as circulating hormones to increase blood pressure and blood volume.

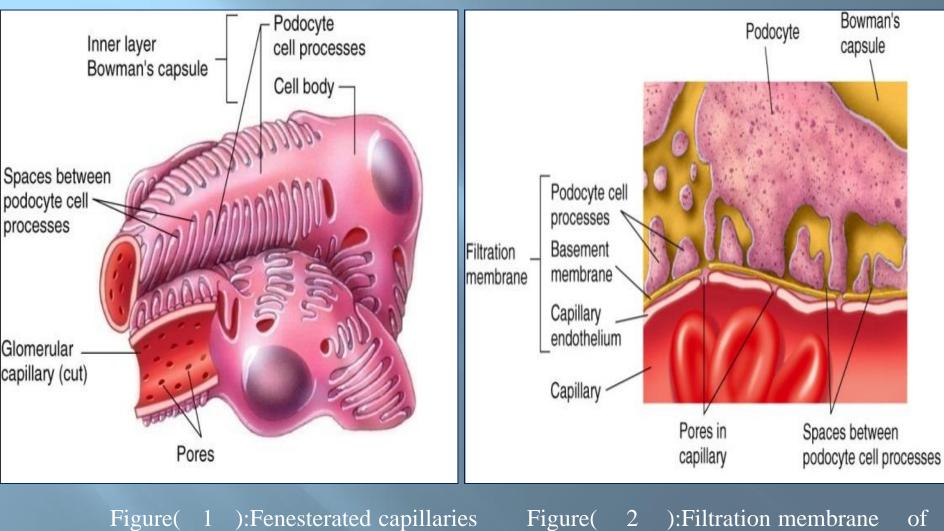


**a:** The renal corpuscle consists of Bowman's capsule and glomerulus, **b:**Bowman,s capsule covers the glomerular capillaries. Juxtaglomerular apparatus consists of cells from the wall of the afferent arteriole and the distal convoluted tubule.

## **Structure of the glomerulus**

# Glomerulus is composed of **fenestratedcapillaries.**

- The filtrated fluid passes from the capillaries into the Bowman,s capsule through the **filtration membrane**.
  - The filtration membrane consists of:
  - 1-Fenestrated glomerular capillary endothelium.
- 2- Basement membrane.
- **3-Podocytes processes**



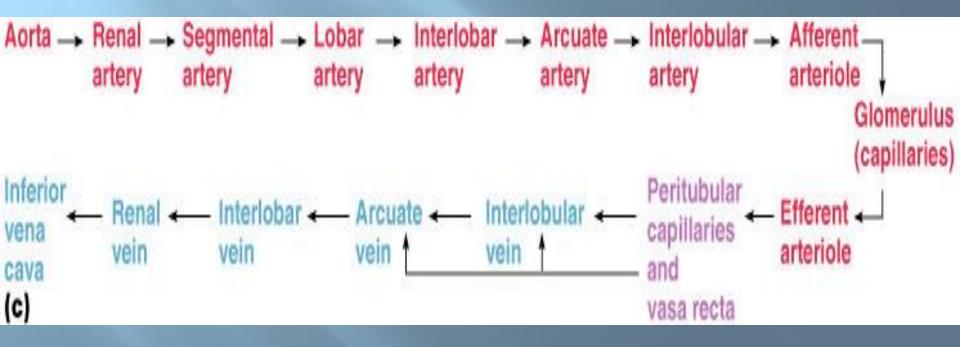
the glomerulus.

### **Renal Blood Supply**

- The **renal artery** enters the kidneys at the **hilum**.
- The renal artery branches to form **interlobar arteries**, which radiate out towards the cortex.
- Interlobar arteries diverge near the base of the pyramid to form **arcuate**.
- Interlobular arteries project from the arcuate.
- Interlobular arteries give rise to the **afferent arterioles** that supply the **glomerular capillaries**.
- **Efferent arterioles** arise from the glomerular capillaries to carry the blood away from the glomeruli.
- When the efferent arteriole exists the glomerulus ,it gives rise to plexus of capillaries, **peritubular capillaries** around the proximal and distal tubules.

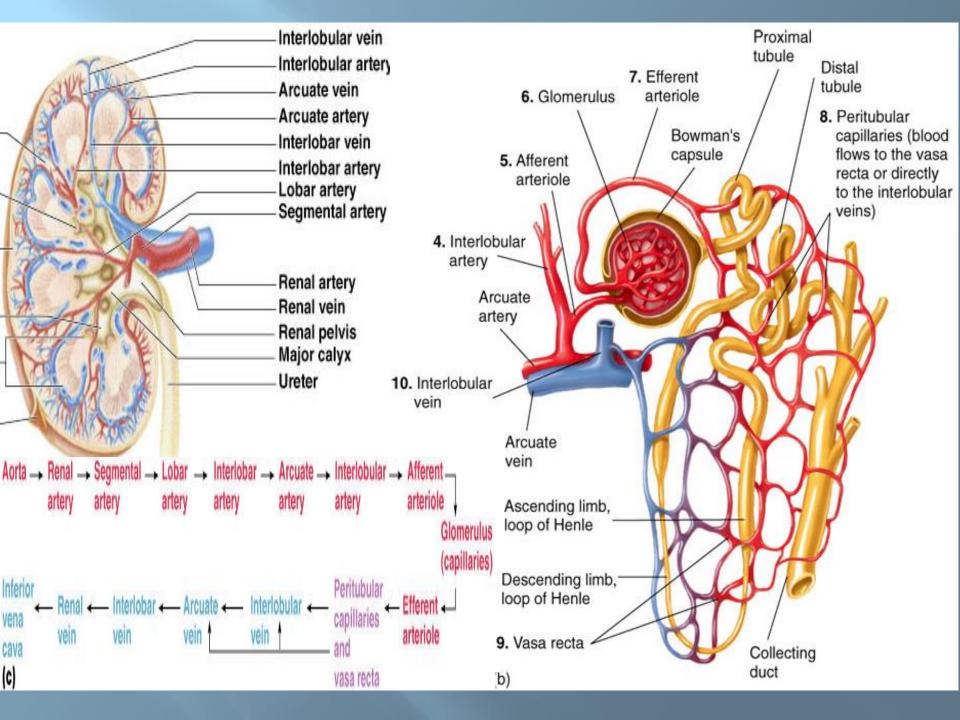
- The efferent arteriole leaving the renal corpuscle enters the **peritubular capillaries** in the cortex (surrounding the proximal and distal tubules), which then flow in to the **vasa recta** capillaries in the medulla (around the loop of Henle and collecting ducts).
- Because of their arrangement ,the vasa recta perform differently from the peritubular capillaries

