Methodology of Formation of Urine in Human Body: 3 Processes (Physiology of Ultra filtration, Reabsobtion and Tubular secretion)

Process # 1. Glomerular Filtration (= ultrafiltration, Fig. 19.14):

On an average 1100-1200 ml of blood is filtered by the kidneys per minute. The glomerular capillaries are narrower than the afferent renal arterioles. Therefore, the blood pressure in the glomerular capillaries becomes very high so that there is continuous process of ultrafiltration (filtration under pressure) through the semi-permeable glomerular capillaries.

Thus water and many dissolved substances from the blood are filtered into the lumen of the Bowman's capsule through its walls. The glomerular filtrate contains a large amount of water and other dissolved substances such as urea, uric acid, creatinine, amino-acids, glucose, sodium, potassium, vitamins, etc. The blood flows into efferent renal arterioles. Thus the glomerular filtrate and blood plasma are similar except that glomerular filtrate does not have proteins and fats.

The amount of the filtrate formed by both the kidneys per minute is called the glomerular filtration rate (GFR). In the normal person, the glomerular filtration rate is about 125 ml. per minute, i.e., 180 litres per day. Auto regulation of Glomerular Filtration. Three important intrinsic mechanisms provide auto regulation of glomerular filtration rate.

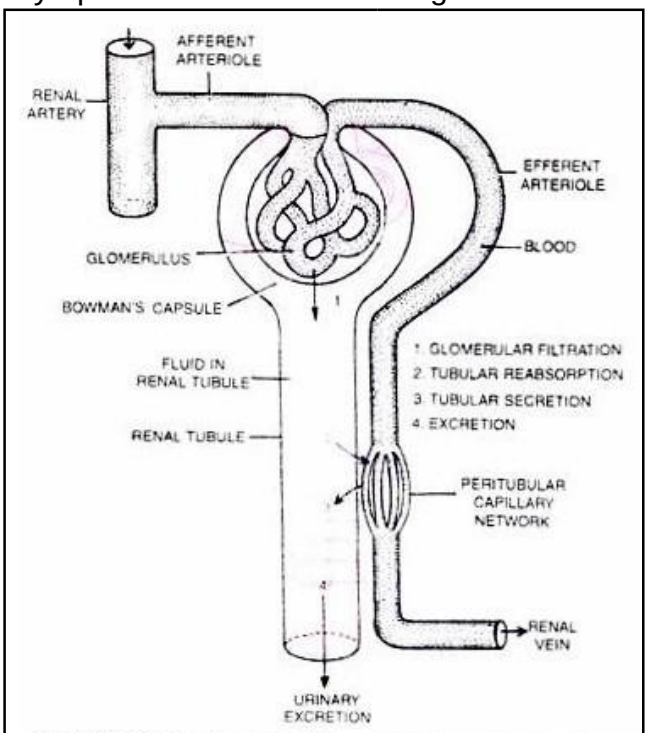

Fig. 19.14. Diagram showing the four processes; glomerular filtration, tubular reabsorption, tubular secretion and urinary excretion.

(i) Myogenic Mechanism:

An increase in blood pressure, tends to stretch the afferent arteriole which increases the blood flow to the glomerulus. When the wall of the arteriole contracts, the diameter of the afferent arteriole is reduced that increases the flow of blood.

(ii) Juxtaglomerular Mechanism:

Juxtaglomerular apparatus (JGA) cells secrete enzymes like renin that modulate blood pressure and thus renal blood flow. This regulates GFR.

(iii) Neural Control:

Blood vessels of the kidney are innervated by nerve fibres of the sympathetic neural system. When activated, the nerve fibres bring about constriction of renal arteries and cause decrease in renal flow and glomerular filtration rate.

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Process # 2. Tubular Reabsorption (Fig. 19.15):

From the Bowman's capsule, the glomerular filtrate enters the proximal convoluted tubule. Absorption of selected materials takes place from the filtrate into the blood of the peritubular capillaries or vasa recta. It is termed the tubular reabsorption.

Reabsorption involves both passive and active transport across the tubular epithelium. As already stated, the glomerular filtrate in the Bowman s capsule resembles blood plasma in composition except for plasma proteins and fats. Therefore, it is almost isotonic to the plasma.

