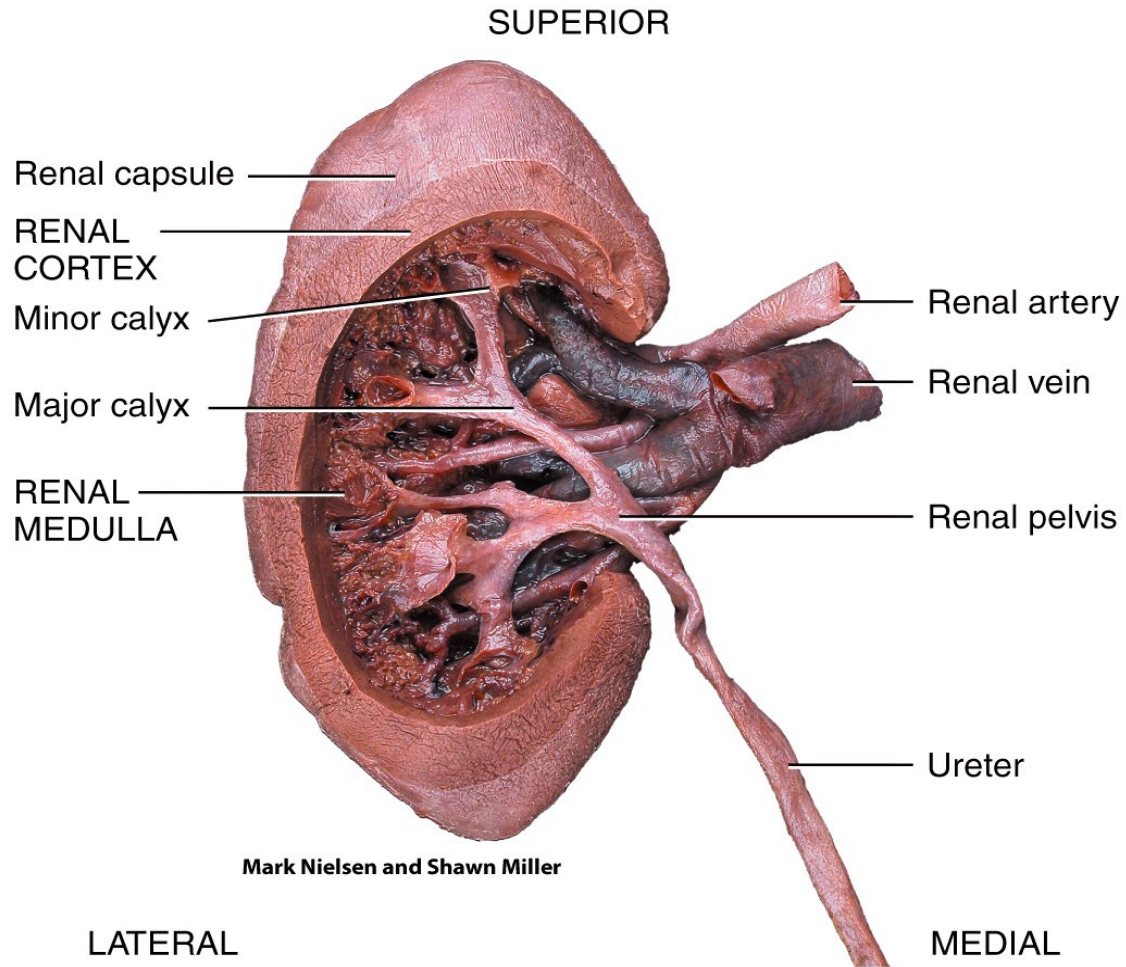


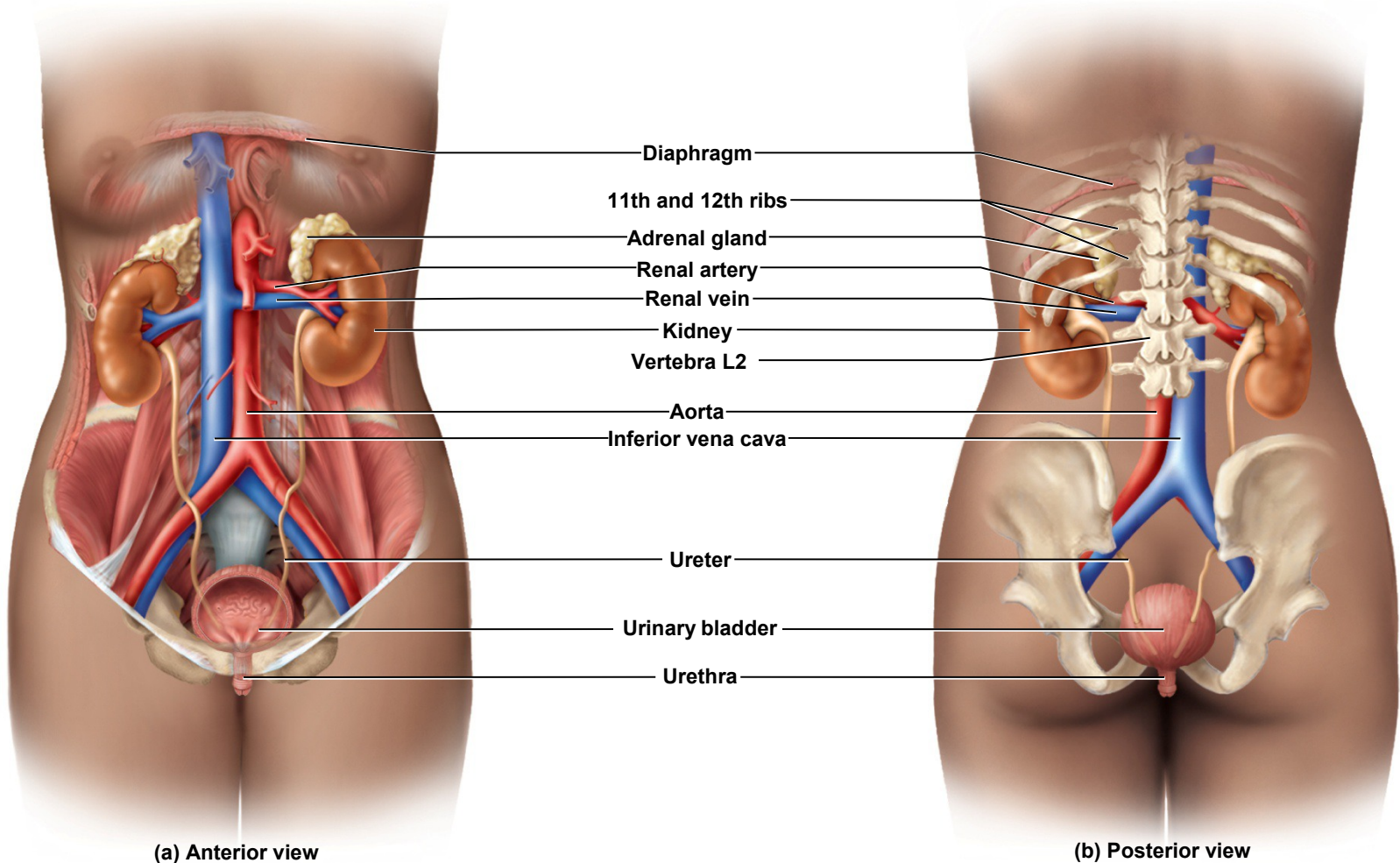
C23

Urinary System



(b) Posterior view of dissection of left kidney

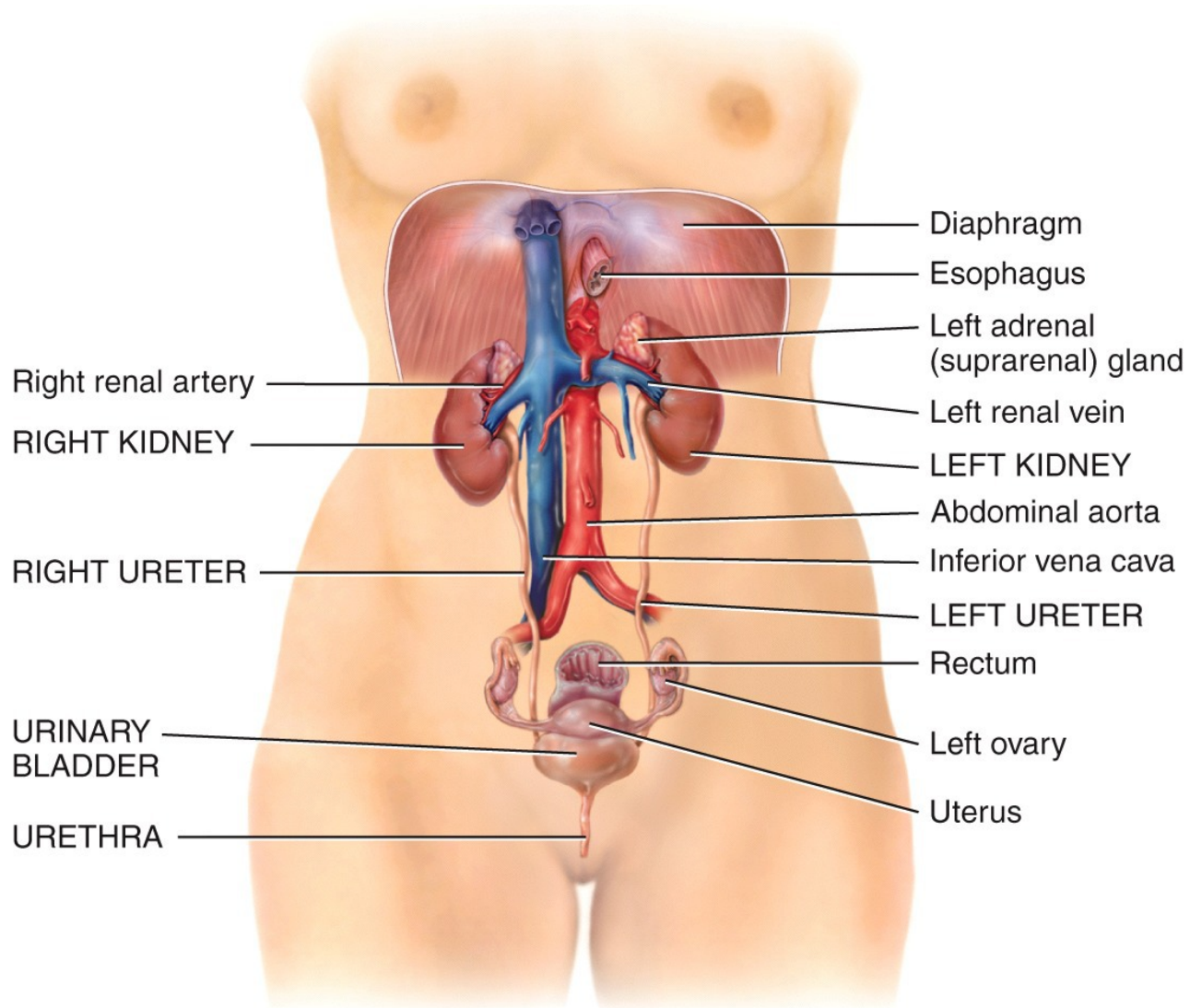
Urinary System



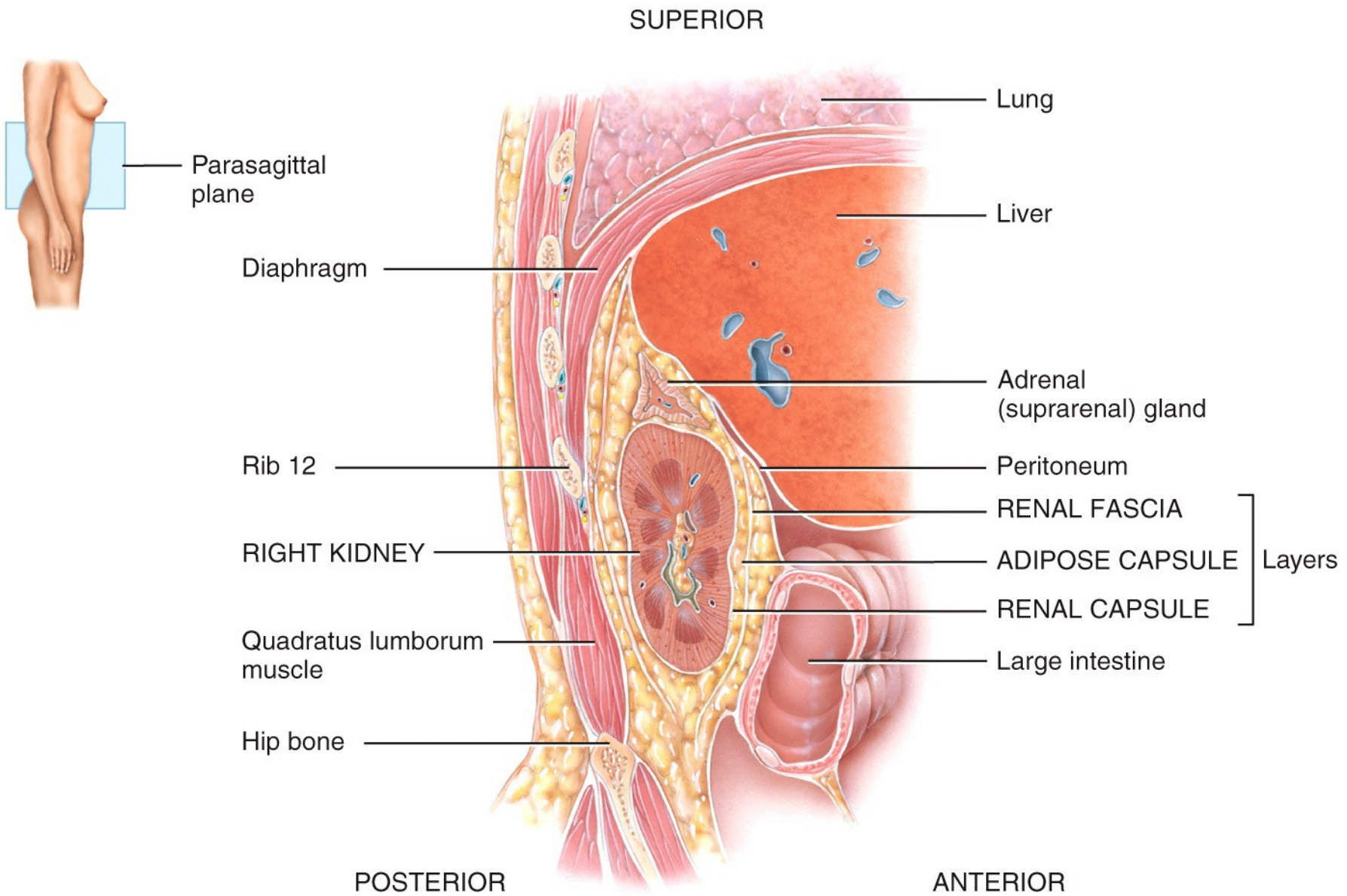
urinary system consists of 6 organs:

2 kidneys, 2 ureters, 1 urinary bladder, and 1 urethra

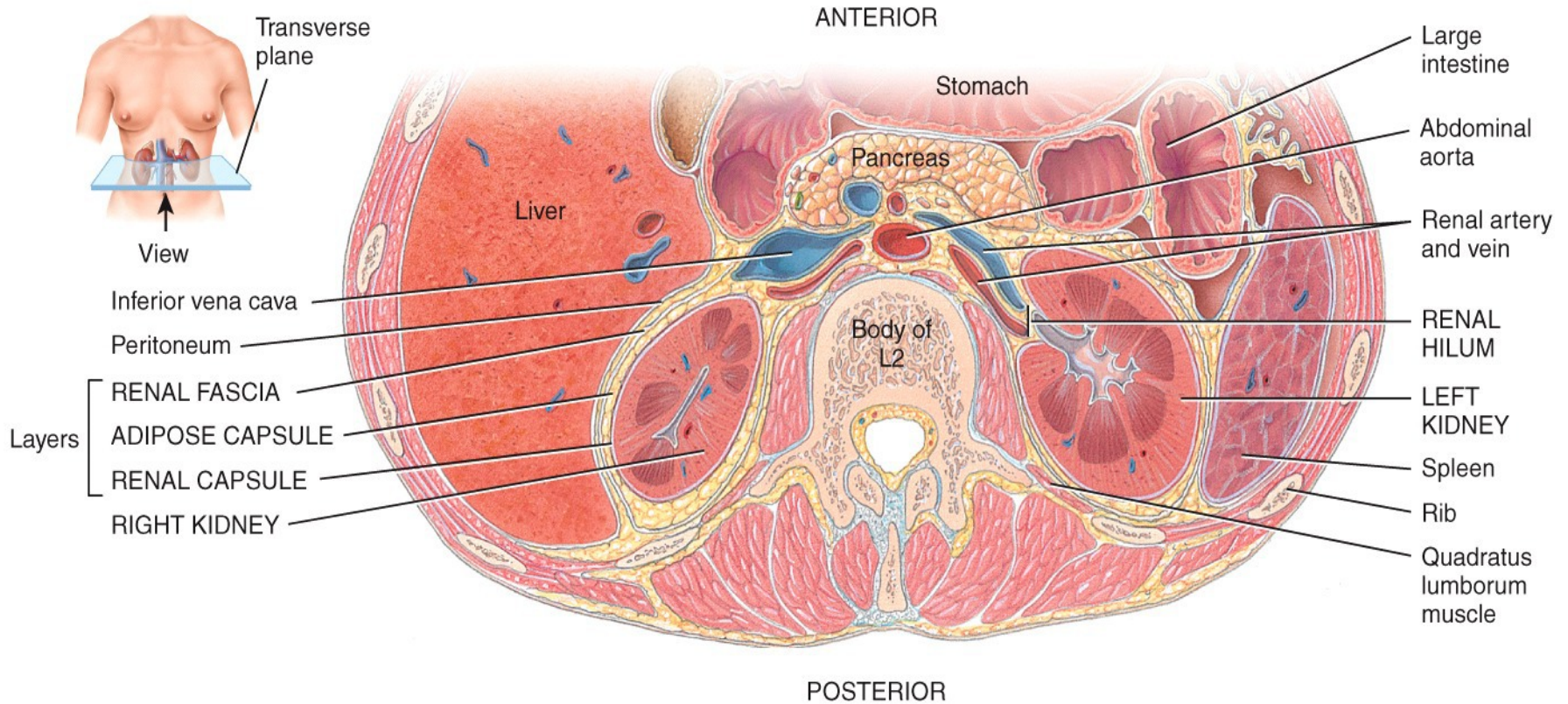
Anatomy of Urinary System



(a) Anterior view of urinary system

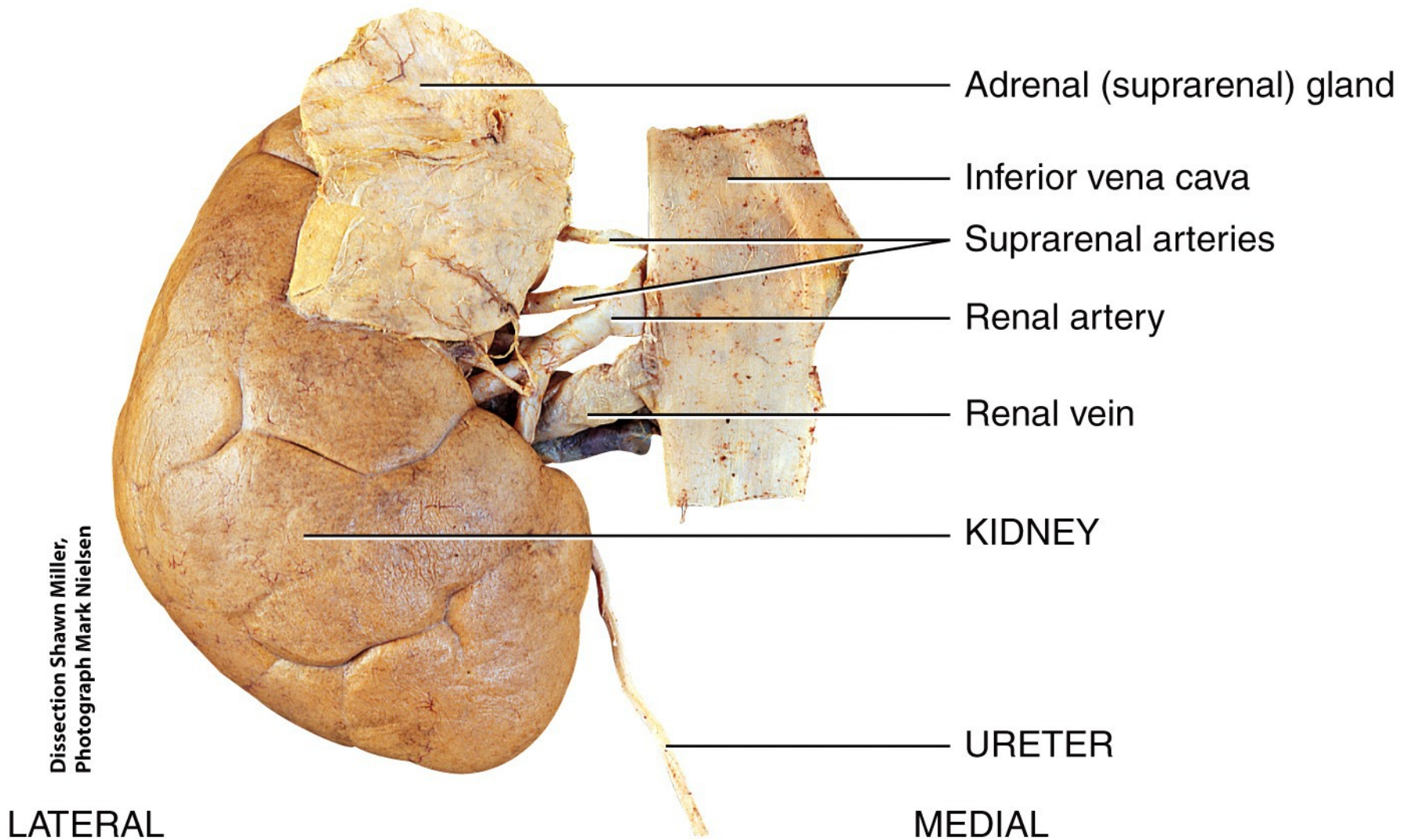


(b) Parasagittal section through right kidney

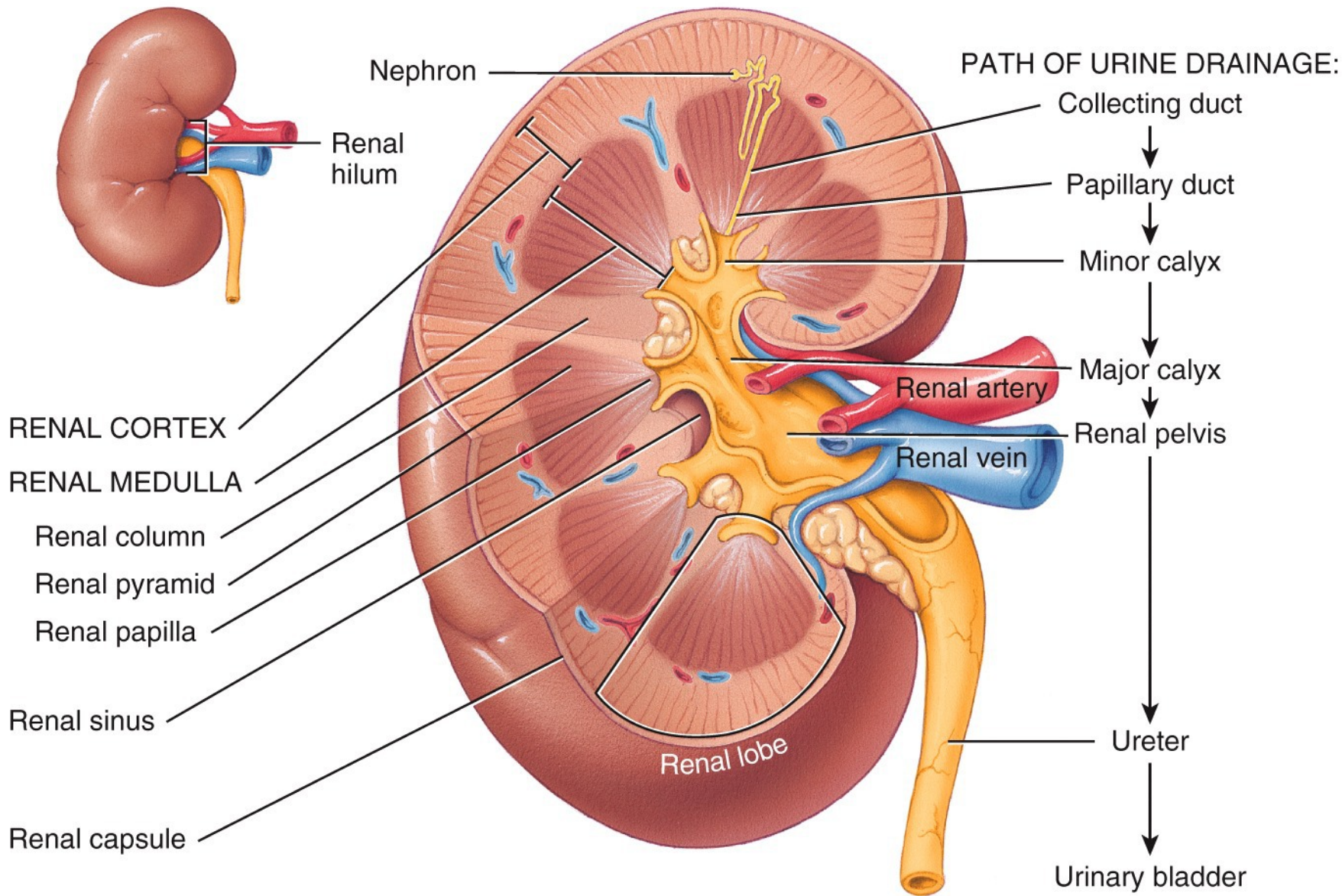


(a) Inferior view of transverse section of abdomen (L2)

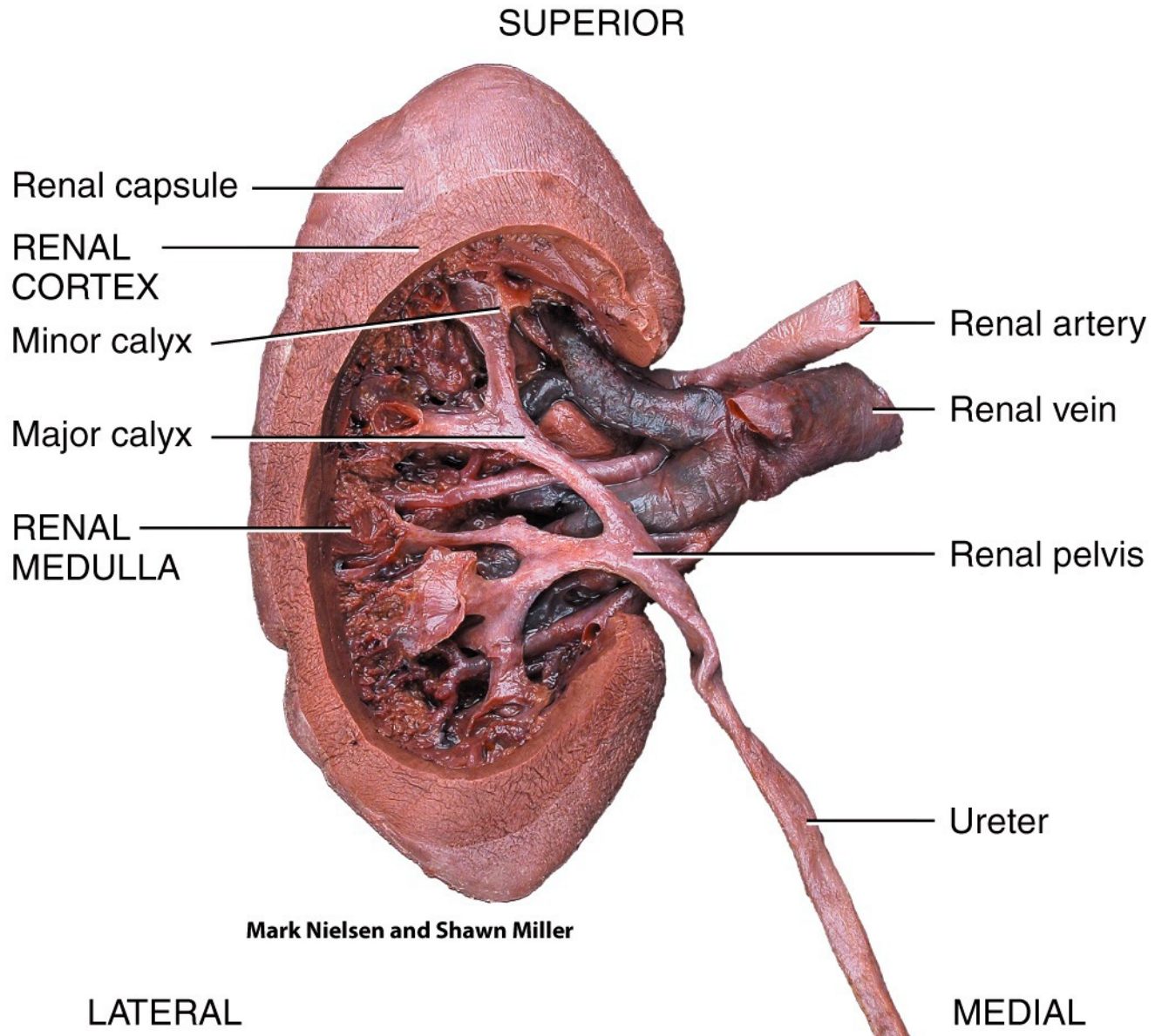
What does retroperitoneal mean?



What is secreted from the adrenal gland?



(a) Anterior view of dissection of right kidney



Mark Nielsen and Shawn Miller

(b) Posterior view of dissection of left kidney

Functions of the Kidney (1 of 2)



- filters blood plasma**, separates toxic waste from useful molecules, conserves useful molecules while eliminating toxic molecules // urine formation
- regulate blood volume** by eliminating or conserving water
- regulate osmolarity** of the body fluids by controlling the amount of water and solutes eliminated
- regulate blood pressure** secretes enzyme, renin, which activates hormonal mechanisms that control blood pressure and electrolyte balance (i.e. renin-angiotensin-aldosterone pathway)

Functions of the Kidney (2 of 2)



- secretes the hormone, ***erythropoietin***, which stimulates the production of red blood cells
- regulate pH and **acid-base balance** of body fluids by its ability to secrete protons into urine
- final step in synthesizing hormone, calcidiol is converted to ***calcitriol in kidney*** // *calcitriol is active form of Vit D* / which contributes to calcium homeostasis
- **gluconeogenesis** // kidney's ability to form new glucose from amino acids – only used in extreme starvation (also function of liver)

How do we eliminate waste from our body?

- *'To live is to metabolize'* // metabolism creates toxic waste products (e.g. nitrogen and organic acids)
- Waste products of metabolism must be removed from the body. These systems remove end metabolic waste products.
 - Respiratory
 - Digestive
 - Sweat glands
 - Urinary system

The nephron is the “structural unit” of a kidney

The tubule start as the glomerular capsule and ends at the distal collection duct (at tip of the pyramid)

