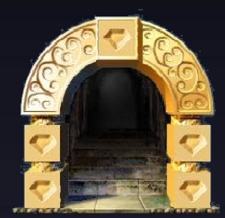
RENAL PHYSIOLOGY
INTRODUCTION



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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

ROLES OF THE KIDNEY

1. Regulation of extracellular fluid volume (ECF) ECF is an important determinant of BLOOD PRESSURE
2. Regulation blood osmolality
3. Maintenance of electrolyte balance (Na^+, K^+, HCO_3^-, Ca^{++})
4. Regulates blood pH

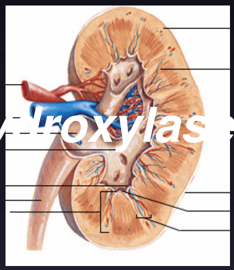
ROLES OF THE KIDNEY (Cont.)

5. Excretes wastes (creatinine, urea, benzoate, penicillin, saccharin)
6. Secretion, metabolism, and excretion of hormones
   - Hormone production (Erythropoietin, Renin)
   - Activation of Vitmain D
7. Gluconeogenesis

Naturally occurring vitamin D (cholecalciferol)

hydroxylation

25-hydroxycholecalciferol 25-OHD3)

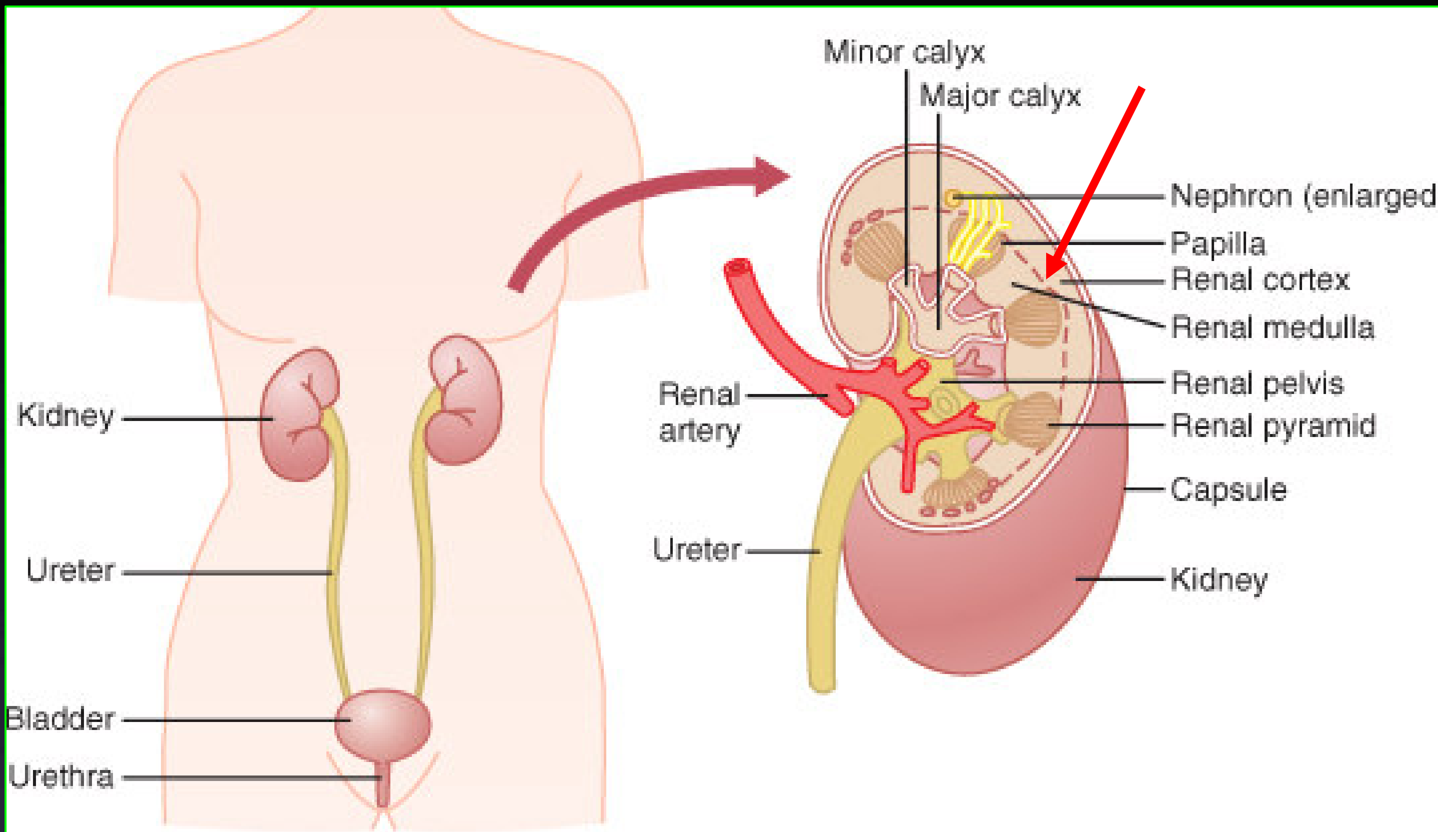


PTH → *1α-hydroxylase enzyme*

