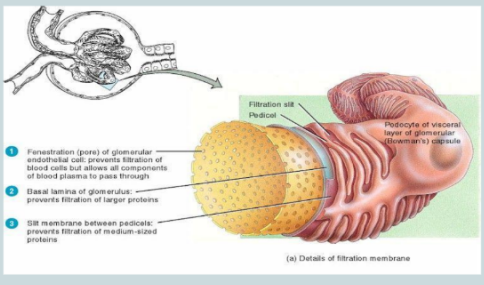
- Kidneys can also use **glutamine** to release glucose in gluconeogenesis.
- kidney is the main regulator of **fluid homeostasis**.
- **Calcitriol**: The active form of vitamin D, important for calcium absorption in the digestive system (the **activation of Vitamin D takes place in the kidney**).
- Filtration process takes place in the **glomerulus.**
- bowman's capsule and the glomerulus are called the **renal corpuscle**.
- Depending on the location of the nephron we have two types of nephros,

1) cortical nephrons (majority).
2) Juxtamedullary nephrons: on the borderline between the cortex and the medulla and those extend very deep in the medulla, **important in concentrating urine.**

The two types of nephrons and their features

Feature	Juxtamedullary nephron	Cortical nephron
Percentage	15%	85%
Renal capsule situation	Inner cortex is near medulla	Outer cortex is near periphery
Tubule blood supply	Vasa recta	Peritubular capillaries
Function	Concentrates urine (mainly), and also forms urine	Forms urine
Loop of Henle	Long Hairpin bend penetrates up to the tip of papilla	short Hairpin bend penetrates only to outer zone of medulla

- peritubular capillaries are called the vasa recta.
- Excretion = filtration - reabsorption + secretion.
- Filtration: **Passive** (depends on the hemodynamic forces, in the glomerulus), variable, **not** selective (except for proteins), averages 20% of RPF (20% filtered and 80% unfiltered).
- Reabsorption: highly variable and selective (because it is mostly an **active** process)
- Secretion: highly variable (because it depends on the availability of the substances that should be secreted)

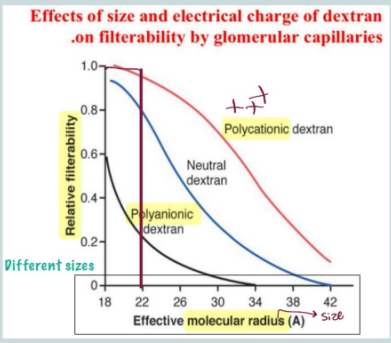


➢ Glomerular or Bowman's capsule:
• Outer: simple Squamous epithelium.
• Inner (Visceral): Podocytes, have projections called pedicles wrap around the glomerular capillaries.
➢ Juxtaglomerular cells: modified smooth muscle cells of the wall of afferent (or efferent) arterioles, proximate to the Macula Densa.
➢ Macula Densa: cells in the final part of thick ascending or DCT (for **renal autoregulation**).
➢ Mesangial cells: **contractile** cells that lie in the clefts btw afferent & efferent arterioles, function to regulate the surface area of filtration.
➢ Basal lamina contains negatively charged fibers, which will prevent negatively charged proteins from passing through (Albumin)
• Proximal Convoluted Tubule (PCT): Simple cuboidal epithelial cells with brush borders.
• Loop of Henle(LH): Simple Squamous (thin), Cuboidal(Thick).
• Distal Convoluted Tubule (DCT): simple cuboidal.
• Last part of DCT and Collecting Duct (CD): Simple cuboidal consisting of:
o Principal Cells: contains receptors for ADH and Aldosterone.
o Intercalated Cells: Blood PH regulation
-Cortical nephrons are Most numerous with short loop of henle.

