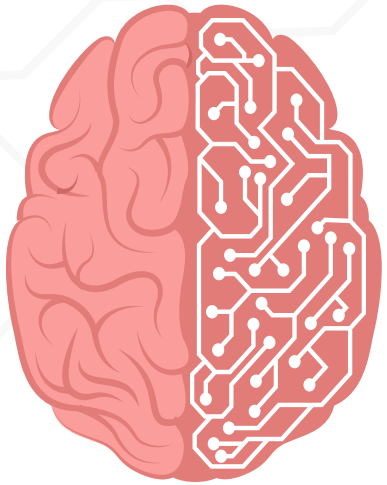

Physiology - GUS

Done By

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Renal Physiology 2
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Renal Handling of Water and Solutes

This table is important

	Filtration	reabsorption	secretion
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	1.8

Do not confuse excretion with secretion. Excretion is whatever is left of the filtered fluid, after filtration, reabsorption and secretion processes. While secretion is an active selective process that removes some of the waste products from the peritubular capillaries, from the blood and that will be eliminated through the filtered fluid. Excretion is the net of all these three processes.

- Water which is the main component of the plasma, which has electrolytes dissolved in it, will be filtered in a rate of 180 L / day through all nephrons in both kidneys, among 180 L filtered, 179 L will be reabsorbed, so only 1 L will be excreted, so we will not lose that much fluid.
- Talking about Na+, most of it will be reabsorbed, only 150 mmol will be excreted.
- Glucose has the same filtration rate of water, but ALL filtered glucose will be reabsorbed leaving nothing to be excreted, and this is the normal physiology of our bodies
- Finally, creatinine, which is a waste product, you can see that it's poorly absorbed because it is a waste product, we want to eliminate it and we don't want to reabsorb it, so 1.8 gm or even more (because of secretion) will be excreted .

Renal Handling of Different Substances

We have 4 main scenarios for renal handling for a substance

- In ex A : some substances can go only through filtration, no reabsorption nor secretion so all the filtered substance will be excreted without added secretions .
- In ex B : you can see that this substance has been filtered but some of it will be reabsorbed (partial reabsorption), so still there is something left to be excreted
- In ex C : the substance is being filtered then completely reabsorbed so nothing left for excretion (complete reabsorption)
- In ex D : this substance went filtration then no reabsorption but further secretion increasing the excretion rate of it.

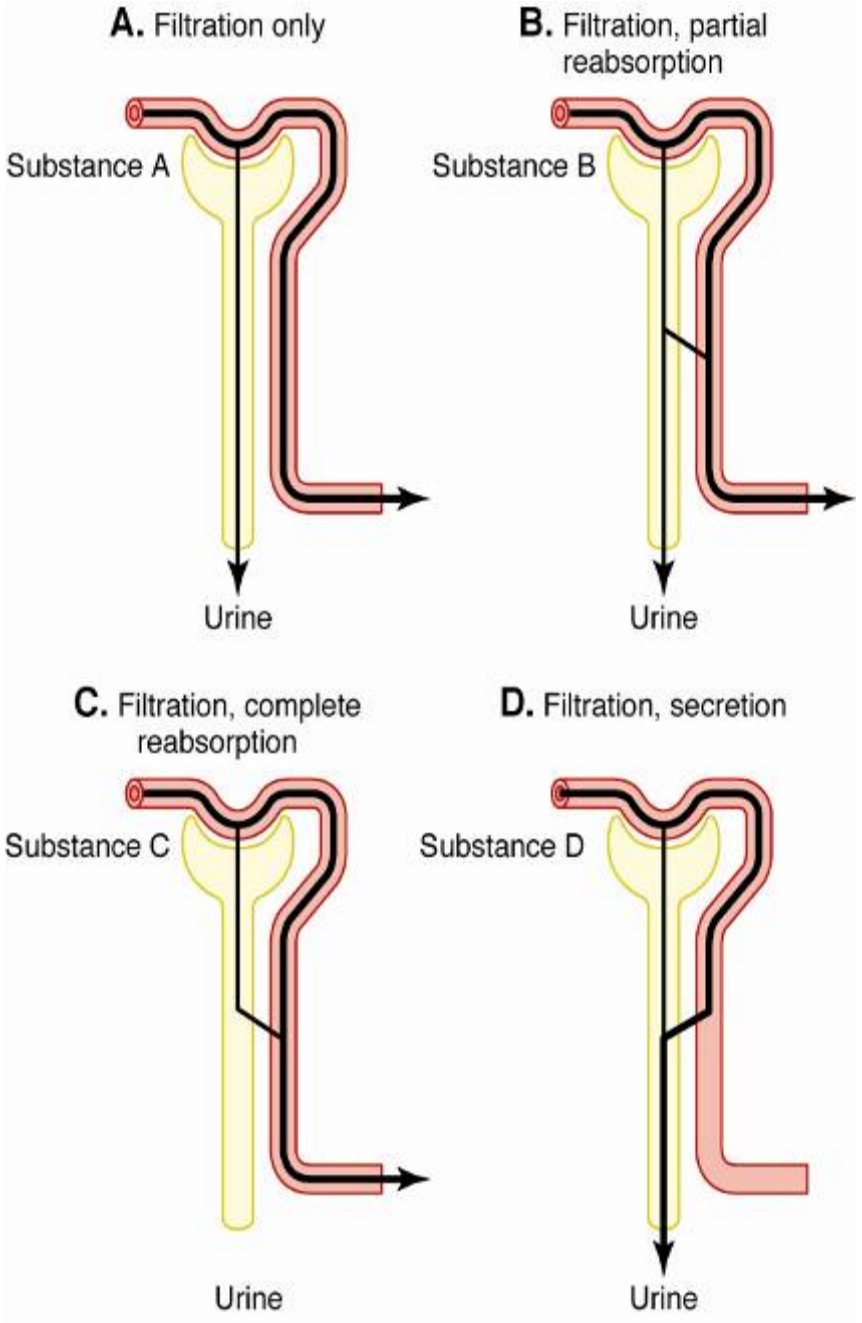


Figure 26-10

Effects of size and electrical charge of dextran on filterability by glomerular capillaries.

Filtration is a passive process depends on the size & charge of the molecules as well as the hemodynamic forces