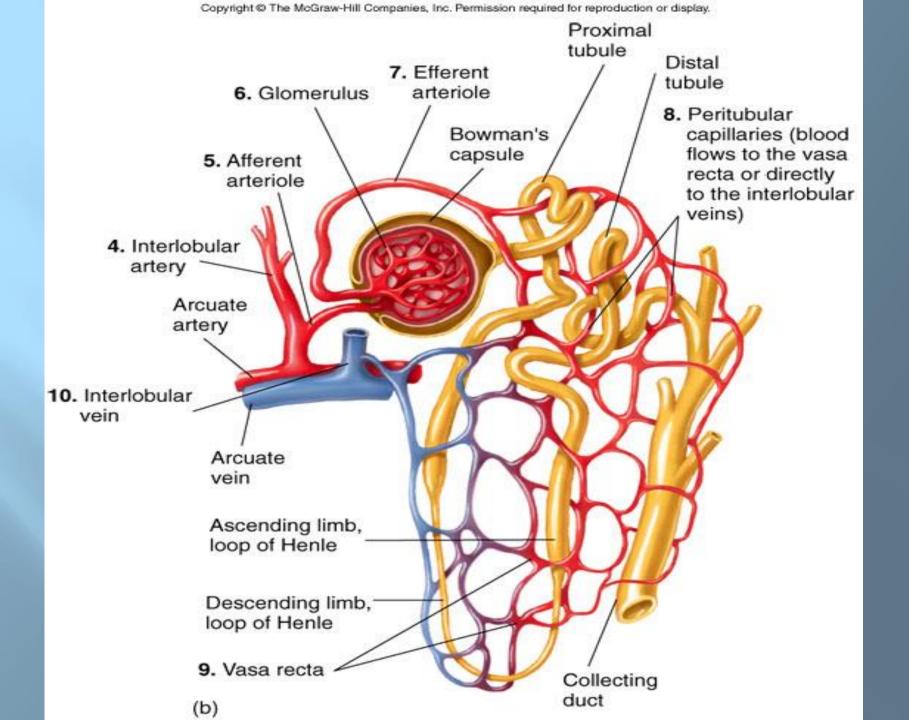
**Vasa recta** is a specialized part of the peritubular capillaries course into the medulla along the loop of Henele of the juxtamedullary nephrons, then back toward the cortex. **Veins form from peritubular capillaries are:** interlobular veins to arcuate vein to interlobar vein to renal vein.



# **Renal nerve supply**

 The kidney has rich sympathetic nonadrenergic innervations which supply renal artery and its branches, juxtaglomerular apparatus and renal tubules.





## **Urine formation**

Three major processes are essential for urine formation: *Filtration*, *tbular reabsorption and tubular secretion* 

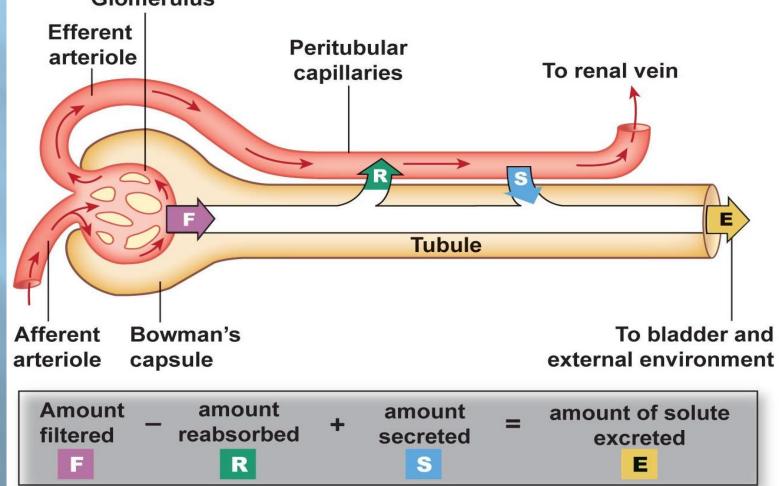
### Filtration

Filtration is the movement of water and small solutes from blood flowing through the glomerulus across the filtration membrane as a result of pressure differences into the Bowman's capsule forming the **filtrate**.

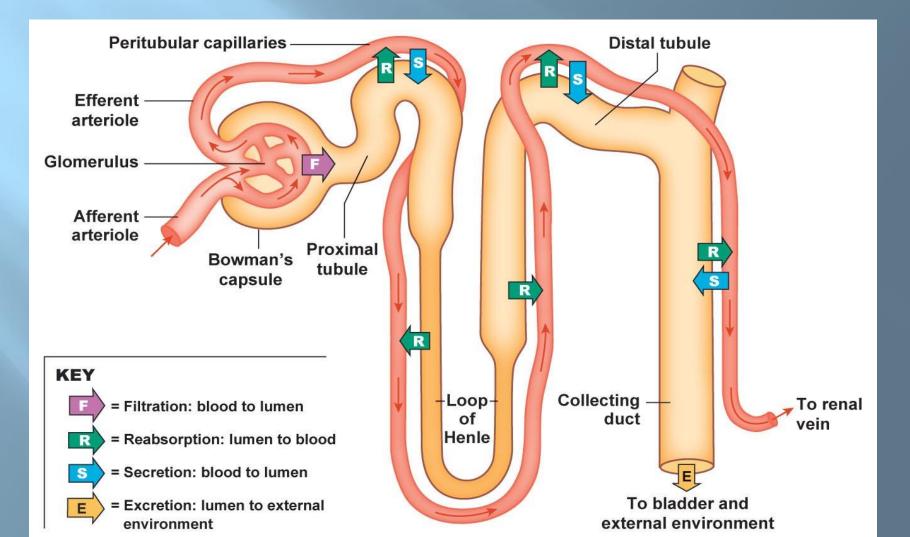
Most substances in the plasma (except for proteins) are freely filtrated ,so their concentrations in the glomerular filtrate in the Bowman's capsule is the same in the plasma.

