# URINE FORMATION

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# INTRODUCTION

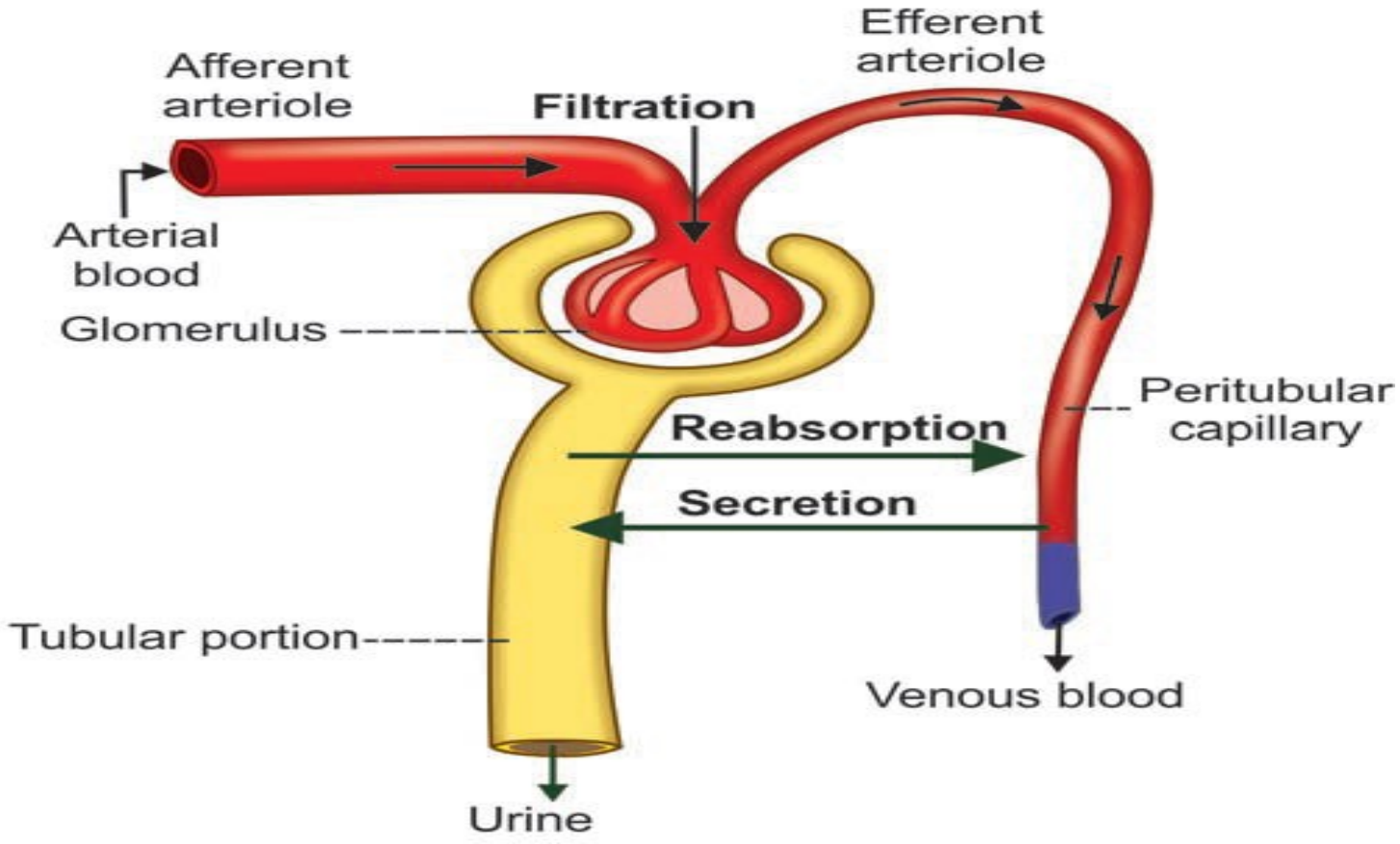
- Urine formation is a blood cleansing function.
- Normally, about 1,300 mL of blood (26% of cardiac output) enters the kidneys.
- Kidneys excrete the unwanted substances along with water from the blood as urine.
- Normal **urinary output** is 1 L/day to 1.5 L/day.

## PROCESSES OF URINE FORMATION

- When blood passes through glomerular capillaries, the plasma is filtered into the Bowman capsule.
- This process is called glomerular filtration.
- From Bowman capsule immature urine passes through the tubular portion of the nephron.

- While passing through the tubule, the filtrate undergoes various changes both in quality and in quantity.
- Many wanted substances like glucose, amino acids, water and electrolytes are reabsorbed from the tubules. This process is called tubular reabsorption.
- And, some unwanted substances are secreted into the tubule from peritubular blood vessels.
- This process is called tubular secretion or excretion.
- Thus, the urine formation includes three processes:

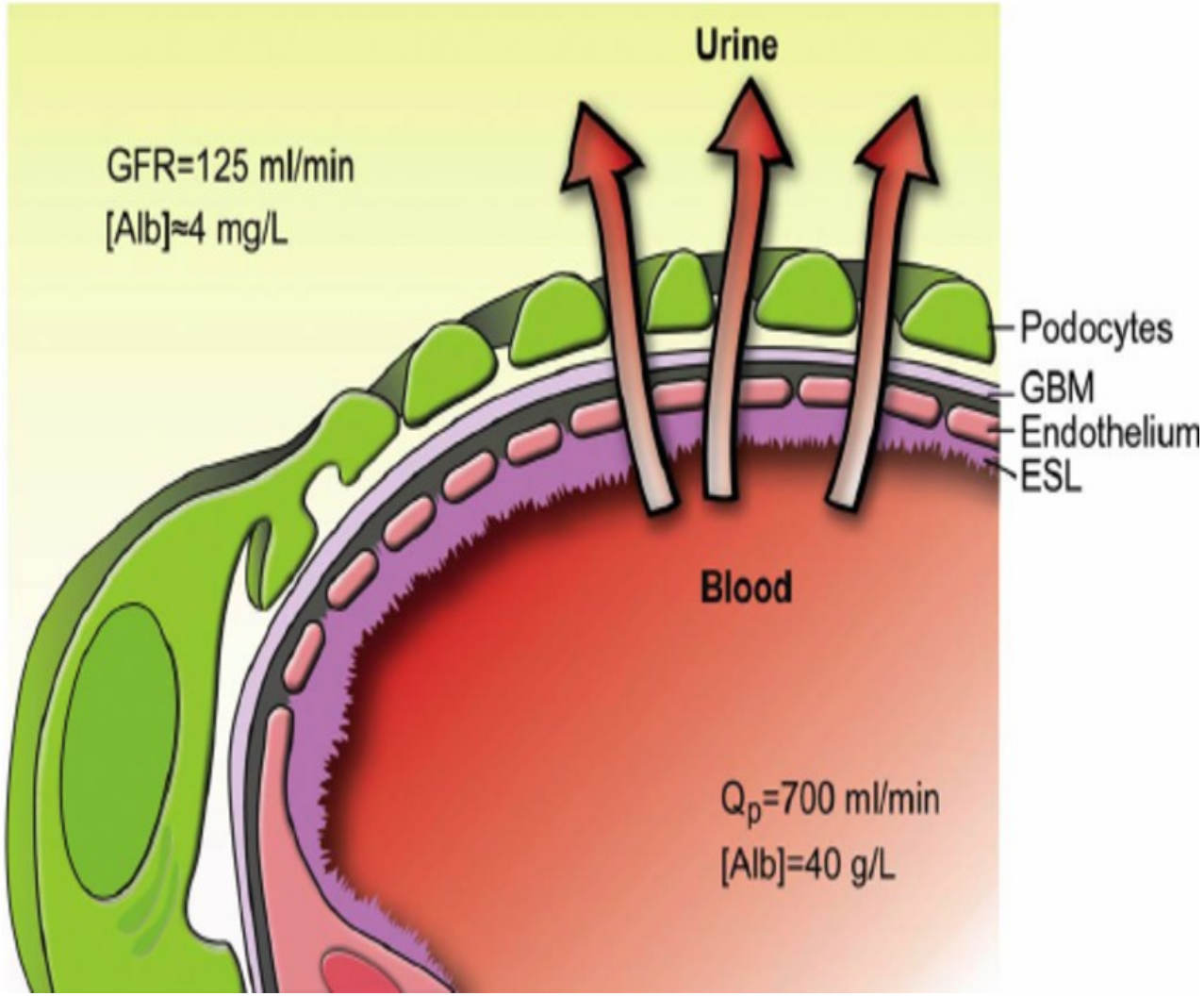
**A. GLOMERULAR FILTRATION**
**B. TUBULAR REABSORPTION**
**C. TUBULAR SECRETION.**



