Renal Physiology

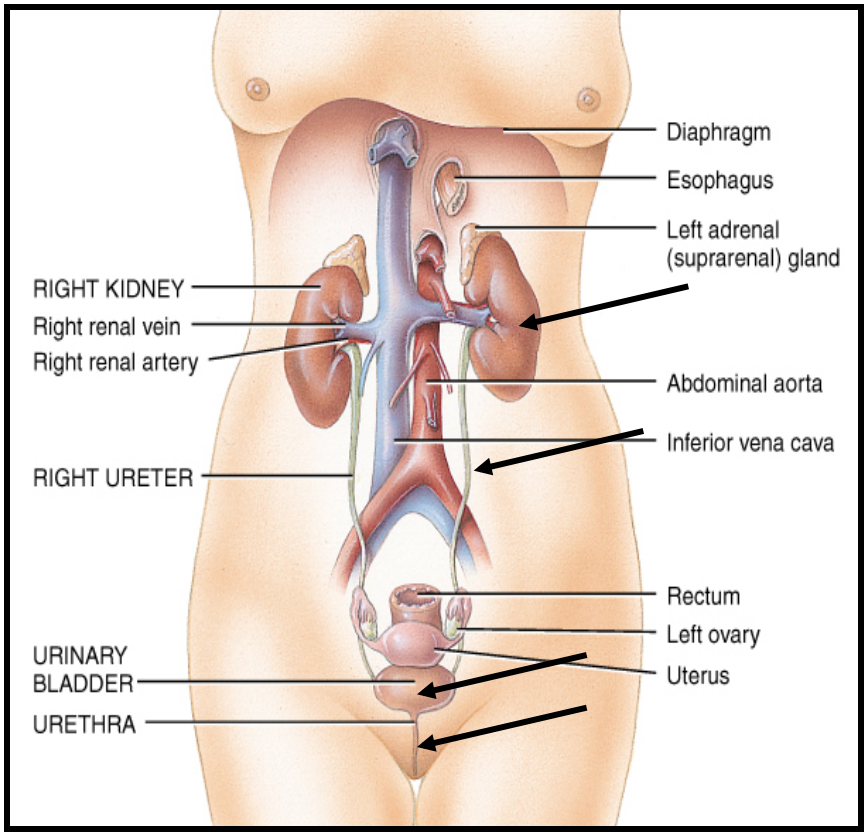
URINARY SYSTEM

- The urinary system consists of:
  - Two kidneys
  - Two ureters
  - Bladder
  - Urethra

The Urinary System

- Urine flows from each kidney, down its ureter to the bladder and to the outside via the urethra

- Filter the blood and return most of water and solutes to the bloodstream



Overview of Kidney Functions

1) Regulation of blood ionic composition
   - Na+, K+, Ca+2, Cl- and phosphate ions

2) Regulation of blood pH, osmolarity & glucose

3) Regulation of blood volume
   - conserving or eliminating water

4) Regulation of blood pressure
   - secreting the enzyme renin
   - adjusting renal resistance

5) Release of erythropoietin & calcitriol

6) Excretion of wastes & foreign substances

The Kidney

More about their functions

Excretion: 1L of urine is produced and excreted per day

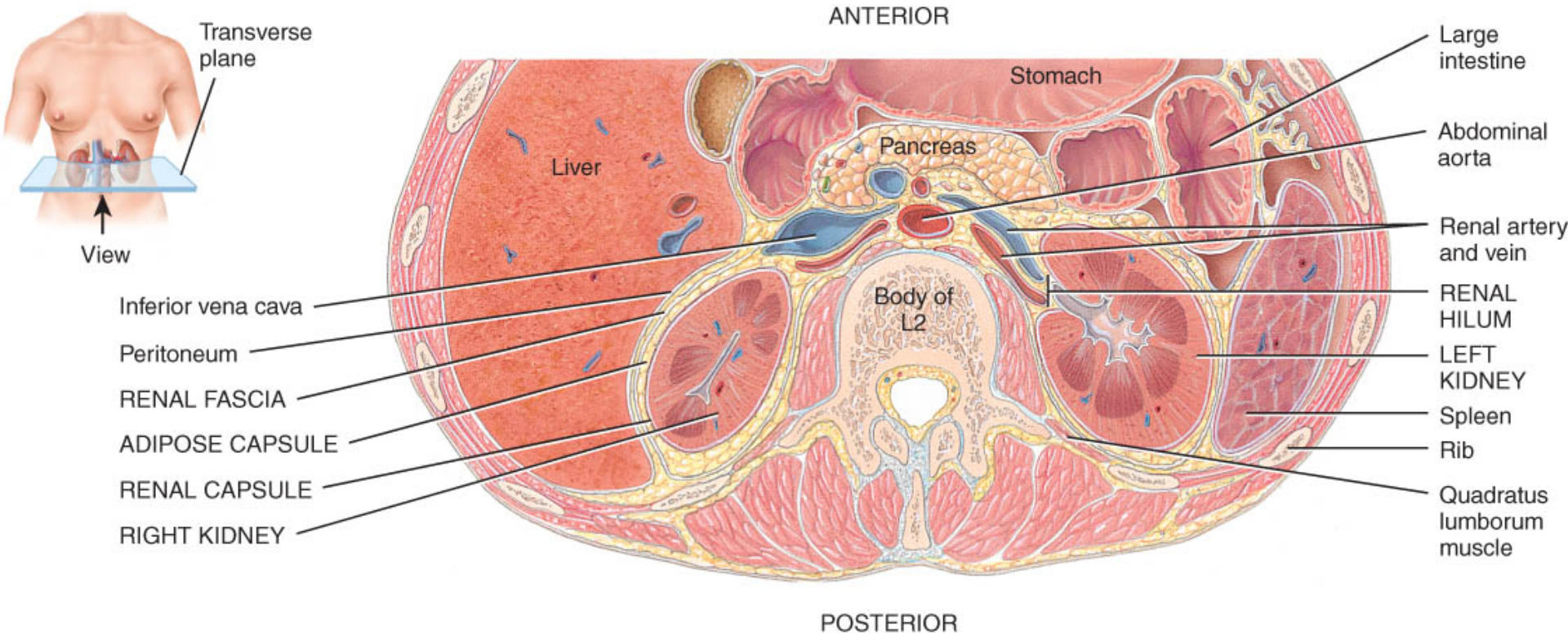
Filtration: Kidneys are vital for filtering and cleaning the blood

total renal blood flow is 1800 L/day
The kidney filters approximately 180 L/day and reabsorbs 99% of plasma ultrafiltrate

Regulatory mechanisms: regulates blood pressure, synthesizes and secretes hormones (renin, erythrpoietin)

Nephrons: the functional unit of the kidney
There are ~ one million nephrons per kidney

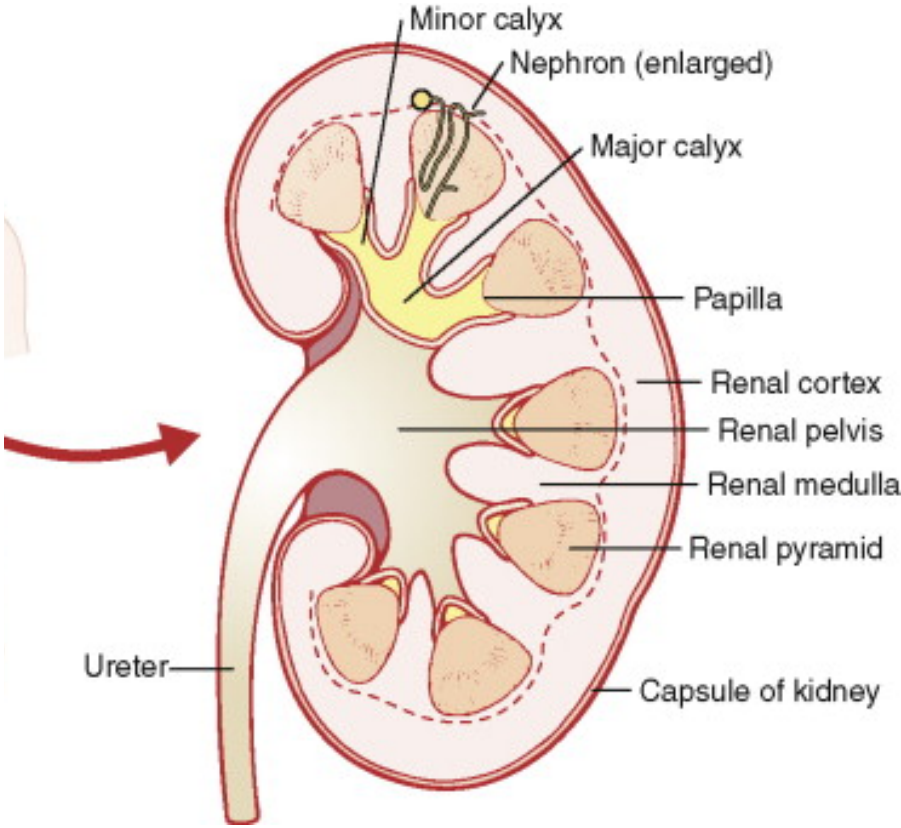
External Anatomy of Kidney



- Blood vessels & ureter enter hilus of kidney
- Renal capsule = transparent membrane maintains organ shape
- Adipose capsule that helps protect from trauma
- Renal fascia = dense, irregular connective tissue that holds against back body wall

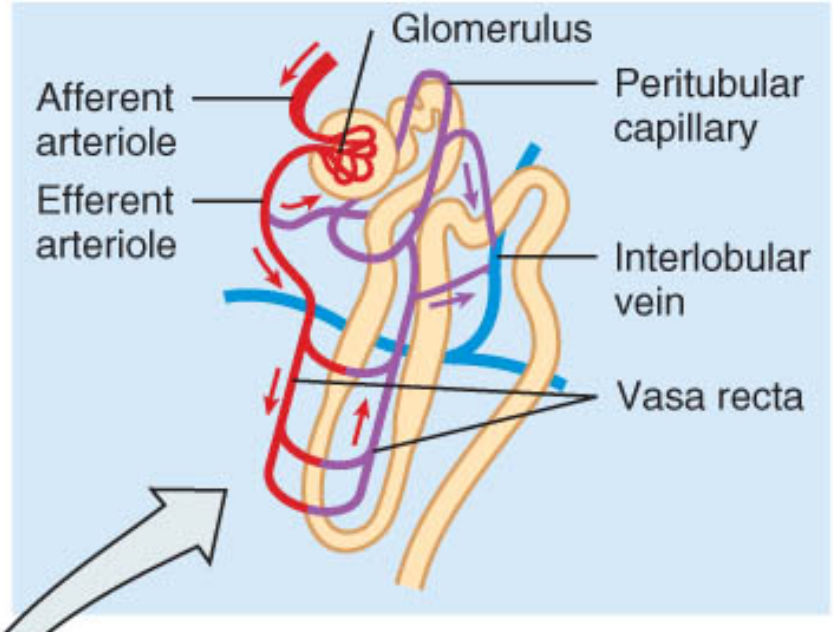
Internal Anatomy of the Kidneys

- Parenchyma of kidney
  1) renal cortex = superficial layer of kidney
  2) renal medulla
     - inner portion consisting of 8-18 cone-shaped renal pyramids separated by renal columns
     - renal papilla point toward center of kidney
- Drainage system fills renal sinus cavity
  - cuplike structure (minor calyces) collect urine from the papillary ducts of the papilla
  - minor & major calyces empty into the renal pelvis which empties into the ureter

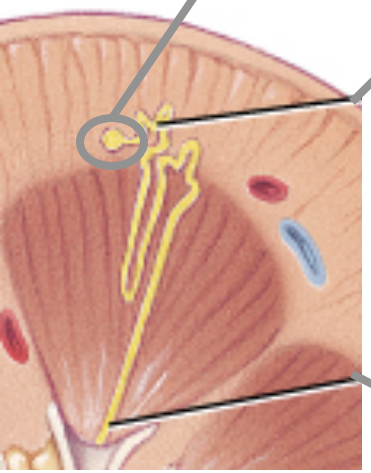


NEPHRON

- The nephron is the basic structural and functional unit of the kidney.
- Each kidney has more than one million nephrons.
- Composed of 2 parts: corpuscle and tubule.

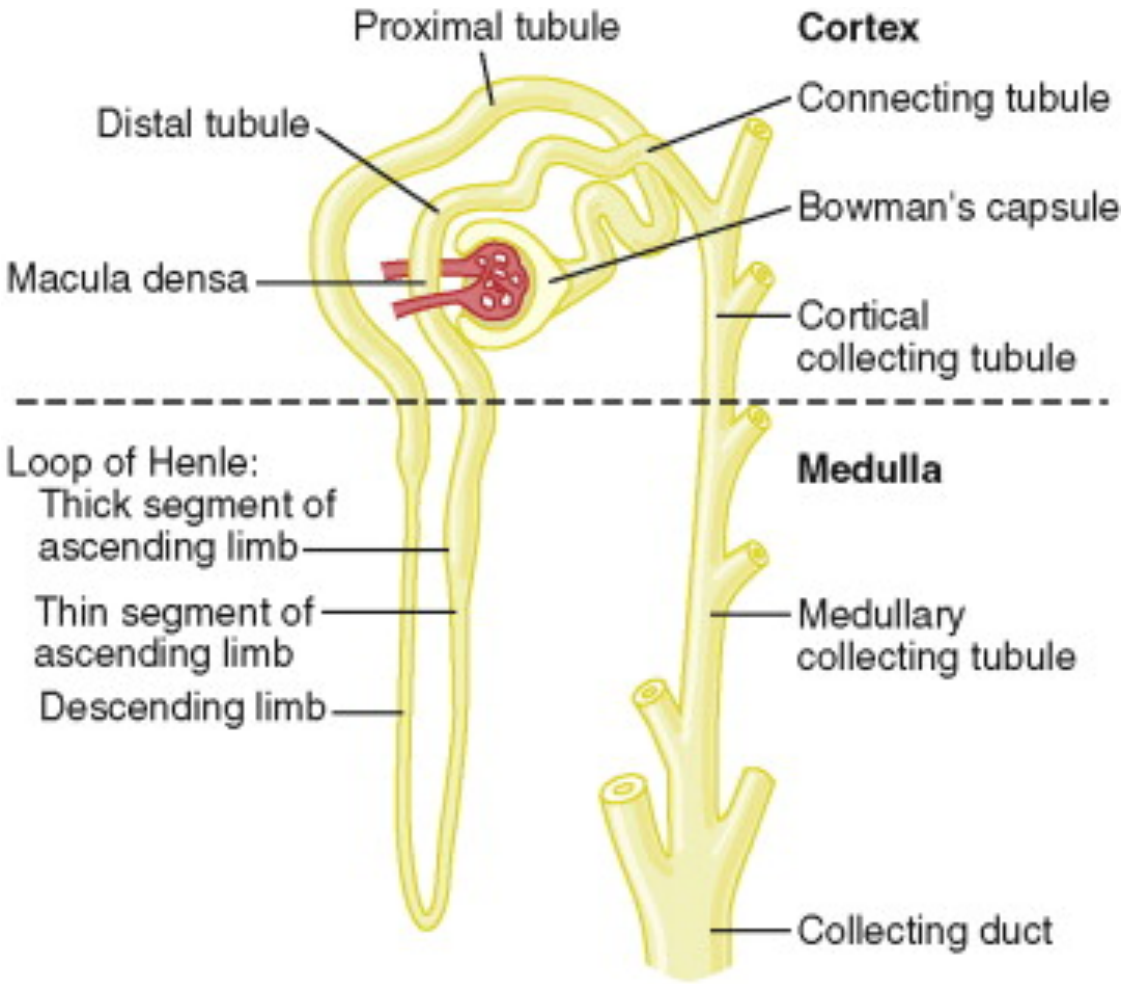


The Nephron



- Kidney has over 1 million nephrons composed of a corpuscle and tubule
- Renal corpuscle = site of plasma filtration
  - glomerulus is a capillary bed where filtration occurs
  - glomerular (Bowman's) capsule is double-walled epithelial cup that collects filtrate
- Renal tubule
  - proximal convoluted tubule
  - loop of Henle dips down into medulla
  - distal convoluted tubule
- Collecting ducts and papillary ducts drain urine to the renal pelvis and ureter. The distal convoluted tubules of several nephrons empty into a single collecting duct and many collecting ducts drain into a small number of papillary ducts.

Basic Segments of the Nephron



Two Types of Nephrons

Cortical Nephrons: This represents 80-85% of all nephrons

The renal corpuscles of cortical nephrons are in the outer portion of the renal cortex

Loops of Henle are short

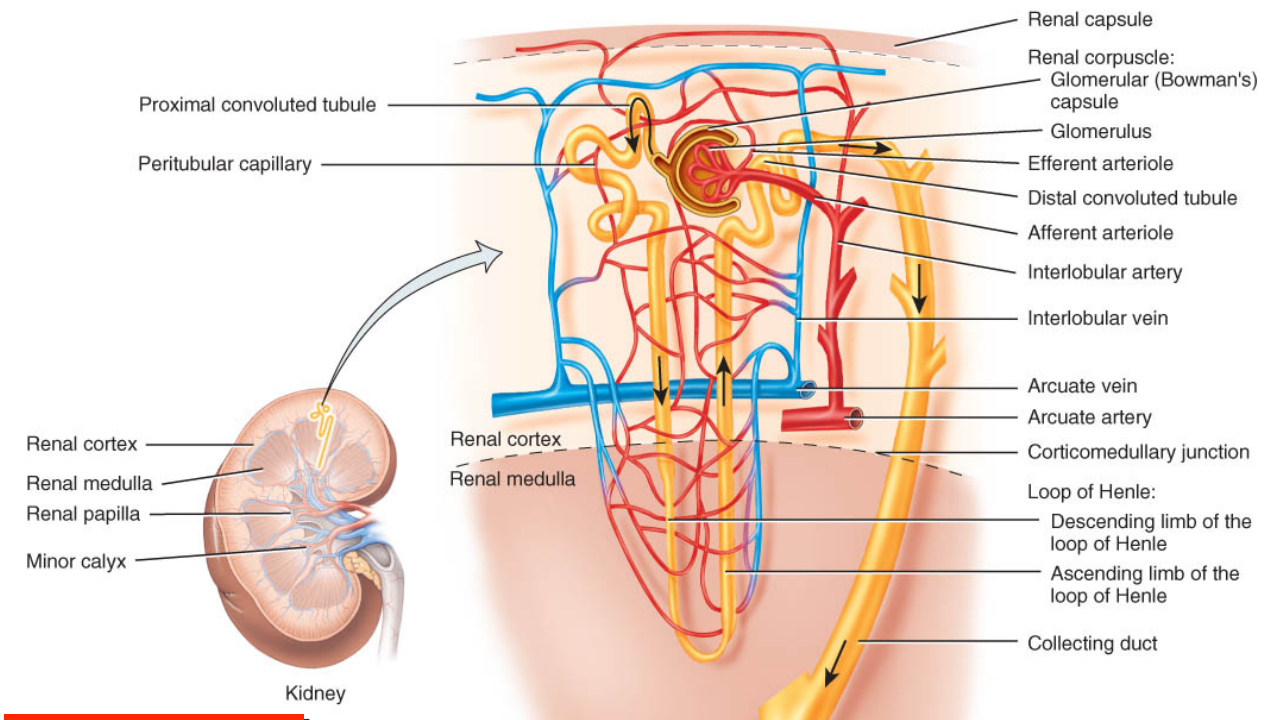
Lie mainly in the cortex and penetrate only into outer region of the renal medulla

