
In The Name Of God

C H A P T E R 2 7

- **Glomerular Filtration, Renal Blood Flow, and Their Control**

هدف کلی جلسه: آشنایی با فیلتراسیون گلومرولی، جریان خون کلیوی و کنترل آنها

اهداف ویژه جلسه
در پایان دانشجو قادر باشد:

- ترکیب فیلترای گلومرولی را شرح دهد
- فرایندهای درگیر در تشکیل ادرار را به تفصیل شرح دهد
- لایه های مختلف تشکیل دهنده سد تصفیه را نام ببرد
- نقش لایه های تشکیل دهنده سد تصفیه در تنظیم فیلتراسیون هر ماده را توضیح دهد
- نیروهای تعیین کننده میزان فیلتراسیون گلومرولی را نام ببرد
- عوامل موثر بر نیروهای تعیین کننده میزان فیلتراسیون گلومرولی را شرح دهد
- عوامل موثر بر میزان جریان خون کلیوی را توضیح دهد
- مکانیسم خودتنظیمی میزان فیلتراسیون گلومرولی و اهمیت آن را توضیح دهد

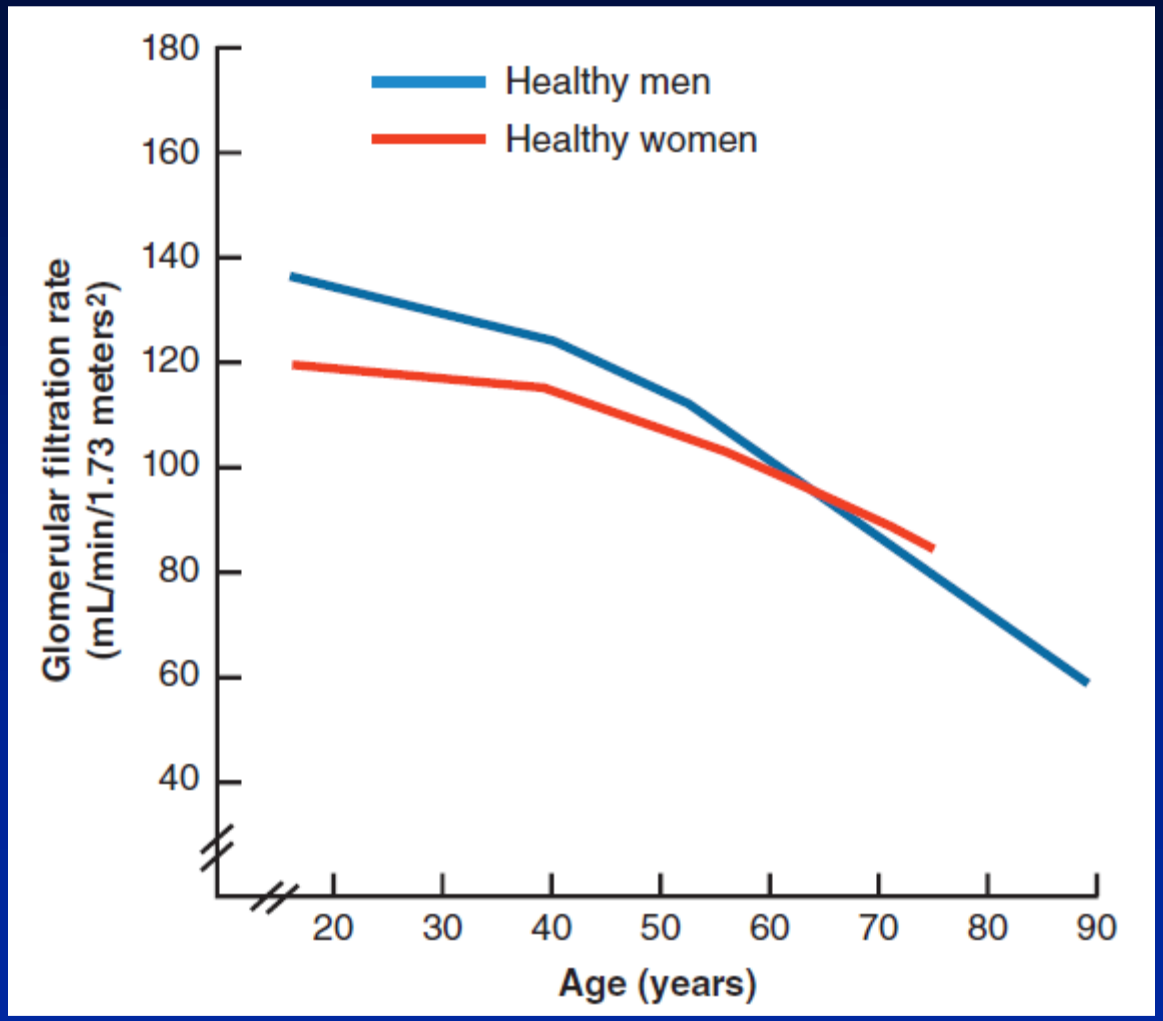
Glomerular Filtration—The First Step in Urine Formation

- **Composition of the Glomerular Filtrate**
- **GFR Is About 20 Percent of the Renal Plasma Flow**

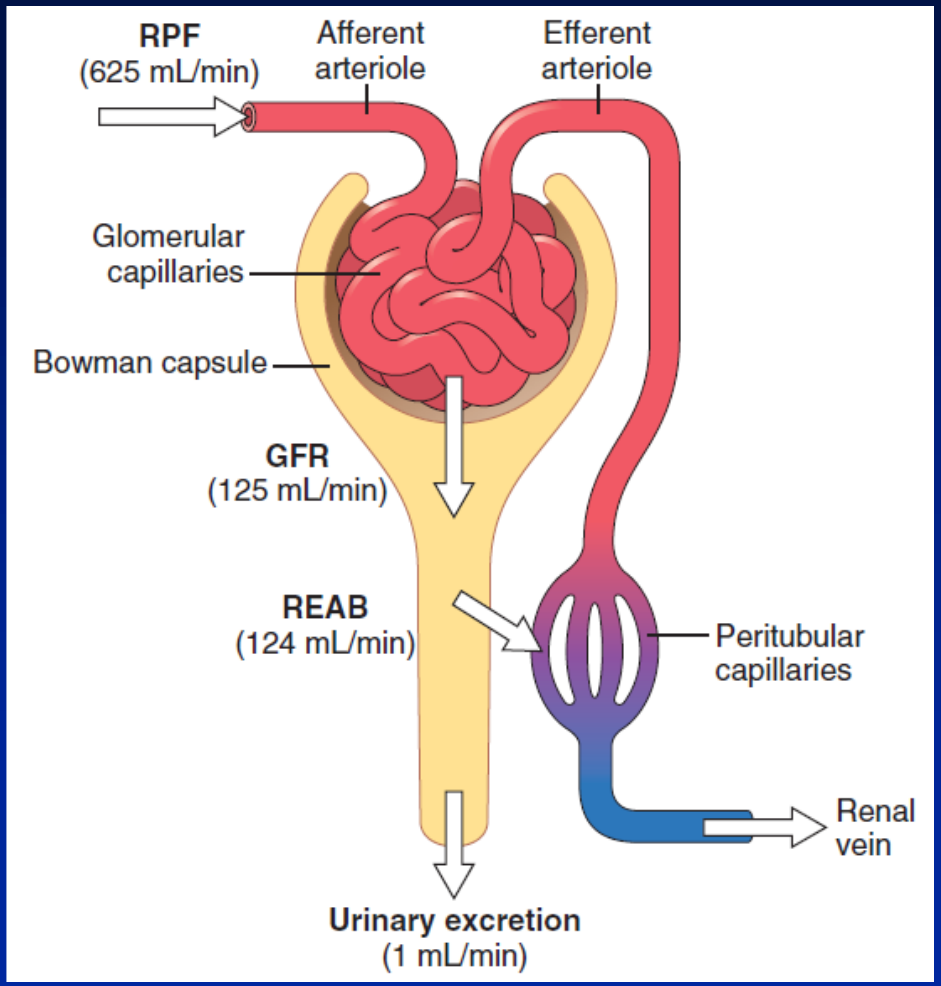
$GFR = NFP \times K_f$ $K_f = K \times S$

