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### **QUESTION**

Explain urine formation and concentration

### **ANSWERS**

#### **URINE FORMATION**

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.

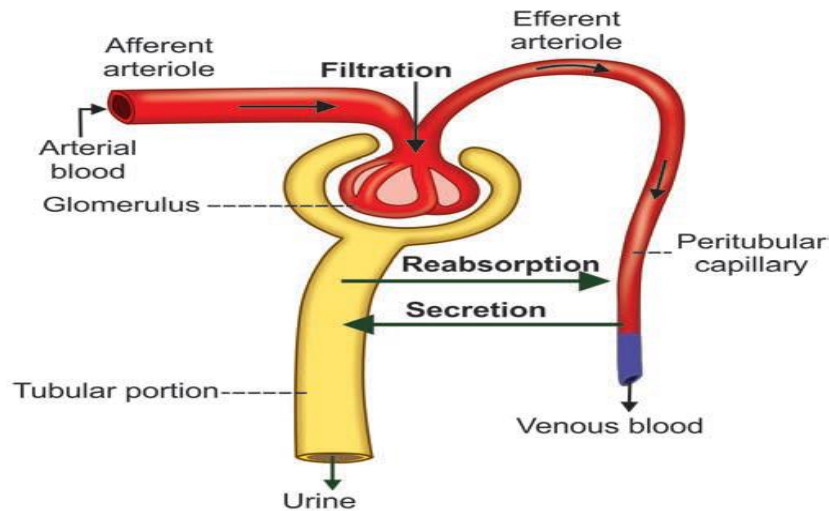
Filtrate from Bowman capsule passes through the tubular portion of the nephron. While passing through the tubule, the filtrate undergoes various changes both in quality and in quantity. Many wanted substances like glucose, amino acids, water and electrolytes are reabsorbed from the tubules. This process 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.



## EVENTS OF URINE FORMATION

### A. 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.

#### Glomerular capillary membrane

Glomerular capillary membrane is formed by single layer of endothelial cells, which are attached to the

#### 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.

#### 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 cleftlike 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 capillaries, 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.

#### FILTRATION FRACTION

Filtration fraction is the fraction (portion) of the renal plasma, which becomes the filtrate. It is the ratio between renal plasma flow and glomerular filtration rate. It is expressed in percentage.

$$\begin{aligned}\text{Filtration fraction} &= \text{GFR} * 100 / \text{Renal plasma flow} \\ &= 125 \text{ mL/min} * 100 / 650 \text{ mL/min} \\ &= 19.2\%\end{aligned}$$

Normal filtration fraction varies from 15% to 20%.

### **B. TUBULAR REABSORPTION**

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. The reabsorbed substances move into the interstitial fluid of renal medulla. And, from here, the substances move into the blood in peritubular capillaries.

Since the substances are taken back into the blood from the glomerular filtrate, the entire process is called tubular 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.

### *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 from the renal tubule are sodium, calcium, potassium, phosphates, sulfates, bicarbonates, glucose, amino acids, ascorbic acid, uric acid and ketone bodies.

### *Passive Reabsorption*

Passive reabsorption is the movement of molecules along the electrochemical (downhill) gradient. This process does not need energy. 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. Transcellular route
2. Paracellular route.