Juxtamedullary nephrons: 15-20% of nephrons

lie deep in the renal cortex near the medulla

Responsible for creating medullary concentration gradient that allows the kidney to change dilution of urine

Cortical Nephron

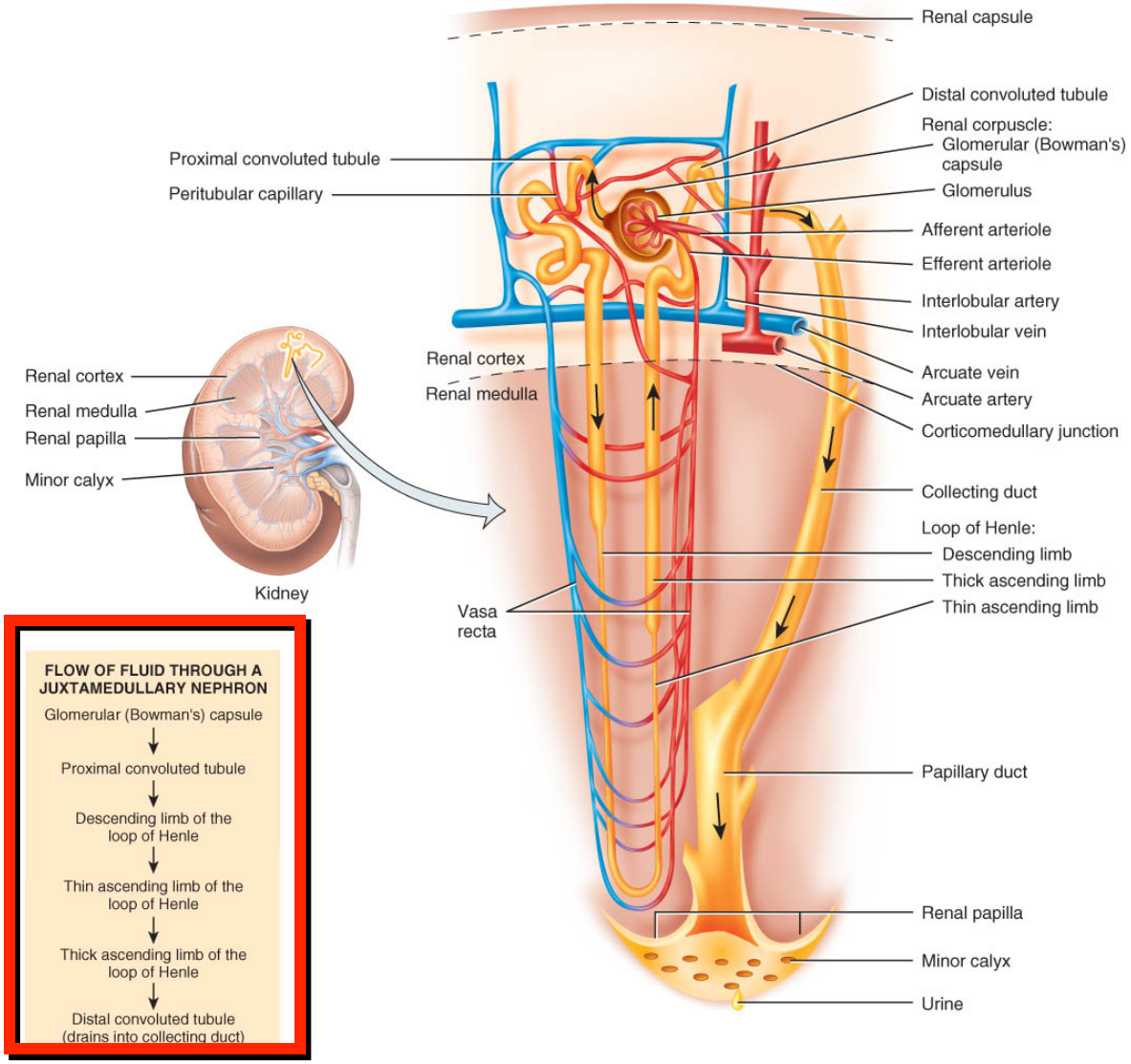


FLOW OF FLUID THROUGH A CORTICAL NEPHRON

Glomerular (Bowman's) capsule
↓
Proximal convoluted tubule
↓
Descending limb of the loop of Henle
↓
Ascending limb of the loop of Henle
↓
Distal convoluted tubule (drains into collecting duct)

- 80-85% of nephrons are cortical nephrons
- Renal corpuscles are in outer cortex and loops of Henle lie mainly in cortex

Juxtamedullary Nephron



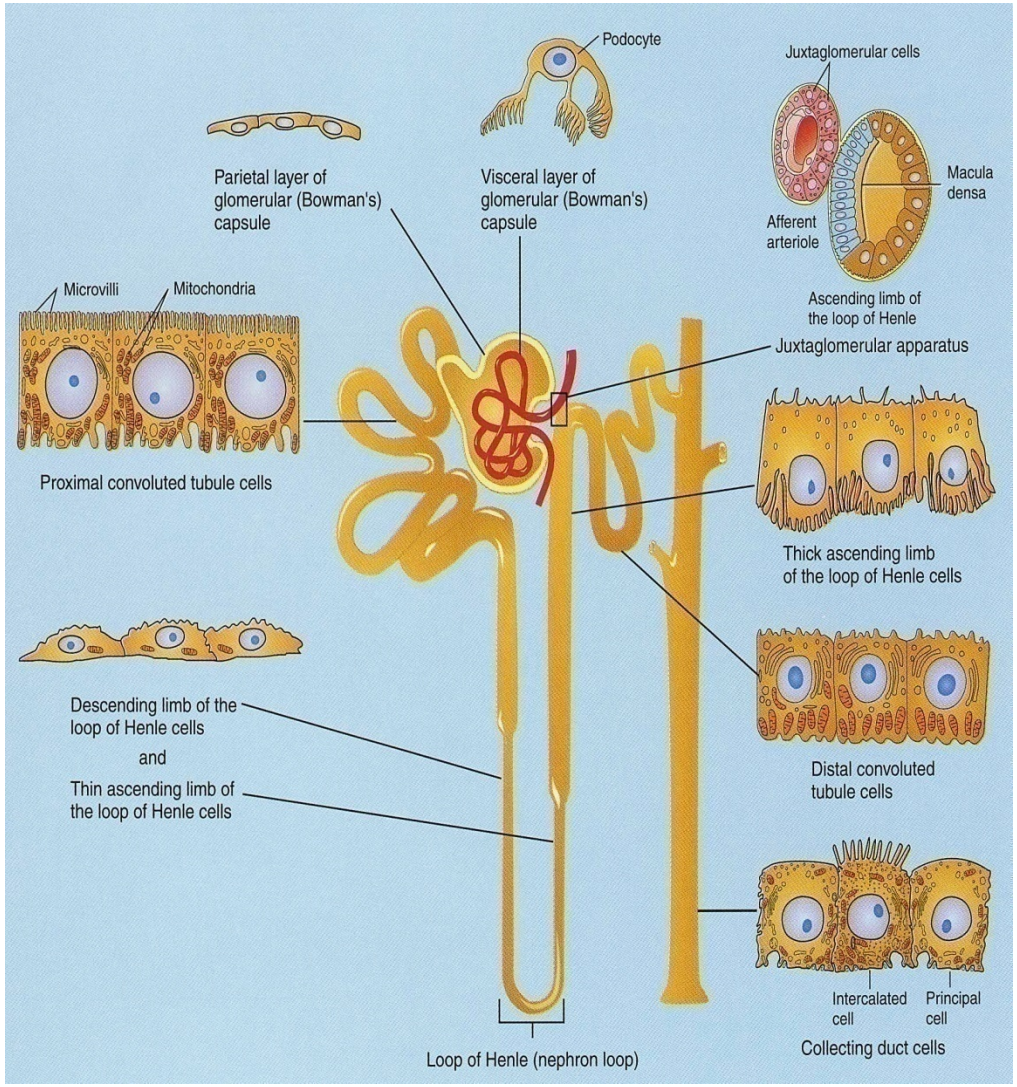
- 15-20% of nephrons are juxtamedullary nephrons
- Renal corpuscles close to medulla and long loops of Henle extend into deepest medulla enabling excretion of dilute or concentrated urine

Number of Nephrons

- Remains constant from birth
  - any increase in size of kidney is size increase of individual nephrons
- If injured, no replacement occurs
- Dysfunction is not evident until function declines by 25% of normal (other nephrons handle the extra work)
- Removal of one kidney causes enlargement of the remaining until it can filter at 80% of normal rate of 2 kidneys

Histology of the Nephron

- Single layer of epithelial cells forms walls of entire tube
- Distinctive features due to function of each region
  - microvilli
  - cuboidal versus simple squamous
  - hormone receptors



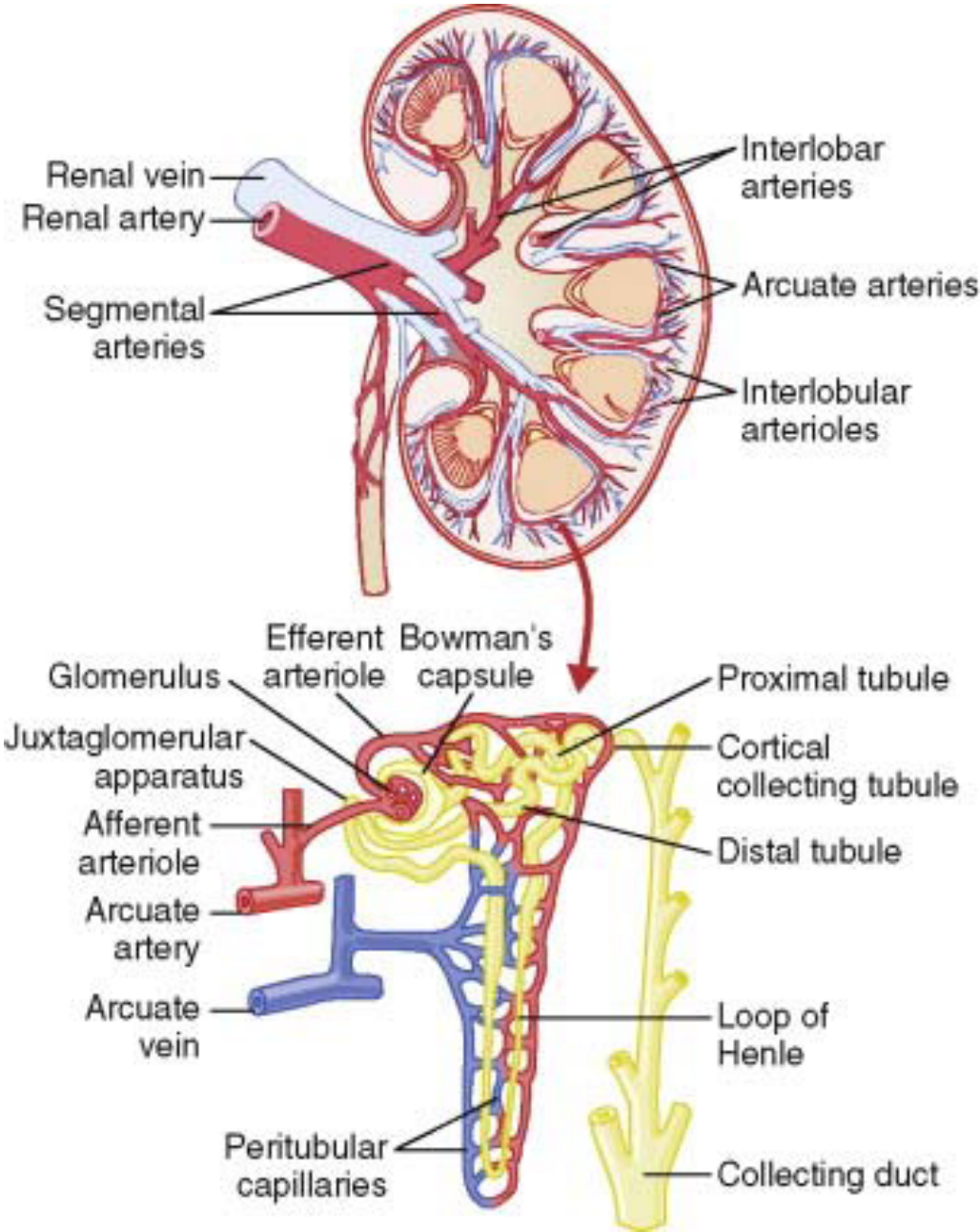
Kidney Blood Supply

Approximately 25% of cardiac output goes through the kidney

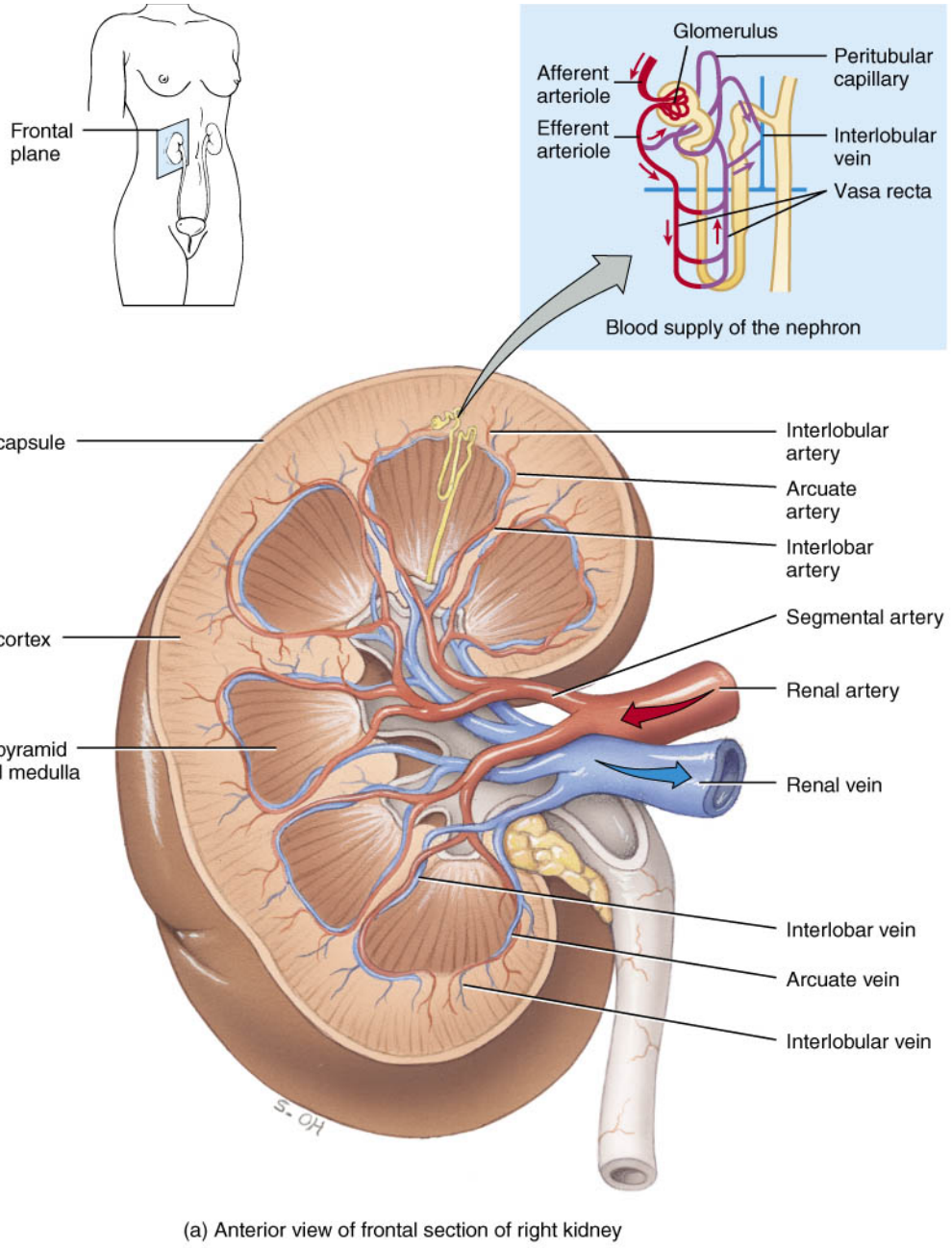
Renal circulation is unique. It has two capillary beds, the **glomerular** and **peritubular** capillaries,

Glomerular capillaries-60 mm Hg

Peritubular capillaries-13 mm Hg



25 % of resting cardiac output flows into the kidneys per minute!