Filtration and partial reabsorption: water and most of electrolytes in our body (Na+ , Cl-).
- The larger size the less filtrability, the lower molecular radius the higher filterability

Renal Handling of Water and Solutes

	Filtration	reabsorption	excretion
L/day Water	180	179	1
+Na mmol/day	25,560	25,410	150
Glucose gm/day	180	180	0
Creatinine gm/day	1.8	0 Poorly absorbed	1.8



- ***Edema***
- Some kidney diseases result in a damage of the glomerular Capillaries leading to an increase in their permeability to large proteins .
- Hence, Bowman's capsule colloid pressure will increase significantly leading to drawing more water from plasma to the capsule (i.e more filtered fluid).
- Proteins will be lost in the urine causing deficiency in the blood colloid pressure which worsens the situation, blood volume decreases and interstitial fluids increases causing ***edema***.

- Neutral dextran depends mainly on <u>size</u>.
- Even if the filtration process is a passive process , it also depends on the size and charge.
- **Filtration fraction (GFR / Renal Plasma Flow)**= 0.2 (i.e. 20% of plasma is filtered) (ratio between filtration rate to plasma flow rate).

*Renal plasma flow is not the same as blood flow (55% of blood is plasma), so blood flow rate = <u>1140</u> ml/min (<u>**55% * BF = PF**</u>; BF= 625ml/min/(55%)=1140 ml/min).
*RBF of 1140 ml/min = 22.8% of 5 liters (cardiac output) is required to have GFR of 125ml/min.
- Plasma flow rate = how much ml of plasma enters the two kidneys per minute.
- Proteinuria: 1) HTN 2) Diabetes 3) pregnancy (gestational proteinuric HTN (or pre-eclampsia)).
- <u>Glomerular blood hydrostatic pressure</u>: Bp that reaches the afferent arterioles from heart, equals 55 mmhg.
- <u>Capsular</u> (bowman's capsule) <u>hydrostatic pressure</u>, opposite in direction to the glomerular hydrostatic pressure and its low (15 mmhg).
- <u>Glomerulus colloid osmatic pressure (oncotic pressure)</u> = 30mmhg.
*no protein in bowman's capsule, so the osmatic pressure is <u>zero</u>.
- Net filtration pressure = +10 towards filtration. (From glomerular into bowman's capsule).

<u>If GFR is too high:</u> kidney will not be able to reabsorb the necessary substances efficiently, then, there will be loss a lot of substances like water, glucose, and amino acids.
<u>If GFR is too low:</u> waste products will stay (harmful) + <u>reabsorption will be more efficient than filtration</u> ➡️ a chance for the waste products to be reabsorbed.

<u>GFR = Net Filtration pressure x Kf</u>

Glomerular Capillary Filtration Coefficient (K_f)

- K_f = hydraulic conductivity x surface area

K_f = GFR/net filt pressure

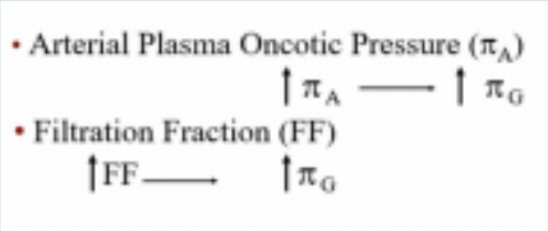
- Normally <u>not</u> highly variable
- Disease that can reduce K_f and GFR
- damage of capillaries, BM thickens,
  - chronic hypertension
  - obesity / diabetes mellitus
  - glomerulonephritis

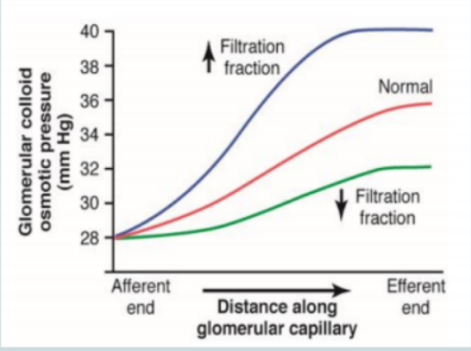
Determinants of Glomerular Filtration Rate

Normal Values:
GFR = 125 ml/min
Net <u>Filt</u>. Press = 10 mmHg
K_f = 12.5 ml/min per mmHg, or 4.2 ml/min per mmHg/ 100gm
(400 x greater than in many tissues)

- Tubular obstruction: increases the hydrostatic pressure (negative factor for the net filtration pressure), there will be reduction in GFR.
- Capillary oncotic pressure: تتناسب عكسيا مع الnet filtration pressure.