- Among these three processes filtration is the function of the glomerulus.
- Reabsorption and secretion are the functions of tubular portion of the nephron.

## GLOMERULAR FILTRATION

- Glomerular filtration is the process by which the blood is filtered while passing through the glomerular capillaries by filtration membrane.
- It is the first process of urine formation.
- The structure of filtration membrane is well suited for filtration.



# FILTRATION MEMBRANE

- Filtration membrane is formed by three layers:

1. **GLOMERULAR CAPILLARY MEMBRANE**
2. **BASEMENT MEMBRANE**
3. **VISCERAL LAYER OF BOWMAN CAPSULE**

## 1. GLOMERULAR CAPILLARY MEMBRANE

- Glomerular capillary membrane is formed by single layer of endothelial cells, which are attached to the basement membrane.
- The capillary membrane has many pores called **fenestrae** or **filtration pores** with a diameter of 0.1 μ.

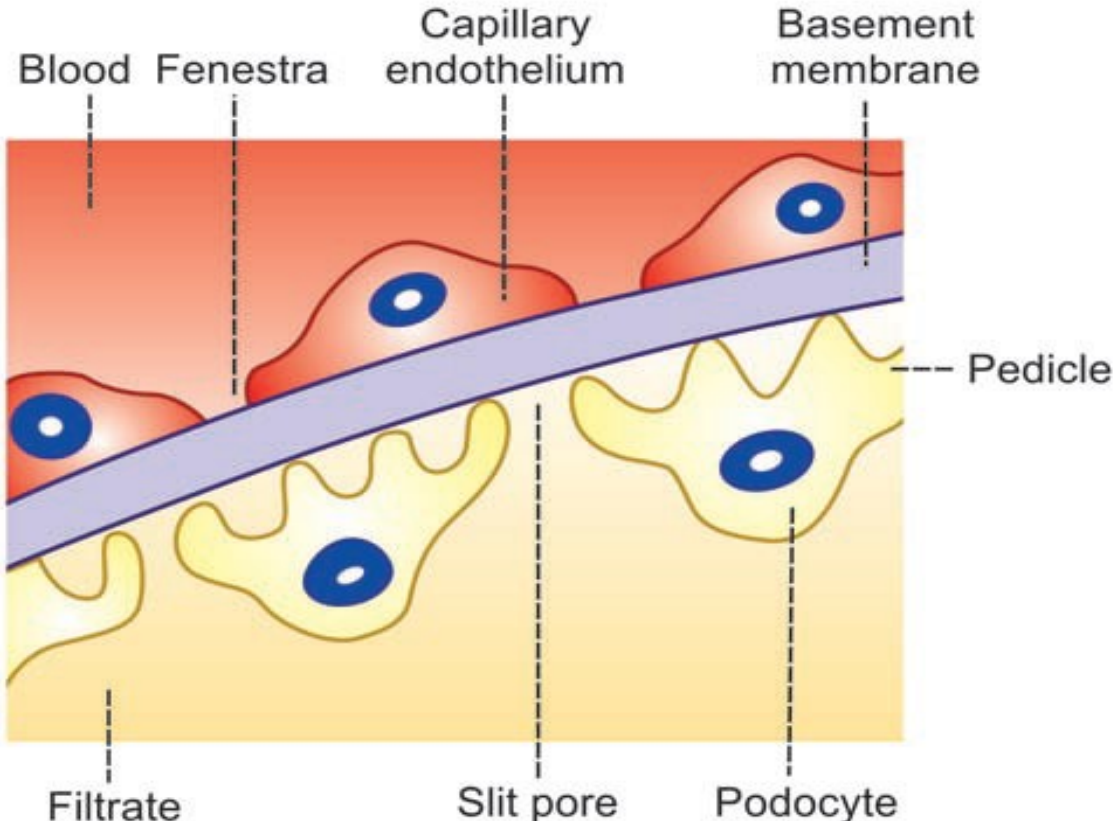



FIGURE : FILTERING MEMBRANE IN RENAL CORPUSCLE.

## 2. BASEMENT MEMBRANE

- Basement membrane of glomerular capillaries and the basement membrane of visceral layer of Bowman capsule fuse together.
- The fused basement membrane separates the endothelium of glomerular capillary and the epithelium of visceral layer of Bowman capsule.

## 3. VISCERAL LAYER OF BOWMAN CAPSULE

- This layer is formed by a single layer of flattened epithelial cells resting on a basement membrane.
- Each cell is connected with the basement membrane by cytoplasmic extensions called **pedicles** or **feet.** Epithelial cells with pedicles are called **podocytes**.
- Pedicles interdigitate leaving small cleft like spaces in between. The cleftlike space is called **slit pore** or **filtration slit.**
- Filtration takes place through these slit pores.