### *Transcellular Route*

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

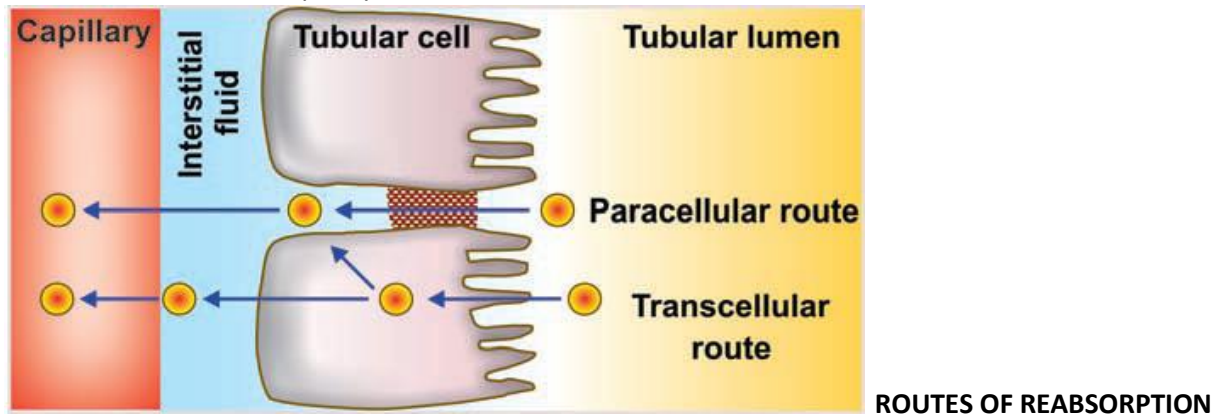
- a. Tubular lumen into tubular cell through apical (luminal) surface of the cell membrane
- b. Tubular cell into interstitial fluid
- c. Interstitial fluid into capillary.

### *Paracellular 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.

1. Substances Reabsorbed from Proximal Convoluted Tubule
2. Substances Reabsorbed from Loop of Henle
3. Substances 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.

### **C. TUBULAR SECRETION**

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:

1. Paraaminohippuric acid (PAH)

2. Diodrast
3. 5hydroxyindoleacetic acid (5HIAA)
4. Amino derivatives
5. Penicillin.

#### SUBSTANCES SECRETED IN DIFFERENT SEGMENTS OF RENAL TUBULES

1. Potassium is secreted actively by sodium potassium 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.

#### **CONCENTRATION OF URINE**

Every day 180 L of glomerular filtrate is formed with large quantity of water. If this much of water is excreted in urine, body will face serious threats. So the concentration of urine is very essential. Osmolarity of glomerular filtrate is same as that of plasma and it is 300 mOsm/L. But, normally urine is concentrated and its osmolarity is four times more than that of plasma, i.e. 1,200 mOsm/L.

Osmolarity of urine depends upon two factors:

1. Water content in the body
2. Antidiuretic hormone (ADH).

Mechanism of urine formation is the same for dilute urine and concentrated urine till the fluid reaches the distal convoluted tubule. However, dilution or concentration of urine depends upon water content of the body.

#### FORMATION OF DILUTE URINE

When, water content in the body increases, kidney excretes dilute urine. This is achieved by inhibition of ADH secretion from posterior pituitary. So water reabsorption from renal tubules does not take place leading to excretion of large amount of water. This makes the urine dilute.

#### FORMATION OF CONCENTRATED URINE

When the water content in body decreases, kidney retains water and excretes concentrated urine. Formation of concentrated urine is not as simple as that of dilute urine.

It involves two processes:

1. Development and maintenance of medullary gradient by countercurrent system
2. Secretion of ADH.

### MEDULLARY GRADIENT

#### *Medullary hyperosmolarity*

Cortical interstitial fluid is isotonic to plasma with the osmolarity of 300 mOsm/L. Osmolarity of medullary interstitial fluid near the cortex is also 300 mOsm/L.

However, while proceeding from outer part towards the inner part of medulla, the osmolarity increases gradually and reaches the maximum at the inner most part of medulla near renal sinus. Here, the interstitial fluid is hypertonic with osmolarity of 1,200 mOsm/L.

This type of gradual increase in the osmolarity of the medullary interstitial fluid is called the medullary gradient. It plays an important role in the concentration of urine.

### DEVELOPMENT AND MAINTENANCE OF MEDULLARY GRADIENT

Kidney has some unique mechanism called countercurrent mechanism, which is responsible for the development and maintenance of medullary gradient and hyperosmolarity of interstitial fluid in the inner medulla.

