GENITOURINARY SYSTEM

Subsystem : Physiology
Lecture Title :Glomerular filtration
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Writer : Leen Asfour
Editor : Abdullah Managreh

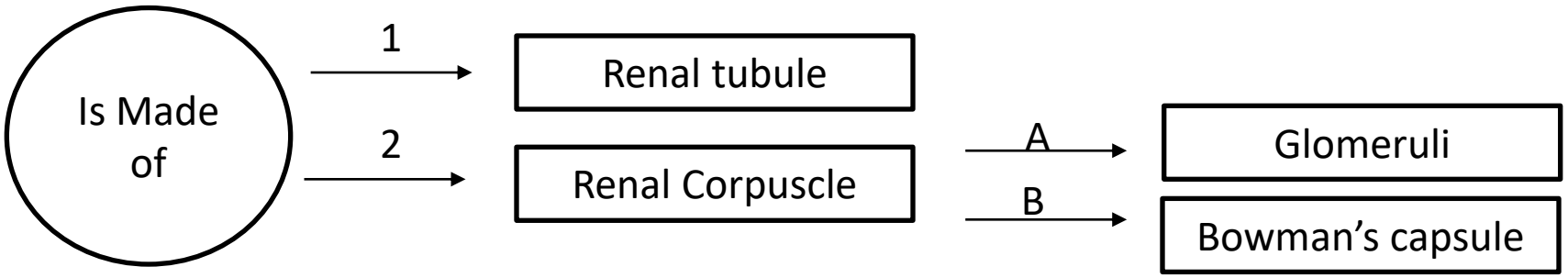
RENAL SYSTEM
Physiology lecture 2
GLOMERULAR FILTRATION

Notes :

- Texts in blue beginning & ending with “ “ within the original slides are all sheet note.

Sheet

- The blood coming to the glomeruli through the afferent arteriole then this blood will be filtrated by the glomeruli passing to bowman's capsule”
- Glomeruli is the first part of the nephron of the kidney
- NEPHRON



GLOMERULAR FILTRATION

1. Composition

Similar to plasma's composition but (no proteins no RBCs), less Ca++ and fatty acids (because partially bound w/proteins) .

2. Glom. Capill. Membrane:

Is made of 3 layers, endothelium, basement , and epithelium (podocyts).

the Glomerular capillaries filtration is 400 to 500 x of that in the other capillaries of the body.

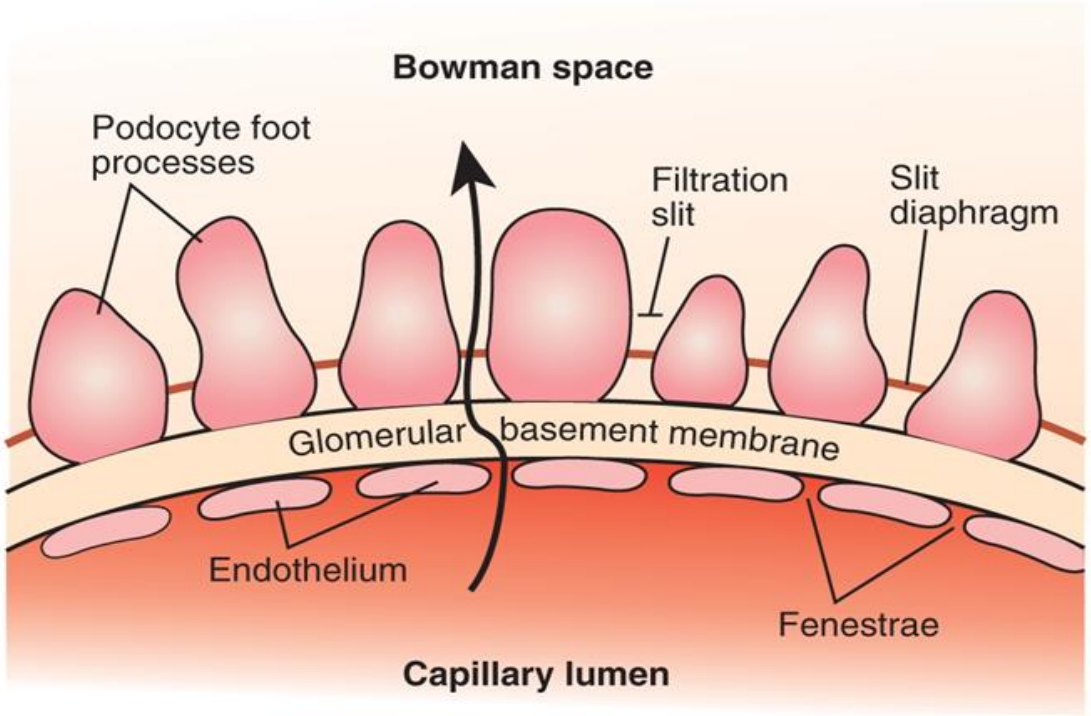
a) small holes (fenestra) in endothelium.

b) Basement w/collagen and Proteoglycan (-) "negatively charged membrane not letting negatively charged ions to pass like proteins"

c) Slit - pores in podocytes (epithelium (-)).

Sheet

- The blood that the afferent arteriole carries must be filtrated through the three layers of the glomeruli “epithelium, basement membrane , endothelium.



Pay attention that the blood first filtration spot is the endothelium then the basement membrane which is negatively charged and lastly the epithelium “podocytes” and then into Bowman’s

Extra sheet for more understanding

- you must be wondering why proteins and RBC are not filtrated

Proteins are negatively charged atoms and the basement membrane of the glomeruli is negatively charged , like charges repel each other preventing the protein to be filtrated

RBCs are large considering the size of the fenestra in the endothelium thus RBCs can’t pass , in other words can't be filtrated