## PROCESS OF GLOMERULAR FILTRATION

- When blood passes through glomerular capillar ies, the plasma is filtered into the Bowman capsule.
- All the substances of plasma are filtered except the plasma proteins.
- The filtered fluid is called **glomerular filtrate.**

## ULTRAFILTRATION

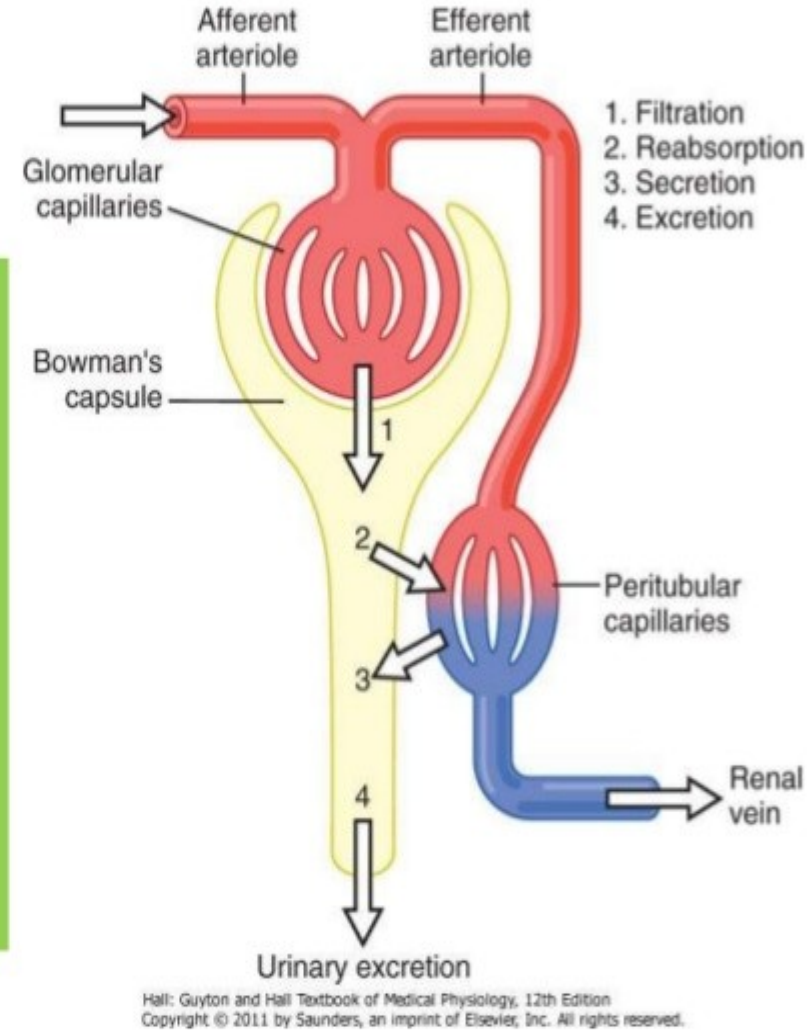
- Glomerular filtration is called ultrafiltration because even the minute particles are filtered. But, the plasma proteins are not filtered due to their large molecular size.
- The protein molecules are larger than the slit pores present in the endothelium of capillaries.
- Thus, the glomerular filtrate contains all the substances present in plasma except the plasma proteins.

# GLOMERULAR FILTRATION RATE

- Glomerular filtration rate (GFR) is defined as the total quantity of filtrate formed in all the nephrons of both the kidneys in the given unit of time.
- Normal GFR is 125 mL/minute or about 180 L/day.

**3 processes involved in Urine formation**

1. **Glomerular filtration**
2. **Tubular reabsorption**
3. **Tubular secretion**



# PRESSURES DETERMINING FILTRATION

- Pressures, which determine the GFR are:

1. Glomerular capillary pressure
2. Colloidal osmotic pressure in the glomeruli
3. Hydrostatic pressure in the Bowman capsule.

- These pressures determine the GFR by either favoring or opposing the filtration.

## 1. GLOMERULAR CAPILLARY PRESSURE

- It was exerted by the blood in glomerular capillaries.
- It is about 60 mm Hg and, varies between 45 and 70 mm Hg.
- Glomerular capillary pressure is the highest capillary pressure in the body.
- This pressure favors glomerular filtration.

## 2. COLLOIDAL OSMOTIC PRESSURE

- It is the pressure exerted by plasma proteins in the glomerular capillaries.
- The plasma proteins are not filtered through the glomerular capillaries and remain in the glomerular capillaries.
- These proteins develop the colloidal osmotic pressure, which is about 25 mm Hg.
- It opposes glomerular filtration.

## 3. HYDROSTATIC PRESSURE IN BOWMAN CAPSULE

- It is the pressure exerted by the filtrate in Bowman capsule.
- It is also called **capsular pressure.**
- It is about 15 mm Hg.
- It also opposes glomerular filtration.

## NET FILTRATION PRESSURE

- Net filtration pressure is the balance between pressure favoring filtration and pressures opposing filtration. It is otherwise known as **effective filtration pressure** or **essential filtration pressure.**

NET FILTRATION PRESSURE = Glomerular Capillary Pressure − Colloidal Osmotic Pressure + Hydrostatic Pressure In Bowman Capsule

= 60 – (25 + 15)

= 20 mm of Hg

# FACTORS REGULATING (AFFECTING) GFR

## 1. RENAL BLOOD FLOW

- It is the most important factor that is necessary for glomerular filtration.
- GFR is directly proportional to renal blood flow.
- Normal blood flow to both the kidneys is 1,300 mL/minute.
- The renal blood flow itself is controlled by **autoregulation.**

## 2. TUBULOGLOMERULAR FEEDBACK

- Tubuloglomerular feedback is the mechanism that regulates GFR through renal tubule and macula densa.
- **Macula densa** is sensitive to the sodium chloride in the tubular fluid.

- When the glomerular filtrate passes through the terminal portion of thick ascending segment, macula densa acts like a sensor.
- It detects the concentration of sodium chloride in the tubular fluid and accordingly alters the glomerular blood flow and GFR.
- When GFR increases, concentration of sodium chloride increases in the filtrate.
- Macula densa releases **adenosine. it** causes constriction of afferent arteriole. It leading to decrease in GFR.
- When GFR decreases, concentration of sodium chloride decreases in the filtrate. Macula densa secretes prostaglandin, bradykinin and renin.
- Prostaglandin and bradykinin cause dilatation of afferent arteriole while Renin induces constriction of efferent arteriole.
- The dilatation of afferent arteriole and constriction of efferent arteriole leads to increase in glomerular blood flow and GFR.