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

PHYSIOLOGIC ANATOMY OF KIDNEYS

- Size Clenched Fist
- Weight 150 grams



RENAL BLOOD SUPPLY

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

Renal artery

Interlobar arteries

Arcuate arteries

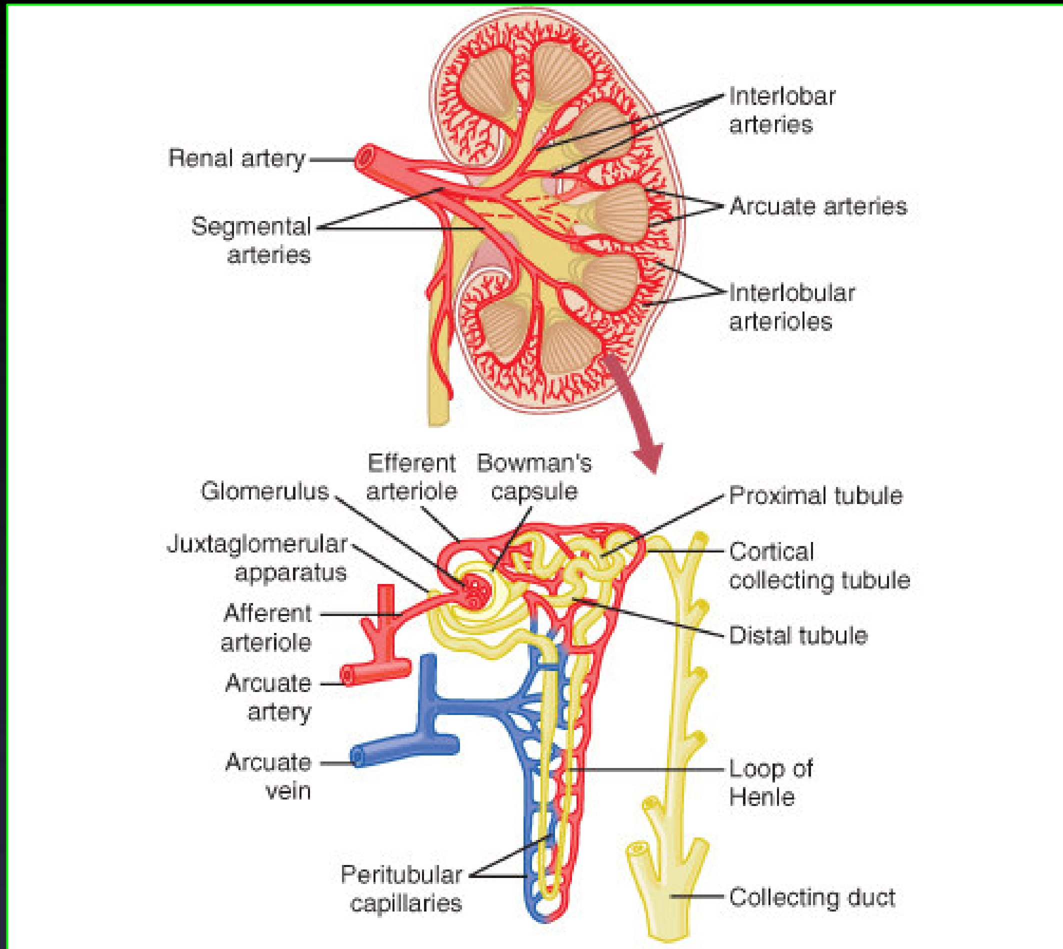
Interlobular arteries

Afferent arterioles

Glomerular capillaries

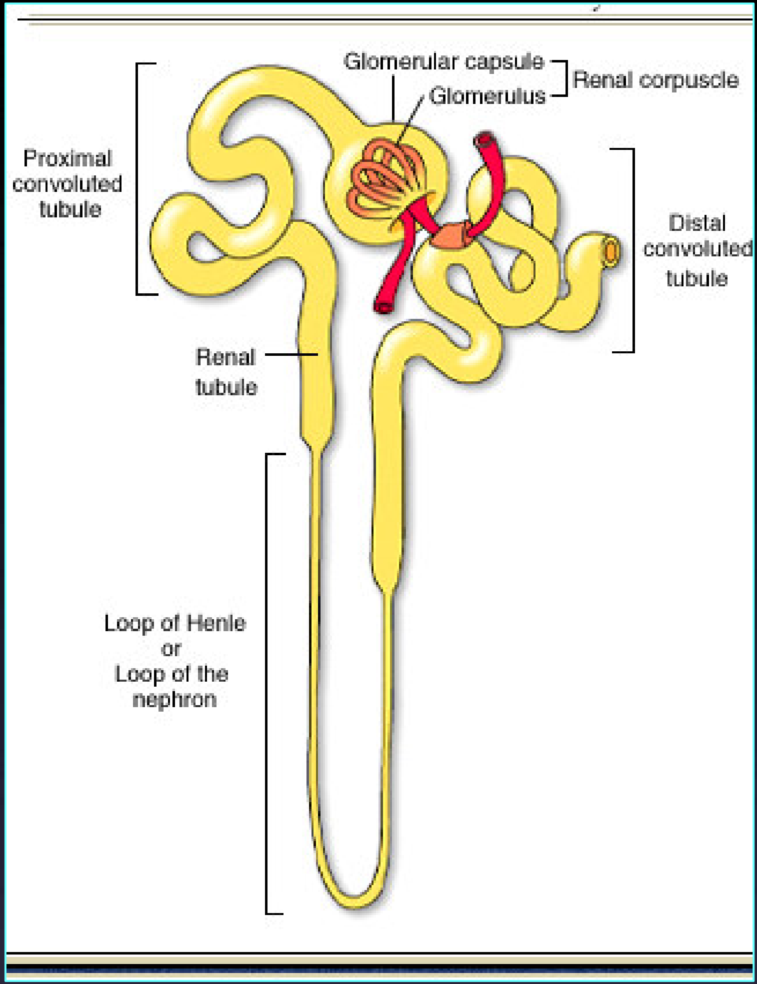
Efferent arteriole

Peritubular capillaries



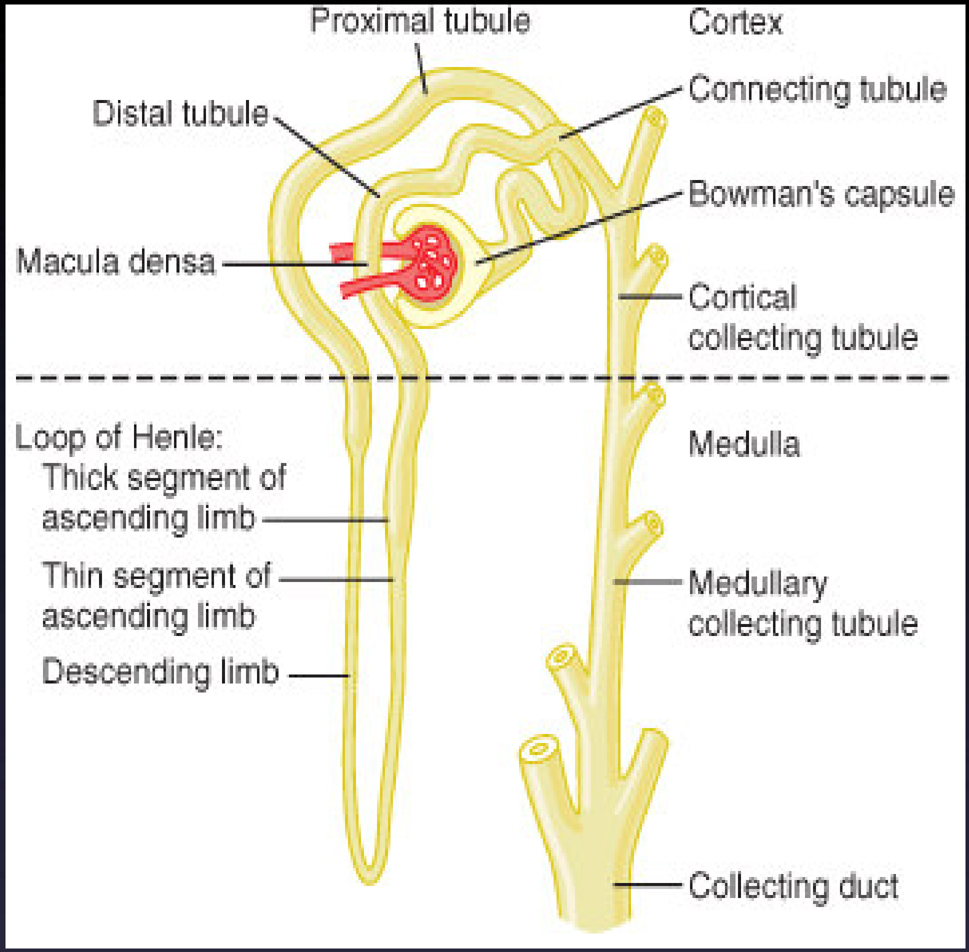
NEPHRON

- 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.

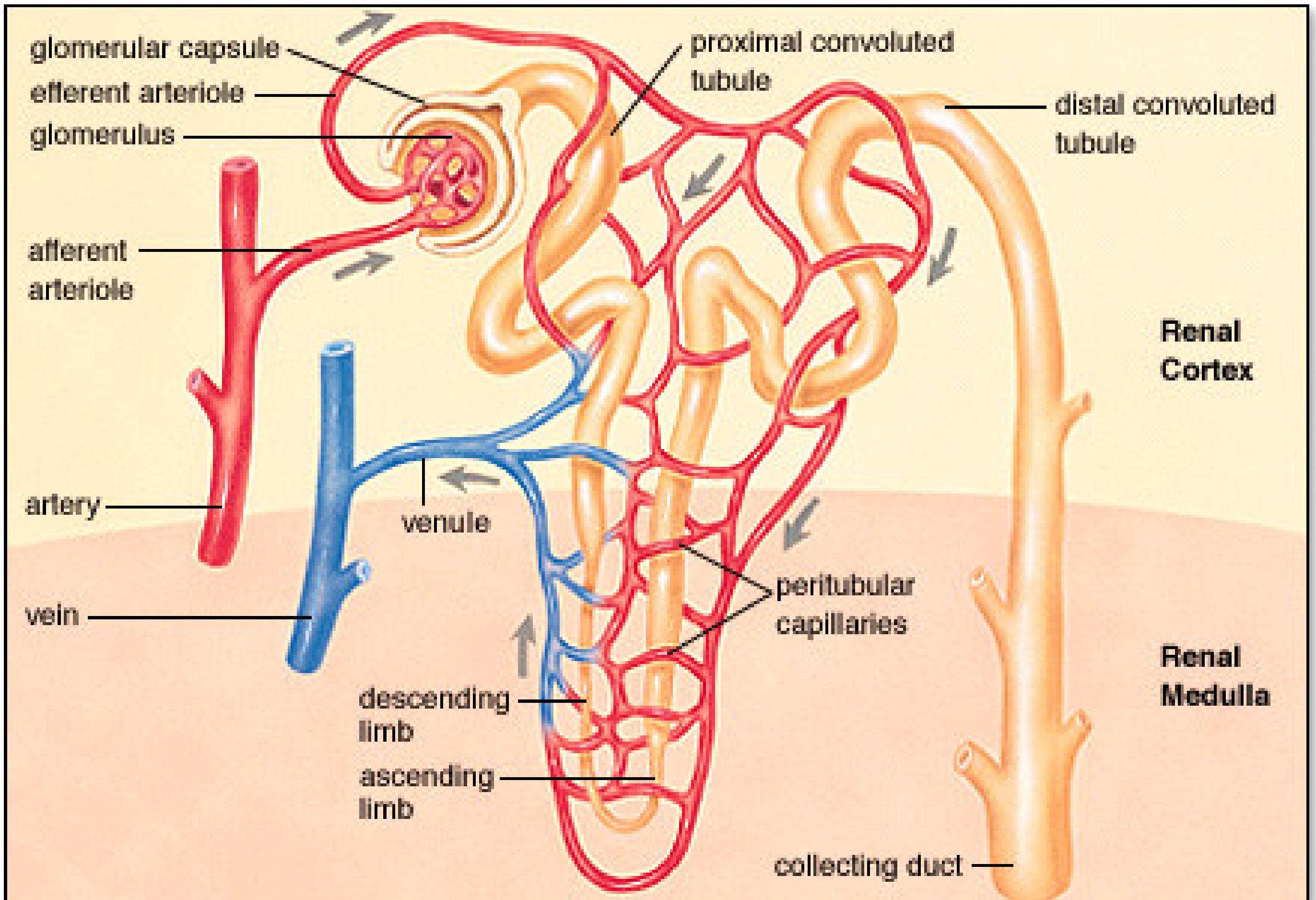


PARTS OF NEPHRON

- The initial parts of 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 progressively larger ducts that eventually empty into the renal pelvis through the tips of the renal papillae. In each kidney, there are about 250 of the very large collecting ducts, each of which collects urine from about 4000 nephrons.*