Filtration fraction = GFR/Renal plasma flow

Age-related changes in glomerular filtration rate (GFR) in healthy men and women

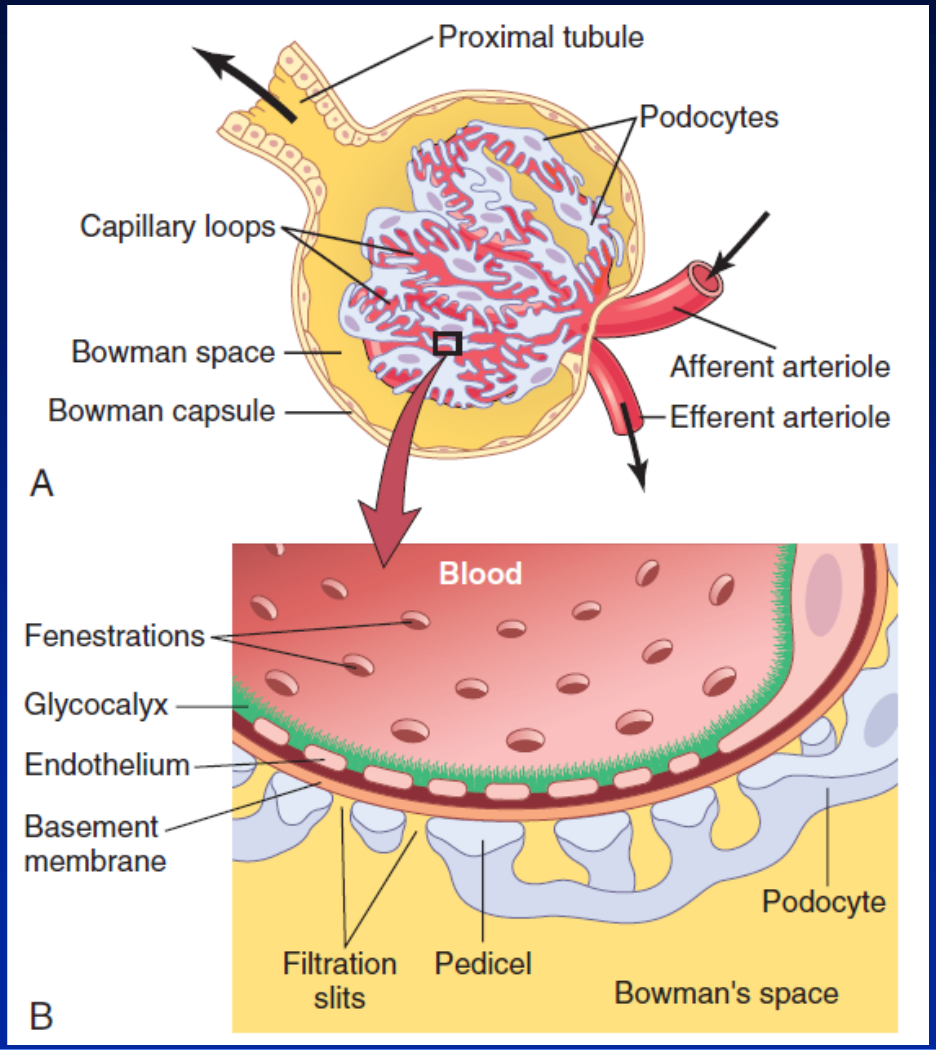


Average values for total renal plasma flow, GFR, tubular reabsorption, and urine flow rate

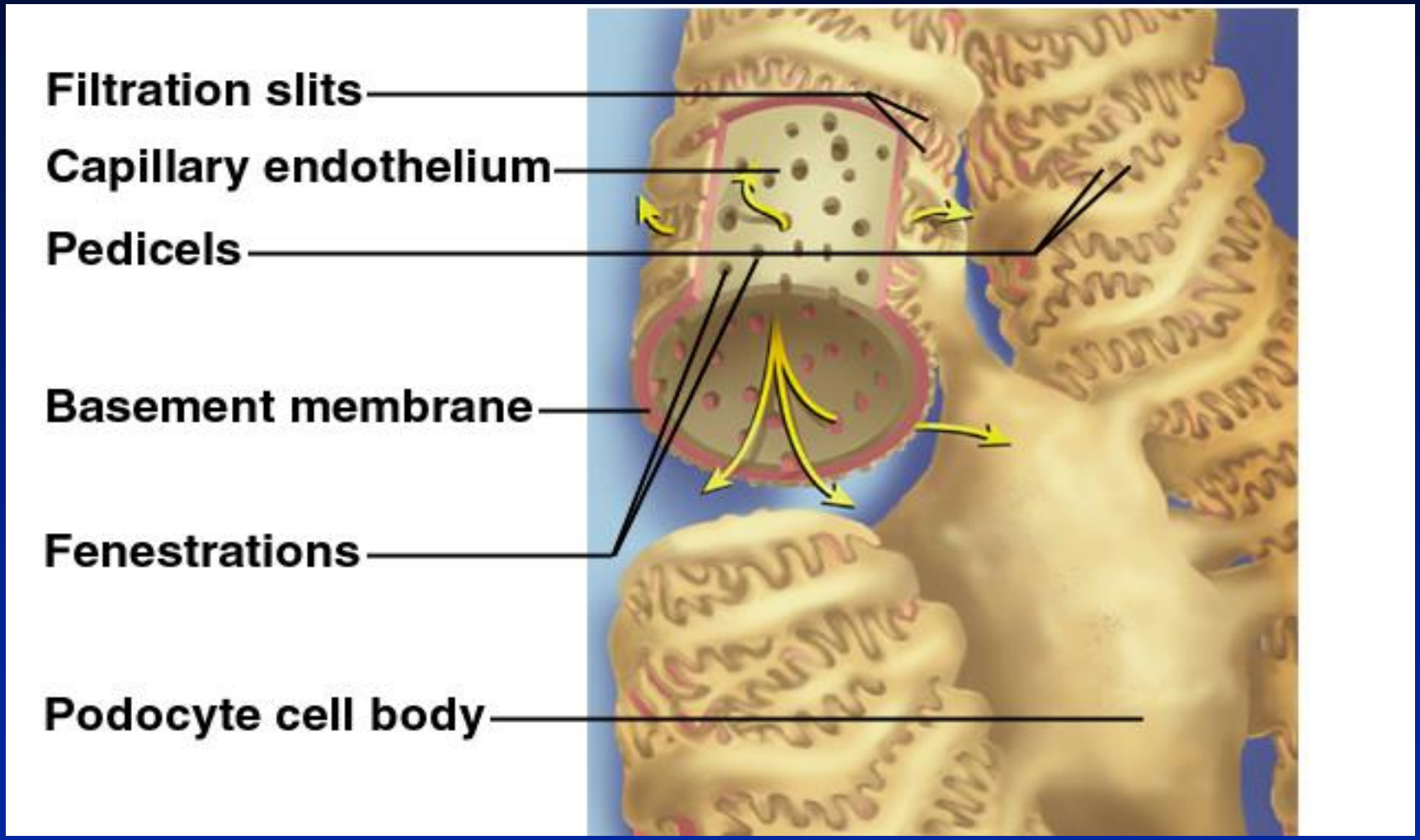


- **Glomerular Capillary Membrane**

A: basic structure of glomerular capillaries
B: the membrane of glomerular capillaries