(a) Anterior view of frontal section of right kidney

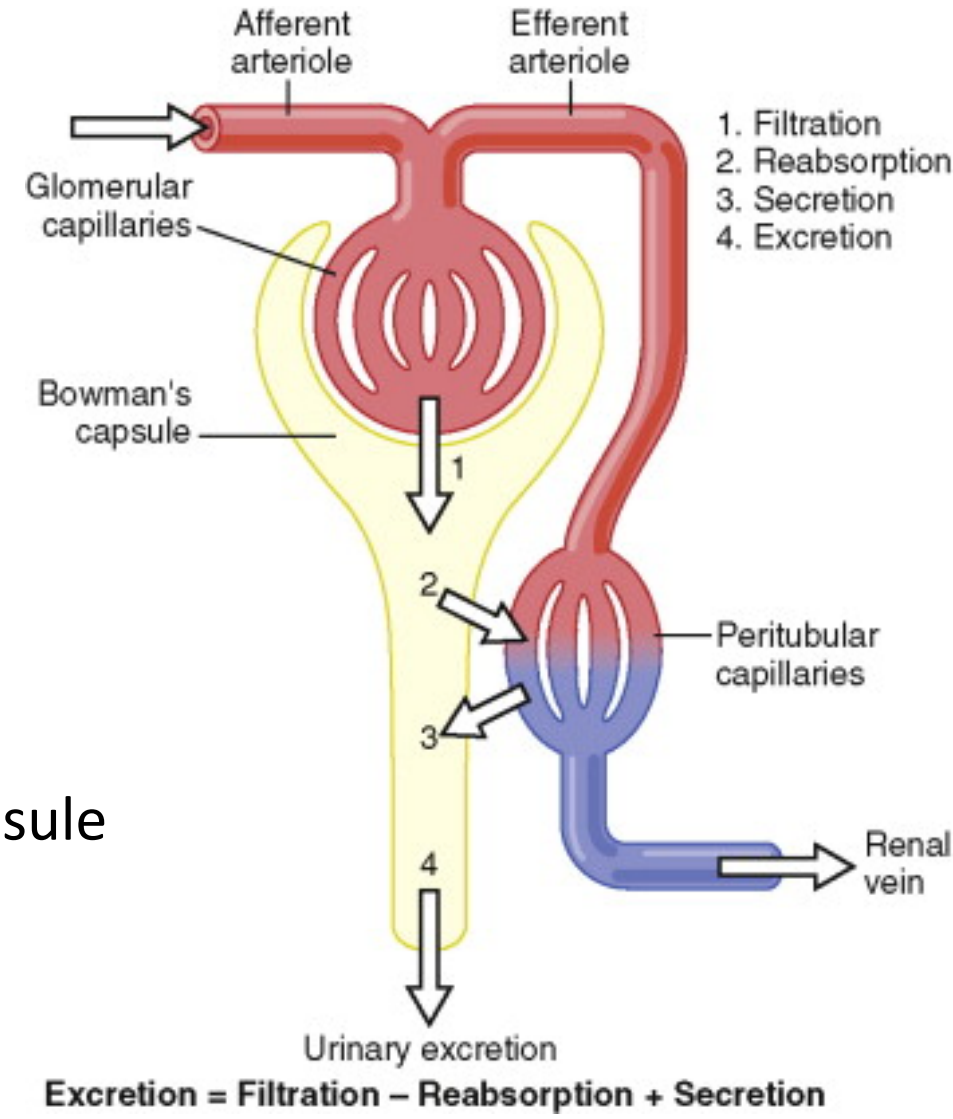
Renal artery
Segmental arteries
Interlobar arteries
Arcuate arteries
Interlobular arteries
Afferent arterioles
Glomerular capillaries
Efferent arterioles
Peritubular capillaries and/or vasa recta
Interlobular veins
Arcuate veins
Interlobar veins
Segmental veins
Renal vein

Blood Supply of the Right Kidney

Basic Kidney Processes

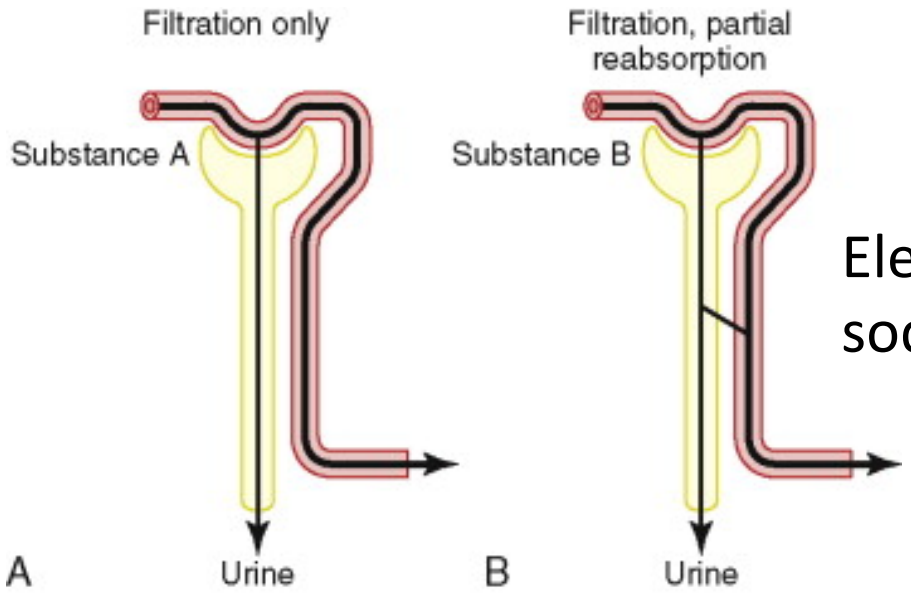
The kidney carries out three basic processes. The sum of these processes determines the rate of excretion

With the exception of proteins, most substances in the plasma are filtered and enter the Bowman's capsule



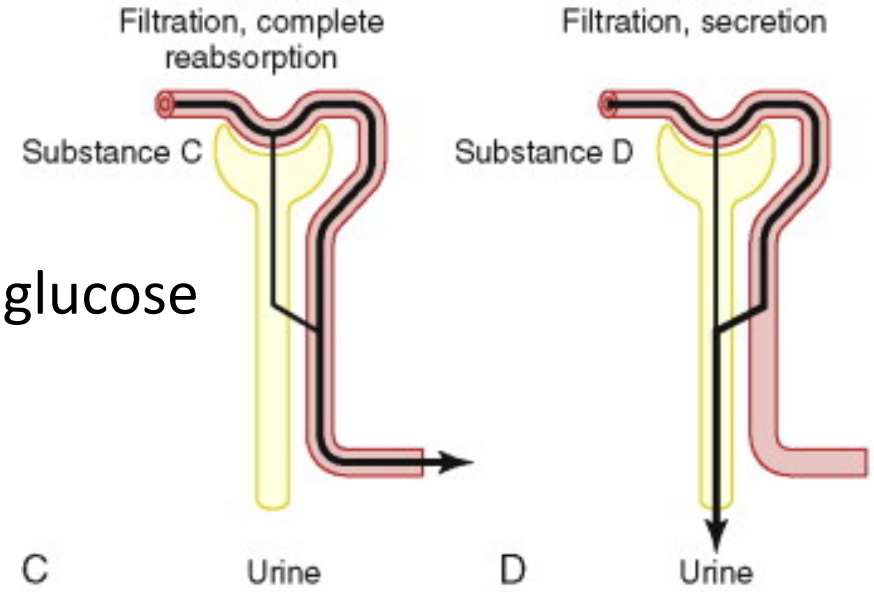
Renal Handling of Substances

Creatine waste



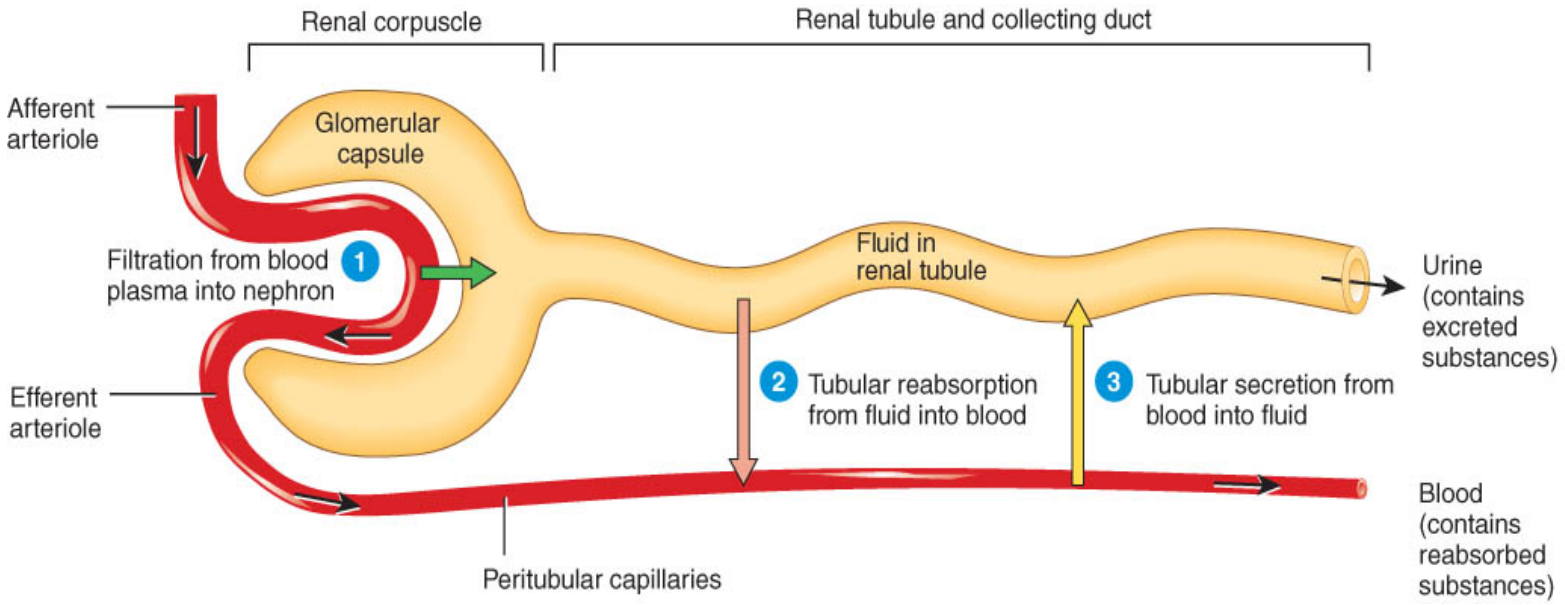
Electrolytes such as sodium and chloride

Amino acids and glucose

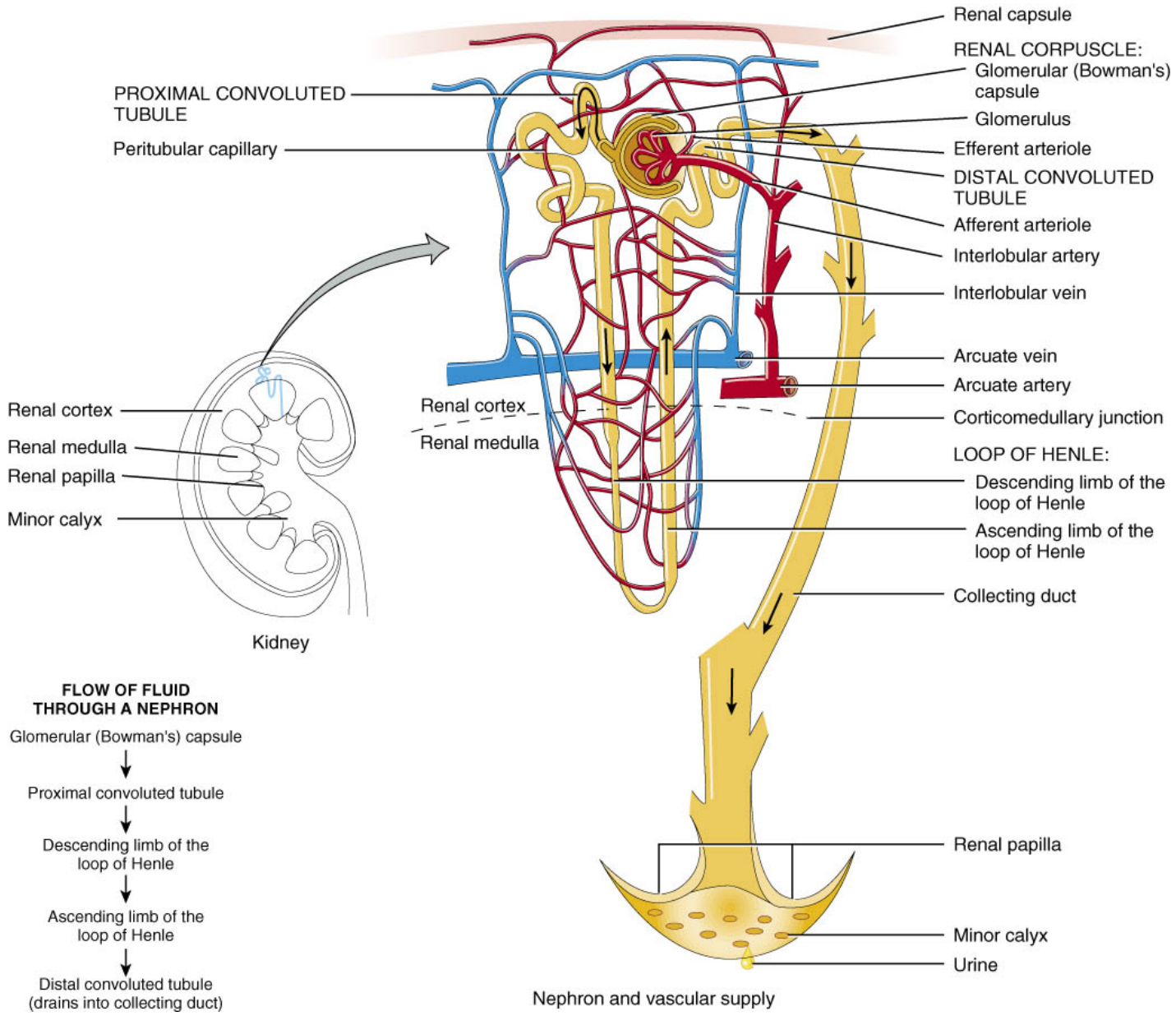


Organic acids and bases

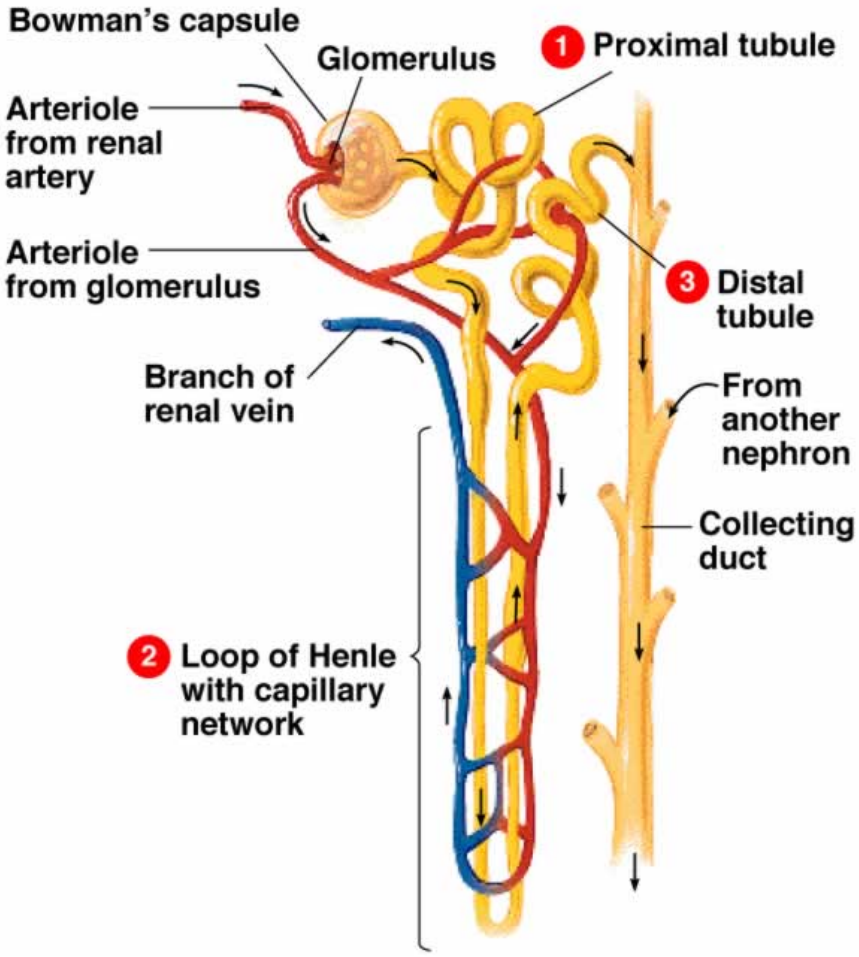
Blood Vessels around the Nephron

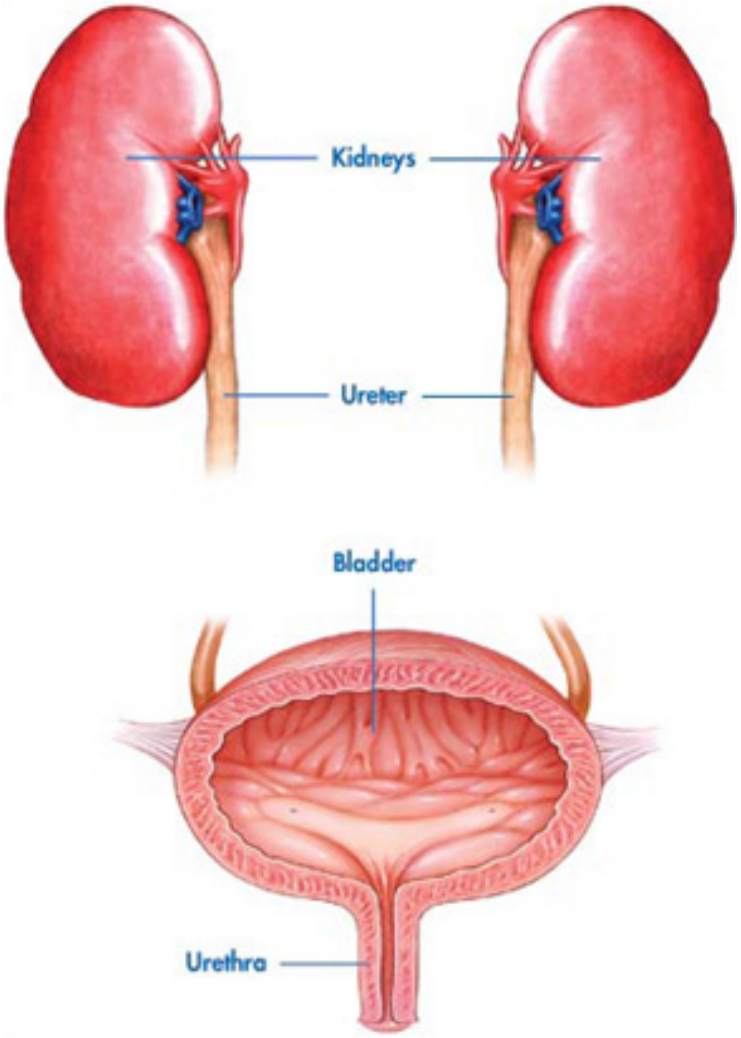


- Glomerular capillaries are formed between the afferent & efferent arterioles
- Efferent arterioles give rise to the peritubular capillaries and vasa recta



The Parts of a Nephron, Collecting Duct, and Associated Blood Vessels


Bowman's capsule
Glomerulus
1 Proximal tubule
Arteriole from renal artery
Arteriole from glomerulus
3 Distal tubule
Branch of renal vein
From another nephron
Collecting duct
2 Loop of Henle with capillary network


Kidneys
Ureter
Bladder
Urethra

Renal Corpuscle

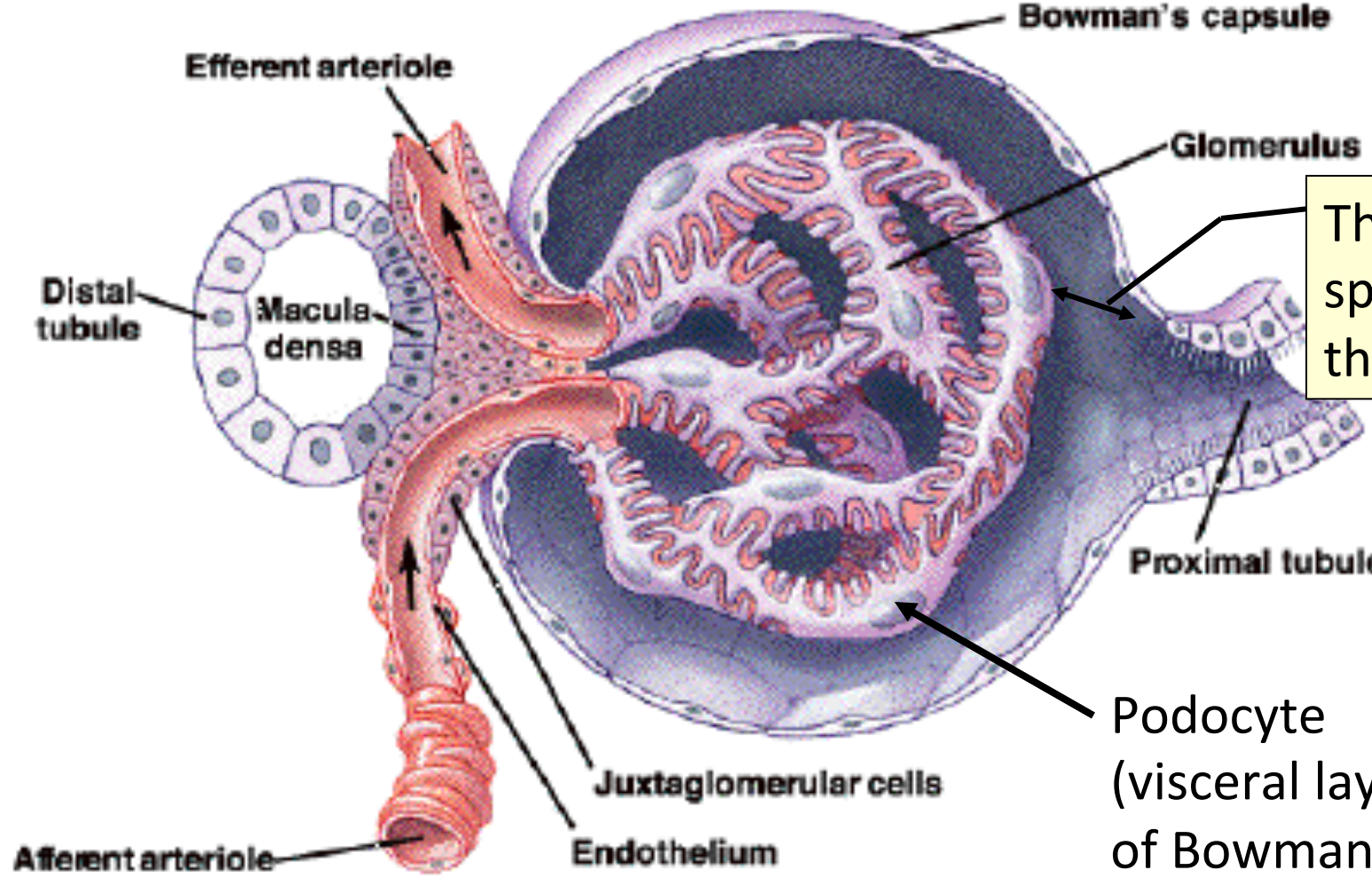
The first part of the nephron

The afferent arteriole leads to the **glomerulus**, which is a specialized capillary bed

Filtration: The hydrostatic force of the blood pressure pushes the fluid from the blood out into Bowman's capsule

Filtrate: The fluid pushed out consists of everything except blood cells and large proteins

Renal Corpuscle



The capsular space contains the filtrate

Podocyte (visceral layer of Bowman's capsule)

Glomerulus

The primary filtering device of the nephron

Blood is transported into the Bowman's capsule from the afferent arteriole

Within the capsule, the blood is filtered through the glomerulus and then passes out via the efferent arteriole.