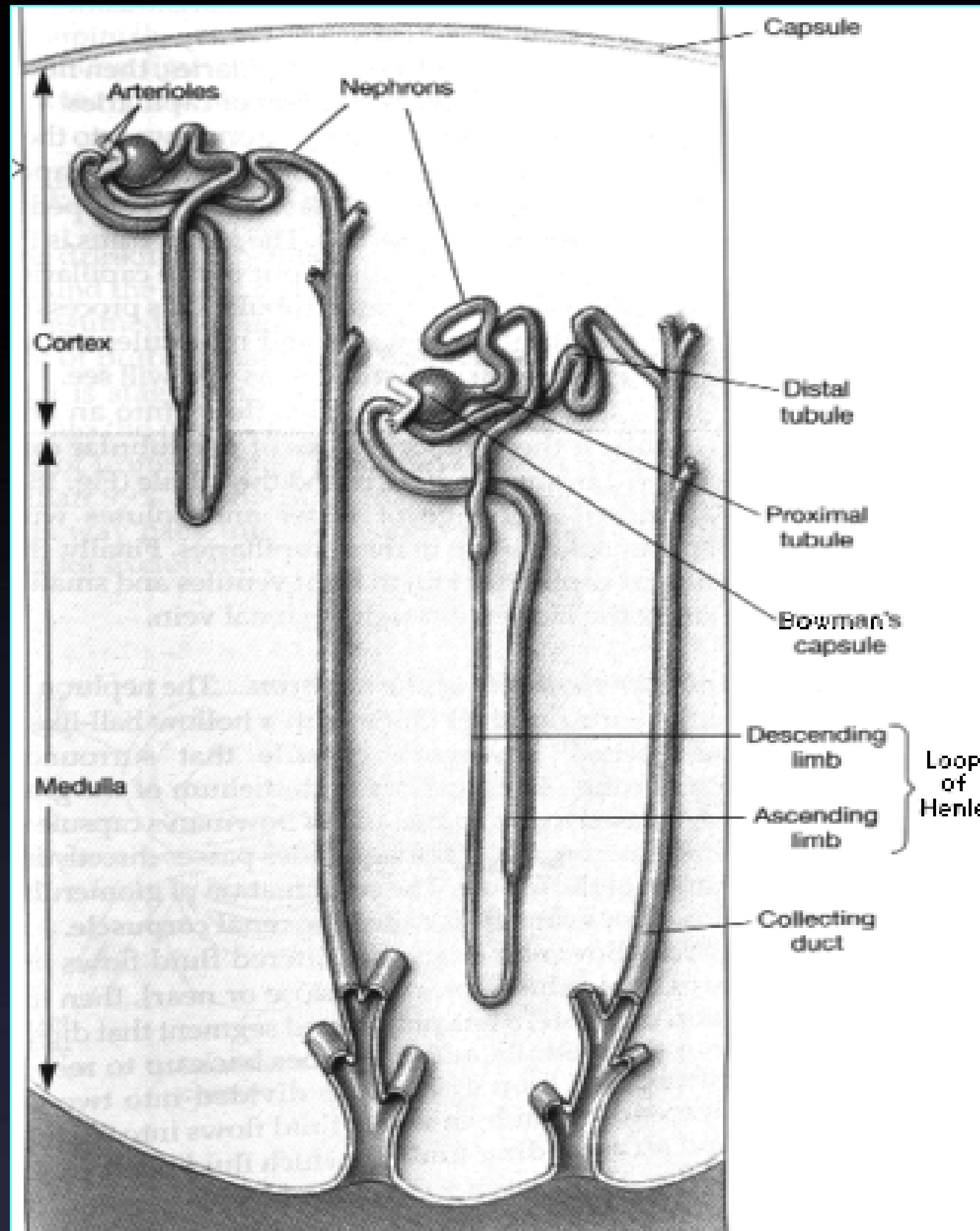


RENAL PORTAL SYSTEM



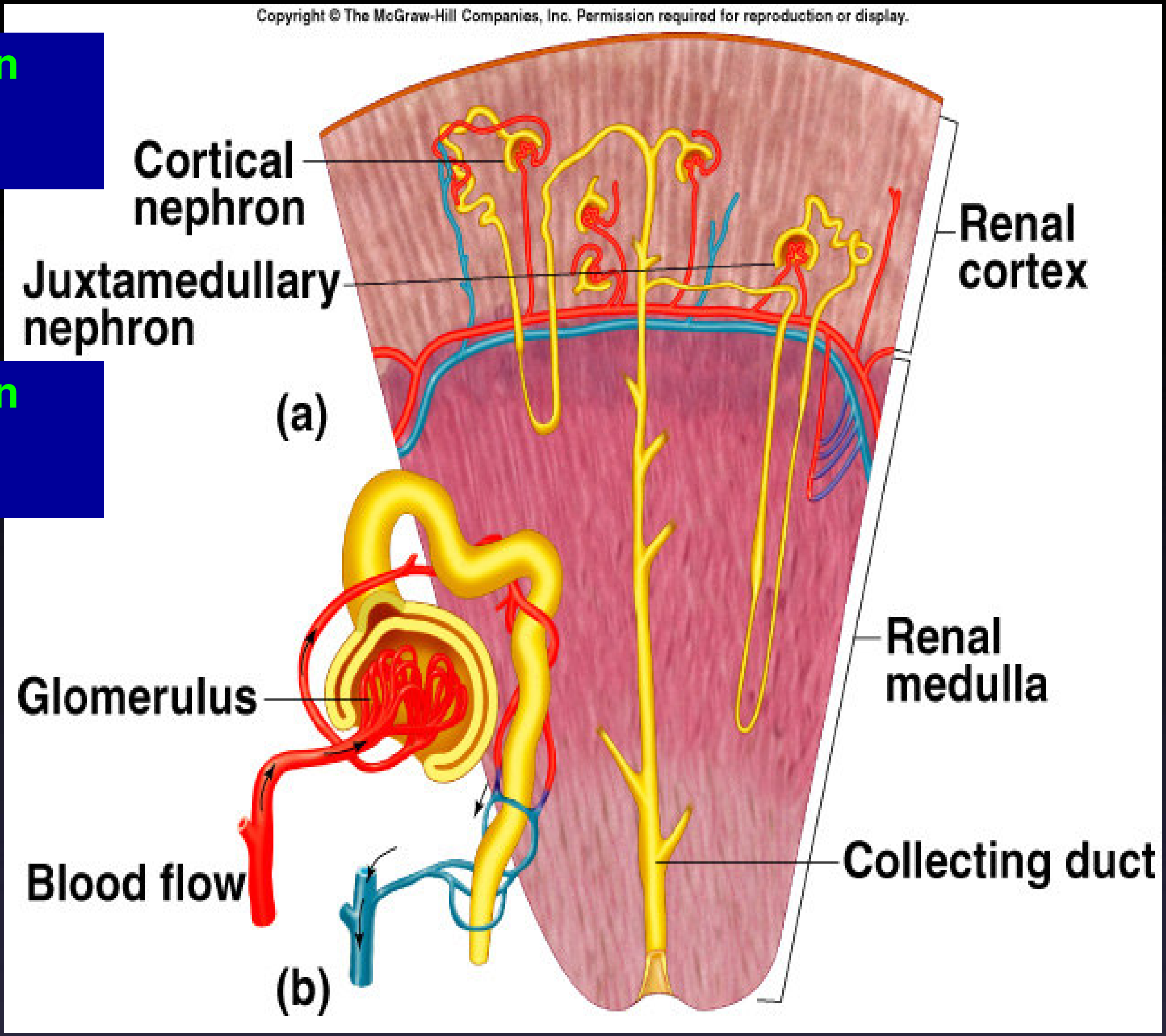
NEPHRON TYPES

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

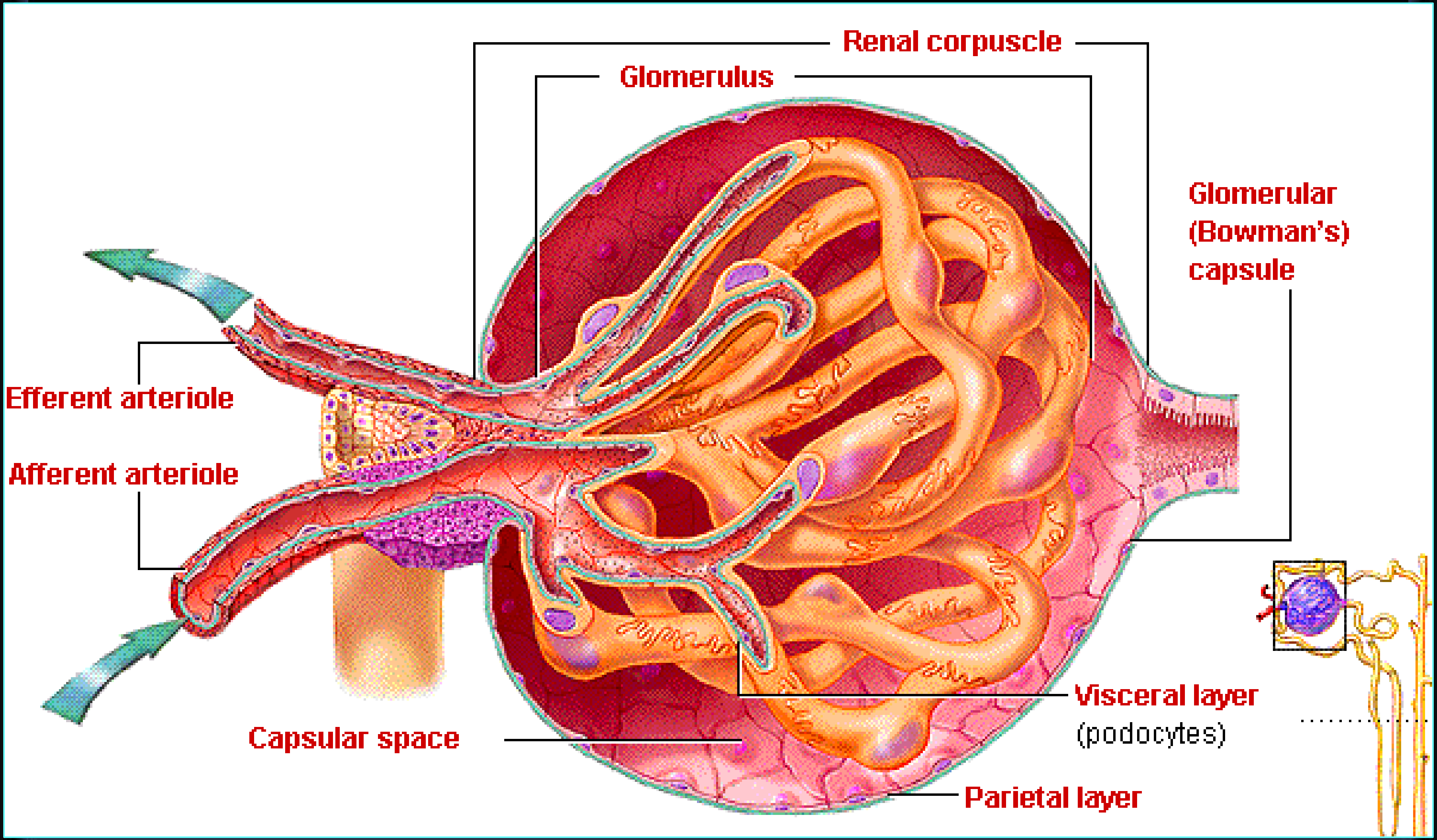

Capsule
Arterioles
Nephrons
Cortex
Medulla
Distal tubule
Proximal tubule
Bowman's capsule
Descending limb
Ascending limb
Loop of Henle
Collecting duct

Originates in outer 2/3 of cortex.

Originates in inner 1/3 of cortex.