Filtration Membrane Diagram



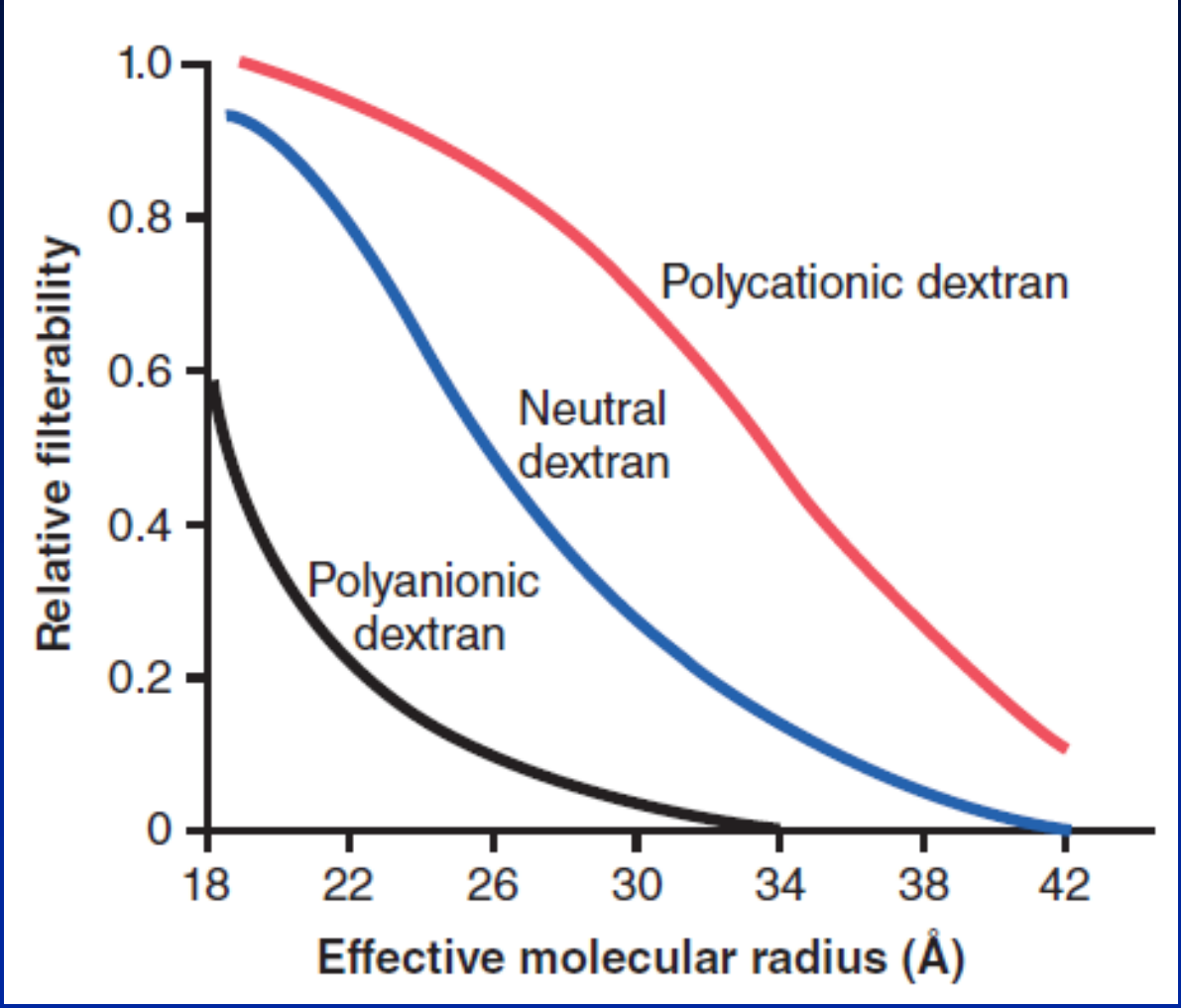
Minimal change nephropathy

Filterability of Solutes Is Inversely Related to Their Size

Substance	Molecular Weight	Filterability
Water	18	1.0
Sodium	23	1.0
Glucose	180	1.0
Inulin	5500	1.0
Myoglobin	17,000	0.75
Albumin	69,000	0.005

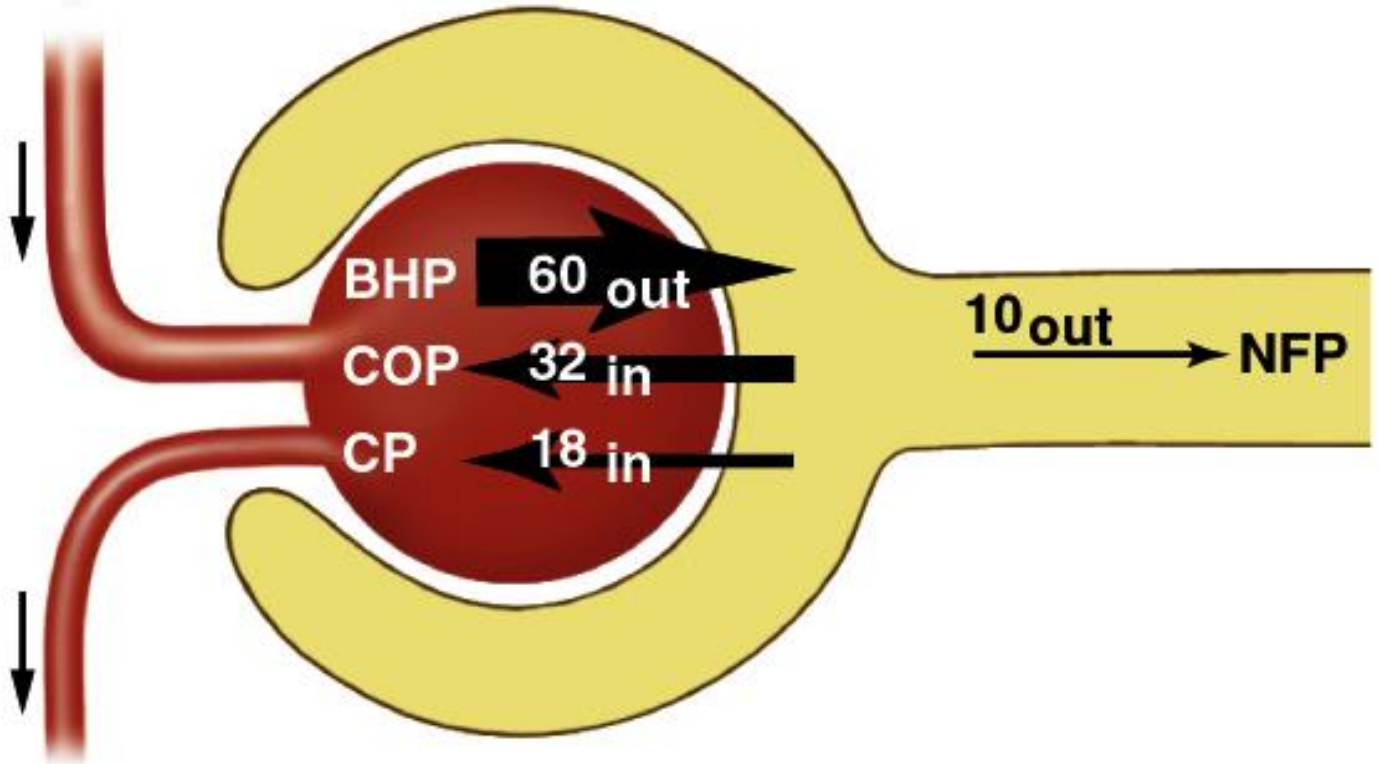
Negatively Charged Large Molecules Are Filtered Less Easily Than Positively Charged Molecules of Equal Molecular Size

Effect of molecular radius and electrical charge on filterability by the glomerular capillaries

