RENAL PHYSIOLOGY
INTRODUCTION
GLOMERLAR FILTRATION

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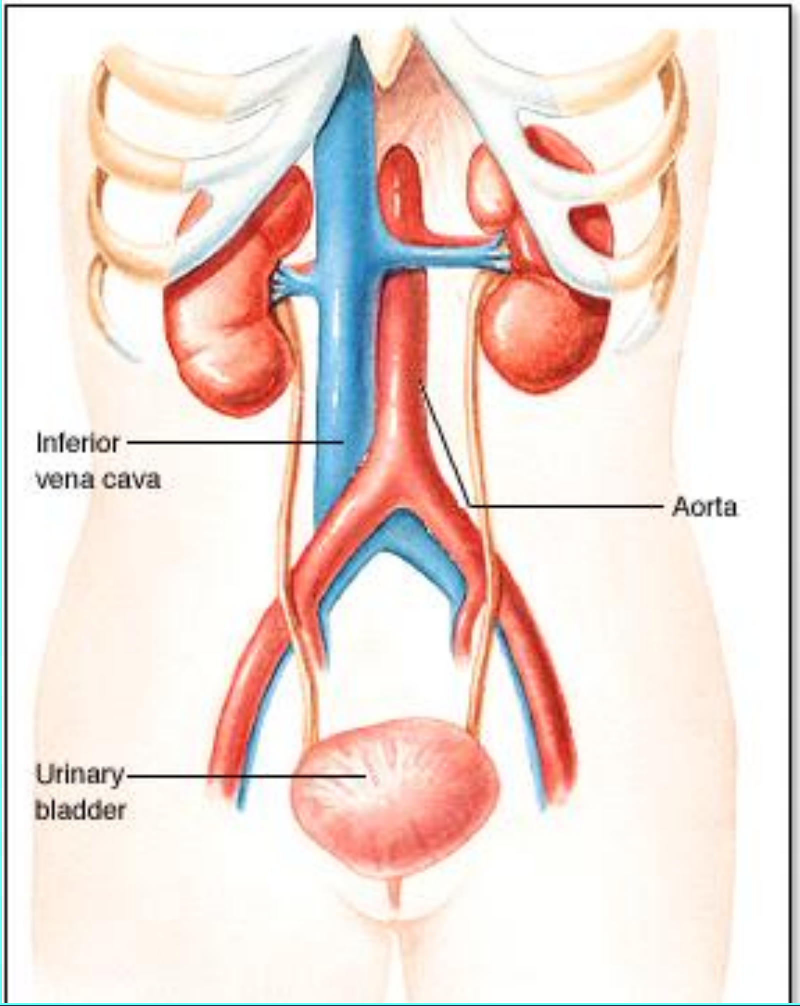
OBJECTIVES

At the end of this lecture you should be able to describe:

- Physiologic anatomy of Urinary system
- Roles of the kidney
- Structure, Parts and Types of Nephrons
- Juxtaglomerular Apparatus
- Filtration Membrane

URINARY SYSTEM



Kidneys: filter blood and remove wastes, producing urine

Ureters: carry urine to bladder from kidneys

Urethra: carries urine from bladder to the exterior

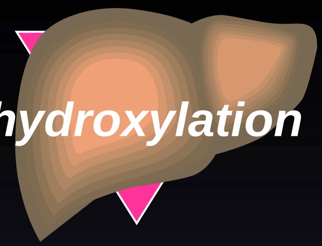
FUNCTIONS OF THE KIDNEY

- Excretion of wastes (creatinine, urea, benzoate, penicillin, saccharin)
- Regulation of water (extracellular fluid volume)
- Maintenance of electrolyte balance (Na^+, K^+, HCO_3^-, Ca^{++})
- Regulation of arterial pressure
- Regulation of blood pH

FUNCTIONS OF THE KIDNEY (Cont.)

- Secretion, metabolism, and excretion of hormones
  - Hormone production (Erythropoietin, Renin)
  - Activation of Vitmain D
- Gluconeogenesis

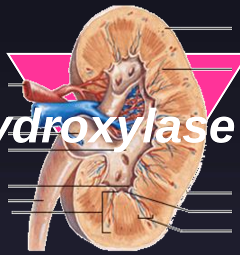
Naturally occurring vitamin D (cholecalciferol)



hydroxylation

25-hydroxycholecalciferol 25-OHD3)

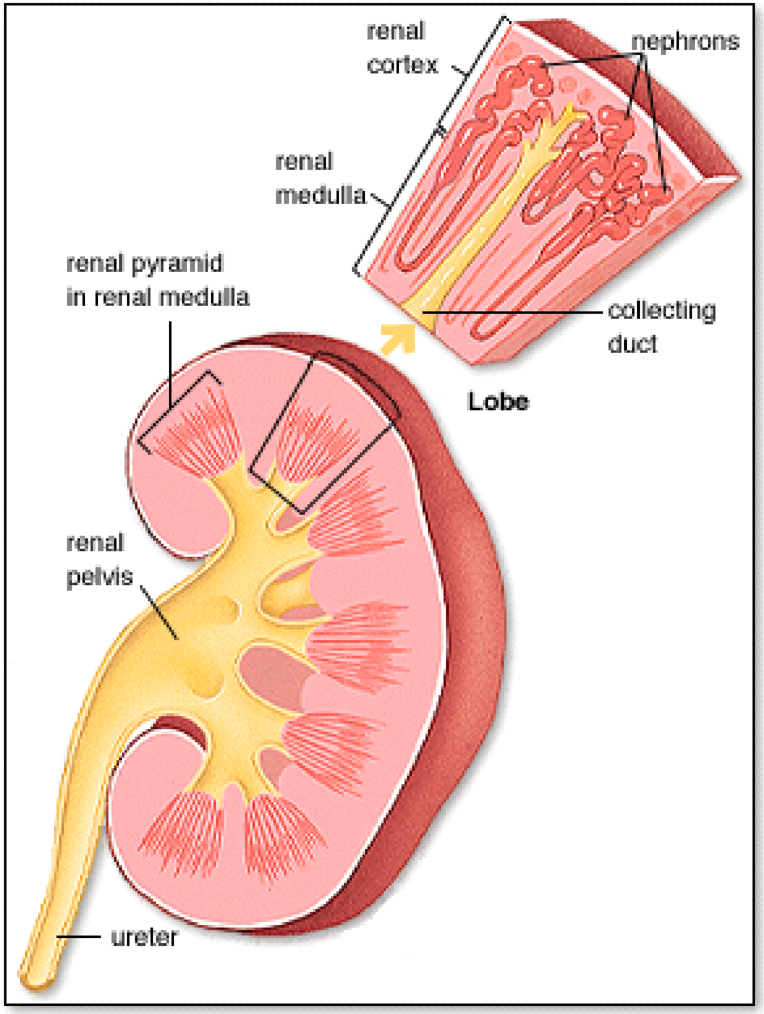
PTH →



1α-hydroxylase enzyme

1,25-dihydroxycholecalciferol (1,25-(OH)2D3)

PHYSIOLOGIC ANATOMY OF KIDNEYS



The outer portion of the kidney is the renal cortex. The medulla lies below the cortex; the many parallel tubes within it give it a striped appearance. The innermost portion is the renal pelvis, which collects the urine and passes it to the ureter. Each kidney lobe contains a large number of nephrons.