- **Glomerular Filtration**
- **Tubular Reabsorption**
- **Tubular Secretion**





# Locations for filtration, reabsorption, secretion & excretion



- Glomerular filtration first step in urine formation
  - forcing of fluids and dissolved solutes through membrane by hydrostatic pressure
  - same process as in systemic capillaries
  - results in a filtrate
  - 180 L/day, about 60 times plasma volume
  - **178-179** L/day is reabsorbed (~99%)

# **Glomerular Filtration**

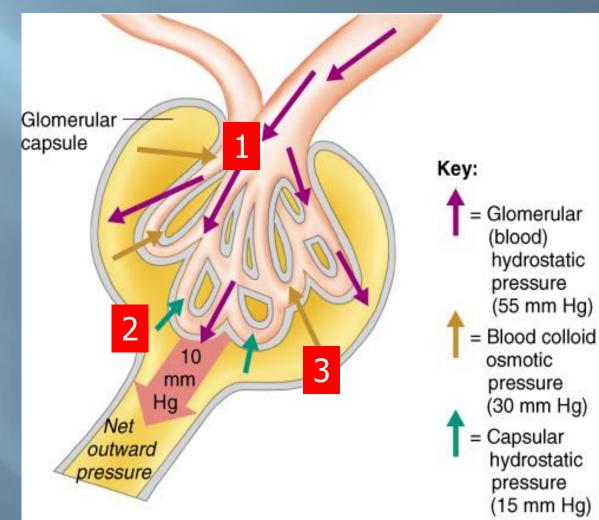
- 3 structural features of the renal corpuscles enhance their filtering capacity:
  - 1) Glomerular capillaries are relatively long which increases their surface area for filtration
  - 2) Filter (endothelium-capsular membrane) is thin and porous
    - Fenestrated glomerular capillaries are 50 times more permeable than regular capillaries
    - > The filtration slits of the basement membrane only permit passage of small molecules
  - 3) Glomerular Capillary blood pressure is high the efferent arteriole diameter is less than the afferent arteriole diameter -- increasing filtration pressure in the renal corpuscle

# **Glomerular Filtration**

Net filtration pressure (NFP) depends on 3 pressures:

- glomerular blood hydrostatic
   pressure (GBHP)
- 2) capsular hydrostatic pressure (CHP)
- 3) blood colloidosmotic pressure(BCOP)

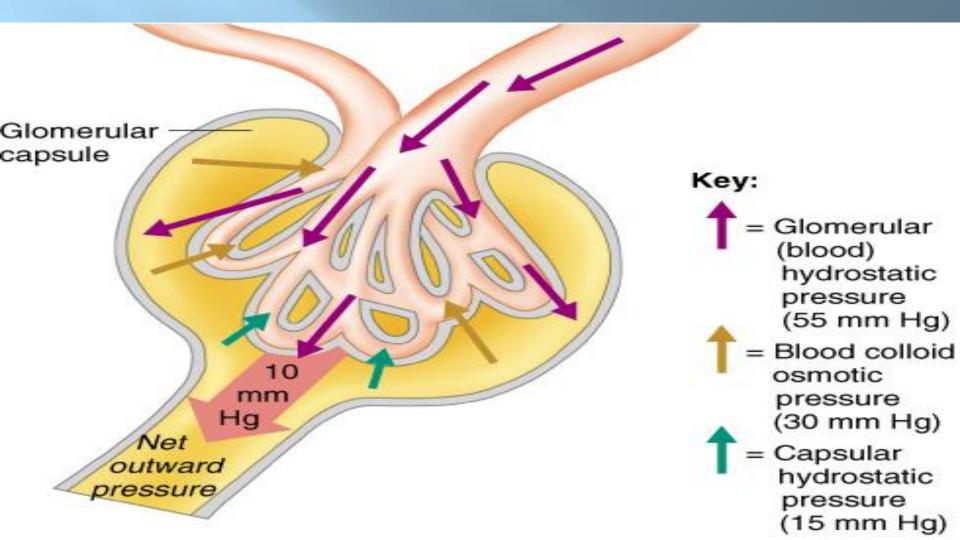
NFP = GBHP - CHP - BCOP10 = 55 - 15 - 30



- Occurs in the glomerulus due to
- Filtration membrane &Net filtration
   pressure (NFP) which depends on 3
   pressures:
  - 1) glomerular blood hydrostatic pressure (GBHP)
  - 2) capsular hydrostatic pressure (CHP)
  - 3) blood colloid osmotic pressure (BCOP)

NFP = GBHP - CHP - BCOP10 = 55 - 15 - 30

# NFP = GBHP - CHP - BCOP10 = 55 - 15 - 30



### **Glomerular blood flow**

The part of the total cardiac output that passes through the kidney is called **renal fraction**.

The normal cardiac output is 5600ml/min, while the renal fraction is 1200 ml/min which represents 21% and varies from 12-30%.

### **Glomerular filtrate**

Glomerular filtrate is the fluid filtrated through the glomerular membrane into Bowman's capsule.
Filtration membrane is composed of three layers ,each of these layer is several hundred times as permeable as the capillary membrane ,which accounts for the volume of the glomerular filtrate formed each minute ,but still of high degree of selectivity for the size of passing molecules.

# The permeability of the G. membrane to substances of different molecular weights =

Concentration of dissolved substance on the filtrate side of the membrane

Its concentration on the plasma side

The reasons for the **high selectivity** of the glomerular membrane are :

1-Size of the pores in the glomerular membrane is large enough to pass molecules with diameter 8 nanometers.

**2-Electrical charges** of the molecules .The pores are lined by glycosylated proteins which have strong negative electrical charges.

Glomerular filtrate has the same components of the plasma except it has no significant amount of proteins. The glomerular filtration rate(GFR)

The glomerular filtration rate (GFR) is the quantity of glomerular filtrate formed each minute in all nephrons of both kidneys. It is 125ml/min in normal person.

Glomerular filtrate formed each day is 180 Lit/day; over 99% of the glomerular filtrate is reabsorbed in the tubules, while remaining is passing into the urine.

Normal plasma flow through the kidney is 650 ml /min and GFR of both kidneys is 125ml/min, so the average filtration fraction is 19%. **Factors that affect the GFR** 

#### GFR= Filtration pressure x Kf

- The factors that determine the filtration pressure (glomerular pressure ,plasma colloid osmotic pressure and Bowman's capsule pressure) will determine the GFR.
- The conditions that affect these pressures and therefore affect the GFR are:
- **Renal blood flow**: an increase in the rate of blood flow through the nephrons increases the GFR by increasing the glomerular pressure which enhances the filtration process.
- Afferent arteriolar constriction decreases the rate of blood flow into the glomerulus and also decreases the glomerular pressure causing a decrease in the filtration rate.
- **Efferent arteriolar constriction** causes an increase in the resistance to outflow from the glomeruli .This increases the glomerular pressure and increase in efferent resistance causes slight increase in the GFR.

- Sympathetic stimulation of the kidneys causes the afferent arterioles to constrict, thereby decreasing the GFR.
- With strong sympathetic stimulation, glomerular blood flow and glomerular pressure are reduced so that glomerular filtration decreases to only a few percent of normal and the urinary output can fall to zero for as long as 5 to 10 minutes.
- Arterial pressure
- When the arterial pressure rises, afferent arteriolar constriction occurs automatically .This prevents a significant rise in glomerular pressure despite the rise in the arterial pressure. Therefore, the GFR increases only few percent even when the mean arterial pressure rises to 150 mmHg. This phenomenon is called autoregulation.
- An increase in arterial pressure can greatly increase the urinary output even though it affects GFR slightly.