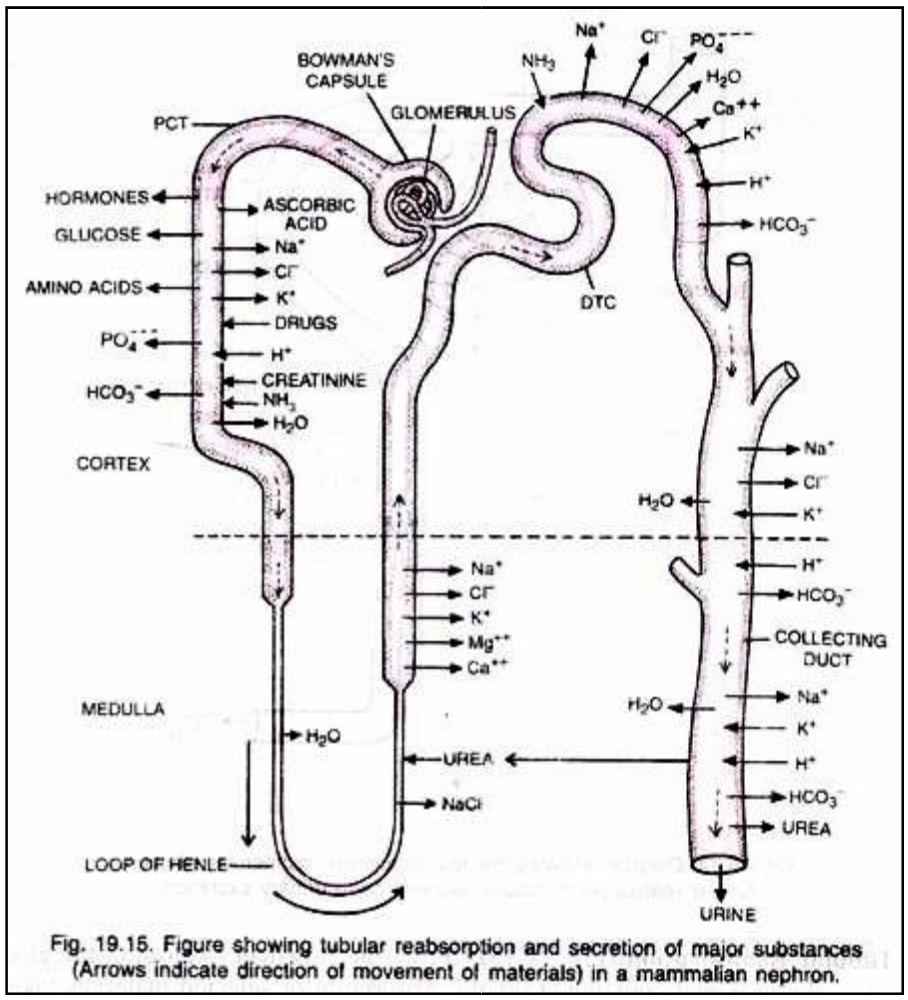


Fig. 19.15. Figure showing tubular reabsorption and secretion of major substances (Arrows indicate direction of movement of materials) in a mammalian nephron.

(i) Proximal Convoluted Tubule (PCT):

About 65 per cent of the glomerular filtrate is normally reabsorbed in the proximal convoluted tubule before reaching the loop of Henle. Glucose, amino acids, vitamins, hormones, sodium, potassium, chlorides, phosphates, bicarbonates, much of water and some urea from the filtrate are absorbed.

Sulphates and creatinine are not reabsorbed. Sodium and potassium are reabsorbed by primary active transport. Glucose and amino acids are reabsorbed by secondary active transport. Water is reabsorbed by osmosis. Chloride ions, urea and other solutes are reabsorbed by diffusion. The filtrate is isotonic to blood plasma.

(ii) Loop of Henle:

It consists of descending limb and ascending limb.

(a) Descending limb of loop of Henle:

As the filtrate flows in it, its water is reabsorbed due to increasing osmolality of interstitial fluid. Sodium and other solutes are not reabsorbed here. The filtrate becomes hypertonic to blood plasma.

(b) Ascending limb of loop of Henle:

It is impermeable to water but permeable to K^+, Cl^- and Na^+ and partially permeable to urea. Thus in the thick ascending limb of the loop of Henle sodium, potassium, calcium, magnesium, and chloride are reabsorbed. The filtrate becomes hypotonic to blood plasma.

(iii) Distal convoluted tubules (DCT):

There is active reabsorption of sodium ions from the filtrate under the influence of aldosterone (hormone secreted by the cortex of adrenal glands). Chloride ions are also reabsorbed in the distal convoluted tubules. Water is reabsorbed here under the influence of antidiuretic hormone (ADH) secreted by posterior lobe of pituitary gland. This makes the filtrate isotonic to blood plasma.

Collecting duct:

From distal convoluted tubule filtrate enters the collecting duct where further reabsorption of water takes place. Now the filtrate becomes more concentrated which makes filtrate hypertonic to blood plasma. The entire duct is permeable to water.

Thus a considerable amount of water is reabsorbed in the collecting duct under the influence of ADH. Sodium is reabsorbed in the collecting duct under the influence of aldosterone. The filtrate is now called urine. Thus urine is hypertonic to blood and isotonic to medullary fluid.

Some substances such as glucose and amino acids are reabsorbed actively into the blood by the active transport and, therefore, they do not appear in the urine. These substances are called the high threshold substances.

Renal threshold of a substance is its highest concentration in the blood up to which it is totally reabsorbed from the glomerular filtrate. The renal threshold of glucose is about 180 mg per 100 ml blood. When this value is exceeded, glucose begins to appear in the urine.

Process # 3. Tubular Secretion:

The cells of the renal tubule no. only remove substances from the filtrate by the process of reabsorption and send them to the blood capillaries (peritubular) but also excrete additional wastes from the blood stream into the filtrate by the process of secretion. Thus tubular secretion is the opposite of tubular reabsorption.

It occurs as follows:

(i) Creatinine, hippuric acid, pigments, drugs including penicillin are actively secreted into the filtrate in the proximal convoluted tubule from the interstitial fluid. Hydrogen ions and ammonia are also secreted into the proximal convoluted tubule.