RENAL BLOOD SUPPLY

22 per cent of the cardiac output, or 1100 ml/min

Renal artery

Interlobar arteries

Arcuate arteries

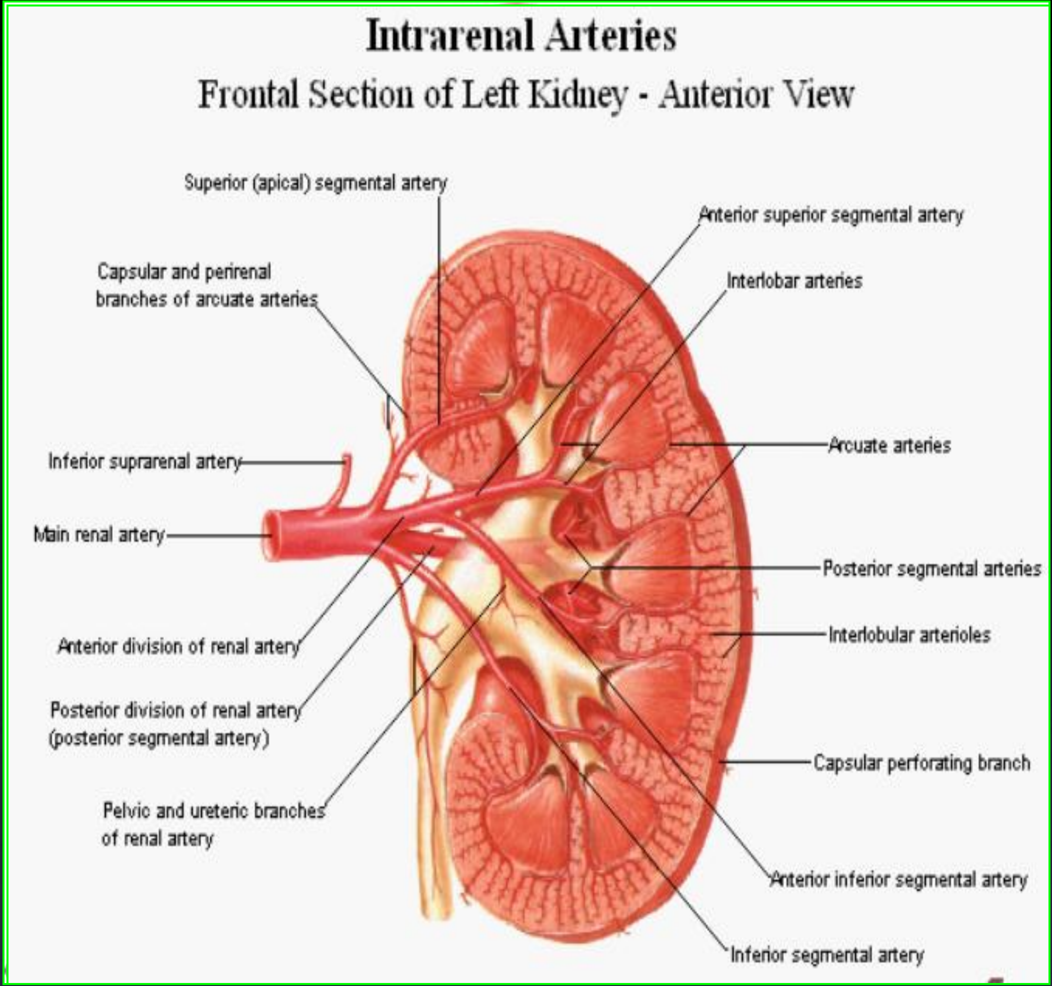
Interlobular arteries

Afferent arterioles

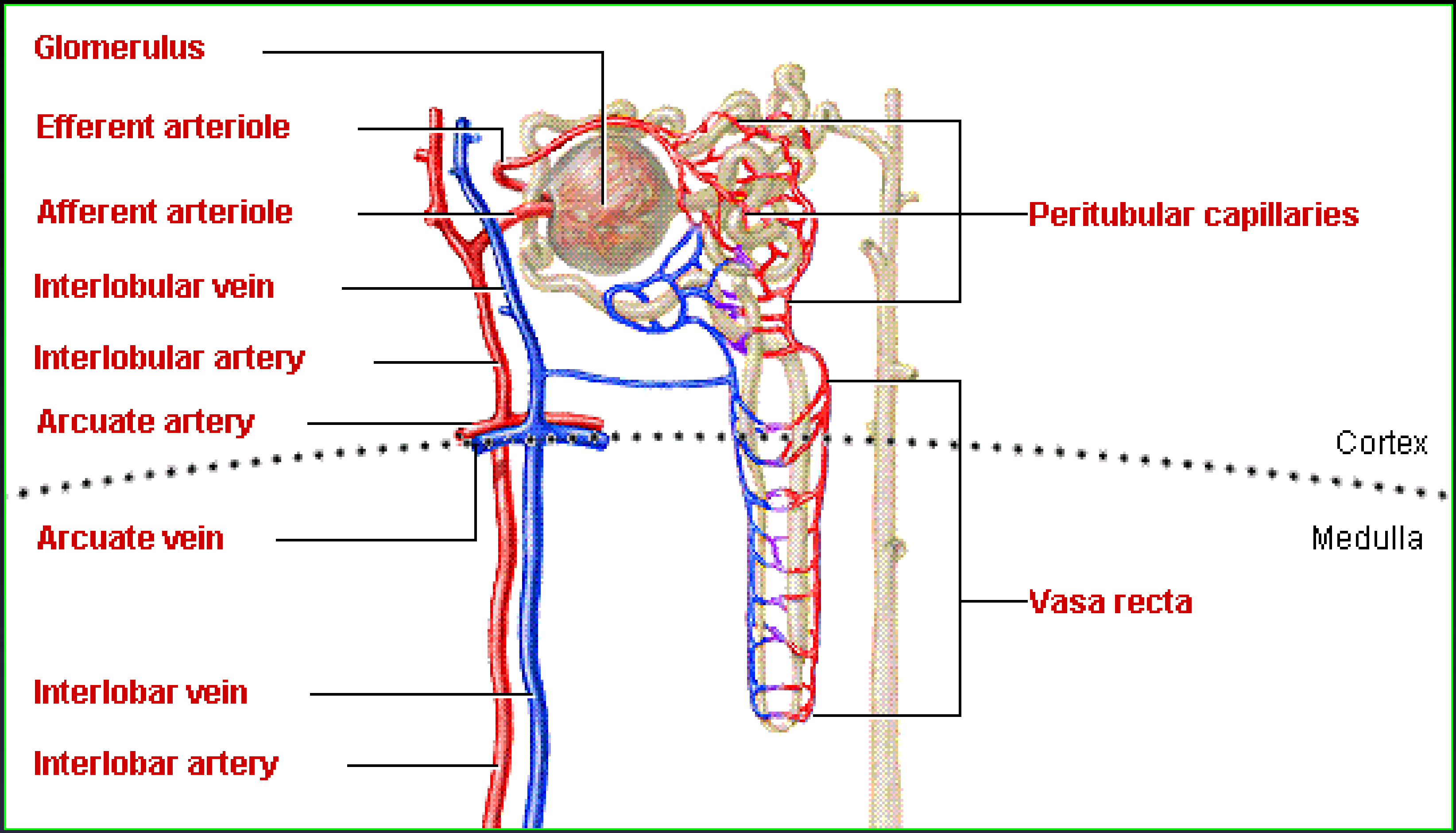
Glomerular capillaries

Efferent arteriole

Peritubular capillaries

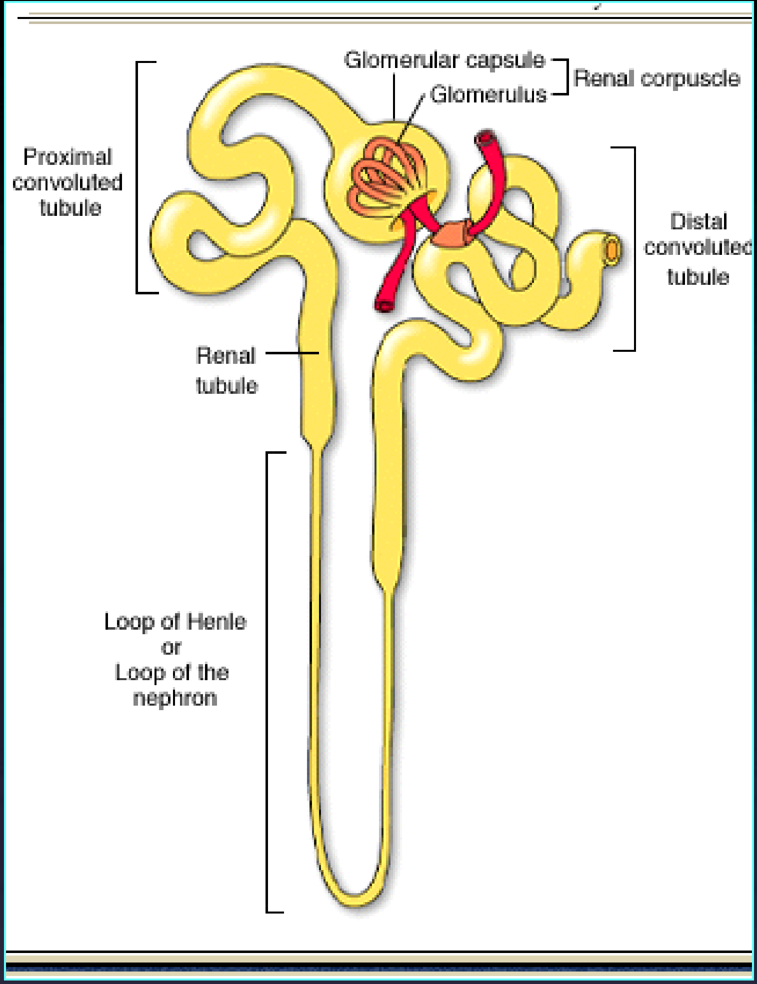


VASCULAR SUPPLY OF KIDNEYS AND NEPHRON



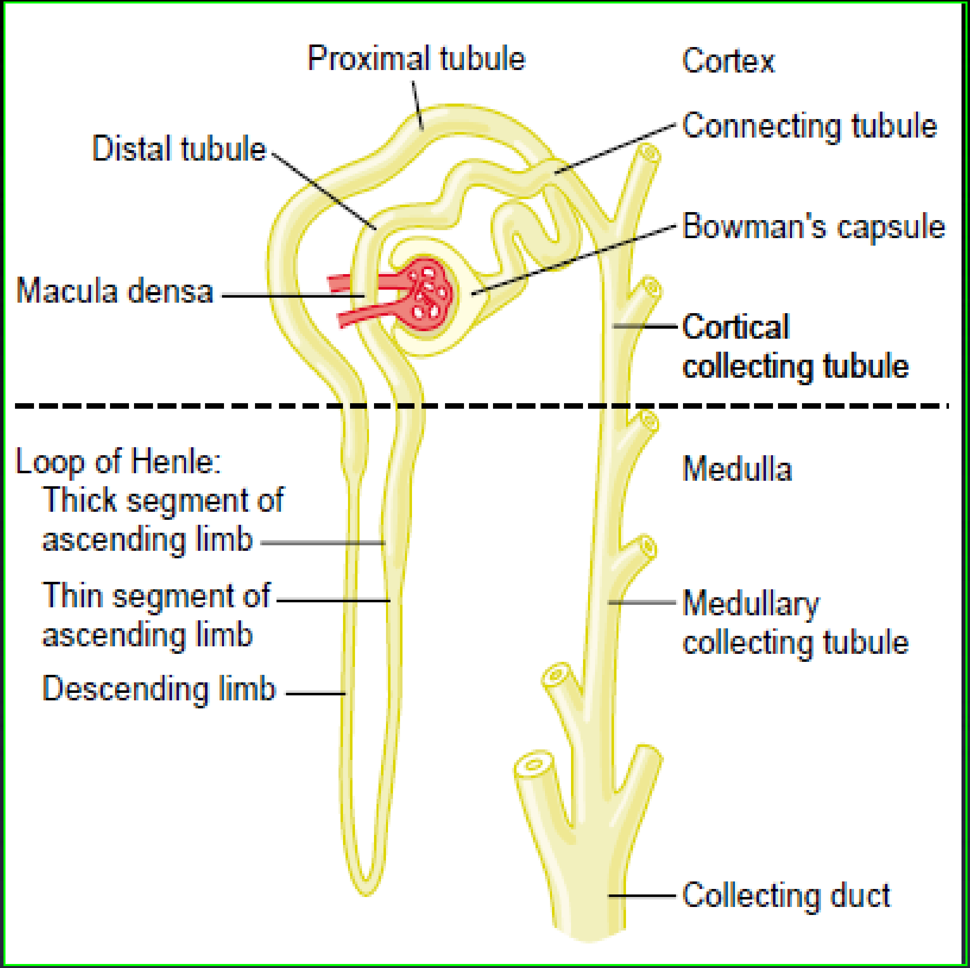
NEPHRON

- Each kidney in the human contains about 1.3 million nephrons, each capable of forming urine.
- The kidney cannot regenerate new nephrons.
- After age 40, the number of functioning nephrons usually decreases about 10 per cent every 10 years; thus, at age 80, many people have 40 per cent fewer functioning nephrons than they did at age 40.

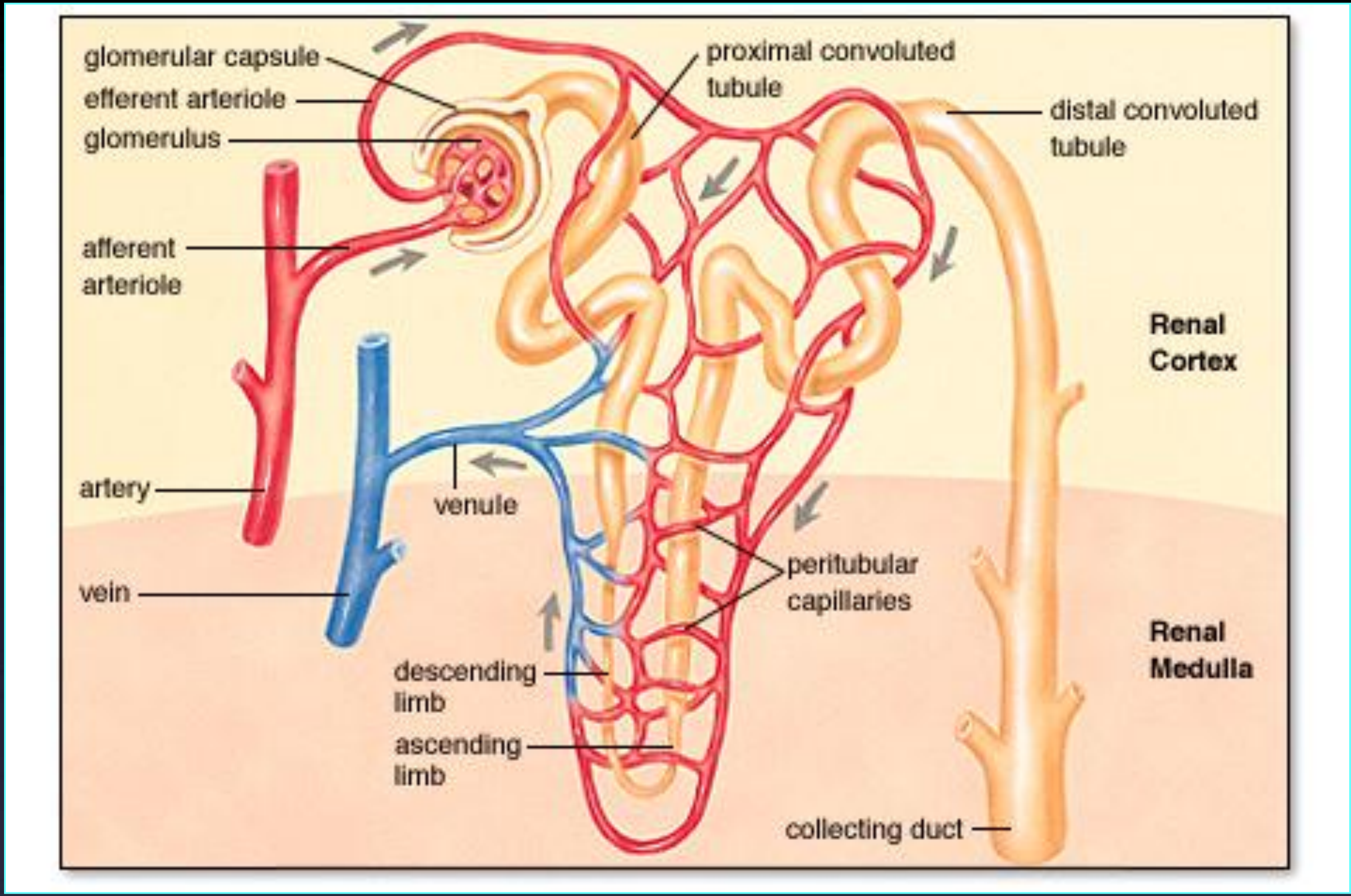


PARTS OF NEPHRON

- **8 to 10 cortical collecting ducts join to form a single larger collecting duct that runs downward into the medulla and becomes the *medullary collecting duct.***
- ***The collecting ducts merge to form larger ducts that eventually empty into the renal pelvis through the tips of the renal papillae.***