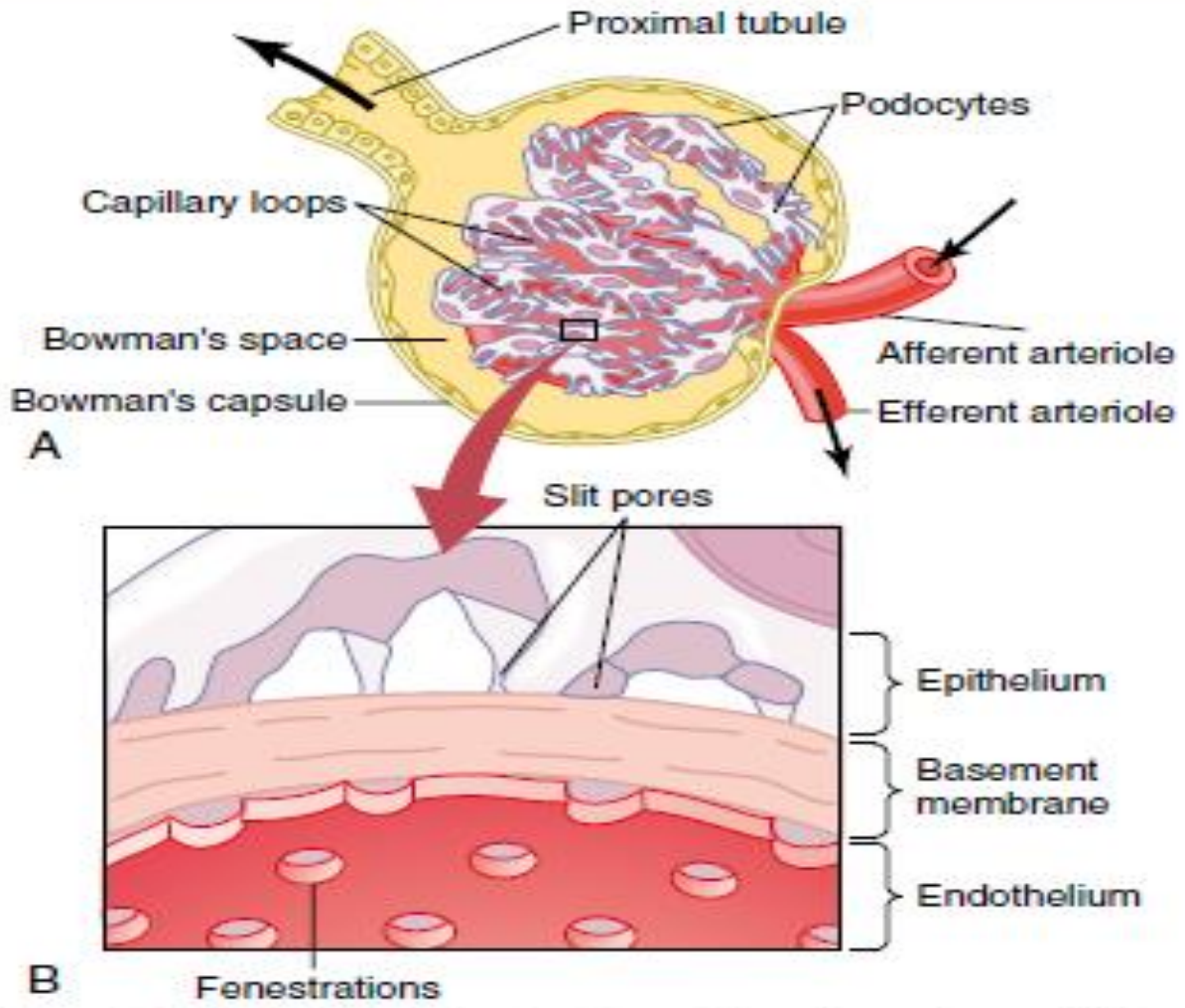


Figure 26-11 *A*, Basic ultrastructure of the glomerular capillaries. *B*, Cross section of the glomerular capillary membrane and its major components: capillary endothelium, basement membrane, and epithelium (podocytes).

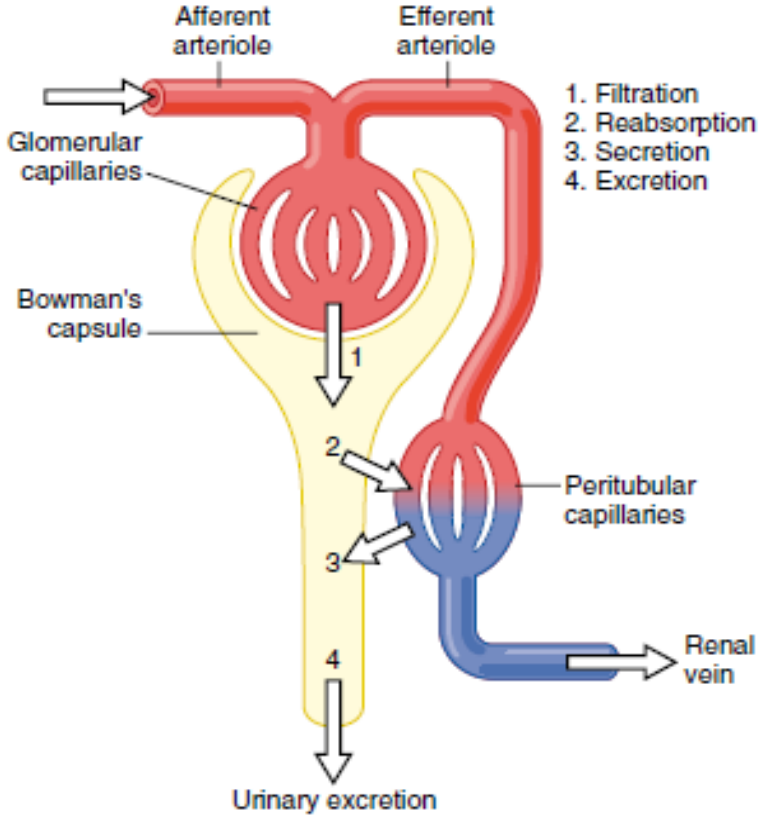


Figure 26-9 Basic kidney processes that determine the composition of the urine. Urinary excretion rate of a substance is equal to the rate at which the substance is filtered minus its reabsorption rate plus the rate at which it is secreted from the peritubular capillary blood into the tubules.

the tubules, it is modified by reabsorption of water and specific solutes back into the blood or by secretion of other substances from the peritubular capillaries into the tubules.

Figure 26-10 shows the renal handling of four hypo-

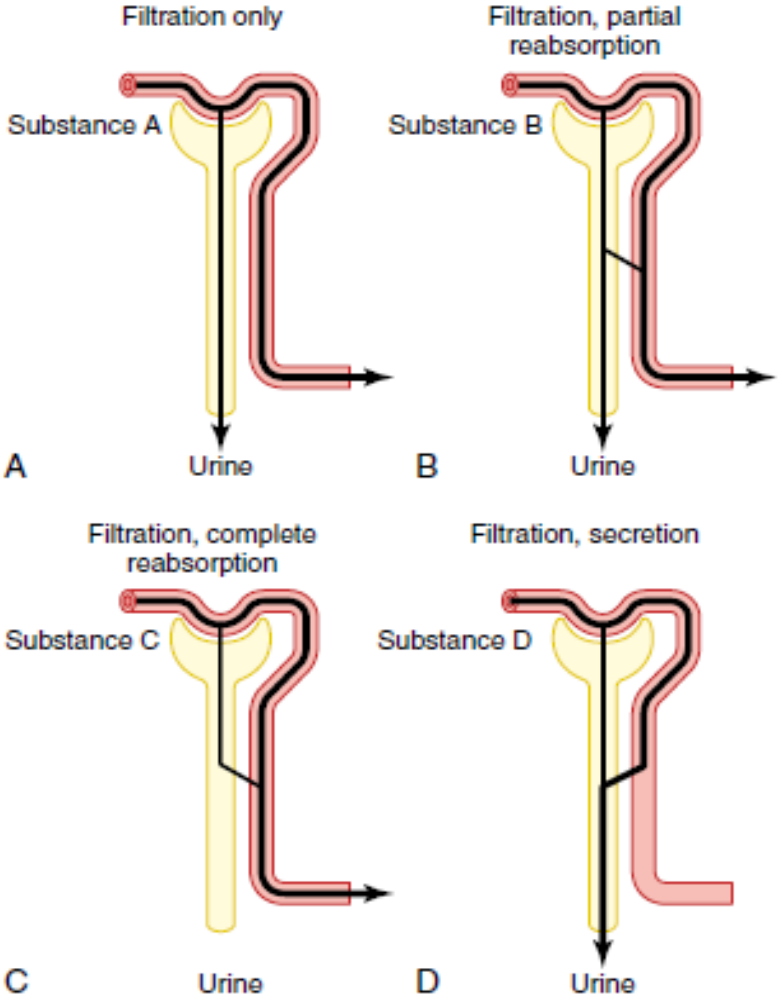
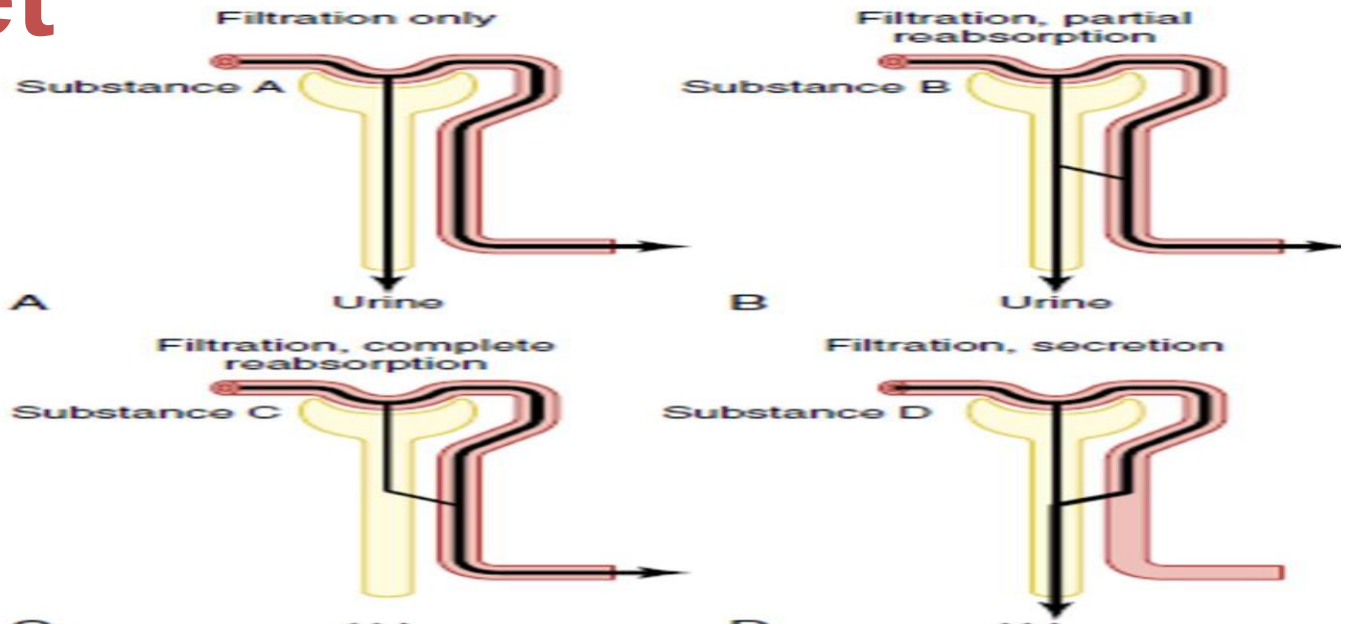