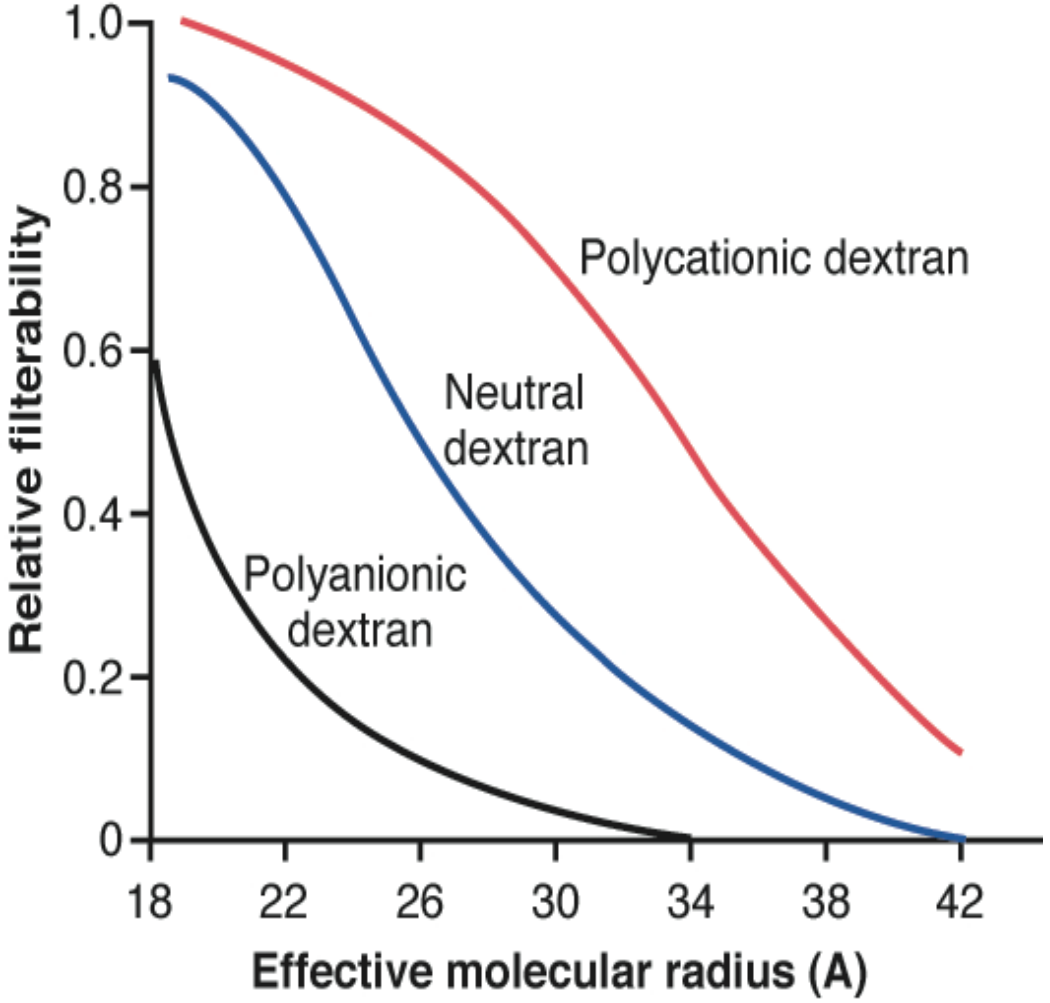


Figure 26-12

As you can see in the graph , on the x axis there is the molecular radius demonstrating the size of the molecules.
On the **y axis** there is the relative filterability (1 = highly filterable and 0 = non-filterable).
In this experiment they dissolved dextran molecules (sugar polymers) in a fluid producing molecules of different sizes and charges , then they measured the relative filterability for each compound. As you can see, as the radius gets bigger, the filterability is declining .

At the same time if you look at the charges, the polyanionic molecule which is highly charged has low filterability (0.6 filterability for the smallest molecules), while for polycationic dextrans, you will have very high filterability =1 for the smallest molecules & **even higher** than the neutral molecules. SO, the higher filterability goes for the more positive charges.

Glomerular Filtration

GFR = 125 ml/min = 180 liters/day

We know that we have about 5 L of plasma and the volume of fluid filtered/day = 180 L= 60 times the volume of plasma so the plasma volume is filtered 60 times/ day → that means the filtration rate is very high and efficient to make sure that no waste products can stay for a long period of time in our bodies (protective mechanism), also important for the maintenance of the different variables in our body, such as volume and the level of electrolytes and adjusting the volume of water and fluids and pH and etc.

- Plasma volume is filtered 60 times per day

- Glomerular filtrate composition is about the same as plasma, except for large proteins

The presence of proteins in urine (proteinuria) is abnormal & indicates something wrong in the kidney.

- **Filtration fraction** (GFR / Renal Plasma Flow) = 0.2 (i.e. 20% of plasma is filtered)

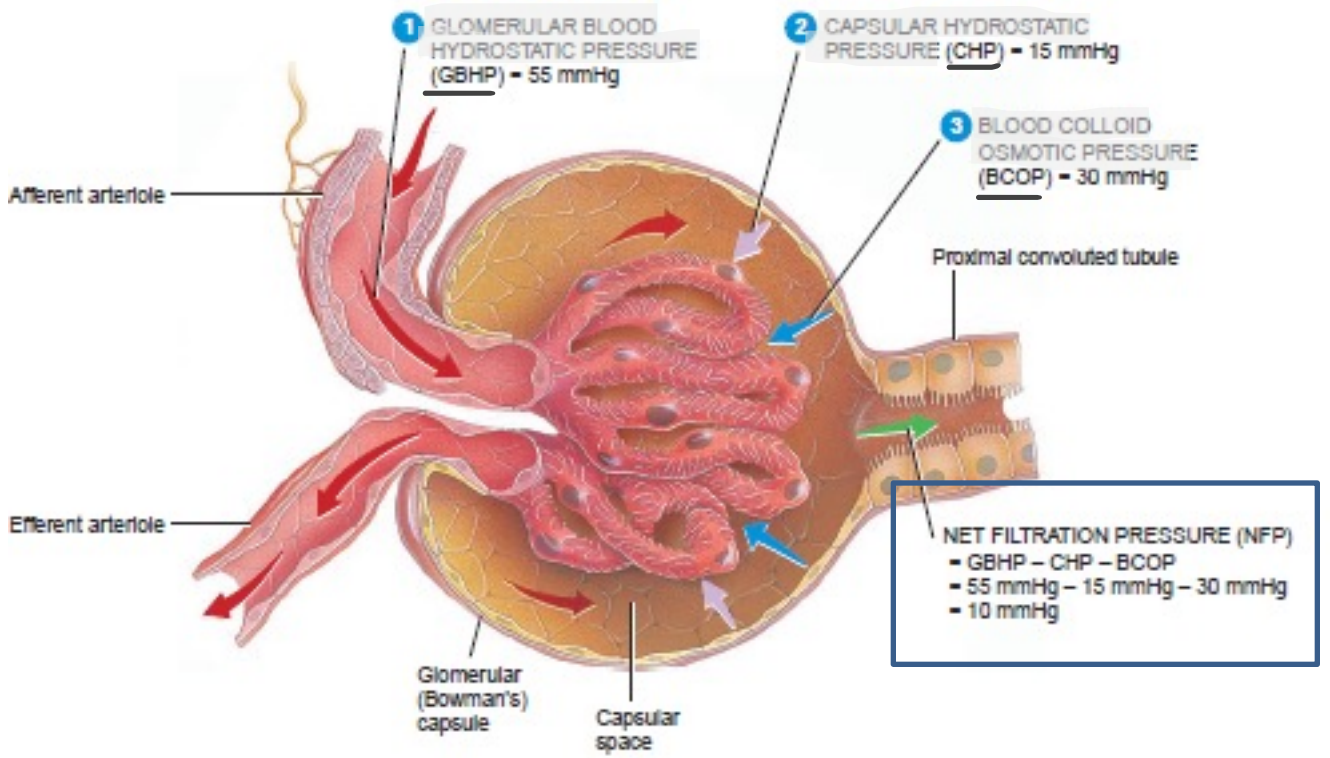
Is almost constant, 20% of renal plasma flow is being filtered, 80% of the plasma is returned back to the inferior vena cava

Clinical Significance of Proteinuria

- Early detection of renal disease in at-risk patients
  - hypertension: hypertensive renal disease
  - diabetes: diabetic nephropathy
  - pregnancy: gestational proteinuric hypertension (pre-eclampsia)
  - annual “check-up”: renal disease can be silent
- Assessment and monitoring of known renal disease

Glomerular Filtration

- As you can see , the blood coming from the afferent arteriole has a hydrostatic pressure of about 55 mmhg (*hydrostatic pressure is the pressure that is exerted on the walls of the blood vessels & originates from the pumping force of the heart and the volume of the blood*) and this pressure will actually push the plasma or the fluids to go outside the capillaries toward the capsular space (the direction is outside the glomerulus)
- The fluid in the capsular space will also exert a hydrostatic pressure on the walls of the glomeruli but to **the opposite direction** (to inside the glomeruli & = 15 mmhg)
- The other type of pressures are related to osmotic colloid pressure (which is the presence of the large proteins), and these proteins are not allowed to leave the glomeruli and exert a pressure that pulls the fluid to inside the glomeruli (against filtration)
- Because of little proteins filtered to the capsule ,the oncotic colloid pressure inside the capsule is very little and can be neglected



- To calculate <u>the net filtration pressure</u>
- Consider any pressure to the direction of filtration (pulling outside the capillaries) is POSITIVE & any pressure against filtration (toward the capillaries = reabsorption) is NEGATIVE
- So GBHP-CHP-BCOP = 55-15-30 = 10mmg
- So this pressure leads to filtration
- If the net pressure is zero , there is no filtration or reabsorption.