RENAL PORTAL SYSTEM

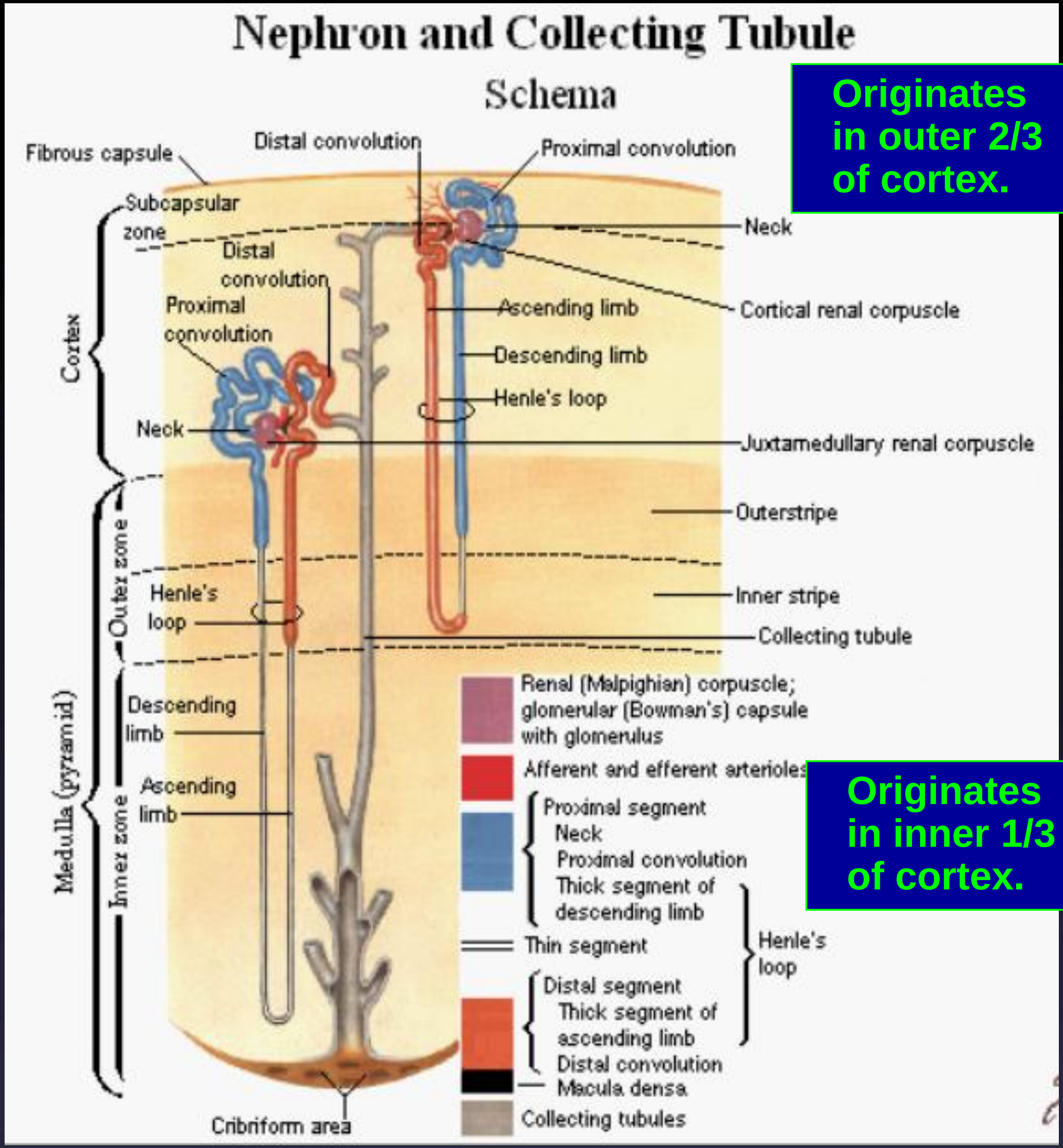


NEPHRON TYPES

- Superficial (cortical) [85 %]
  - Capable of forming dilute urine
- Juxtamedullary [15 %]
  - Capable of forming concentrated (> 300 mOsm/kg) urine

NEPHRON TYPES
Cortical and Juxtamedullary Nephrons

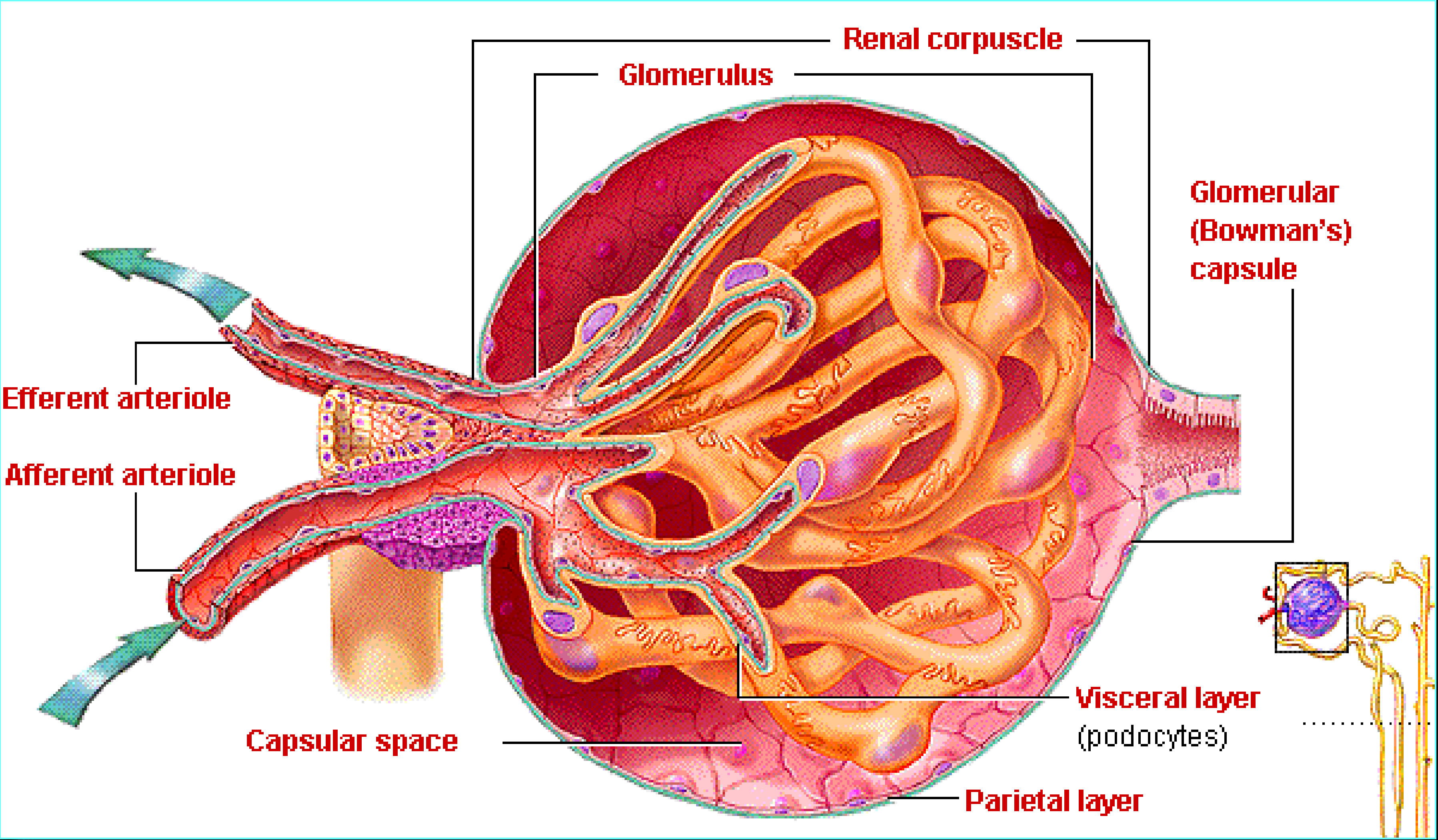
1-2 % Blood Flows Through Juxta Medullary Nephrons



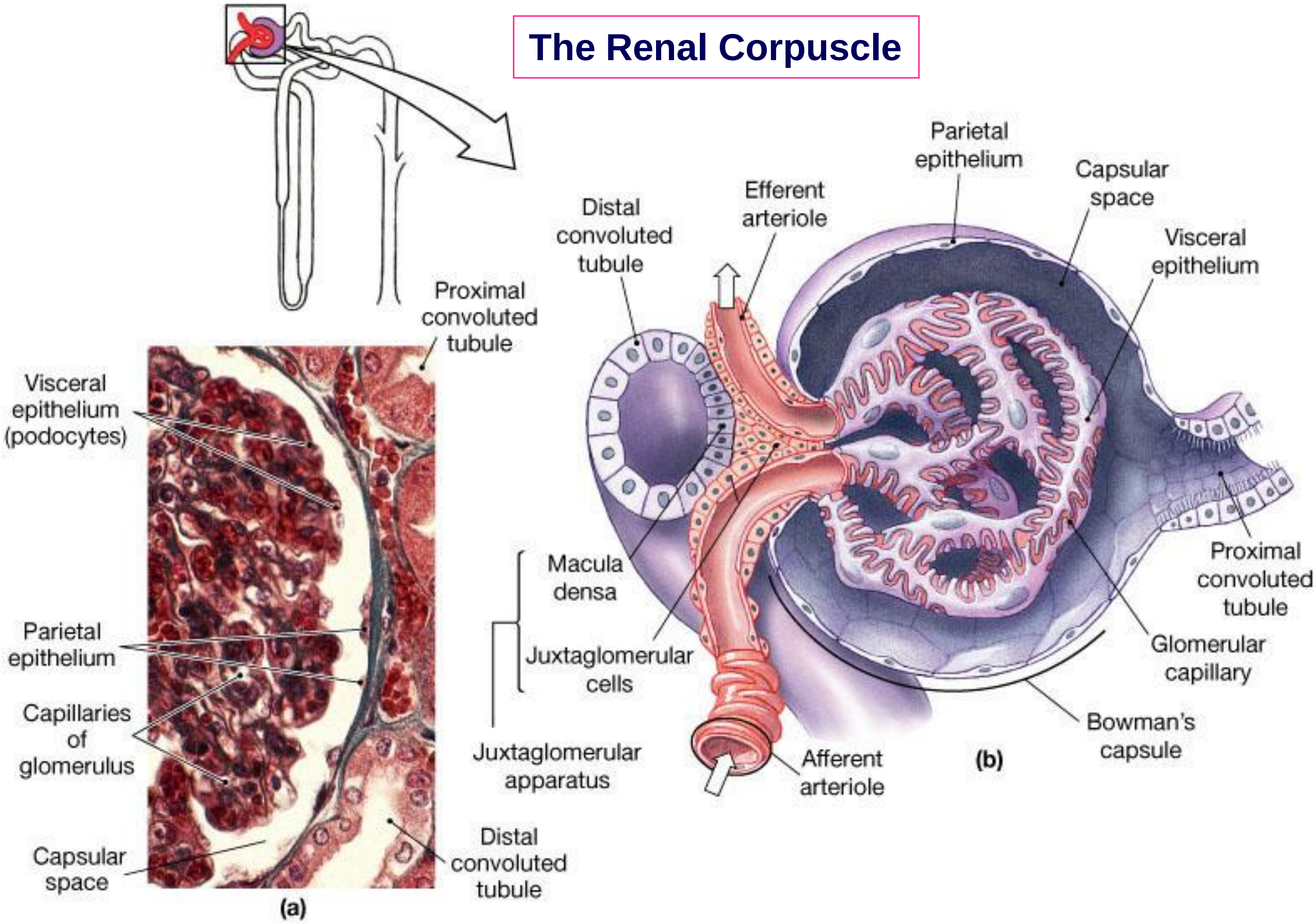
Originates in outer 2/3 of cortex.

Originates in inner 1/3 of cortex.