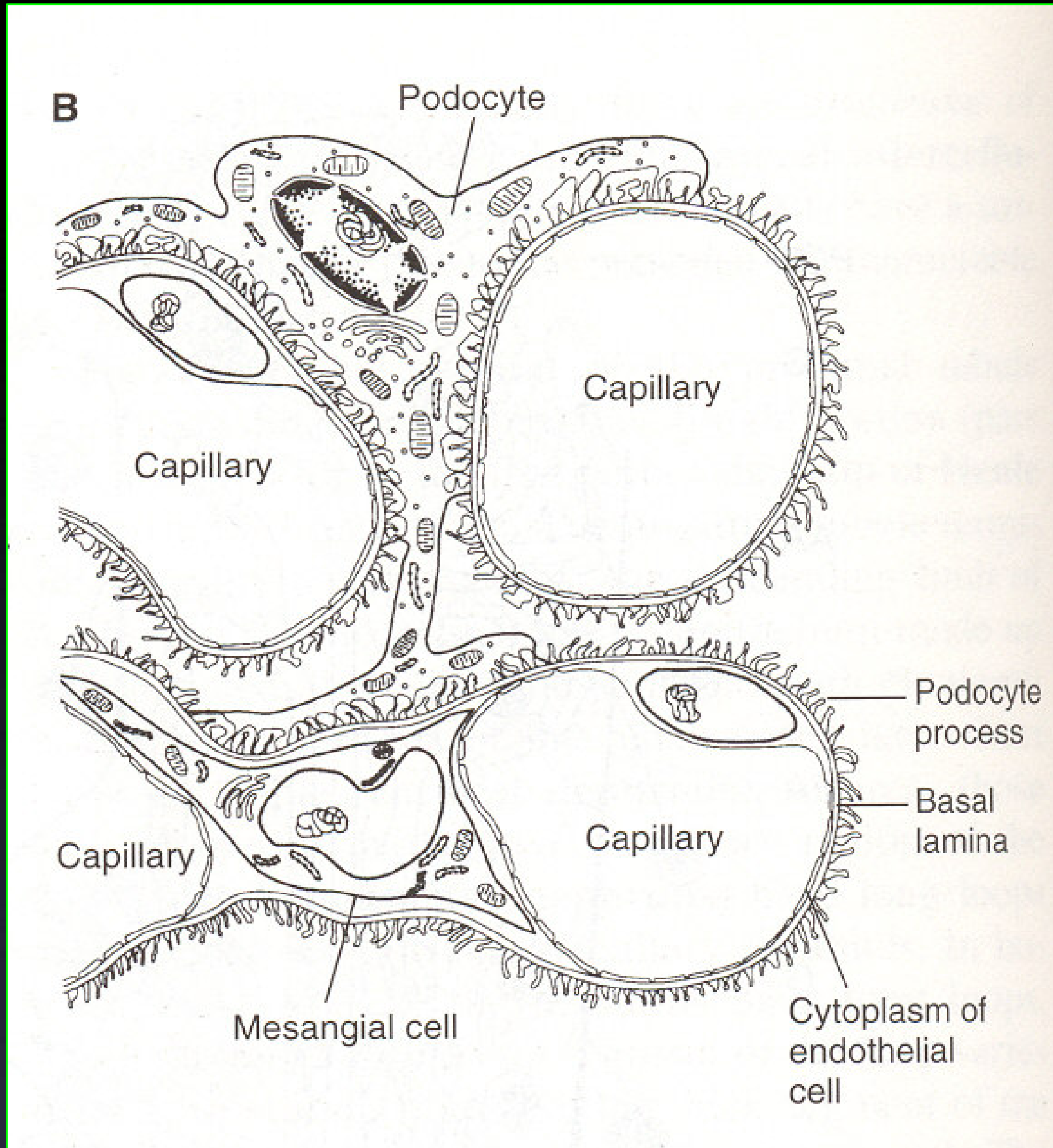
BOWMAN'S CAPSULE



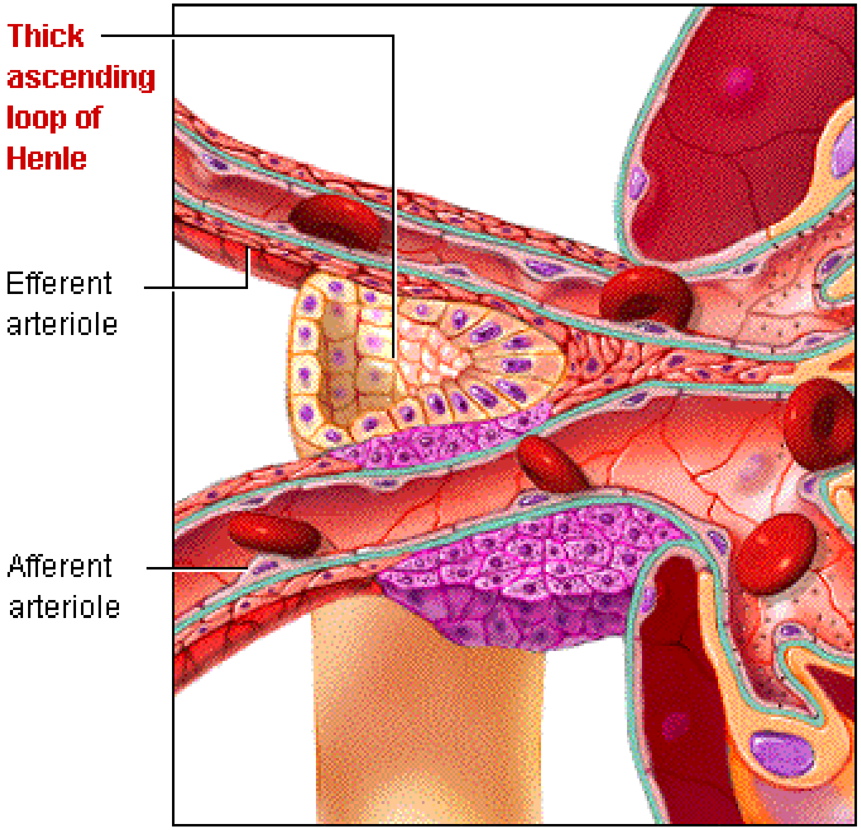
THE Renal Corpuscle COMPRISES FOUR MAIN CELL TYPES

1) **Endothelial cells** which are fenestrated with 500-1000 Å pores;
2) **Visceral epithelial cells (podocytes)** which support the delicate glomerular basement membrane by means of an extensive trabecular network (foot processes);
3) **Parietal epithelial cells** which cover the Bowman's capsule;
4) **Mesangial cells** are contractile cells

Type I Medullary Intyerstitial Cells secrete PGE2

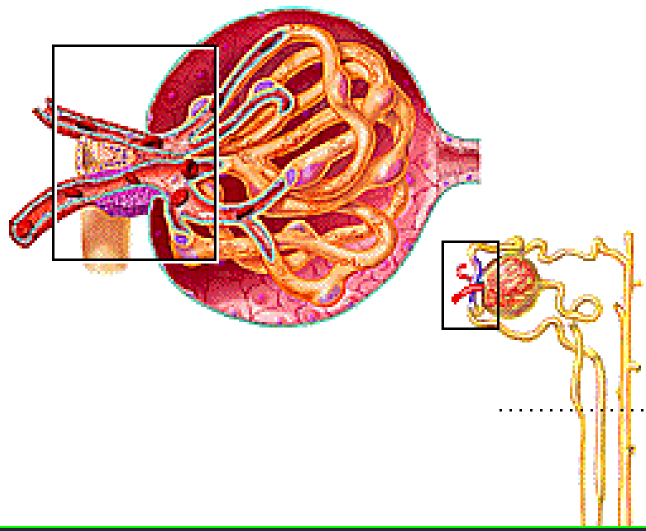

B
Podocyte
Capillary
Capillary
Podocyte process
Basal lamina
Capillary
Capillary
Mesangial cell
Cytoplasm of endothelial cell

JUXTA GLOMERULAR APPARATUS



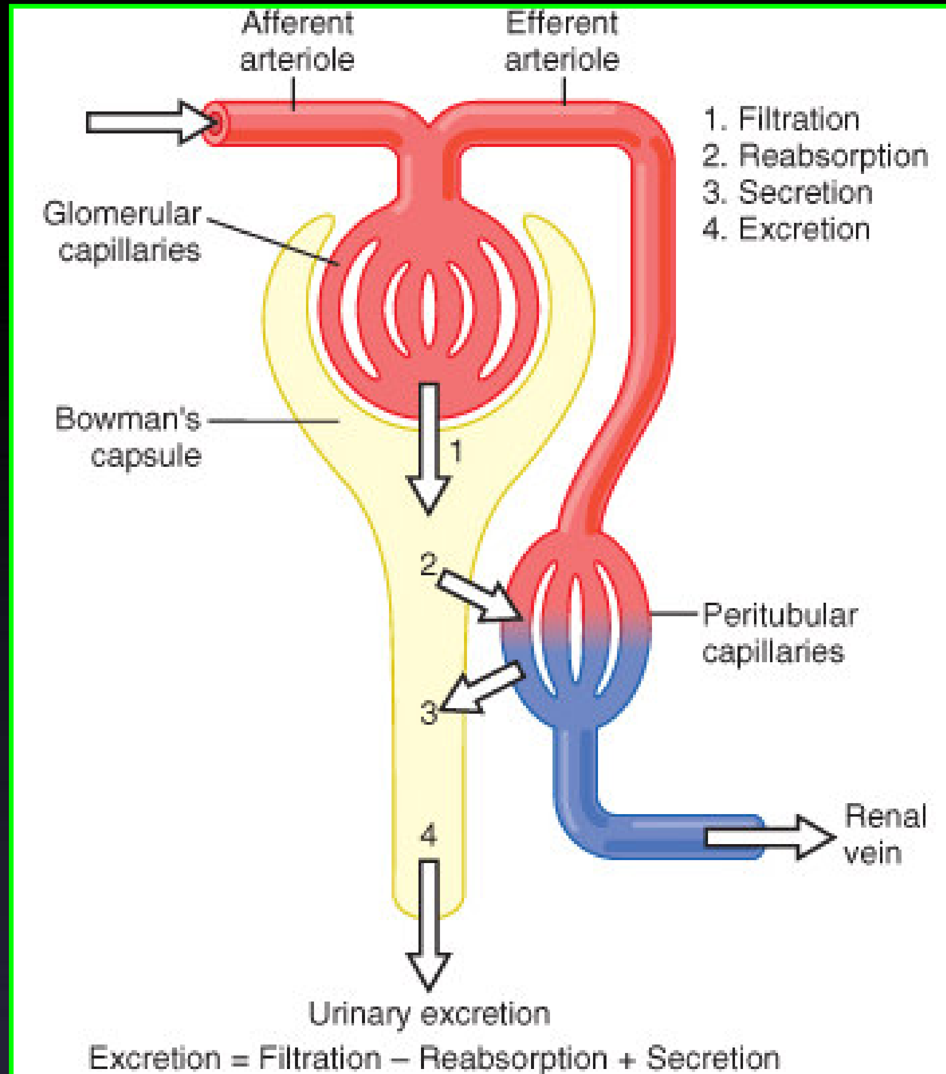
As the thick ascending loop of Henle transitions into the early DCT, the tubule runs adjacent to the afferent and efferent arterioles.

Where these structures are in contact they form the monitoring structure called the **juxtaglomerular apparatus (JGA)**, which is composed of macula densa and JG cells.