- You can find some differences in numbers between books

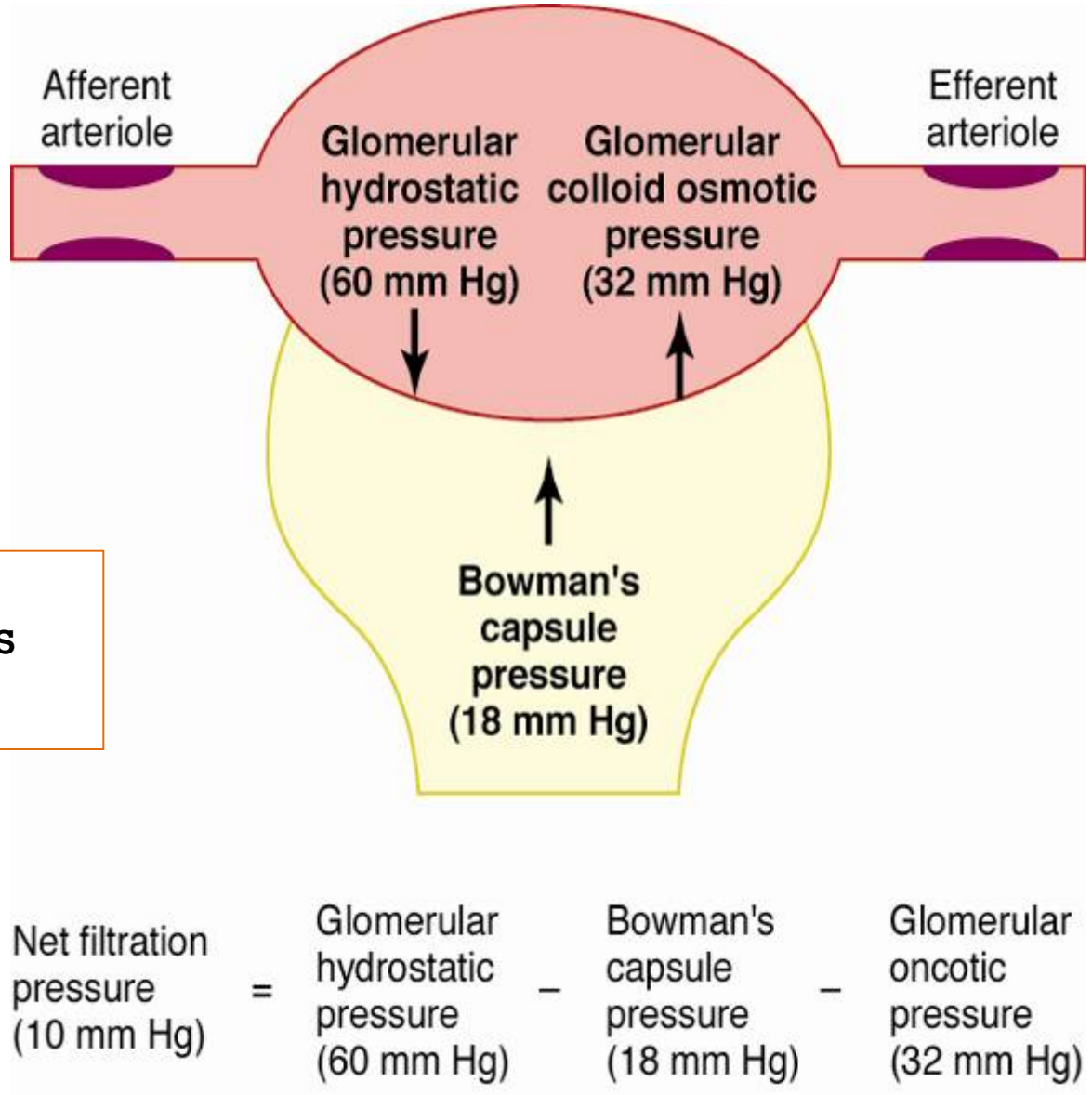


Figure 26-13

+ colloid capsular pressure (0)

Glomerular Filtration Rate (GFR)

- **Filtration Fraction (FF)= Fraction** of blood plasma in the afferent arterioles that becomes filtrate= 16-20%.
- **GFR** =The volume (ml) of fluid filtered through all the corpuscles of both kidneys per minute.
- The volume of fluid filtered daily through all the corpuscles of both kidneys per day **= 180 L**
- **Hence, GFR**= 180 L/24hours * (1000 ml/ L)*(1hour/60 min)= **125 ml/min (Males)**
- For 125ml/min; renal plasma flow = **625ml/min**

  FF * PF=GFR, PF= 125/(20%)=625 ml/min

FF = GFR/ renal plasma flow

- 55% of blood is plasma, so blood flow = 1140ml/min

  55% * BF= PF; BF= 625ml/min/ (55%)=1140 ml/min
- Renal Blood Flow of **1140 ml/min** = (22.8 % of 5 liters (the CO)) is required to have GFR of 125ml/min.

Renal blood flow should equal 1140ml/min in order to have a normal GFR

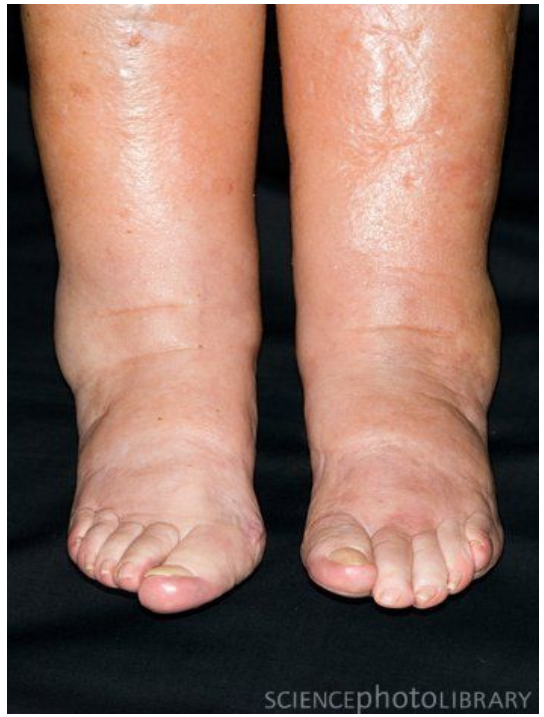
Clinical Application

- ***Edema***
- Some kidney diseases result in a damage of the glomerular capillaries leading to an increase in their permeability to large proteins .

For ex in diabetes

Or damage in podocytes or basement membrane

- 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***.



Regulation of Glomerular Filtration

- Homeostasis of body fluids requires constant GFR by kidneys.
- If the GFR is too high, needed substances cannot be reabsorbed quickly enough and are lost in the urine.
- If the GFR is too low -everything is reabsorbed, including wastes that are normally disposed of.