BOWMAN'S CAPSULE



The Renal Corpuscle

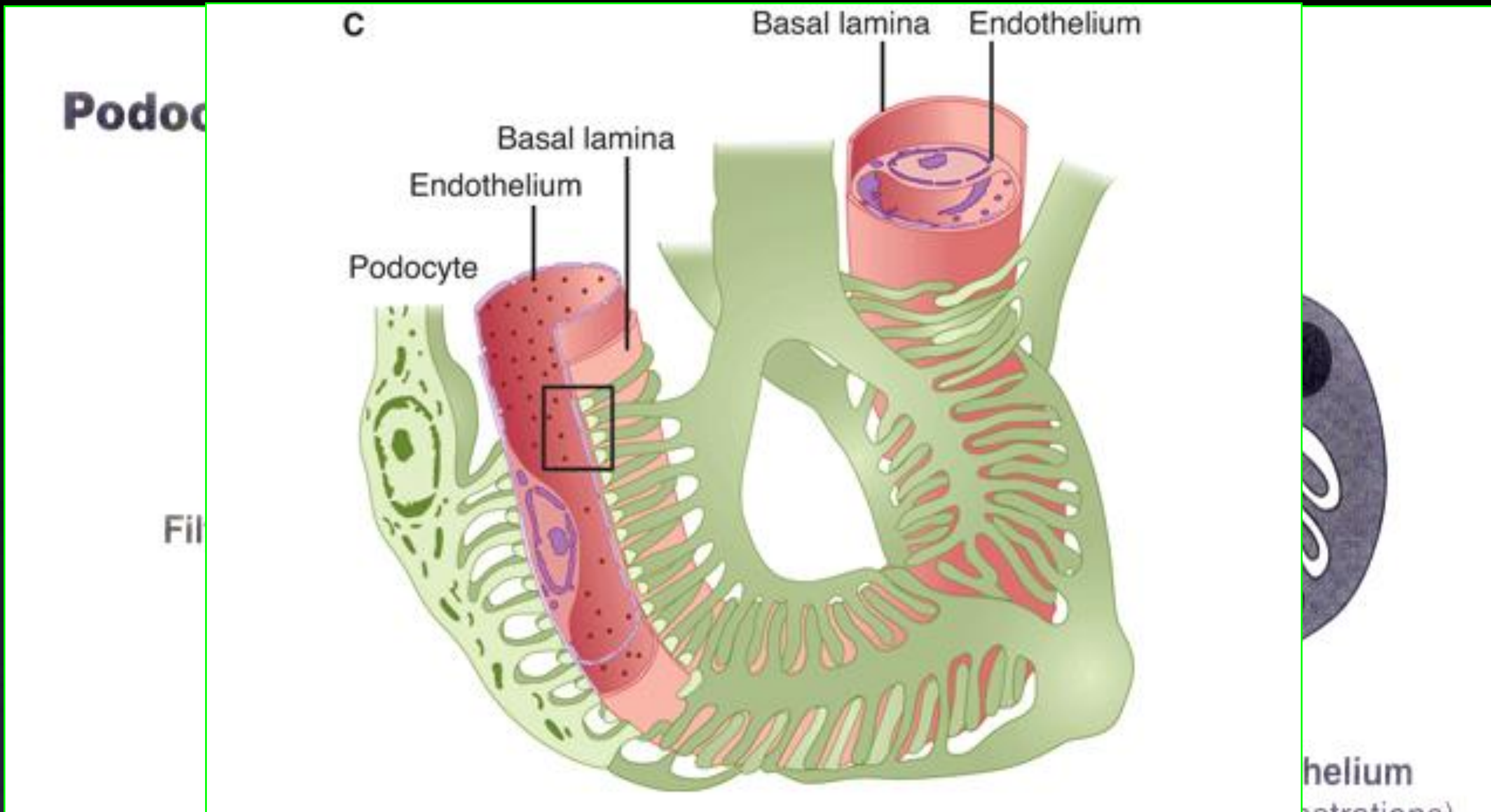


THE RENAL CORPUSCLE COMPRISES FOUR MAIN CELL TYPES

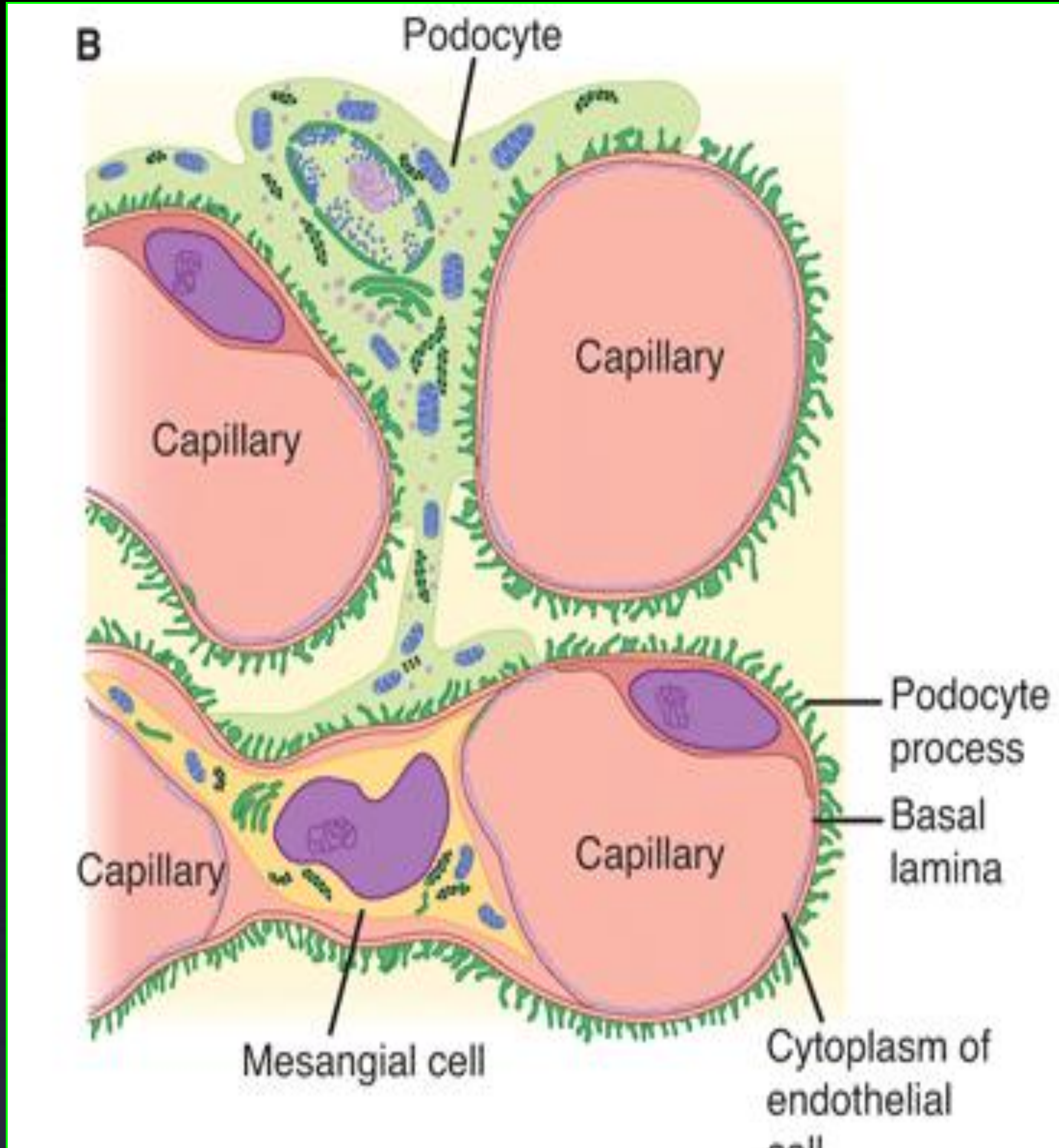
1) **Endothelial cells** which are fenestrated
2) **Visceral epithelial cells (podocytes)** which support the delicate glomerular basement membrane by means of foot processes
3) **Parietal epithelial cells** which cover the Bowman's capsule;
4) **Mesangial cells** are contractile cells

Type I Medullary Interstitial Cells secrete PGE2

PODOCYTES



C
Basal lamina
Endothelium
Basal lamina
Endothelium
Podocyte



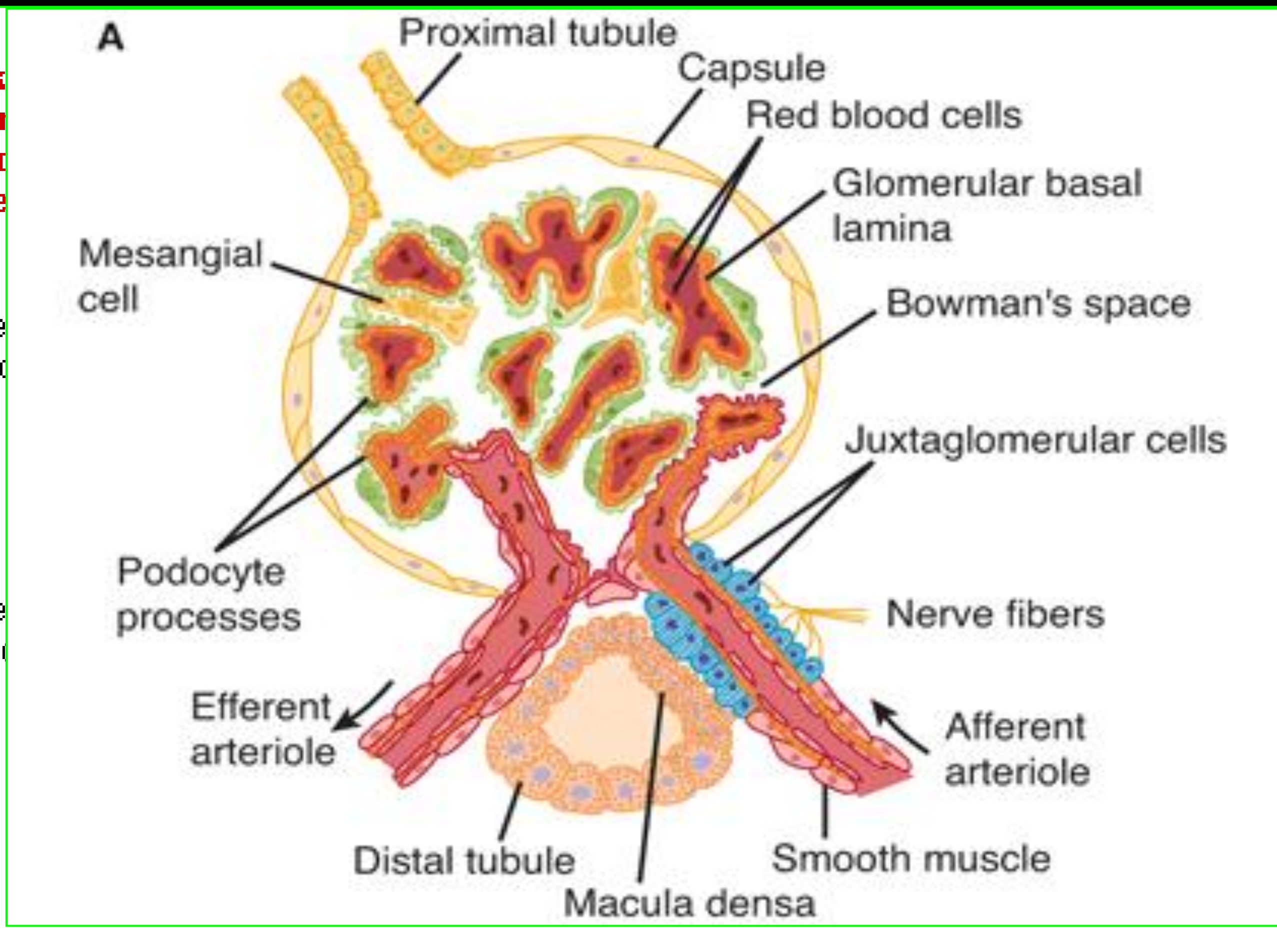
B
Podocyte
Capillary
Capillary
Podocyte process
Basal lamina
Capillary
Capillary
Mesangial cell
Cytoplasm of endothelial cell