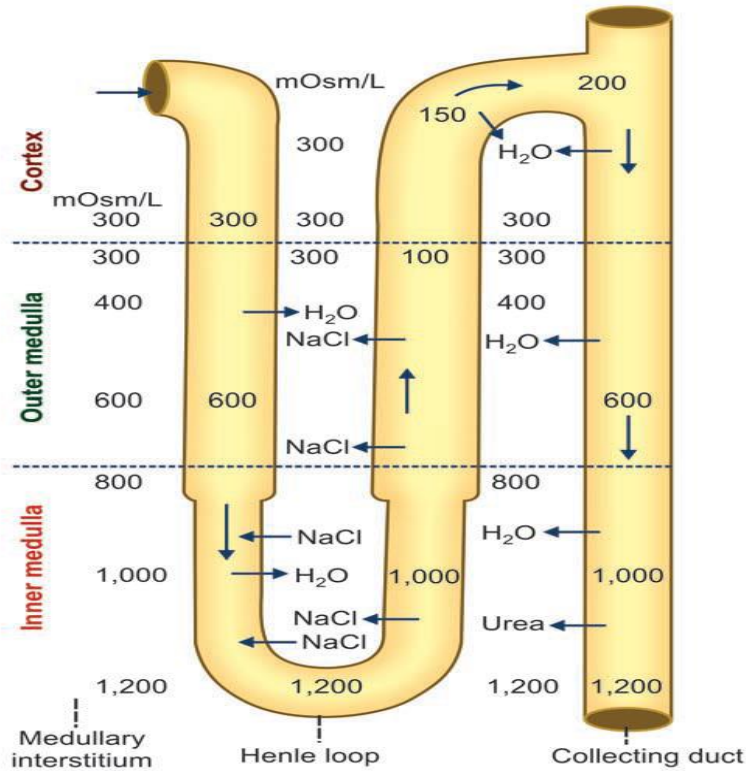
### COUNTERCURRENT MECHANISM

#### *Countercurrent flow*

A countercurrent system is a system of 'U-shaped tubules (tubes) in which, the flow of fluid is in opposite direction in two limbs of the 'U-shaped tubules.

#### *Divisions of Countercurrent System*

1. Countercurrent multiplier formed by loop of Henle
2. Countercurrent exchanger formed by vasa recta.

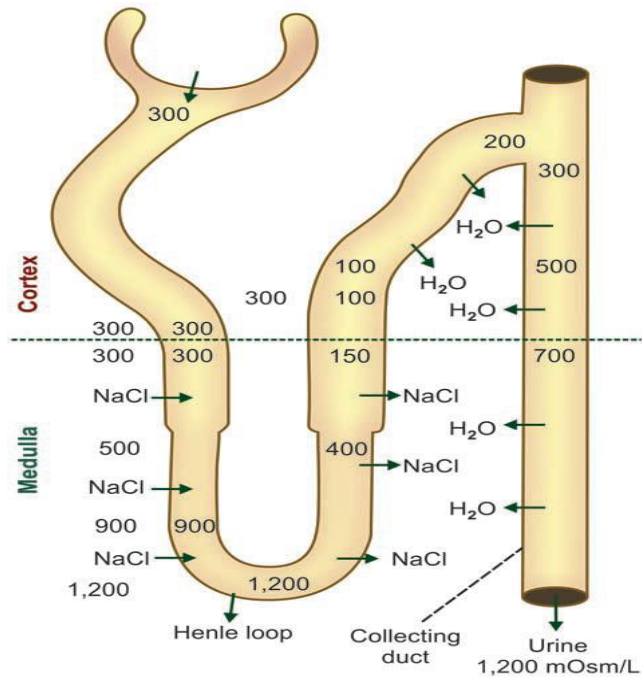


**COUNTERCURRENT MULTIPLIER. NUMERICAL INDICATE OSMOLARITY (MOSM/L)**

### ROLE OF ADH

Final concentration of urine is achieved by the action of ADH. Normally, the distal convoluted tubule and collecting duct are not permeable to water. But the presence of ADH makes them permeable, resulting in water reabsorption. Water reabsorption induced by ADH is called facultative reabsorption of water. A large quantity of water is removed from the fluid while passing through distal convoluted tubule and collecting duct. So, the urine becomes hypertonic with an osmolarity of 1,200 mOsm/L.