#### Reabsorption and secretion in the tubules

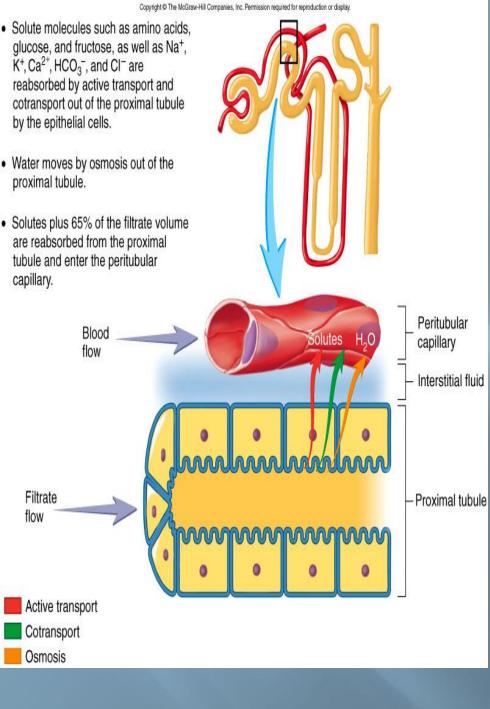
- The filtrate entering the nephrons flows through the following tubules:
- The proximal tubule
- The loop of Henele
- The distal tubule
- The collecting tubule
- The collecting duct.
- Substances are selectively reabsorbed or secreted by the tubular epithelium.
- Reabsorption plays greater role than does secretion in the formation of urine, but secretion is important in the determining the amounts of K<sup>+</sup> and H<sup>+</sup>.
- The resulting fluid entering the pelvis is urine
- The tubules separate the substances that are to be conserved in the body from those be eliminated in the urine.
- Water in the glomerular filtrate is reabsorbed in about 99% as it passes through the tubules.
- Glucose and amino acids are entirely reabsorbed.

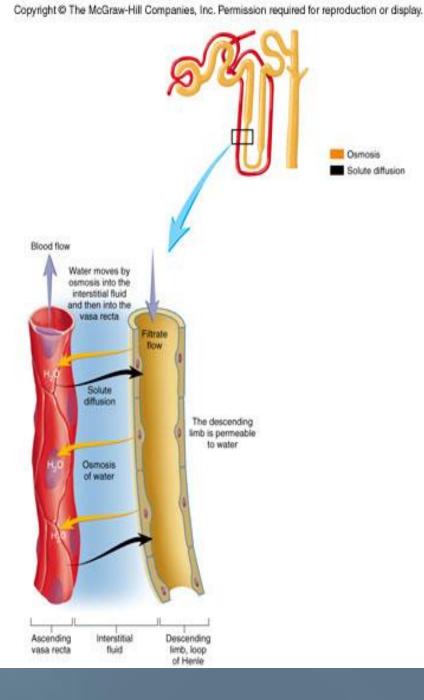
## Reabsorption.The Proximal tubule

Useful substances are reabsorbed by **active transport and cotransport**. Thus the cells of the proximal tubule have microvilli (give a large surface area) and large numbers of mitochondria (ATP for active transport).

■ Separate pumps are found for each of the different types of foods e.g. glucose, fructose, aminoacids, and for different ions e.g. Na<sup>+</sup>, Ca<sup>2+</sup>, HCO<sub>3</sub><sup>-</sup>. Foods are thus normally completely reabsorbed, unless the capability of the pump is exceeded. Thus the maximum reabsorption of glucose produces a blood concentration of 150mg/ 100ml, so if a higher level of glucose enters the kidney (after eating too many sweets), the excess will be excreted in the urine.

- The ionic pumps increase the concentrations of ions outside the nephron and produce a low concentration inside the tubule. This produces an osmotic pressure sucking water out of the tubule into the plasma surrounding the tubule. In this way,
- 65% of the water in the filtrate is reabsorbed by osmosis. The reabsorbed substances are taken up by the peritubular capillaries and so removed from the cortex back in to the blood.
- The filtrate leaving the proximal tubule is isotonic (has the same osmotic pressure as the blood plasma = 300 mOsm). This is because salt and water were removed at the same rate from the filtrate.





#### Loop of Henle

The loop of Henle consists of a descending loop, descending deep in to the medulla, and an ascending loop, returning back towards the cortex. The ascending loop is subdivided into a short section of thin segment and a longer thick segment. The medulla has high concentrations of NaCl + small quantities of urea (that have leaked out of the collecting ducts), so that its osmotic pressure increases from 300 mOsm (near the cortex) to 1200 near the central pelvis. This is because the vasa recta only remove water from the medulla, leaving behind most of the salt (unlike the peritubular capillaries of the cortex).

## Thus water reabsorption occurs in 3 stages:

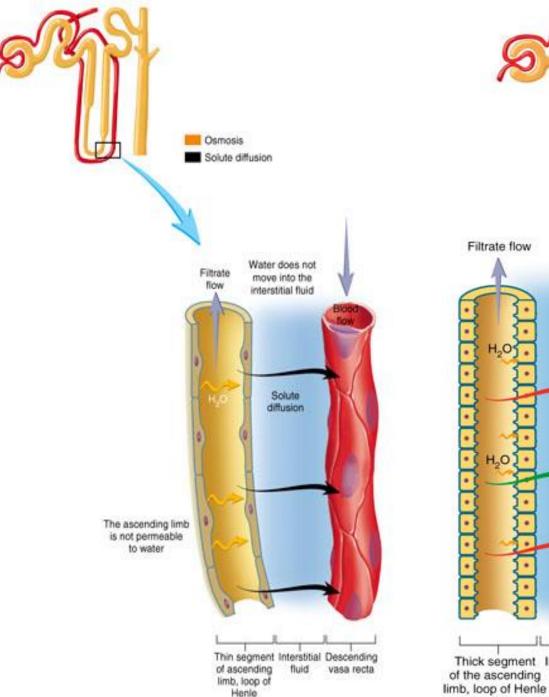
• The **descending loop** has walls permeable to water, but only a very low permeability to salts. As the filtrate descends in to progressively higher and higher OP's, water is sucked out, but only small quantities of salt can diffuse in. By the **bottom** of the loop, the OP of the filtrate has increased to 1200 mOsm. 15% of the water is reabsorbed in the descending loop of **Henle**, so the volume of filtrate is now only 20% of the original.

