Glomerular filtration

Means filtration of fluid from the blood in the glomerular capillaries to the cavity of Bowman's capsule by pressure gradient.

Glomerular filtration rate (GFR):-

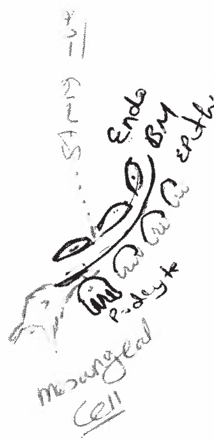
It is the volume of fluid filtered in all nephrons of both kidneys each minute.

Normal value of GFR:-

125 ml/ minute = 180 liters / day. In the everage sized normal man. It is 10% lower in woman.

Its magnitude correlates fairly well with the surface area of the body.

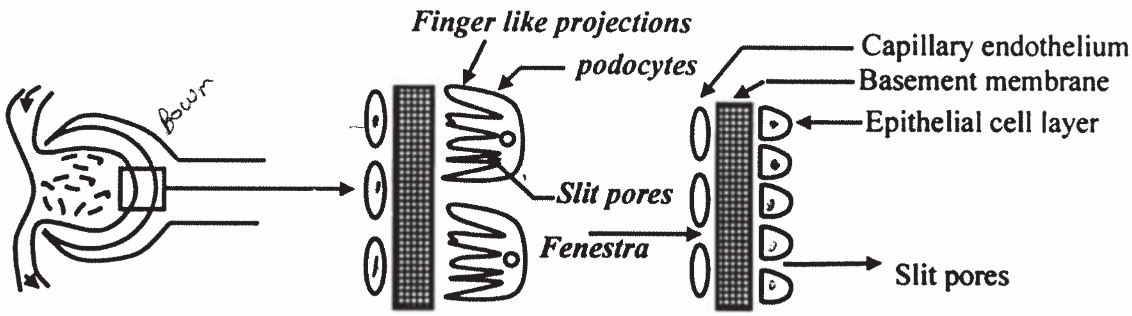
Glomerular membrane:-



It is the membrane through which filtration occur.

Structure:- It is formed of 3 layers:-

1. The capillary endothelial cells lining the glomerular capillaries:- They are perforated by thousands of small holes called fenestrae.
2. The basement membrane:- Composed mainly of a meshwork of fine fibrils that has large spaces through which fluid can filter.
3. Epithelial cells that line the outer surface consists mainly of finger-like projections that cover the basement membrane. These fingers form slits called slit pors through which fluid can filter.



It has 2 important characters:-

1) High permeability:- 100-500 times the permeability of usual tissue capillaries
2) High degree of selectivity for the molecules passing through it:-
   1. Molecules with MW 10,000 or less pass the membrane freely (as easily as water).
   2. Molecules with MW more than 10,000, their permeability is inversely proportionate to their MW.
   3. Molecules with MW more than 80,000 cannot pass through membrane.

MW	Permeability	Example
5000	**1(100%)**	**Inulin**
30.000	**0.5(50%)**	**Small proteins**
65.000	**0.05(5%)**	**Hemoglobin**
69.000	**0.005(0.5%)**	**Albumin**
80.000	**0**	**Globulins**

The causes of this high degree of selectivity are:-

1. **The sizes of the pores** in the membrane:- 8 nanometers (80 angstroms).
2. **The strong negative charge of the proteins lining the pores:-** It repels negatively charged substances. The negative charge of albumin explain its poor permeability through glomerular membrane in relation to its MW.

Note:- Mesengial cells:- they are stellate cells that send processes between the endothelium and basement membrane. They are found between capillary loops. They are contractile and also secrete various substances.

Composition of the filtrate: -

It is similar to plasma except: -

1. It contains only minute amount of albumin (0.03gm%) (0.5%that of the plasma).
2. The negatively charged ions (Cl^- and HCO_3^-) are 5% more and the positively charged ions (Na^+ and K^+) are 5% less in the filtrate than in the plasma. This is due to the non diffusibility of the plasma proteins (which is negatively charged), which lead to a Donnan effect on the diffusable ion distribution.

For all practical purposes, **it is enough to say that the glomerular filtrate is composed of Plasma minus plasma proteins.**

Filtration fraction:-

It is the fraction of renal plasma flow that becomes glomerular filtrate

$$= \frac{GFR}{RPF} = \frac{125}{650} = \frac{1}{5} \text{ OR } 20\%$$

Filtration forces (pressures):-

- **Forces helping filtration:-**
  1. The glomerular capillary blood pressure = 60 mm Hg
  2. Osmotic pressure of proteins in Bowman's capsule = zero normally
- **Forces opposing filtration:-**
  1. Osmotic pressure of plasma proteins in the glomerular capillary blood = 32 mm Hg.
  2. Pressure in Bowman's capsule = 18 mm Hg.

Net filtration pressure = 60 + 0 – 32 – 18 = **10 mm Hg**.

- **Filtration coefficient (K_f):-** It is the fluid filtered by all nephrons in both kidneys per minute **if the filtration pressure is only 1 mm Hg**.