Figure 26-10 Renal handling of four hypothetical substances. *A*, The substance is freely filtered but not reabsorbed. *B*, The substance is freely filtered, but part of the filtered load is reabsorbed back in the blood. *C*, The substance is freely filtered but is not excreted in the urine because all the filtered substance is reabsorbed from the tubules into the blood. *D*, The substance is freely filtered and is not reabsorbed but is secreted from the peritubular capillary blood into the renal tubules.

Sheet



- There are 4 faiths for filtrated substances :
- A- Only filtrated in the renal tubule without being reabsorbed, pathway for inulin and creatinine “what’s filtrated is secreted”
- B- Filtrated and partially reabsorbed , other than that will be excreted , pathway for most of electrolytes, ”concentration of these sub. in urine is less than plasma”
- C- Filtration and complete reabsorption, no excretion, pathway for glucose and amino acids, “the substance in the plasma doesn’t appear in urine “all reabsorbed”
- D- Filtrated and then secreted , concentration of the sub. In the urine is more than the plasma ”

Filtration fraction (FF) = the fraction of the renal plasma flow that is filtered, about 20% of plasma flow.

FF= GFR/Renal plasma flow

“A portion of the blood that passes through the glomeruli will go through filtration , 20% of that portion will be filtrated →
“In other words the plasma flow through the afferent arteriole is 1200 ml/min , 625 ml of it will go to the glomeruli the other 575 ml will leave the circulation through the efferent arteriole, 20% of the 625 ml will be filtrated which is equal to 125 ml/min”

Filterability depends on size and charges

GFR = Kf x Net filtration pressure

Kf: Filtration coefficient is a measure of the product of the hydraulic conductivity and surface area of glom capill. ml/min/mmHg

Net filtration pressure

= Glomerular hydrostatic pressure "to the outside 60"

= Bowman's capsular pressure "to the inside 18"

= Glomerular oncotic pressure "or glomerular colloid pressure to the inside 32"

NEF = 60 - 18 -32 = 10 mmHg = "the force that's responsible for filtrating the plasma from the glomerular capillaries to bowman's Capsule

"Extra, Outside means out of the body through bowman's capsule"

Table 26-1 Filterability of Substances by Glomerular Capillaries Based on Molecular Weight

Substance	Molecular Weight	Filterability
Water	18	1.0
Sodium	23	1.0
Glucose	180	1.0
Inulin	5,500	1.0
Myoglobin	17,000	0.75
Albumin	69,000	0.005

More molecular weight ,less filtration as with albumin and myoglobin.

Determinants of the GFR

- **GFR is determined by (1) sum of the hydrostatic and colloid forces across the glomerular membrane (net filtration pressure), and (2) the glomerular capillary filtration coefficient.**

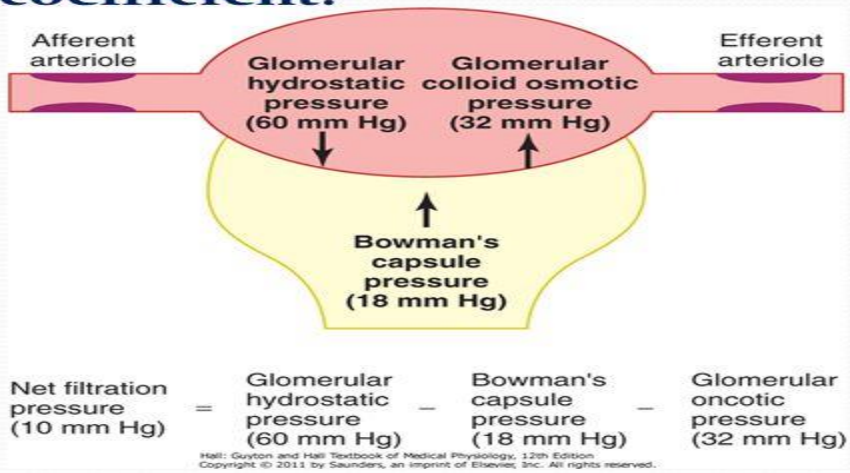


Fig. 26.13

First filtration step takes place in the endothelium of the glomeruli leading to an increase in the colloid osmotic pressure, so at first the colloid will be 28 “near the afferent arteriole and 36 at the efferent arteriole ,the pressure gradually inc. due to the more filtrated plasma, the more plasma proteins the more osmotic pressure.

Pressure”avg. is 32”

Extra

colloid osmotic pressure Is the pressure generated from the substances that couldn’t be filtrated like albumin

“The more colloid osmotic pressure the less filtration rate and vice versa.
So near the afferent end —> less colloid osmotic pressure, more filtration rate

Near the efferent end —> more colloid osmotic pressure , less filtration”

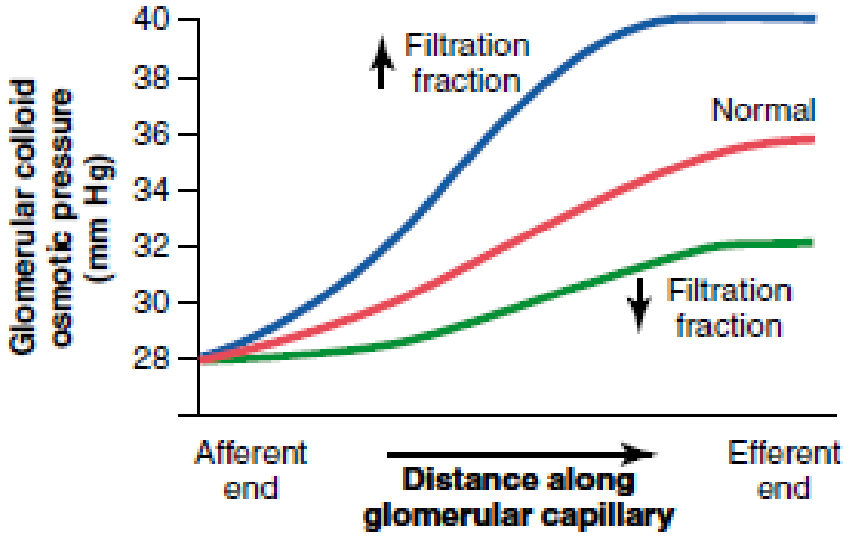


Figure 26-14 Increase in colloid osmotic pressure in plasma flowing through the glomerular capillary. Normally, about one fifth of the fluid in the glomerular capillaries filters into Bowman's capsule, thereby concentrating the plasma proteins that are not filtered. Increases in the filtration fraction (glomerular filtration rate/renal plasma flow) increase the rate at which the plasma colloid osmotic pressure rises along the glomerular capillary; decreases in the filtration fraction have the opposite effect.