divided into five regions

Glomerular capsule 1

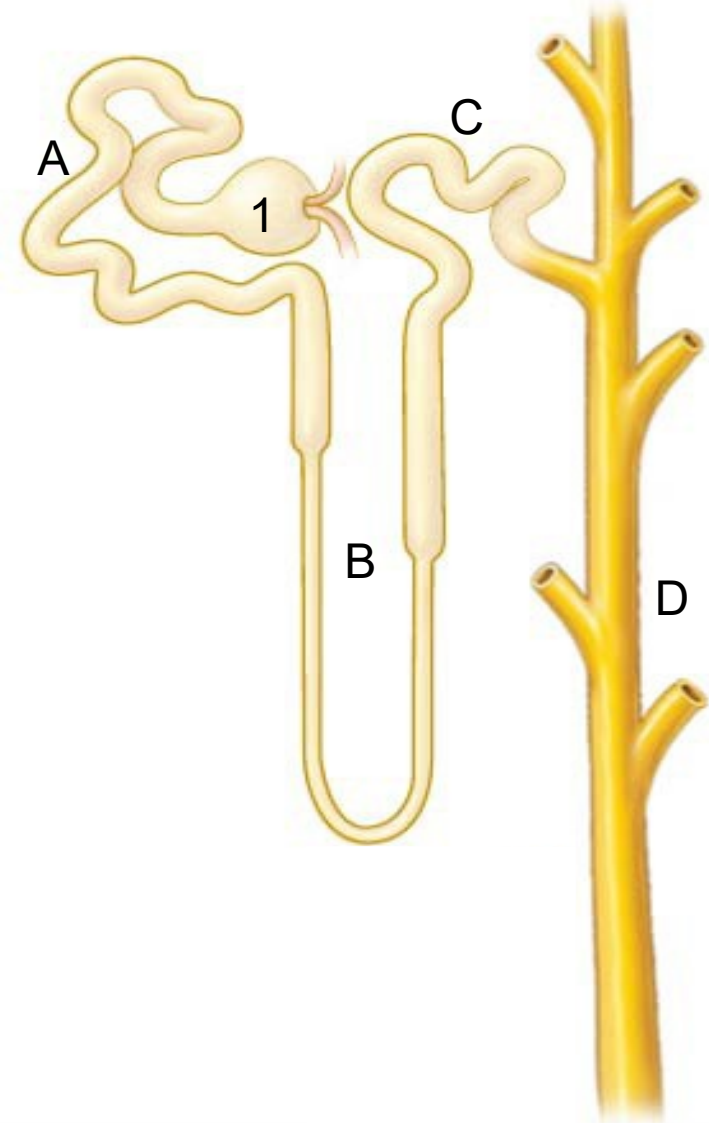
proximal convoluted tubule A

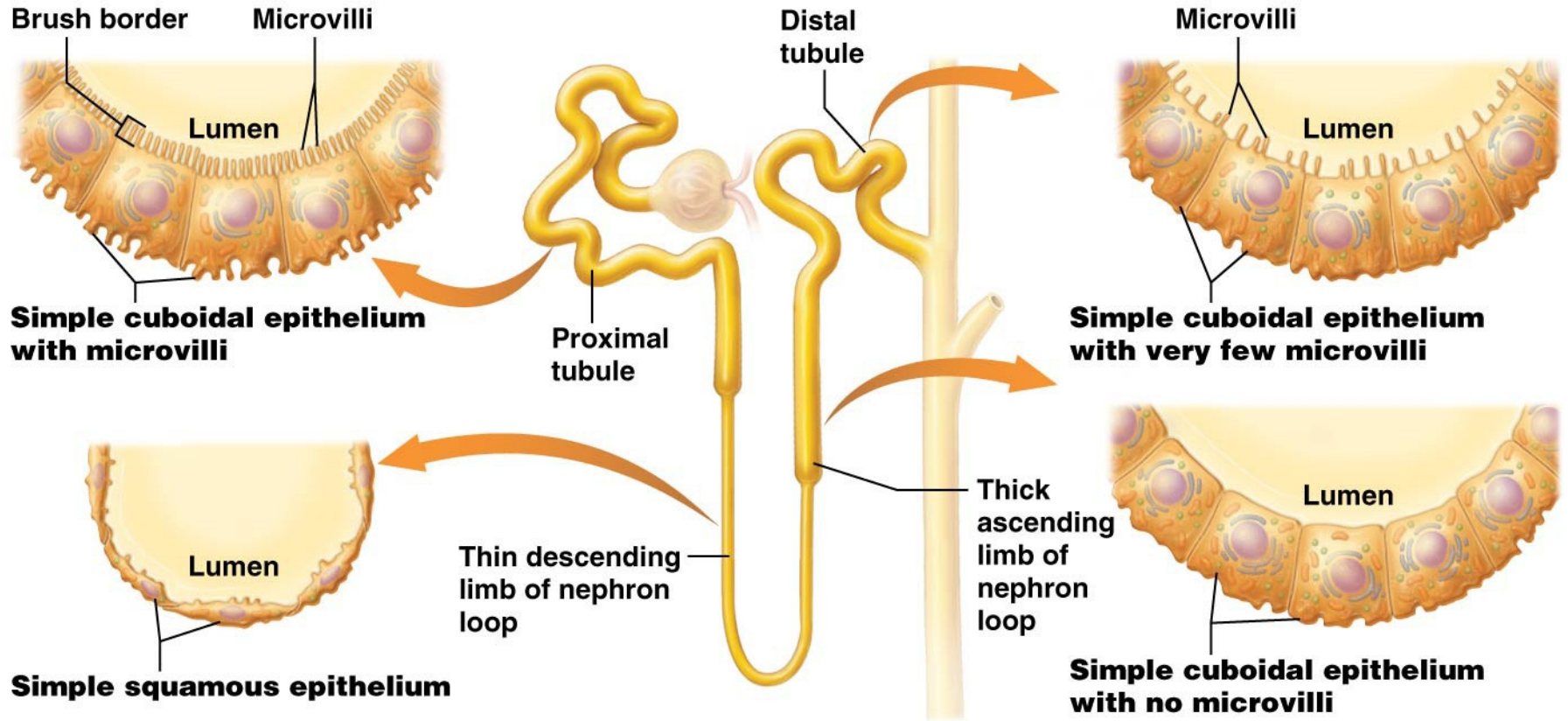
nephron loop B

distal convoluted tubule C

collecting duct D

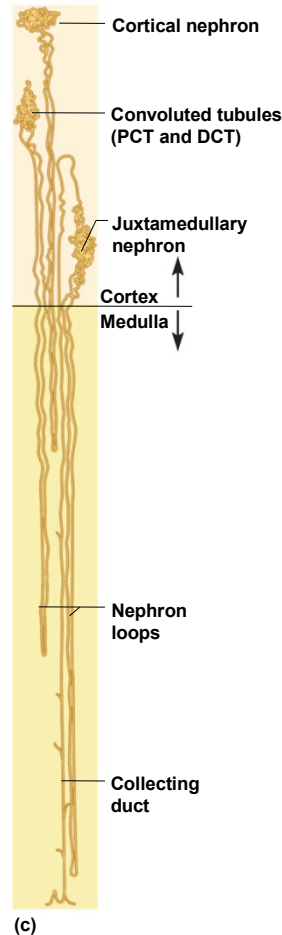
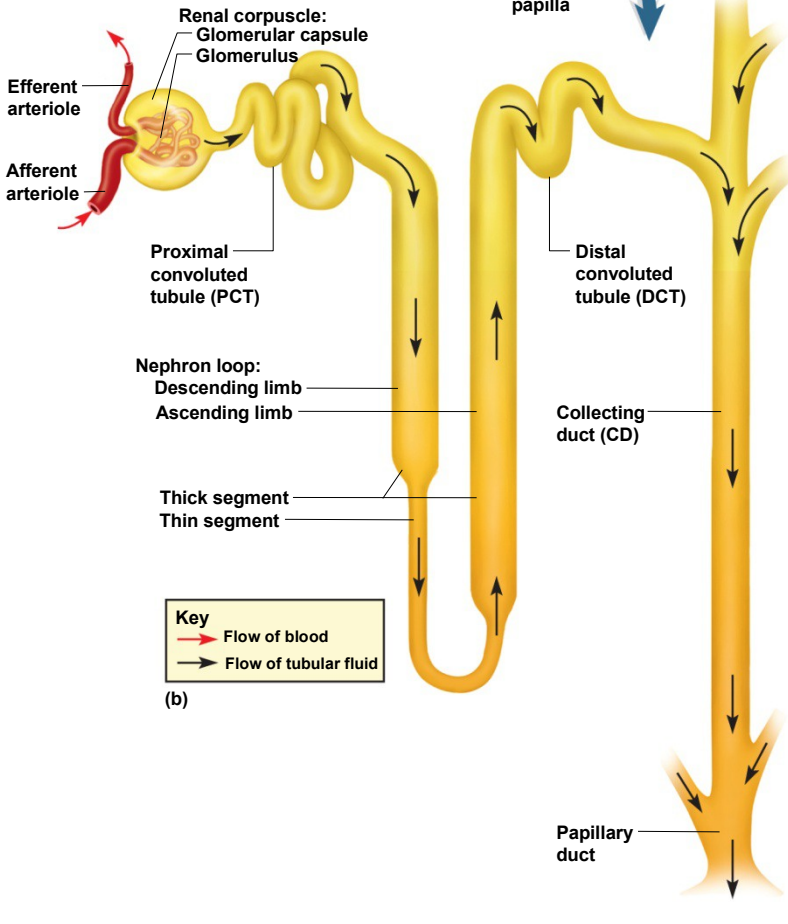
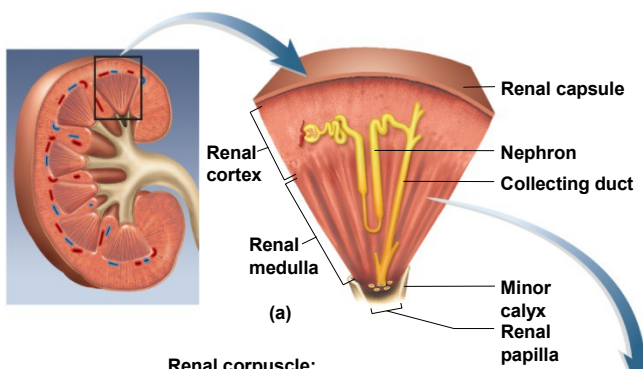
Tubules of the Nephron







The Nephron



Each kidney has about 1.2 million nephrons // may survive with as few as 25%

The nephron has two parts:

renal corpuscle – filters the blood plasma // needs vascular glomerulus // creates filtrate

renal tubules – long coiled tubes that convert the filtrate into urine

The structural nephron also requires a system of blood vessels in order to make urine. These blood vessels are closely associated with the tubular nephron.



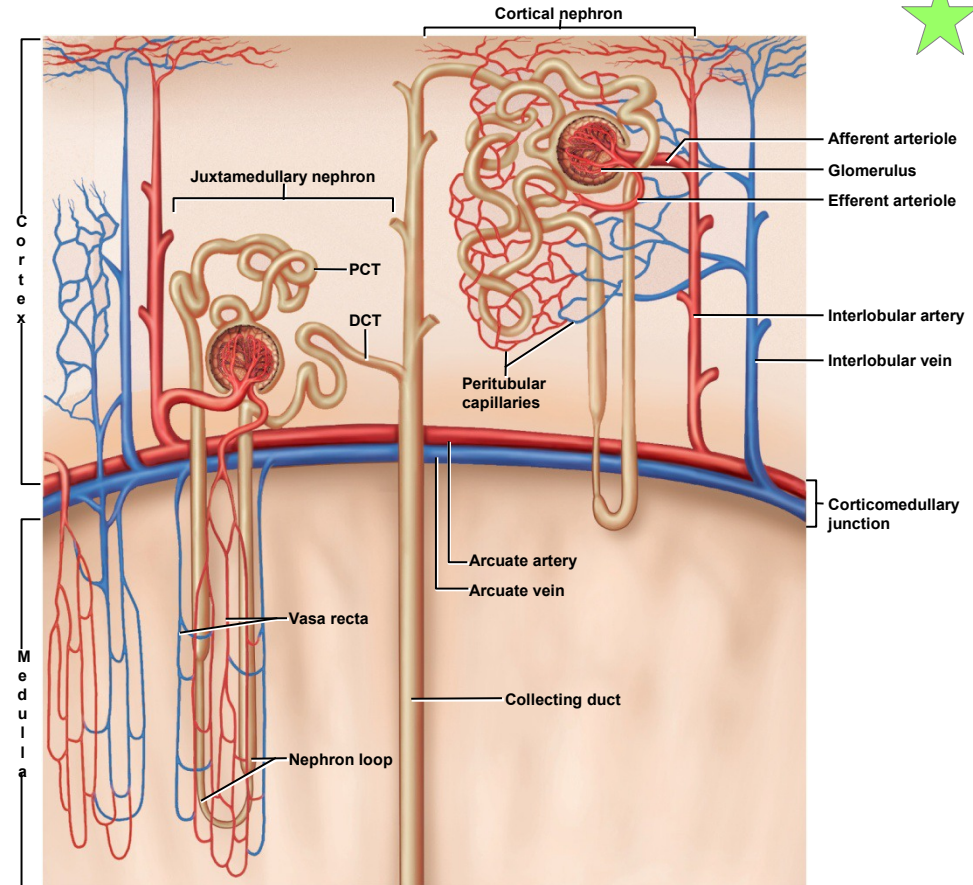
Proximal convoluted tubule (PCT)

arises from glomerular capsule

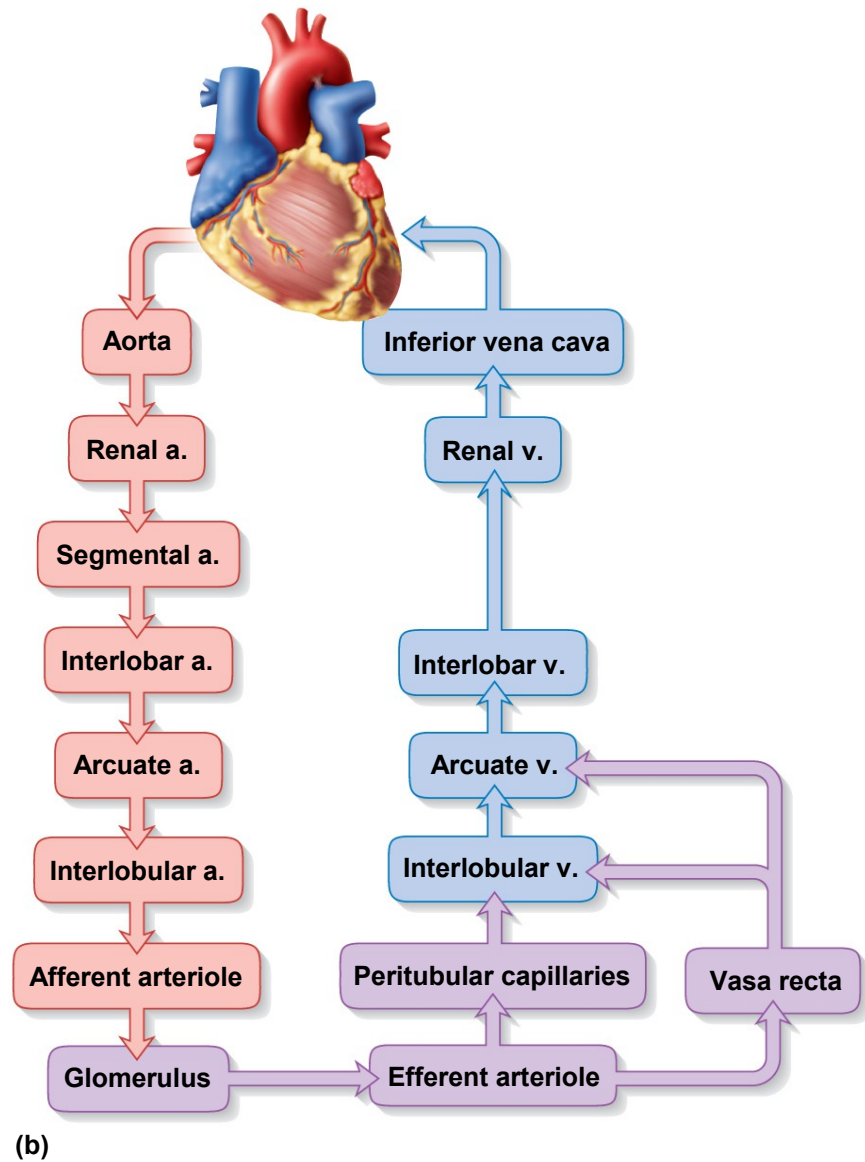
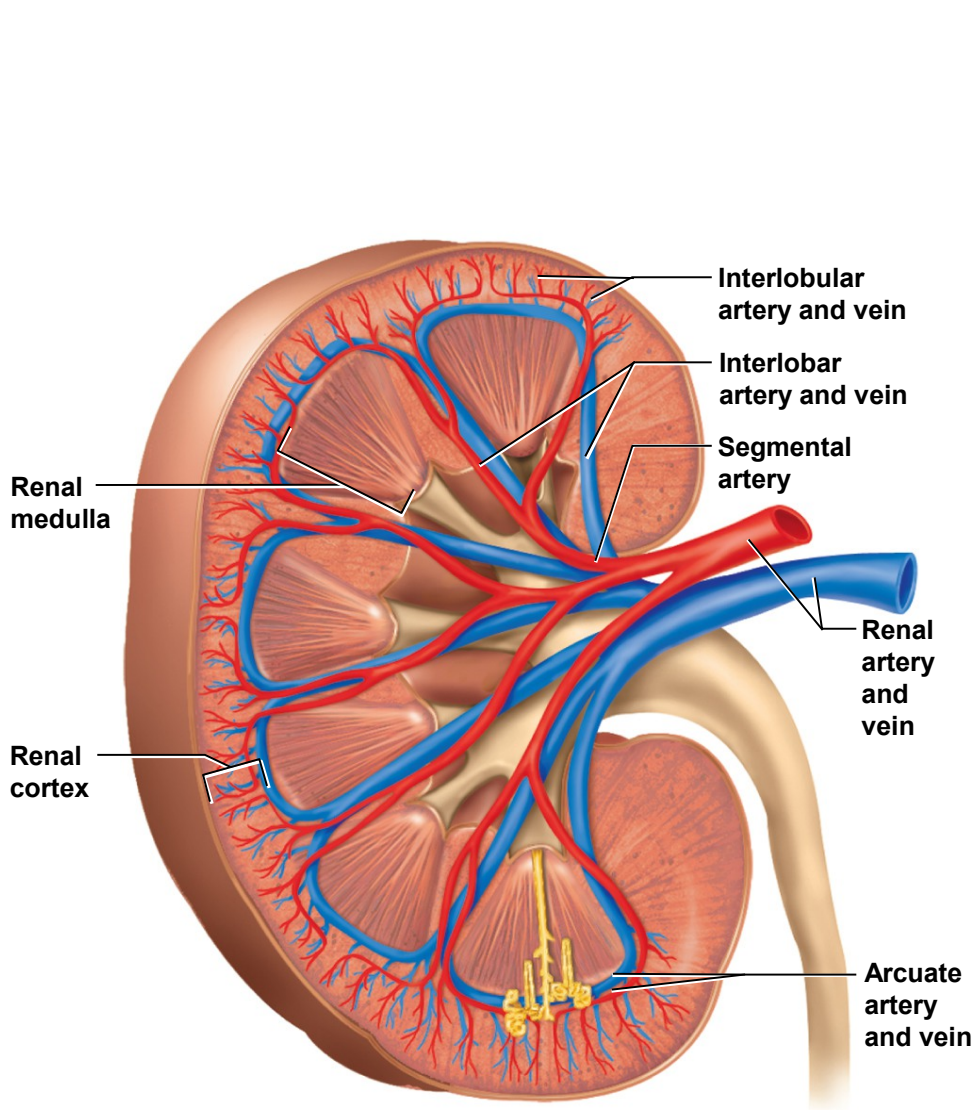
longest and most coiled region

simple cuboidal epithelium with prominent microvilli for reabsorption

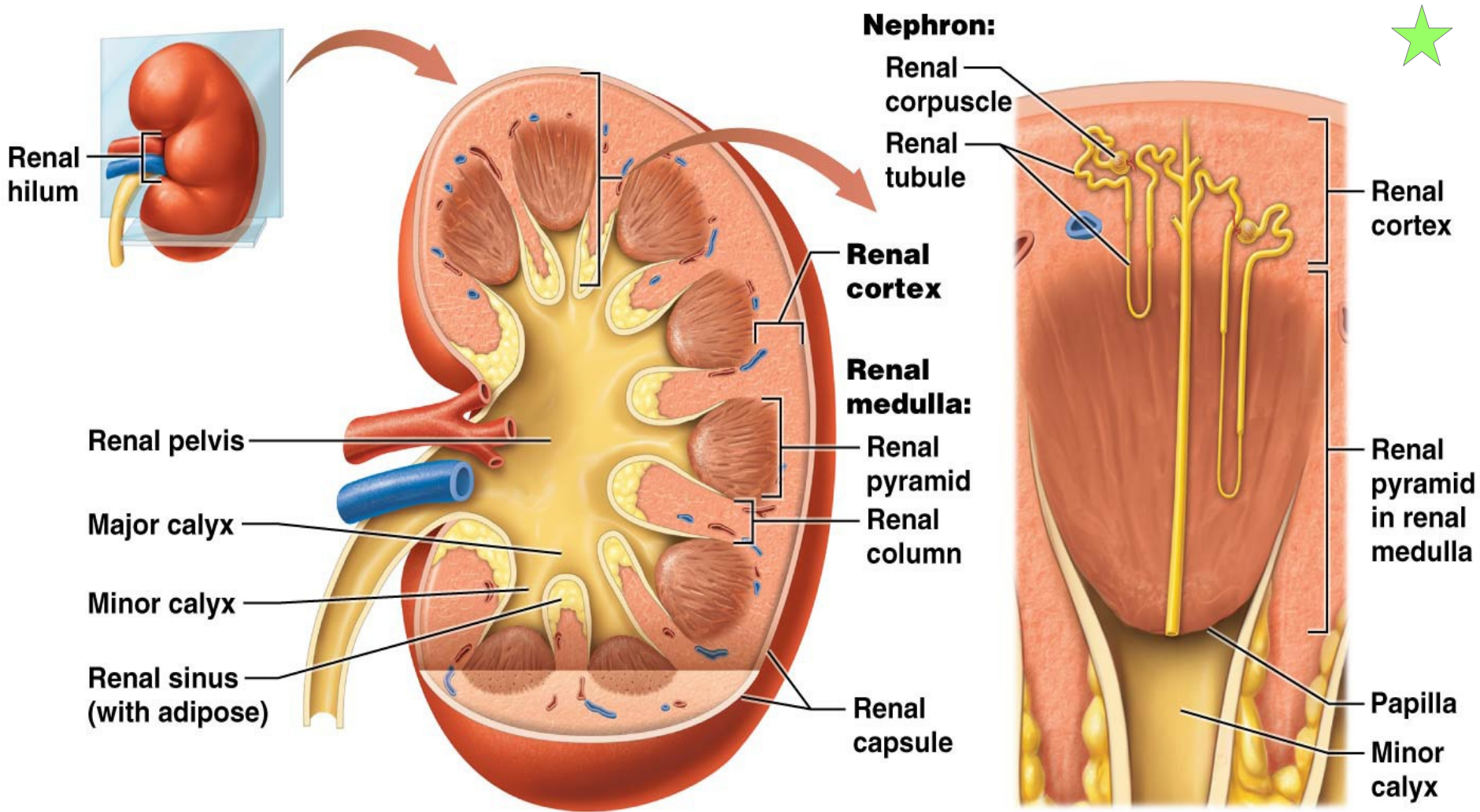
PCT of cortical nephrons responsible for most of the reabsorption of the filtrate