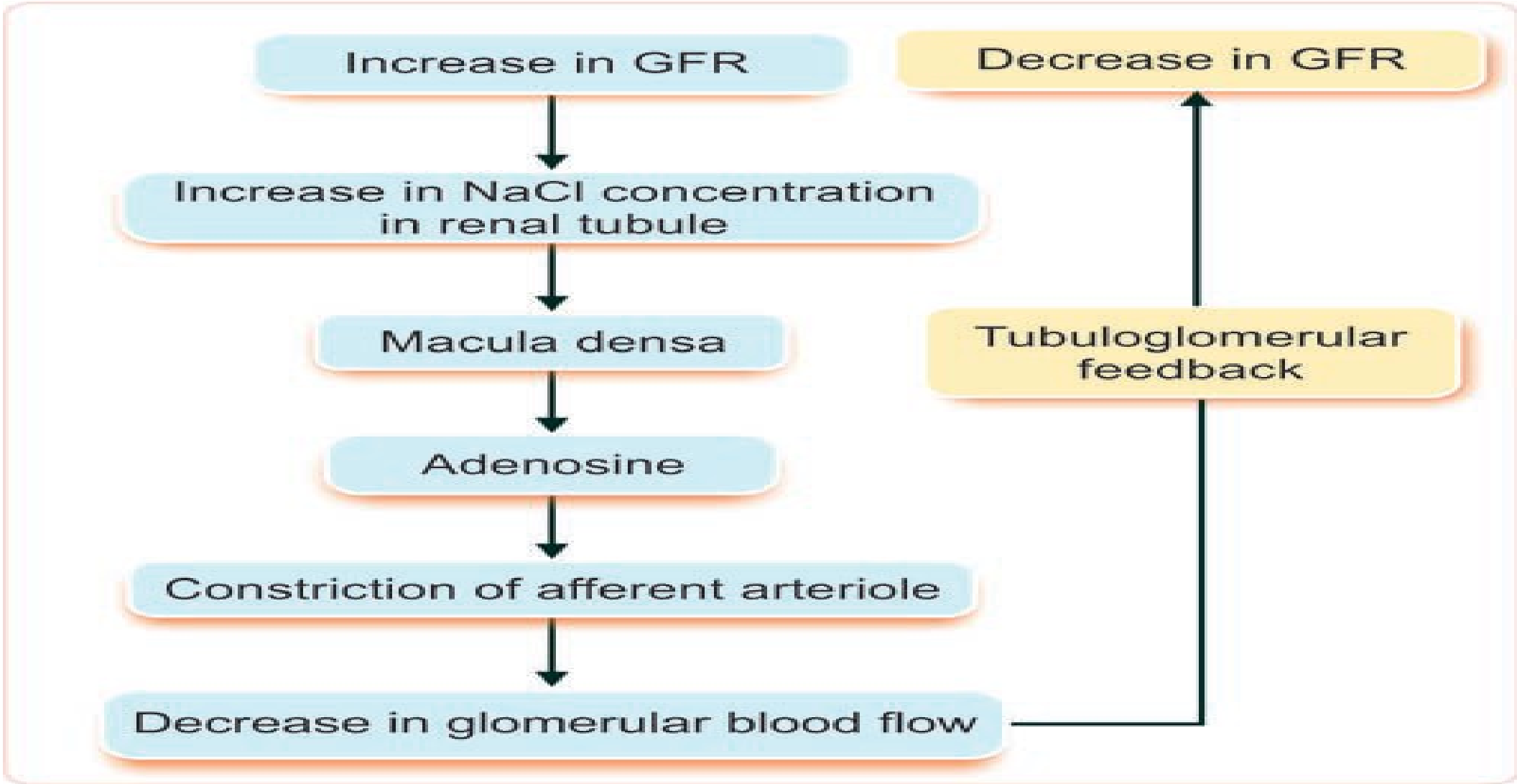



**FIGURE : TUBULOGLOMERULAR FEEDBACK**

(NaCl = Sodium chloride, GFR = Glomerular filtration rate)

## 3. SYSTEMIC ARTERIAL PRESSURE

- Renal blood flow and GFR are not affected as long as the mean arterial blood pressure is in between 60 and 180 mm Hg due to the autoregulatory mechanism.
- Variation in pressure above 180 mm Hg or below 60 mm Hg affects the renal blood flow and GFR accordingly, because the autoregulatory mechanism fails beyond this range.

## 4. SURFACE AREA OF CAPILLARY MEMBRANE

- GFR is directly proportional to the surface area of the capillary membrane.
- If the glomerular capillary membrane is affected as in the cases of some renal diseases, the surface area for filtration decreases. So there is reduction in GFR.

## 5. SYMPATHETIC STIMULATION

- Afferent and efferent arterioles are supplied by sympathetic nerves.
- The mild or moderate stimulation of sympathetic nerves does not cause any significant change either in renal blood flow or GFR.
- Strong sympathetic stimulation causes severe constriction of the blood vessels by releasing the neurotransmitter substance, noradrenaline.
- The effect is more severe on the efferent arterioles than on the afferent arterioles.
- However, if the stimulation is continued for more than 30 minutes, there is recovery of both renal blood flow and GFR. It is because of reduction in sympathetic neurotransmitter.

## 6. PERMEABILITY OF CAPILLARY MEMBRANE

- GFR is directly proportional to the permeability of glomerular capillary membrane.
- In many abnormal conditions like hypoxia, lack of blood supply, presence of toxic agents, etc. The permeability of the capillary membrane increases.
- In such conditions, even plasma proteins are filtered and excreted in urine.

## 7. CONTRACTION OF GLOMERULAR MESANGIAL CELLS

- Glomerular mesangial cells are situated in between the glomerular capillaries.
- Contraction of these cells decreases surface area of capillaries resulting in reduction in GFR.

## 8. HORMONAL AND OTHER FACTORS

- Many hormones and other secretory factors alter GFR by affecting the blood flow through glomerulus.

**Factors increasing GFR by vasodilatation**

i. Atrial natriuretic peptide
ii. Brain natriuretic peptide cAMP
iii. Dopamine
iv. Prostaglandin (PGE2)

**Factors decreasing GFR by vasoconstriction**

i. Angiotensin II
ii. Noradrenaline
iii. Platelet activating factor
iv. Prostaglandin (PGF2).

# TUBULAR REABSORPTION

## INTRODUTION

- Tubular reabsorption is the process by which water and other substances are transported from renal tubules back to the blood.
- When the glomerular filtrate flows through the tubular portion of nephron, both quantitative and qualitative changes occur.
- Large quantity of water (more than 99%), electrolytes and other substances are reabsorbed by the tubular epithelial cells.
- Since the substances are taken back into the blood from the glomerular filtrate, the entire process is called tubular reabsorption.

## SELECTIVE REABSORPTION

- Tubular reabsorption is known as selective reabsorption because the tubular cells reabsorb only the substances necessary for the body.
- Essential substances such as glucose, amino acids and vitamins are completely reabsorbed from renal tubule.
- Whereas the unwanted substances like metabolic waste products are not reabsorbed and excreted through urine.

## MECHANISM OF REABSORPTION

- Basic transport mechanisms involved in tubular
- reabsorption are of two types:

1. Active reabsorption
2. Passive reabsorption.

## 1. ACTIVE REABSORPTION

- Active reabsorption is the movement of molecules against the **electrochemical (uphill) gradient.**
- It needs liberation of energy, which is derived from ATP.

### SUBSTANCES REABSORBED ACTIVELY

- Substances reabsorbed actively from the renal tubule are sodium, calcium, potassium, phosphates, sulfates, bicarbonates, glucose, amino acids, ascorbic acid, uric acid and ketone bodies.

## 2. PASSIVE REABSORPTION

- Passive reabsorption is the movement of molecules along the **electrochemical (downhill) gradient.**
- This process does not need energy.