Filtration coefficient (Kf) a measure of a membrane's permeability to water; specifically, the volume of fluid **filtered** in unit time through a unit area of membrane per unit pressure difference, and it defined as the glomerular **filtration** rate (GFR) for both **kidney** per millimeter of mercury (mmHg) of **filtration** ...

"Filtration coefficient in other words : how much fluid is filtrated considering the surface area of all the glomerular capillaries when a change in pressure occurs."

FILTRATION COEFFICIENT Kf

Kf: Is a measure of the product of the hydraulic conductivity and surface area of glomerular capillaries

Kf = GFR / Net filtration pressure

Kf=125 /10 =12.5ml/min/mmHg "for the whole kidney

Kf= 4.2ml/min/mmHg/100gm of kidney

"Note that the glomerular Kf is 400 to 500 X than that of the tissues"

Kf=0.01ml/min/mmHg/100gr in other tissues

Factors affect GFR

1. Increasing the Glomerular capillary filtration coefficient increases GFR .

   Chronic uncontrolled hypertension & DM decrease coefficient and GFR (increase the thickness of glomerular capillary basement membrane)

2. Increasing Bowman's capsule hydrostatic pressure decreases GFR as in formation of (stones) in urinary tract mainly ureter.

   "CHP pushes the fluid inside so less filtration"

Factors affect GFR Cont

3. Increasing Glomerular capillary colloid osmotic pressure decreases GFR:

COP is 28 near the afferent arteriole, more filtration. The filtration will gradually decrease as the COP increases reaching its minimum rate near the efferent end ” COP is 36 near the efferent arteriole” average is 32 mmHg and this pressure is determined by:

a. Arterial plasma colloid osmotic pressure

b. Fraction of plasma filtered (filtration Fraction)

“The more filtered plasma —> more plasma proteins the more COP”

Factors affect GFR Cont

4. Increasing Glomerular capillary hydrostatic pressure increases GFR : this pressure is determined by:

a. Arterial pressure. "Pressure normally found in all arteries"

b. Afferent arteriolar resistance

"if there's constriction , less blood flow to the glomeruli, less filtration"

c. Efferent arteriolar resistance this has biphasic effect:

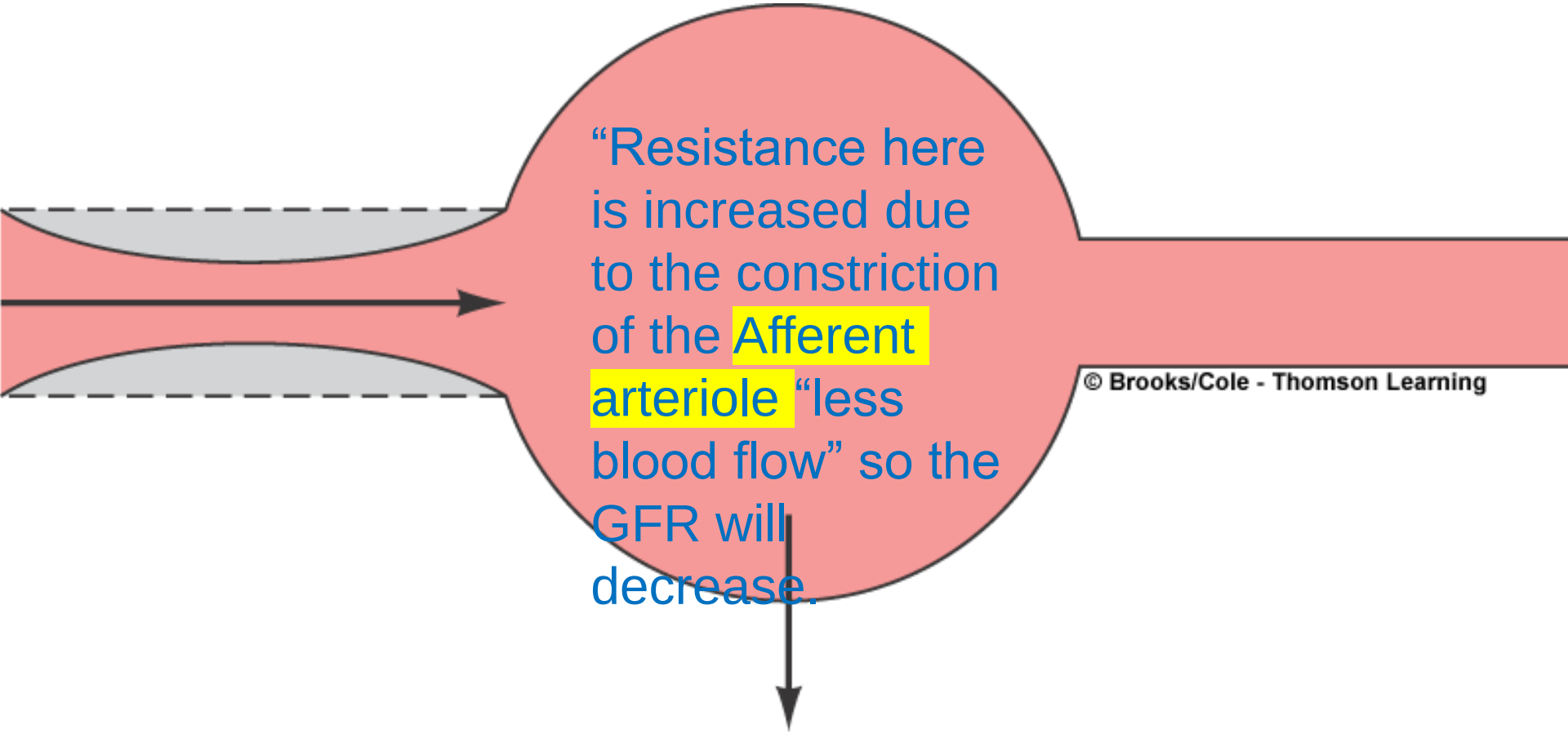
A- Moderate increase In the efferent arteriole resistanceleads to moderate increase in CHP which in turn increases the GFR