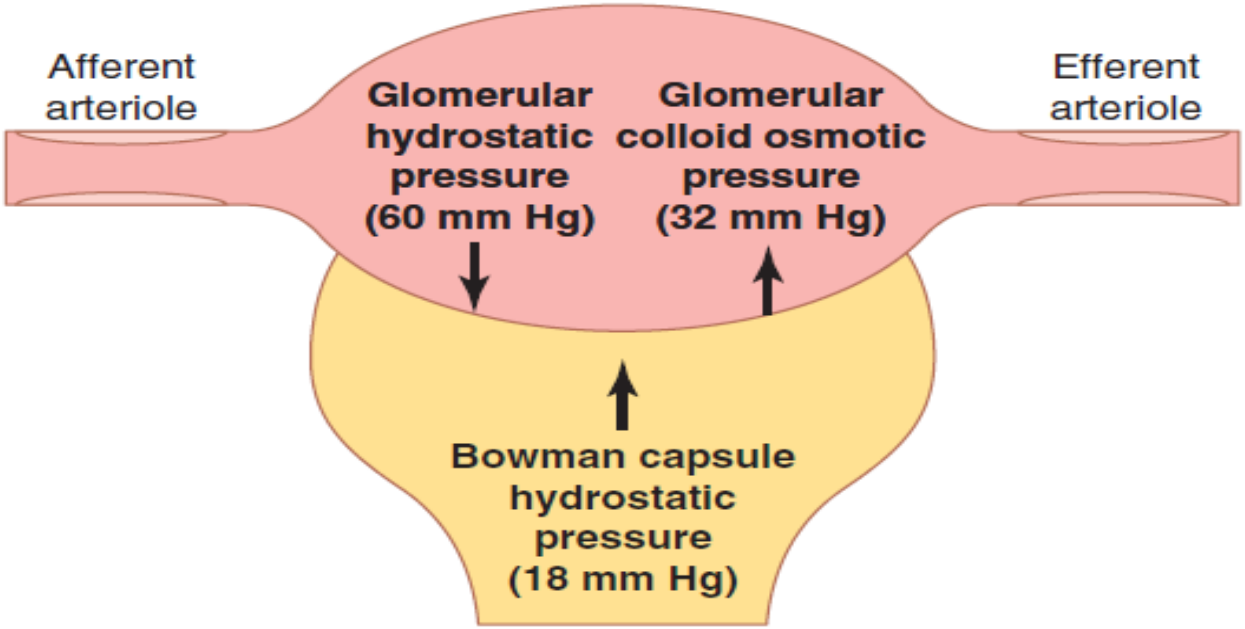


Determining factors for GFR:

1- net filtration pressure 2- filtration coefficient



Blood hydrostatic pressure (BHP)	60 mmHg out
Colloid osmotic pressure (COP)	–32 mmHg in
Capsular pressure (CP)	–18 mmHg in
Net filtration pressure (NFP)	10 mmHg ou



Net filtration pressure (10 mm Hg)	=	Glomerular hydrostatic pressure (60 mm Hg)	–	Bowman capsule hydrostatic pressure (18 mm Hg)	–	Glomerular colloid osmotic pressure (32 mm Hg)

$GFR = K_f \times$ Net filtration pressure

$$GFR = 12.5 \times (60 - 18 - 32 + 0) = 125$$

ml/min/mmHg mmHg ml/min

$$K_f = K \cdot S$$

- **Increased Glomerular Capillary Filtration Coefficient Increases GFR (400 times of sys.)**

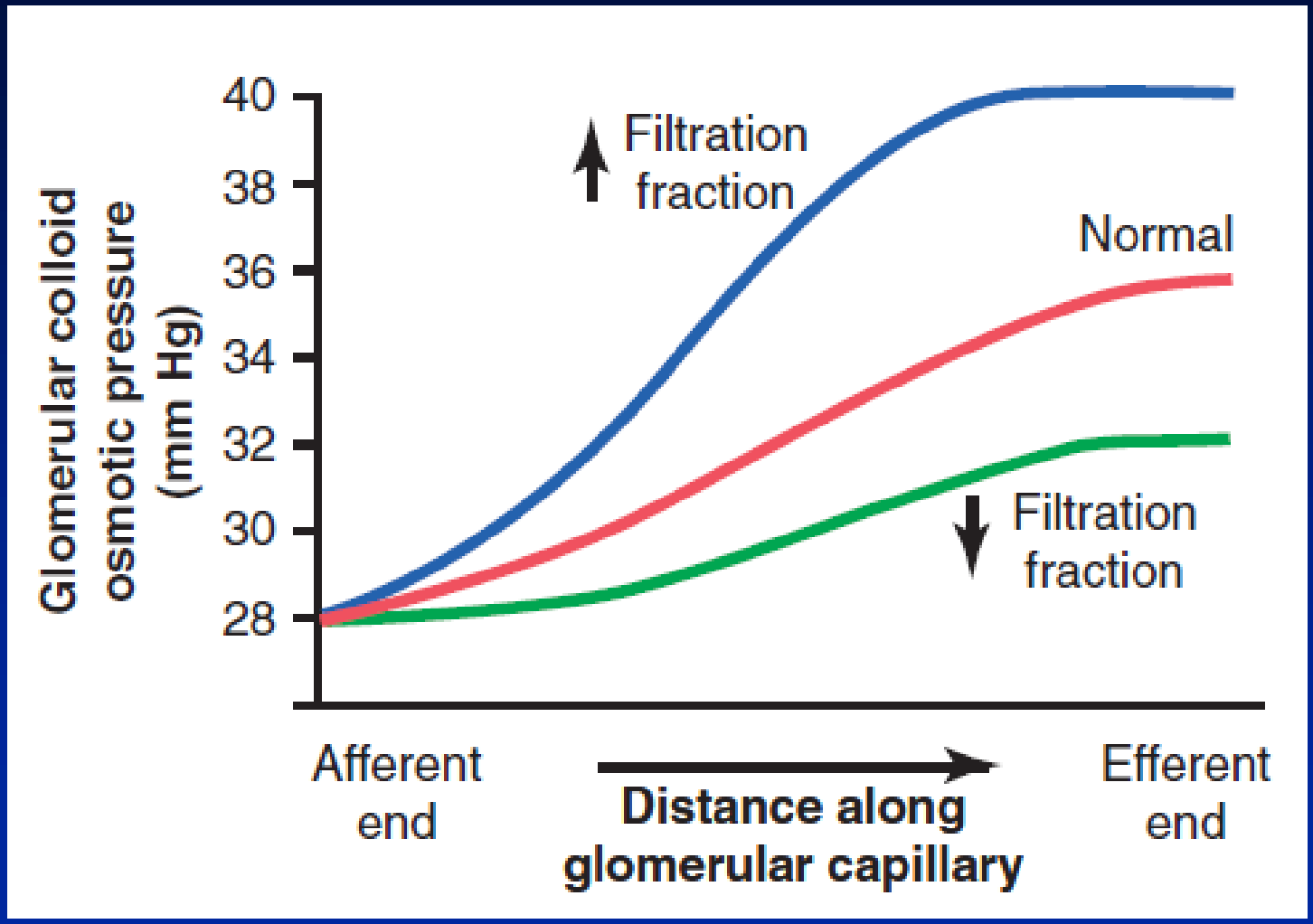
$$K_f = K \cdot S$$

K_f = GFR / Net filtration pressure

- **Increased Bowman's Capsule Hydrostatic Pressure Decreases GFR (18 mmHg)**

- **Increased Glomerular Capillary Colloid Osmotic Pressure Decreases GFR**

Increase of osmotic-colloid pressure in plasma that circulate in glomerular capillary



