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 selective 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.

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 fltration.

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 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. 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.

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.**

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***

Glomerular capillary pressure is the pressure 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 glomeruli. 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.

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 = GCP -- COP + HP

$$\left\{ \text{Glomerular capillary pressure} - \text{Colloidal osmotic pressure} + \text{Hydrostatic pressure in Bowman capsule} \right\}$$

$$= 60 - (25 + 15) = 20 \text{ mm Hg.}$$

<u>Factors regulating (affecting) GFR</u>

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 :- Tubulo glomerular feedback is the mechanism that regulates GFR through renal tubule and macula densa . Macula densa of juxtaglomerular apparatus in the terminal portion of thick ascending limb 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. Macula densa detects the sodium chloride concentration via **Na+K+ 2Cl– cotransporter (NKCC2).** When the concentration of sodium chloride increases in the filtrate the GFR increases, concentration of sodium chloride increases in the filtrate. Macula densa **releases adenosine** from ATP. Adenosine causes constriction of afferent arteriole. So the blood flow through glomerulus decreases leading to decrease in GFR. Adenosine acts on afferent arteriole **via adenosine A1 receptors**. There are several other factors, which increase or decrease the sensitivity of tubule glomerular feedback.

Factors increasing the sensitivity of tubule glomerular feedback:

i. Adenosine

ii. Thromboxane

iii. Prostaglandin E2

iv. Hydroxyeicosatetranoic acid.

Factors decreasing the sensitivity of tubule glomerular feedback:

i. Atrial natriuretic peptide

ii. Prostaglandin I2

iii. Cyclic AMP (cAMP)

iv. Nitrous oxide.

When the concentration of sodium chloride decreases in the filtrate the GFR decreases, concentration of sodium chloride decreases in the filtrate. **Macula densa secretes prostaglandin (PGE2), bradykinin and renin. PGE2 and bradykinin cause dilatation of afferent arteriole. Renin induces the formation of angiotensin II, which causes constriction of efferent arteriole**. The dilatation of afferent arteriole and constriction of efferent arteriole leads to increase in glomerular blood flow and GFR.

3. Glomerular Capillary Pressure:-

Glomerular filtration rate is directly proportional to glomerular capillary pressure. Normal glomerular capillary pressure is 60 mm Hg. When glomerular capillary pressure increases, the GFR also increases. Capillary pressure, in turn depends upon the renal blood flow and arterial blood pressure.

4. Colloidal Osmotic Pressure :-

Glomerular filtration rate is inversely proportional to colloidal osmotic pressure, which is exerted by plasma proteins in the glomerular capillary blood. Normal colloidal osmotic pressure is 25 mm Hg. When colloidal osmotic pressure increases as in the case of dehydration or increased plasma protein level GFR decreases. When colloidal osmotic pressure is low as in hypoproteinemia, GFR increases.

5. Hydrostatic Pressure in Bowman Capsule :-

GFR is inversely proportional to this. Normally, it is 15 mm Hg. When the hydrostatic pressure increases in the Bowman capsule, it decreases GFR. Hydrostatic pressure in Bowman capsule increases in conditions like obstruction of urethra and edema of kidney beneath renal capsule.

6. Constriction of Afferent Arteriole:-

Constriction of afferent arteriole reduces the blood flow to the glomerular capillaries, which in turn reduces GFR.

7. Constriction of Efferent Arteriole:-

If efferent arteriole is constricted, initially the GFR increases because of stagnation of blood in the capillaries. Later when all the substances are filtered from this blood, further filtration does not occur. It is because, the efferent arteriolar constriction prevents outflow of blood from glomerulus and no fresh blood enters the glomerulus for filtration.

8. 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.

9. 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. So, initially there is increase in filtration but later it decreases. 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.

10. 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.

11. 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.

12. 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

13. Hormonal and Other Factors Many hormones and other secretory factors alter GFR by affecting the blood flow through glomerulus.