B- Severe inc. in the efferent arteriole resistance decreases GFR

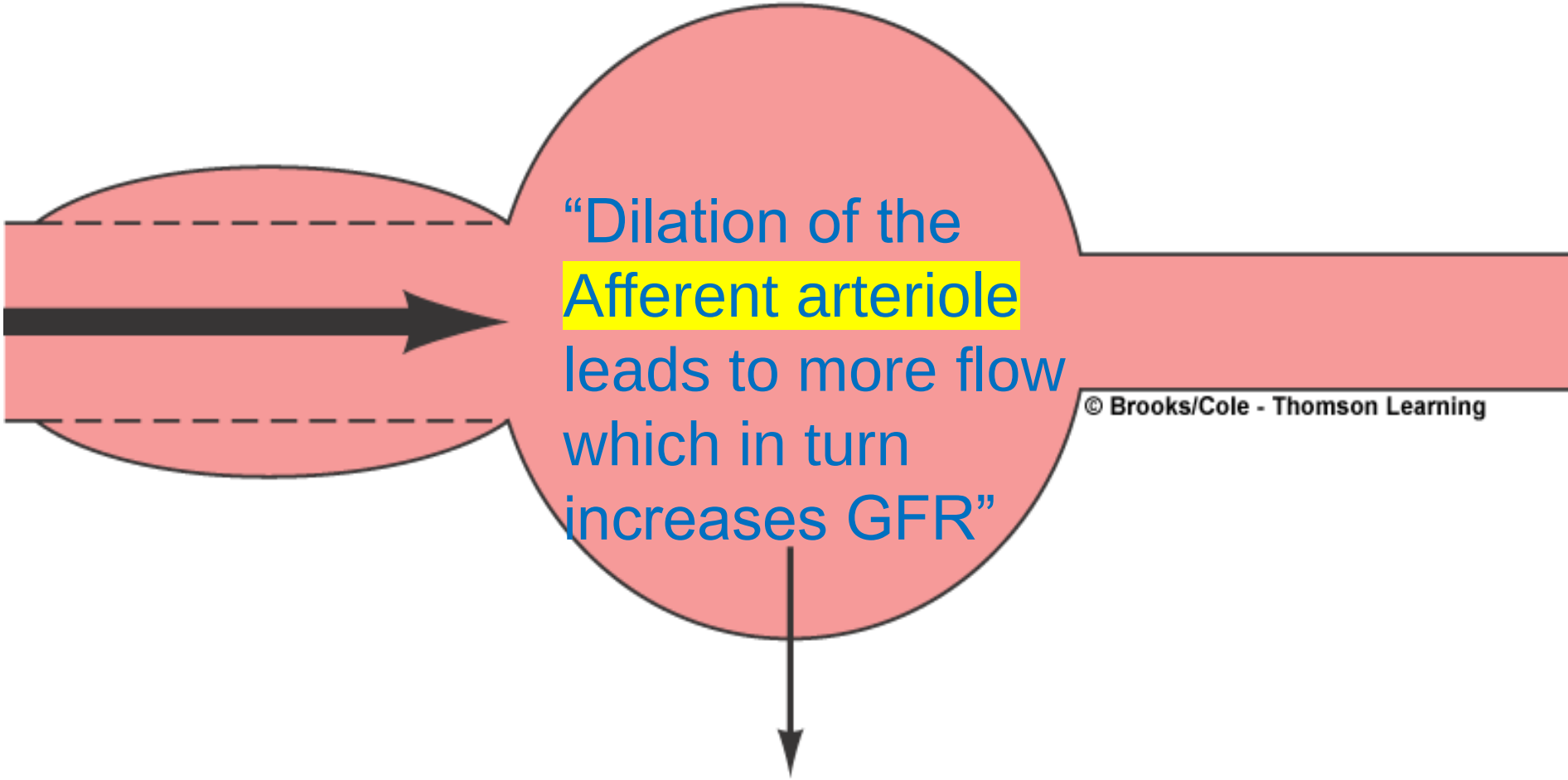
"by time there'll be more plasma proteins, this accumulation of plasma proteins increases the colloid osmotic pressure leading to the decrease of GFR"

"in this case the COP will be equal or a bit less than the glomerular CHP"

Factors affect GFR Cont



Factors affect GFR Cont



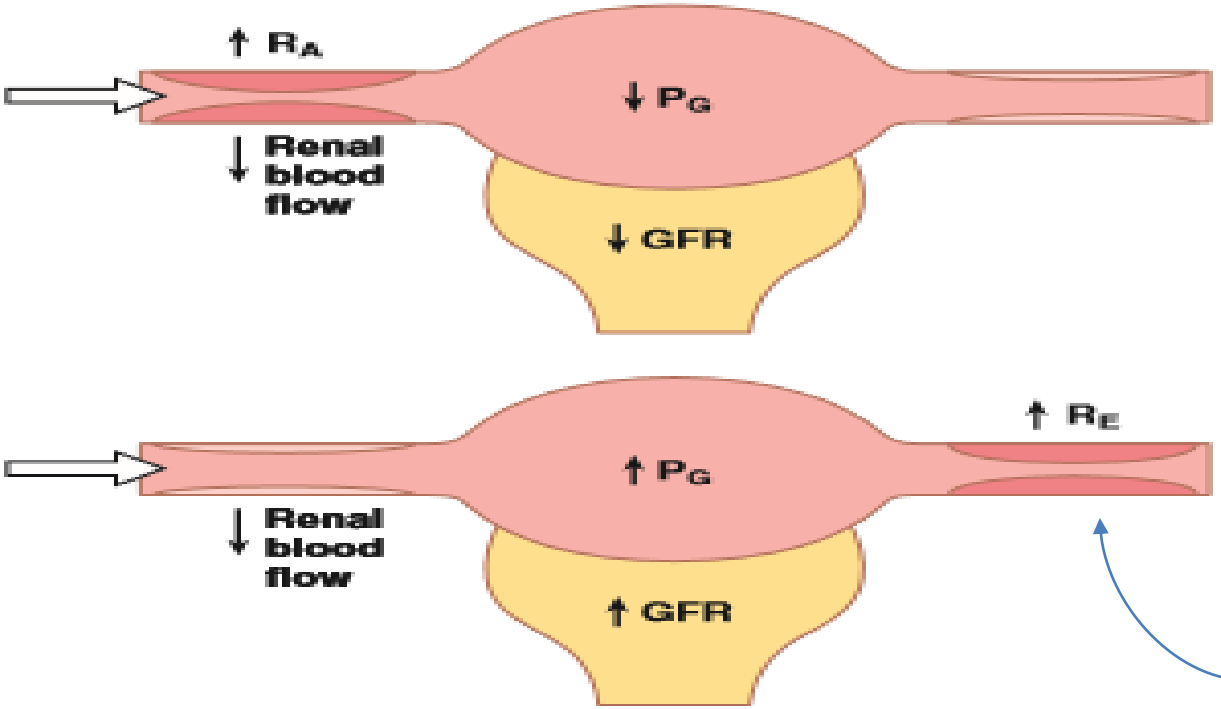
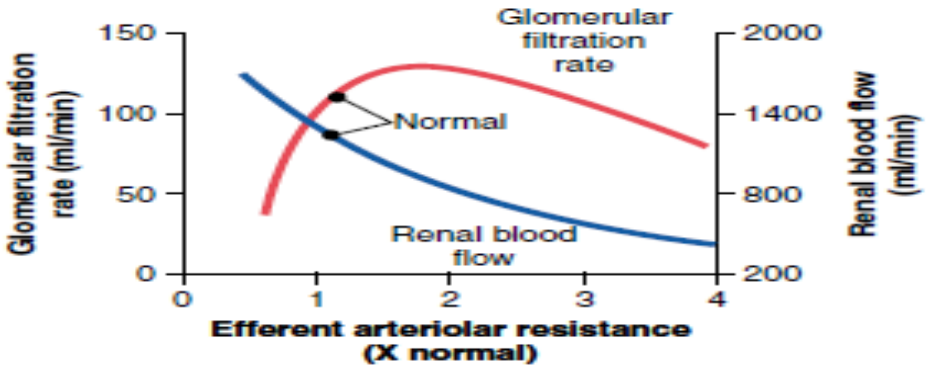


Figure 27-6. Effect of increases in afferent arteriolar resistance (R_A, top panel) or efferent arteriolar resistance (R_E, bottom panel) on renal blood flow, glomerular hydrostatic pressure (P_G), and glomerular filtration rate (*GFR*).

"Increase the Afferent arteriole resistance, less blood flow, less GFR"

"As mentioned before the increase in efferent arteriole resistance is biphasic , here's phase 1 where moderate increase In the efferent arteriole resistance leads to moderate increase in glomerular CHP which in turn increases the GFR"



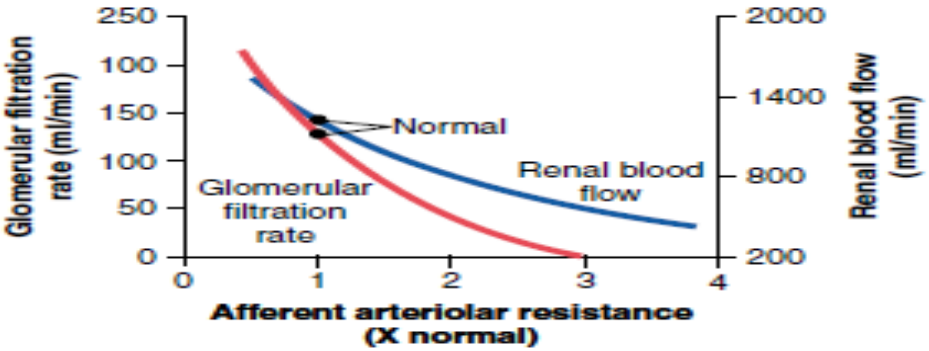


Figure 26-15 Effect of change in afferent arteriolar resistance or efferent arteriolar resistance on glomerular filtration rate and renal blood flow.