RENAL PROCESSES

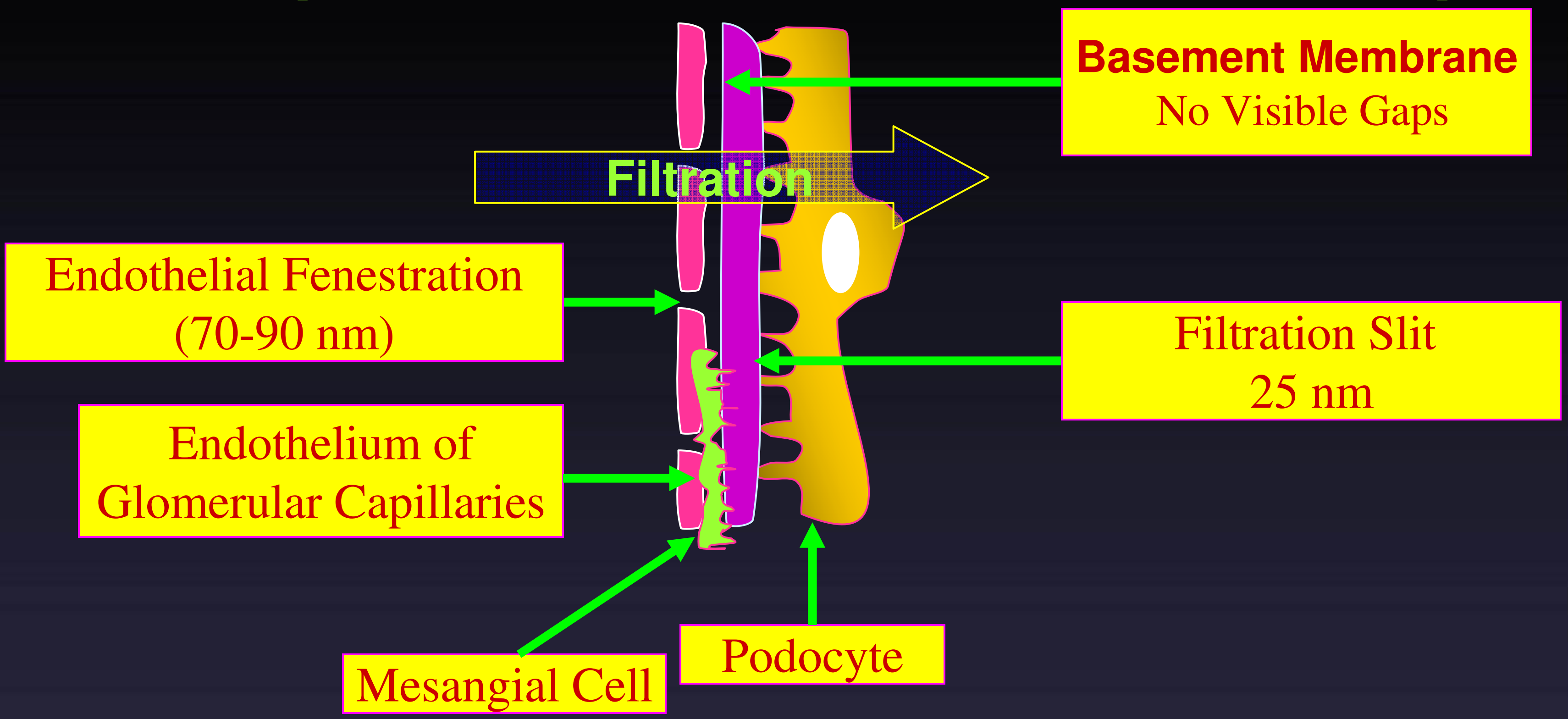
1. Filtration
2. Reabsorption
3. Secretion
4. Excretion



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

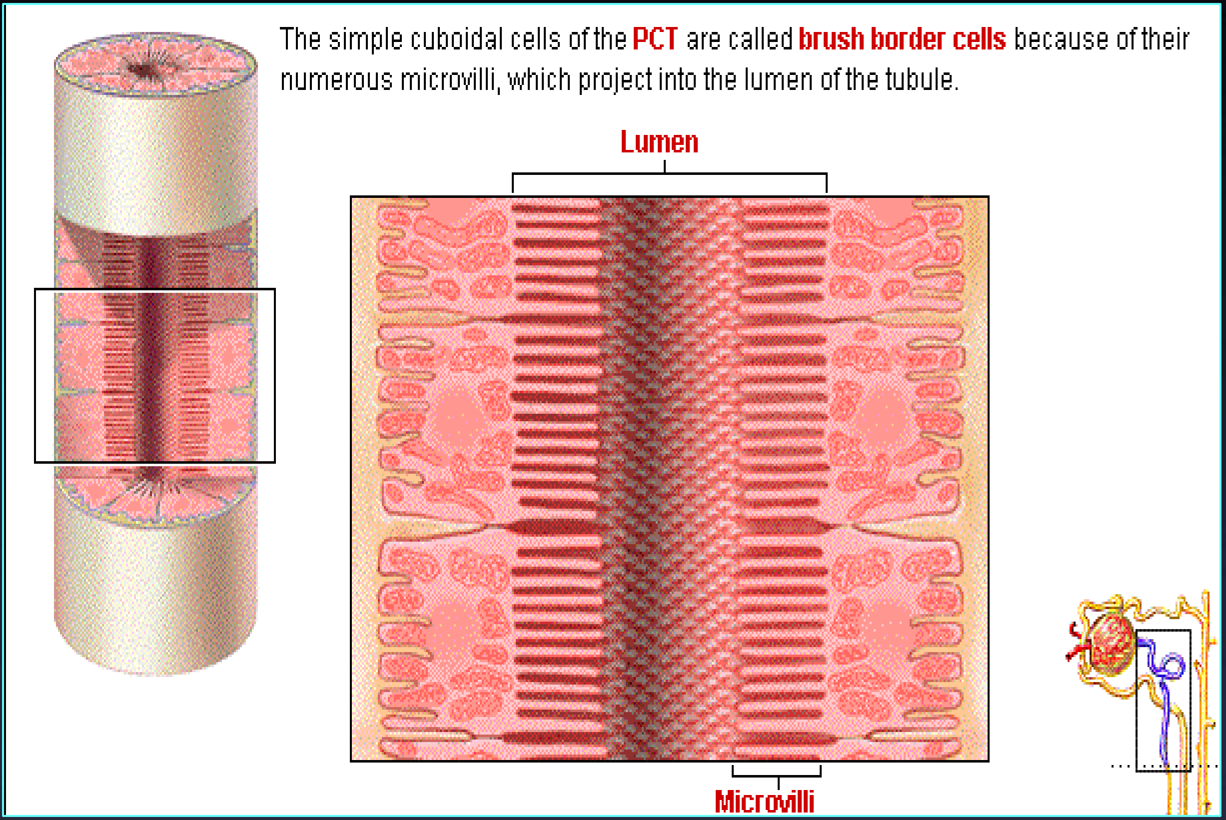
FILTRATION MEMBRANE

4-8 nm particles can size can be filtered easily



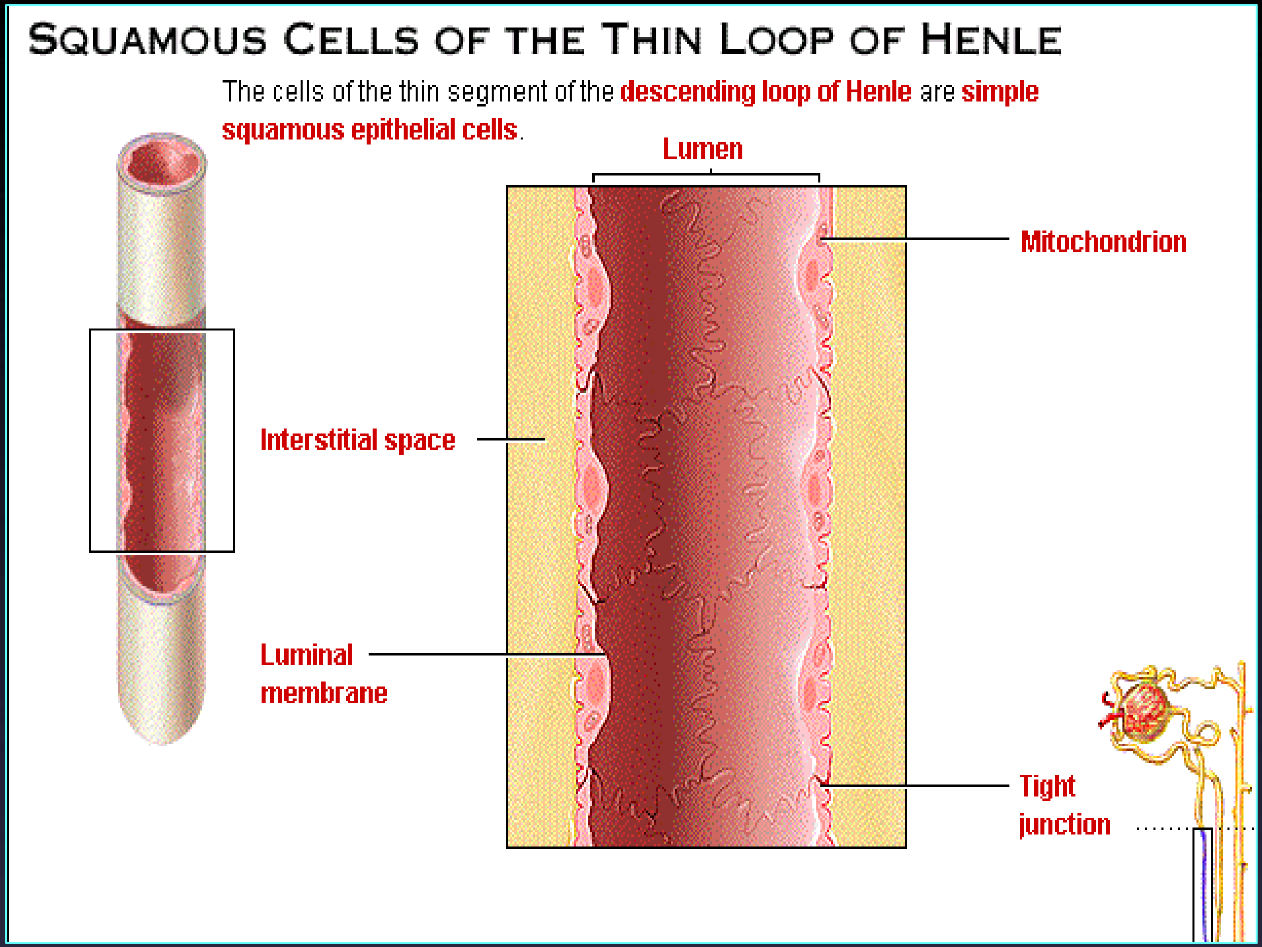
PROXIMAL CONVOLUTED TUBULE

- many mitochondria
- brush border
- tight junctions
- lateral intercellular spaces.