Determinants of Glomerular Filtration Rate

Normal Values:

GFR = 125 ml/min

Net Filt. 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)

There is a direct relationship between GFR and net filtration press which will result in a constant called Kf (coefficient of filtration)

Kf = GFR /Net filt. Press

Glomerular Capillary Filtration Coefficient (K_f)

- K_f = hydraulic conductivity x surface area

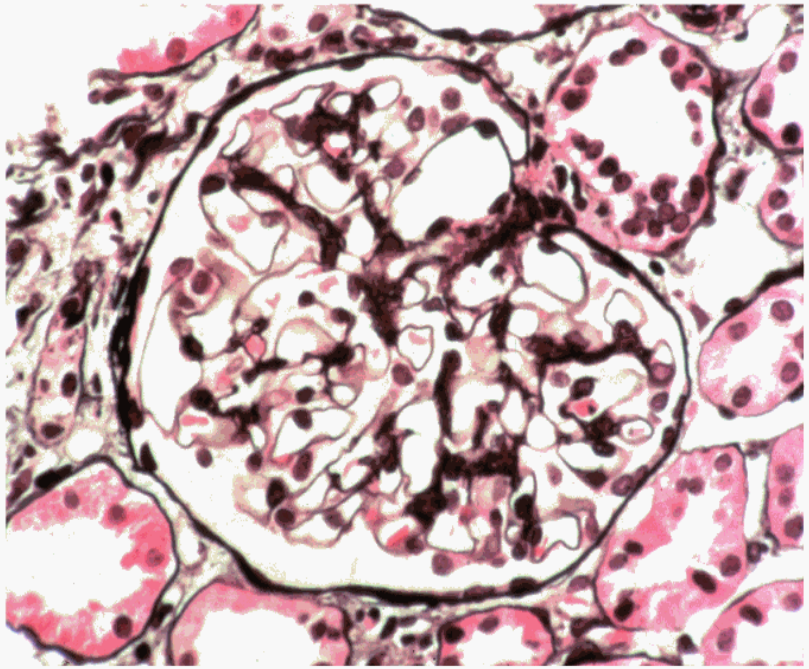
K_f = GFR/net filt pressure

The normal range is similar between people, normally Kf is not a determinant for GFR

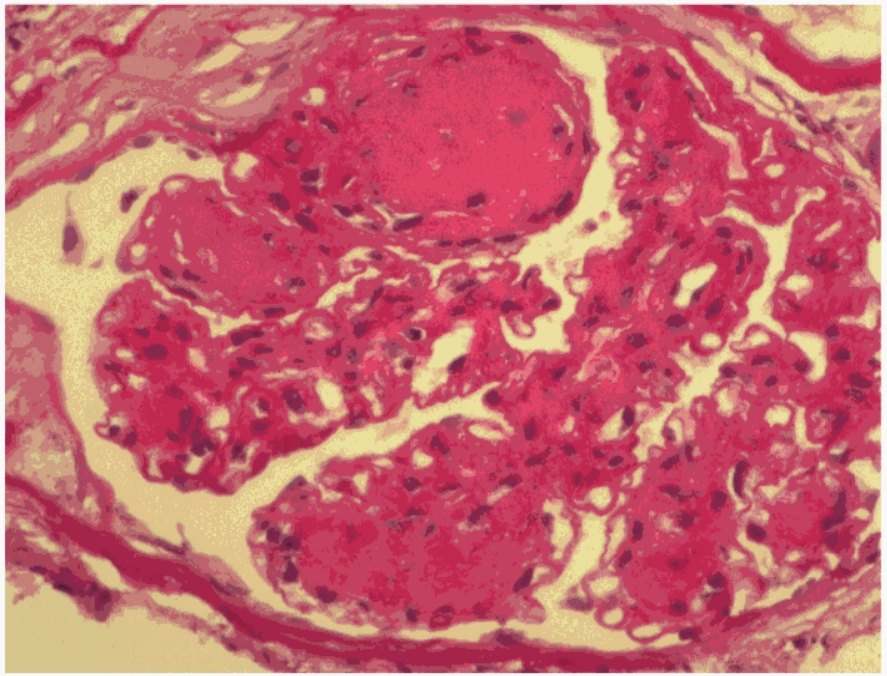
- Normally not highly variable
- Disease that can reduce K_f and GFR
- damage of capillaries, BM thickens,
  - chronic hypertension
  - obesity / diabetes mellitus
  - glomerulonephritis

Glomerular Injury in Chronic Diabetes

Normal glomerulus



Diabetic nephropathy



This pathology is caused either from damage to glomerular capillaries or fibrosis in the basement (deposition of fibrous tissue in the matrix) which will decrease the surface area for filtration and cause reduction of GFR

Bowman's Capsule hydrostatic Pressure (P_B)

- Normally changes as a function of GFR, not a physiological regulator of GFR

Increases with increasing GFR

- Increases with Tubular Obstruction

- Kidney stones
- Tubular necrosis
- Reducing GFR

In some pathological conditions, there is increase in capsular hydrostatic pressure which will reduce the net filtration press resulting in reducing GFR (remember the equation of net filt. Press)

- Urinary tract obstruction

Prostate hypertrophy/cancer

Factors Influencing Glomerular Capillary Oncotic Pressure (Π_G)

Not regulator for GFR; it influences it but doesn't regulate it

- Arterial Plasma Oncotic Pressure (π_A)

$\uparrow \pi_A \longrightarrow \uparrow \pi_G$

The blood inside the glomeruli is the same blood of arteries so an increase in the arterial plasma oncotic pressure will increase the glomerular oncotic pressure

- Filtration Fraction (FF)

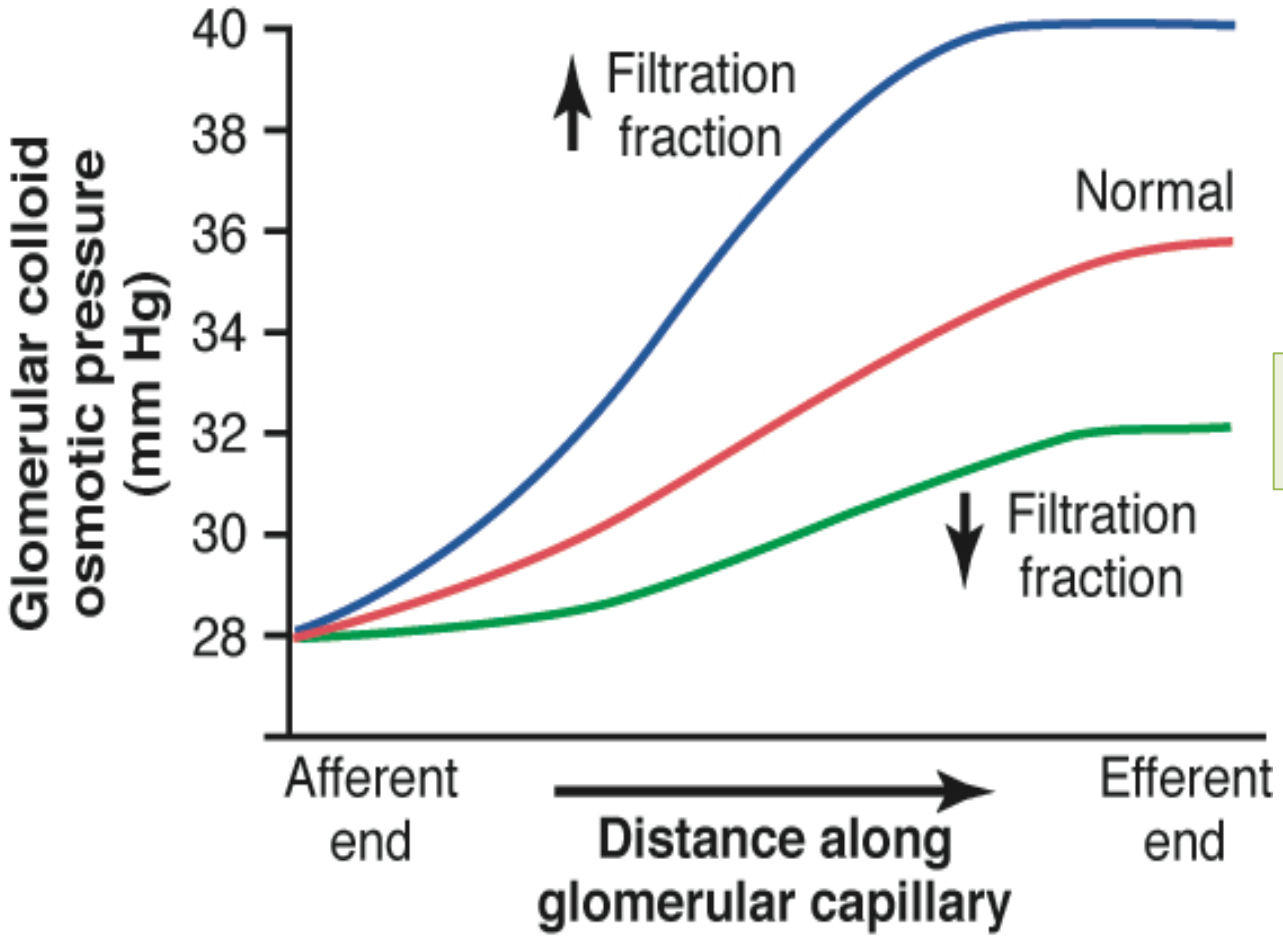
$\uparrow FF \longrightarrow \uparrow \pi_G$