(ii) Urea enters the filtrate by diffusion in the thin segment of the ascending limb of loop of Henle.

(iii) Potassium, hydrogen ions, ammonia, HCO_3" ions are secreted by active transport into the filtrate in the distal convoluted tubule.
Maximum hydrogen secretion occurs in the proximal convoluted tubule. Removal of hydrogen ions and ammonia from the blood in the proximal convoluted tubule and distal convoluted tubule helps to maintain the pH of the blood between 6 to 8 (pW of blood is usually 7.4)

Tubular secretion probably plays a minor role in the function of human kidneys but in animals like marine fishes and desert amphibians, whose nephrons do not possess developed glomeruli, their urine is formed mainly by the tubular secretion of urea, creatinine and mineral ions. Kidneys excrete about 1.5 litres of urine in a day.

Essay # 1. Introduction to Kidney:

A large number of waste products are produced in the body as a result of metabolic activities. The main waste products are carbon dioxide, water, and nitrogenous compounds. The retention of these products produces a harmful effect on the normal health.

Therefore, the removal of these products from the body is a must. Carbon dioxide is removed mainly through lungs and water as well as nitrogenous compounds are removed through urogenital system. The kidneys are the most important component of this system.

The kidneys are two in number, usually bean shaped, and exist behind the peritoneum on either side of the vertebral column extending from the 12th thoracic to the 3rd lumbar vertebra. Each kidney weighs about 120-170 grams and is about 11-13 cms. long, the left being larger than the right one.

Each kidney is found to consist of two main parts by section. The outer part is called cortex and the inner one is medulla. The cortex consists of a large number of glomeruli and convoluted tubules. The medulla is composed of renal tubules projecting into a cavity towards the inner region of the kidney called the pelvis, the region where the renal artery and vein enters and leaves the kidney respectively.

Nephron –Basic Unit of Kidney:

It is a functional basic unit of kidney. Each kidney is provided with about one million nephrons containing the glomerulus and the tubule. The glomerulus is a network of afferent and efferent capillaries.

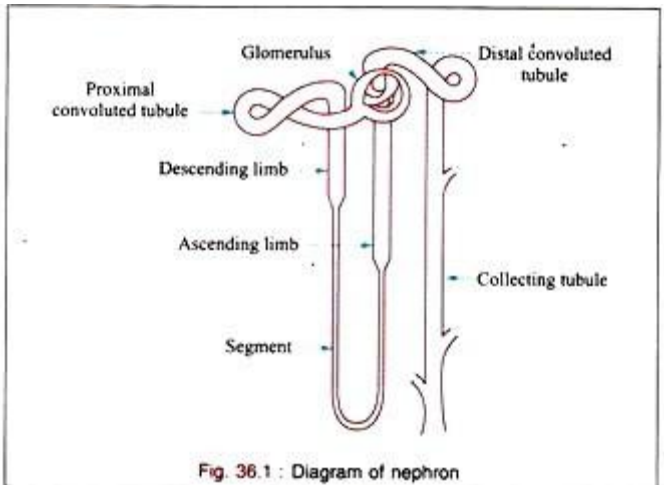


Fig. 36.1 : Diagram of nephron

Each glomerulus is surrounded by a double-walled epithelial sac known as Bowman 's Capsule which leads to the tubule which is divided into three

parts—proximal convoluted tubule, loop of Henle, and the distal convoluted tubule.

The Proximal Convoluted Tubule (PCT) is about 45 mm long and 50 mm in diameter. This lies in the cortex along with glomerulus. Its lumen is continuous with that of the Bowman's Capsule. It consists of cells with scalloped outline and brush border. The brush border is formed by numerous microvilli which increases the surface enormously for absorption.

The loop of Henle consists of three parts—the descending limb, a thin segment, and an ascending limb. The proximal convoluted tubule opens into the descending limb which is continued into the thin segment from where the ascending limb arises. The whole loop of Henle is lined by a single layer of flattened epithelial cells.

The ascending limb of the loop of Henle continues into the distal convoluted tubule (DCT) which finally opens into a collecting tubule or duct which carries the urine to the renal pelvis from where it is carried to the bladder by the ureter.

The distal convoluted tubule commences near the pole of the glomerulus and establishes a close proximity to the afferent arteriole of its parent glomerulus. The DCT contains cuboidal epithelium.

Nephrons are mainly of two types—cortical and juxtamedullary. The loop of Henle of the juxtamedullary is long and dips deep into the substance of the medulla. But the loop of Henle of cortical is short and only a very small part of it dips into the medullary tissue and the greater part remains embedded in the cortical substances.

Moreover, the glomeruli of the juxtamedullary lie very close to the medulla while those of cortical lie close to the surface of the kidney. The juxtamedullary nephrons constitute 20 per cent of nephrons, while the cortical nephrons constitute 80 per cent of the total nephrons. These two types of nephrons have the same common function.

Blood Supply of the Kidneys:

The short renal artery arising from the abdominal aorta supplies the blood to the kidney. The renal artery after entering the kidney divides into a number of arterioles—the afferent arterioles which further branch into capillaries and enter into each glomerulus.