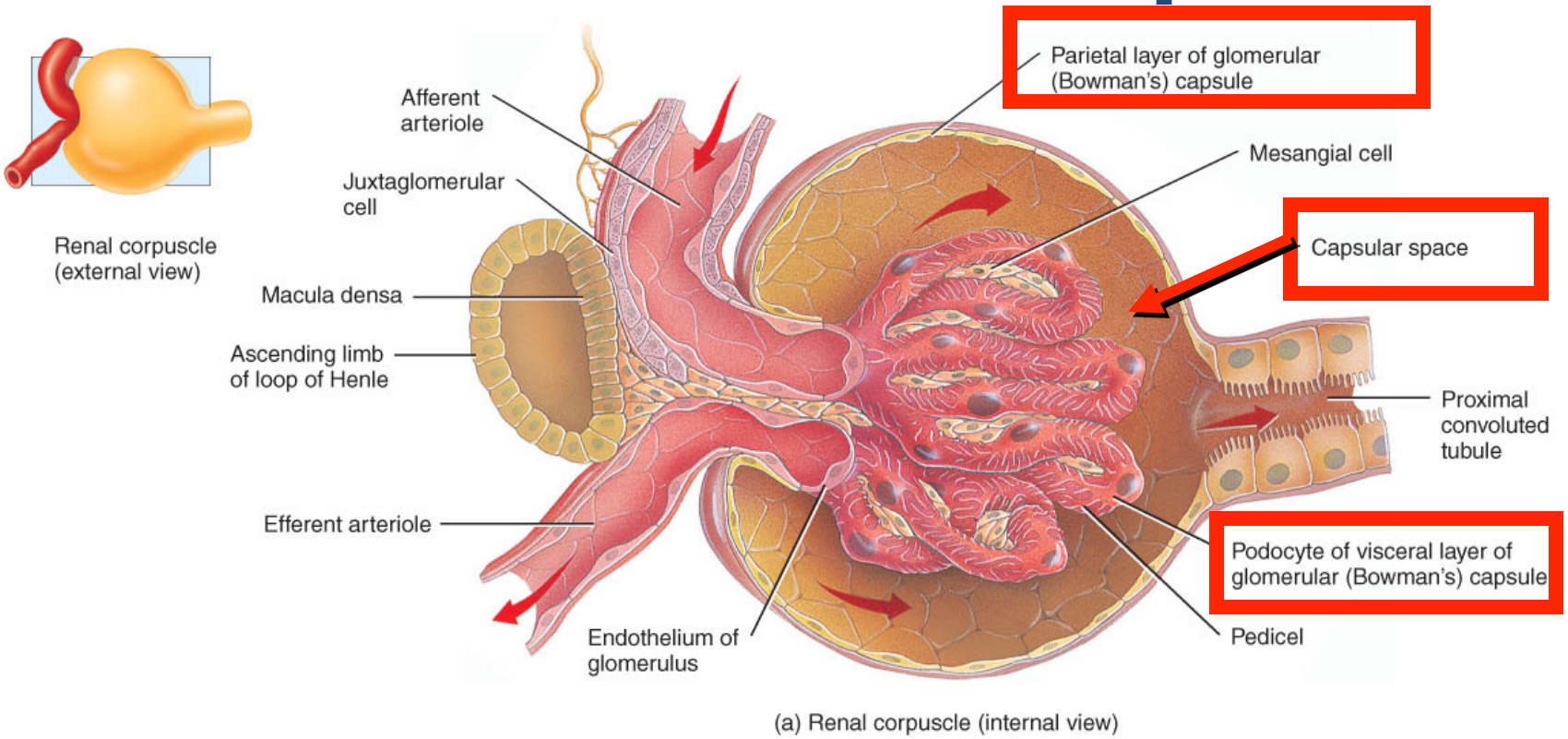
Filtered water and aqueous wastes are passed out of the Bowman's capsule into the proximal convoluted tubule

Histology of the Capsule

- Glomerular Capsule
  - The *glomerular capsule* consists of visceral and parietal layers (Figure 26.6).
  - The visceral layer consists of modified simple squamous epithelial cells called *podocytes*.
  - The parietal layer consists of simple squamous epithelium and forms the outer wall of the capsule.

- Fluid filtered from the glomerular capillaries enters the *capsular space*, the space between the two layers of the glomerular capsule.

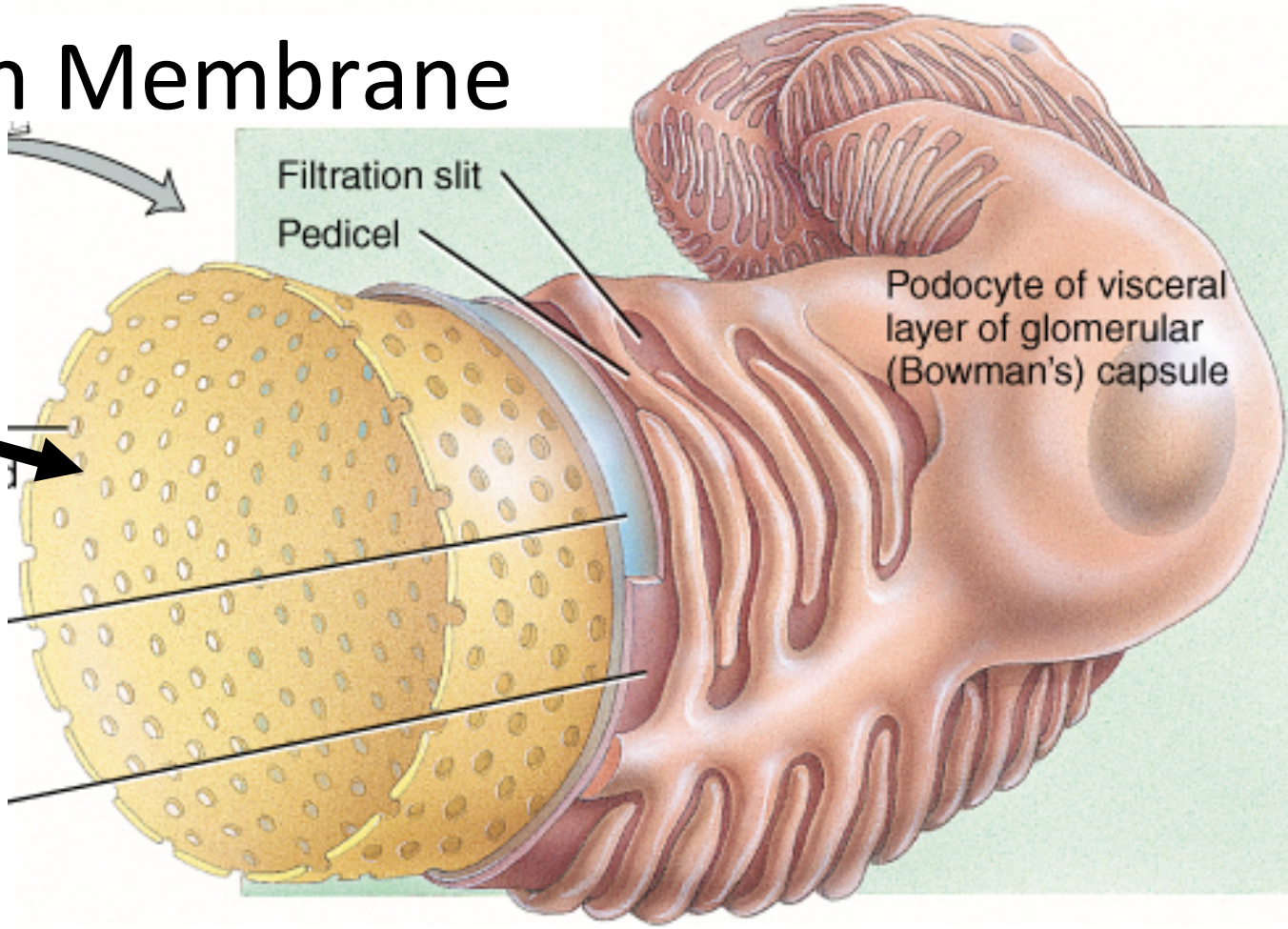
Structure of Renal Corpuscle



- Bowman's capsule surrounds capsular space
  - podocytes cover capillaries to form visceral layer
  - simple squamous cells form parietal layer of capsule
- Glomerular capillaries arise from afferent arteriole & form a ball before emptying into efferent arteriole

Filtration Membrane

Fenestrations: holes in the capillary endothelium



Podocyte

Filters all cells and platelets

Filters large and medium-sized proteins, but not small ones

Glomerular Capillary Membrane

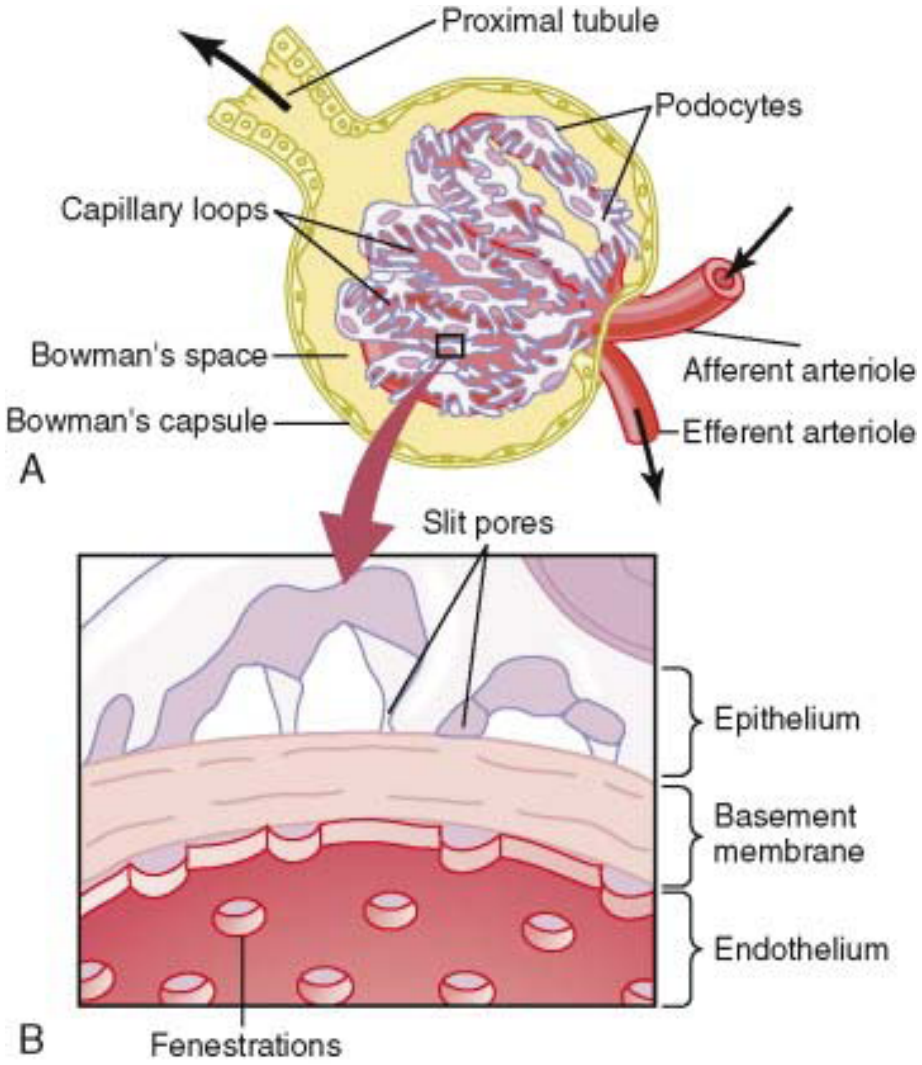
Has three major layers

These make up the filtration barrier

Allows passage of several hundred fold more water than typical capillary

Filtration is mediated by fenestrations

Negative charges block passage of proteins

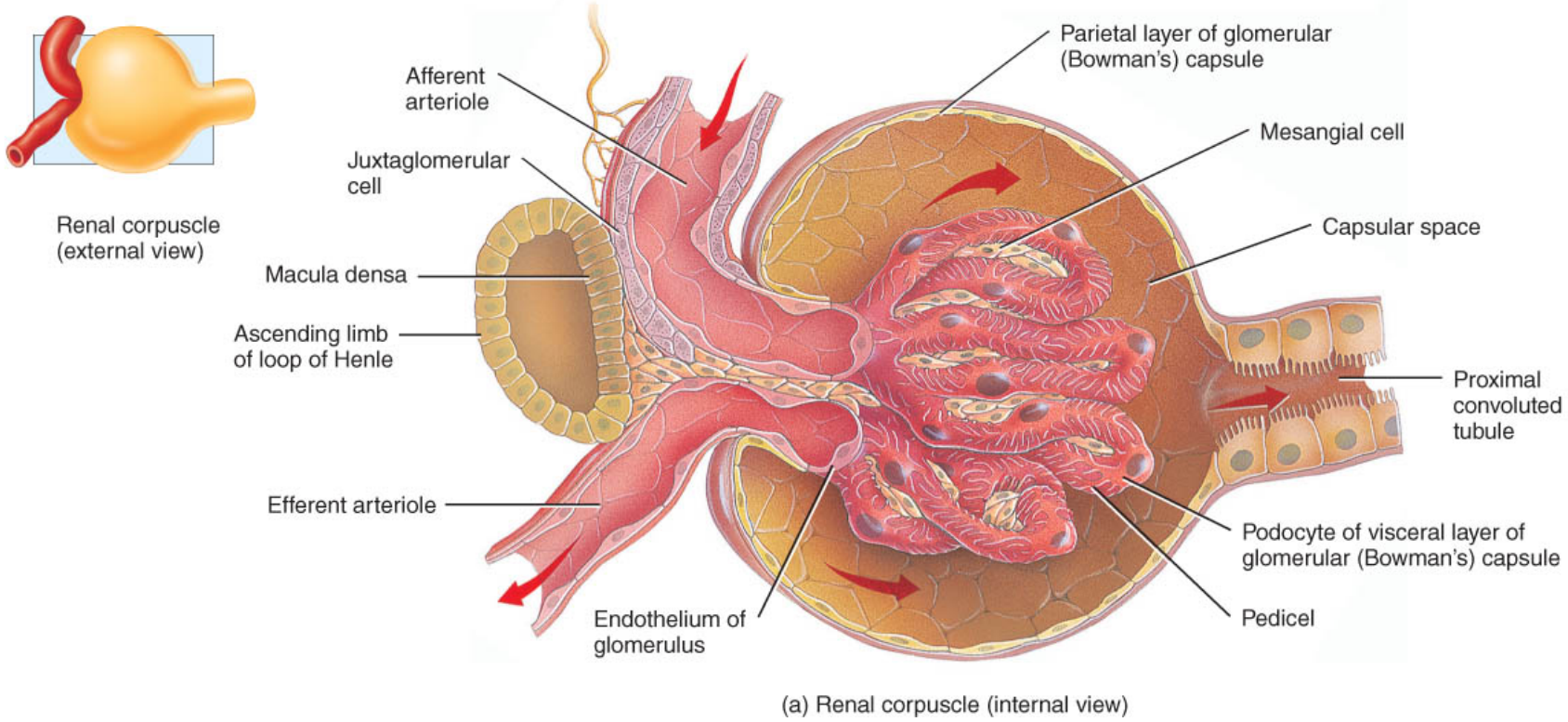


Special Cells of the Renal Tubule

- The *juxtaglomerular apparatus* (*JGA*) consists of the *juxtaglomerular cells* of an afferent arteriole and the *macula densa*. The JGA helps regulate blood pressure and the rate of blood filtration by the kidneys

- Most of the cells of the distal convoluted tubule are *principal cells* that have receptors for ADH and aldosterone. A smaller number are *intercalated cells* which play a role in the homeostasis of blood pH.