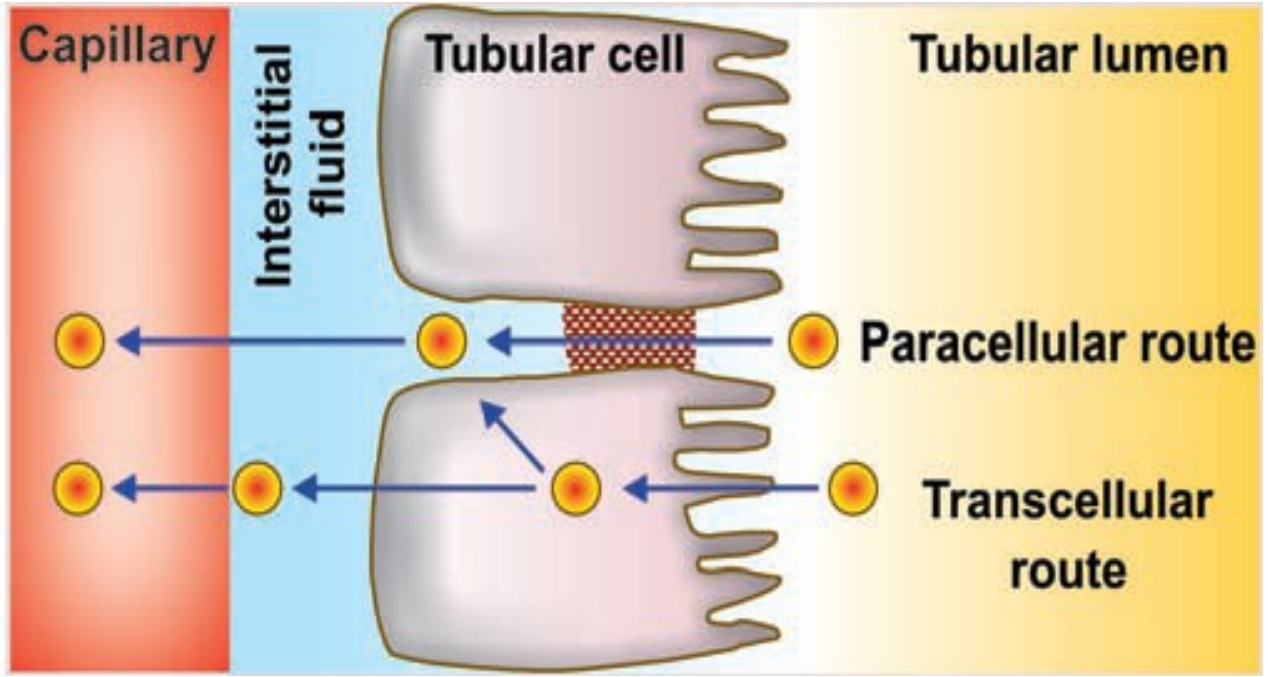
## SUBSTANCES REABSORBED PASSIVELY

- Substances reabsorbed passively are chloride, urea and water.

## ROUTES OF REABSORPTION

- Reabsorption of substances from tubular lumen into the peritubular capillary occurs by two routes:

1. TRANSCELLUAR ROUTE
2. PARACELLULAR ROUTE



## 1. TRANSCELLULAR ROUTE

- In this route the substances move through the cell.
- It includes transport of substances from:

i. Tubular lumen into tubular cell through apical (luminal) surface of the cell membrane.
ii. Tubular cell into interstitial fluid.
iii. Interstitial fluid into capillary.

## 2. PARACELLUAR ROUTE

- In this route, the substances move through the intercellular space.
- It includes transport of substances from:

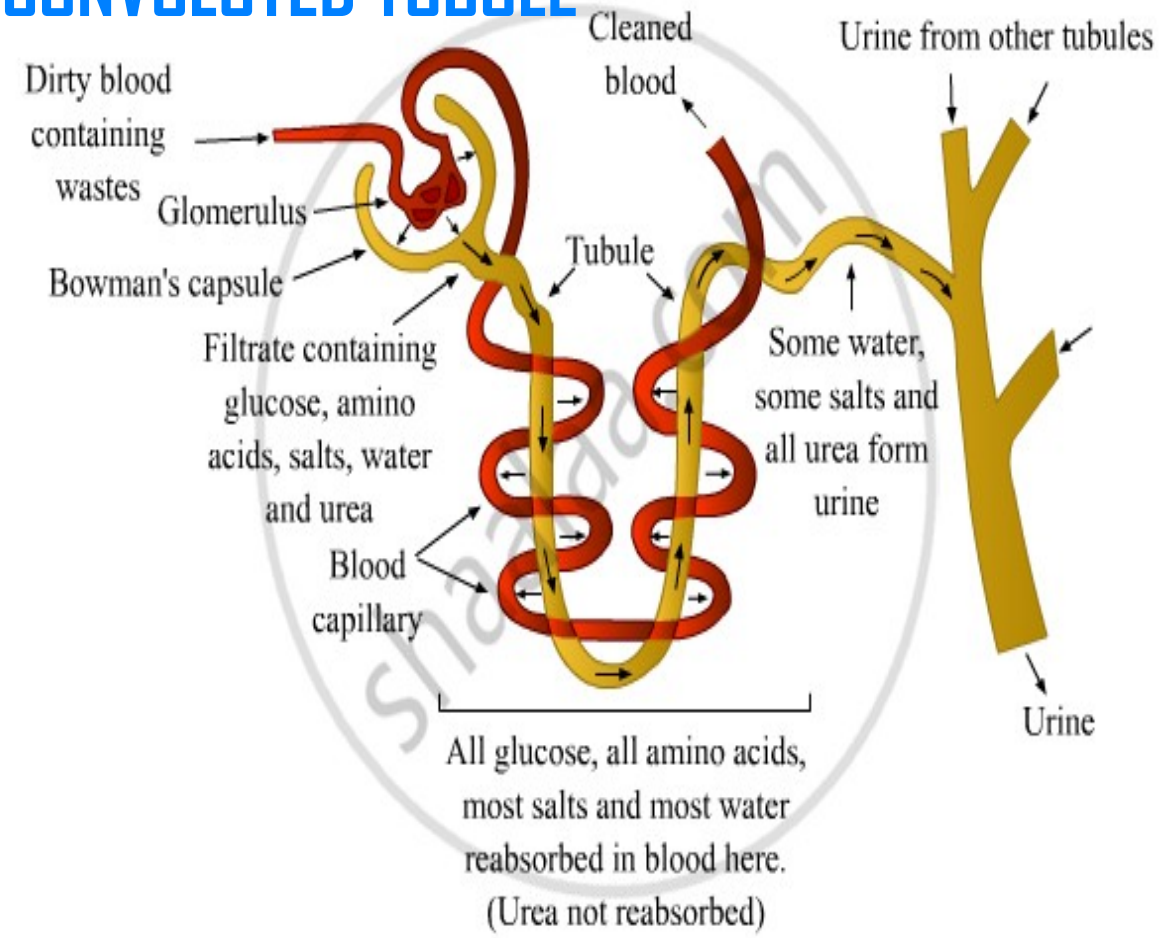
i. Tubular lumen into interstitial fluid present in lateral intercellular space through the tight junction between the cells.
ii. Interstitial fluid into capillary.

## SITE OF REABSORPTION

- Reabsorption of the substances occurs in almost all the segments of tubular portion of nephron.

## SUBSTANCES REABSORBED FROM PROXIMAL CONVOLUTED TUBULE

- About 88% of the filtrate is reabsorbed in proximal convoluted tubule.
- The brush border of epithelial cells in proximal convoluted tubule increases the surface area and facilitates the reabsorption.
- Substances reabsorbed from proximal convoluted tubule are glucose, amino acids, sodium, potassium, calcium, bicarbonates, chlorides, phosphates, urea, uric acid and water.



## 2. SUBSTANCES REABSORBED FROM LOOP OF HENLE

- Substances reabsorbed from loop of Henle are sodium and chloride.

## 3. SUBSTANCES REABSORBED FROM DISTAL CONVOLUTED TUBULE

- Sodium, calcium, bicarbonate and water are reabsorbed from distal convoluted tubule.