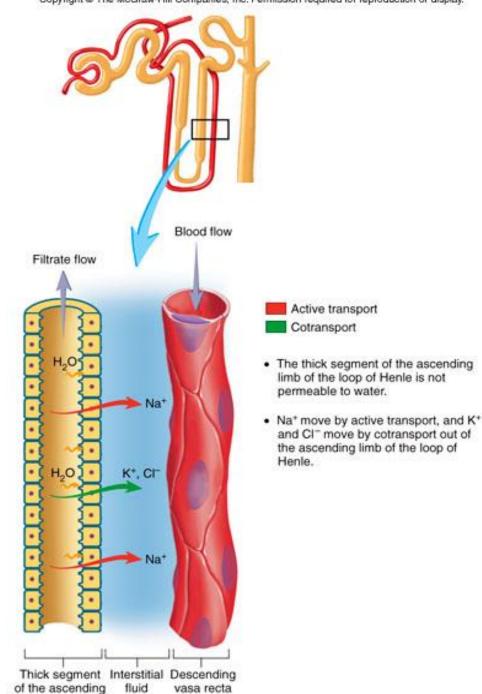
In the thin segment of the ascending loop, the walls are not permeable to water, so as it moves up through progressively lower salt concentrations, some salt will diffuse out, to reduce its OP (but not change its volume).

- In the **thick segment** of the ascending loop, there are Na<sup>+</sup> pumps (like in the proximal tubule). Na<sup>+</sup> is **pumped out**, while Cl<sup>-</sup> follows passively; K<sup>+</sup> also moves out by cotransport. This progressively dilutes the filtrate (water will not be removed because the walls throughout the ascending loop are not permeable). By the **top** of the loop (as the tubule reenters the cortex), the filtrate will now be hypotonic (100 mOsm).
- The descending loop thus loses water (and thus reduces its volume); the ascending loop loses salt (no further change in volume

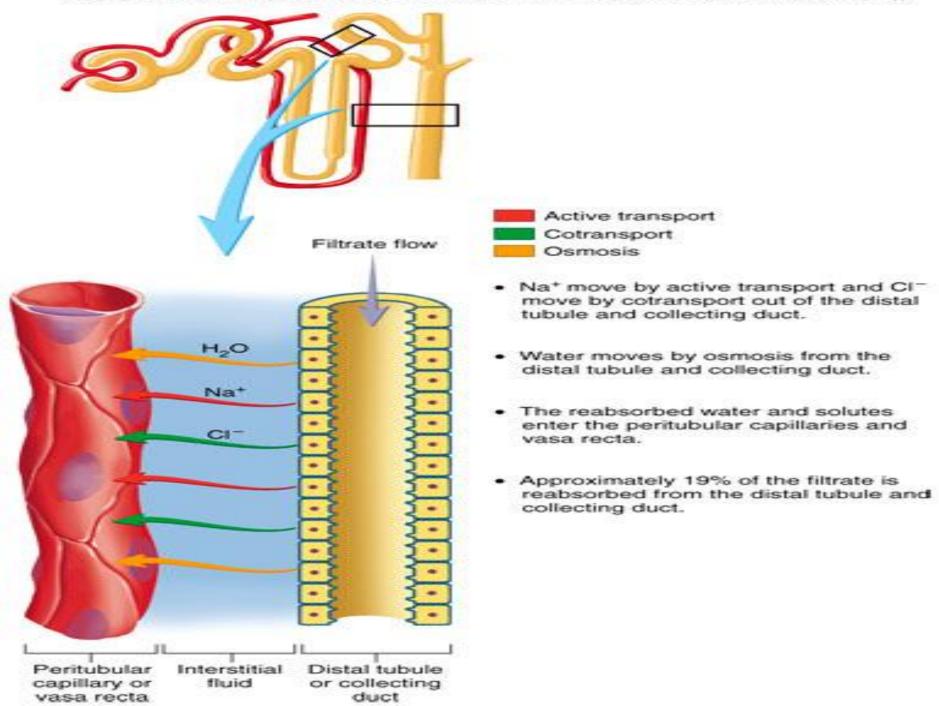
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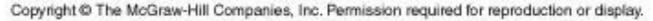


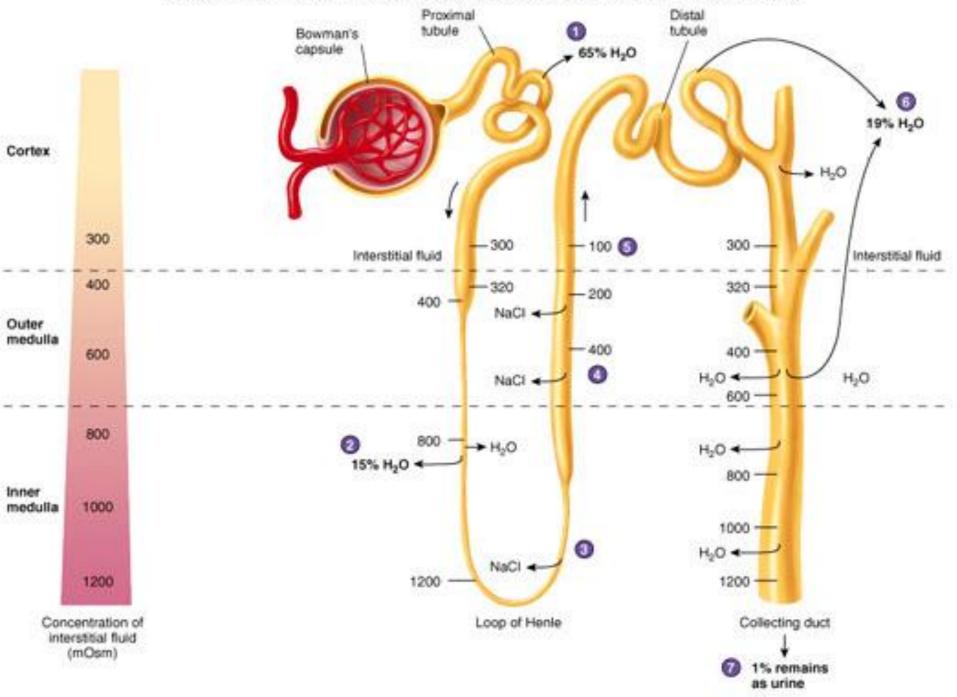
#### Distal tubule.

Because the OP of the filtrate is now less than the surrounding plasma, some water will diffuse out (and some salt diffuse in) to return the OP to 300 mOsm. However, aldosterone can act in this section (and the collecting duct) by activating Na<sup>+</sup>/K<sup>+</sup> pumps (so Na<sup>+</sup> out, but K<sup>+</sup> in - unlike loop of Henle)

#### Collecting duct.

The **collecting duct** re-enters the medulla, but this time passes right through the medulla. As it passes through the deepest layers of the medulla, which have the very highest concentrations of NaCl, the maximum reabsorption of water by osmosis will occur (raising the OP of the filtrate to over **1200 mOsm**). A further **19%** of the filtrate may be reabsorbed, leaving just 1% of the original remaining. However, the permeability to water of the collecting duct walls is controlled by the hormone **ADH**.