"These curves shows the effect of efferent and afferent arterioles resistance to the GFR and glomerular filtration rate"

Table 26-2 Factors That Can Decrease the Glomerular Filtration Rate (GFR)

Physical Determinants*	Physiologic/Pathophysiologic Causes
$\downarrow K_f \rightarrow \downarrow$ GFR	Renal disease, diabetes mellitus, hypertension
$\uparrow P_B \rightarrow \downarrow$ GFR	Urinary tract obstruction (e.g., kidney stones)
$\uparrow \pi_G \rightarrow \downarrow$ GFR	↓ Renal blood flow, increased plasma proteins
$\downarrow P_G \rightarrow \downarrow$ GFR	
$\downarrow A_p \rightarrow \downarrow P_G$	↓ Arterial pressure (has only small effect due to autoregulation)
$\downarrow R_E \rightarrow \downarrow P_G$	↓ Angiotensin II (drugs that block angiotensin II formation)
$\uparrow R_A \rightarrow \downarrow P_G$	↑ Sympathetic activity, vasoconstrictor hormones (e.g., norepinephrine, endothelin)

*Opposite changes in the determinants usually increase GFR.
K_f, glomerular filtration coefficient; P_B, Bowman's capsule hydrostatic pressure; π_G, glomerular capillary colloid osmotic pressure; P_G, glomerular capillary hydrostatic pressure; A_p, systemic arterial pressure; R_E, efferent arteriolar resistance; R_A, afferent arteriolar resistance.

Increasing colloid osmotic pressure

Less GFR

Decreases in GFR

"Here's the factors that dec. the GFR "
"As the doctor said sometimes kidney stones leads to dec. in GFR due to it effect on the bowman's capsular pressure increasing it, these stones leads to the increase of the kidneys size"

Renal blood flow and GF Controlled by

Renal blood flow: 1200 ml/min = 21% C.O "cardiac output"

1-2% in vasa recta "we'll talk about it in the upcoming lectures"

O2 consumption by the kid mainly related to active Na reabsorption by renal tubules.

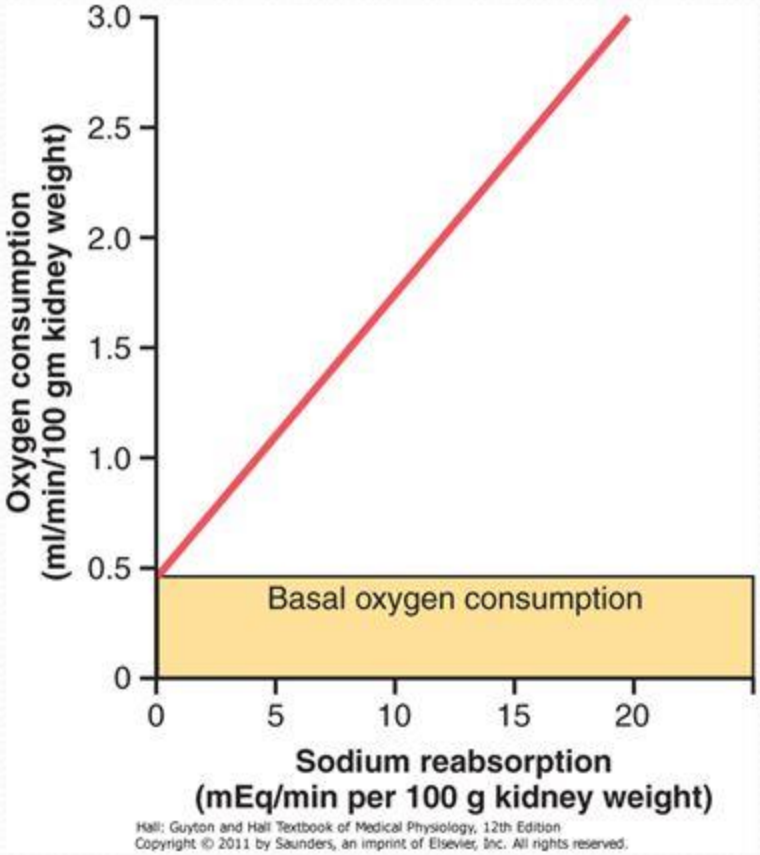
"More Na reabsorption increases oxygen consumption which increases the renal blood flow"

- **1. Sympathetic N.S :**

- Strong activation, decreases GFR and flow as in hemorrhage and CNS ischemia
- Moderate activation : little effect (normal person)

Renal Blood Flow

- **Renal Blood Flow and Oxygen Consumption**



In normal people

Fig. 26.16 Relationship between sodium reabsorption and oxygen consumption

RENAL BLOOD FLOW =

RAP-RVP / Total renal vascular resistance

“Renal arterial pressure – Renal venous pressure”

“Renal vascular resistance is difference in resistance between afferent and efferent arteriole”

“Extra From google its ameasurement of the degree to which the blood vessels of the kidneys impede the flow of blood through them.

Table 26-3 Approximate Pressures and Vascular Resistances in the Circulation of a Normal Kidney

Vessel	Pressure in Vessel (mm Hg)		Percent of Total Renal Vascular Resistance
	Beginning	*End*	
Renal artery	100	100	≈0
Interlobar, arcuate, and interlobular arteries	≈100	85	≈16
Afferent arteriole	85	60	≈26
Glomerular capillaries	60	59	≈1
Efferent arteriole	59	18	≈43
Peritubular capillaries	18	8	≈10
Interlobar, interlobular, and arcuate veins	8	4	≈4
Renal vein	4	≈4	≈0

"Significant resistance"

"Capillaries surrounding renal tubules"

"Renal artery and renal vein resistance is zero"

2. Hormonal and autacoid:

a. Norepinephrine , epinephrine, endothelin constrict renal blood vessels and decreases GFR

b. Angiotensin II constricts efferent arterioles "not the afferent" leading to the inc. Of GFR – and Na and H_2O reabsorption

c. Endothelial - Derived Nitric oxide decreases resistance "increases the blood flow" which Inc. GFR

d. Prostaglandins, bradykinin cause vasodilators "dec. the resistance, inc. the GFR"

3. Autoregulation of GFR and Renal blood flow :

- Arterial pressure 75 - to 160 mmHg changes GFR very few% .

"Bcz of the autoregulation"

- Normally GFR is 180 L/day "in normal pressure" if pressure inc. by 25% so GFR will inc. to 225 L/day. If reabsorption constant "or dec. to prevent the excess pressure effect " so urine formation 46.5 L/day. "Normally the urine formation is 1.5 L/day"
- Autoregulation and ^ or adaptive changes in reabsorption will not cause significant increase in urine output (pressure Diuresis) or (pressure Natriuresis) .

"Auto regulation : regulation of the blood flow to the tissues according to their need not according the diff. In pressure"

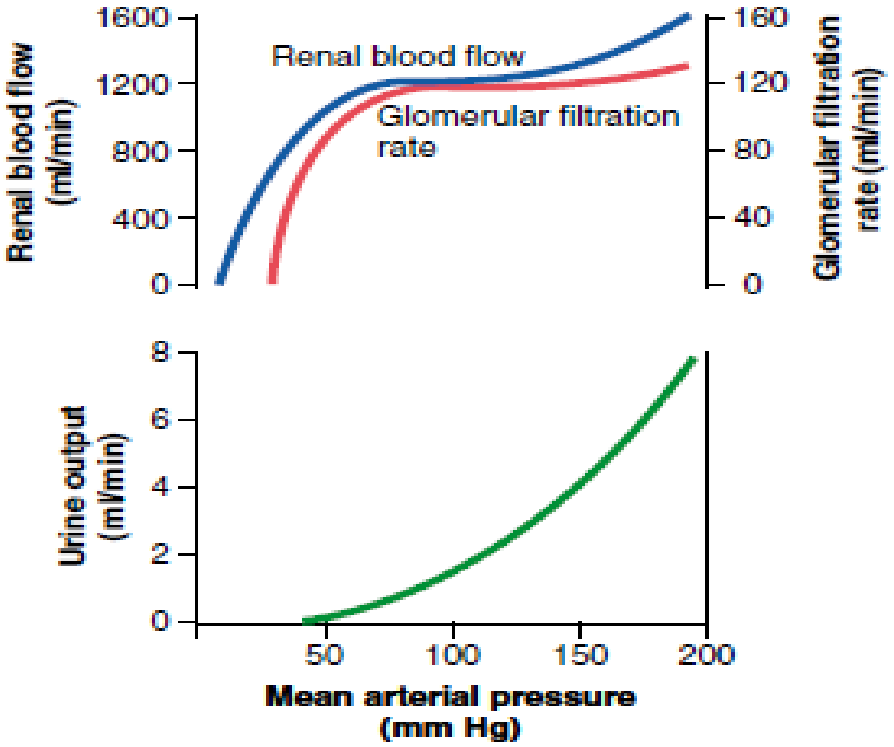


Figure 26-17 Autoregulation of renal blood flow and glomerular filtration rate but lack of autoregulation of urine flow during changes in renal arterial pressure.

