Glomerular filtration rate (GFR) is the volume of plasma that is filtrated by all glomeruli each minute.

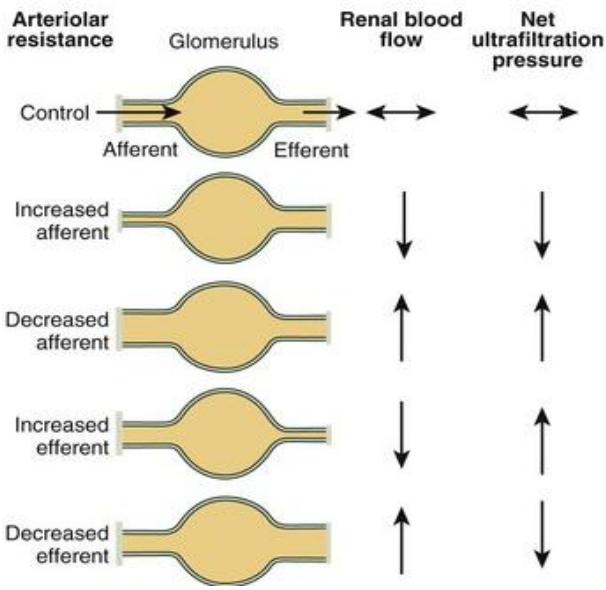
- GFR=125 ml/min in male (female is 10%less) or 180 L/day while normal urine volume is 1L/day → 99%of glomerular filtrate is normally reabsorbed by tubule and 1% is excreted.
- GFR = filtration pressure X kf (membrane permeability x S.A)

Factors affecting GFR :

1. ↑ Kf raises GFR and ↓ Kf reduces GFR.
   - It is not change greatly from normal except when the kidneys become diseased by ↓the number of functional glomerular capillaries (↓ the surface area) or by ↑ the thickness of the glomerular capillary basement membrane. Ex: DM and Hypertension
   - If one kidney is removed (half of the functioning nephrons lost), GFR decreases only about 25% because the other nephrons compensate

2. Glomerular capillary hydrostatic pressure ,which is affected by
   I. Systemic blood pressure (its effect is buffered by autoregulatory mech.)
   II. Renal blood flow.
   III. Afferent arteriole resistance:
   - Constriction (sympathetic stimulation) →↓blood flow→↓ G.pr.→↓ GFR.
   - Dilatation → ↑Blood flow .→↑ G.pr.→↑ GFR.

   IV. Efferent arteriole resistance :
   - Mild Constriction →↑ resistance to out flow from the glomeruli→↑ G.pr. → ↑GFR.↓RBF
   - But in moderate or sever constriction the blood flow ↓at the same time →plasma will remain for a long period of time in the Glomerulus →large portion of plasma will be filtered out →↑colloid osm.pr. in the glomeruli→ paradoxical ↓GFR
   - Dilation →↓GFR



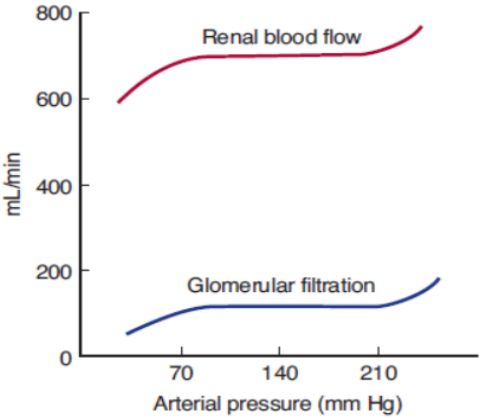
3. Glomerular capillary Colloid osmotic pressure :Affected by
    - plasma colloid osmotic pressure .
    - Filtration fraction (FF) : The fraction of plasma filtered by the glomerular capillaries . ↑fraction of filtered plasma →↑oncotic pressure in the glomerular capillaries→↓GFR
4. Bowman Capsule hydrostatic pressure: when ↑like in renal tubular obstruction (ex: stone) →↓GFR.