The capillaries then join to form another arteriole—the efferent arteriole which opens into another set of capillaries called peritubular capillaries surrounding the proximal tubule, the loop of Henle, and the distal tubule. Ultimately, the capillary set opens into a venule which joins with other venules to form the renal vein. The renal vein then opens into the inferior vena cava.

Blood Flow to Kidney through the Nephron:
The blood flows through both the kidneys of an adult weighing 70 kg at the rate of about 1200 ml/mt. The portion of the total cardiac output (about 560 ml/ mt.) which passes through the kidneys is called the renal fraction. This is about 560/1200 ml per minute, i.e., about 21 per cent.

There are two sets of capillaries—the glomerulus and the peritubular. These two capillaries are separated from each other by the efferent arteriole which contributes sufficient resistance to blood flow. The glomerular capillary bed provides a high pressure of about 70 mm Hg, while the peritubular bed provides a low pressure about 13 mm Hg.

The pressures in the artery and vein are 100 mm of Hg. and 8 mm of Hg respectively. The high pressure in the glomerulus exerts the filtering of fluids continually into the Bowman's Capsule. The low pressure in the peritubular capillary system, on the other hand, functions in the same way as the usual venous ends of the tissue capillaries with the fluid being absorbed continually into the capillaries.

Functions of Kidney:
a. Kidney eliminates excess of certain nutrients such as sugar and amino acids when their concentration increases in the blood.

b. It removes certain non-volatile waste products such as urea, uric acid, creatinine, and sulphates, etc. from the body.

c. It eliminates certain foreign or toxic substances such as iodides, pigments, drugs, and bacteria, etc. from the blood.

d. It regulates hydrogen ion concentration of the blood by removing excess of nonvolatile acids and bases.

e. It maintains the osmotic pressure of the blood by regulating the excretion of water and inorganic salts and thus preserves the constant volume of the circulating blood.

f. It regulates the arterial blood pressure by causing the secretion of the hormone renin.

g. It maintains the erythrocyte production by excreting the secretion of the hormone erythropoietin.

Hormonal regulation:: The function of kidney is regulated by three important hormones. These hormones are aldoster-one (from adrenal cortex), parathormone (from parathyroid), and vasopressin (from hypophyseal posterior lobe).

Aldosterone restricts the excretion of Na+ and stimulates the excretion of K+. Parathormone stimulates excretion of phosphate. Vasopressin, the antidiuretic hormone, is held responsible mainly

for the reabsorption of water. In the absence of this hormone, a large amount of very dilute urine is excreted.

Mechanism of Action of Diuretics: a. Diuretics, the drugs, enhance losses of water and salt via the urine through inter-ference with normal reabsorptive mecha-nisms.

b. Osmotic diuretics are nonreabsorbable substances which increase tubular osmolarity. The osmotic substances which limit the amount of water. Osmotic diuresis is responsible for the serious dehydration which accompanies diabetic ketoacidosis.

c. Diamox is the inhibitor of carbonic anhydrase. It blocks both HCO_3^- reabsorption in the proximal tubule and regeneration in the distal tubule.

d. Thiazide diuretics, furosemide, ethacrynic acid and mercurials all inhibit chloride rea-bsorption in the ascending limb.

Urine is a liquid byproduct of the body secreted by the kidneys through a process called urination and excreted through the urethra. The normal chemical composition of urine is mainly water content, but it also includes nitrogenous molecules, such as urea, as well as creatinine and other metabolic waste components. Other substances may be excreted in urine due to injury or infection of the glomeruli of the kidneys, which can alter the ability of the nephron to reabsorb or filter the different components of blood plasma.

Normal Chemical Composition of Urine: Urine is an aqueous solution of greater than 95% water, with a minimum of these remaining constituents, in order of decreasing concentration:

- Urea 9.3 g/L., Chloride 1.87 g/L., Sodium 1.17 g/L., Potassium 0.750 g/L., Creatinine 0.670 g/L .
- Other dissolved ions, inorganic and organic compounds (proteins, hormones, metabolites).

Urine is sterile until it reaches the urethra, where epithelial cells lining the urethra are colonized by facultatively anaerobic gram-negative rods and cocci. Urea is essentially a processed form of ammonia that is non-toxic to mammals, unlike ammonia, which can be highly toxic. It is processed from ammonia and carbon dioxide in the liver.

ABNORMAL TYPES OF URINE: There are several conditions that can cause abnormal components to be excreted in urine or present as abnormal characteristics of urine. They are mostly referred to by the suffix -uria. Some of the more common types of abnormal urine include:

- Proteinuria—Protein content in urine, often due to leaky or damaged glomeruli.
- Oliguria—An abnormally small amount of urine, often due to shock or kidney damage.
- Polyuria—An abnormally large amount of urine, often caused by diabetes.
- Dysuria—Painful or uncomfortable urination, often from urinary tract infections.
- Hematuria—Red blood cells in urine, from infection or injury.
- Glycosuria—Glucose in urine, due to excess plasma glucose in diabetes, beyond the amount able to be reabsorbed in the proximal convoluted tubule.