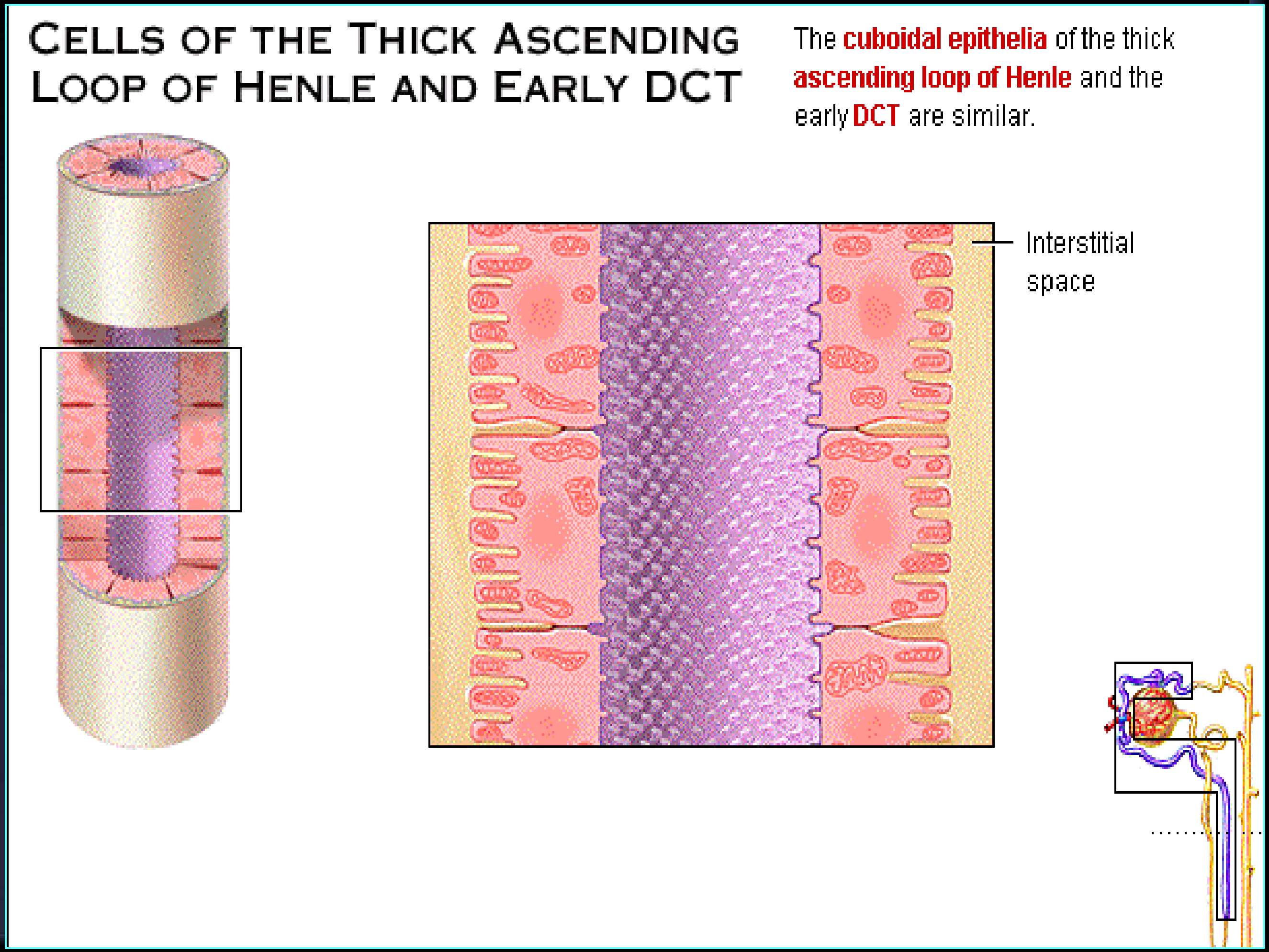
THIN LOOP OF HENLE

- few mitochondria
- flattened with few microvilli

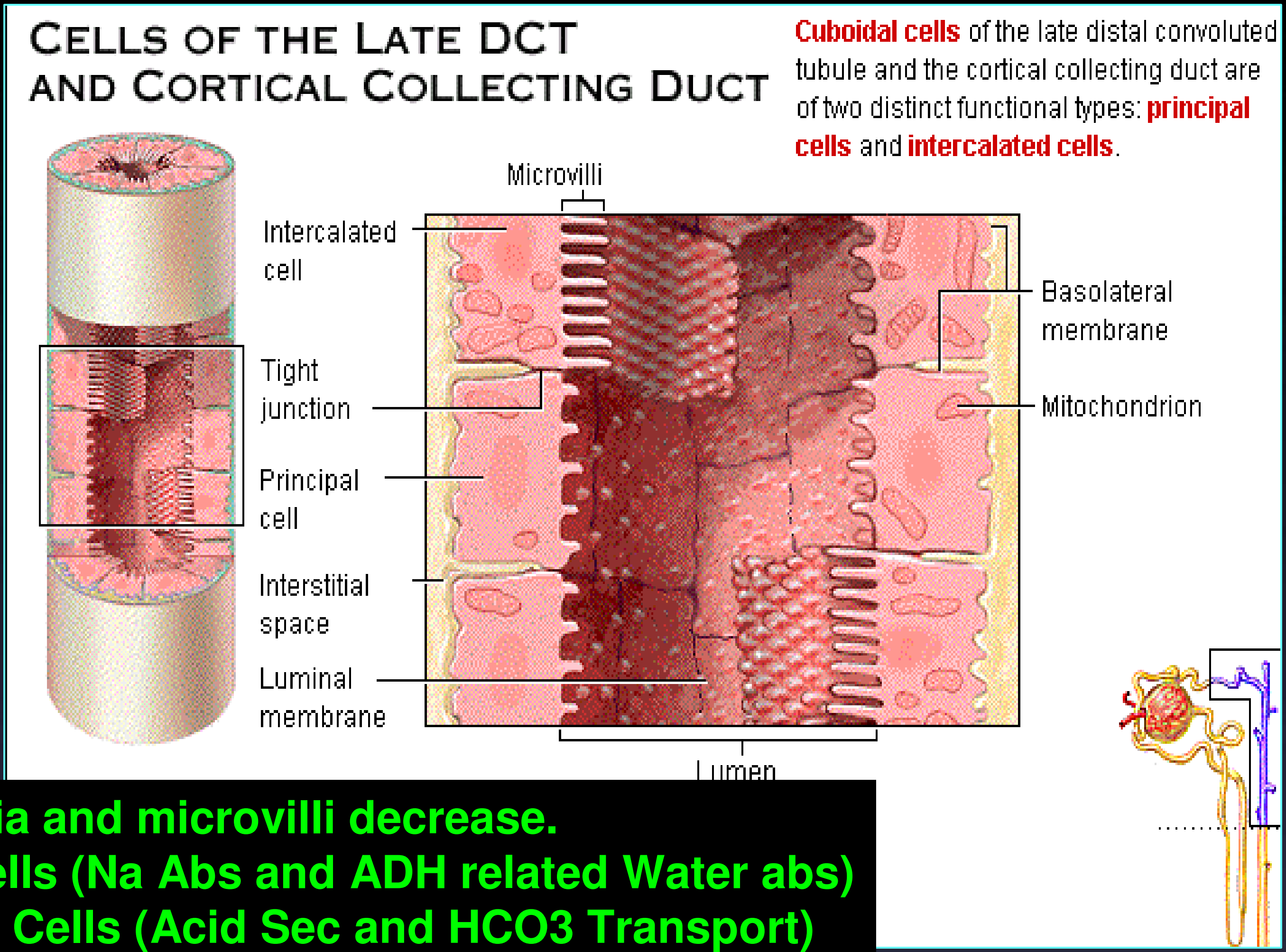


THICK ASCENDING LOOP OF HANLE AND EARLY DCT

Many mitochondria and microvilli, but fewer than in the proximal tubule

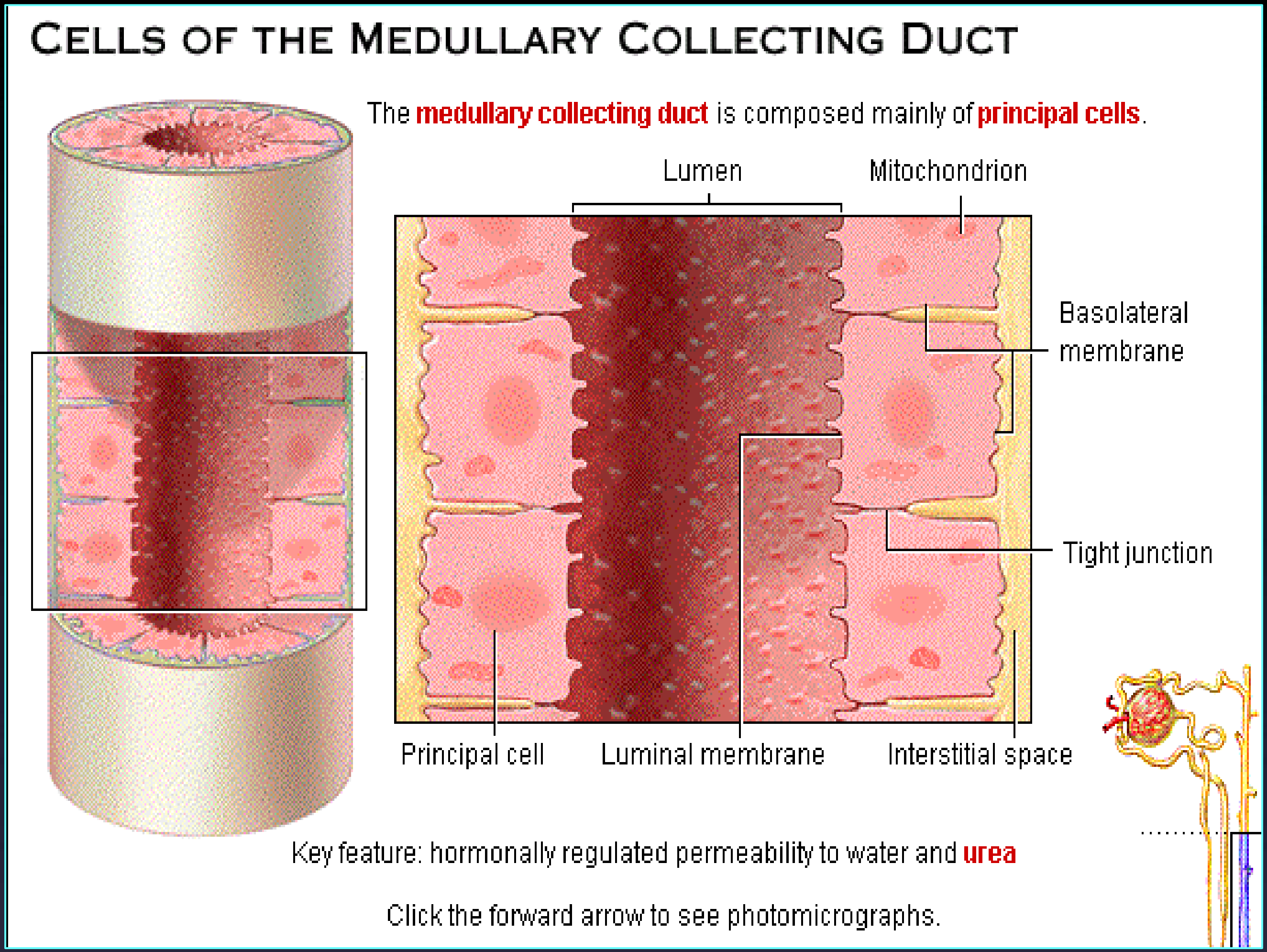


LATE DCT AND CORTICAL COLLECTING DUCT



- Mitochondria and microvilli decrease.
- Principal Cells (Na Abs and ADH related Water abs)
- Intercalated Cells (Acid Sec and HCO3 Transport)