JUXTA GLOMERULAR APPARATUS

Thick
ascen
loop o
Henle

Effere
arteri

Affere
arteri



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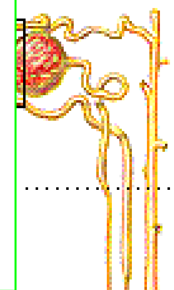
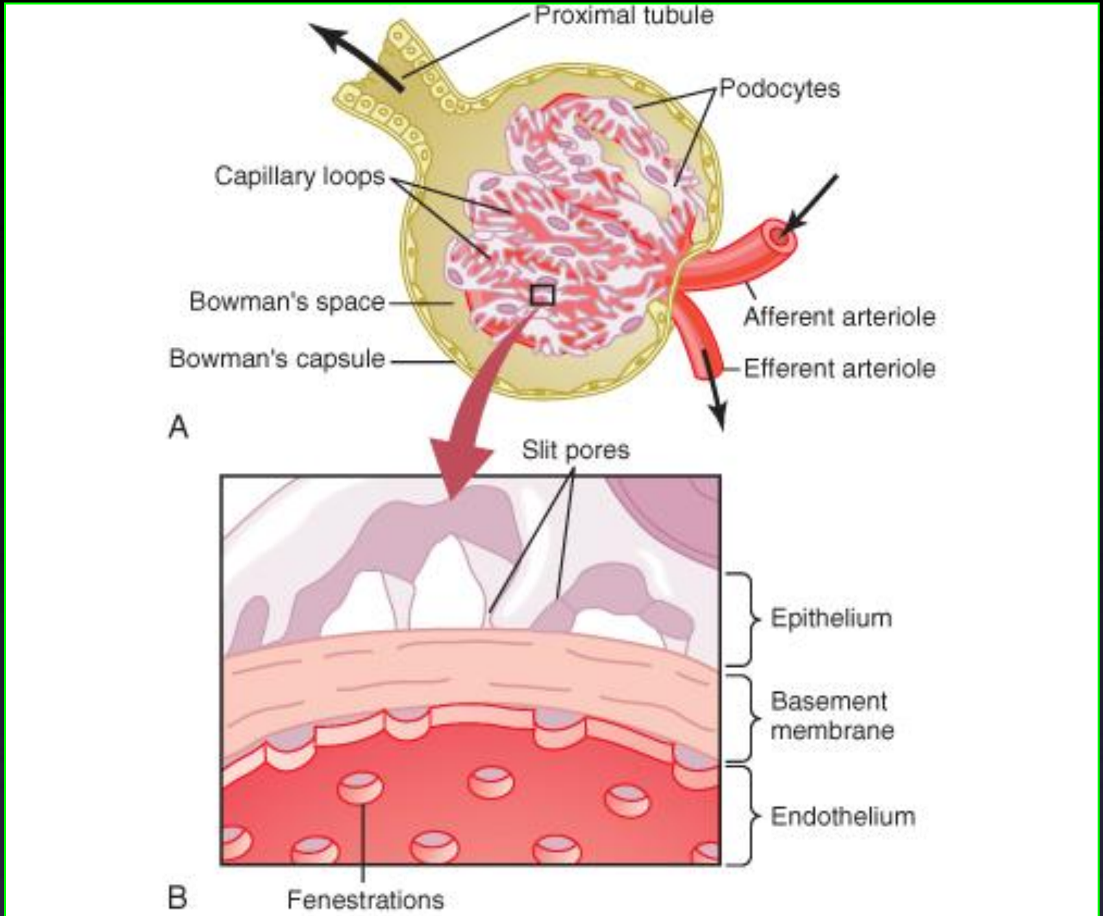
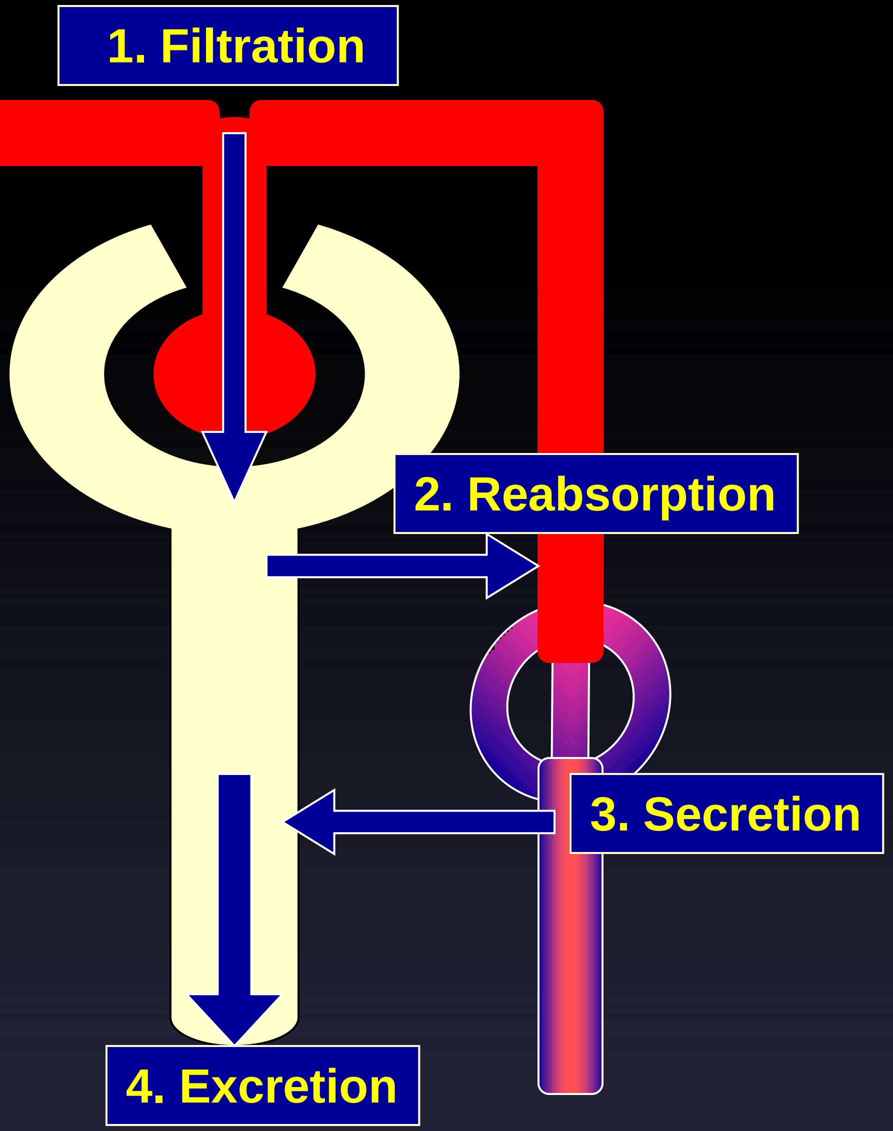


RENAL CORPUSCLE



RENAL PROCESSES

1. Filtration
2. Reabsorption
3. Secretion
4. Excretion



Urinary Excretion Rate = Filtration Rate – Reabsorption Rate + Secretion Rate

INVESTIGATIONS

- EXAMINATION OF THE URINE
- BLOOD AND QUANTITATIVE TESTS
- IMAGING TECHNIQUES
- TRANSCUTANEOUS RENAL BIOPSY

RENAL PHYSIOLOGY

GLOMERULAR FILTRATION

OBJECTIVES

At the end of this lecture you should be able to describe:

- Filtration Membrane
- GFR, Ff, Kf, Plasma Clearance
- Control of GFR
- Regulation of Renal Blood Flow and GFR

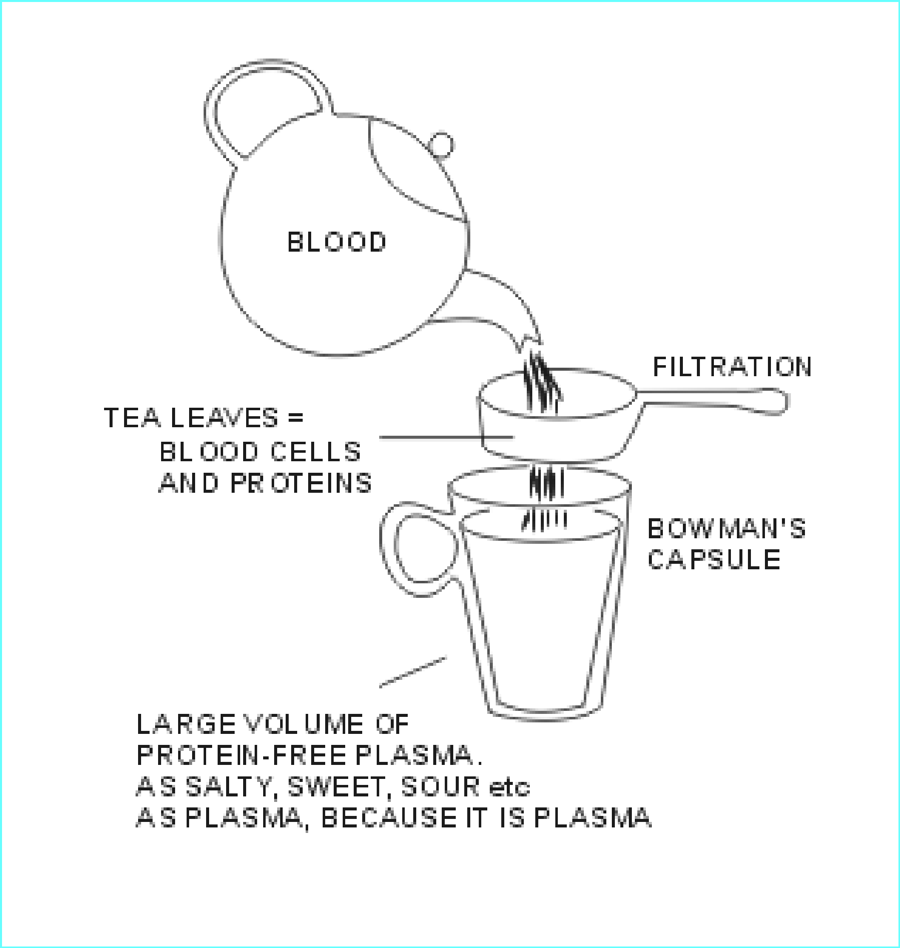
NEXT

FILTRATION AND OSMOSIS

At a molecular level, filtration is the bulk flow of fluid through a membrane or other barrier that selectively impedes the movement of some molecules, the largest being impeded most. This process is sometimes called **ULTRAFILTRATION**.

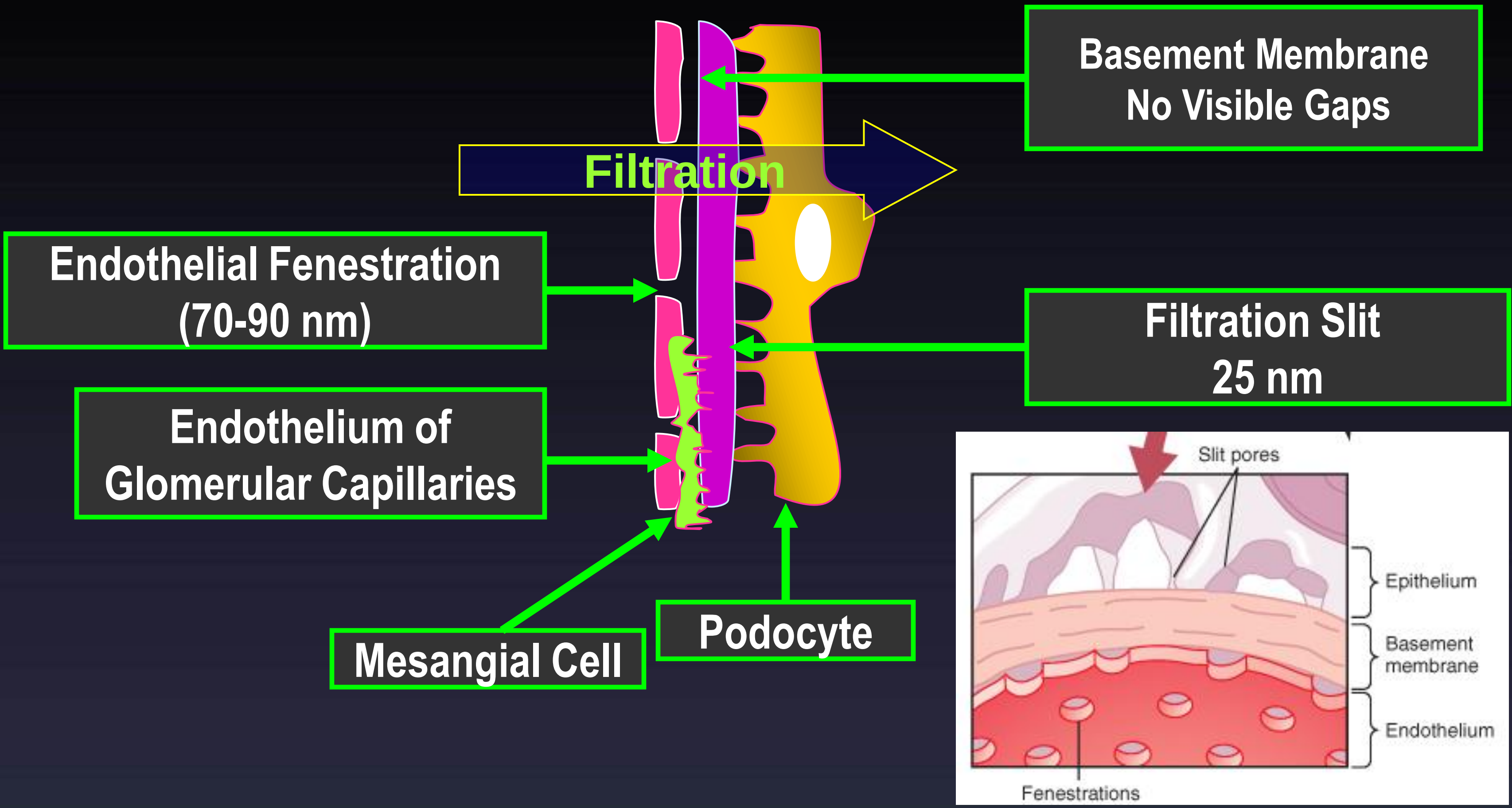
In the average adult human, the GFR is about 125 ml/min