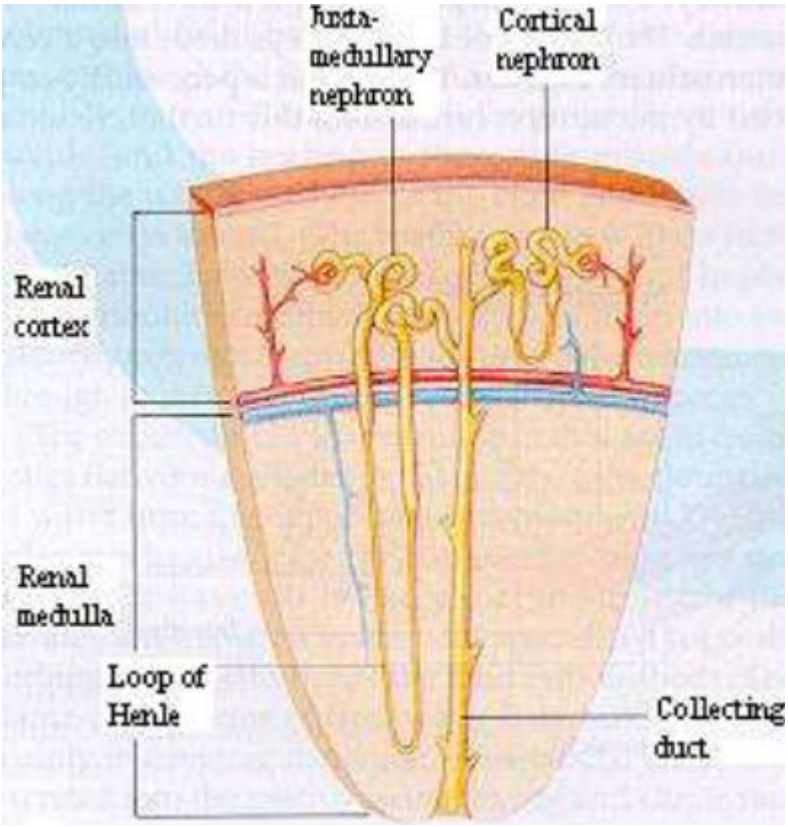
The two types of Nephrons

Cortical

•The loop of Henle does not extend past the cortex of the kidney.

Juxtamedullary

•Loop of Henle extends past the cortex and into the medulla of the kidney



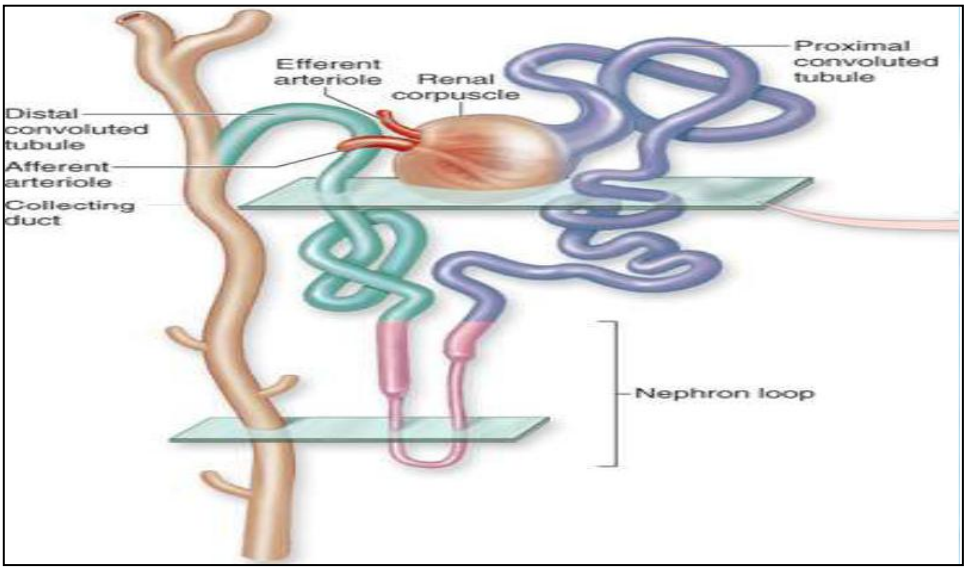
Physiology

The nephrons are the functional units of the kidney and are the site of:

1. Filtration of blood
2. Maintenance of Renal blood pressure
3. Formation of urine
4. Counter current mechanism
5. Acid-base balance
6. Regulation of electrolytes
7. Reabsorption of materials
8. Secretion of materials (production of hormones)
9. Excretion of wastes