## REGULATION OF TUBULAR REABSORPTION

- Tubular reabsorption is regulated by three factors:

1. **GLOMERULOTUBULAR BALANCE**
2. **HORMONAL FACTORS**
3. **NERVOUS FACTORS.**

# 1. GLOMERULOTUBULAR BALANCE

- Glomerulotubular balance is the balance between the filtration and reabsorption of solutes and water in kidney.
- When GFR increases, the tubular load of solutes and water in the proximal convoluted tubule is increased. It is followed by increase in the reabsorption of solutes and water.
- This process helps in the constant reabsorption of solute particularly sodium and water from renal tubule.

## MECHANISM OF GLOMERULOTUBULAR BALANCE

- It occurs because of osmotic pressure in the peritubular capillaries. When GFR increases, Consequently, the osmotic pressure increases in the blood (due to plasma proteins).
- The elevated osmotic pressure in the peritubular capillaries increases reabsorption of sodium and water.

# 2. HORMONAL FACTORS

- Hormones, which regulate GFR are listed in Table.

| Hormone | Action |
|---|---|
| Aldosterone | Increases sodium reabsorption in ascending limb, distal convoluted tubule and collecting duct |
| Angiotensin II | Increases sodium reabsorption in proximal tubule, thick ascending limb, distal tubule and collecting duct (mainly in proximal convoluted tubule) |
| Antidiuretic hormone | Increases water reabsorption in distal convoluted tubule and collecting duct |
| Atrial natriuretic factor | Decreases sodium reabsorption |
| Brain natriuretic factor | Decreases sodium reabsorption |
| Parathormone | Increases reabsorption of calcium, magnesium and hydrogen<br>Decreases phosphate reabsorption |
| Calcitonin | Decreases calcium reabsorption |

## 3. NERVOUS FACTOR

- Activation of sympathetic nervous system increases the tubular reabsorption (particularly of sodium) from renal tubules.
- It also increases the tubular reabsorption indirectly by stimulating secretion of renin from juxtaglomerular cells.
- Renin causes formation of angiotensin II, which increases the sodium reabsorption.

## THRESHOLD SUBSTANCES

- Depending upon the degree of reabsorption, various substances are classified into three categories:

1. **HIGHTHRESHOLD SUBSTANCES**
2. **LOWTHRESHOLD SUBSTANCES**
3. **NONTHRESHOLD SUBSTANCES**

## 1. HIGH-THRESHOLD SUBSTANCES

- Highthreshold substances, which do not appear in urine under normal conditions.
- The food substances like glucose, amino acids, acetoacetate ions and vitamins are completely reabsorbed and do not appear in urine under normal conditions.
- They found in urine, only if their concentration in plasma is abnormally high or in renal diseases. So, these substances are called high threshold substances.

## 2. LOW-THRESHOLD SUBSTANCES

- Lowthreshold substances are the substances, which appear in urine even under normal conditions.
- The substances such as urea, uric acid and phosphate are reabsorbed to a little extend. So, these substances appear in urine even under normal conditions.

## 3. NON-THRESHOLD SUBSTANCES

- Nonthreshold substances are those substances, which are not at all reabsorbed and are excreted in urine irrespective of their plasma level.
- The metabolic end products such as creatinine are the nonthreshold substances.

# REABSORPTION OF IMPORTANT SUBSTANCES

## REABSORPTION OF SODIUM

- From the glomerular filtrate, 99% of sodium is reabsorbed.
- Two thirds of sodium is reabsorbed in proximal convoluted tubule and remaining one third in other segments (except descending limb) and collecting duct.
- Sodium reabsorption occurs in three steps:

## 1. TRANSPORT FROM LUMEN OF RENAL TUBULES INTO THE TUBULAR EPITHELIAL CELLS

- Active reabsorption of sodium ions from lumen into the tubular cells occurs by two ways:

i. In exchange for hydrogen ion by **antiport** (sodium counterport protein) – in proximal convoluted tubules.

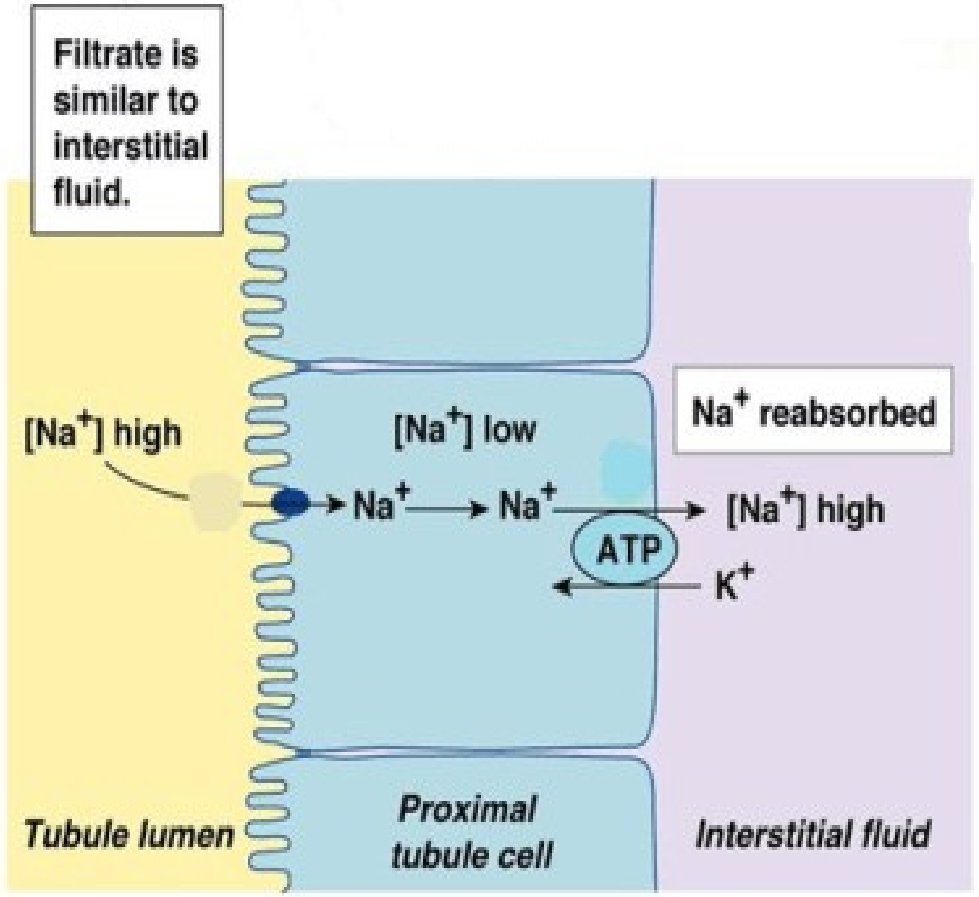
ii. Along with other substances like glucose and amino acids by **symport** (sodium cotransport protein) – in other segments and collecting duct.