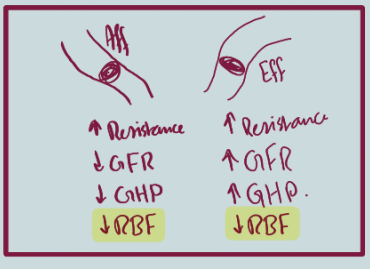
- Factors than increase oncotic pressure:
*In normal filtration fraction as we move away from afferent end, the colloid pressure will increase.
*net filtration pressure decreases as we move toward the efferent end because oncotic pressure increases.
- oncotic pressure is NOT easily regulated in the body, so body can't use it to regulate GFR.
- glomerulare hydrostatic pressure is a physiological regulator. (Arterial p↗; GHP↗; Net filt. Pressure↗; GFR↗).
Note: changes in the arterial pressure wouldn't affect GFR directly (effect is buffered by autoregulation).

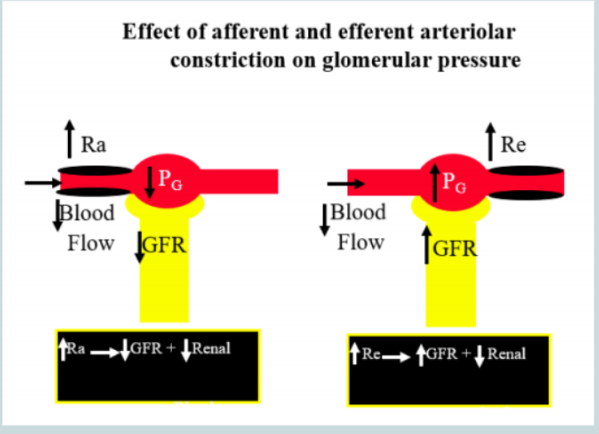




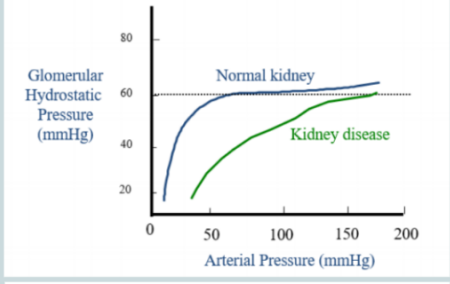
- afferent arteriolar resistance
When the diameter decreases, resistance increases, perfusion decreases and Glomerular Hydrostatic Pressure decreases. So Glomerular Hydrostatic Pressure will increase when we decrease afferent arteriolar resistance.

If we increase resistance at efferent arterioles , blood that entered the glomerulus will not be able to pass ; so there will be building up of pressure and the Glomerular Hydrostatic pressure will increase.





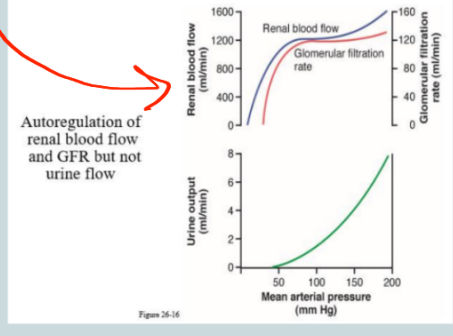
increases too, but in fact when the kidney is normal and when there is an increase in arterial pressure from 50 to 150 or to 180 the Glomerular Hydrostatic pressure does not increases. (plateau)
This is due to autoregulation that fixes pressure inside capillaries on wide range of

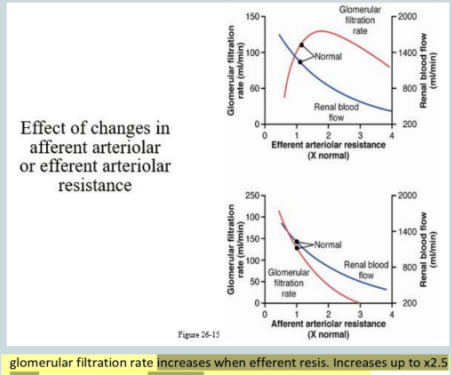


*When mean arterial pressure increases more than 50 until 100, renal blood flow will increase in a direct relation. then plateau starts to 200 or 180.
*glomerular filtration curve? From 50 to 90 or 100 there will be increase in glomerular filtration rate then at 90 to 200 plateau phase.