Blood Supply Diagram



kidneys receive 21% of cardiac output

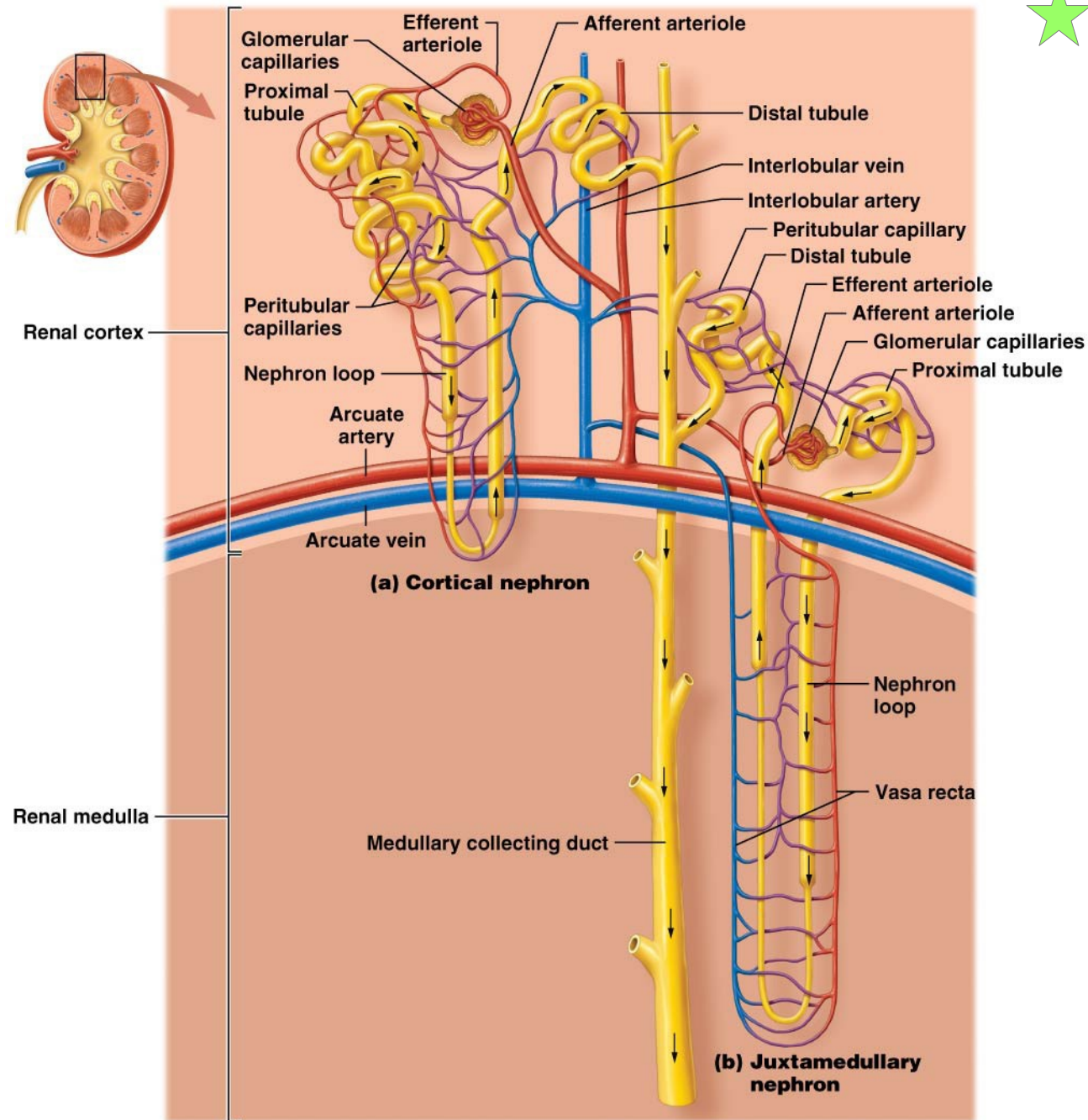


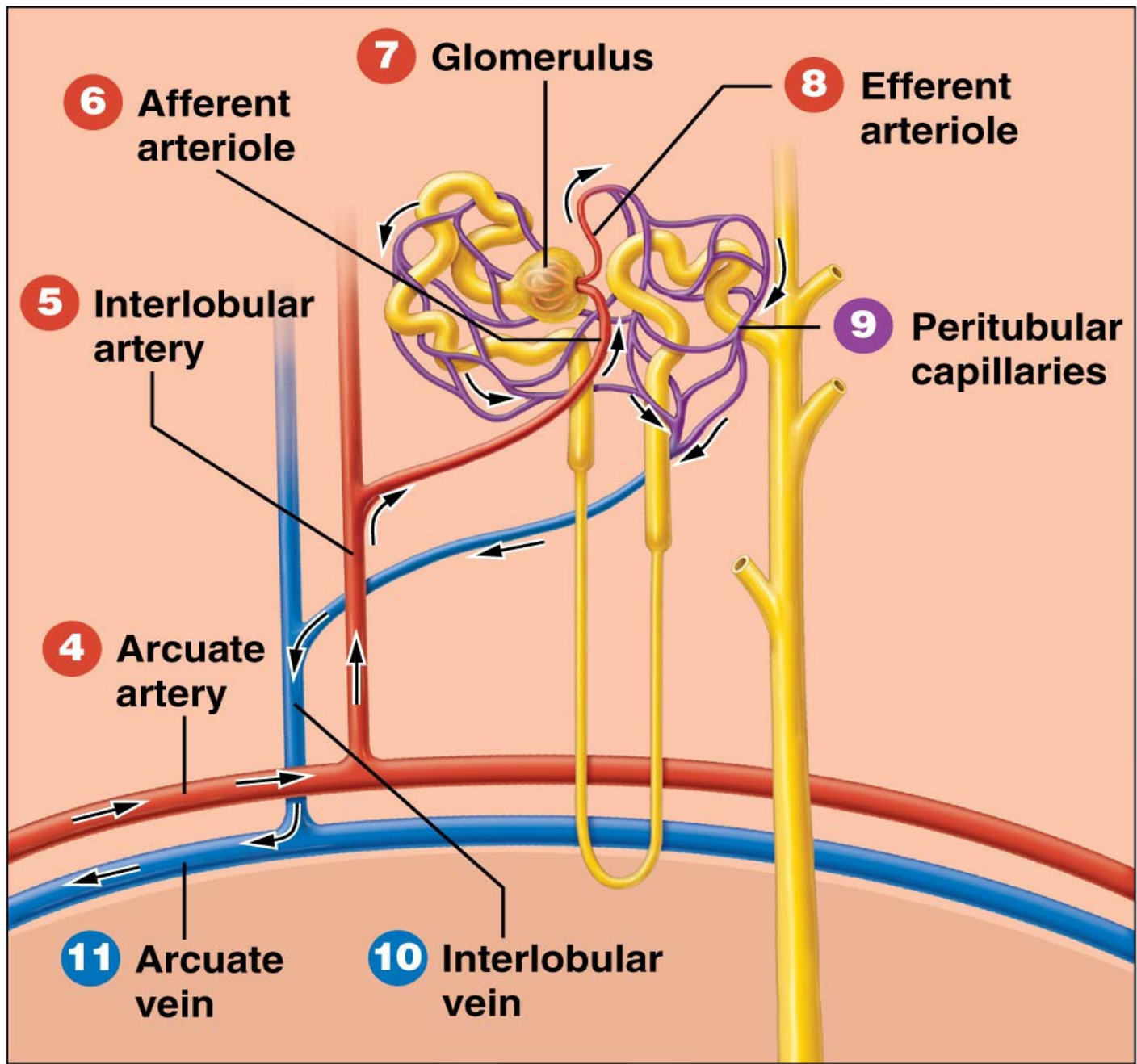
(a) Kidney, frontal section

(b) Section of the renal cortex and renal pyramid showing nephrons



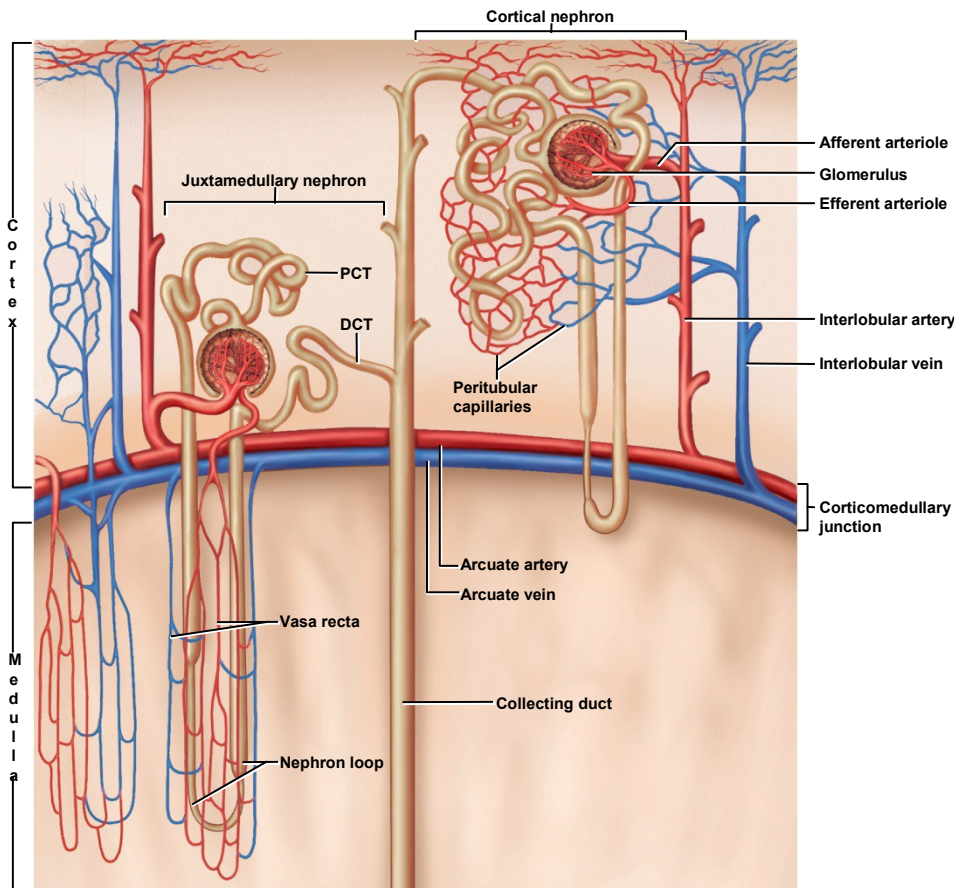
- Two nephron types
- **Cortical nephron** // receives 85% of blood /// responsible for producing most of the filtration volume
- **Juxtamedullary nephron** // responsible for making the deep medulla hypertonic





(b) Blood flow around nephron

The Nephron's Blood Vessels



The **functional nephron** requires a complex arrangement of blood vessels which interacts with the nephron at specific locations along the nephron.

Interlobular artery

afferent arteriole

glomerulus (capillaries)

efferent arteriole

(option #1) peritubular capillaries'
blood flows into interlobular vein then
into arcuate vein

(option #2) vasa recta capillaries'
blood flows into the arcuate vein

Interlobular vein

Distal Convolved Tubule

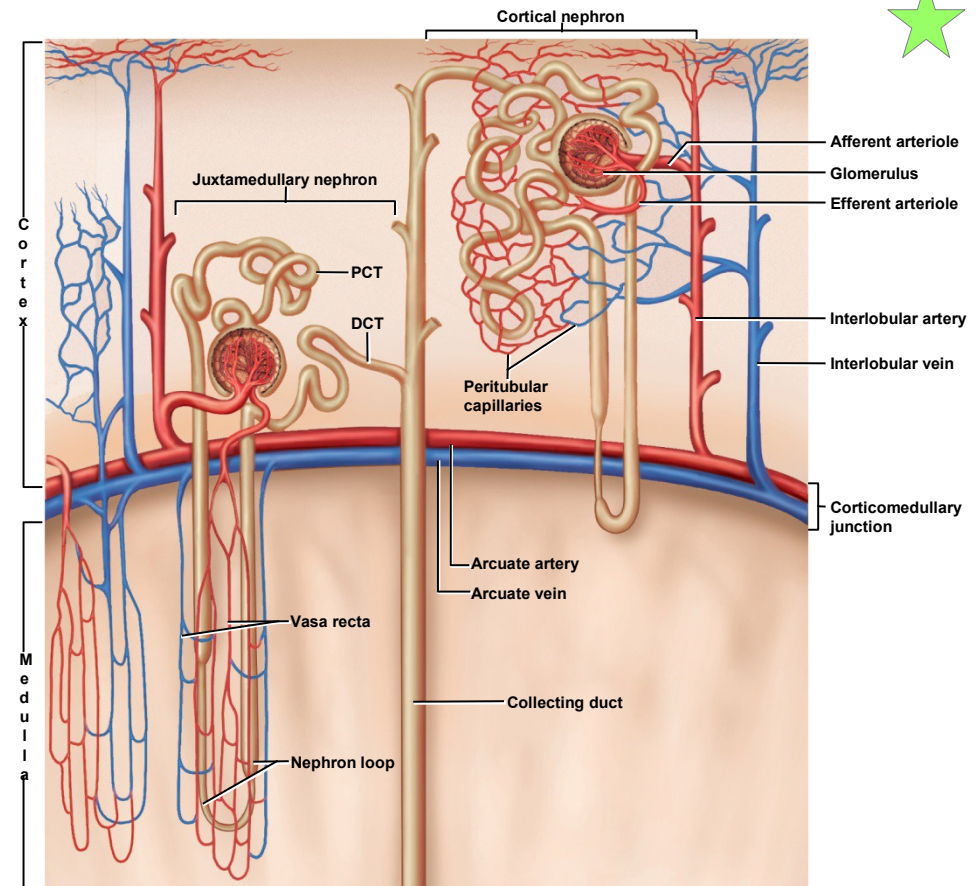
- many of the nephron's DCT will drain into a single collecting duct
- hormone receptors are found at the distal end of the distal convolved tubules of cortical nephrons

Collecting Duct

- hormone receptors are located in tubular collecting duct of cortical nephron
- **primary function is to conserve water** // antidiuretic hormone uses aquaporins to recover water // aldosterone recovers water by reabsorbing sodium ions

Loop of Henle

- counter current mechanisms in medulla recovers water from collecting duct and uses vasa recta capillaries to return water to systemic circuit.



Osmotic gradient in the cortex is 300 mOsm and deep in the medulla is 1,200 mOsm .

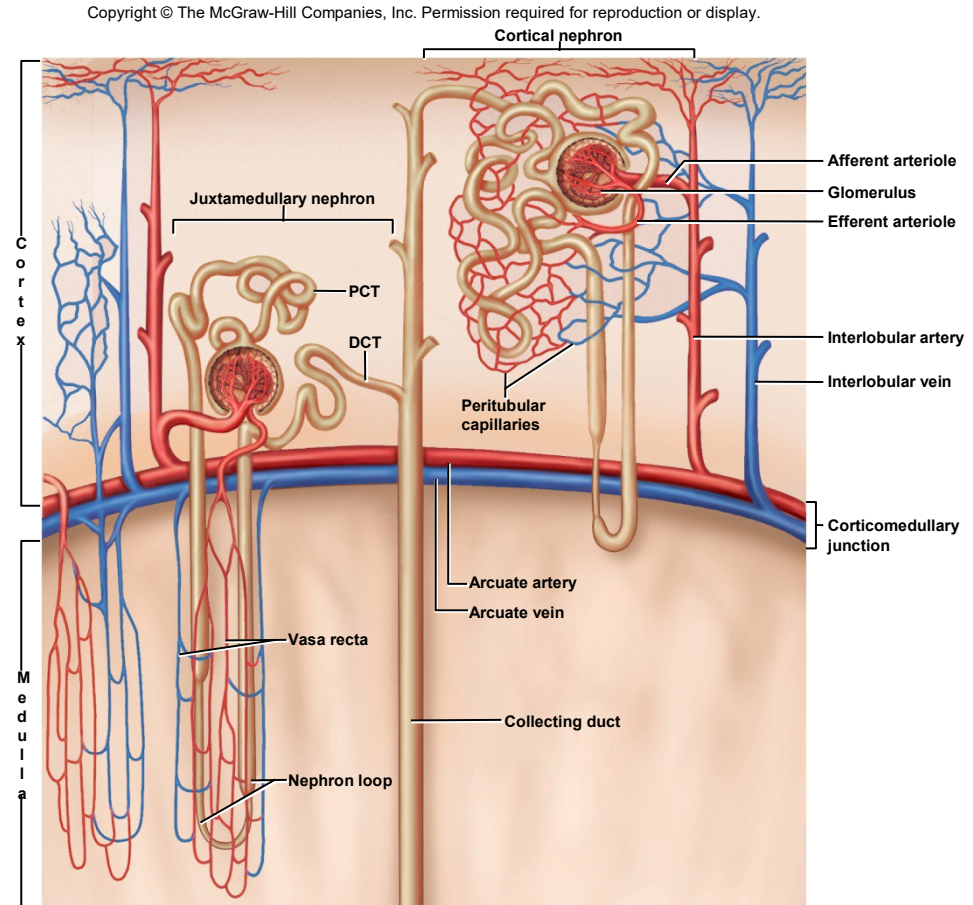
Why is this significant?

Think about why water may move across a plasma membranes!

What is the structure and function of the two capillary beds surrounding the nephron's tubules?



- In the cortex, **peritubular capillaries** branch off the cortical nephron's efferent arterioles // these capillaries surround the proximal and distal convoluted tubules // provide exchange of substances between blood and tubular fluid (filtrate)
- In medulla, **vasa recta capillaries** branch off the juxtamedullary nephron's efferent arteriole to form capillaries around loop of Henle // provide mechanism to create extreme **hypertonic** environment within the interstitial space (counter current multiplication and counter current exchange).