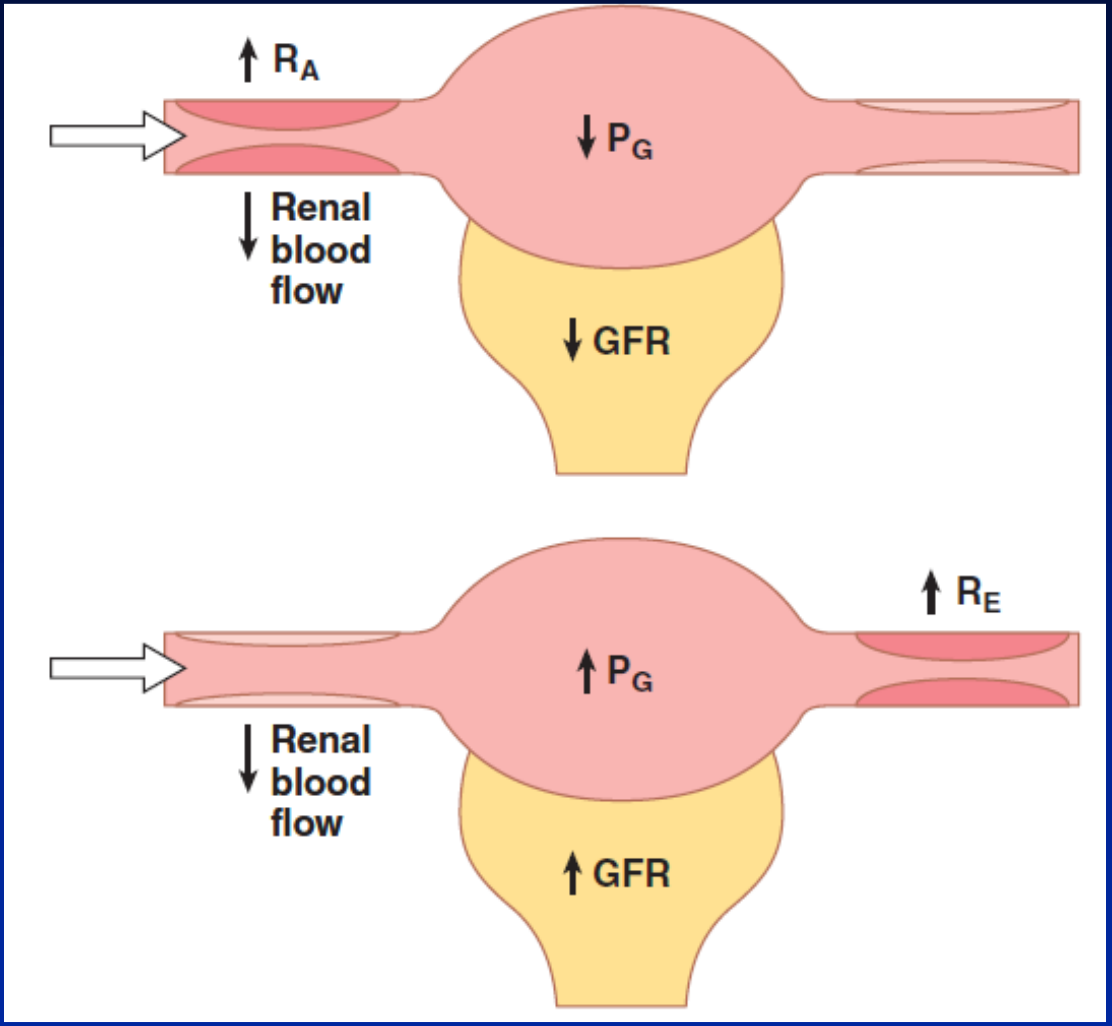
- Two factors that influence the glomerular capillary colloid osmotic pressure:

(1) the arterial plasma colloid osmotic pressure

(2) filtration fraction

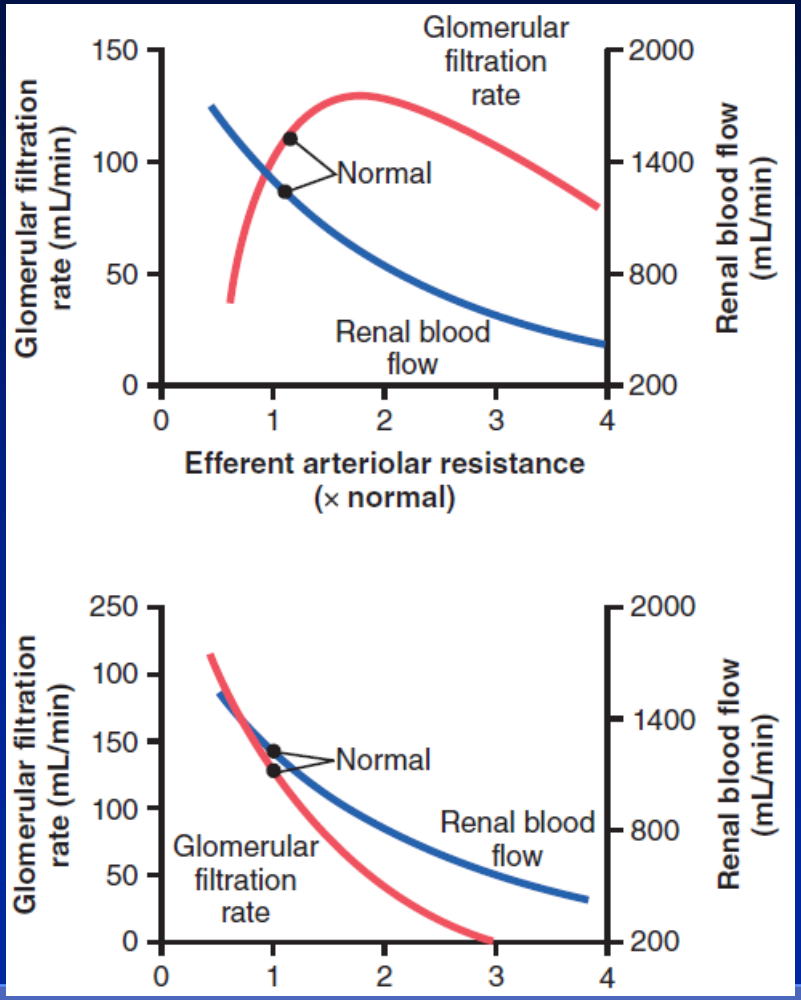
- Therefore, changes in renal blood flow can influence GFR independently of changes in glomerular hydrostatic pressure

Effect of increase in afferent or efferent arteriolar resistance on GFR



Increased Glomerular Capillary Hydrostatic Pressure

(by arterial pressure, afferent arteriolar resistance, and efferent arteriolar resistance) **Increases GFR**