1. Filtration of Blood

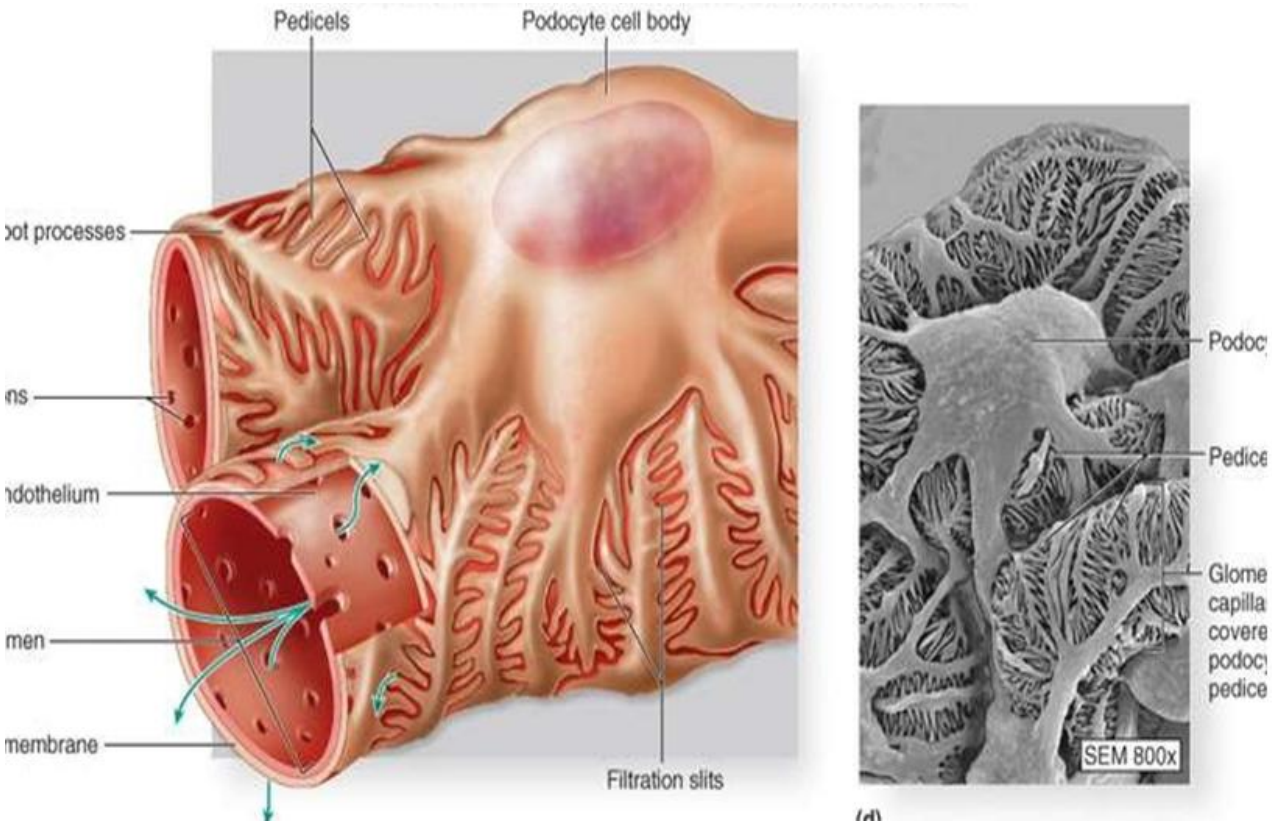
The glomerulus is the site of filtration of blood.



The Bowman’s capsule (basement membrane + podocytes)
• filters blood,
• hold back large molecules such as proteins,
• passes through small molecules such as water, salts, and sugar
• Aids in the formation of urine

PODOCYTES:

• Also known as visceral epithelial cells
• Cells in the Bowman's capsule in the kidneys that wrap around the capillaries of the glomerulus leaving slits between them.
• They are involved in regulation of glomerular filtration rate (GFR). When podocytes contract, they cause closure of filtration slits. This decreases the GFR by reducing the surface area available for filtration**.**



2. Maintenance of Renal Blood Pressure

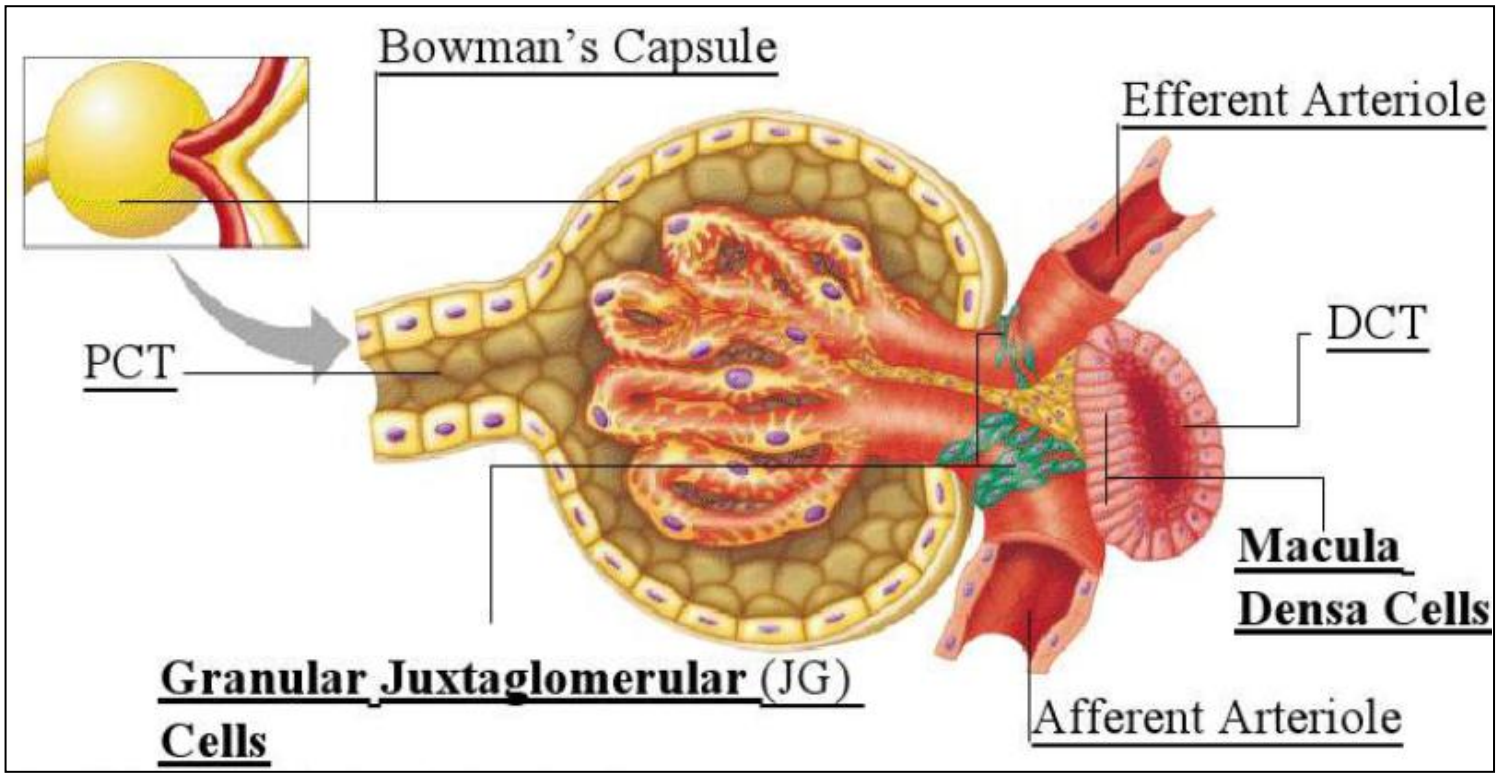
• This process is achieved by the Juxtaglomerular apparatus.