When we have higher FF , more than 20% we will have higher glomerular oncotic press

FF = GFR / Renal plasma flow

= 125 / 650 ~ 0.2 (or 20%)

In this graph we see different curves indicating different FF



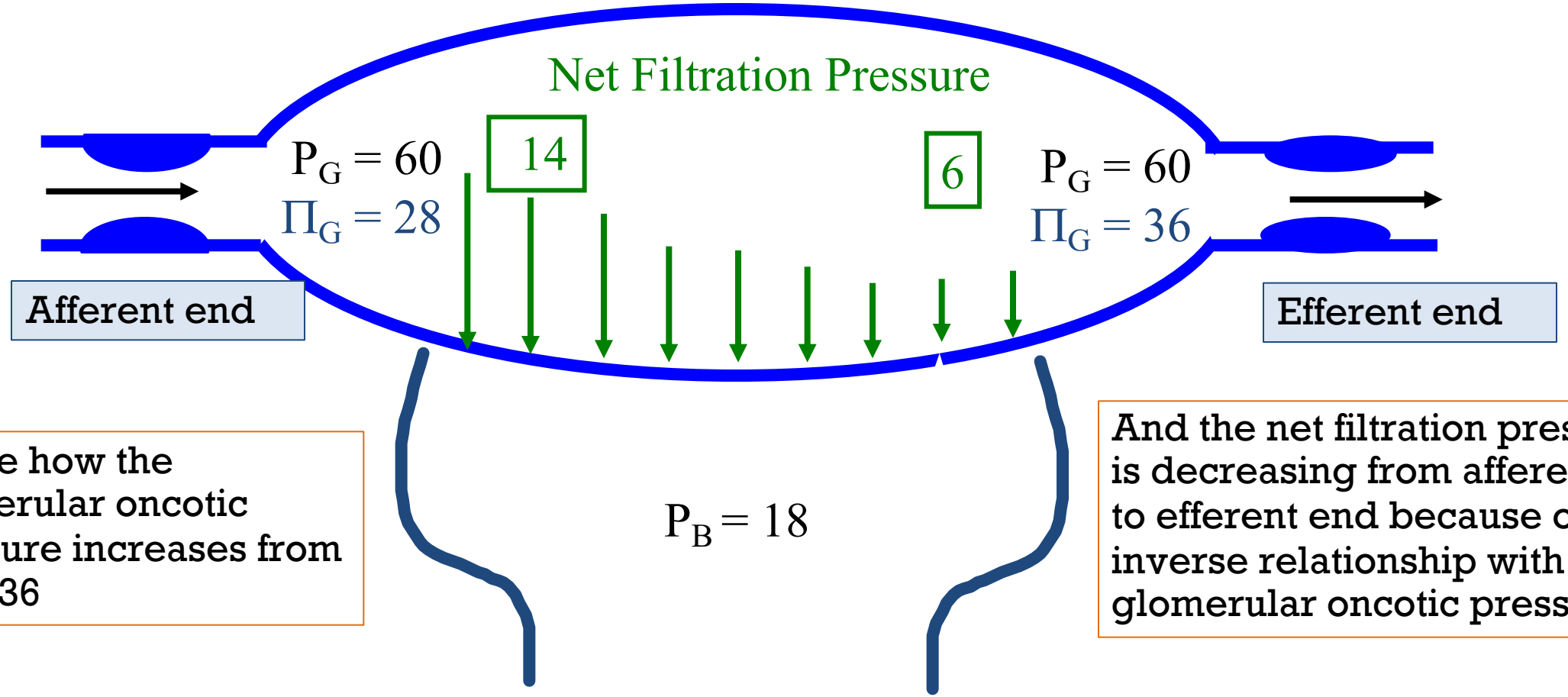
When we have higher FF , the glomerular oncotic pressure is elevated

When we have lower FF , the glomerular oncotic pressure is reduced

The higher point of glomerular oncotic press is at the efferent end of the higher FF curve

In all curves when we go from afferent to efferent, the pressure is increasing → because of more filtration

Figure 26-14



Notice how the glomerular oncotic pressure increases from 28 to 36

And the net filtration pressure is decreasing from afferent end to efferent end because of the inverse relationship with the glomerular oncotic pressure

Microalbuminuria

- Definition: urine excretion of > 30 but < 150 mg albumin per day

- Causes: early diabetes, hypertension, glomerular hyperfiltration

Prognostic Value: diabetic patients with microalbuminuria are 10-20 fold more likely to develop persistent proteinuria

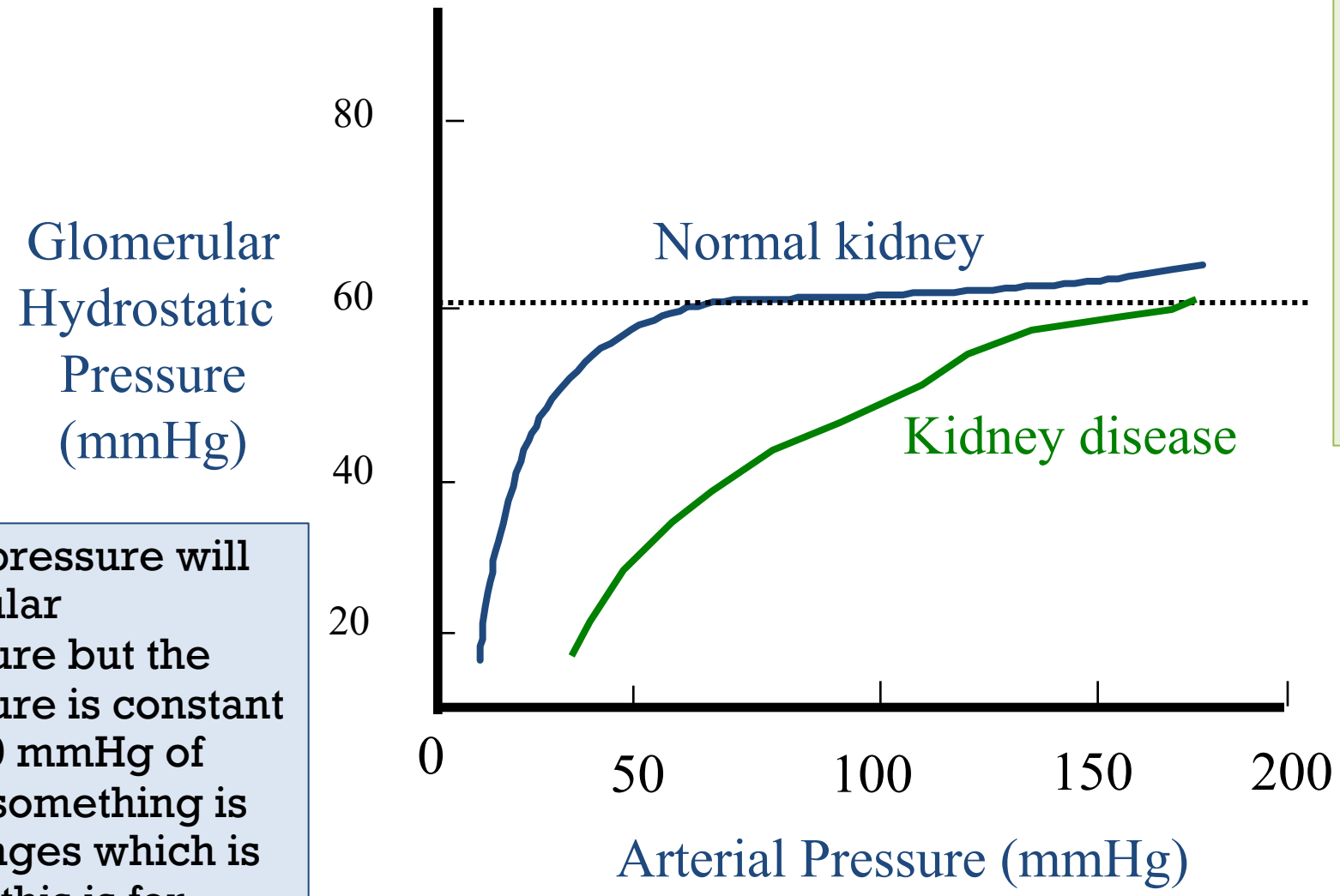
Glomerular Hydrostatic Pressure (P_G)