GFR determining factors

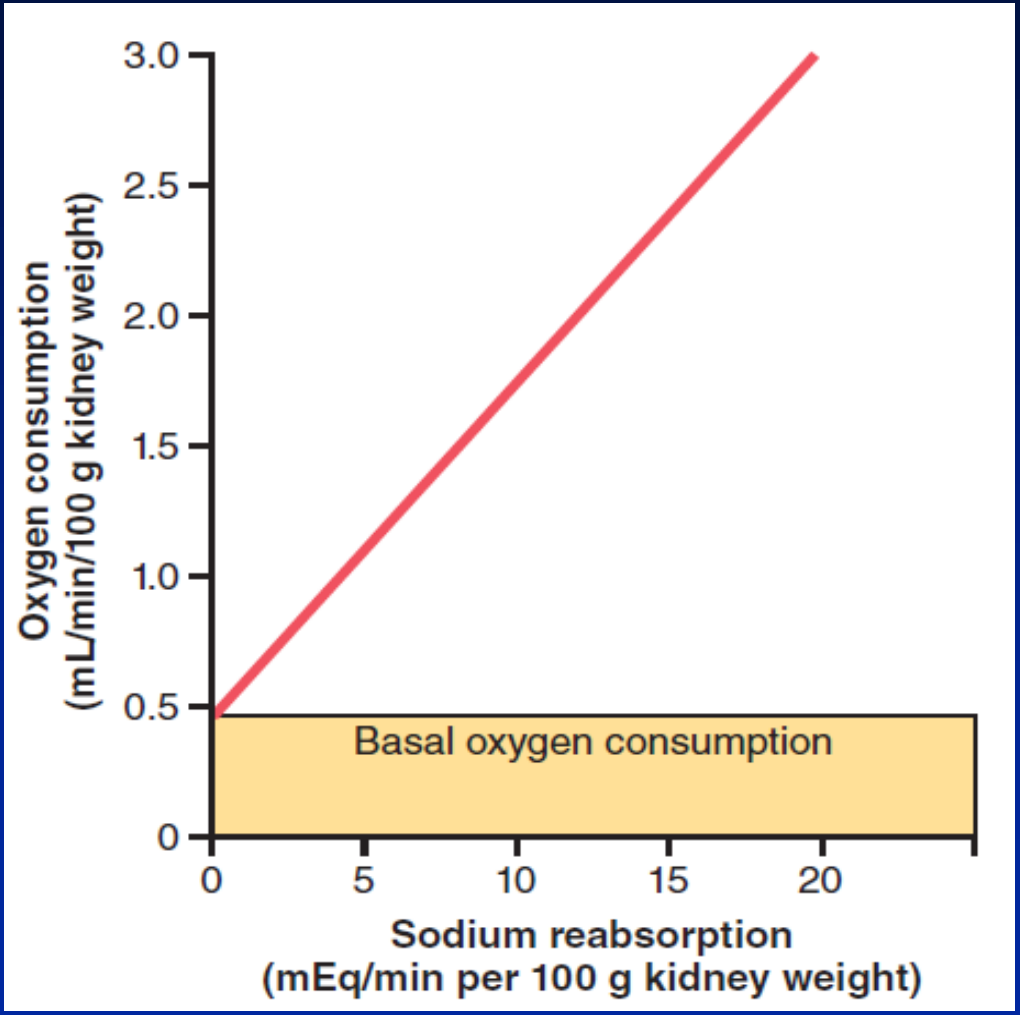
- ↑ BP → ↑P_{GC} → ↑GFR
- ↑Protein concentration → ↑Π_{GC} → ↓GFR
- ↑renal blood flow → ↑P_{GC} → ↑GFR
- Tubular occlusion → ↑P_{BS} → ↓GFR
- Mesangial cell contraction → ↓ K_f → ↓GFR
- Sympathetic nerve activation → ↓K_f → ↓GFR
- Ang II → ↑P_{GC} → Prevent decrease GFR

Factors That Can Decrease the Glomerular Filtration Rate

Physical Determinants[a]	Physiological or Pathophysiological Causes
$\downarrow K_f \rightarrow \downarrow$ GFR	Renal disease, diabetes mellitus, hypertension, aging
$\uparrow P_B \rightarrow \downarrow$ 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 a small effect because of 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)

- **Renal Blood Flow Rate**
- **Renal Blood Flow and Oxygen Consumption**

Relationship between oxygen consumption and sodium reabsorption



Approximate Pressures and Vascular Resistances in Circulation of a Normal Kidney

Vessel	*Pressure in Vessel (mm Hg)*		Percentage 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

$$\frac{\text{(Renal artery pressure} - \text{Renal vein pressure)}}{\text{Total renal vascular resistance}}$$

- **Blood Flow in the Vasa Recta of the Renal Medulla Is Very Low Compared with Flow in the Renal Cortex (1-2%)**

- **Physiologic Control of GFR and Renal Blood Flow**

- Glomerular hydrostatic pressure

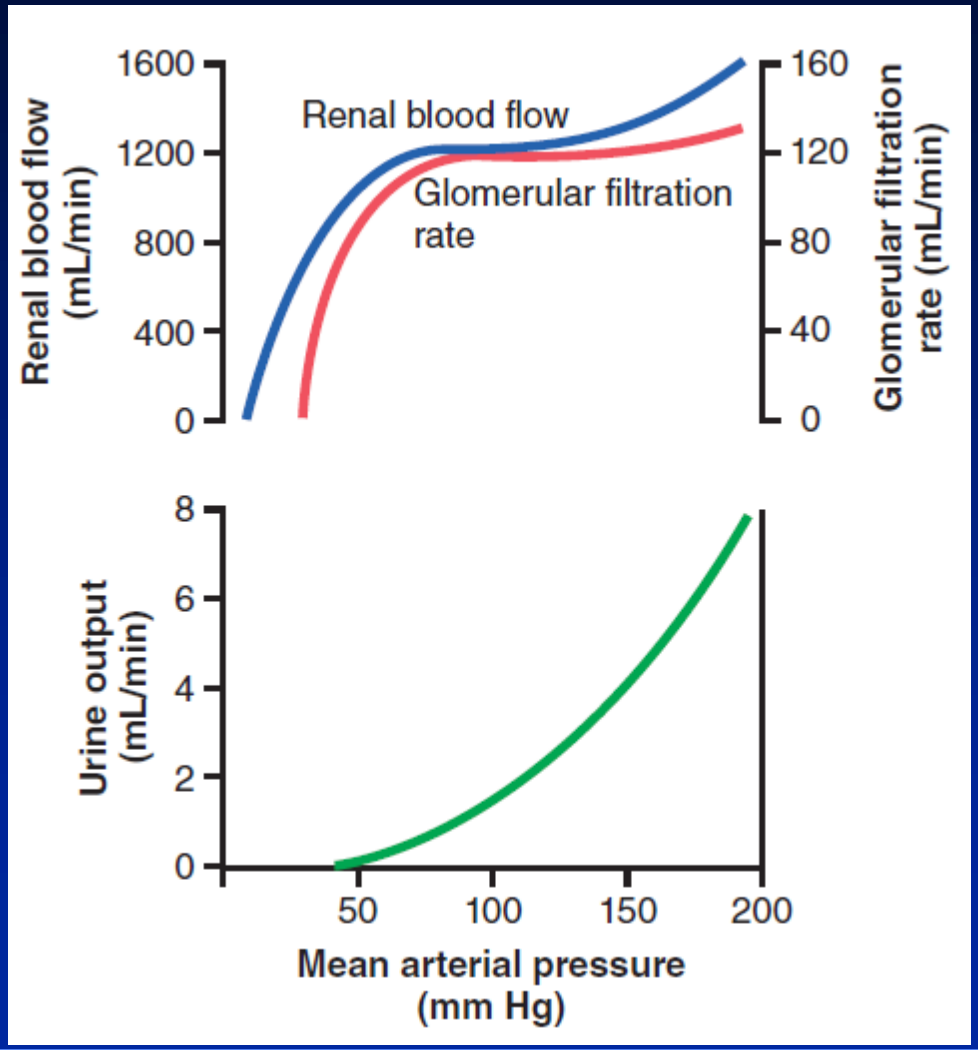
- Glomerular capillary colloid-osmotic pressure

- **Sympathetic Nervous System Activation Decreases GFR**

Hormones and Autacoids That Influence the GFR and Renal Blood Flow

Hormone or Autacoid	Effect on GFR	Effect on RBF
Norepinephrine	↓	↓
Epinephrine	↓	↓
Endothelin	↓	↓
Angiotensin II	↔ (prevents ↓)	↓
Endothelial-derived nitric oxide	↑	↑
Prostaglandins	↑	↑