The three cellular components of the apparatus are the

1. juxtaglomerular cells

2. macula densa,

3. extraglomerular mesangial cells



Function of the JC cells

1. Release of Renin

Stimulus : Low blood pressure

Action : Release of Renin

Angiotensin ⟶ Angiotensin I ⟶ Angiotensin II

Angiotensin II

- It acts as a vasoconstrictor to raise blood pressure.
- It stimulates the release of aldosterone hormone from the adrenal cortex.

2. Release of Aldosterone hormone

- It stimulates the DCT to reabsorb salt

3. Reabsorption of salt (NaCl)

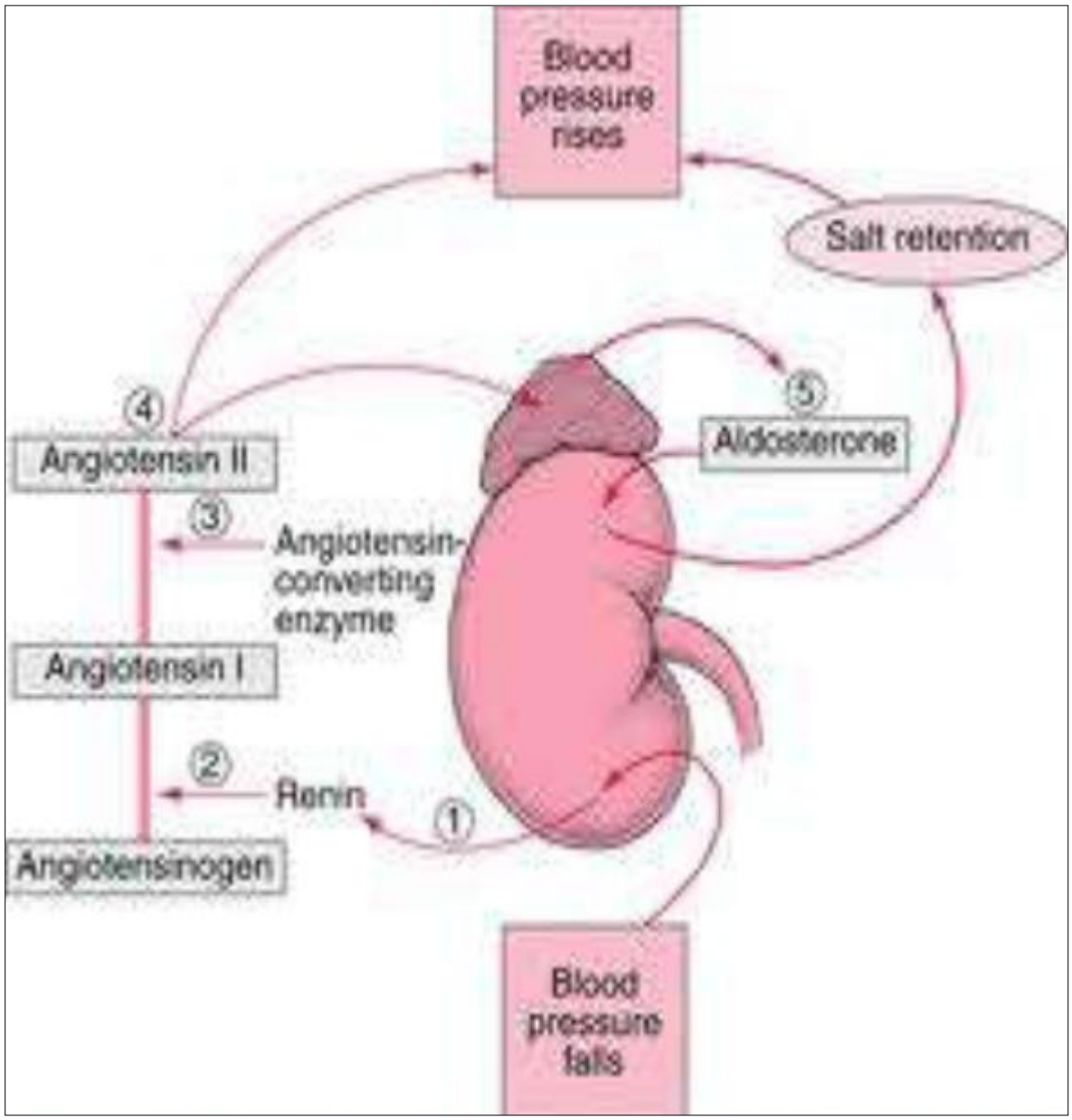
- Salt reabsorbtion induces the movement of water to the blood by osmosis thereby raising the blood volume and hence increasing the blood pressure.