MEDULLARY COLLECTING DUCT



RENAL PHYSIOLOGY

GLOMERULAR FILTRATION

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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

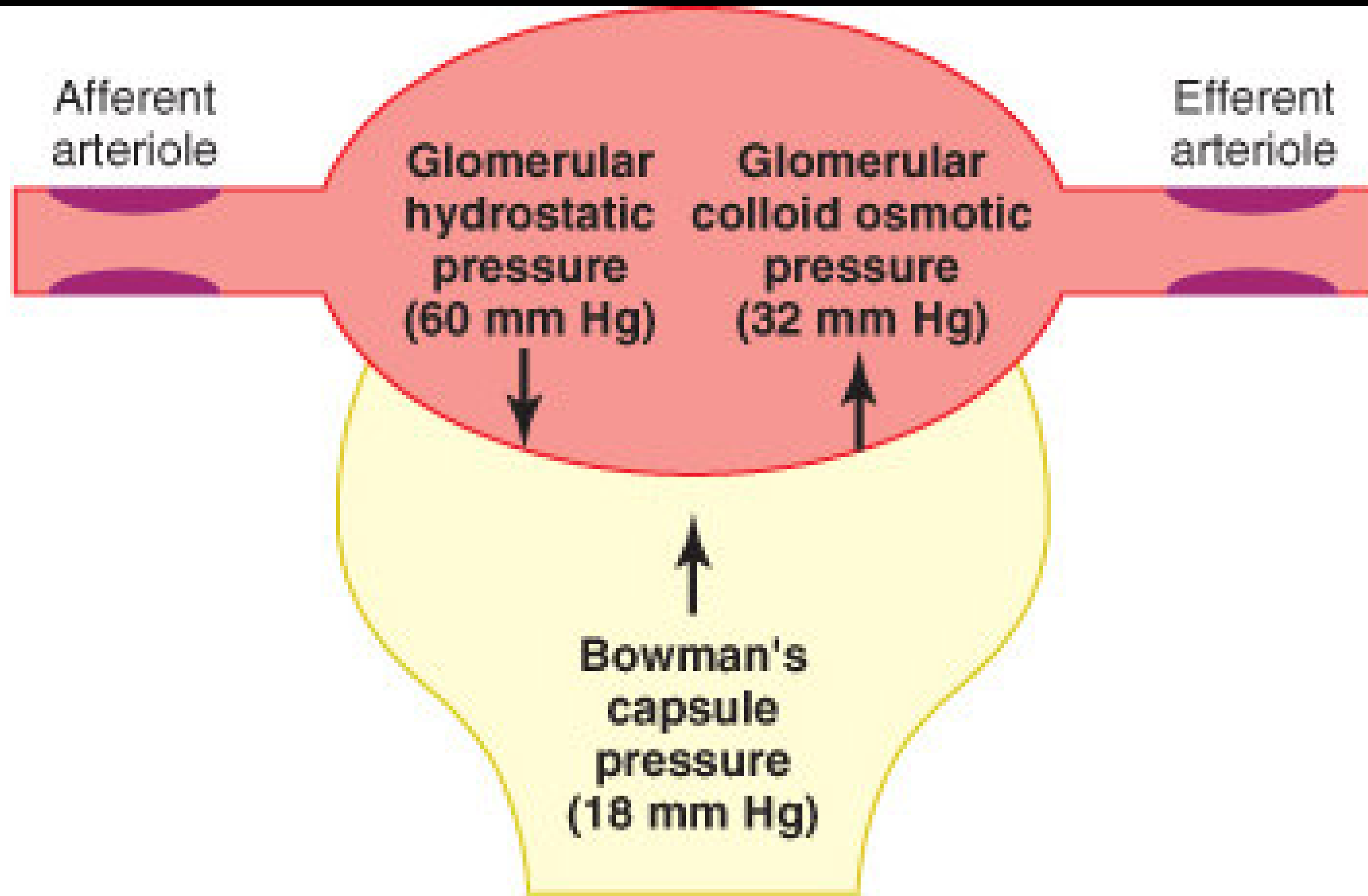
At a molecular level, filtration is the bulk flow of fluid through a membrane or other barrier that selectively impedes the movement of some molecules, the largest being impeded most. This process is sometimes called ultrafiltration.

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.

- RBF=1100 ml/minX60=66000ml
- RPF=650ml/minX60X24=871200ml
- GFR=125ml/min
- Filtration Fraction=GFR/RPF=125/650=19.3=20 %
- GFR/day=125X60X24=180000mlor180 liters/day
- Filterate Reabsorbed=180-1.5=178.5 liters
- Less than 1 % of GF becomes urine more than 99 % is reabsorbed
- N Urinary Output=1.5 liters
- Obligatory UO = .5-.6 Liters
- Anuria and Oliguria < 0.3 liters



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)

Determinants of the 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	

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 (6 nm)	69,000	0.005

Rx Glucose

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.

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

PLASMA CLEARANCE

- The Volume of Plasma that is completely cleared of any substance by the Kidneys per minute is called the clearance of that particular substance

Clearance = Urine Conc. X Vol of Urine/ Plasma Conc

CONTROL OF GFR

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

(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

- Glomerular Filtration Rate in both kidneys per mm Hg Filtration Pressure

Kf = GFR/ Filtration Pressure

= 125 ml per min/ 10 mm Hg

= 12.5 ml/min/mm Hg of filtration Pr

Increased Glomerular Capillary Filtration Coefficient Increases GFR

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

$$K_f = GFR \, / \, \text{net filtration pressure}$$

increased Kf raises GFR and decreased Kf reduces GFR

FACTORS AFFECTING GFR

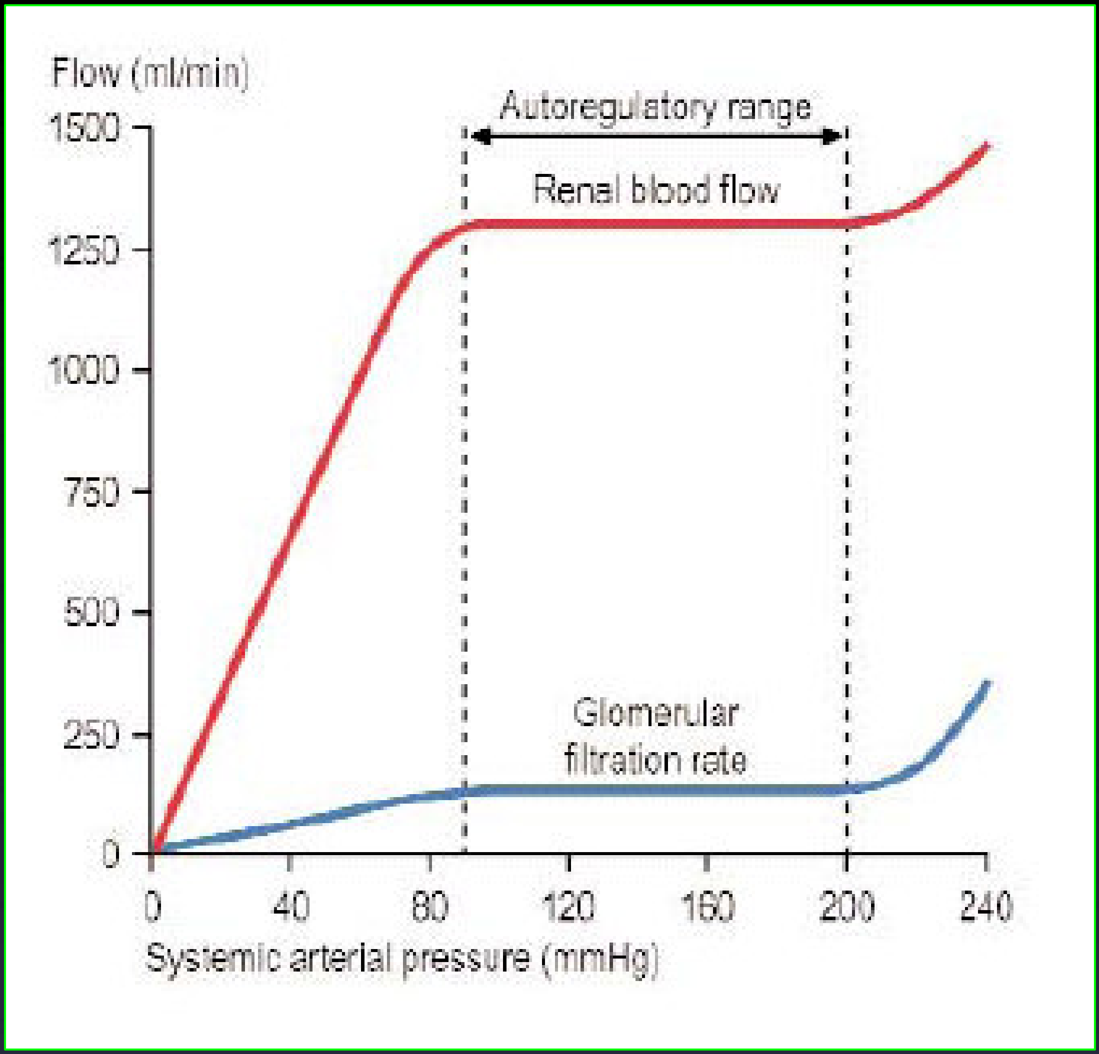
- Changes in renal blood flow
- Changes in Glomerular Capillary hydrostatic pressure
- Changes in hydrostatic pressure in bowman’s Capsule
- Changes in concentration of plasma proteins (Dehydration, Hypoproteinemia etc.)
- Changes in kf (Permeability and Surface Area)

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)