Juxtaglomerular Apparatus

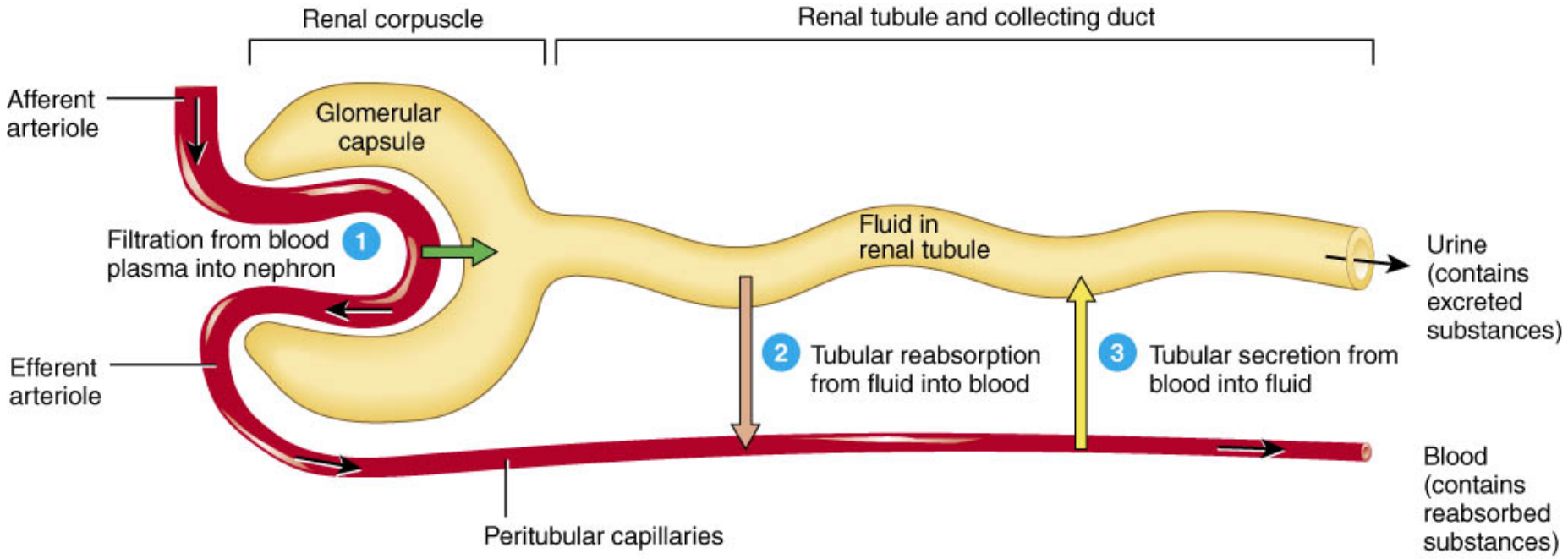


- Structure where afferent arteriole makes contact with ascending limb of loop of Henle
  - macula densa is thickened part of ascending limb
  - juxtaglomerular cells are modified muscle cells in arteriole
  - Regulates blood pressure within the kidneys

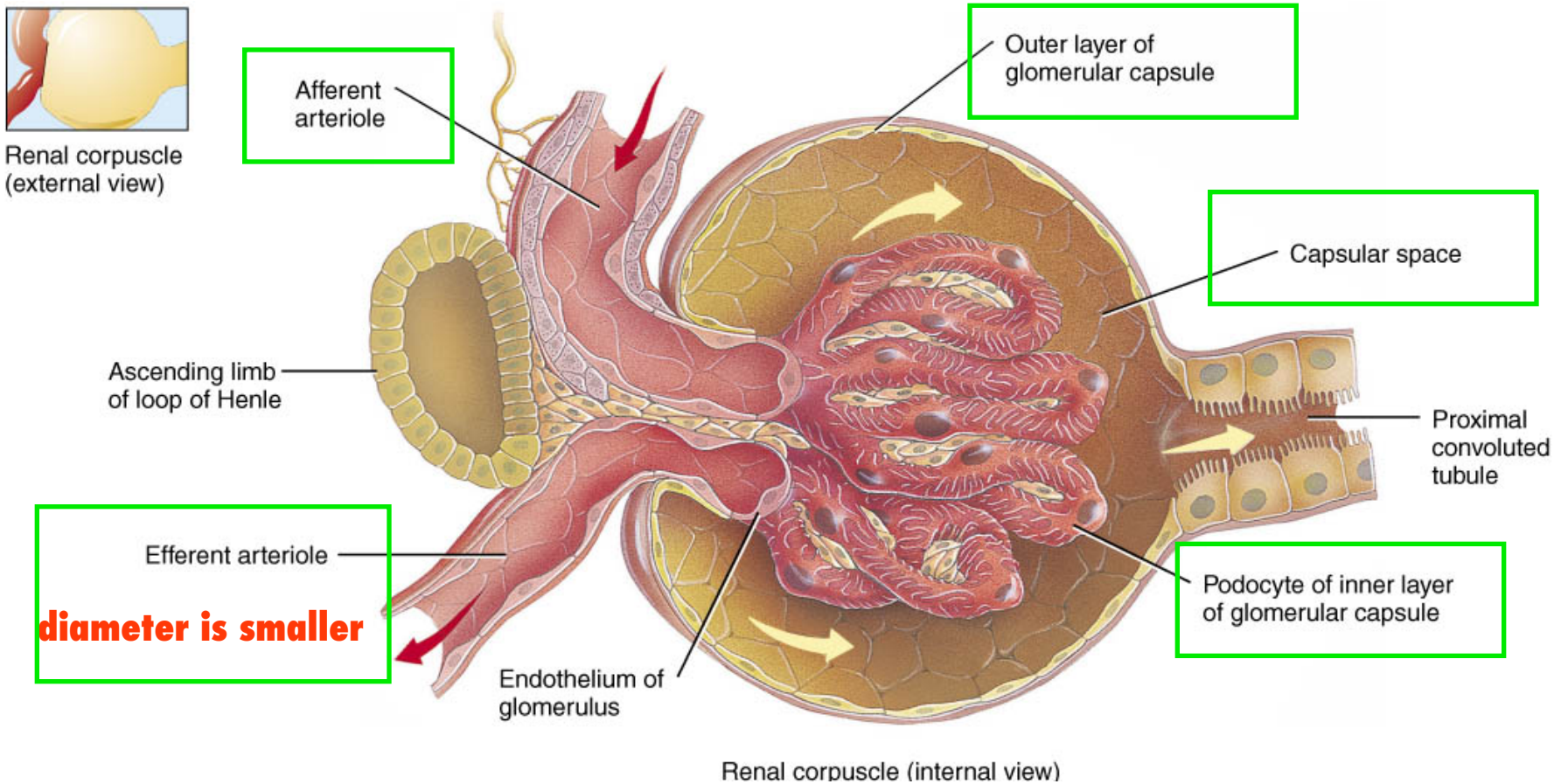
OVERVIEW OF RENAL PHYSIOLOGY

- 3 processes of urine formation

1) Filtration by the glomerulus
2) Tubular Reabsorption (from filtrate into blood)
3) Tubular Secretion (from blood into filtrate)



Overview of Functions of a Nephron



•The fluid that enters the capsular space is termed *glomerular filtrate*.

•The fraction of plasma in the afferent arterioles of the kidneys that becomes filtrate is termed the *filtration fraction*)

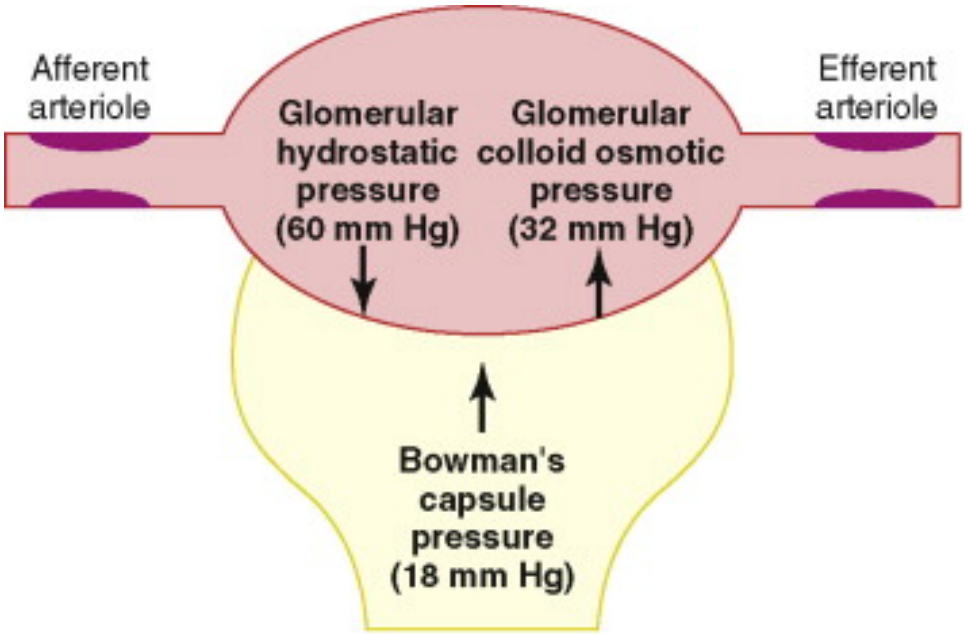
Glomerular Filtration, the First Step in Urine Formation

Summary of Forces Causing Glomerular Filtration

Changes in glomerular hydrostatic pressure serve as the primary means for physiologic regulation of GFR

This can be affected by

1. Arterial pressure
2. Afferent arteriolar resistance
3. Efferent arteriolar resistance



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)

Increased resistance of afferent arterioles reduces glomerular hydrostatic pressure and decreases the GFR. Conversely, **dilation of the afferent arterioles** increases both glomerular hydrostatic pressure and GFR. **Constriction of the efferent arterioles** increases the resistance to outflow from the glomerular capillaries. This mechanism raises glomerular hydrostatic pressure. As long as the increase in efferent resistance does not reduce renal blood flow too much, GFR increases slightly.

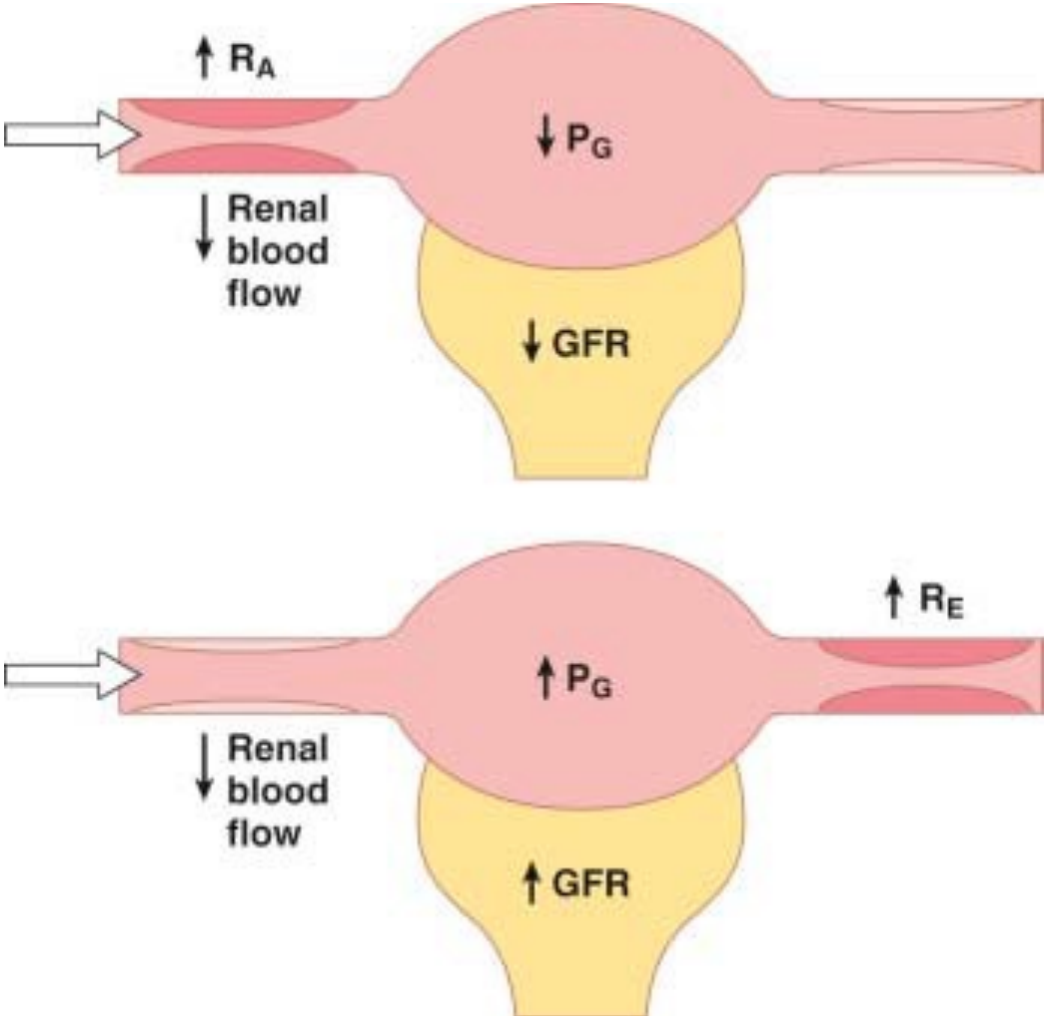
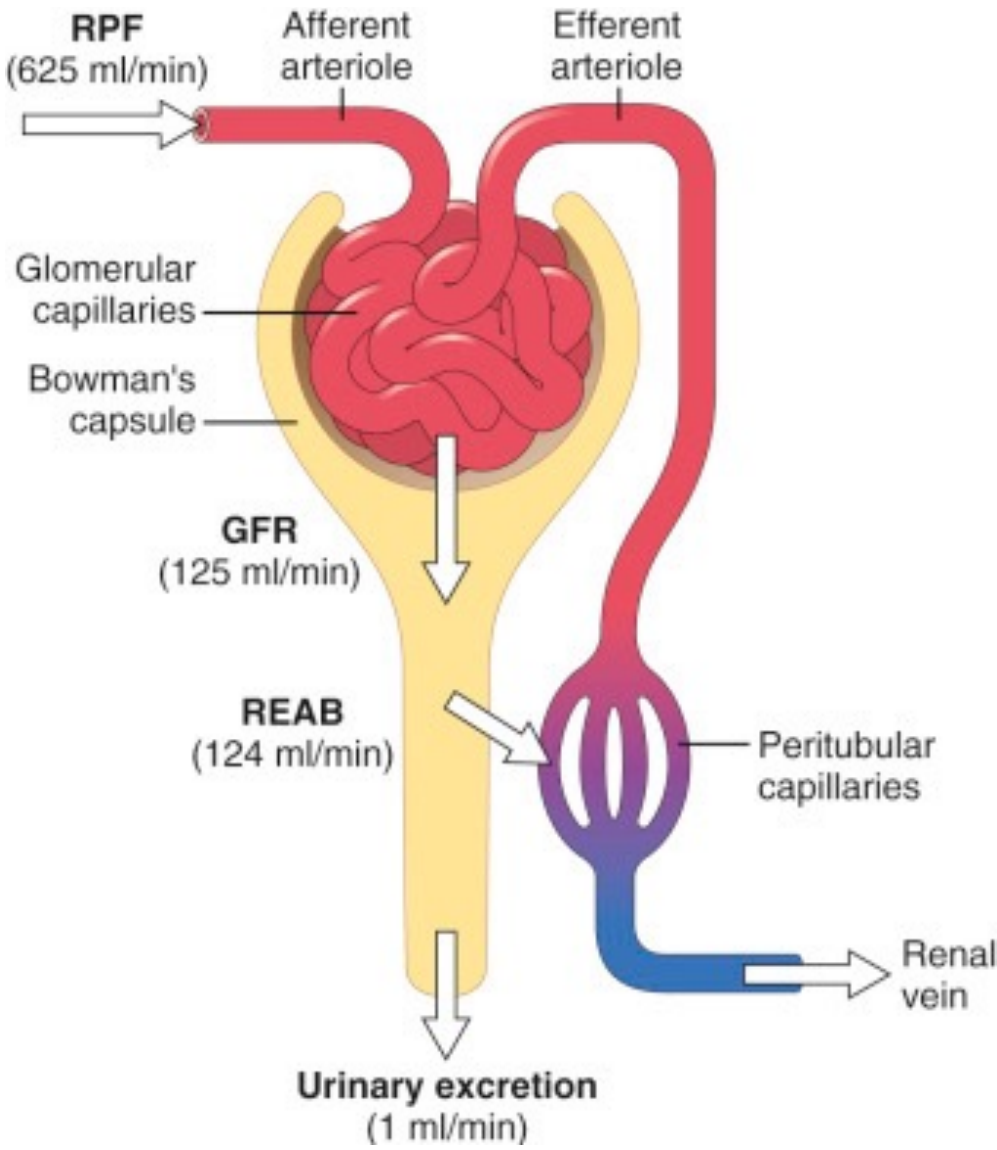


Figure 27-1 Average values for total **renal plasma flow** *(RPF)* , **glomerular filtration rate** *(GFR)* , **tubular reabsorption** *(REAB)* , and **urine flow rate**.

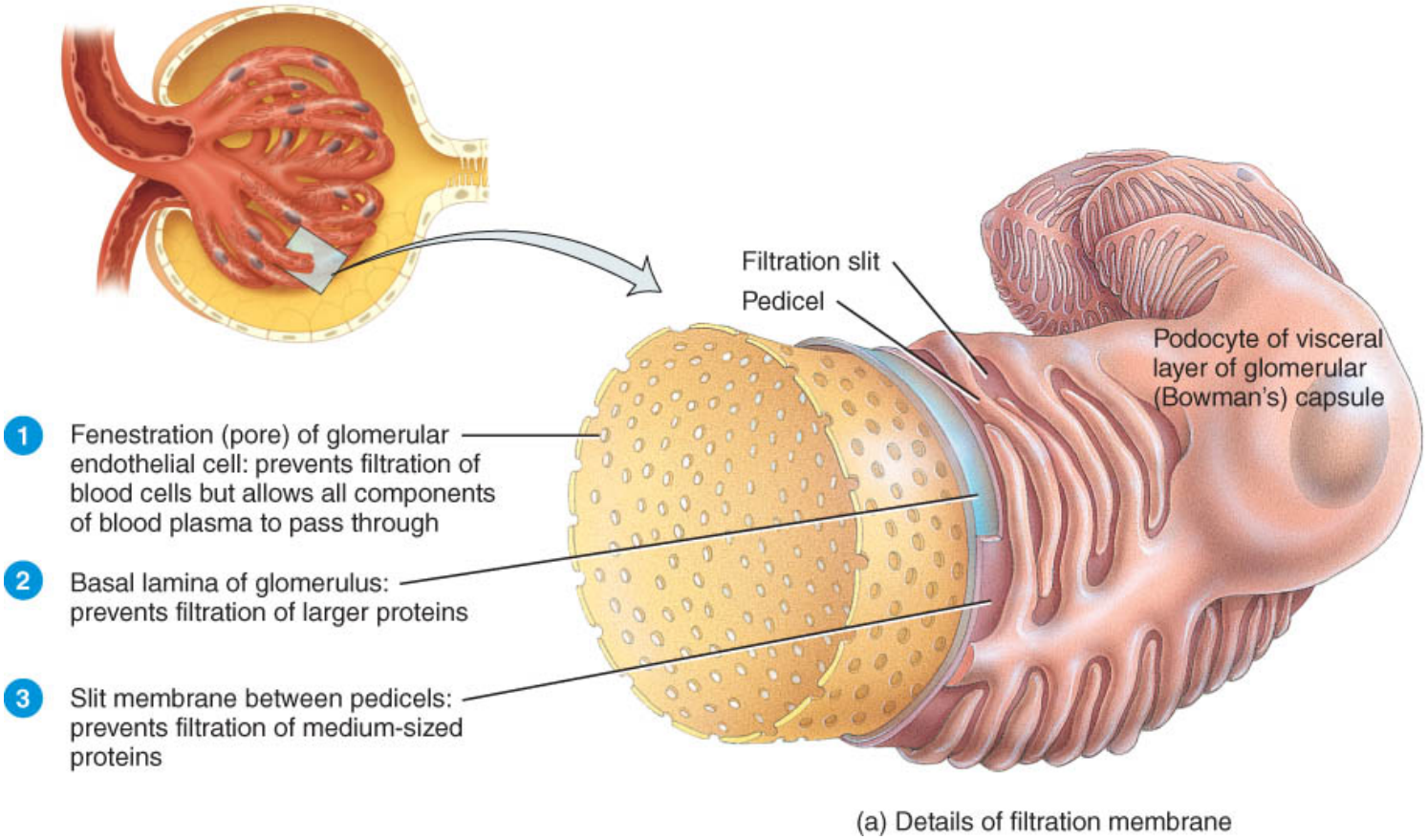
RPF is equal to renal blood flow × (1 – Hematocrit).

