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#### Explain urine formation and concentration

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.

#### **1. 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  $0.1 \mu$ .

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 cleft like space is called slitpore 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.

#### 2. 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.

#### " METHOD OF COLLECTION OF TUBULAR FLUID

There are two methods to collect the tubular fluid for analysis.

1. Micropuncture Technique: A micropipette is inserted into the Bowman capsule and different parts of tubular portion in the nephrons of experimental animals, to collect the fluid. The fluid samples are analyzed and compared with each other to assess the changes in different parts of nephron.

2. Stop-flow Method: Ureter is obstructed so that the back pressure rises and stops the glomerular filtration. The obstruction is continued for 8 minutes. It causes some changes in the fluid present in different parts of the tubular portion. Later, the obstruction is released and about 30 samples of 0.5 mL of urine are collected separately at regular intervals of 30 seconds. The first sample contains the fluid from collecting duct. Successive samples contain the fluid from distal convoluted tubule, loops of Henle and proximal convoluted tubule respectively. All the samples are analyzed.

## **3.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. Para-aminohippuric acid (PAH)
- 2. Diodrast
- 3. 5-hydroxyindoleacetic acid (5-HIAA)
- 4. Amino derivatives
- 5. Penicillin



FIGURE 52.1: Events of urine formation

# **Urine concentration**

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.

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

#### 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 SEGMENTOF 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. The urine becomes hypertonic to plasma.