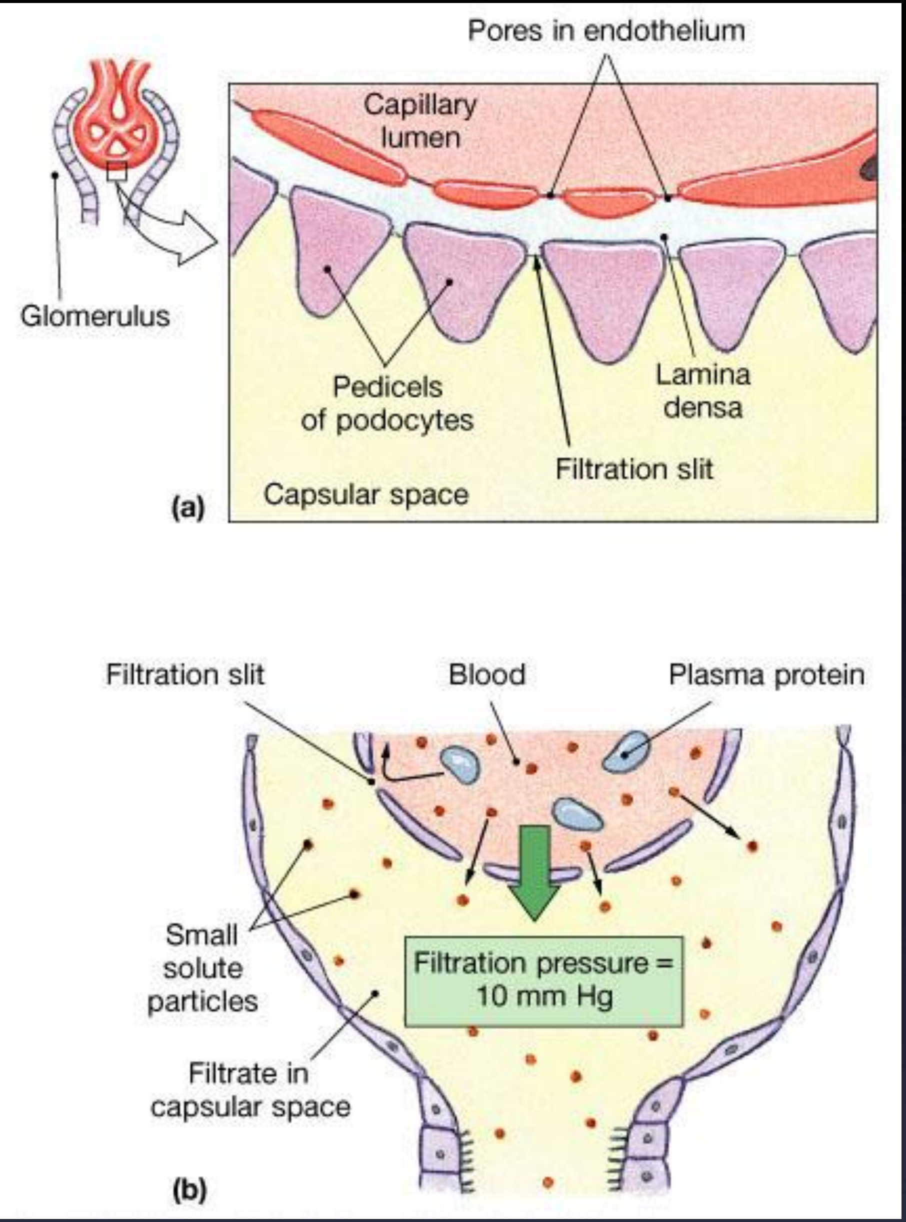
FILTRATION


BLOOD
FILTRATION
TEA LEAVES =
BLOOD CELLS
AND PROTEINS
BOWMAN'S
CAPSULE
LARGE VOLUME OF
PROTEIN-FREE PLASMA.
AS SALTY, SWEET, SOUR etc
AS PLASMA, BECAUSE IT IS PLASMA

FILTRATION MEMBRANE

4-8 nm size particles can be filtered easily



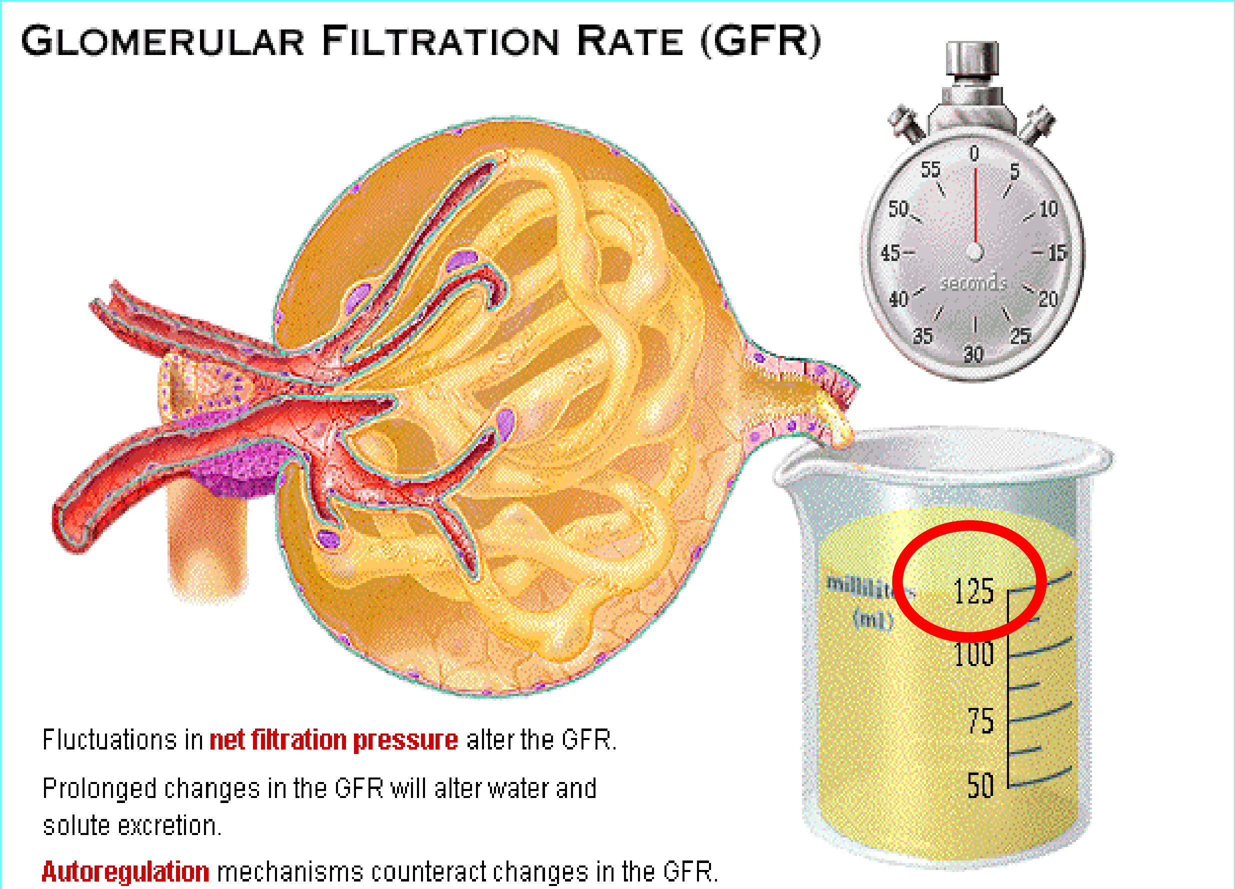

Pores in endothelium
Capillary lumen
Glomerulus
Pedicels of podocytes
Lamina densa
Filtration slit
Capsular space
(a)
Filtration slit
Blood
Plasma protein
Small solute particles
Filtration pressure = 10 mm Hg
Filtrate in capsular space
(b)

Why Are Large Amounts of Solutes Filtered and Then Reabsorbed by the Kidneys?

It allows the kidneys to rapidly remove waste products from the body that depend primarily on glomerular filtration for their excretion. Most waste products are poorly reabsorbed by the tubules and, therefore, depend on a high GFR for EFFECTIVE REMOVAL from the body.

It allows all the body fluids to be FILTERED AND PROCESSED BY THE KIDNEY MANY TIMES EACH DAY. Because the entire plasma volume is only about 3 liters, whereas the GFR is about 180 L/day, the entire plasma can be filtered and processed about 60 times each day.

GLOMERULAR FILTRATION RATE



Fluctuations in **net filtration pressure** alter the GFR.

Prolonged changes in the GFR will alter water and solute excretion.

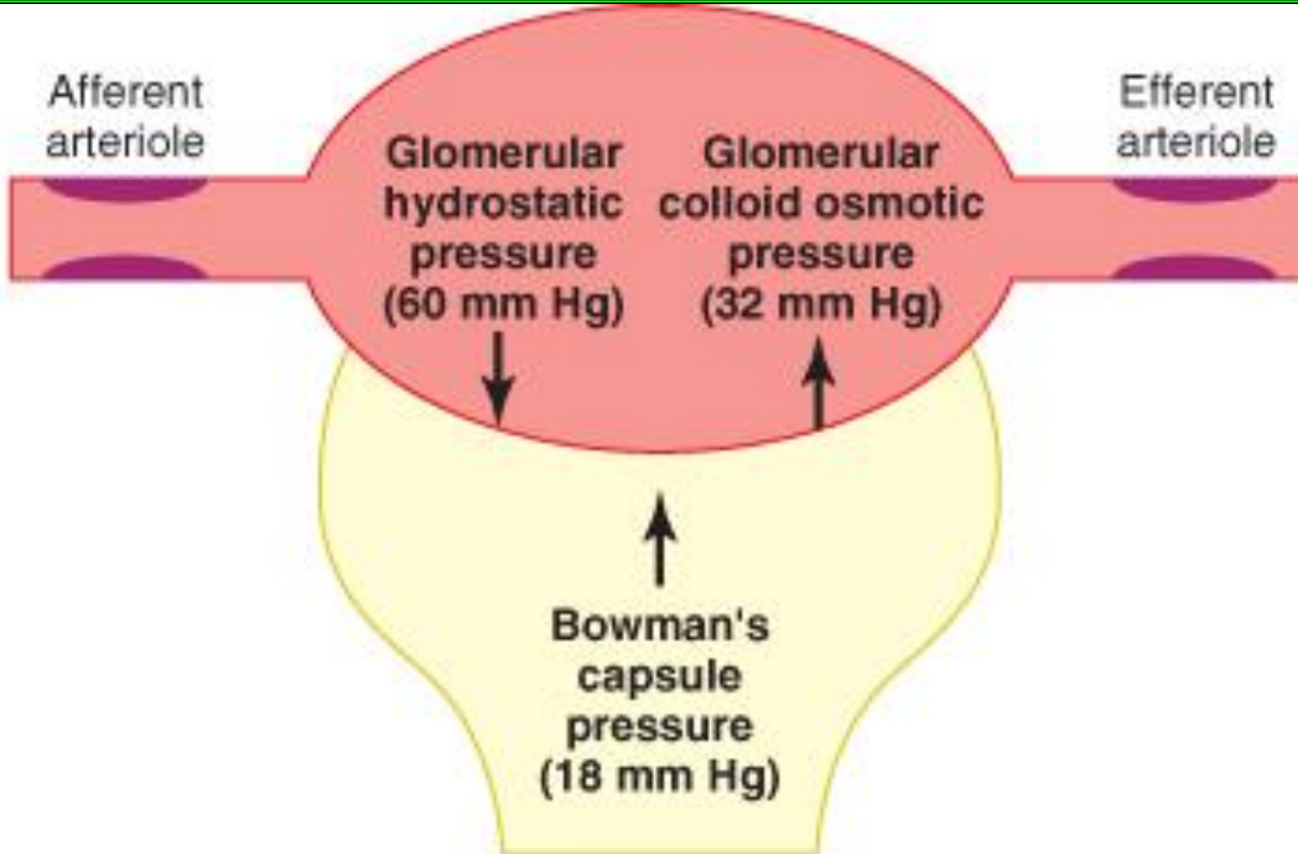
Autoregulation mechanisms counteract changes in the GFR.