Plateau refers to autoregulation.

**no regulation on urine output. (Urine output increases as mean pressure increases).
* we call the behavior in **efferent** arteriole resistance - glomerular filtration rate a **biphasic behavior**.
Because: When resistance of efferent is increased , this will lead to an increase in the oncotic pressure also (not only the hydrostatic pressure), so the continuous increase in the resistance will lead to high increase in the oncotic pressure which **has more effect** on the glomerular filtration rate than the increase of hydrostatic pressure.
*the result is decrease of GFR because high oncotic pressure works against filtration (at resistance more than 3).



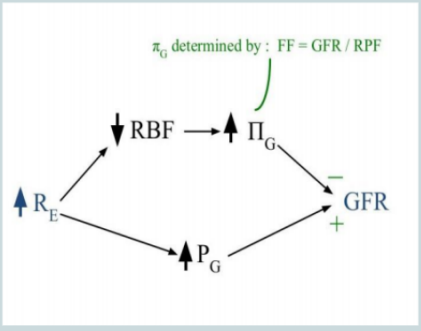


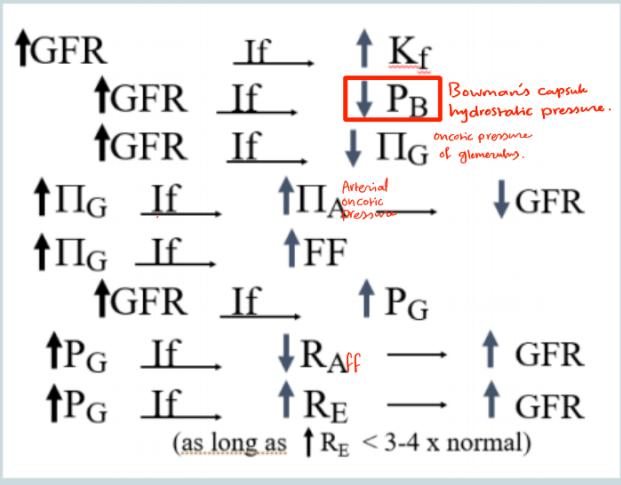
glomerular filtration rate increases when efferent resis. Increases up to x2.5 or x3 then there will be reduction in glomerular filtration rate.

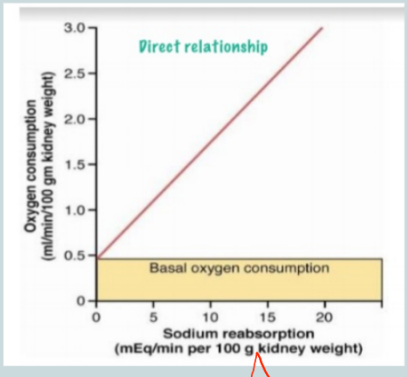
To sum up:

any increase in resistance from 1 to 2.5 or 3 → increased glomerular filtration rate

Any increase in the resistance above 3 → decreased glomerular filtration rate, due to increase of oncotic pressure.







- Note: when RBF is reduced , FF will increase **Filtration fraction (GFR / Renal Plasma Flow).**
➡️ increase in FF will lead to the increase of oncotic pressure.
- Generally: if hydrostatic pressure overcomes oncotic pressure GFR increases.
If oncotic pressure overcomes the hydrostatic pressure, GFR decreases.

Renal blood flow = P / R
= (renal artery pressure - renal venous pressre)/total renal vascular resistance (in the 2 kidneys)(= R afferent + R efferent + R vein).
*A large fraction of renal oxygen consumption is related to renal tubular sodium reabsorption. (High sodium reabsorption needs high energy and high oxygen).