Note that GFR averages about 20% of the RPF, while urine flow rate is less than 1% of the GFR. Therefore, more than 99% of the fluid filtered is normally reabsorbed.

The filtration fraction is the GFR/ RPF.



Filtration Membrane



- #1 Stops all cells and platelets
- #2 Stops large plasma proteins
- #3 Stops medium-sized proteins, not small ones

Glomerular Filtration Rate

- Amount of filtrate formed in all renal corpuscles of both kidneys/ minute
  - average adult male rate is 125 mL/min; 105 mL/ min in females

- Homeostasis requires GFR that is constant
  - too high & useful substances are lost due to the speed of fluid passage through nephron
  - too low and sufficient waste products may not be removed from the body

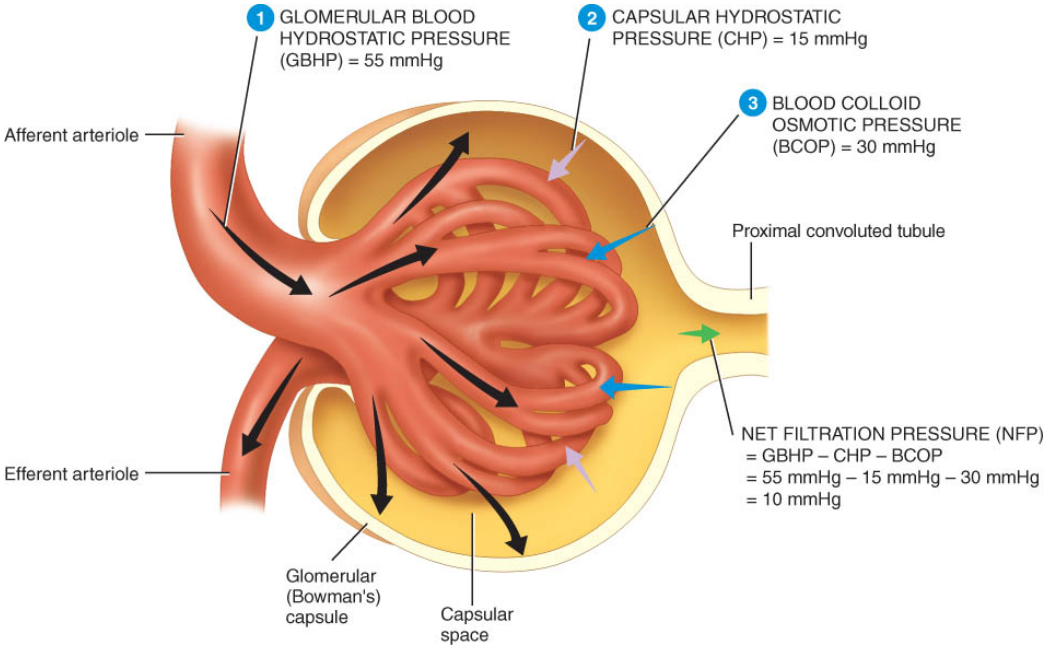
- Changes in net filtration pressure affects GFR
  - filtration stops if capillary hydrostatic pressure drops too much (severe hemorrhage=renal failure)

Net Filtration Pressure

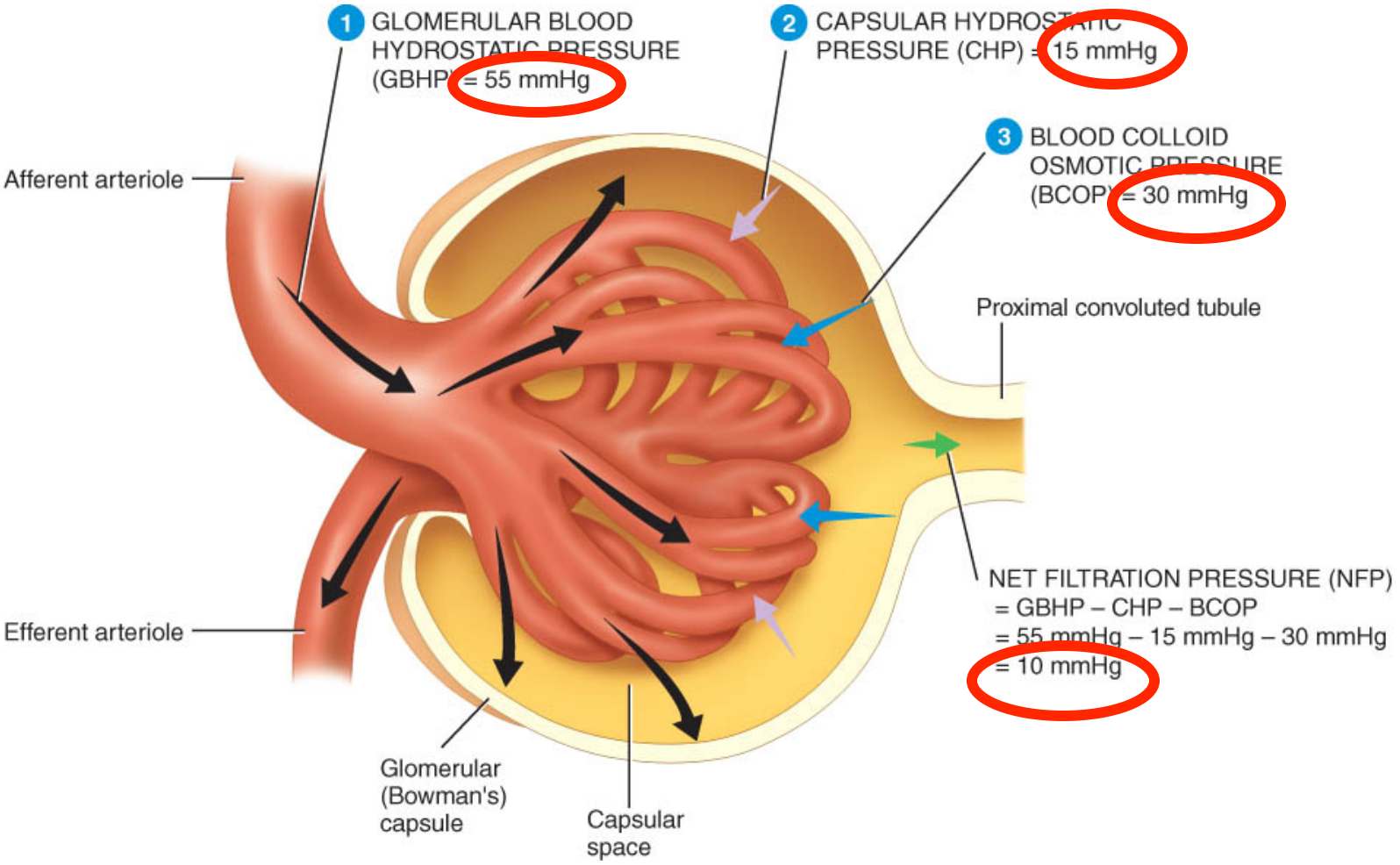
•Glomerular filtration depends on three main pressures, one that promotes and two that oppose filtration

•Filtration of blood is promoted by *glomerular blood hydrostatic pressure* (*BGHP*) and opposed by *capsular hydrostatic pressure* (*CHP*) and blood colloid osmotic pressure (*BCOP*).

•The *net filtration pressure* (*NFP*) is about 10 mm Hg.



Net Filtration Pressure



- NFP = total pressure that promotes filtration
- NFP = GBHP - (CHP + BCOP) = 10mm Hg

Regulation of GFR

- The mechanisms that regulate GFR: adjust blood flow into and out of the glomerulus and alter the glomerular capillary surface area available for filtration.
- The three principal mechanisms that control GFR are *renal autoregulation, neural regulation,* and *hormonal regulation.*

Regulation of GFR

Strong activation of the renal sympathetic nerves can constrict the renal arterioles and decrease renal blood flow and GFR.

Moderate or mild sympathetic stimulation has little influence on renal blood flow and GFR. In the healthy resting person, sympathetic tone appears to have little influence on renal blood flow.

Several hormones and autacoids can influence GFR and renal blood flow

Hormonal Factors

Angiotensin II - Preferentially **constricts efferent arterioles** in most physiological conditions.

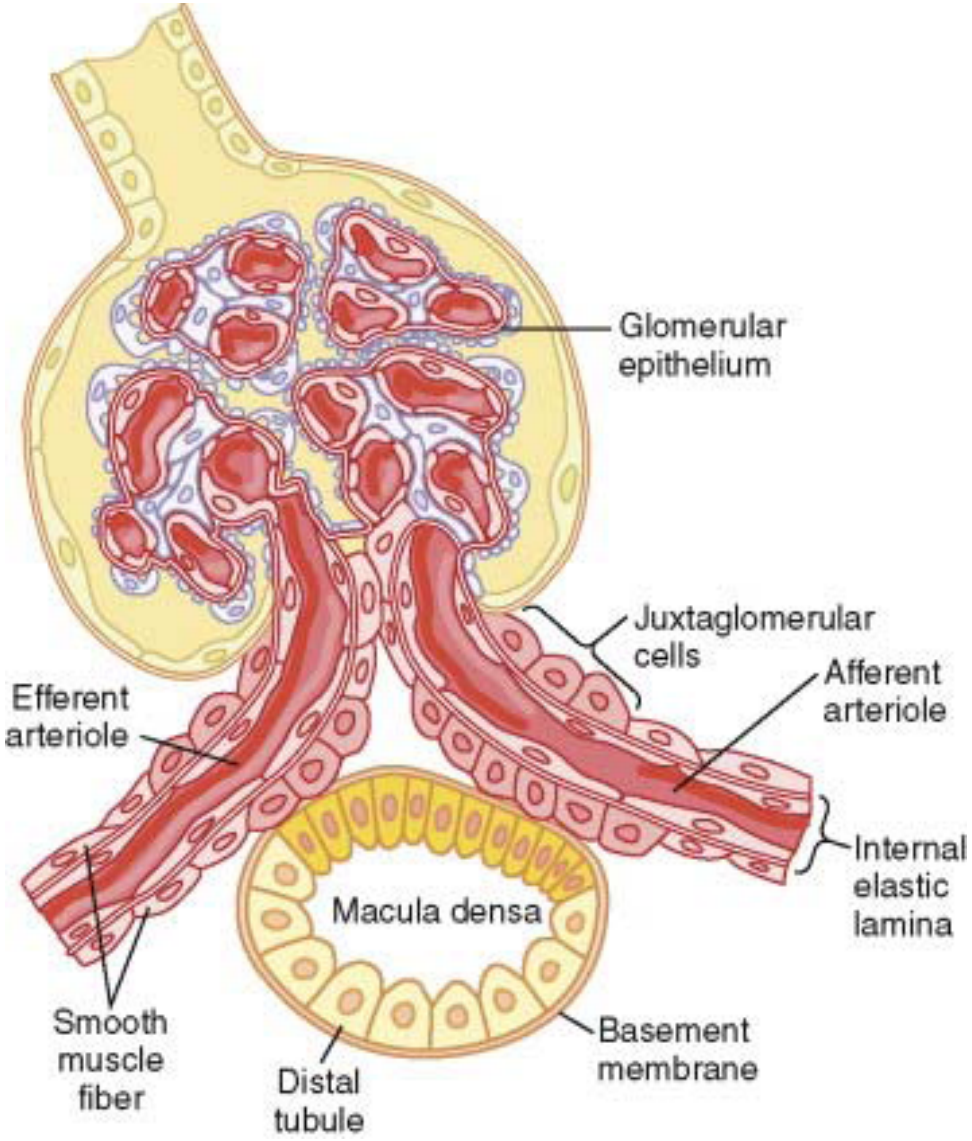
Typically, increased angiotensin II levels **raise glomerular hydrostatic pressure** while **reducing renal blood flow**.

Endothelial-Derived Nitric Oxide - Decreases renal vascular resistance and increases GFR.

Prostaglandins and Bradykinin - Decrease renal vascular resistance and tend to increase GFR.

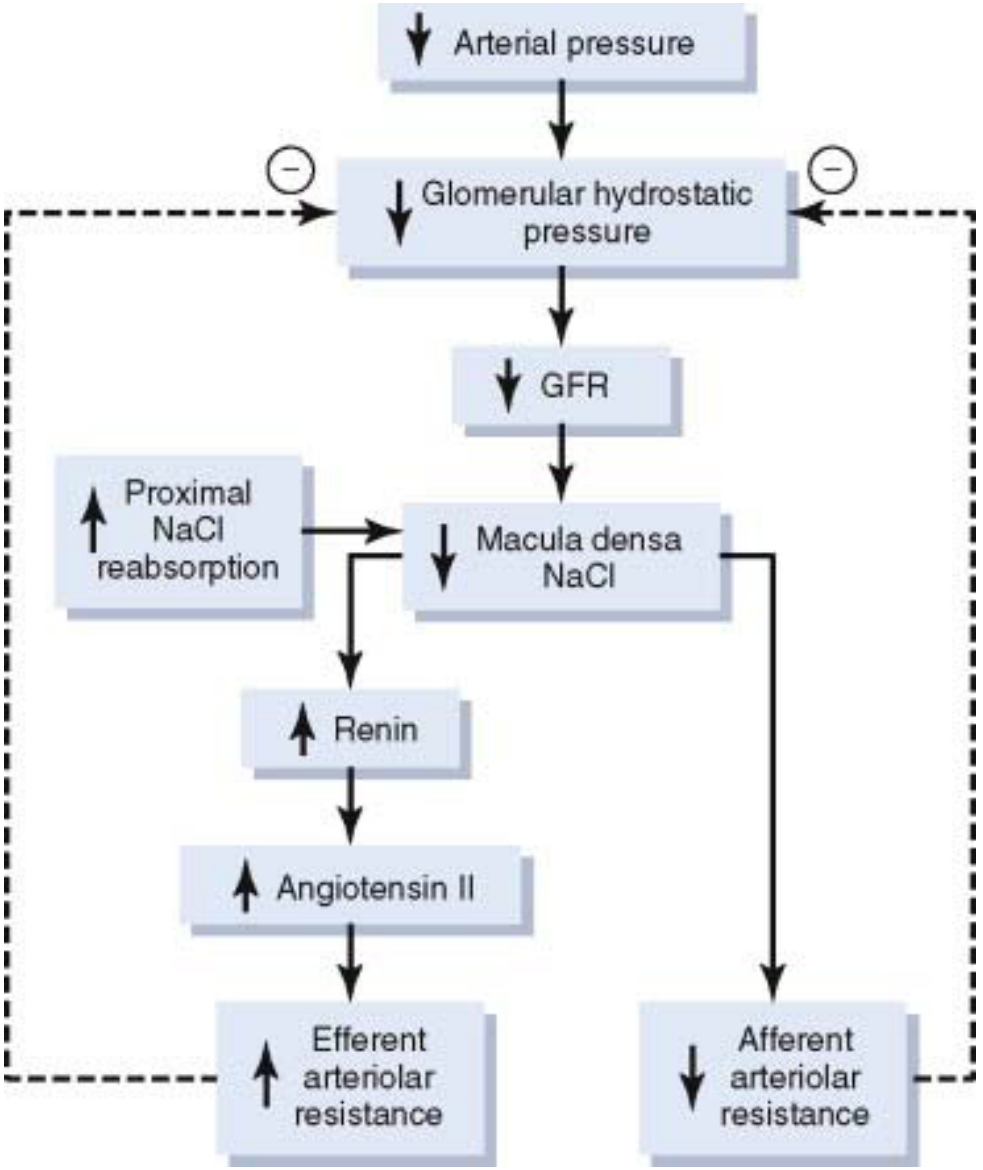
The Juxtaglomerular Apparatus

The juxtaglomerular complex consists of **macula densa cells** in the initial portion of the distal tubule, and **juxtaglomerular cells** in the walls of the afferent and efferent arterioles.



Macula Densa Feedback

Decreased macula densa sodium chloride causes dilation of afferent arterioles which raises glomerular hydrostatic pressure. Decreased sodium chloride also increases renin release from the juxtaglomerular cells of the afferent and efferent arterioles.