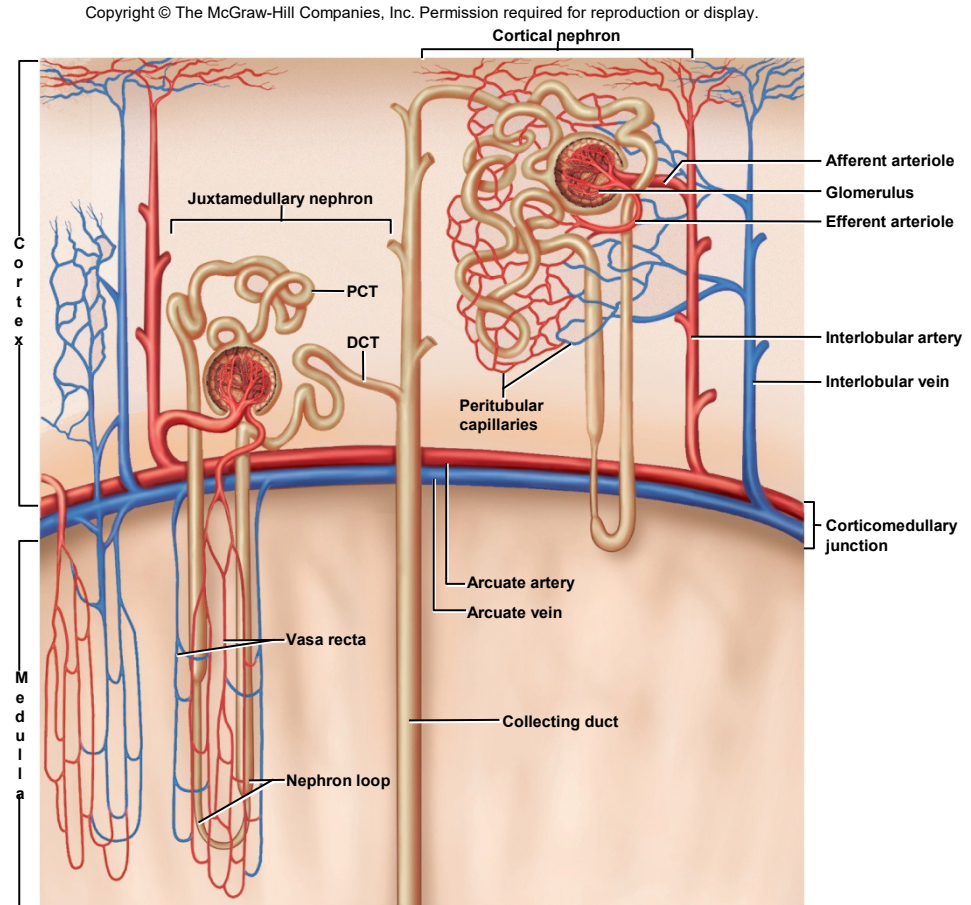


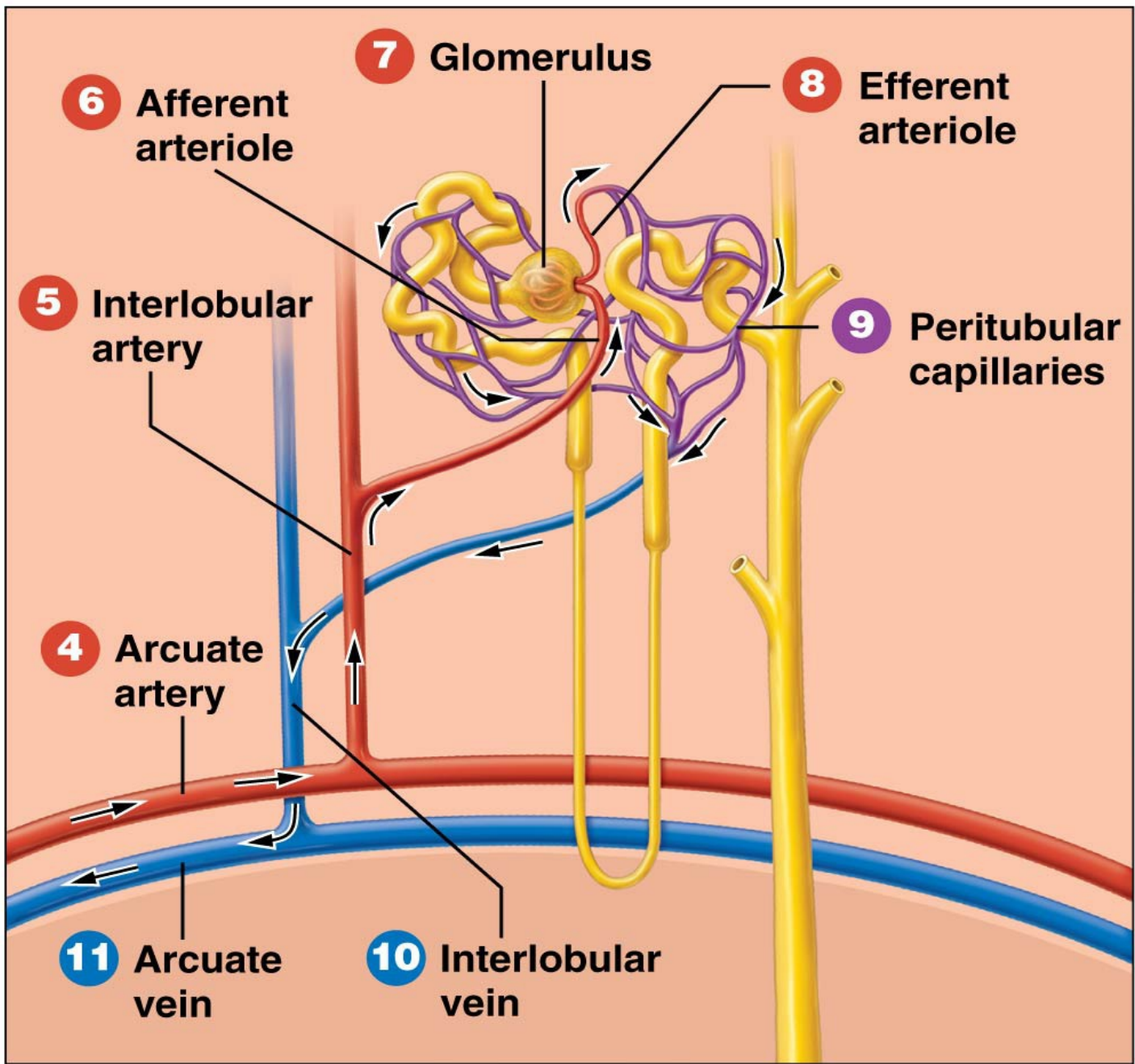
What is the structure and function of the two capillary beds surrounding the nephron's tubules?



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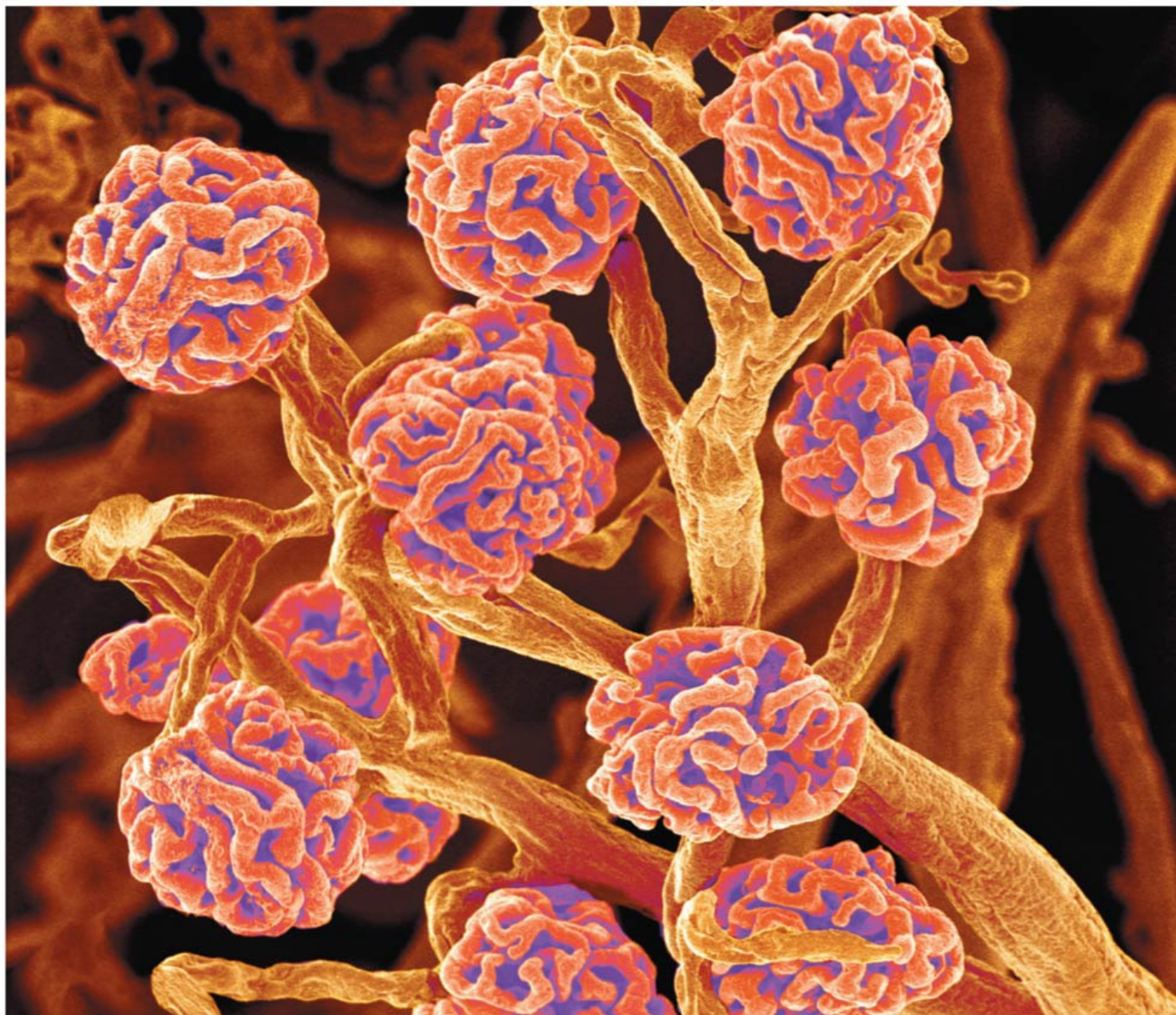
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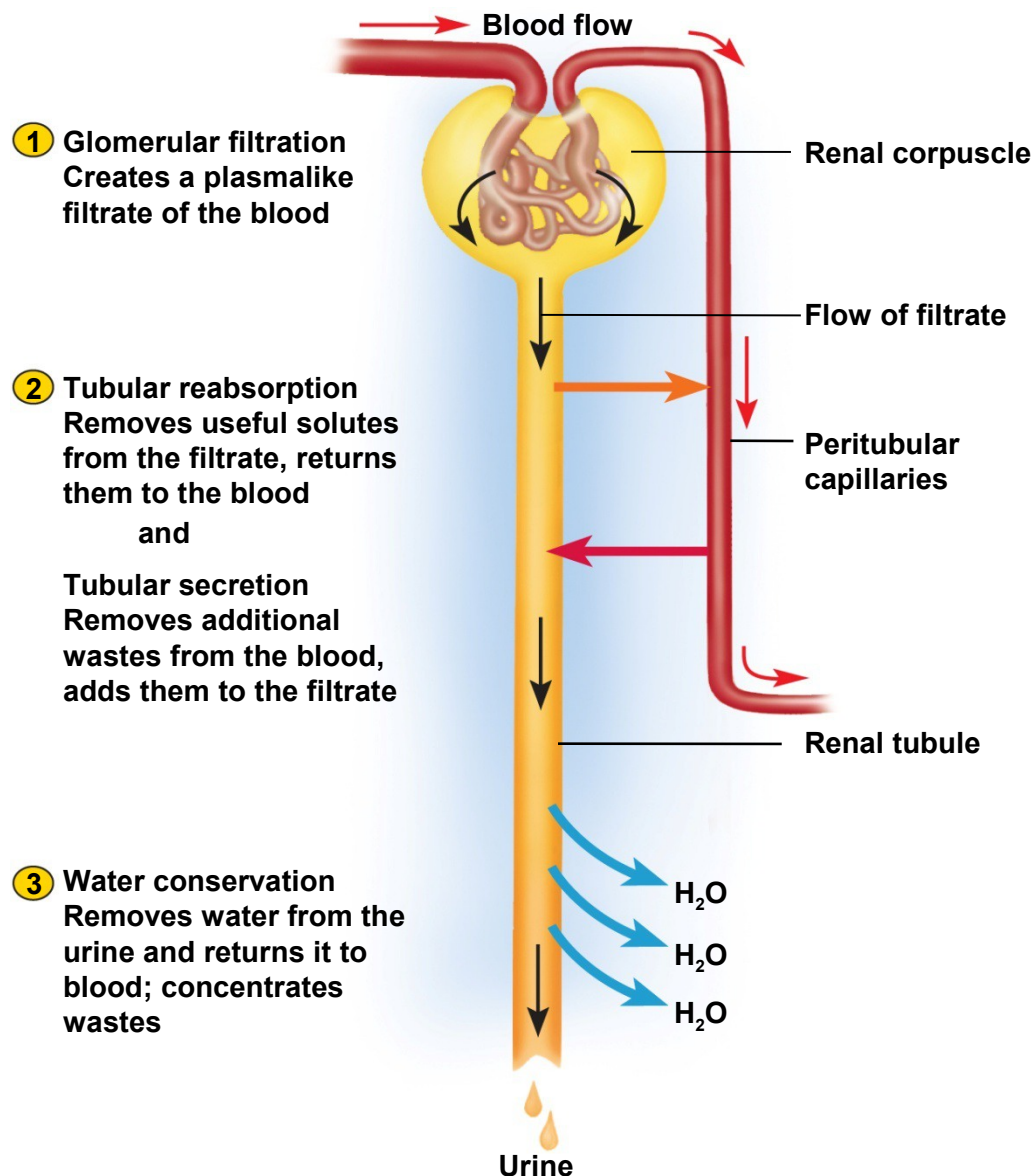


(b) Blood flow around nephron

This scanning electron micrograph shows glomeruli, the filtering units of the kidneys.



Overview of Urine Formation



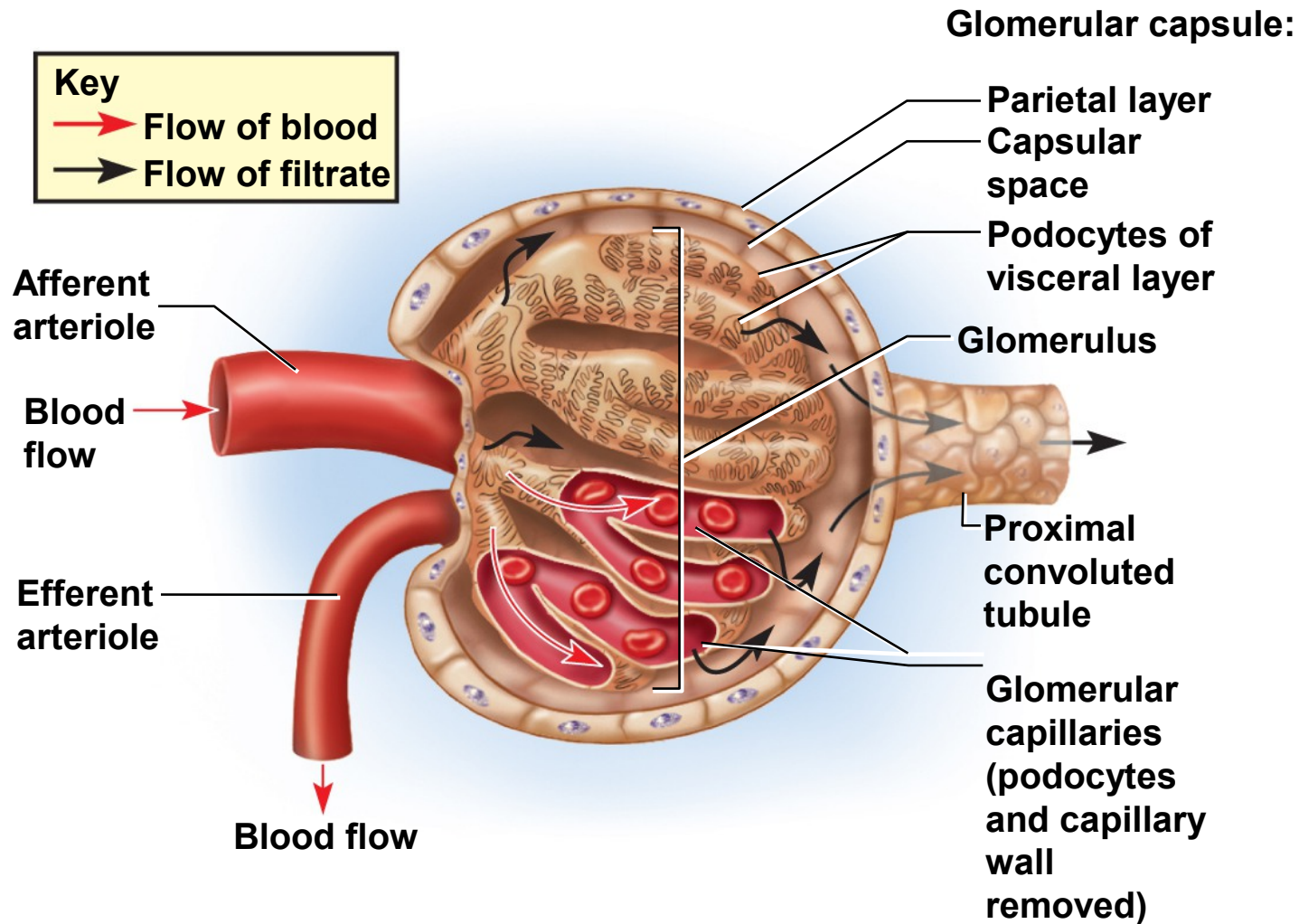
- kidneys convert's filtrate of blood plasma into urine in four stages
 - glomerular filtration
 - tubular reabsorption
 - tubular secretion
 - water conservation
- **glomerular filtrate** // fluid in capsular space // blood plasma without protein
- **tubular fluid** // fluid in renal tubule // starts as glomerular filtrate but tubular cells remove and add substances as fluid moves through tubules
- **urine** // once tubular fluid enters the collecting duct it is called urine // only remaining change is water conservation

Renal Tubules

This is the path for the flow of filtrate from the glomerular capillaries to the point where urine leaves the body:

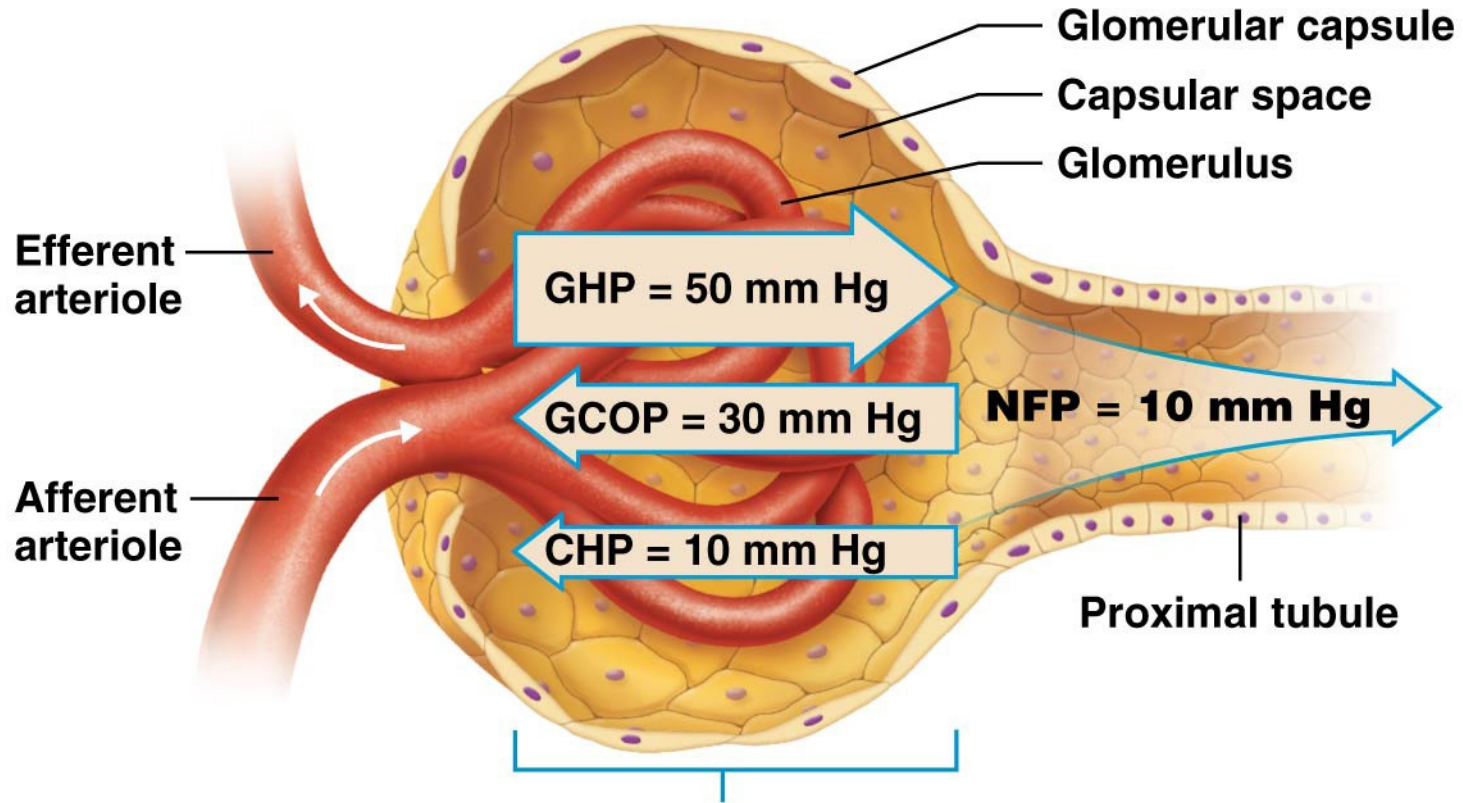
glomerular capsule →
proximal convoluted tubule →
nephron loop →
distal convoluted tubule →
collecting duct →
papillary duct →
minor calyx →
major calyx →
renal pelvis →
ureter →
urinary bladder →
urethra → (*pass urine from body*)

Renal Corpuscle = Glomerular Capsule + Glomerulus (capillaries)



- The glomerular filtrate collects in capsular space, flows into proximal convoluted tubule. /// Note the vascular and urinary poles. /// Note the afferent arteriole is larger than the efferent arteriole.

Net filtration pressure in the glomerular capillaries.

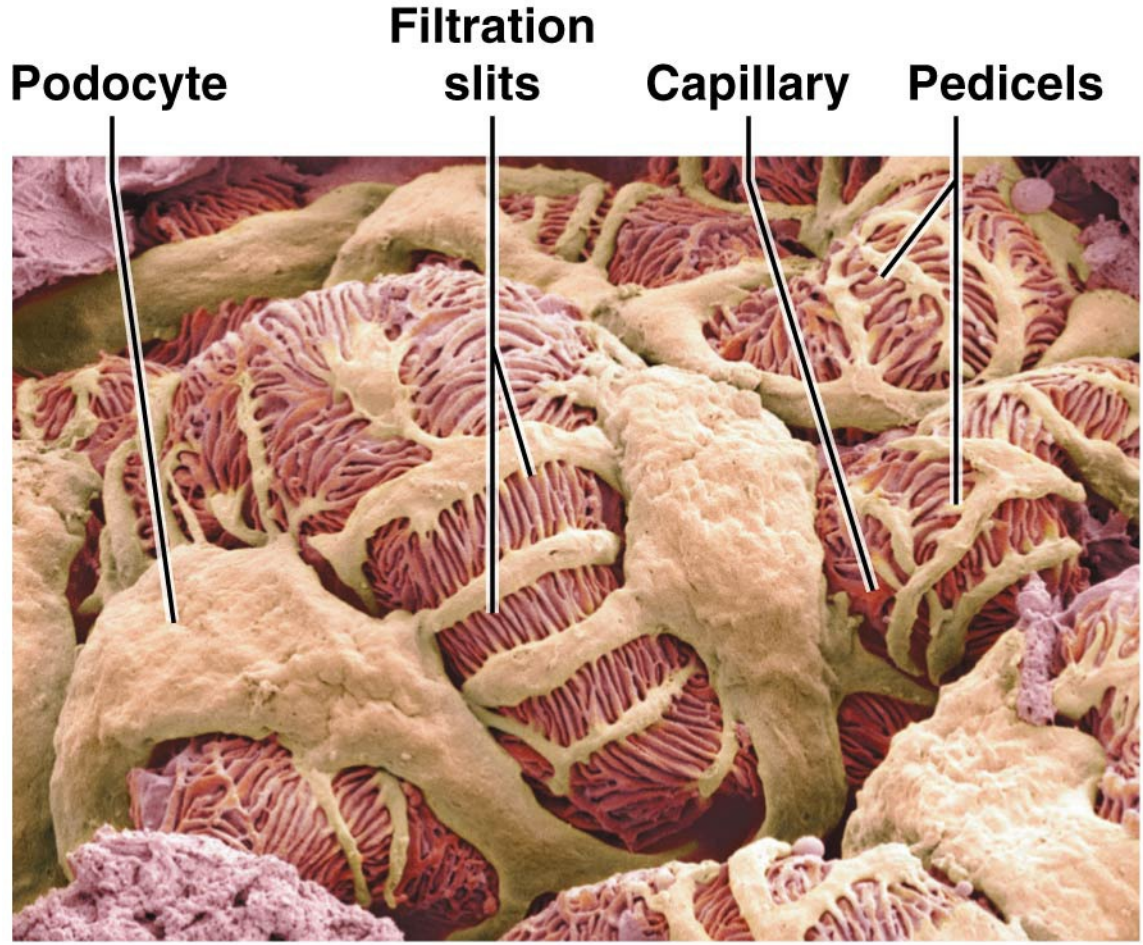


The three forces in the renal corpuscle = NFP

- Glomerular capillary hydrostatic pressure
- Glomerular capillary colloidal pressure
- Capsular space hydrostatic pressure

What is glomerular filtration rate (GFR)?

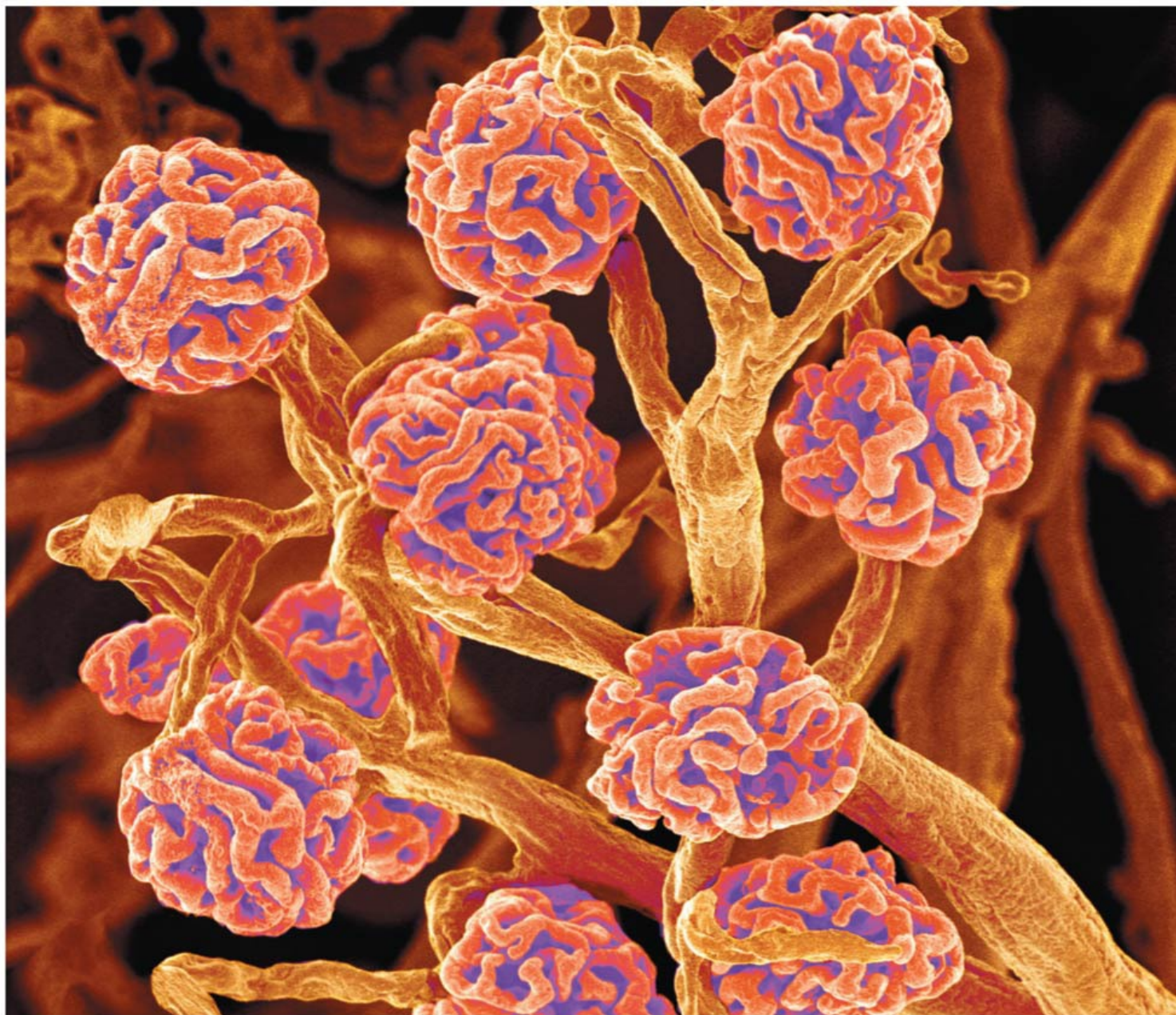
The renal corpuscle.



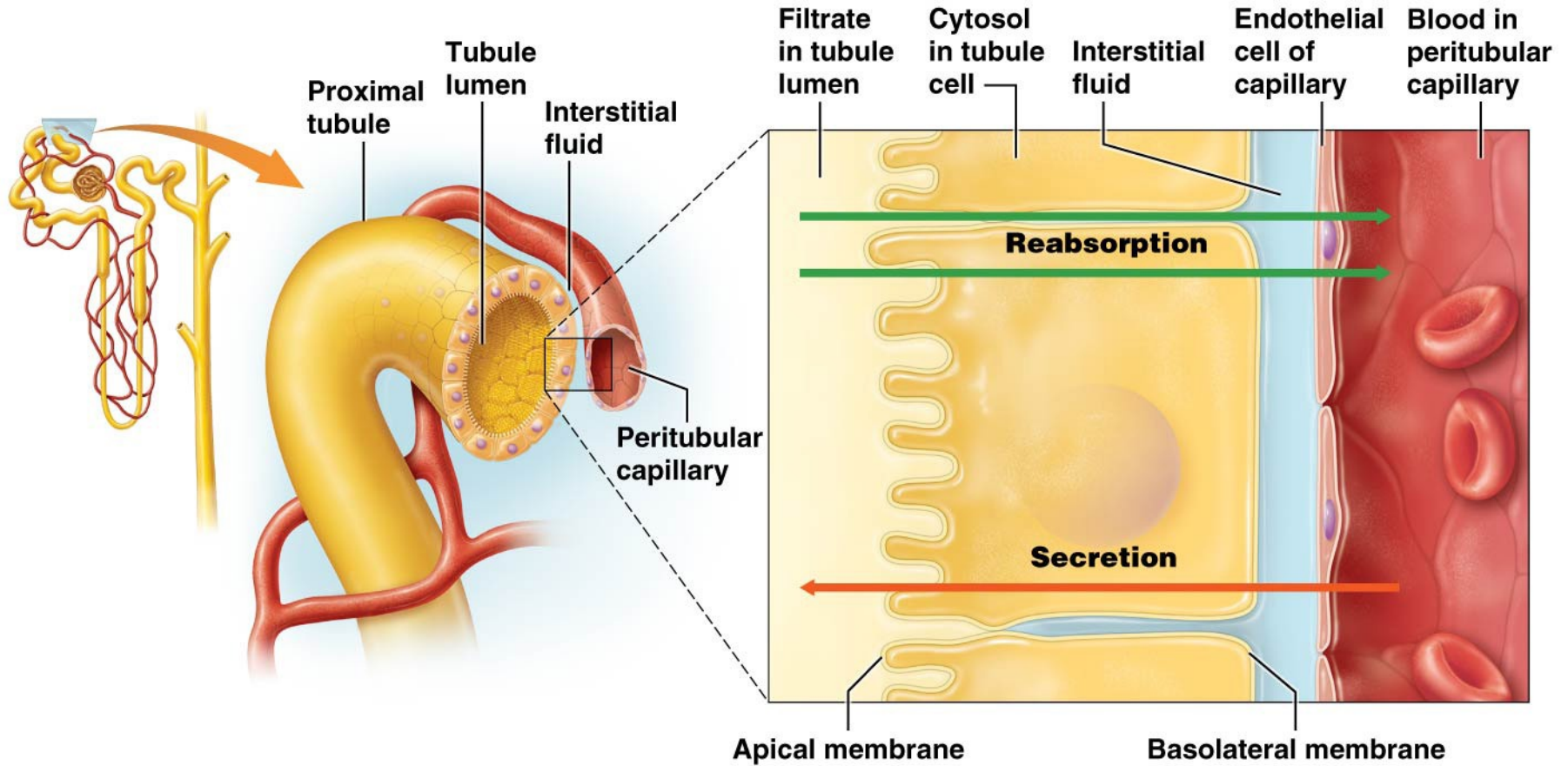
SEM (92,000x)

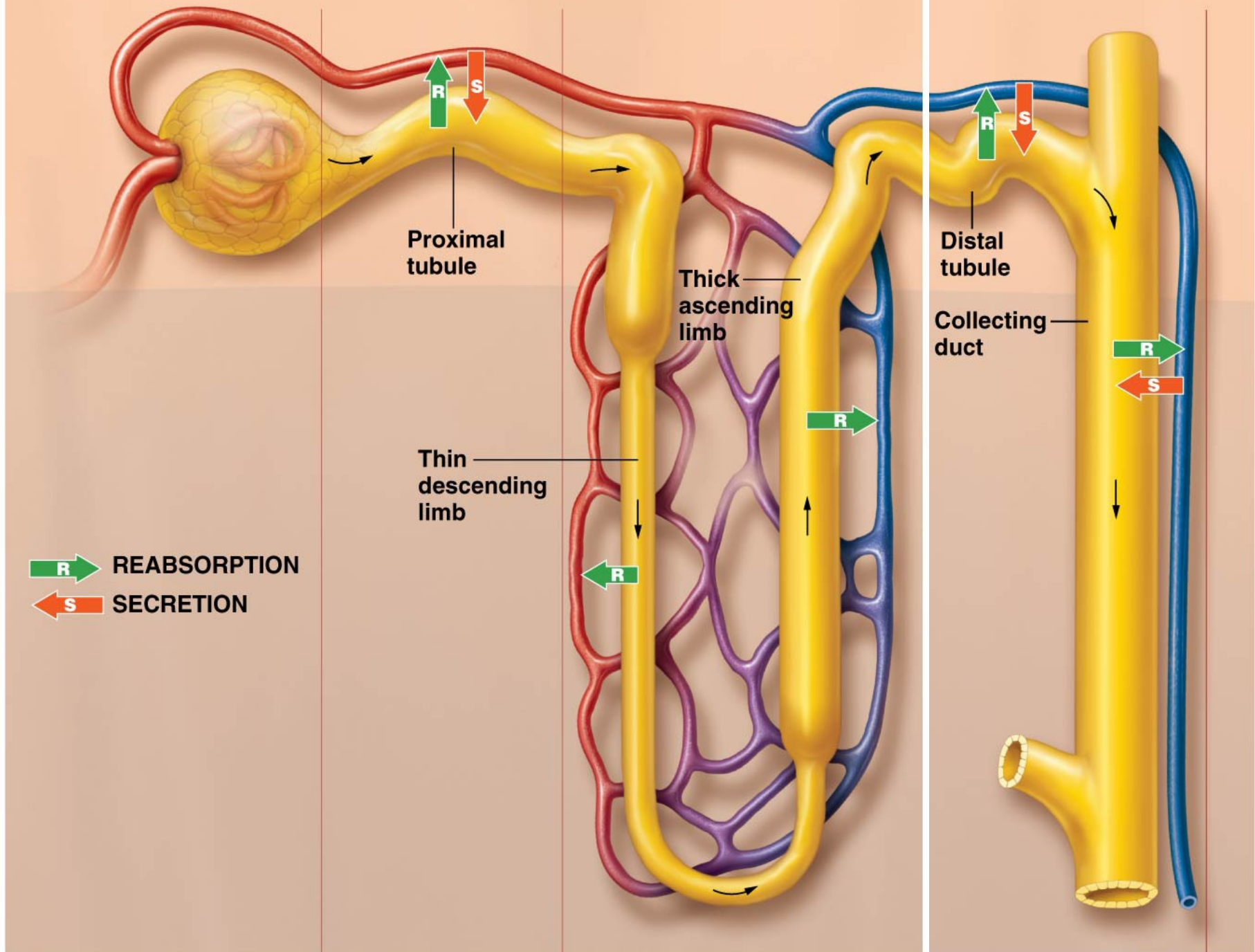
(b) SEM of capillary surrounded by podocytes



This scanning electron micrograph shows glomeruli, the filtering units of the kidneys.