**ROLE OF ADH IN THE FORMATION OF CONCENTRATED URINE. ADH INCREASES THE PERMEABILITY FOR WATER IN DISTAL CONVOLUTED TUBULE AND COLLECTING DUCT. NUMERICAL INDICATE OSMOLARITY (MOSM/L)**

### SUMMARY OF URINE CONCENTRATION

When the glomerular filtrate passes through renal tubule, its osmolarity is altered in different segments

#### 1. BOWMAN CAPSULE

Glomerular filtrate collected at the Bowman capsule is isotonic to plasma. This is because it contains all the substances of plasma except proteins. Osmolarity of the filtrate at Bowman capsule is 300 mOsm/L.

#### 2. PROXIMAL CONVOLUTED TUBULE

When the filtrate flows through proximal convoluted tubule, there is active reabsorption of sodium and chloride followed by obligatory reabsorption of water.

So, the osmolarity of fluid remains the same as in the case of Bowman capsule, i.e. 300 mOsm/L. Thus, in proximal convoluted tubules, the fluid is isotonic to plasma.

#### 3. THICK DESCENDING SEGMENT

When the fluid passes from proximal convoluted tubule into the thick descending segment, water is reabsorbed from tubule into outer medullary interstitium by means of osmosis. It is due to the increased osmolarity in the medullary interstitium, i.e. outside the thick descending tubule. The osmolarity of the fluid inside this segment is between 450 and 600 mOsm/L. That means the fluid is slightly hypertonic to plasma.

#### 4. THIN DESCENDING SEGMENT OF HENLE LOOP

As the thin descending segment of Henle loop passes through the inner medullary interstitium (which is increasingly hypertonic) more water is reabsorbed. This segment is highly permeable to water and so the osmolarity of tubular fluid becomes equal to that of the surrounding medullary interstitium. In the short loops of cortical nephrons, the osmolarity of fluid at the hairpin bend of loop becomes 600 mOsm/L. And, in the long loops of juxtamedullary nephrons, at the hairpin bend, the osmolarity is 1,200 mOsm/L. Thus in this segment the fluid is hypertonic to plasma.

#### 5. THIN ASCENDING SEGMENT OF HENLE LOOP

When the thin ascending segment of the loop ascends upwards through the medullary region, osmolarity decreases gradually. Due to concentration gradient, sodium chloride diffuses out of tubular fluid and osmolarity decreases to 400 mOsm/L. The fluid in this segment is slightly hypertonic to plasma.

#### 6. THICK ASCENDING SEGMENT

This segment is impermeable to water. But there is active reabsorption of sodium and chloride from this. Reabsorption of sodium decreases the osmolarity of tubular fluid to a greater extent. The osmolarity is between 150 and 200 mOsm/L. The fluid inside becomes hypotonic to plasma.

#### 7. DISTAL CONVOLUTED TUBULE AND COLLECTING DUCT

In the presence of ADH, distal convoluted tubule and collecting duct become permeable to water resulting in water reabsorption and final concentration of urine. It is found that in the collecting duct, Principal (P) cells are responsible for ADH induced water reabsorption. Reabsorption of large quantity of water increases the osmolarity to 1,200 mOsm/L (Fig. 53.3). The urine becomes hypertonic to plasma.

### APPLIED PHYSIOLOGY

1. Osmotic Diuresis
2. Polyuria
3. Syndrome of Inappropriate Hypersecretion of ADH (SIADH)
4. Nephrogenic Diabetes Insipidus
5. Bartter Syndrome