Regulation of renal blood flow and GFR

1. Auto regulation of renal blood flow and GFR

Is the tissue capacity to regulate its own blood flow despite a wide variation of systemic blood pressure. At a blood pressure range between 80-180 mmHg ,the renal vascular resistance change with the pressure so the renal blood flow and GFR is maintained constant .Theories of auto regulation are:

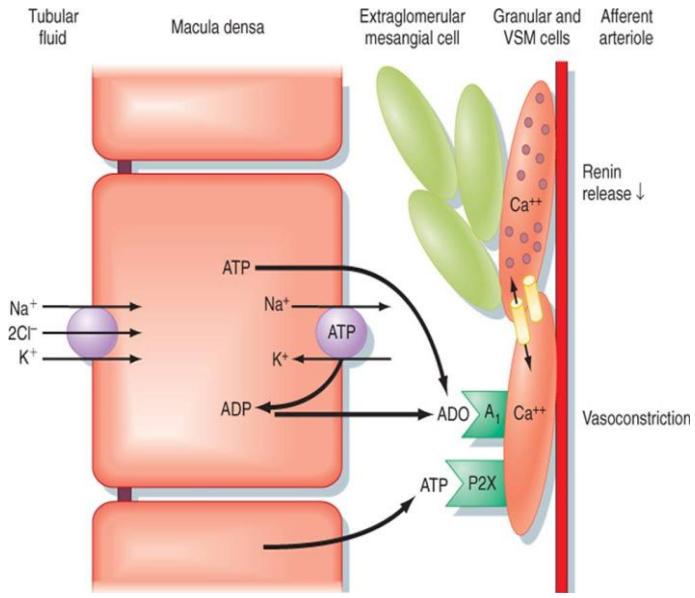
a) **Myogenic theory**: is property of the arteriolar smooth muscle to contract when it is stretched.
    - ↑blood pressure →stretching of the afferent arteriole wall → contraction of the smooth muscle →prevent ↑in RBF and GFR
    - ↓blood pressure →dilation of the afferent arteriole →prevent ↓in RBF and GFR.



b) **Tubuloglomerular feedback** : it links changes in Na ,CL concentration at the macula densa with the control of renal arteriolar resistance. How ?

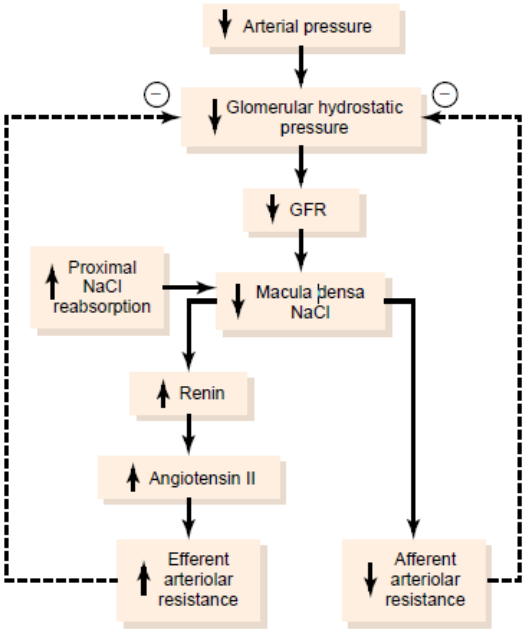
- ↑ MBP →↑ GFR →↑ Na, Cl in the macula densa→ enhances uptake of NaCl across the apical cell membrane of macula densa cells by (Na-K-2Cl cotransport) and ↑ Na-K ATPase activity → ATP hydrolysis and release of **adenosine** which acts on **adenosine A1** receptors in the plasma membrane of smooth muscle cells

surrounding the afferent arteriole → ↑ Ca ions → contraction & ↓GRF. Also adenosine inhibit renin release by granular cells in the afferent arteriole



- ↓ MBP →↓ in GFR →↓NaCl reaching the macula densa cells →:
  I.↓ the resistance to blood flow in the **afferent** arteriole which ↑ the hydrostatic pressure and help return GFR to normal
  II. Renin secretion from JGA, which convert angiotensinogen to angiotensin I which then converted to angiotensin II that → vasoconstriction of **efferent** arterioles→ raise the hydrostatic pressure and return GFR to normal.

2. Sympathetic stimulation : →constrict the renal arterioles and ↓ renal blood flow and GFR



Note : effect of sympathetic stimulation :

i. Direct simulation of juxtaglomeular cells through β1 adrenergic receptors →renin secretion
ii. ↑Na reabsorption
iii. Vasoconstriction mainly afferent arterioles

Estimation of GFR :

- Estimation of GFR are used clinically as an index of renal function and to assess the severity and the course of renal disease
- ↓ GFR means the disease is progressing while ↑GFR indicate recovery
- Estimation of GFR depends on the concept of clearance.

