

■ 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.

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

Normal filtration fraction varies from 15% to 20%.

■ 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.

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 =

$$\left\{ \begin{array}{l} \text{Glomerular capillary pressure} \\ \text{—} \\ \text{Colloidal osmotic pressure} \\ \text{+} \\ \text{Hydrostatic pressure in Bowman capsule} \end{array} \right\}$$

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

Net filtration pressure is about 20 mm Hg and, it varies between 15 and 20 mm Hg.

Starling Hypothesis and Starling Forces

Determination of net filtration pressure is based on Starling hypothesis. Starling hypothesis states that the net filtration through capillary membrane is proportional to hydrostatic pressure difference across the membrane minus oncotic pressure difference. Hydrostatic pressure within the glomerular capillaries is the glomerular capillary pressure.

All the pressures involved in determination of filtration are called **Starling forces**.

■ FILTRATION COEFFICIENT

Filtration coefficient is the GFR in terms of net filtration pressure. It is the GFR per mm Hg of net filtration pressure. For example, when GFR is 125 mL/min and net filtration pressure is 20 mm Hg.

$$\begin{aligned} \text{Filtration coefficient} &= \frac{125 \text{ mL}}{20 \text{ mm Hg}} \\ &= 6.25 \text{ mL/mm Hg} \end{aligned}$$

■ 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**. Refer previous chapter for details.

2. Tubuloglomerular Feedback

Tubuloglomerular feedback is the mechanism that regulates GFR through renal tubule and macula densa (Fig. 52.2). **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 $\text{Na}^+\text{-K}^+\text{-2Cl}^-$ cotransporter (NKCC2).

When the concentration of sodium chloride increases in the filtrate

When GFR increases, concentration of sodium chloride increases in the filtrate. Macula densa releases **adenosine**

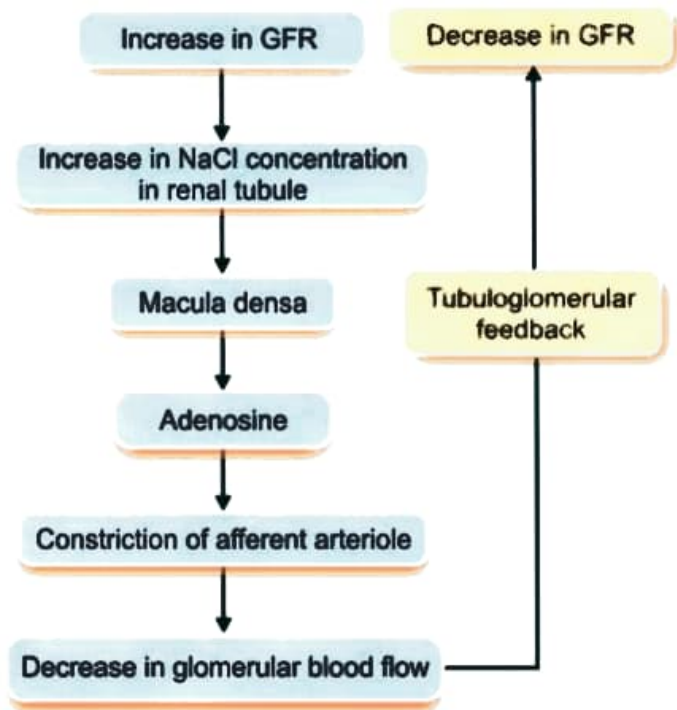


FIGURE 52.2: Tubuloglomerular feedback.

NaCl = Sodium chloride, GFR = Glomerular filtration rate.

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 A_1 receptors.

There are several other factors, which increase or decrease the sensitivity of tubuloglomerular feedback.

Factors increasing the sensitivity of tubuloglomerular feedback:

- i. Adenosine
- ii. Thromboxane
- iii. Prostaglandin E_2
- iv. Hydroxyeicosatetraenoic acid.

Factors decreasing the sensitivity of tubuloglomerular feedback:

- i. Atrial natriuretic peptide
- ii. Prostaglandin I_2
- iii. Cyclic AMP (cAMP)
- iv. Nitrous oxide.

When the concentration of sodium chloride decreases in the filtrate

When GFR decreases, concentration of sodium chloride decreases in the filtrate. Macula densa secretes prostaglandin (PGE_2), bradykinin and renin.

PGE_2 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 (Chapter 51). 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 (refer Chapter 51 for details).

13. 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
- iii. cAMP
- iv. Dopamine
- v. Endothelial-derived nitric oxide
- vi. Prostaglandin (PGE_2).

Factors decreasing GFR by vasoconstriction

- i. Angiotensin II
- ii. Endothelins
- iii. Noradrenaline
- iv. Platelet-activating factor
- v. Platelet-derived growth factor
- vi. Prostaglandin (PGF_2).