Ttubular reabsorption and secretion.

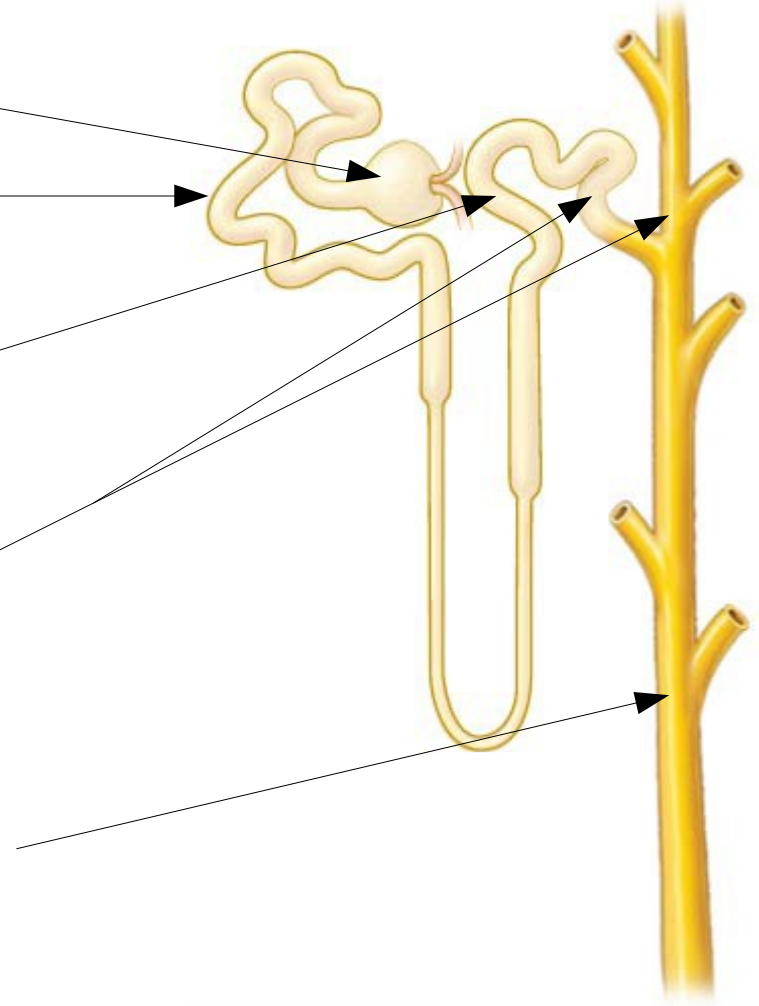




TUBULAR SEGMENTS	PROXIMAL TUBULE	NEPHRON LOOP		DISTAL TUBULE AND COLLECTING DUCT
		Thin descending limb	Thick ascending limb	
SUBSTANCES REABSORBED 	<ul style="list-style-type: none"> • 65% of H₂O in the filtrate • Nearly 100% of glucose, amino acids, and other organic solutes • About 90% of bicarbonate ions (HCO₃⁻) • 65% or more of Na⁺, K⁺, Ca²⁺, Cl⁻, and Mg²⁺ 	<ul style="list-style-type: none"> • 20% of H₂O in the filtrate 	<ul style="list-style-type: none"> • 25% of Na⁺ and Cl⁻ 	<ul style="list-style-type: none"> • Most of remaining H₂O • Nearly all of the remaining Na⁺, Cl⁻, and Ca²⁺ • Bicarbonate ions (HCO₃⁻)
SUBSTANCES SECRETED 	<ul style="list-style-type: none"> • Hydrogen ions (H⁺) • Nitrogenous wastes such as uric acid • Some drugs 			<ul style="list-style-type: none"> • K⁺ and H⁺ (regulated by hormones)

Where does filtration, reabsorption, and secretion occur?

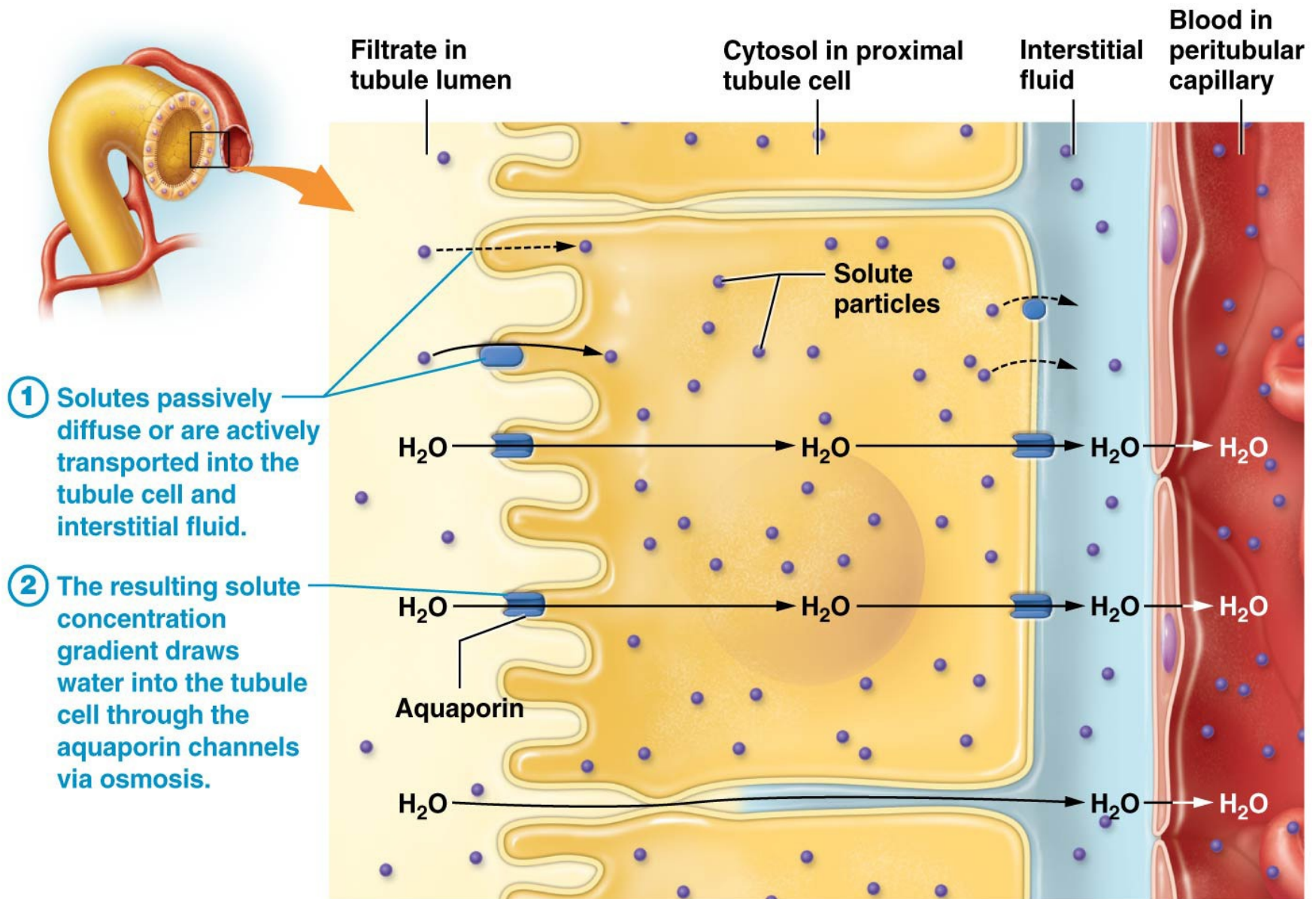
- Filtration occurs in the renal corpuscle.
- Most water and solute reabsorption (e.g. sodium) occur in the PCT of cortical nephrons // active co-transport mechanisms
- Some reabsorption and secretions occurs in the DCT of cortical nephrons.
- The DCT and cortical collecting duct have receptors for aldosterone and ADH. /// These areas able to reabsorb sodium and water using different mechanisms.
- Water reabsorption (water conservation) occurs by controlling the number of aquaporins in the collecting duct's plasma membrane /// aquaporins allow water to move into hypertonic area (deep medulla)





Water Reabsorption

- Kidneys receive 25% of cardiac output (kidney weighs 150 g)
- 180 L of water filtered in renal corpuscle
- 1.8 L of water leaves body as urine (1% of filtrate)
- **99% of filtered water is reabsorbed** and much of the solute (much of the water recovery is a direct consequence of sodium active transport within PCT)
- Kidneys use about 20% of the body's ATP at rest
- Water reabsorbed in the PCT is a **function of sodium co-transport mechanisms**. As solute is recovered, water molecules follow the sodium ions back into the peritubular capillaries. // obligatory water reabsorption



Obligatory water reabsorption in the proximal tubule.

Water Conservation

- The kidney must **eliminates metabolic wastes** from the body
- The kidney must also **prevent excessive water loss**
- Kidney must creates large volume of filtrate and return most of the water to the systemic circuit
- Any fluid not recovered will remain in the renal tubules and will pass into the collecting duct and exit body as urine /// may cause dehydration
- As water is conserved then the tubular fluid (i.e. the urine) is concentrated!
- Most of the filtrate is recovered in the proximal convoluted tubules

The Role of Sodium in Reabsorption

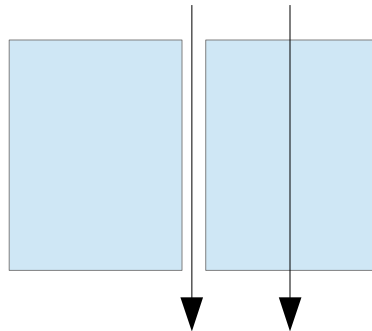
- Sodium reabsorption is used to reabsorb water and as a co-transporter to reabsorb other solutes in **PCT**
- In proximal convoluted tubules – Two types of transport proteins in the apical cell surface are responsible for sodium uptake
 - **symports** that simultaneously bind Na^+ and another solute such as glucose, amino acids or lactate
 - a **Na^+ - H^+ antiport** that pulls Na^+ into the cell (reabsorb) while pumping out H^+ (secretion) into tubular fluid
- Aldosterone receptors in **collecting duct** sodium activate transport mechanisms to recover sodium and water follows the sodium

Water Reabsorption

Kidney uses active transport mechanisms to reabsorb sodium in PCT reabsorption

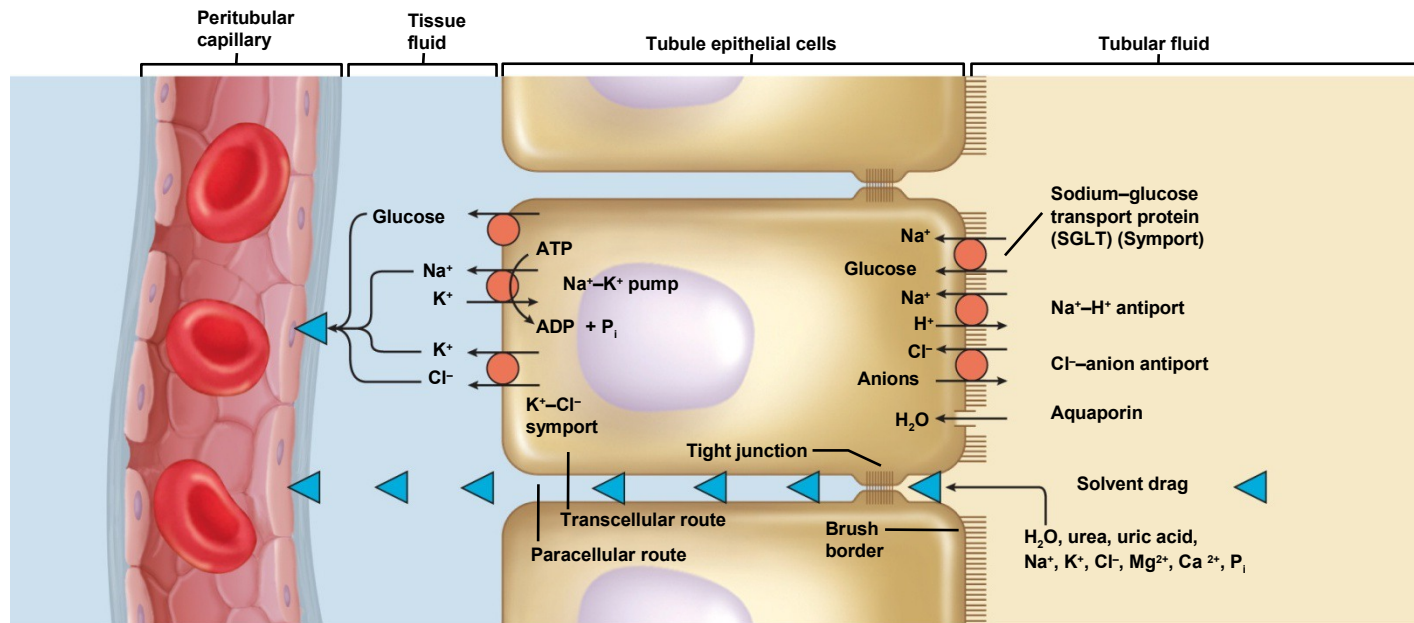
water follows solutes through paracellular and transcellular routes // transcellular route uses water channels called **aquaporins**

in PCT, water is reabsorbed at constant rate called obligatory water reabsorption

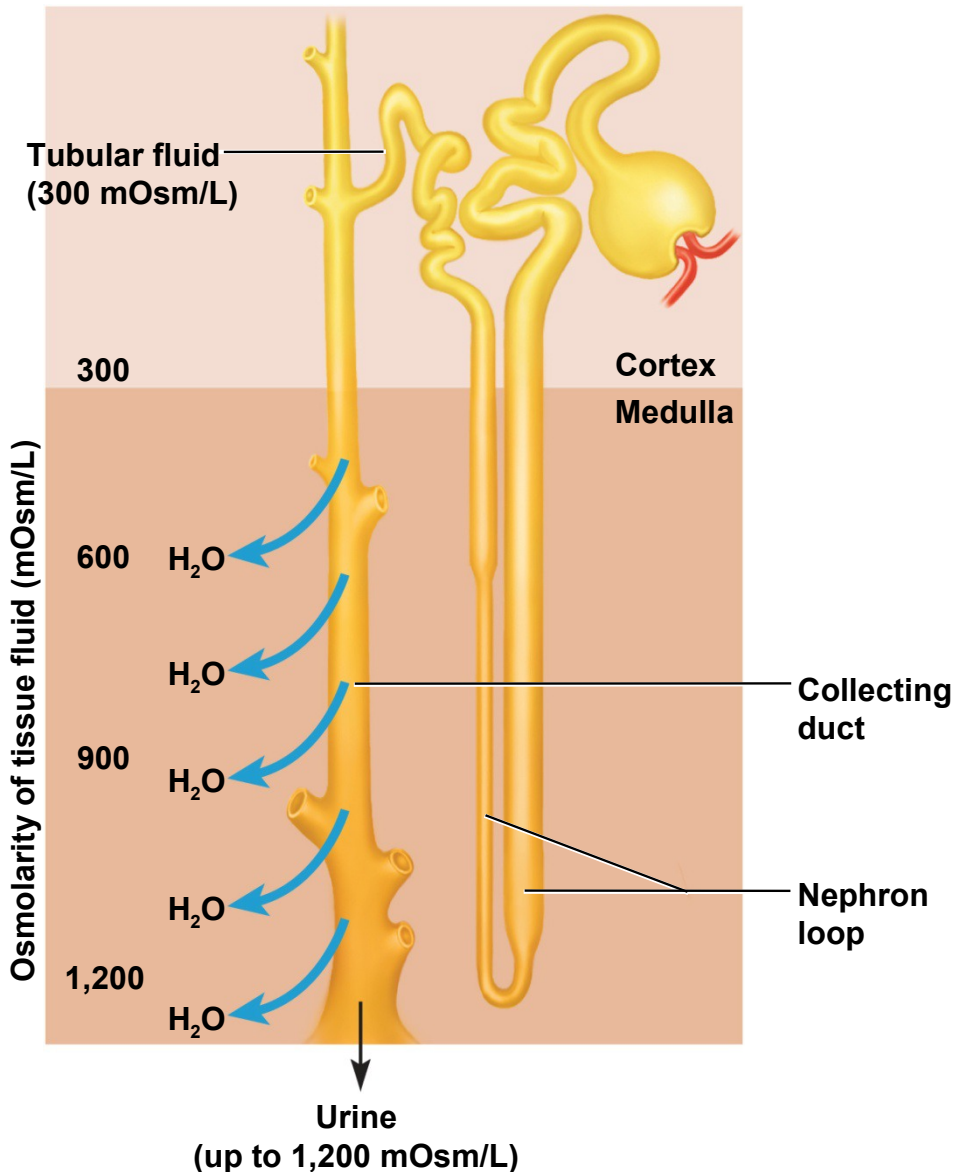


Reabsorption in the PCT

- potassium, magnesium, and phosphate ions diffuse through the paracellular route with water
- phosphate is cotransported into the epithelial cells with Na^+
- some calcium is reabsorbed through the paracellular route in the PCT, but most Ca^{+2} occurs later in the nephron
- urea diffuses through the tubule epithelium with water – reabsorbs 40 – 60% in tubular fluid /// **kidneys remove about half of the urea from the blood - creatine is not reabsorbed at all**



Water Reabsorption at the Collecting Duct



- collecting duct (CD) begins in the cortex where it **receives tubular fluid from many nephrons**
- as dilute urine passes through CD into the medulla, water is **reabsorbed and urine is concentrated**
- medullary portion of CD is more permeable to water than to NaCl
- Deeper in the medulla the interstitial space becomes more hypertonic // aquaporins allow for osmosis /// further concentrates urine
- This process is regulated by hormones with receptors located at the end of the distal convoluted tubules and cortical portion of the collecting duct
- Function of antidiuretic hormone and aldosterone will be covered in another section

Control of Water Loss

- *Urine volume depends on the status of your hydration.*
- Water diuresis – drinking large volumes of water will produce a large volume of **hypotonic urine**
- If you do not hydrate then the kidneys will produce a low volume of **hypertonic urine**.