  Normally K_f = 12.5 ml/min/mmHg.

  GFR = Kf x filtration pressure = 12.5 x 10 = **125ml/min**.

Factors affecting glomerular filtration:-

1- Glomerular capillary pressure:-

↑glomerular capillary pressure→↑GFR and vice versa. Glomerular capillary pressure is affected by:-

1) Renal blood flow:- ↑ renal blood flow →↑glom blood flow →↑glomerular capillary pressure →↑GFR and vice versa.

2) Diameter of afferent arteriole:-

- Dilatation →↑glomerular blood flow →↑gom. cap.p. →↑GFR.
- Constriction has a reverse effect.

3) Diameter of efferent arteriole:-

- **Dilatation** →↓**glom cap.p.** →↓GFR.
- Constriction:-
  - **Mild constriction** →↑glom. Cap.P. →only slight ↑in GFR due to **associated ↓in glom. blood flow.**
  - **Moderate and severe constriction** →↓GFR due to marked ↓ in glom. blood flow.

4)Sympathetic stimulation:- Leads to constriction of afferent arteriole →↓ glom.cap. pressure →↓GFR.

5) Arterial blood pressure (ABP):-

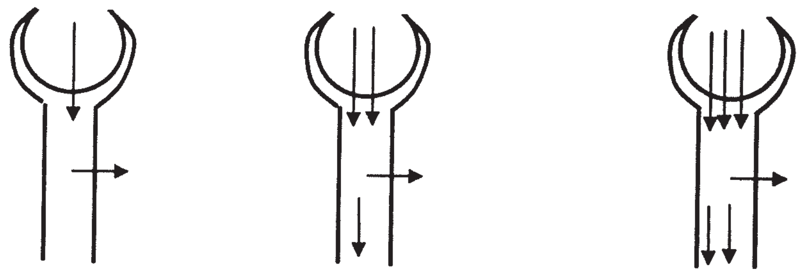
Changes in ABP **within the physiological range** (80- 180 mm Hg) has a **little effect** on renal blood flow or GFR due to autoregulation mechanism.

***Autoregulation** is a mechanism by which RBF and GFR are maintained at a nearly constant rate inspite of changes in ABP within the physiological range.

***Significance of autoregulation of GFR:-**

It allows the glomerular filtrate to flow into the tubular system at an appropriate rate for tubular function thus allowing the unwanted substances to pass in urine , while reabsorping the wanted substances.

- Too little GFR →Slow tubular flow → all of it will be absorbed → reabsorption of unwanted substances.
- In contrast, too high GFR →rapid tubular flow →loss of wanted substances in urine.



Too low GFR→reabs. Of Unwanted subs. — *Normal GFR* — *Too high GFR→loss of wanted subs. In urine*

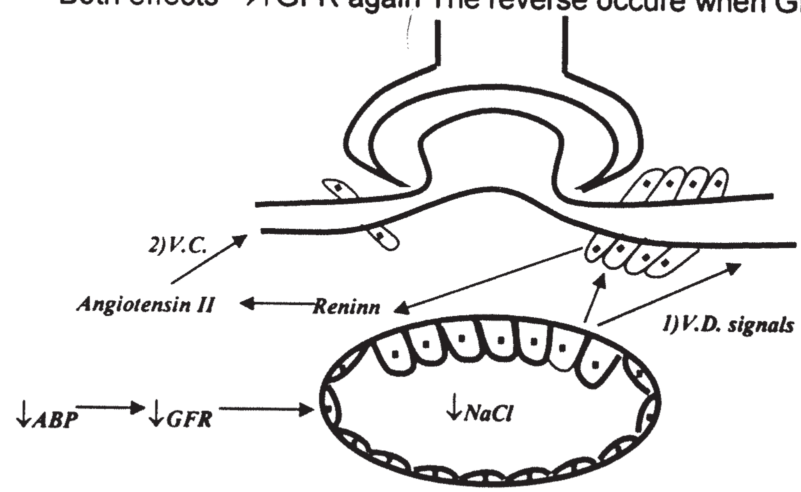
Mechanism of autoregulation:- 2 mechanisms

a. Tubuloglomerular feedback mechanism:-

↓ GFR→ overabsorption of Na Cl in the ascending limb of loop of Henle →↓Na Cl load at macula densa. This leads to:-

1. Dilatation of afferent by signals from macula densa.
2. Constriction of efferent through renin secretion from JG cells → formation of angiotensin II which constricts the efferent only (the afferent is not sensitive to angiotensin.II).

Both effects →↑GFR again The reverse occure when GFR↓.



b. Myogenic mechanism:-

↑ABP→ stretch of the wall of the afferent →secondary contraction of afferent →↓RBF→no change in GFR. The reverse occur with ↓ ABP.

However this mechanism has not yet been proved.

2- Osmotic pressure of proteins in Bowman's capsule:-

When increased → ↑ GFR and vice versa.

3- Osmotic pressure of plasma proteins:-

↓Osmotic pressure of plasma proteins:- as in hypoproteinemia →↑GFR and vice versa.