Function of the Macula Densa Cells

- It monitors the salt content of the blood.
- If concentration of salt is raised, the macula densa cells inhibit the release of renin from the JC cells.
- No release of renin No angiotensin II , No aldosterone . Blood pressure decreases until it is sent back to normal

Function of the extra glomerular mesangial cells

- It secretes erythropoietin
- Erythropoietin is a glycoprotein hormone which controls erythropoiesis or red blood cell production.



8. Secretion of substances

Release of several substances occur in order to aid in the functions of the kidney:

1. Calcitriol (activated form of vitamin D promotes intestinal absorption of calcium and the renal reabsorption of phosphate)

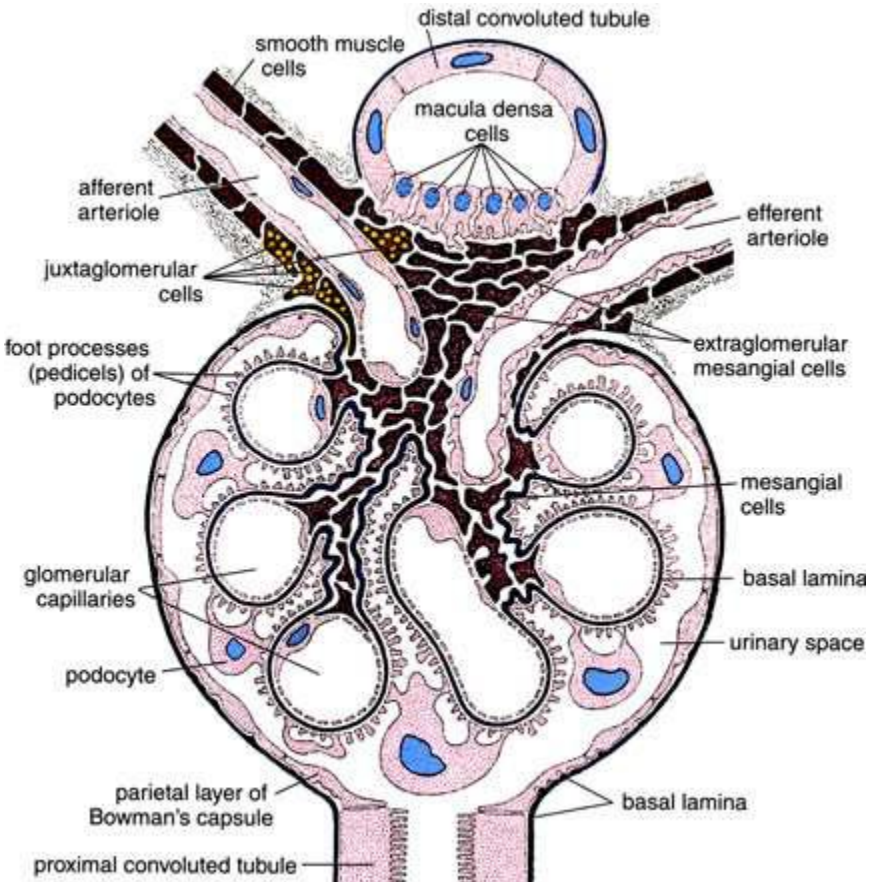
2. renin,

3. Erythropoietin

4. ADH

5. Prostaglandins

6. Kinins
7. 1,25-dihydroxyvitamin D3



Excretion of wastes

The kidney is also involved in the excretion of wastes such as:

1. Urea (from protein metabolism)
2. Uric acid (from nucleic acid metabolism)
3. Creatinine (from metabolic breakdown of creatine phosphate)
4. End-products of Hb metabolism
5. Metabolites of hormones
6. Foreign substances: drugs, pesticides, other chemicals ingested in food

Finding the amount of a substance excreted per unit time

Given

- Amount filtered in gNaCl/day
- Amount reasorbed in gNaCl/day
- Amount excreted in gNaCl/day

Amount excreted = Amount filtered – Amt reabsorbed