Plasma clearance :

Renal clearance of a substance is the volume of plasma that is completely cleared of the substance by the kidneys per unit time

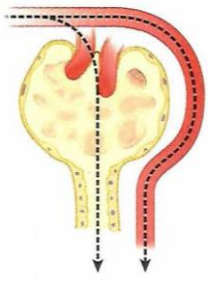
Us: Concentration of the substance in urine
V: urine flow rate
Ps: Concentration of the substance in plasma

- **Clearance = Us x V (excretion rate) / Ps** .

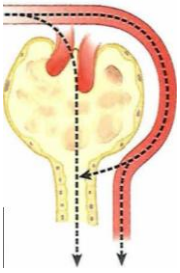
- Ideal substance to use is not toxic , not metabolized ,stable plasma conc., easily measured in the plasma and urine, completely filtered ,Neither reabsorbed nor secreted by the tubules (The amount Sub filtered /min = amount of Sub excreted in urine/min)
  Ps × GFR =Us × Vu
  GFR = Us x Vu / Ps = clearance .

Substances used to determine GFR

1. **Inulin:**
   - polysaccharide molecule present in the root of certain plants
   - Gold standard to determined GFR ;it fits the above criteria (completely filtered but neither reabsorbed nor secreted) but it is not used clinically .
   - Not produced by the body and it administered IV .
   - GFR = C inulin =125 ml/min

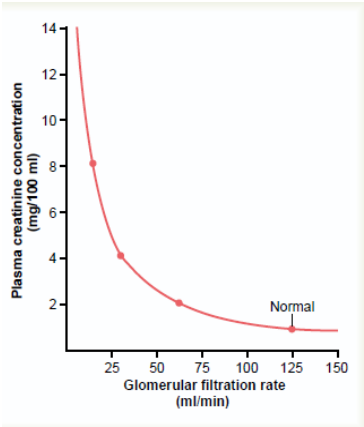


2. **Creatinine:** Is a by-product of muscle metabolism (endogenously produced →**It is a preferred indicator used to estimated GFR**
   - There is some secretion of creatinine by renal tubule →amount of creatinine excreted is a little > filtered (clearance > GF =140 ml /min)
   - Plasma creatinine concentration (PCr) can be obtained as an approximation of changes in GFR which is inversely proportional to



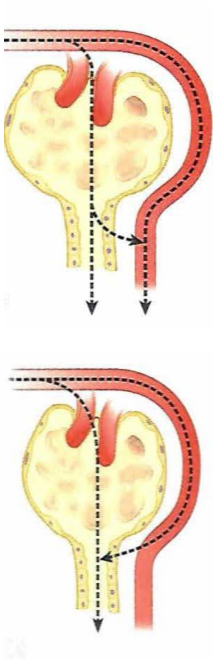
GFR: If GFR ↓by 50%, the kidneys will excrete only half as much creatinine →accumulation of creatinine in the body fluids →↑plasma concentration.

- Plasma creatinine is not a very sensitive measure of reduced GFR. At the beginning a large ↓of GFR produces a modest ↑ serum creatinine conc.
- It is best to do cretinine clearance (urine volume , plasma Cr conc.,urine Cr. conc.)



3. Urea :

- is a waste product formed during protein metabolism
- Easily filtered, not metabolized, not secreted but reabsorbed
- C urea < GFR = GFR-plasma reabsorbed C urea = 75 ml/min.
- Urea depends on protein metabolism and intake .



4. Para-aminohippurate (PAH) :

- PAH(exogenous substance) is completely filtered and secreted into the renal tubule by in the PCT. (90% cleared from plasma during a single pass)
- Used to measure renal plasma flow (RPF).
- C PAH =plasma filtered +secreted
  = GFR + secreted
  =125+475 = 600 ml/min =effective renal plasma flow

<u>Total Renal plasma flow</u> : clearance of PAH/ extraction ratio

- The extraction ratio (ER) : is calculated as the difference between the renal arterial conc and renal venous concentrations, divided by the renal arterial concentration
- ER = renal arterial PAH conc – Renal Venous PAH conc ./Reanl arterial PAH conc. = 90%
- Total Renal plasma flow = 600 ml/min / 90%
  = 660 ml/min

<u>Total blood flow</u> : total renal plasma flow /1- hematocrit

- Hct 0.45 and the total renal plasma flow is 660 ml/min, the total blood flow through both kidneys is 660/(1 - 0.45)= 1200 ml/min.