until now we couldn't find a regulator for GFR

- Is the determinant of GFR most subject to physiological control

Affects GFR by affecting net filtration press

- Factors that influence P_G
  - arterial pressure (effect is buffered by autoregulation)
  - afferent arteriolar resistance
  - efferent arteriolar resistance



By logic, arterial pressure will affect the glomerular hydrostatic pressure but the hydrostatic pressure is constant between 50 to 200 mmHg of arterial press, so something is buffering the changes which is autoregulation … this is for normal kidney

In kidney disease the efficiency of auto-regulation is affected, we can't see the plateau and at normal levels of arterial pressures the glomerular hydrostatic pressure is reduced

Here we are examining the relationship of arterial pressure **(x axis)** with both (the glomerular filtration rate & renal blood flow) **(y axis)**, and you can appreciate how they are almost constant at 125 & 1200 respectively because of auto regulation

Autoregulation of renal blood flow and GFR but not urine flow

And here we examine the relationship of urine output with arterial pressure, and you can see the direct relation, no auto regulation

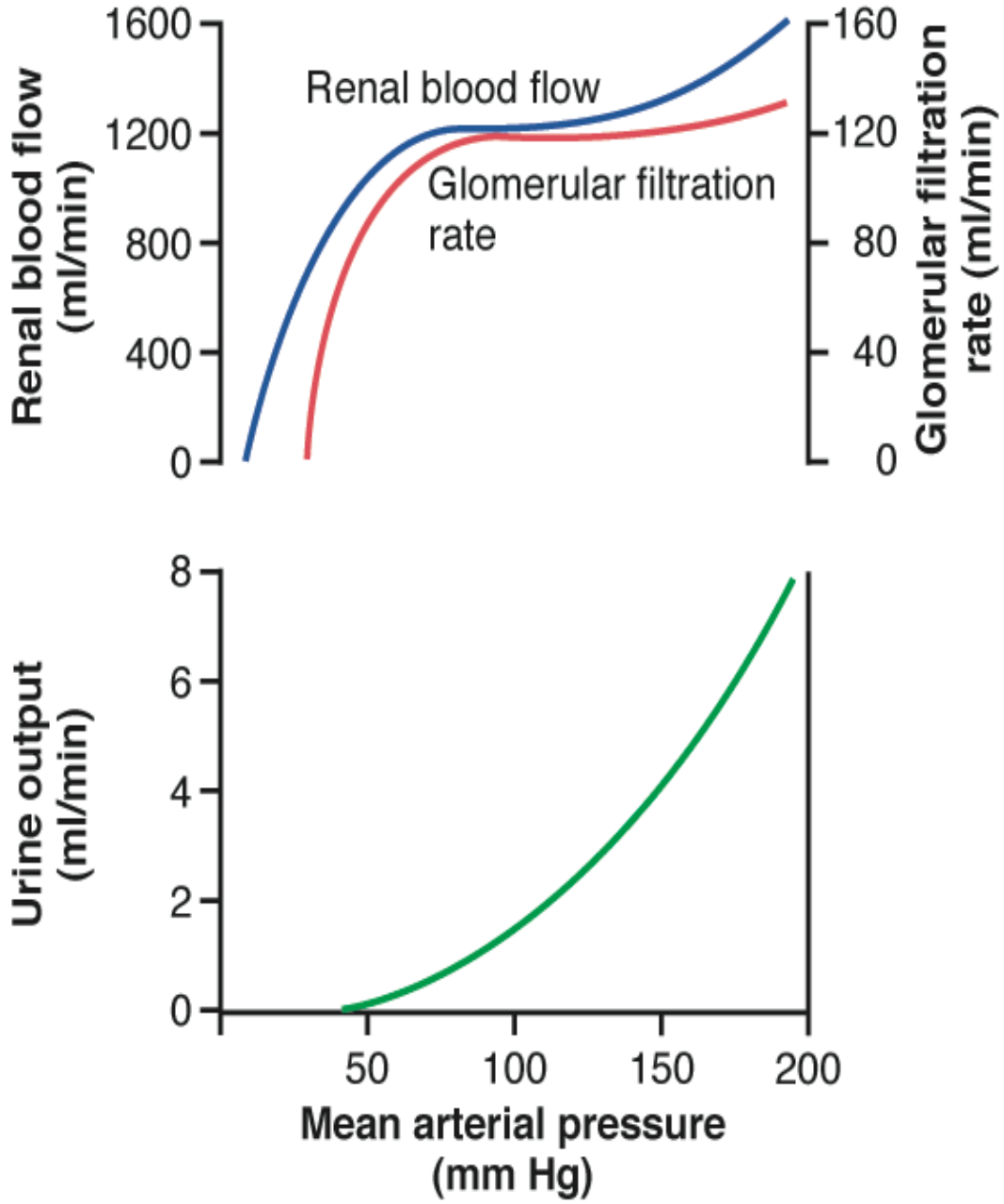
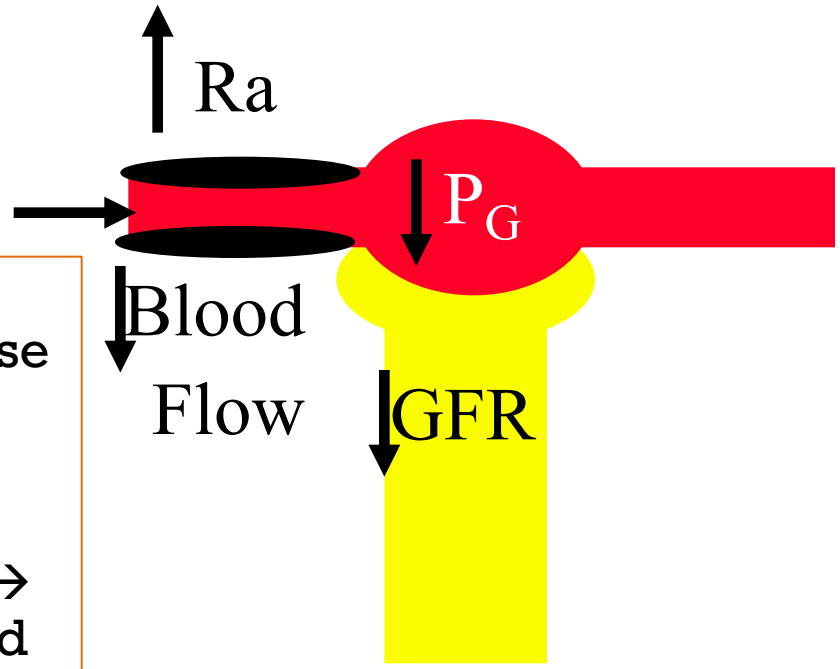