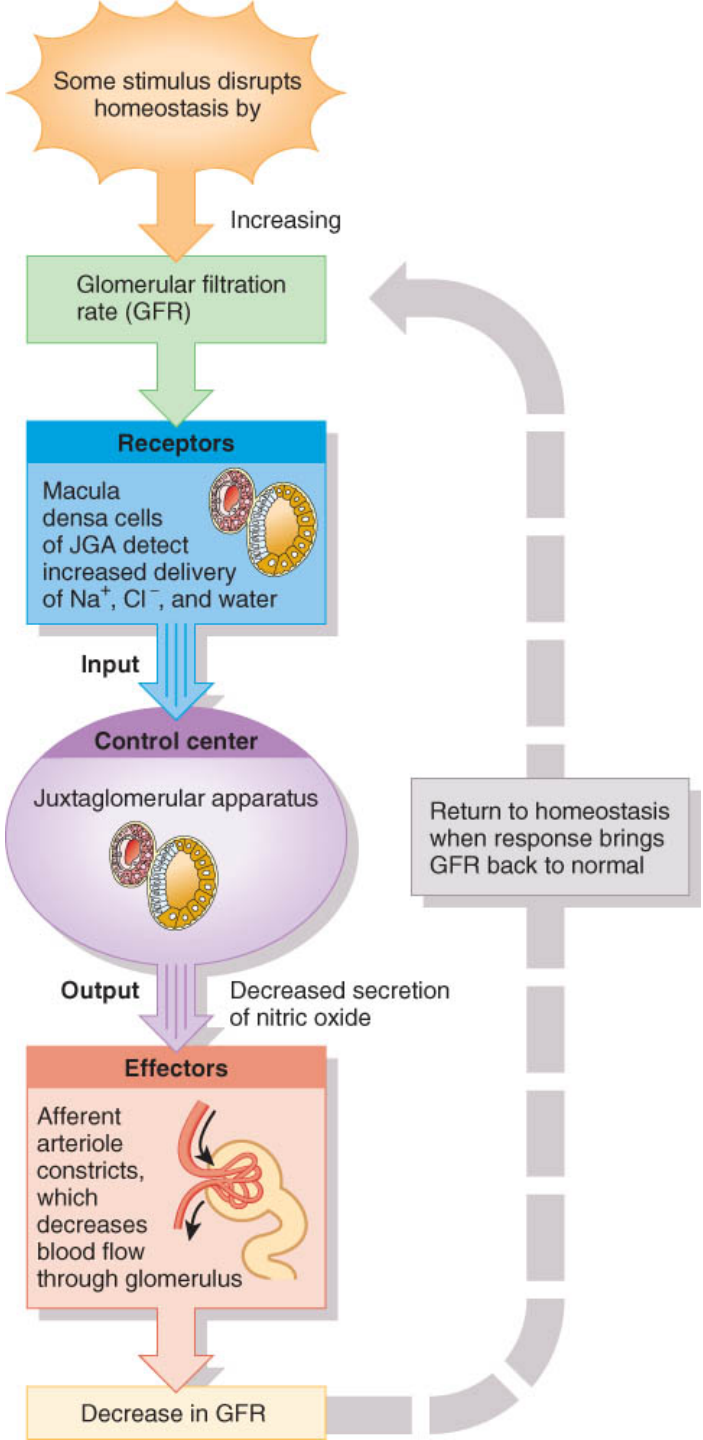
Renal Autoregulation of GFR

allows kidneys to maintain constant GFR w/ everyday changes

1) myogenic mechanism
   - systemic increases in BP, stretch the afferent arteriole
   - smooth muscle contraction reduces the diameter of the arteriole returning the GFR to its previous level in seconds

2) tubuloglomerular feedback
   - elevated systemic BP raises the GFR so that fluid flows too rapidly through the renal tubule & Na+, Cl- and water are not reabsorbed
   - macula densa detects that difference
   - afferent arterioles constrict & reduce GFR

Auto-Regulation of GFR



Neural Regulation of GFR

- Blood vessels of the kidney are supplied by sympathetic fibers that cause vasoconstriction of afferent arterioles
- At rest, renal BV are maximally dilated because sympathetic activity is minimal
  - renal autoregulation prevails
- With moderate sympathetic stimulation, both afferent & efferent arterioles constrict equally
  - decreasing GFR slightly
- With extreme sympathetic stimulation (exercise or hemorrhage), vasoconstriction of afferent arterioles reduces GFR significantly
  - lowers urine output & permits blood flow to other tissues

Hormonal Regulation

- Atrial natriuretic peptide (ANP)
- Renin-Angiotensin II-Aldosterone
- ADH
- Calcitriol
- Erythropoietin
- and sympathetic stimulation (not hormonal)

Hormonal Regulation of GFR

- Atrial natriuretic peptide (ANP) increases GFR
  - stretching of the atria that occurs with an increase in blood volume causes hormonal release
    - increases capillary surface area of glomerulus for more filtration = **increasing** GFR

Hormonal Regulation of GFR

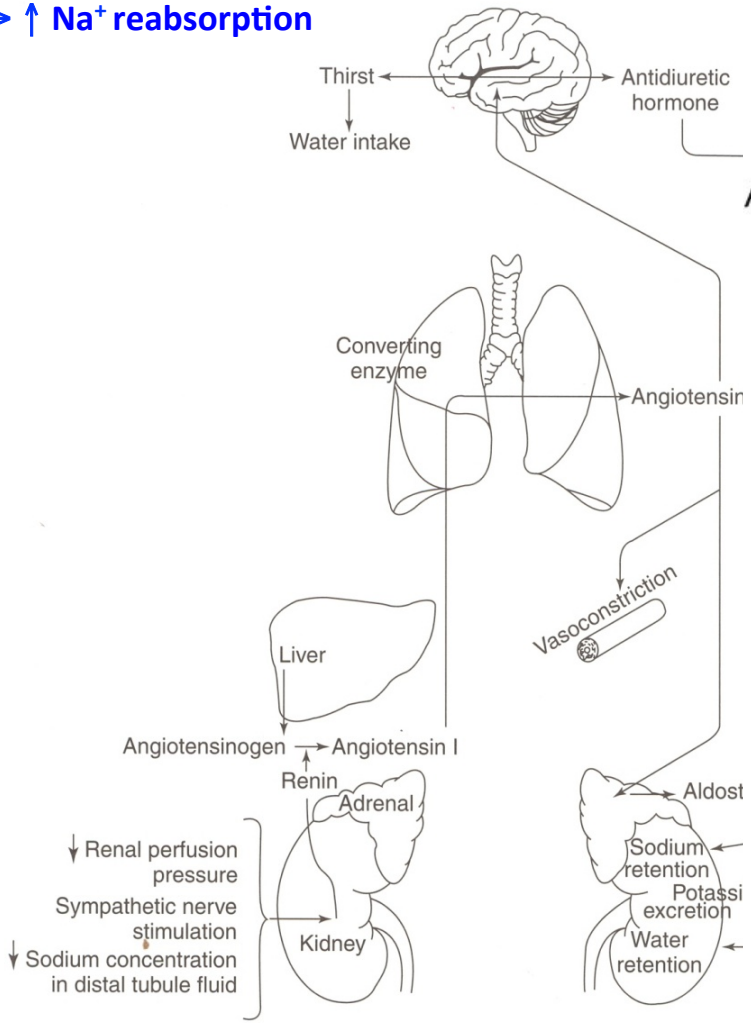
Angiotensin II reduces GFR

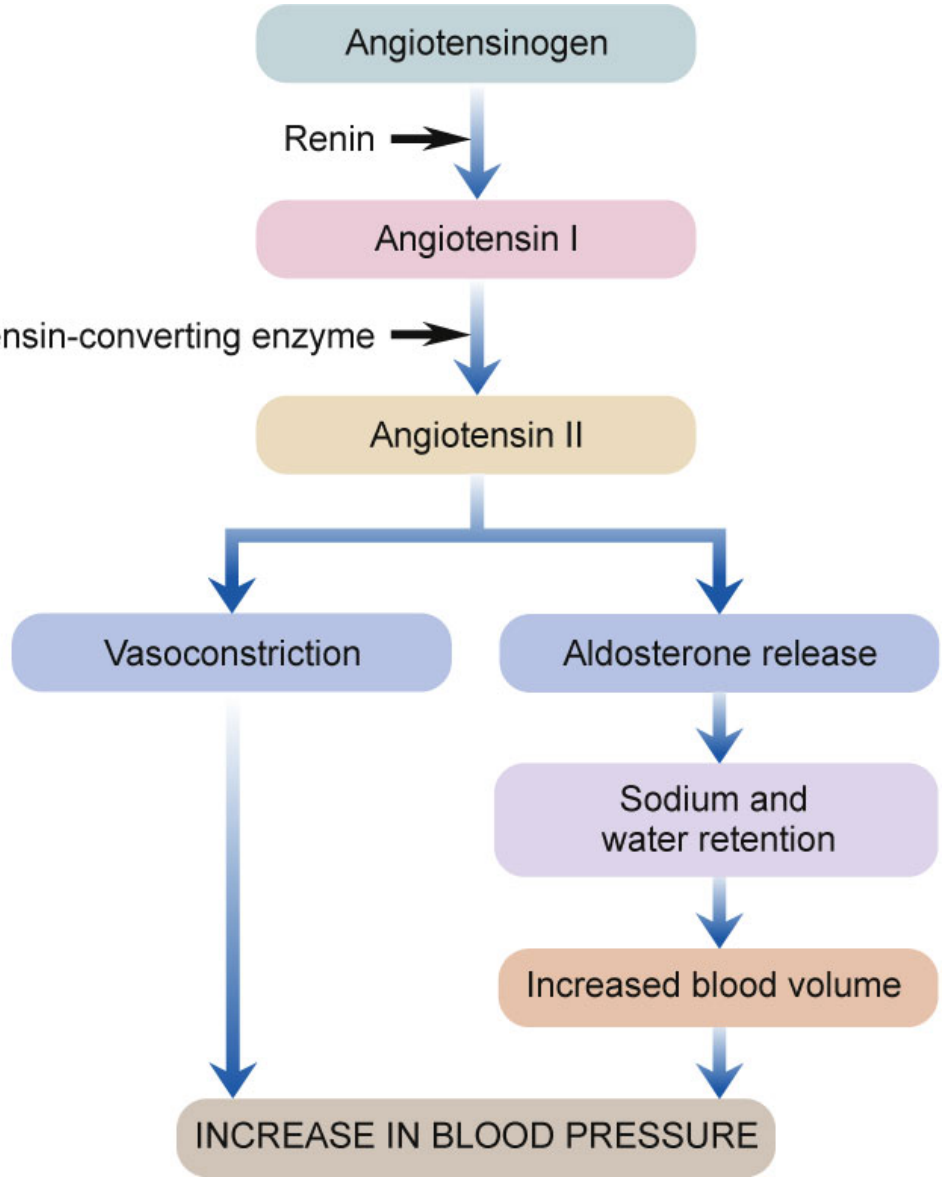
- potent vasoconstrictor that narrows both afferent & efferent arterioles **reducing** GFR

Renin–angiotensin–aldosterone system

It functions as a neurohormonal regulatory mechanism for body water and Na^+:

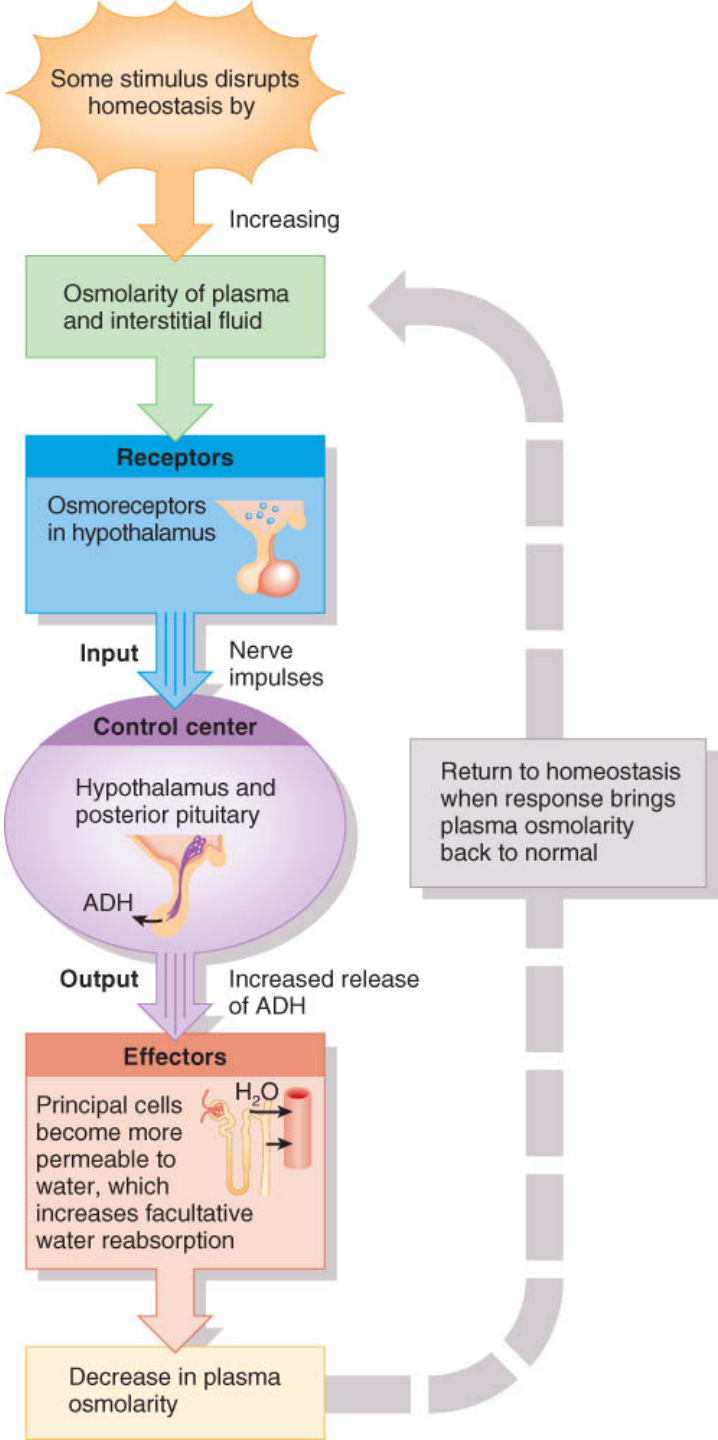
- → ↑ water volume
- → ↑ Na^+ reabsorption





Antidiuretic Hormone

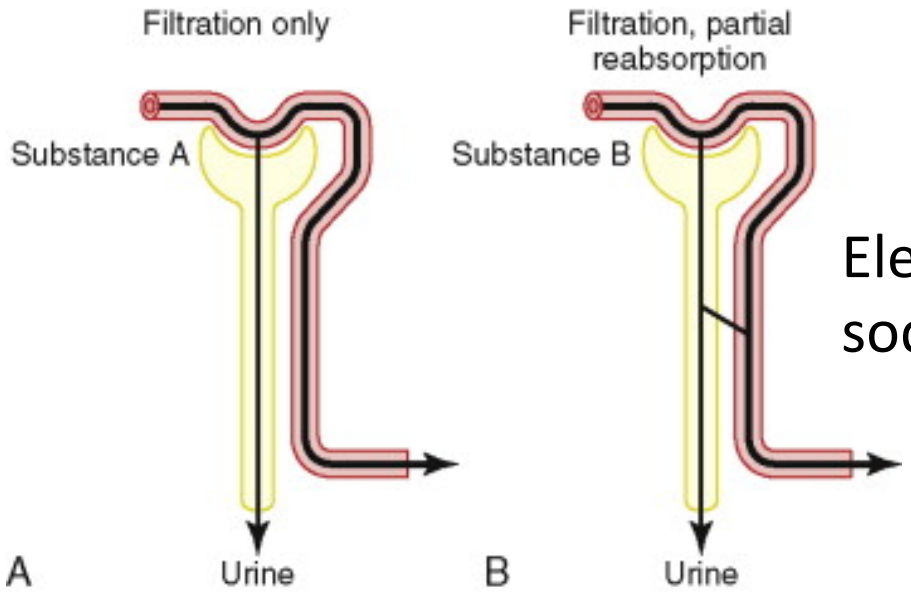
- Increases water permeability of principal cells so regulates facultative water reabsorption
- Stimulates the insertion of aquaporin-2 channels into the membrane
  - water molecules move more rapidly
- Stimulated by decreased blood volume or severe dehydration.



Urine formation

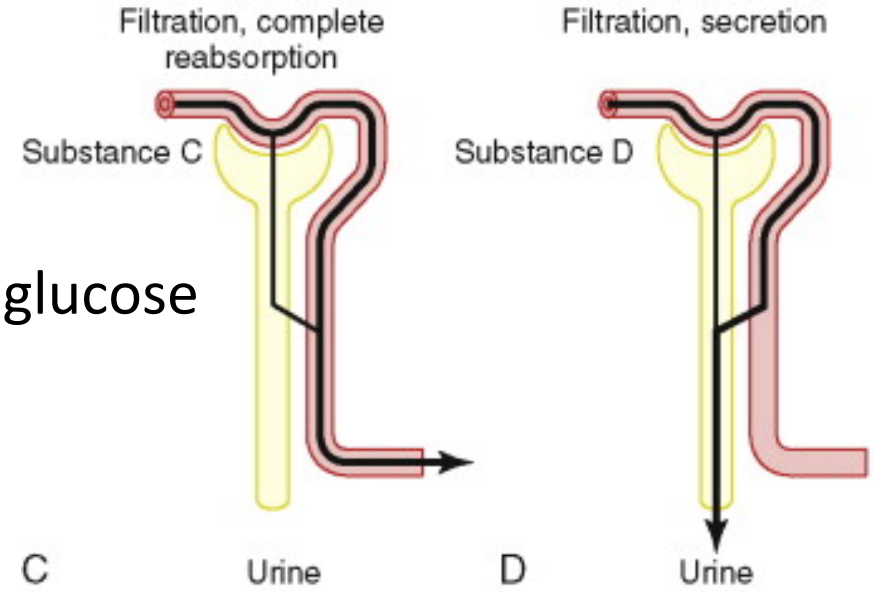
Secretion and Reabsorption

Creatine waste



Electrolytes such as sodium and chloride

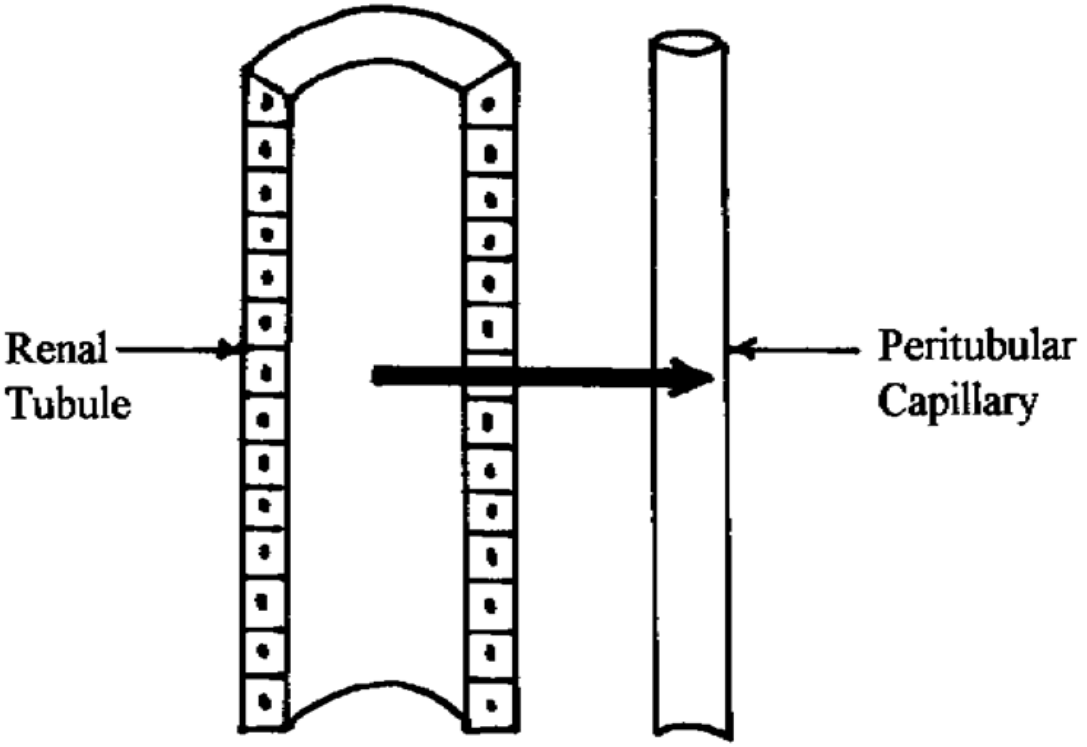
Amino acids and glucose



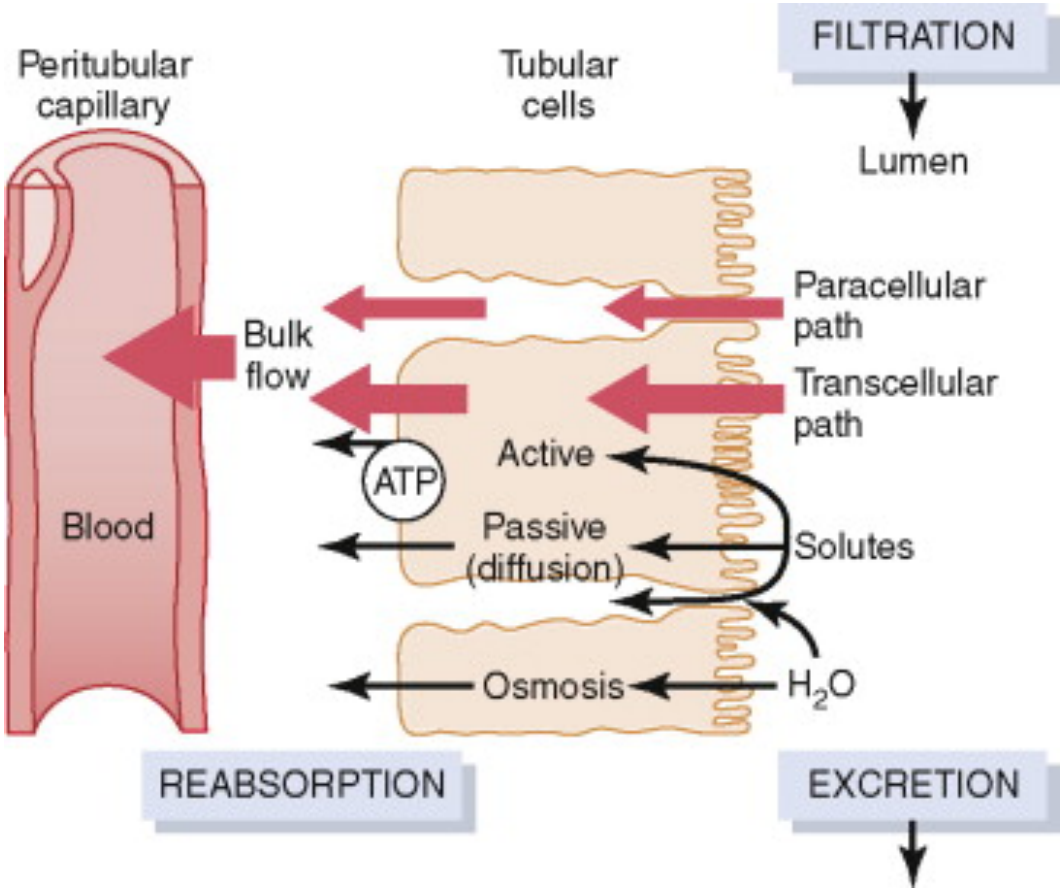
Organic acids and bases

Reabsorption

Reabsorption is the process of moving substances from the filtrate back into the blood