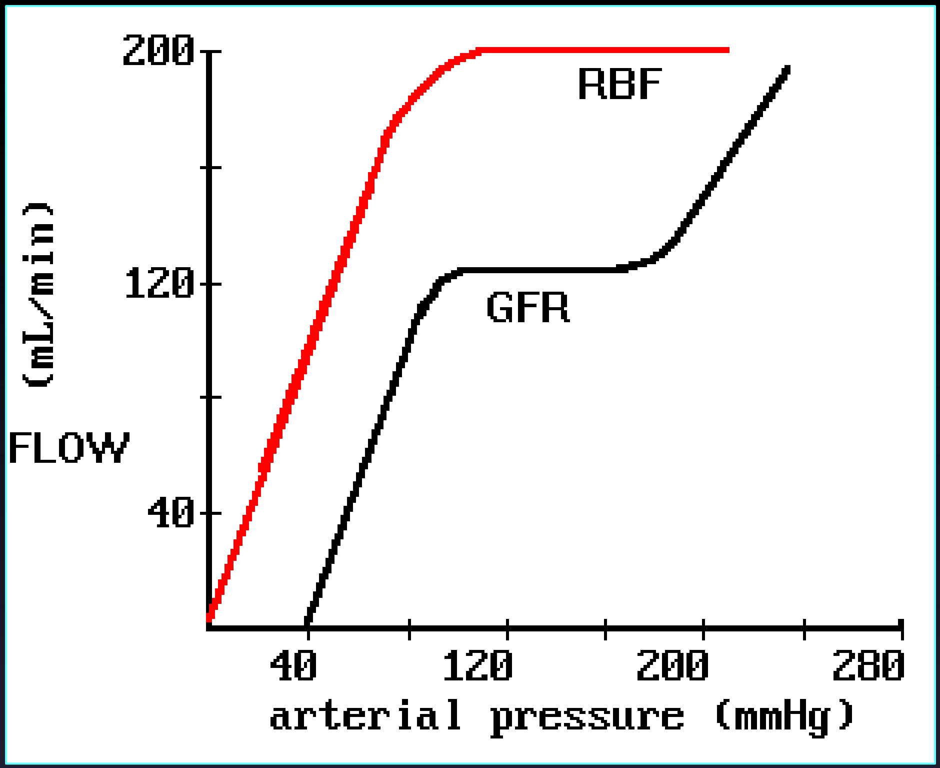
Kf, glomerular filtration coefficient; **PB**, Bowman's capsule hydrostatic pressure; **πG**, glomerular capillary colloid osmotic pressure; **PG**, glomerular capillary hydrostatic pressure; **AP**, systemic arterial pressure; **RE**, efferent arteriolar resistance; **RA**, afferent arteriolar resistance.

* Opposite changes in the determinants usually increase GFR.

AUTOREGULATION OF RBF AND GFR



GFR AUTOREGULATION



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

GFR REGULATION: *INTRINSIC*

1) **MYOGENIC:**
   - **Intrinsic property of mesangial (smooth muscle) cells 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

GFR Regulation by Hormones or Autacoids

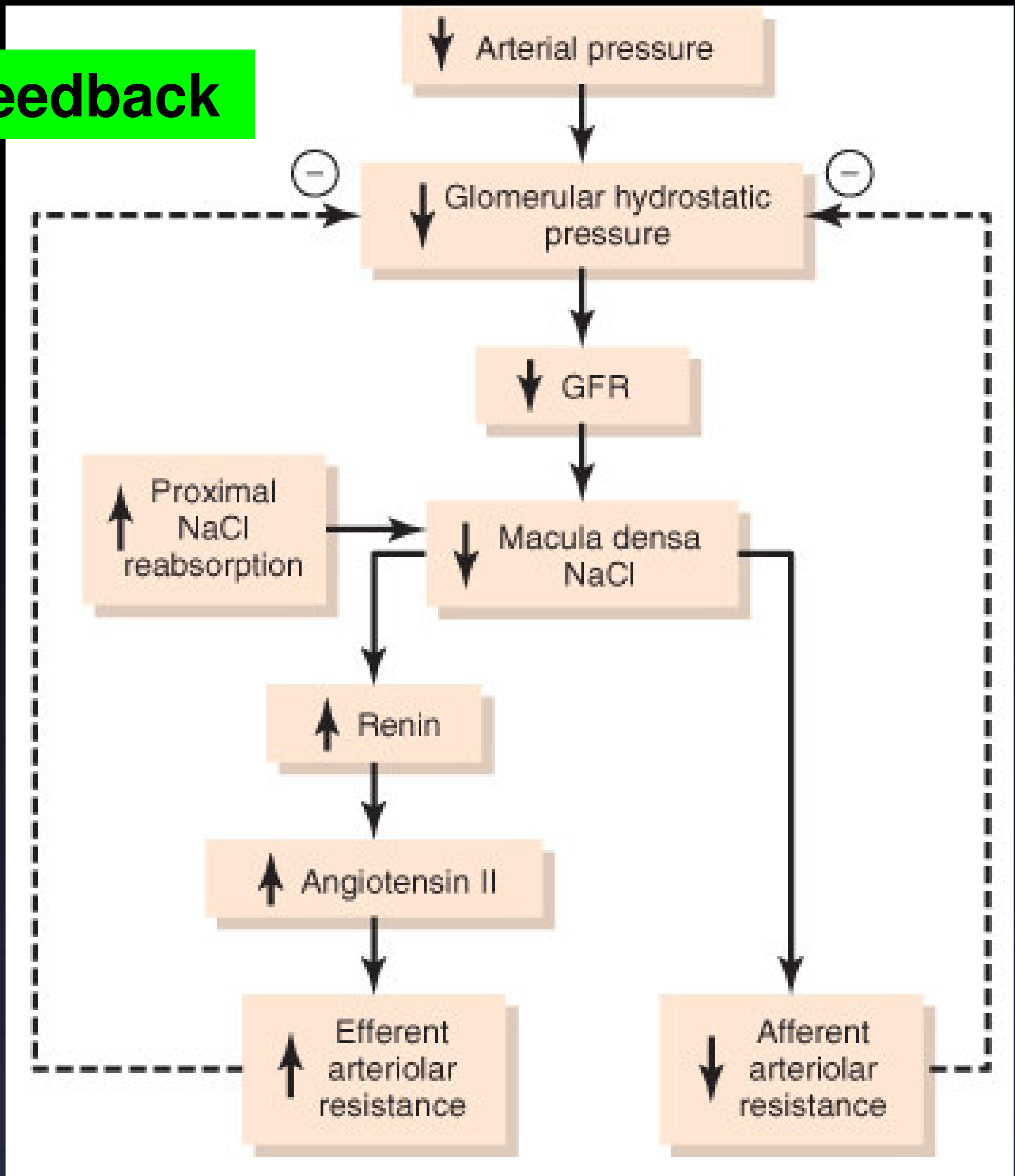
Hormone or Autacoid	Effect on GFR
Norepinephrine	↓
Epinephrine	↓
Endothelin	↓
Angiotensin II	↔ (prevents ↓)
Endothelial-derived nitric oxide	↑
Prostaglandins	↑

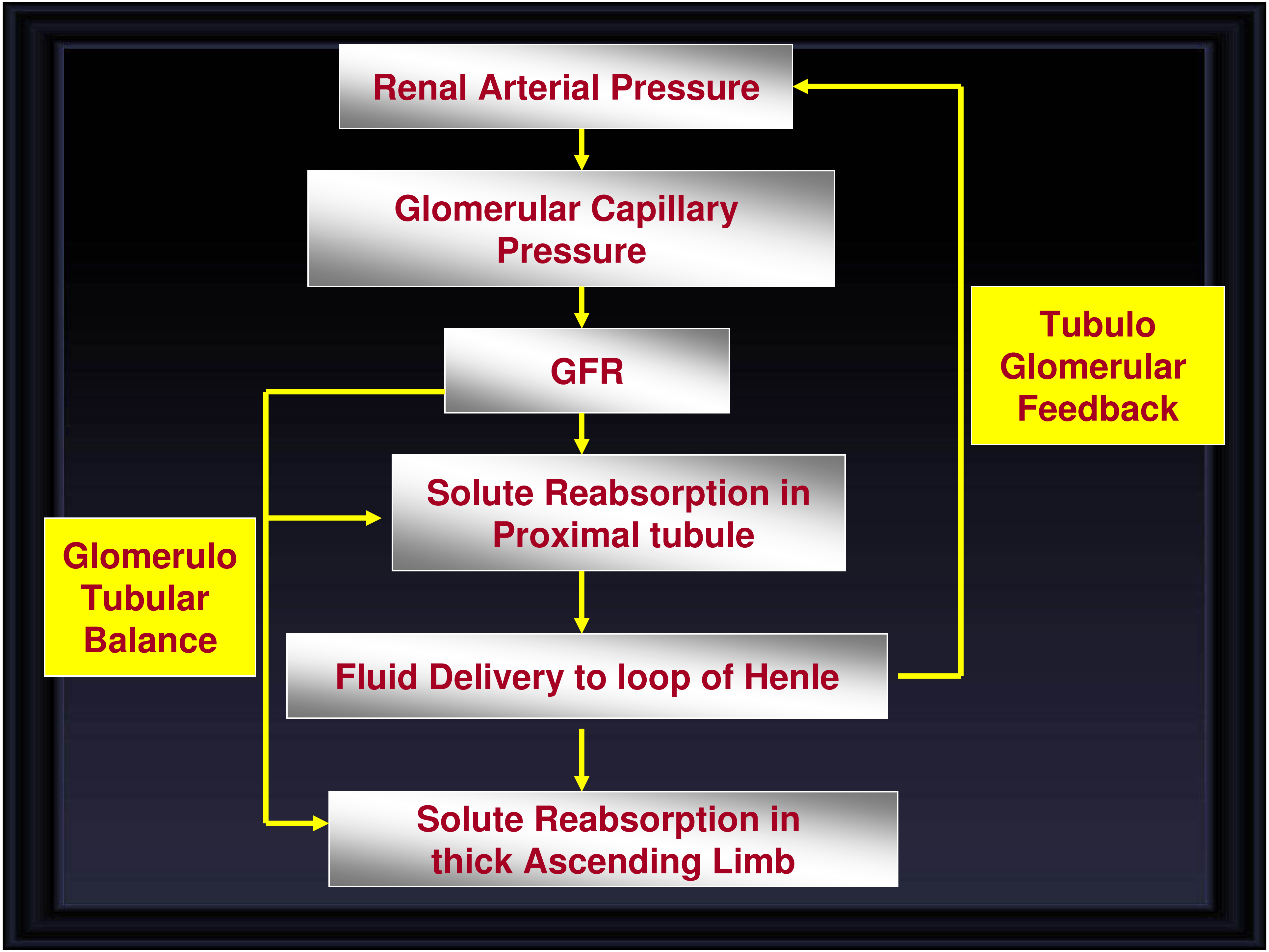
AGENTS AFFECTING MESANGIAL CELLS

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

TUBULOGLOMERULAR FEEDBACK

tubuloglomerular feedback




Renal Arterial Pressure
Glomerular Capillary Pressure
GFR
Solute Reabsorption in Proximal tubule
Fluid Delivery to loop of Henle
Solute Reabsorption in thick Ascending Limb
Tubulo Glomerular Feedback
Glomerulo Tubular Balance