- **GFR=125ML/MIN**
- **OR 125X60X24=180000=180L/DAY**
- **Normal Urinary Output = 1.5 L/day**
- **Daily Reabsorption 180-1.5=178.5 L/day**
- **Percent Reabsorbed = 178.5/180x100=99.2%**
- **Percent Excreted = 100-99.2=0.8% (Less than 1 % becomes urine)**

- Obligatory Urinary Output = 0.5-0.6L
- Oliguria = <300 ml/day
- Anuria = Less than 50 ml/day
- RBF = 1100 ML/MIN
- RPF = 1100x0.55=620 ML/MIN
- FILTRATION FRACTION =125/620X100=20%
- 137x60x24=198 L/day if tubular reabsorption remains constant urine volume will increase from 1.5 to 19.5 L/day

DETERMINANTS OF GFR

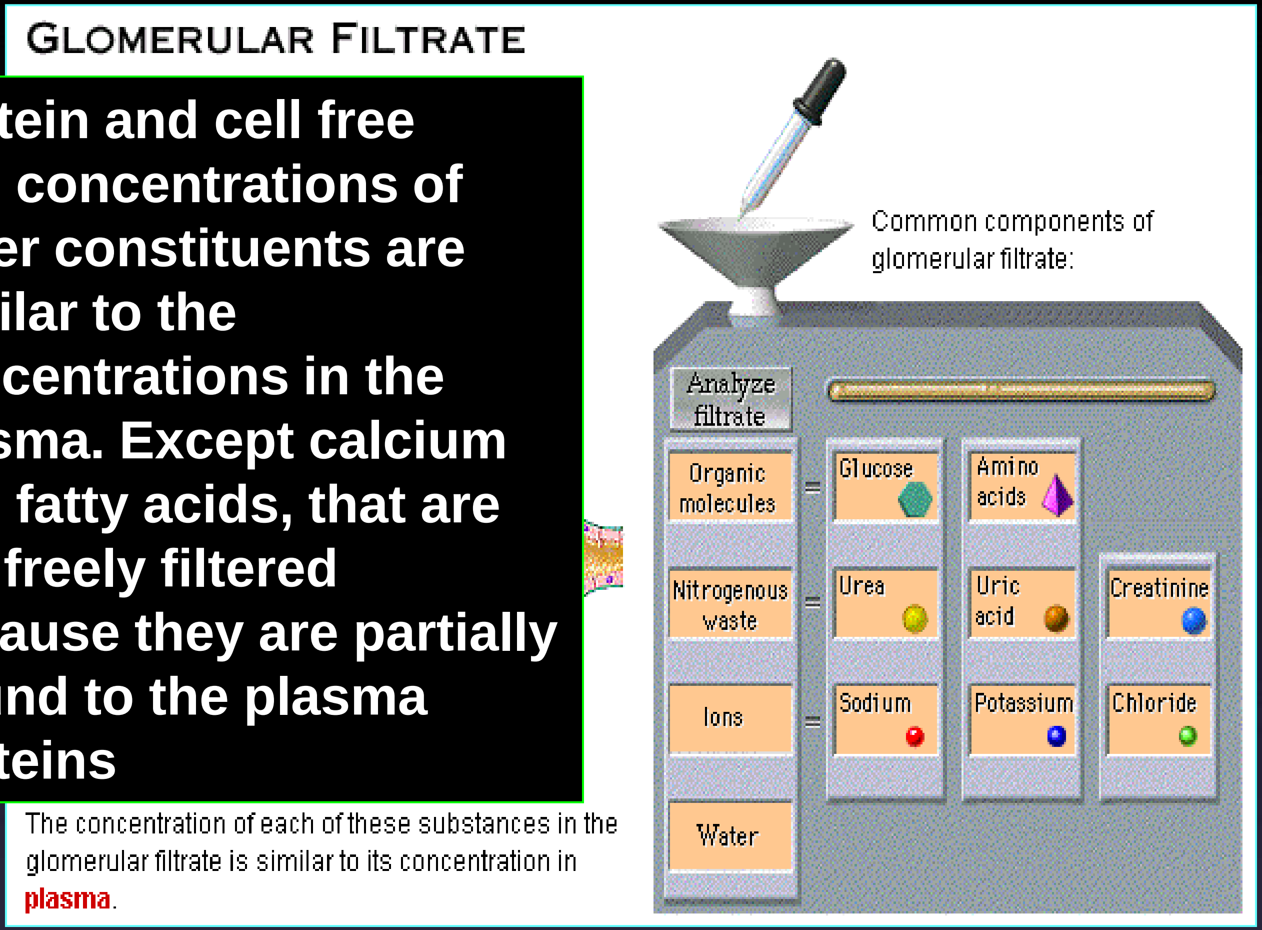
Forces Favoring Filtration (mm Hg)	
Glomerular hydrostatic pressure	60
Bowman's capsule colloid osmotic pressure	0
Forces Opposing Filtration (mm Hg)	
Bowman's capsule hydrostatic pressure	18
Glomerular capillary colloid osmotic pressure	32
Net Filtration Pressure = 60 – (18 + 32) = +10 mm Hg	



Net filtration pressure (10 mm Hg) = Glomerular hydrostatic pressure (60 mm Hg) – Bowman's capsule pressure (18 mm Hg) – Glomerular oncotic pressure (32 mm Hg)

GLOMERULAR FILTRATE

1. Protein and cell free
2. The concentrations of other constituents are similar to the concentrations in the plasma. Except calcium and fatty acids, that are not freely filtered because they are partially bound to the plasma proteins

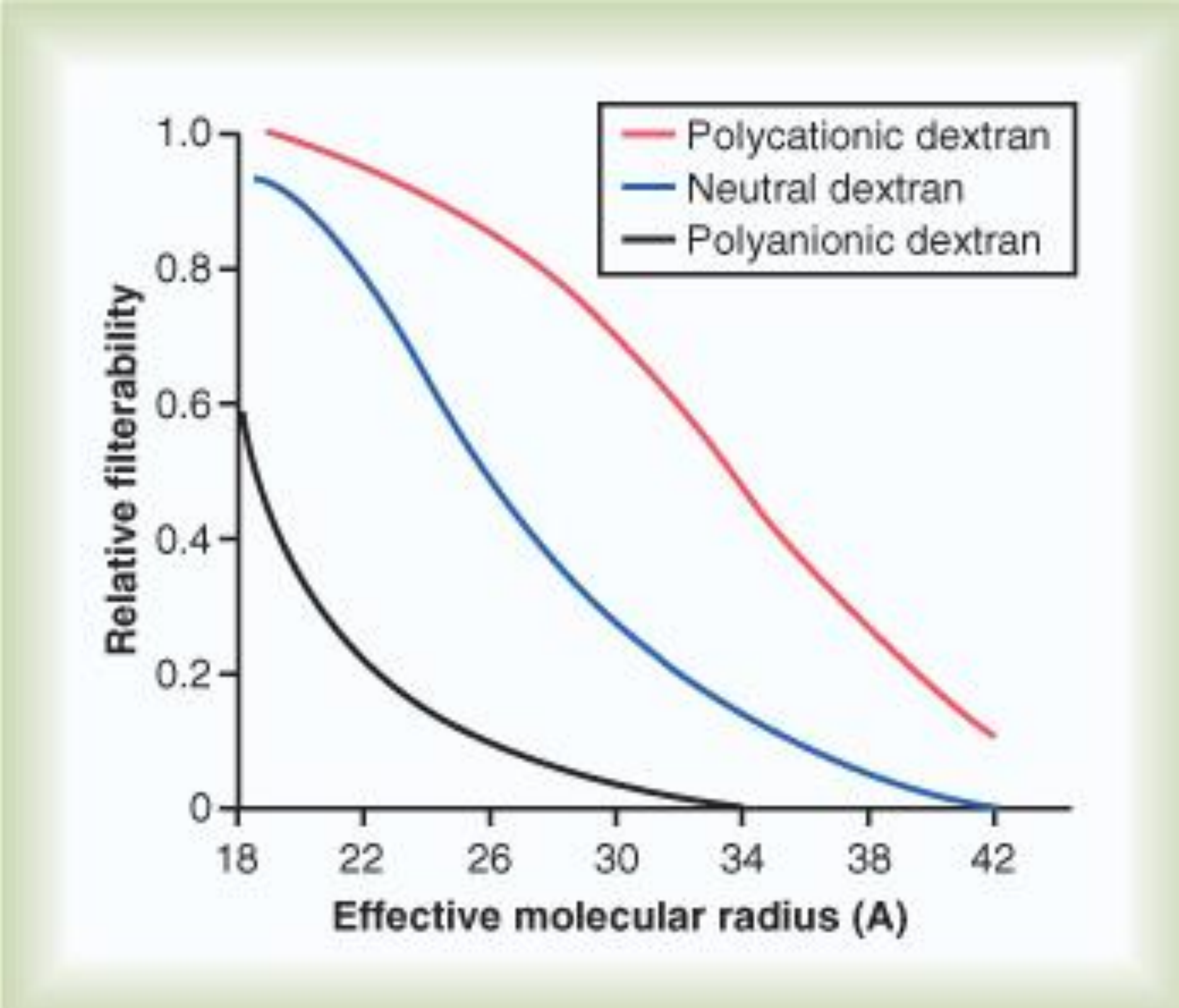


SUBSTANCE	MOLECULAR WEIGHT	MOLECULAR SIZE nm	FILTERABILITY
Water	18	0,15	1.0
Sodium	23	0,1	1.0
Glucose	180	0,33	1.0
Inulin	5,500	1.48	1.0
Myoglobin	17,000	1.88	0.75
Albumin (6 nm)	69,000	3.55	0.005

Filterability of Solutes Is Inversely Related to Their Size

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

Dextrans are polysaccharides that can be manufactured as neutral molecules or with negative or positive charges.



Polycationic dextran
Neutral dextran
Polyanionic dextran
Relative filterability
1.0
0.8
0.6
0.4
0.2
0
18
22
26
30
34
38
42
Effective molecular radius (A)

FILTRATION FRACTION

- **Fraction of renal plasma that becomes Glomerular Filtrate**

Ff = GFR/Renal Plasma Flow

= 125 ml per min/650 ml per min

= 19.2 or approximately 20 %

About 20 per cent of the plasma flowing through the kidney is filtered through the glomerular capillaries

CONTROL OF GFR

$$GFR = Kf \times [(P_G - P_B) - (\pi_G - \pi_B)]$$

GFR = Kf x [(60-18)-(32- 0)]

(1) Hydrostatic pressure inside the glomerular capillaries (glomerular hydrostatic pressure, PG), which promotes filtration

(2) The hydrostatic pressure in bowman's capsule (PB) outside the capillaries, which opposes filtration

(3) The colloid osmotic pressure of the glomerular capillary plasma proteins (πg), which opposes filtration

(4) The colloid osmotic pressure of the proteins in bowman's capsule (πb), which promotes filtration

FILTRATION COEFFICIENT (Kf)

Glomerular Filtration Rate in both kidneys per mm Hg Filtration Pressure

The Kf is a measure of the product of the Permeability and surface area of the glomerular capillaries. The Kf cannot be measured directly

Kf = GFR / net filtration pressure

= 125 ml per min/ 10 mm Hg

= 12.5 ml/min/mm Hg of filtration Pr

increased Kf raises GFR and decreased Kf reduces GFR

FACTORS AFFECTING GFR

- Renal blood flow
- Glomerular Capillary & bowman's Capsule hydrostatic and osmotic pressures
- Sympathetic Nervous system ↓ GFR
- Hormonal & Autocoid Control
- Changes in concentration of plasma proteins (Dehydration↓ , Hypoproteinemia↓ etc.)
- Changes in kf (Permeability and Surface Area)
- Misc: High Protein Diet↑, Hyperglycemia↑, Glucocorticoids↑, Fever↑, Aging ↓