## 2. TRANSPORT FROM TUBULAR CELLS INTO THE INTERSTITIAL FLUID

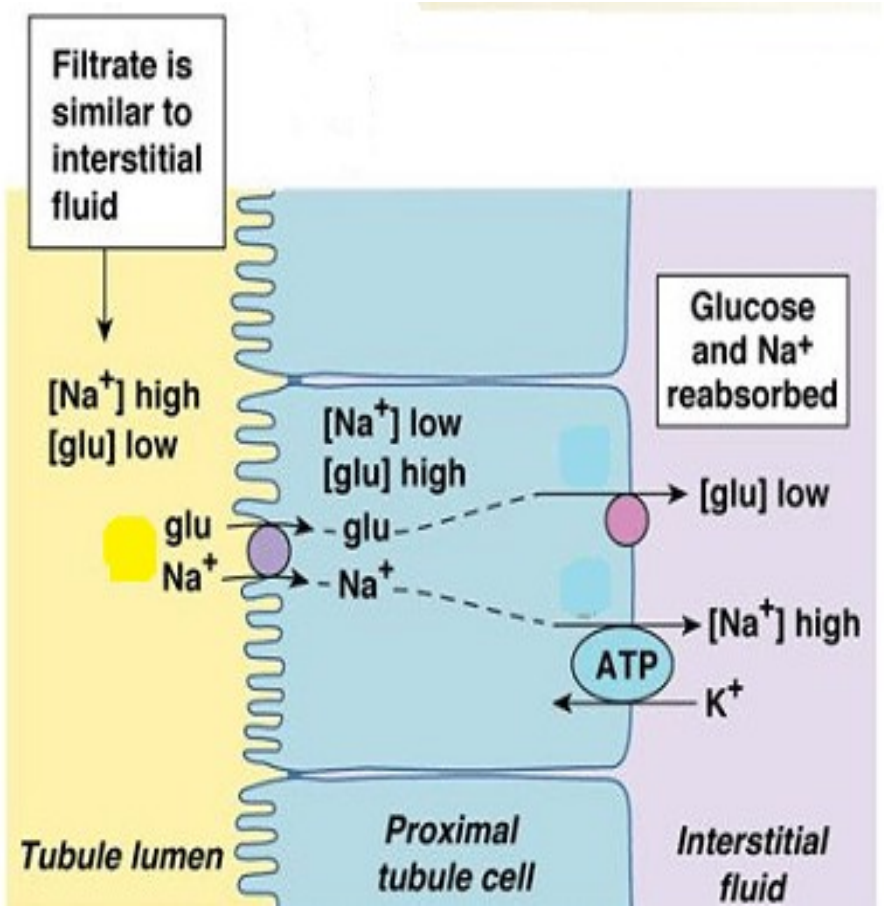
- Sodium is pumped outside the cells by sodium-potassium pump.
- Transport of sodium out of the tubular cell by sodium potassium pump, decreases the sodium concentration within the cell.
- This develops an electrochemical gradient between the lumen and tubular cell resulting in diffusion of sodium into the cell.

# 3. TRANSPORT FROM INTERSTITIAL FLUID TO THE BLOOD

- From the interstitial fluid, sodium ions enter the peritubular capillaries by concentration gradient.




ANTIPORT




SYMPORT

# REABSORPTION OF WATER

- Reabsorption of water occurs from proximal and distal convoluted tubules and in collecting duct.

**i. Reabsorption of water from proximal convoluted tubule – obligatory water reabsorption**

- Obligatory reabsorption is the type of water reabsorption in proximal convoluted tubule, which is secondary (obligatory) to sodium reabsorption.
- When sodium is reabsorbed from the tubule, the osmotic pressure decreases.
- It causes osmosis of water from renal tubule.

**ii. Reabsorption of water from distal convoluted tubule and collecting duct – facultative water reabsorption**

- Facultative reabsorption is the type of water reabsorption in distal convoluted tubule and collecting duct that occurs by the activity of antidiuretic hormone (ADH).
- Normally, the distal convoluted tubule and the collecting duct are not permeable to water. But in the presence of ADH, these segments become permeable to water, so it is reabsorbed.

# REABSORPTION OF GLUCOSE

- Glucose is completely reabsorbed in the proximal convoluted tubule.
- It is transported by secondary active transport (sodium cotransport) mechanism.
- Glucose and sodium bind to a common carrier protein in the luminal membrane of tubular epithelium and enter the cell.
- The carrier protein is called **sodium-dependant glucose cotransporter 2** (SGLT2).
- From tubular cell glucose is transported into medullary interstitium by another carrier protein called **glucose transporter 2** (GLUT2).

## RENAL THRESHOLD FOR GLUCOSE

- Renal threshold for glucose is 180 mg/dL in venous blood.
- When the blood level reaches 180 mg/dL glucose is not reabsorbed completely and appears in urine.

## REABSORPTION OF AMINO ACIDS

- Amino acids are also reabsorbed completely in proximal convoluted tubule.
- Amino acids are reabsorbed actively by the secondary active transport mechanism along with sodium.

## REABSORPTION OF BICARBONATES

- Bicarbonate is reabsorbed actively, mostly in proximal tubule.
- It is reabsorbed in the form of carbon dioxide.
- In the tubular cells, carbon dioxide combines with water to form carbonic acid.
- It immediately dissociates into hydrogen and bicarbonate.
- Bicarbonate from the tubular cell enters the interstitium.
- There it combines with sodium to form sodium bicarbonate.