"This curve shows the relationship bt. The renal blood flow, glomerular filtration and mean arterial pressure , urine formation"

As can be seen in here a slight inc. in mean arterial pressure increases urine formation drastically in this way the renal blood flow and GFR will remain some how constant utoregulation "

Juxtaglomerular complex:

Tubuloglomerular feedback:

1. Afferent arteriolar feedback mechanism
2. Efferent arteriolar feedback mechanism

Juxtaglomerular complex:

Macula densa cells (proximal distal tubule)

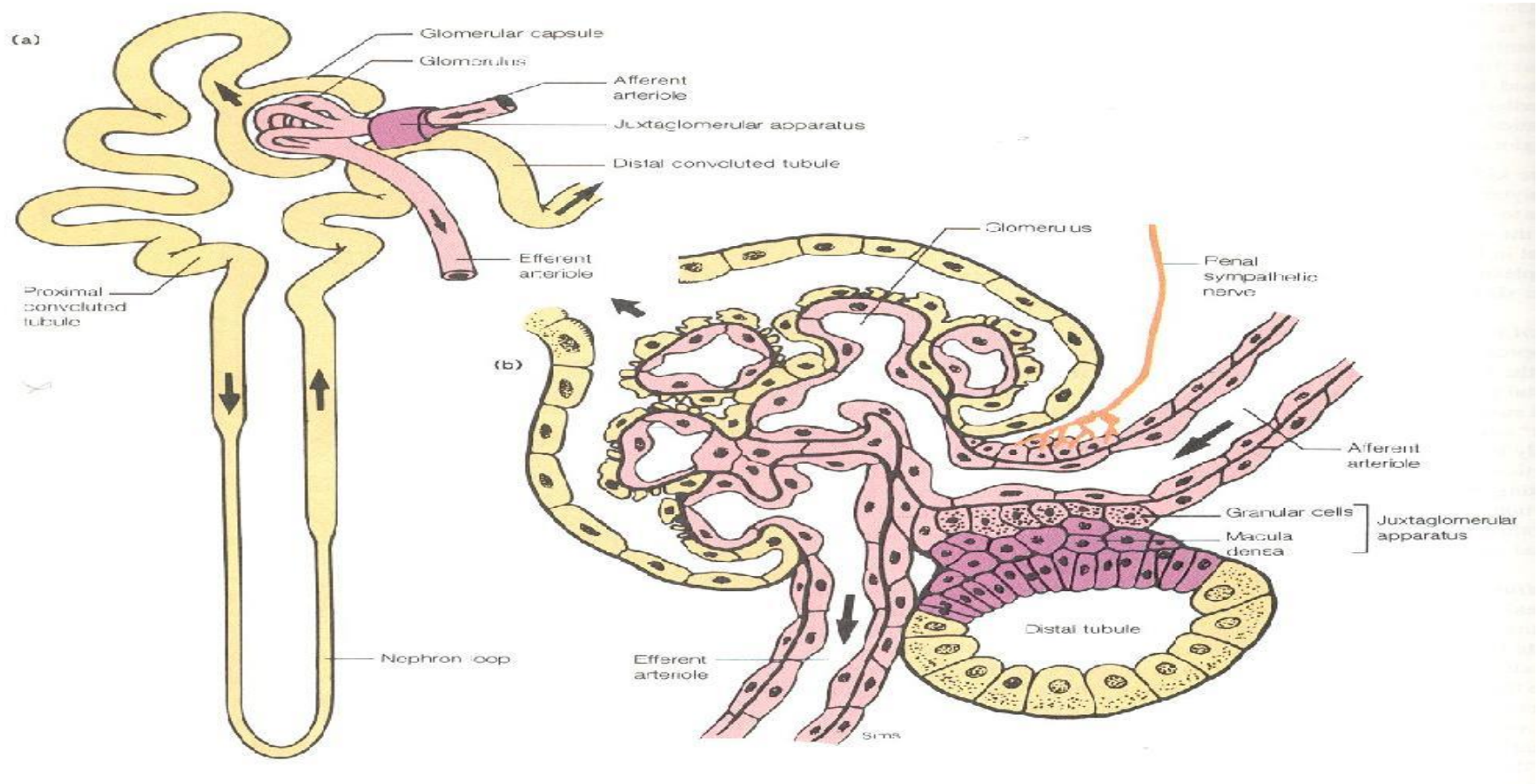
Juxtaglomerular cells (in the wall of efferent & afferent arterioles) decrease [NaCl] stimulate macula densa :

- 1. Dilates afferent arteriole

"from book, dilating the afferent arteriole, dec. the resistance, more blood flow, raises glomerular hydrostatic pressure, helps return GFR to its normal rate"

- 2. Releases renin(from glomerular. Cells)→angiotensin I-→Angiotensin II → Constricts efferent . "inc. glomerular hydrostatic pressure, helping GFR return to normal , "from book""

"The macula densa cells are sensitive to the concentration of sodium in the blood flow passing through it, thus a change in Na concentration inc. or dec. the blood flow"



"Juxtaglomerular apparatus, proximal part of distal tubule"