GFR REGULATION BY HORMONES OR AUTACOIDS

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

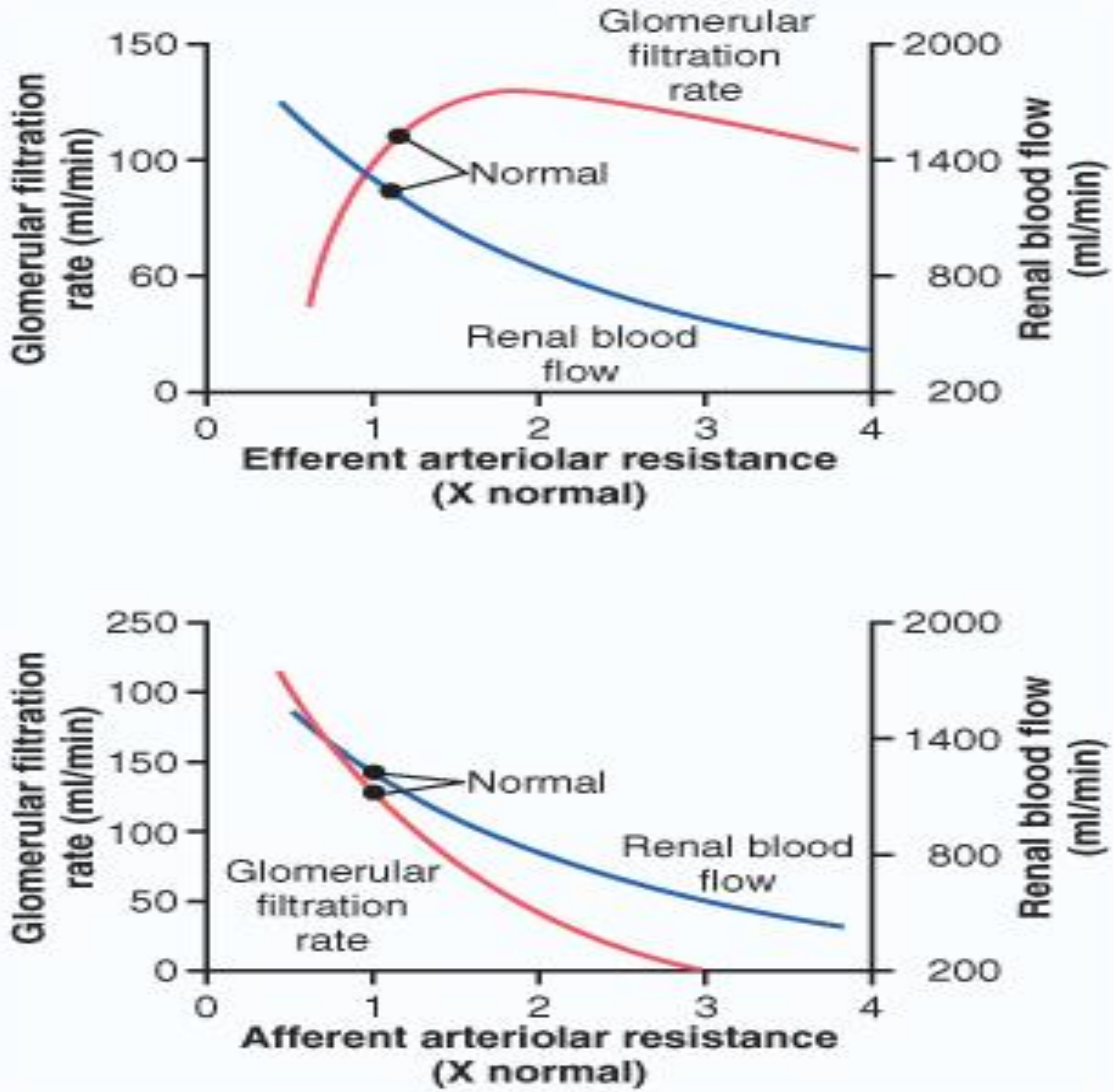
AGENTS AFFECTING MESANGIAL CELLS

CONTRACTION	RELAXATION
▪ Endothelins	▪ ANP
▪ Angiotensin II	▪ Dopamine
▪ Vasopressin	▪ PGE2
▪ Norepinephrine	▪ cAMP
▪ Platelet-activating factor	
▪ Thromboxane A2	
▪ PGF2	
▪ Histamine	
▪ Leukotriene C4&D4	

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

Kf, glomerular filtration coefficient; **PB**, Bowman's capsule hydrostatic pressure; **πG**, glomerular capillary colloid osmotic pressure; **PG**, glomerular capillary hydrostatic pressure; **AP**, systemic arterial pressure; **RE**, efferent arteriolar resistance; **RA**, afferent arteriolar resistance.

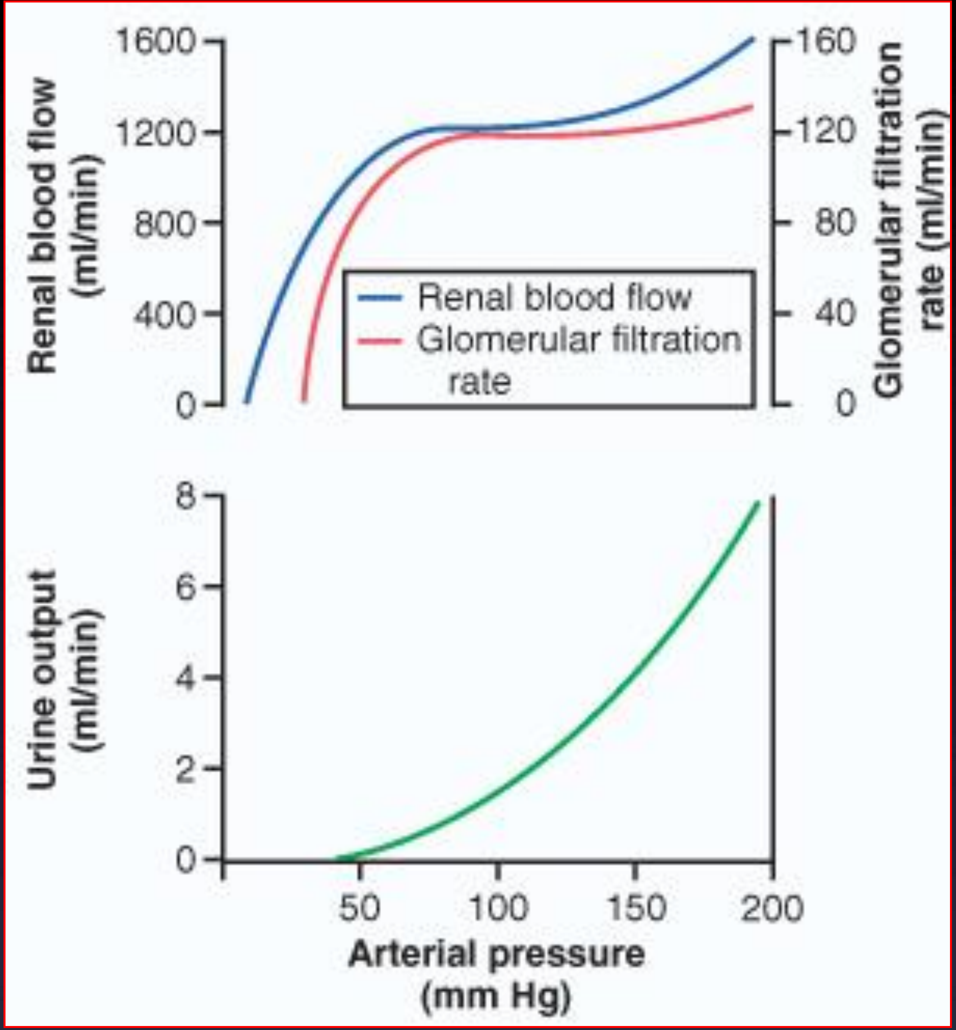
* Opposite changes in the determinants usually increase GFR.



Glomerular filtration rate (ml/min)
150
100
60
0
Glomerular filtration rate
2000
1400
800
200
Renal blood flow (ml/min)
Normal
Renal blood flow
0
1
2
3
4
Efferent arteriolar resistance (X normal)
Glomerular filtration rate (ml/min)
250
100
150
100
50
0
2000
1400
800
200
Renal blood flow (ml/min)
Normal
Renal blood flow
Glomerular filtration rate
0
1
2
3
4
Afferent arteriolar resistance (X normal)

AUTOREGULATION OF GFR

- GFR remains constant over a large range of values 75-160
- Autoregulation largely occurs by the regulation of renal vascular resistance



GFR REGULATION: *INTRINSIC*

1) **MYOGENIC:**
   - **Intrinsic property of mesangial (smooth muscle) cells and in afferent arteriole**
   - **Reflex contraction induced by increased blood pressure reduces filtration**

2) **TUBULOGLOMERULAR FEEDBACK:**
   - **Flow rate sensed by macula densa (part of juxtaglomerluar apparatus), sends chemical signal to alter afferent arteriole resistance**

GFR REGULATION: *EXTRINSIC*

- **SYMPATHETIC INNERVATION**
  - **Sympathetic stimulation/ epinephrine released from adrenal medulla cause arteriole vasoconstriction and reduced GFR**
- **ANGIOTENSIN II**
  - **Produced as a result of renin release from kidney**
  - **Constricts efferent ↑ arteriole; prevent decrease in GFR**

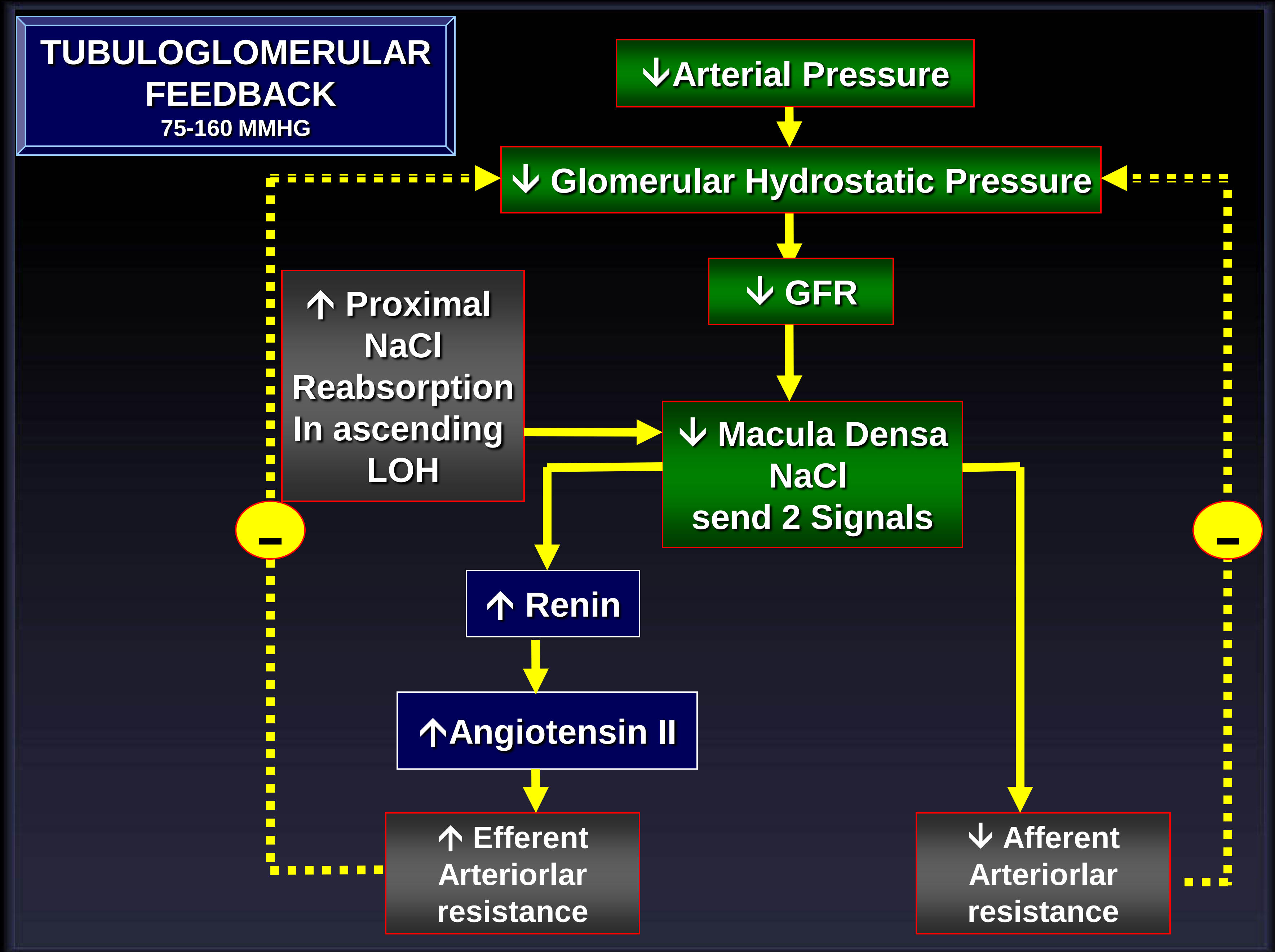
GFR REGULATION: *EXTRINSIC*

(Cont.)

- **NITRIC OXIDE (NO)**
  - **Causes arteriolar vasodilation**
  - **Elevated NO may result in hyperfiltration of early Diabetes Mellitus**
  - **Reduced NO after salt intake may lead to hypertension**

TUBULOGLOMERULAR FEEDBACK

A feedback mechanism that links changes in sodium chloride concentration at the macula densa with the control of renal arteriolar resistance


TUBULOGLOMERULAR FEEDBACK
75-160 MMHG
↓Arterial Pressure
↓ Glomerular Hydrostatic Pressure
↓ GFR
↑ Proximal NaCl Reabsorption In ascending LOH
↓ Macula Densa NaCl send 2 Signals
–
–
↑ Renin
↑Angiotensin II
↑ Efferent Arteriorlar resistance
↓ Afferent Arteriorlar resistance