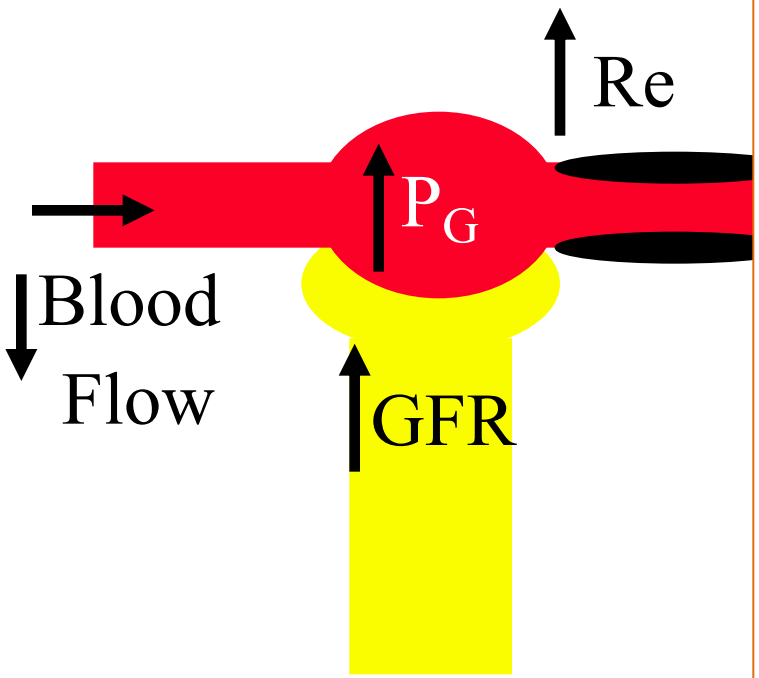
Figure 26-16

Effect of afferent and efferent arteriolar constriction on glomerular pressure

We can see there is increase in the afferent arteriolar resistance (constriction) → decrease blood flow → decrease glomerular hydrostatic pressure → decrease GFR



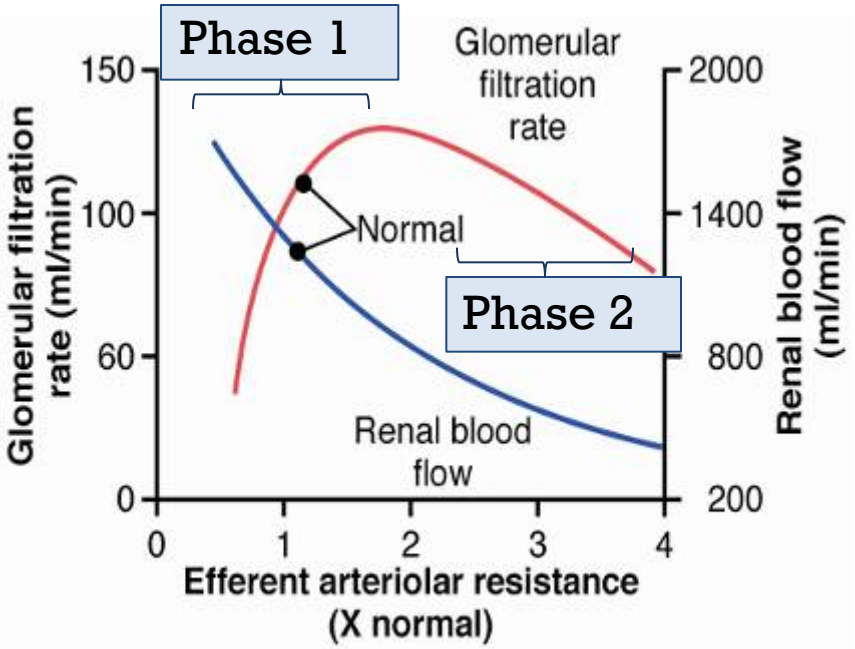
Ra → GFR + Renal



Re → GFR + Renal

We can see there is increase in the efferent arteriolar resistance (constriction) → increase in glomerular hydrostatic pressure because of the difficulty of getting the blood out → increase GFR [But the blood flow is decreased because of the constriction]

This figure represents the changes of renal blood flow (blue) and the glomerular filtration rate (red) due to changes in the efferent arteriolar resistance, the renal blood flow decreases by increasing the efferent arteriolar resistance but with GFR we can notice 2 phases, there's an increase in GFR and a decrease, any increase in the efferent arteriolar resistance above the double, there will be decrease in GFR



Effect of changes in afferent arteriolar or efferent arteriolar resistance

This figure represents the changes of renal blood flow (blue) and the glomerular filtration rate (red) due to changes in the afferent arteriolar resistance , both of them will decrease by increasing the afferent arteriolar resistance

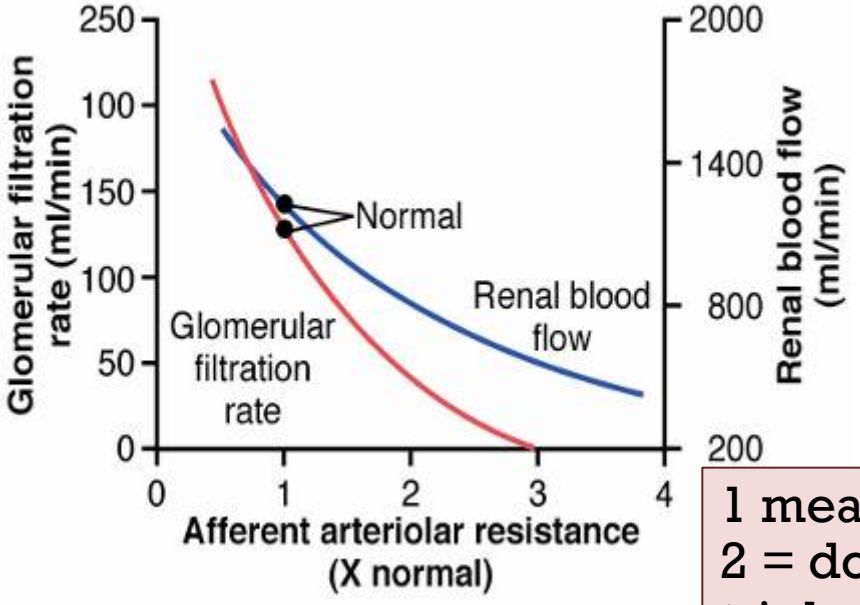
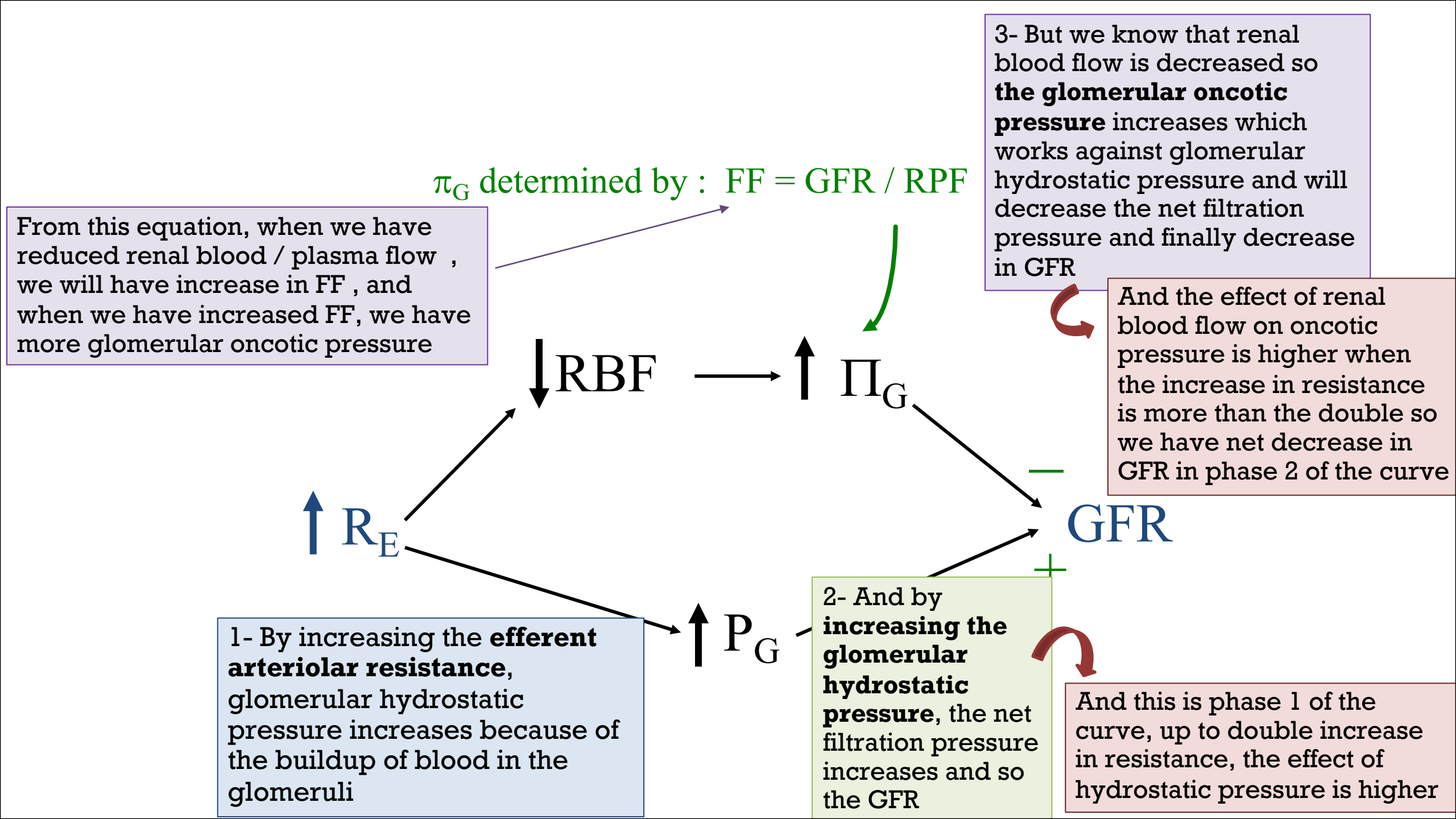