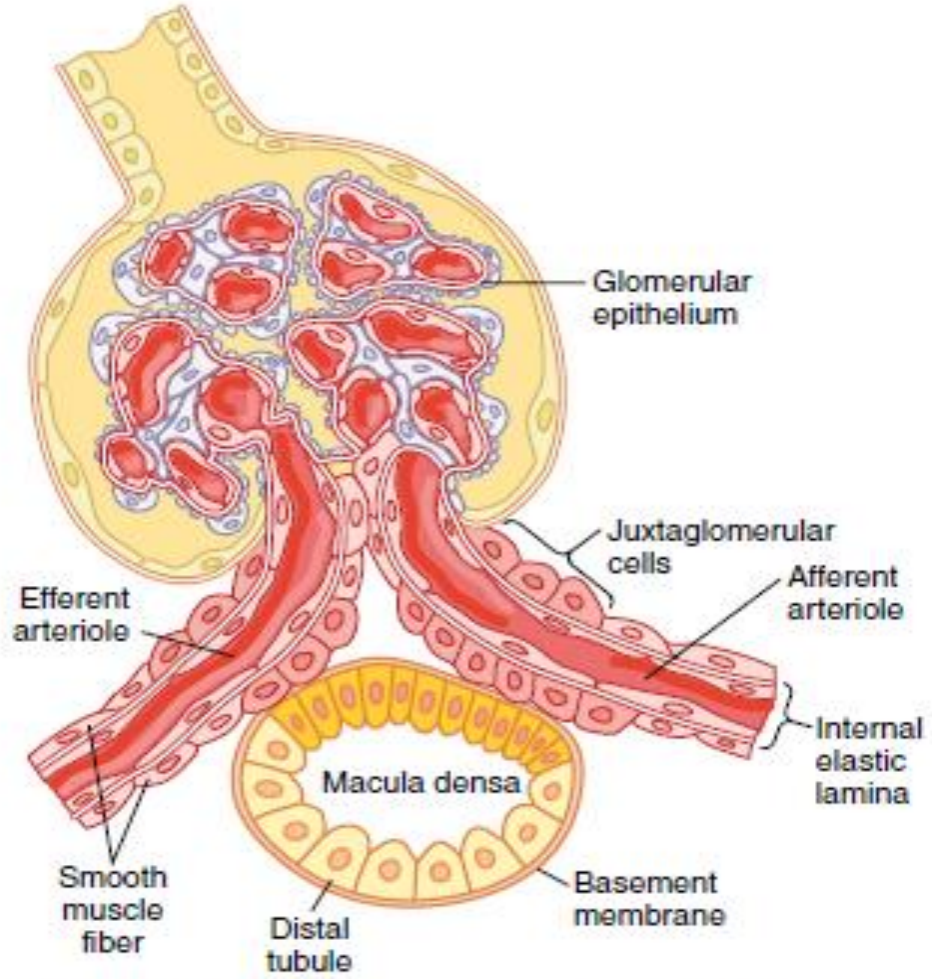
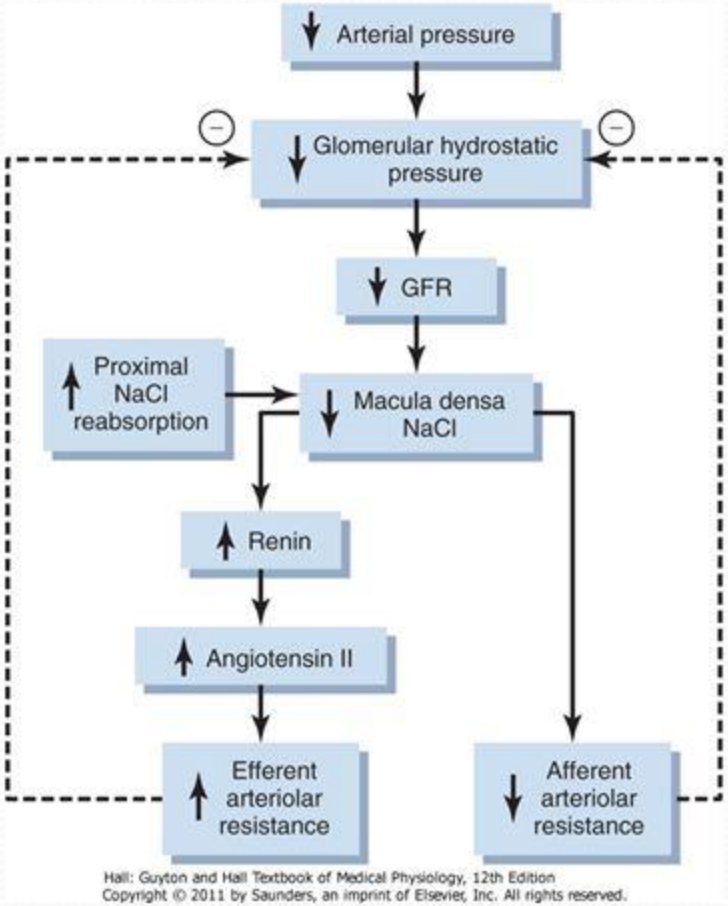


Figure 26-18 Structure of the juxtaglomerular apparatus, demonstrating its possible feedback role in the control of nephron function.

- **Decreased macula densa NaCl causes dilation of afferent arterioles and increased renin release**



"To keep the glomerular hydrostatic pressure high"

Fig. 26.19

"Inc. the blood flow"

4. Myogenic autoregulation :

When arterial pressure increases it will contract vessels & prevent increase renal blood flow.

”as in CVS , the inc. in arterial pressure leads to the stretch of muscles surrounding the walls of the arteries Constricting them which reduces the resistance , preventing the inc. in renal blood flow”

“ From the book, this contraction prevents excessive stretch of the vessel and at the same time, by raising vascular resistance helps prevent excessive increases in renal blood flow and GFR when arterial pressure increases.”

5. Other factors :

1. A. any substance that inc. Protein intake →inc. in blood flow and GFR→inc. of a.a→inc. reabsorption water/Na →decrease Na→ autoregulation by stimulate macula densa to decrease afferent arteriole and so increase RBF “renal blood flow” & GFR

B. inc. Blood glucose: same mechanism .

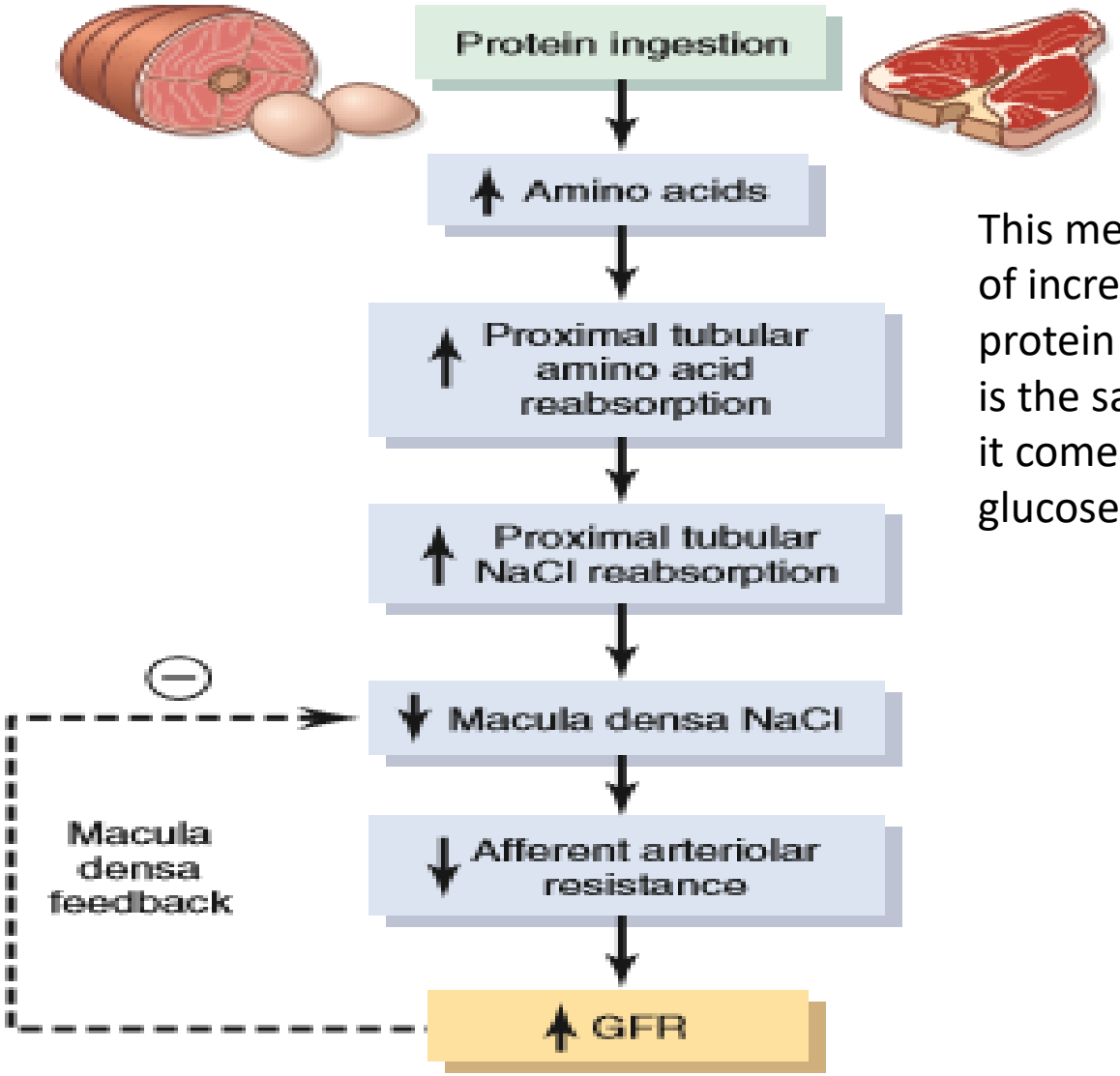


Figure 27-12. Possible role of macula densa feedback in mediating increased glomerular filtration rate *(GFR)* after a high-protein meal.

This mechanism of increased protein ingestion is the same when it comes to glucose