## **Active secretion.**

The distal tubule secretes **toxins** in to the tubule by **active transport**. These include **H**<sup>+</sup> (which interferes with respiration and enzyme activity), K<sup>+</sup> (nerve conduction requires a low conc of K<sup>+</sup> in the plasma), **histamine** (acts locally in the body, so should then be removed), creatinine, etc. In addition, some toxins, such as **ammonia** (produced by the breakdown of aminoacids), will passively diffuse into the tubule.

## **Control of urine production.**

- Your body needs to control:
- Your blood volume = reduce water loss when dehydrated; increase loss when over-hydrated. This is mainly due to ADH and to aldosterone/ ANH, but is affected by blood pressure (through ultrafiltration).
- The amount of salts in the blood and therefore lost in the urine e.g. Na<sup>+</sup>, K<sup>+</sup>. This is mainly controlled by aldosterone and ANH.

#### ADH

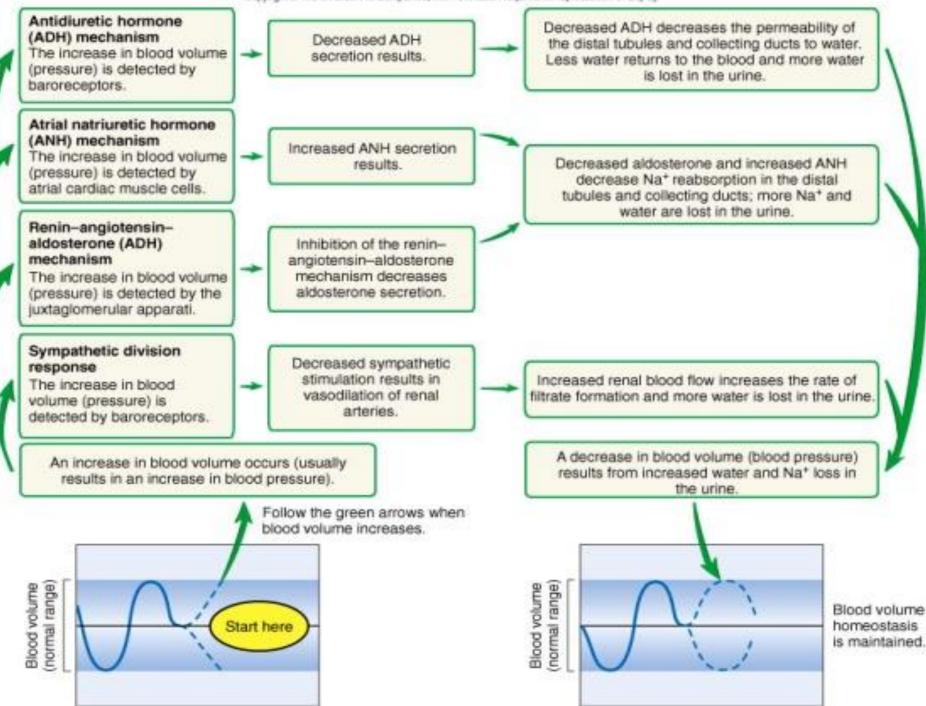
- ADH is secreted by the **hypothalamus** and stored and released from the posterior pituitary, in response to either **high blood OP** or **low blood pressure** detected by the hypothalamus (both indicate dehydration).
- ADH makes the walls of the collecting duct permeable to water, so that a total of 99% of the water in the urine is reabsorbed. When overhydrated, the absence of ADH results in 20% water loss (= 19% from the collecting duct + the 1% unrecoverable water).

## **Controlling sodium chloride by** Aldosterone + ANH.

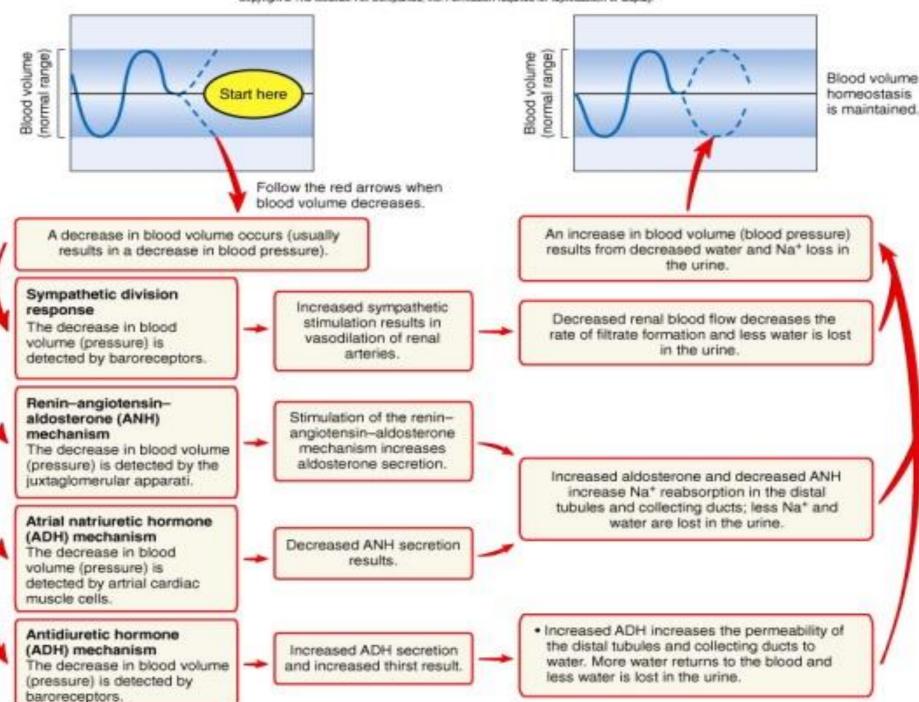
- A low blood pressure results in the juxtamedullary apparatus (attached to the glomerulus) releasing the enzyme renin into the blood. This activates the hormone angiotensin, which cause the adrenal glands to release aldosterone.
- Aldosterone increases reabsorption of sodium ions from the distal tubule and collecting duct (Note: the Na<sup>+</sup> pumps in the proximal tubule and loop of Henle are unaffected). As well as increasing blood Na<sup>+</sup>, it increases the blood volume by increasing reabsorption of water alongside the Na

- If blood pressure is high, then no aldosterone is secreted. Instead, cardiac cells in the heart secrete ANH (atrial natriuretic hormone), which inhibits absorption of sodium from the urine. The resulting high sodium in the filtrate increases its osmotic pressure, so less water is reabsorbed from the filtrate and thus more water is excreted in the urine.
- Aldosterone and ANH are thus antagonistic hormones responsible for controlling blood sodium, but in doing so, they alter water reabsorption by the kidney.