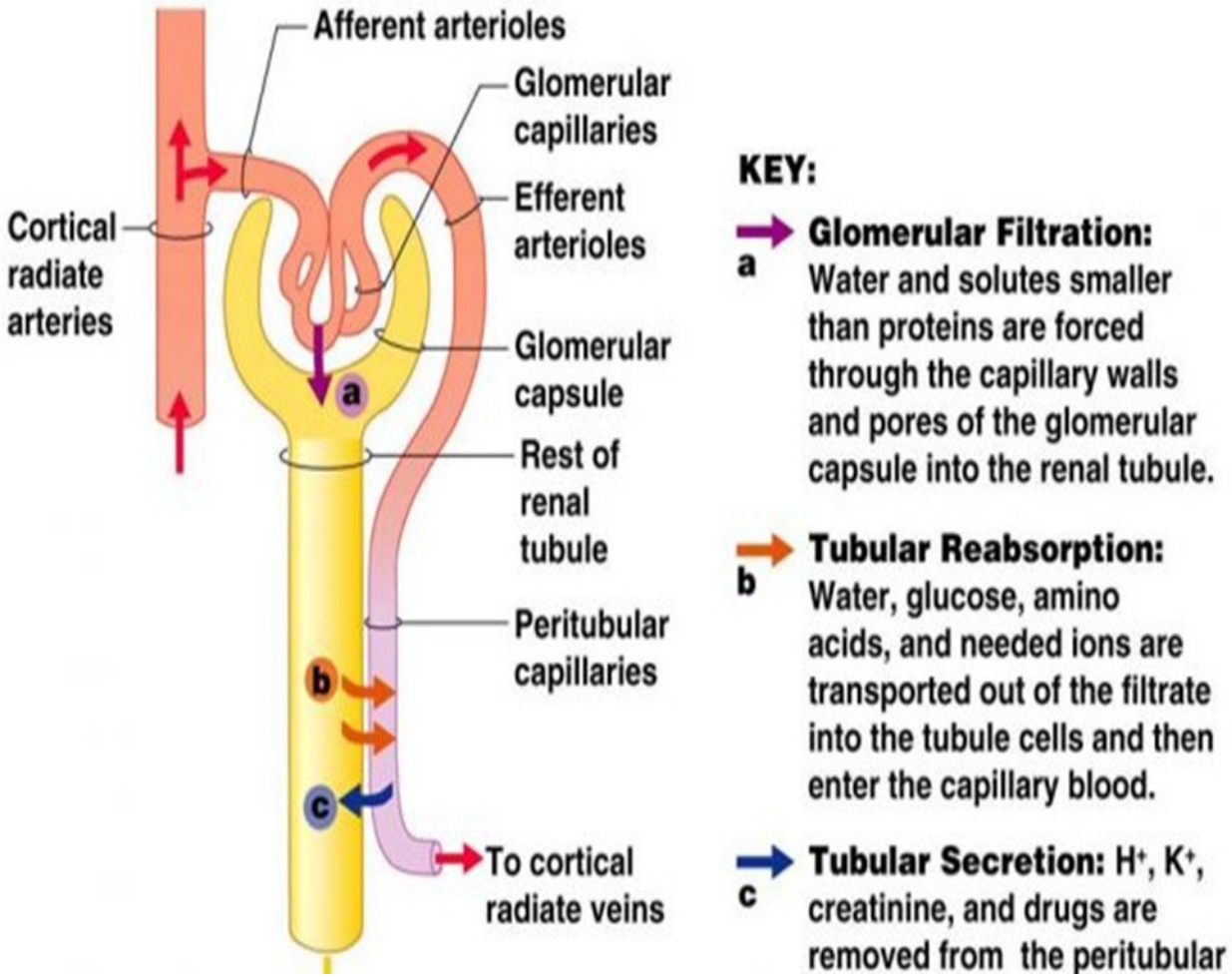
# TUBULAR SECRETION

## INTRODUCTION

- Tubular secretion is the process by which the substances are transported from blood into renal tubules.
- It is also called tubular excretion.
- In addition to reabsorption from renal tubules, some substances are also secreted into the lumen from the peritubular capillaries through the tubular epithelial cells.
- **Dye phenol red** was the first substance found to be secreted in renal tubules in experimental conditions.
- Later many other substances were found to be secreted.
- Such substances are Paraaminohippuric acid (PAH), Diodrast, 5-hydroxyindoleacetic acid (5HIAA), Amino derivatives, Penicillin.

# SUBSTANCES SECRETED IN DIFFERENT SEGMENTS OF RENAL TUBULES

1. Potassium is secreted actively by sodiumpotassium pump in proximal and distal convoluted tubules and collecting ducts.
2. Ammonia is secreted in the proximal convoluted tubule.
3. Hydrogen ions are secreted in the proximal and distal convoluted tubules. Maximum hydrogen ion secretion occurs in proximal tubule.
4. Urea is secreted in loop of Henle.




- Thus, urine is formed in nephron by the processes of glomerular filtration, selective reabsorption and tubular secretion.

# SUMMARY OF URINE FORMATION

- Urine formation takes place in three processes:

## 1. GLOMERULAR FILTRATION

- Plasma is filtered in glomeruli and the substances reach the renal tubules along with water as filtrate.

## 2. TUBULAR REABSORPTION

- The 99% of filtrate is reabsorbed in different segments of renal tubules.

## 3. TUBULAR SECRETION

- Some substances are transported from blood into therenal tubule. With all these changes, the filtrate becomes urine.

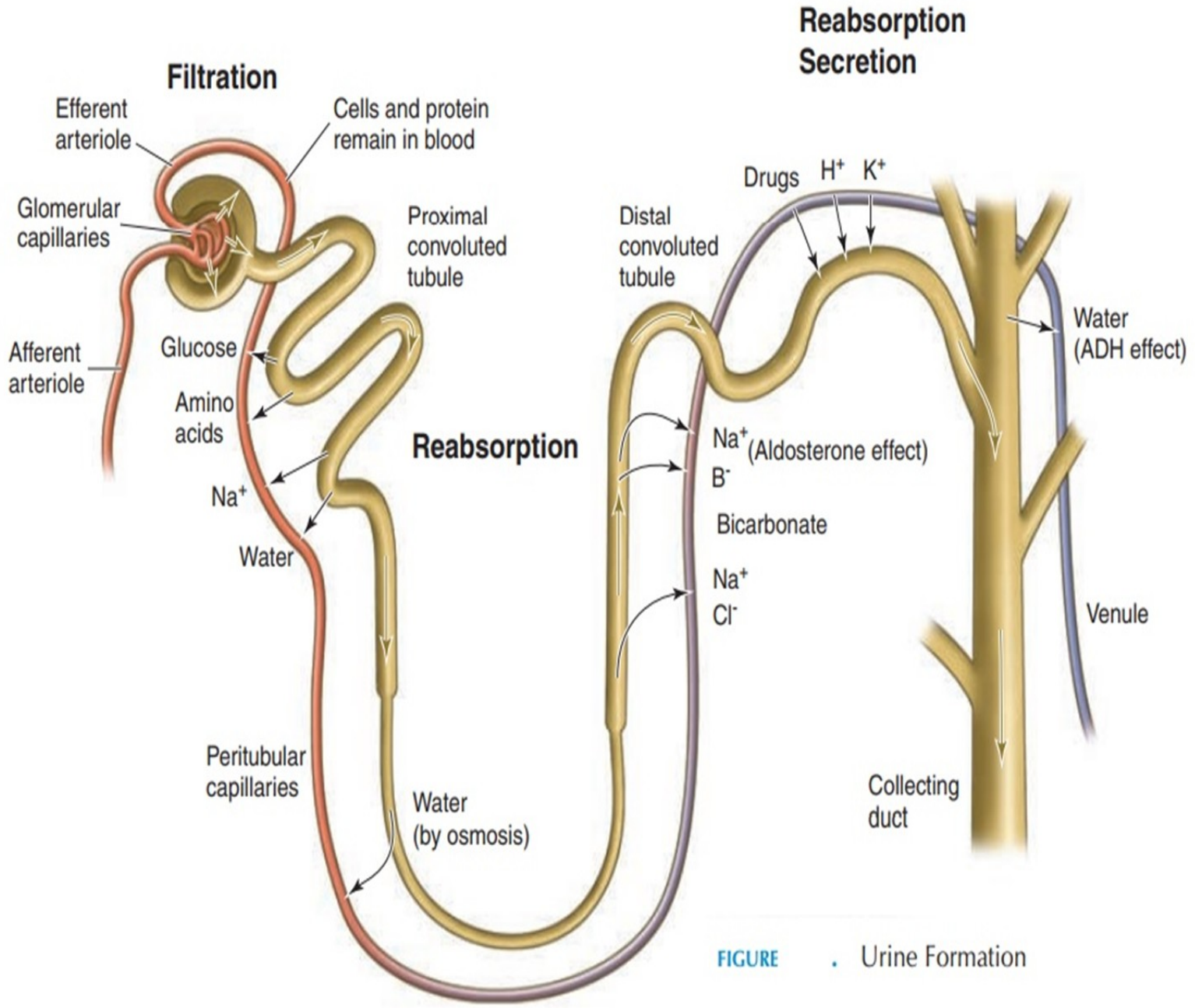



FIGURE . Urine Formation

# THANK YOU