Figure 26-15

1 means normal 2 = double, 3 = triple and so on


π_G determined by : FF = GFR / RPF
From this equation, when we have reduced renal blood / plasma flow , we will have increase in FF , and when we have increased FF, we have more glomerular oncotic pressure
3- But we know that renal blood flow is decreased so **the glomerular oncotic pressure** increases which works against glomerular hydrostatic pressure and will decrease the net filtration pressure and finally decrease in GFR
And the effect of renal blood flow on oncotic pressure is higher when the increase in resistance is more than the double so we have net decrease in GFR in phase 2 of the curve
↓RBF
↑ Π_G
↑ R_E
GFR
−
+
↑ P_G
1- By increasing the **efferent arteriolar resistance**, glomerular hydrostatic pressure increases because of the buildup of blood in the glomeruli
2- And by **increasing the glomerular hydrostatic pressure**, the net filtration pressure increases and so the GFR
And this is phase 1 of the curve, up to double increase in resistance, the effect of hydrostatic pressure is higher

All of this is discussed previously

Summary of Determinants of GFR

↑GFR If → ↑ K_f

Physiologically it's constant unless there is a disease

↑GFR If → ↓ P_B

↑GFR If → ↓ Π_G

↑ Π_G If → ↑ Π_A → ↓GFR

↑ Π_G If → ↑FF

↑GFR If → ↑ P_G

↑ P_G If → ↓ R_A → ↑ GFR

↑ P_G If → ↑ R_E → ↑ GFR

(as long as ↑ R_E < 3-4 x normal)

Remember phase 2

Determinants of Renal Blood Flow (RBF)

$$RBF = \Delta P / R$$

Ohm's law

ΔP = difference between renal artery pressure and renal vein pressure

R = total renal vascular resistance
= Ra + Re + Rv
= sum of all resistances in kidney vasculature

Inverse relationship with renal blood flow

Renal blood flow

- High blood flow (~22 % of cardiac output)
- High blood flow needed for high GFR

We discussed it previously

- Oxygen and nutrients delivered to kidneys normally greatly exceeds their metabolic needs

To maintain effective filtration and elimination of wastes

- A large fraction of renal oxygen consumption is related to renal tubular sodium reabsorption

Reabsorption is selective and active process (needs energy & oxygen)

Renal oxygen consumption and sodium reabsorption

Direct relationship

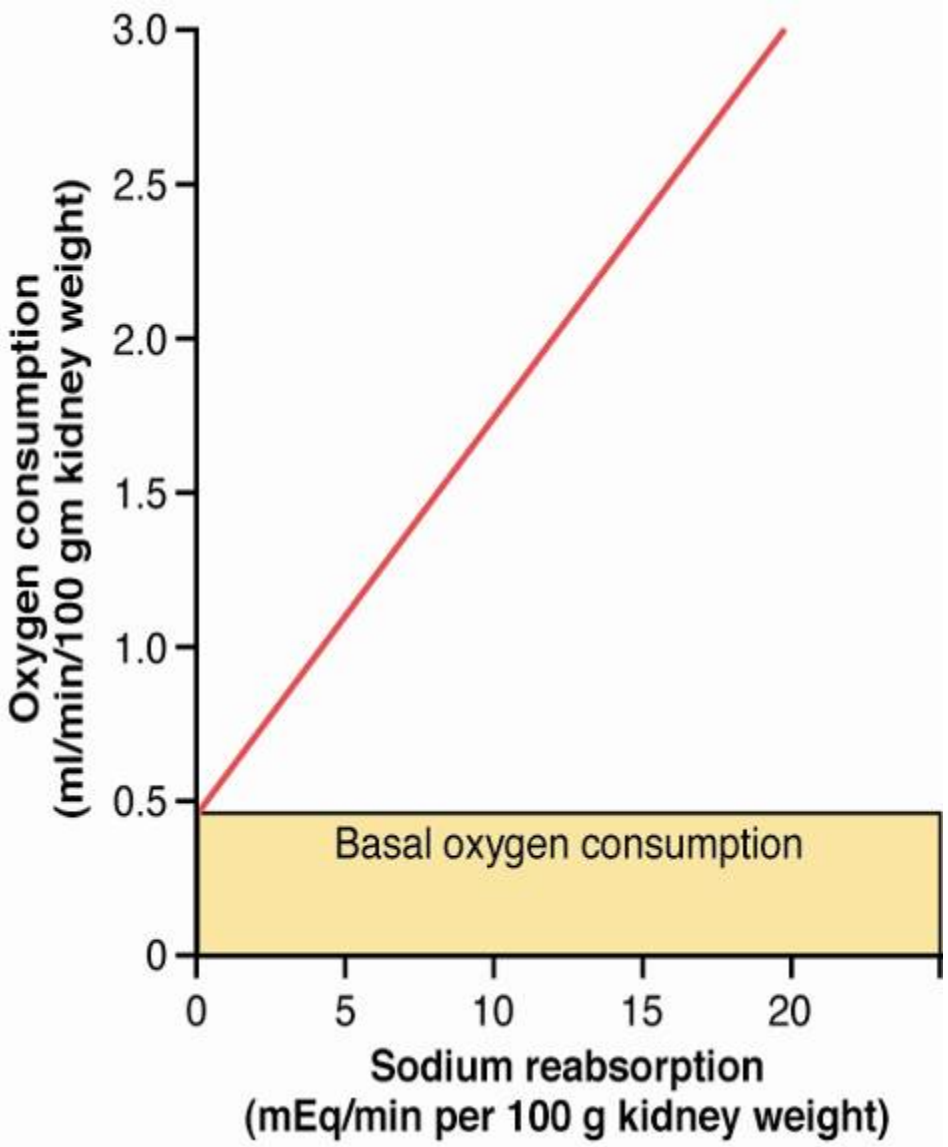


Figure 26-16