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#### **Blood pressure**

- When there are temporary changes in blood pressure, the afferent arteriole in to the renal corpuscle stabilises ultrafiltration by constricting when pressure rises and dilating when pressure drops.
- However, the arteriole is also controlled by the sympathetic nervous system from the hypothalamus (measuring the overall blood pressure). If there is a severe drop in pressure due to heavy bleeding or extensive inflammation, increased sympathetic stimulation increases vasoconstriction to reduce filtration and thus reduce further urine loss. This also happens during intense physical activity, when there is a high blood pressure, in order to maintain the high pressure and thus rapid O<sub>2</sub> transport.
- Conversely, continuous high pressure (when not active) decreases sympathetic stimulation → vasodilation → greater urine production → reduced blood volume and thus pressure.

#### Thirst center in hypothalamus.

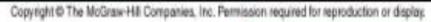
- Overall control of water balance is by the hypothalamus. The Thirst center in the hypothalamus responds to:
- Low blood pressure.
- High osmotic pressure of the blood.
- Dehydration of the mucosa of the mouth.
- These all stimulate the feeling of "thirst" so you drink water and increase your blood volume.

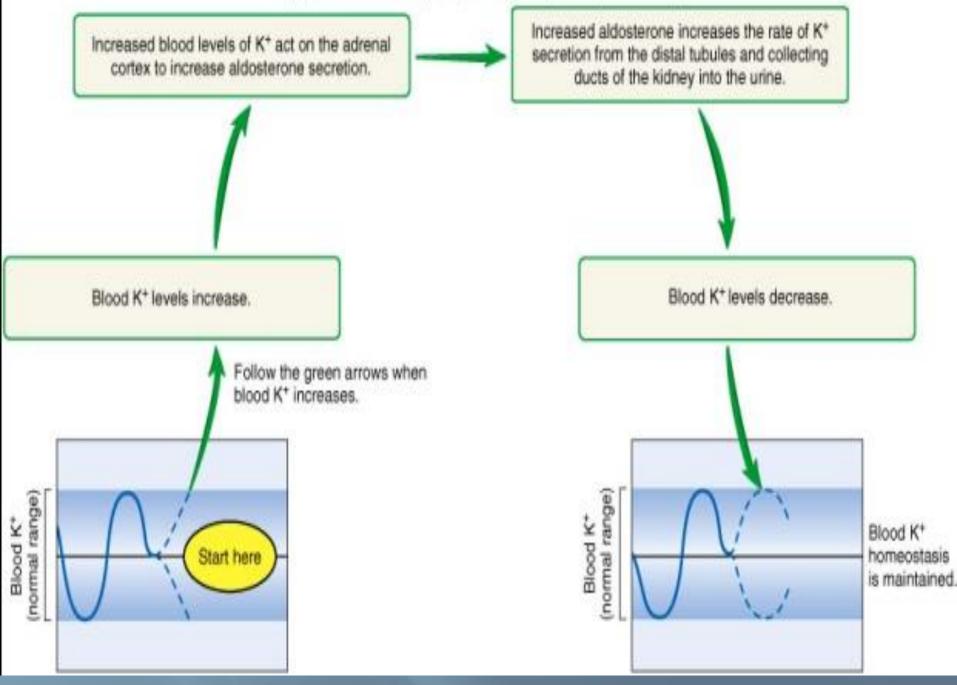
# Regulation of ions (summary).Sodium ions.

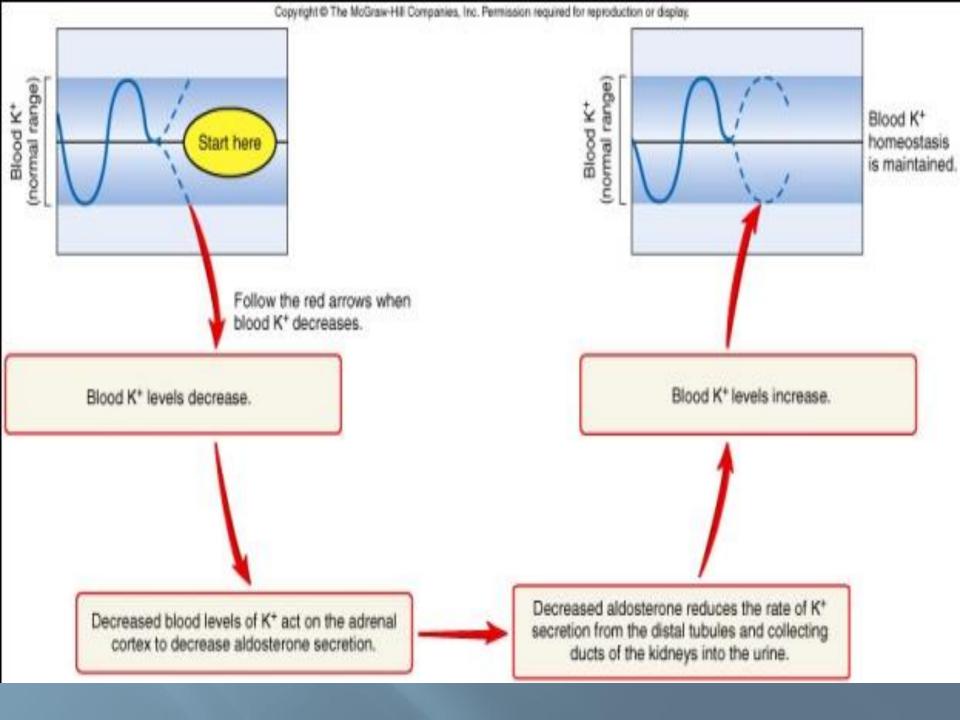
- This is the major cation in the extracellular fluid and thus gives 90% of its OP. Low bp → increased angiotensin → increased aldosterone → increased reabsorption in the distal tubules and collecting ducts, so less Na<sup>+</sup> is lost. High bp → increased ANH → opposite effect.
- Some Na<sup>+</sup> is also lost during sweating, but the concentration varies depending on body availability.

#### Potassium ions.

- Extracellular K<sup>+</sup> must be kept low to maintain the resting potential of the body cells, but is required inside the cell. Dehydration increases the conc of plasma K<sup>+</sup>, which must thus be excreted.
- Aldosterone → increased loss from the distal tubules and collecting ducts (at the same time as Na<sup>+</sup> is reabsorbed).