Reabsporption Across Tubular Epithelial Cells

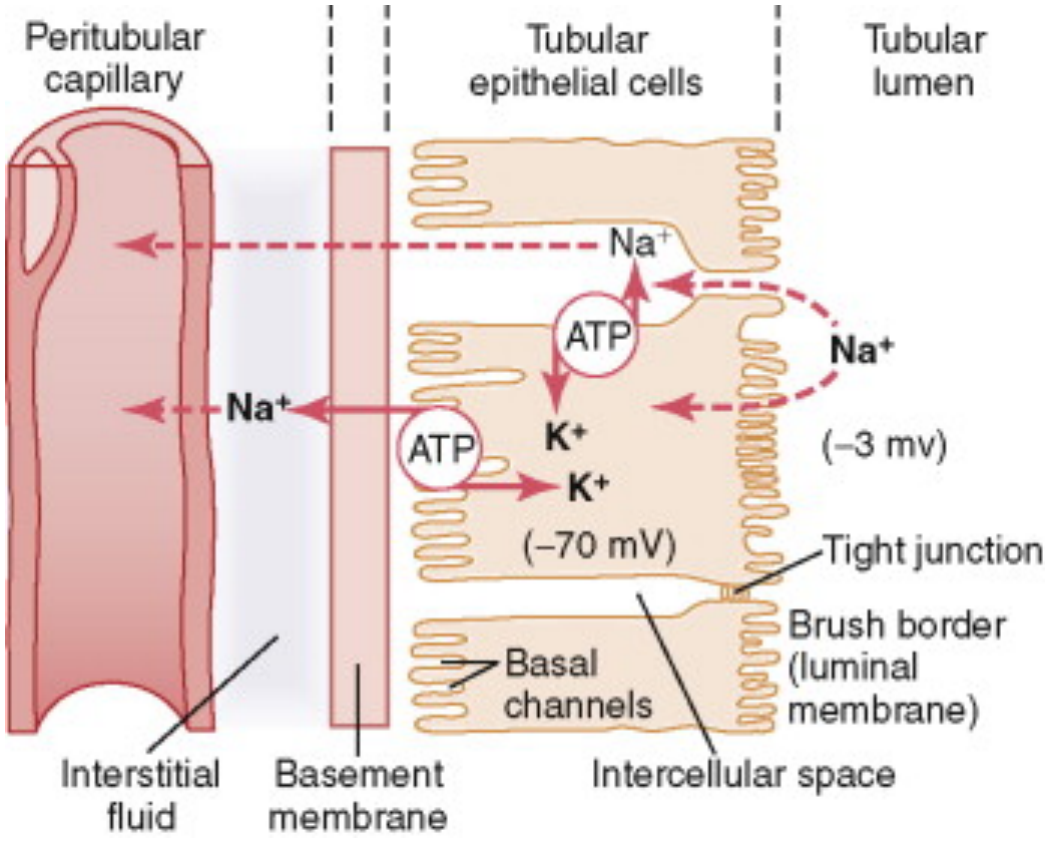


Active Transport of Sodium

1. Sodium diffuses across the luminal membrane *down an* electrochemical gradient

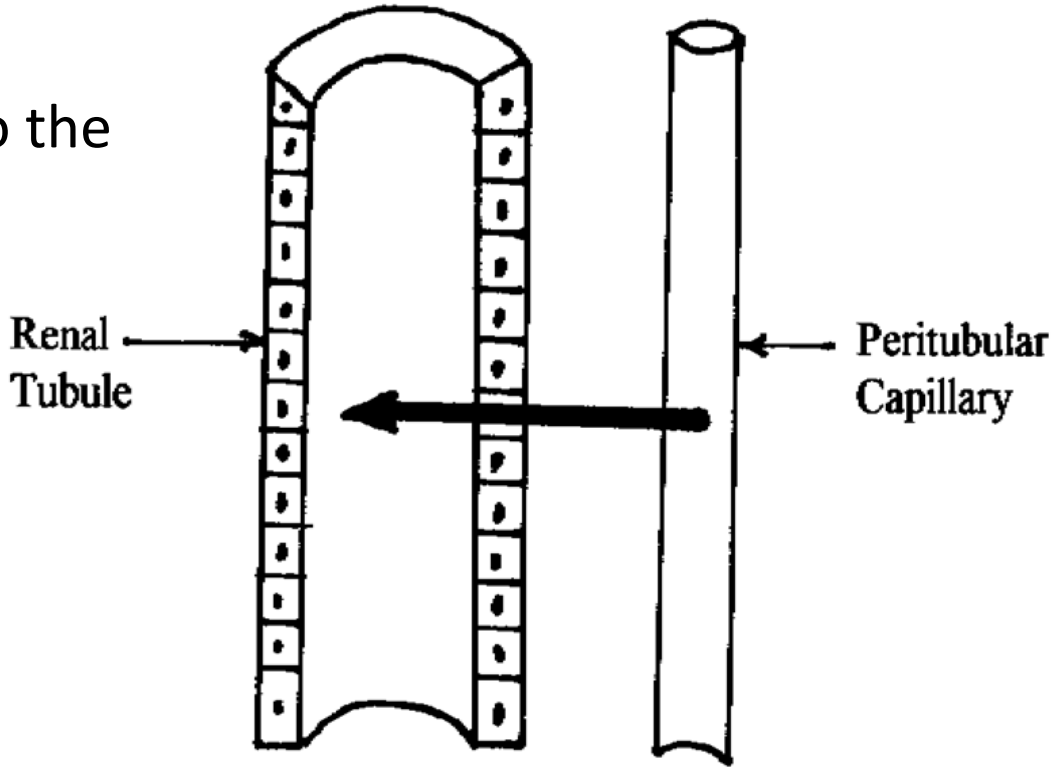
2. Sodium is transported across the basolateral membrane by the sodium potassium ATPase pump.

3. Sodium, water, and other substances are reabsorbed from the interstitial fluid into the peritubular capillaries by ultrafiltration



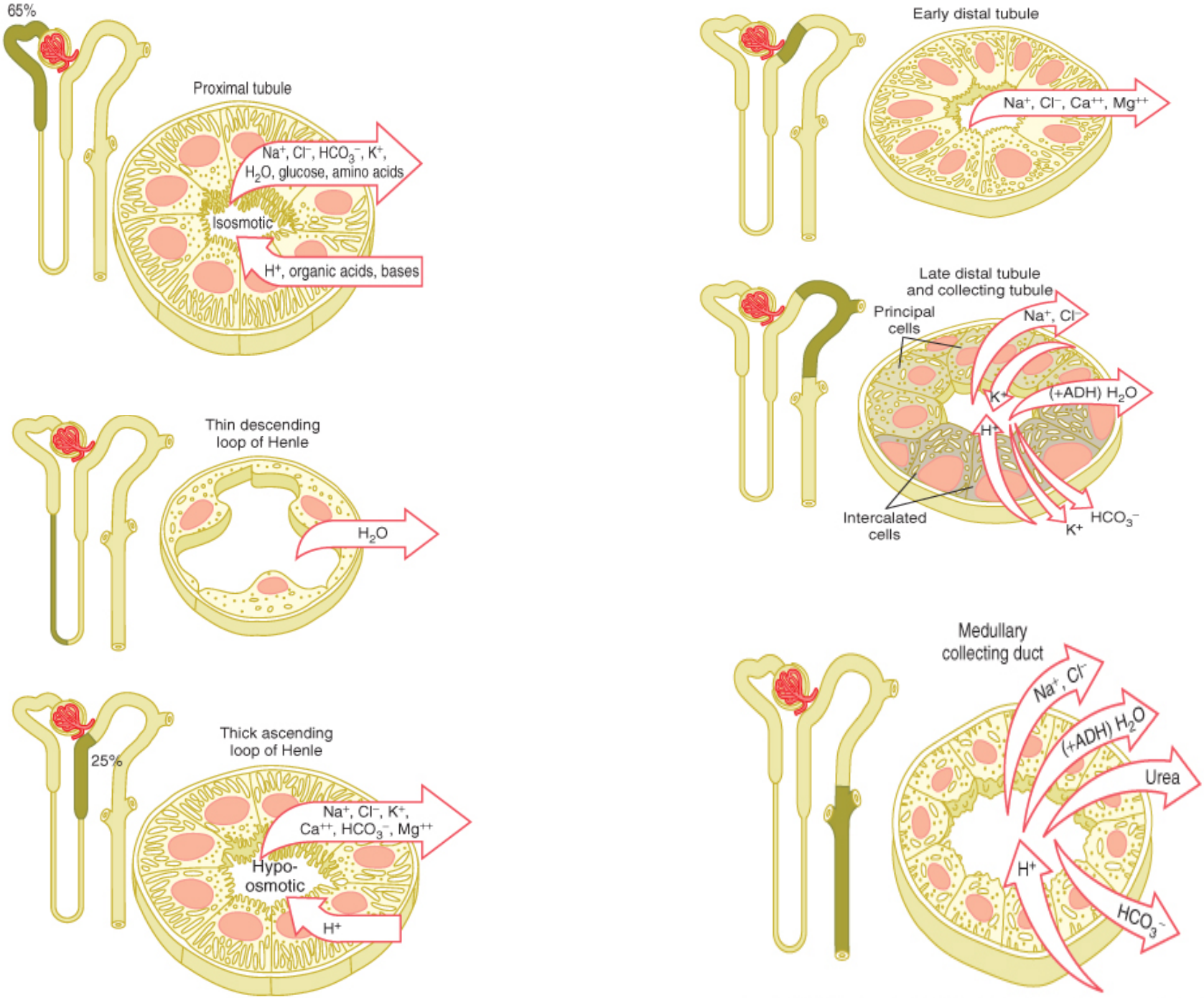
Secretion

Secretion is the transfer of substances from the blood into the filtrate

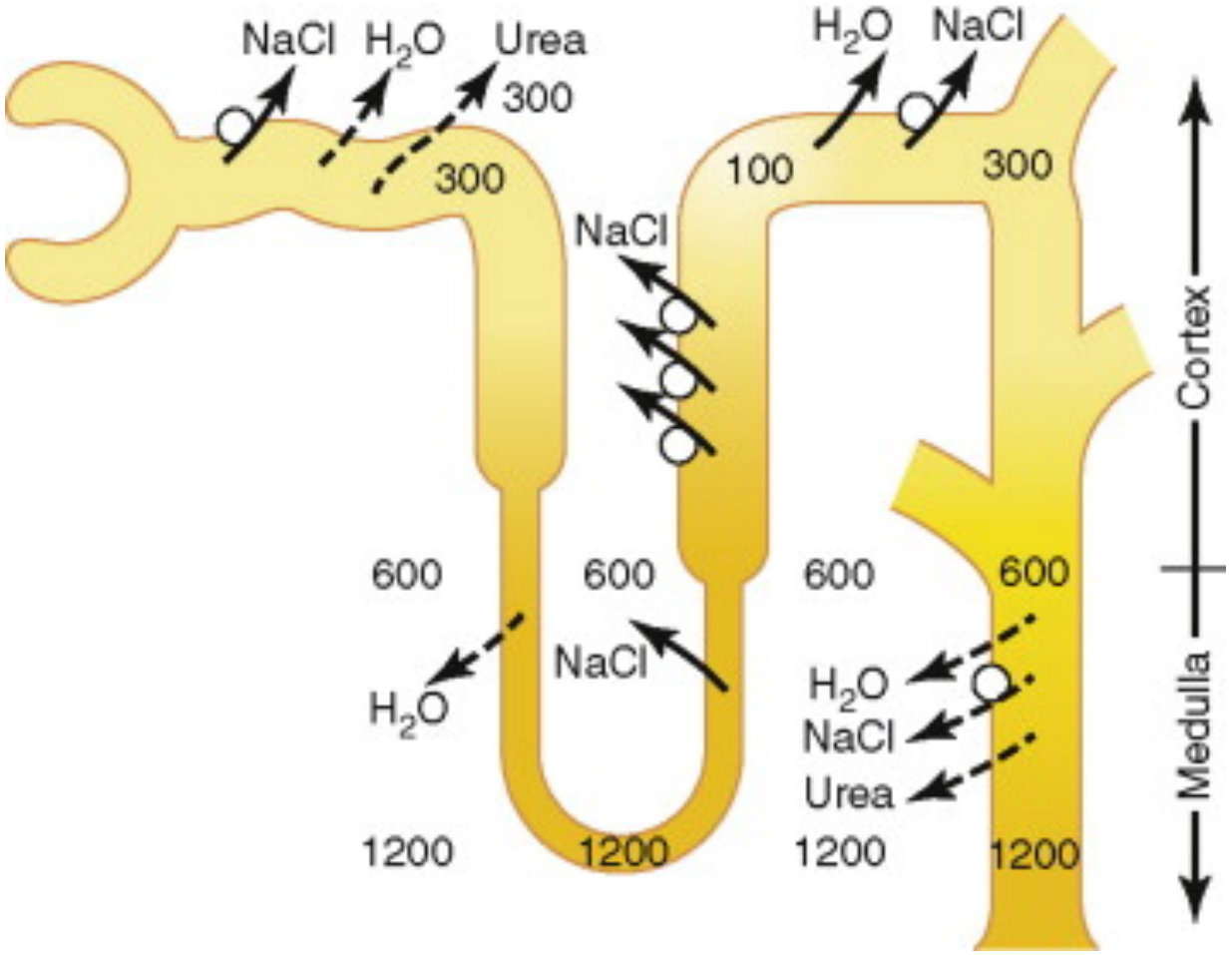


Important for removal of organic acids and bases such as bile salts, oxalate, urate, and catecholamines from the blood

Secreted substances must pass through 3 membranes to reach the filtrate

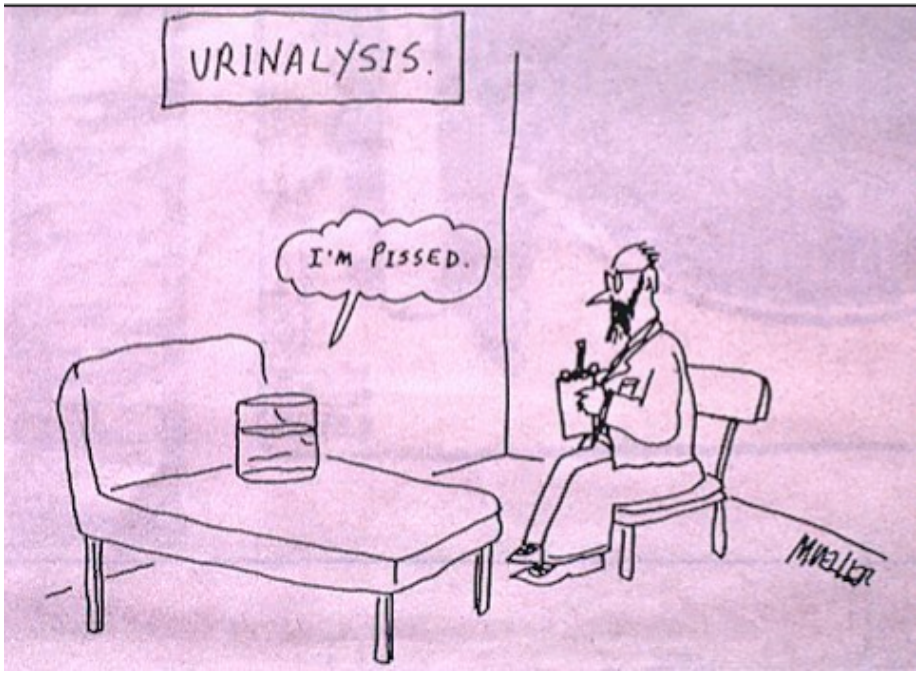

65%
Proximal tubule
Na+, Cl−, HCO3−, K+,
H2O, glucose, amino acids
Isosmotic
H+, organic acids, bases
Thin descending
loop of Henle
H2O
25%
Thick ascending
loop of Henle
Na+, Cl−, K+,
Ca++, HCO3−, Mg++
Hypo-
osmotic
H+
Early distal tubule
Na+, Cl−, Ca++, Mg++
Late distal tubule
and collecting tubule
Principal
cells
Na+, Cl−
K+
(+ADH) H2O
H+
Intercalated
cells
K+
HCO3−
Medullary
collecting duct
Na+, Cl−
(+ADH) H2O
Urea
H+
HCO3−

Formation of Concentrated Urine



Urinalysis

- An analysis of the volume and physical, chemical, and microscopic properties of urine, called *urinalysis*, reveals much about the state of the body.



Collection method: cystocentesis
Time collected: 09:30 am

========== URINALYSIS ==========

COLOR	TURBIDITY	SP GRAV	pH-STIX	PROT-STIX
md. yellow	sl.cldy	1.040	7.0	neg.

PROT-SSA	GLUC-STIX	KET-STIX	BILI-STIX	BILI-ICTO
neg.	neg.	neg.	neg.	neg.

BLOOD-STIX	WBC/HPF	RBC/HPF	BACTERIA	EPITH CELL
neg.	<5	<5	none seen	few

FAT DROP	DEBRIS	SPERM
few	none seen	none seen

CASTS/LPF: none seen

CRYSTALS: few struvite

EVALUATION OF KIDNEY FUNCTION

- Two *blood screening tests* can provide information about kidney function.
  - One screening test is the blood urea nitrogen (BUN), which measures the level of nitrogen in blood that is part of urea from breakdown of proteins.
  - Another test is measurement of plasma creatinine which results from catabolism of creatinine phosphate in skeletal muscle.

- *Renal plasma clearance* expresses how effectively the kidneys remove (clear) a substance from blood plasma.
  - The clearance of creatinine gives the glomerular filtration rate. (it is filtered, not reabsorbed and only minimally secreted)