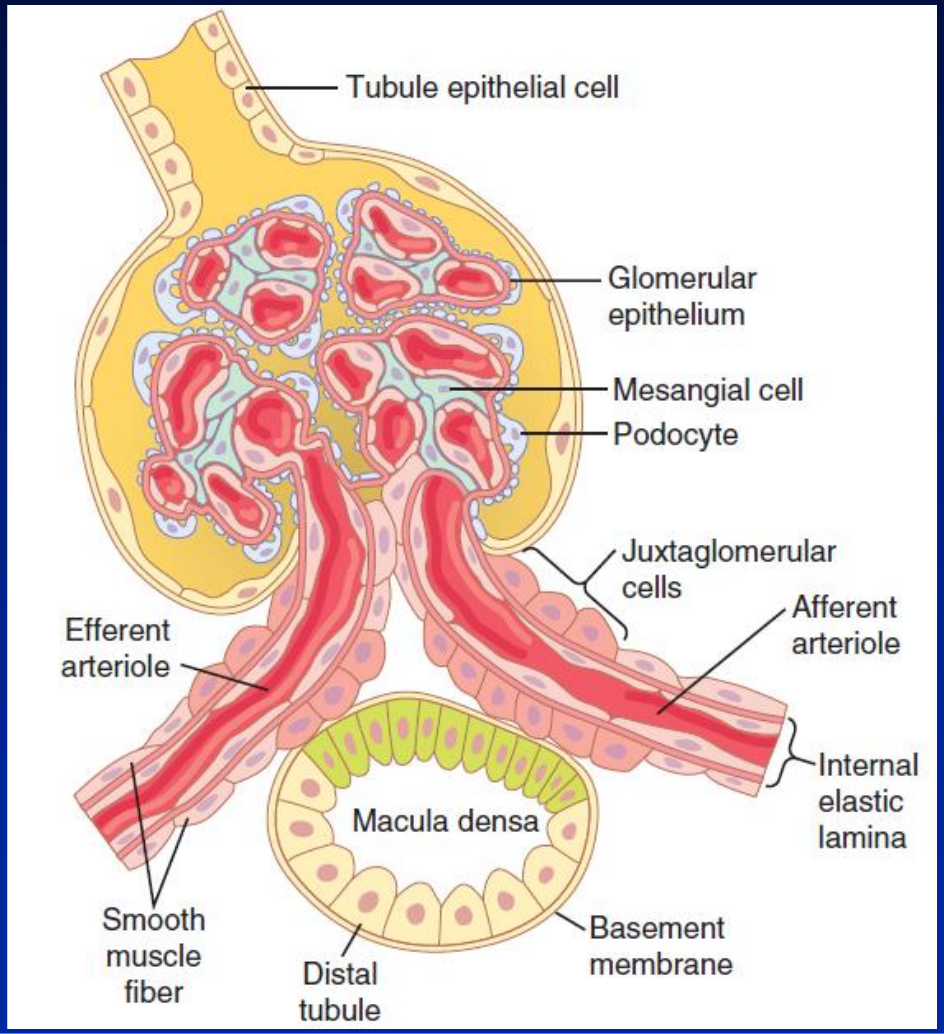
Autoregulation of GFR and Renal Blood Flow



- **Importance of GFR Autoregulation in Preventing Extreme Changes in Renal Excretion**

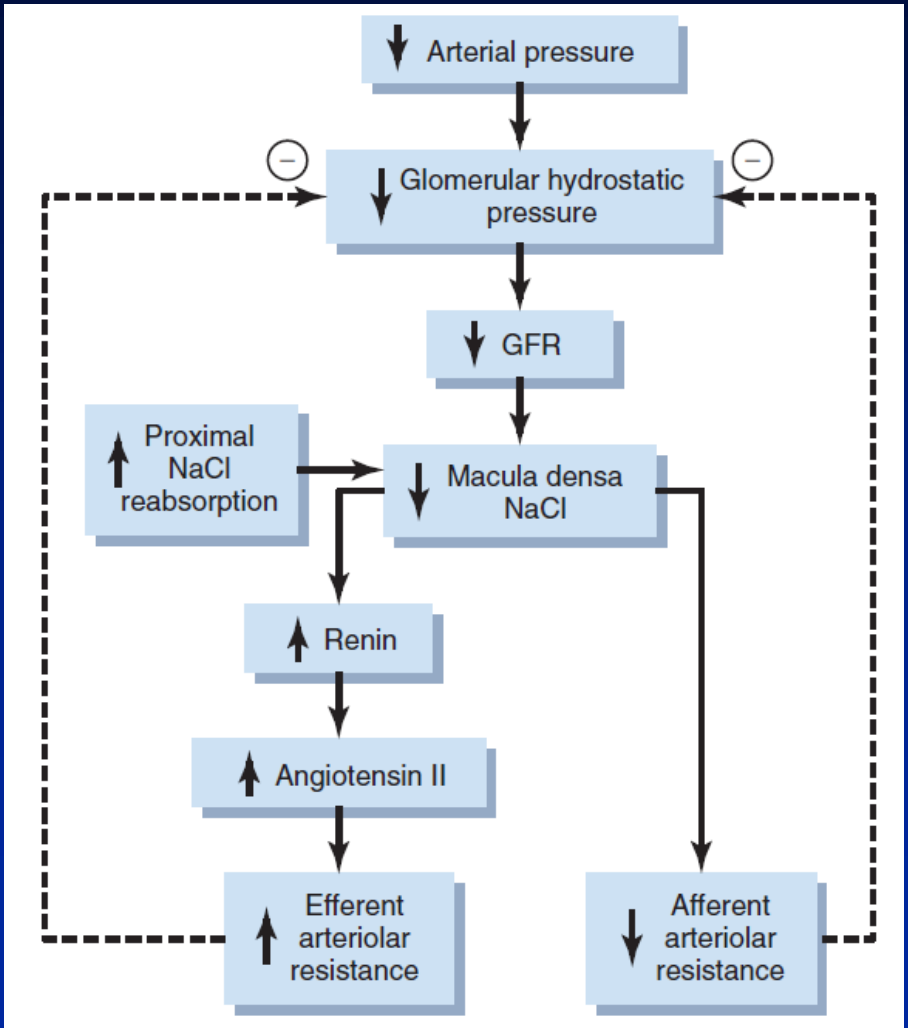
- **1- Role of Tubuloglomerular Feedback in Autoregulation of GFR**

Structure of juxtaglomerular apparatus and its role in the control of nephron function