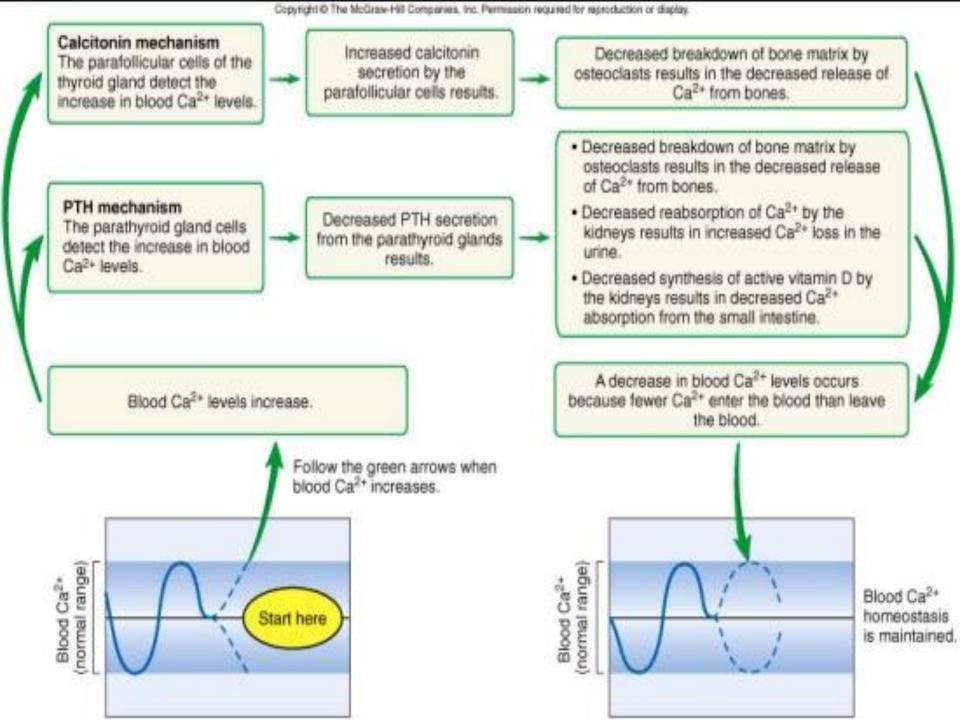


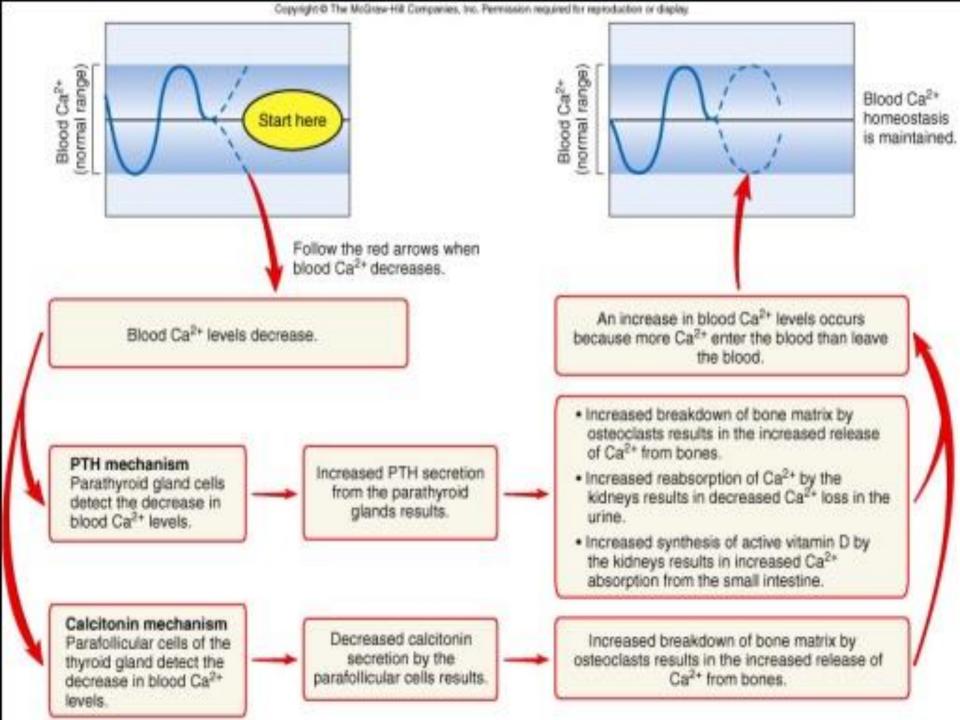


## **Calcium ions.**

• Ca<sup>2+</sup> conc. is of major importance in nerves(especially the synapses) and muscles, and affects the permeability of the cell membrane to Na<sup>+</sup> and so is closely controlled. Parathyroid hormone increases as Ca<sup>2+</sup> decreases to stimulate osteoclasts to release Ca<sup>2+</sup> from bones, reduce loss in the urine and increase uptake from the gut (by stimulating vitamin D).

 Excessive Ca<sup>2+</sup> reduces PTH but increases calcitonin to reverse these 3 processes.





#### **Urine collection and Micturition**

#### **Passage of urine from kidney to bladder**

- •Urine moves from the collecting ducts of the renal tubules to the renal pelvis by hydrostatic pressure.
- •Urine moves from the **pelvis** into the **ureter** by the **smooth muscles contraction**.
- •The **peristaltic wave** which propagates along the ureters length propels urine into the bladder to store the urine.

### **Micturition**

•The flow of urine to the urinary bladder is relatively continuous.

•The urinary bladder acts as a reservoir for urine until it can be eliminated at appropriate time.

•The bladder can distend to accommodate the large volume of fluid .The maximum volume it can contain is 1L, and discomfort begins when urine volume exceeds 500ml. •The capacity of the urinary bladder to distend is due to the following factors:

•The walls of the bladder contain large folds, which unfold to enlarge the lumine of the urinary bladder.

•The lining of urinary bladder is stretchable transitional epithelium.

•Smooth muscle wall of the urinary bladder stretch to accommodate the fluid volume.

•The bladder expands as the urine flows into it, but the internal pressure does not increase(because its structure) until the bladder volume becomes large.

#### **Micturition reflex**

•Micturition reflex is activated when the bladder wall is stretched resulting in elimination of urine from the urinary bladder (micturition).

•Integration of the micturition reflex occurs in the sacral region of the spinal cord and modified in the pons of cerebrum.(Figure 10.14).

•When urine fills the bladder stimulates **stretch receptors** which produce action potential.

•Action potential is carried by sensory neurons to **spinal cord** through the **pelvic nerves**.

•Action potential is carried to the bladder through parasympathetic fibers

• Parasympathetic stimulation causes contraction of smooth muscles of the bladder and decrease somatic motor action potentials causing the external urinary sphincter to relax.

Urine flows from the bladder to the urethra by increase the pressure.
The micturition reflex produces a series of contractions of the urinary bladder.