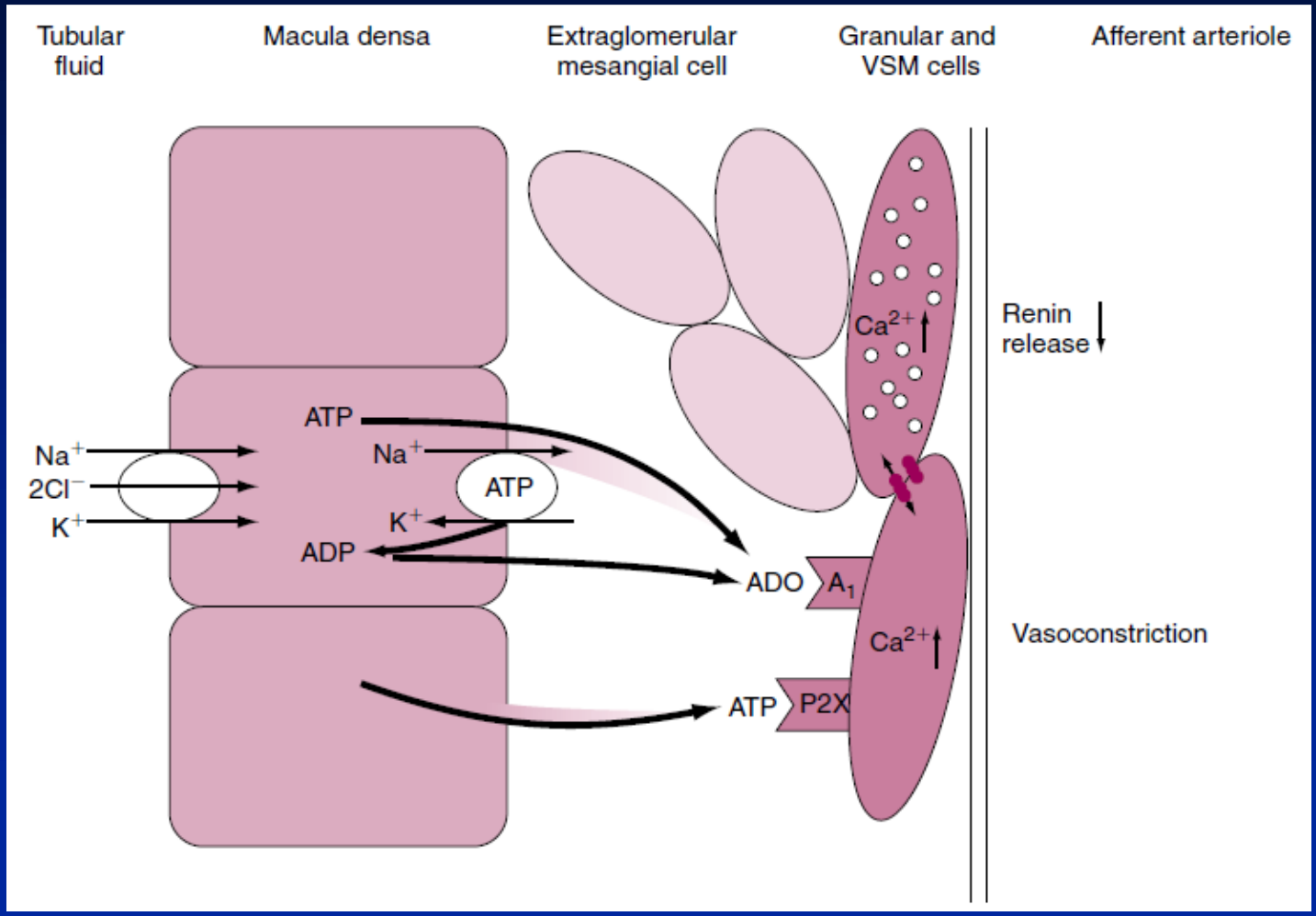


- **Decreased Macula Densa Sodium Chloride Causes Dilation of Afferent Arterioles and Increased Renin Release**

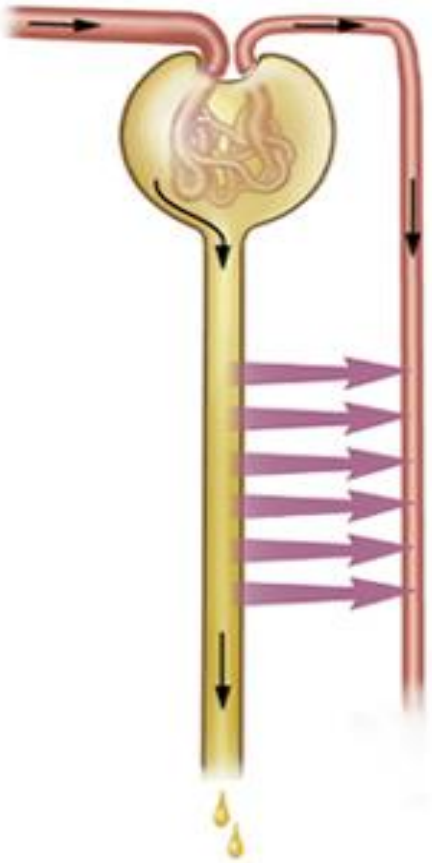
Macula densa feedback for autoregulation of glomerular hydrostatic pressure and GFR



Mechanism of autoregulation feedback in kidney



Effects of Angiotensin II



Angiotensin II → Causes constriction of efferent arteriole

↓

Increases glomerular blood pressure and filtration and Reduces blood pressure in peritubular capillary

↓

Reduces resistance to tubular reabsorption

↓

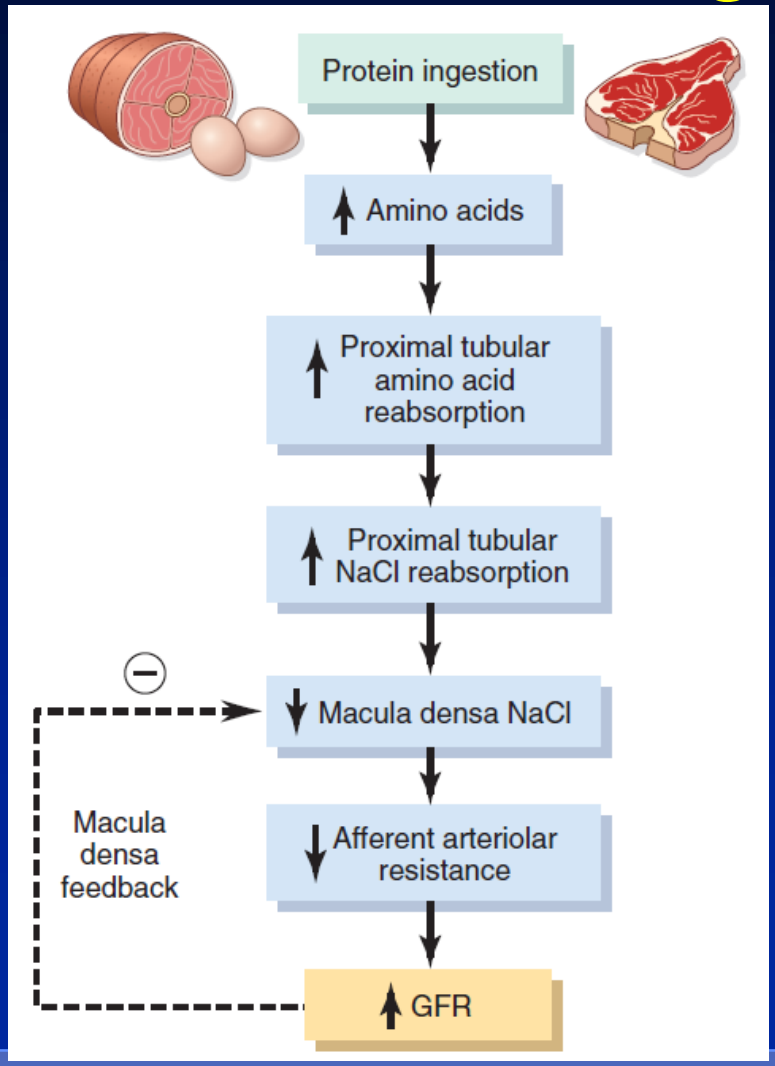
Tubular reabsorption increases

↓

Urine volume is less but concentration is high

- **Blockade of Angiotensin II Formation Further Reduces GFR During Renal Hypoperfusion**
- **2- Myogenic Autoregulation of Renal Blood Flow and GFR**
- **Other Factors That Increase Renal Blood Flow and GFR: High Protein Intake and Increased Blood Glucose**

Possible role of macula densa feedback in mediating increased GFR after a high protein meal



Other factors that influence renal blood flow and glomerular filtration rate

Condition	RBF	GFR
Aging	↓	↓
High dietary protein	↑	↑
Hyperglycemia[a]	↑	↑
Obesity[a]	↑	↑
High NaCl intake[a]	↑	↑
Glucocorticoids	↑	↑
Fever, pyrogens	↑	↑


Thanks for your attention

1. Decreased GFR

- Less NaCl delivery and reabsorption in macula densa cells
- Upregulation of NOS by macula densa cells
- Creates NO, which catalyses formation of prostaglandins
- Diffuse to granular cells and activate a specific Gs receptor
- Increased cAMP level
- cAMP augments renin release
- PGs and NO also vasodilate afferent arteriole
- Efferent arteriole are spared from this effect by renin release $\longrightarrow$ increase GFR

2. Excessive GFR or inadequate uptake of Na^+ in PT or TAL

- Increased delivery of NaCl to macula densa
- Apical NKCC move sodium into macula densa cells
- Macula densa cells do not have enough Na/K pumps
- Cell osmolarity increases and water flows into cell
- Cell swelling, opening of a stretch activated non selective anion channel on basolateral surface
- ATP escape into and converted to adenosine
- Vasoconstricts the afferent arteriole via A1 receptor and vasodilates efferent arteriole via A2
- Decrease GFR

- Also, adenosine inhibits renin release in JG cells via A1 receptor using Gi pathway.

- When macula densa cells detect higher concentration of NaCl, they inhibit NOS which decrease renin release.