Control of Water Loss



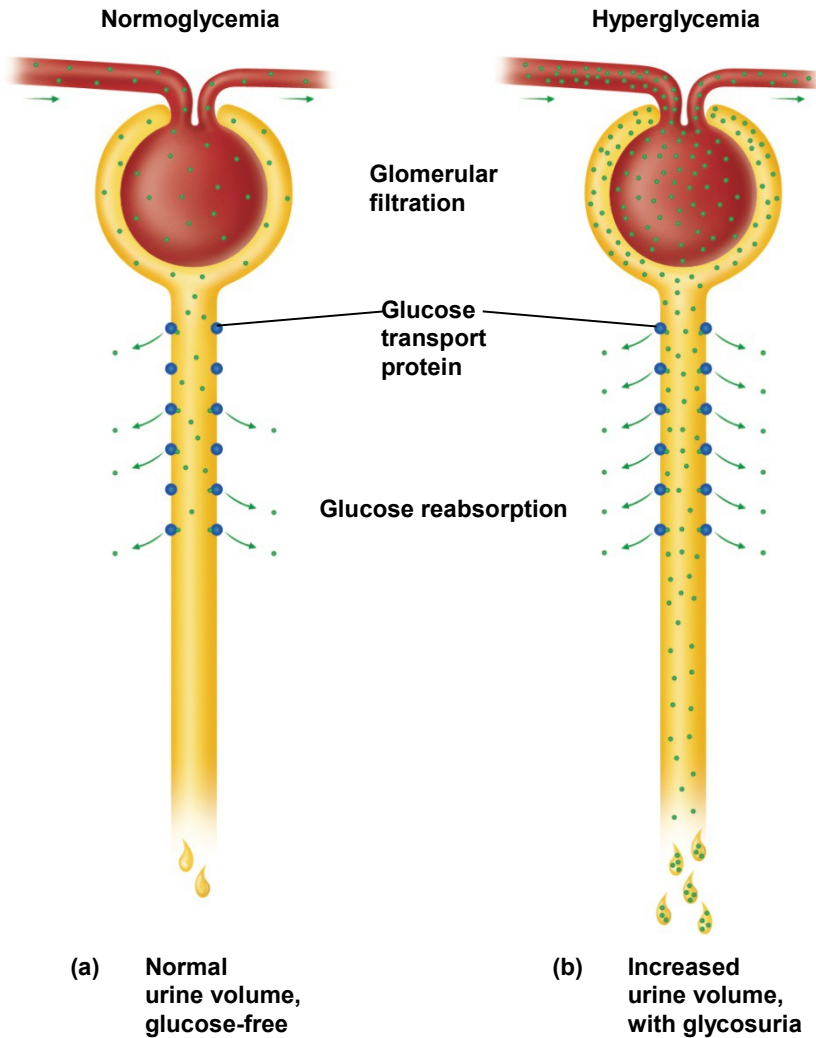
- What will cause urine to be hypertonic?
 - dehydration will cause a low urine volume and it will be more concentrated // darker color
 - dehydration will also cause high blood osmolarity. // High blood osmolarity will stimulate posterior pituitary to **release ADH** /// result in an increase in the number of **aquaporin channels** placed in the collecting duct
 - water moves through the aquaporin channels and is reabsorbed from collecting duct into interstitial space /// water moves from interstitial space into vasa recta /// this returns water to systemic circuit
 - urine becomes more concentrated in this process
- **If BP is low in a dehydrated person, Glomerular Filtration Rate will also be low** /// filtrate now moves more slowly through nephron and there is more time for reabsorption /// more salt reabsorbed with water following the ions /// net result is more water reabsorbed and **less urine is produced but more concentrated (i.e. darker color)**

Control of Water Loss



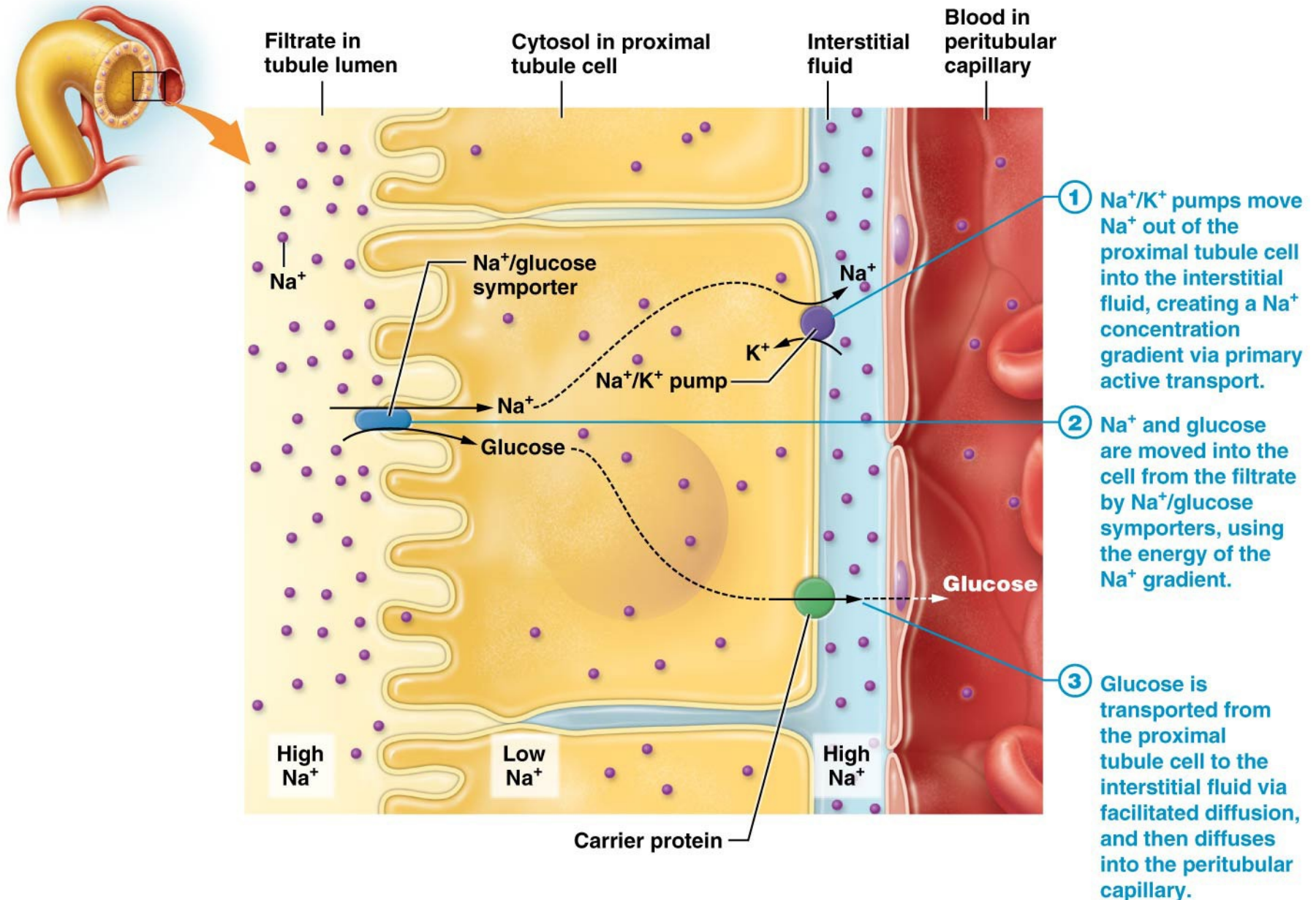
- *The amount of solids in the urine (i.e. urine concentration) depends on body's state of hydration:*
 - water diuresis – drinking large volumes of water will produce a large volume of **hypotonic urine**
 - cortical portion of CD reabsorbs Na and Cl ions, but it is impermeable to water
 - salt removed from the urine // water stays in the CD
 - urine concentration may be as low as 50 mOsm/L in cortical portion of CD

Glucose Reabsorption and the Glucose Transport Maximum



- Glucose can only be “reabsorbed” in the proximal convoluted tubules
- Glucose uses a symport for secondary co-transport
- Limited number of symports // under normal blood glucose concentration (70 – 100 mg/dL) symports able to capture all glucose
- If blood glucose concentration exceeds glucose transport maximum (T_m) then some glucose will pass PCT
- Now glucose becomes an osmotic diuretic // explain
- Blood glucose concentrations above 220 mg/dL causes glycosuria
- Doctor's use to taste urine to see if patients were diabetic

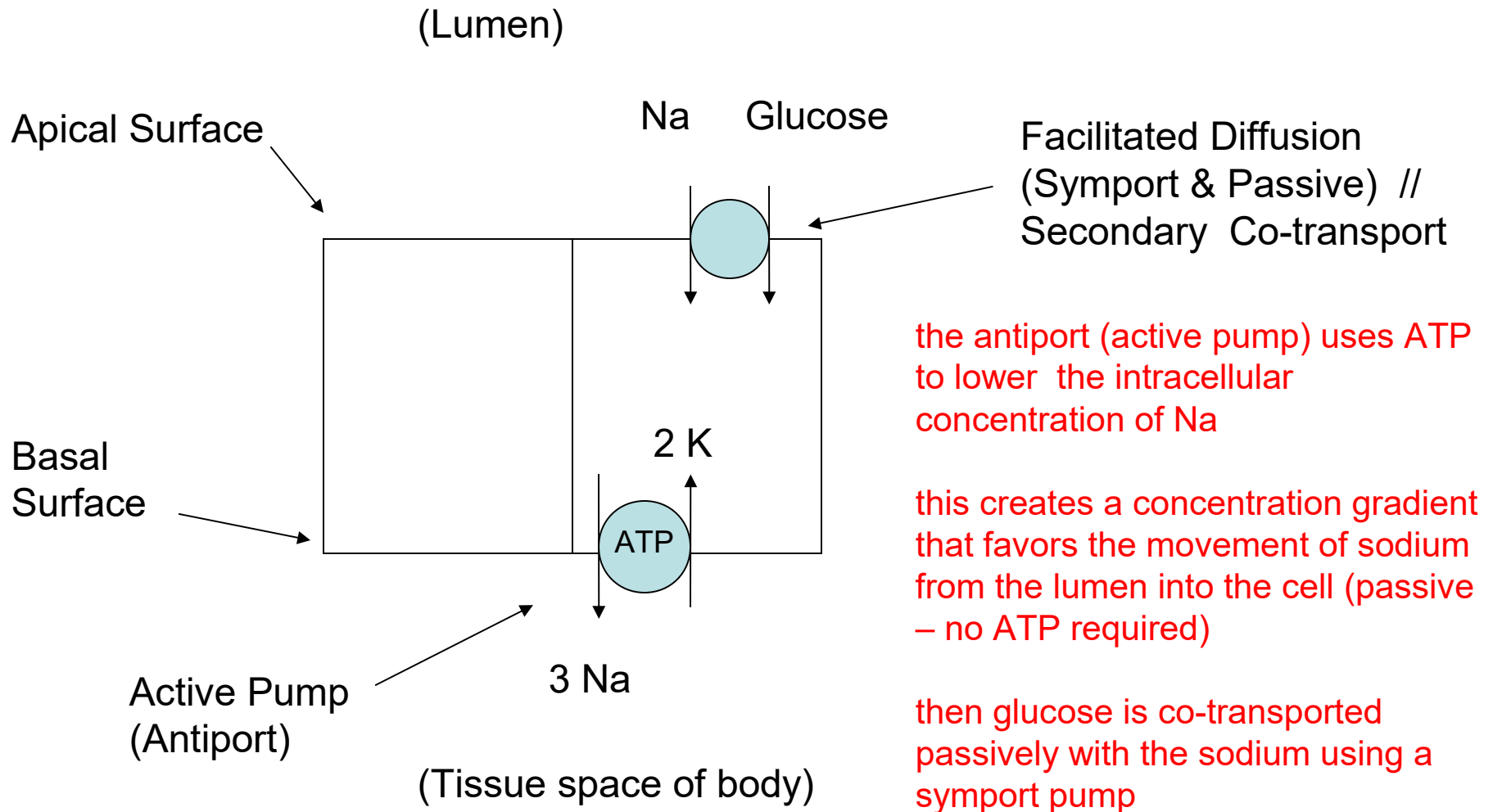
Glucose reabsorption in the proximal tubule.





Secondary Co-Transport

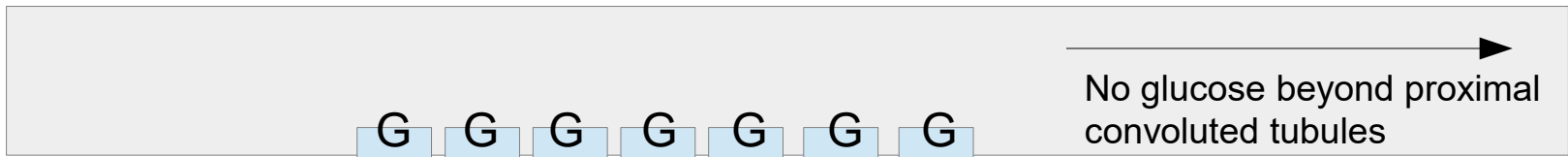
(Powered by the Sodium Potassium ATP Pump)



What is the Significance of the Glucose Transport Maximum? (Glucose Tm)



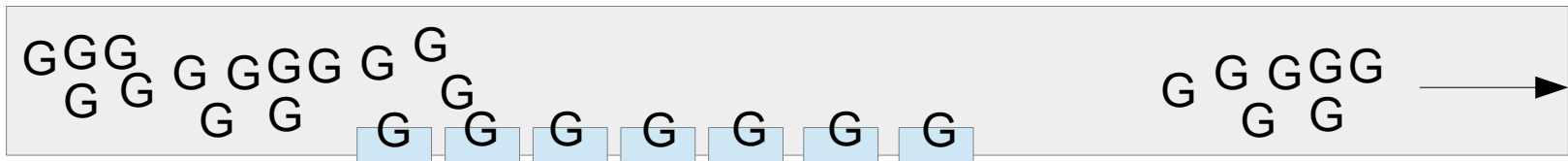
Enough transporters to capture all glucose // These glucose transporters only in PCT



All glucose reabsorbed

Blood glucose concentration exceeds Tm

Glucose not captured now pass proximal convoluted tubules

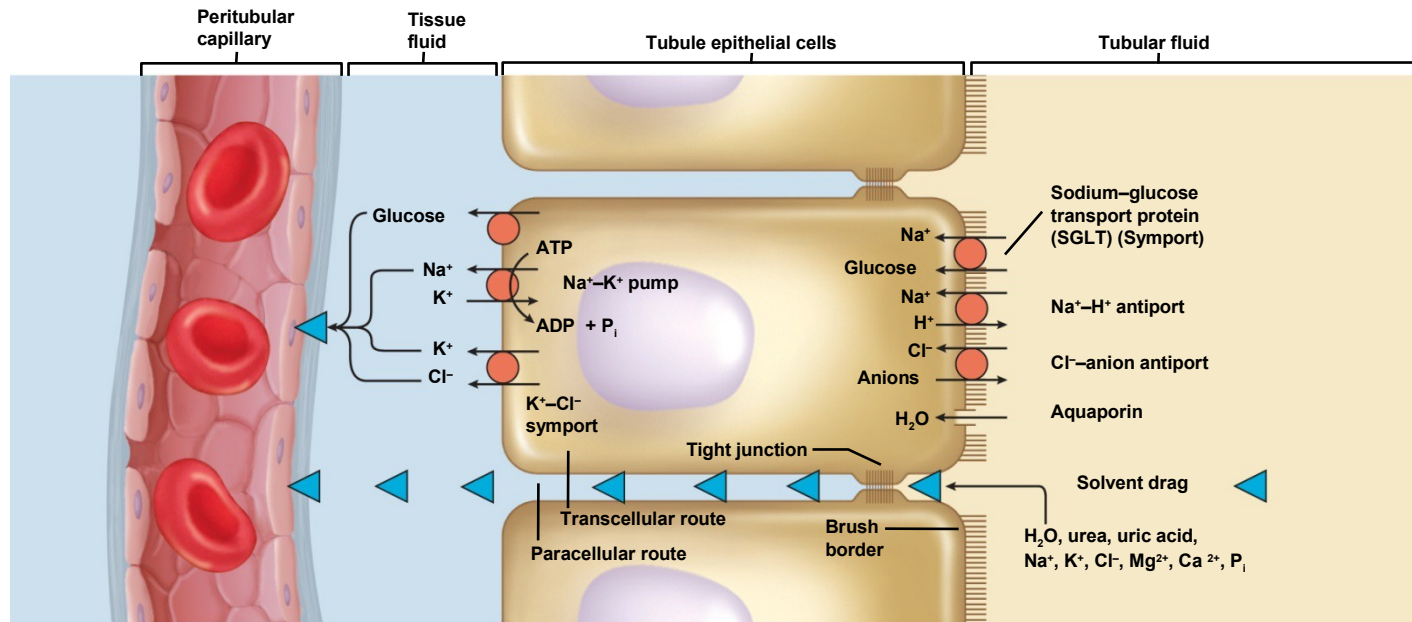


Some glucose reabsorbed

These glucose molecules "spill" into urine and may now be called an osmotic diuretic. Why?

Other Ions, and Urea Reabsorption in the PCT

- potassium, magnesium, and phosphate ions diffuse through the paracellular route with water
- phosphate is cotransported into the epithelial cells with Na^+
- some calcium is reabsorbed through the paracellular route in the PCT, but most Ca^{+2} occurs later in the nephron
- urea diffuses through the tubule epithelium with water – reabsorbs 40 – 60% in tubular fluid /// kidneys remove about half of the urea from the blood - creatine is not reabsorbed at all





Urine Volume Is Influenced By Glomerular Filtration Rate

- Glomerular filtration rate is 125 ml/min (180 L per day)
 - this filtration rate is regulated by **autoregulation, autonomic nervous system, and hormones**
 - GFR is important because **this volume** of filtrate is necessary in order for kidneys to eliminate metabolic waste from blood
- **If GFR too high**
 - fluid flows through the renal tubules too rapidly /// unable to reabsorb the usual amount of water and solutes
 - urine output rises
 - greater chance of dehydration and electrolyte depletion
- **If GFR too low**
 - wastes not filtered
 - wastes stay in plasma
 - azotemia may occur (i.e. high nitrogen concentration in blood)

This is why we need to regulate GFR!

Can you explain a similar logic about cardiac output and tidal volume?



Regulation of Glomerular Filtration

GFR controlled by adjusting glomerular blood pressure from moment to moment

GFR regulated by three homeostatic mechanisms

- renal autoregulation (myogenic or tubuloglomerular feedback)
- sympathetic nervous system control
- hormonal control

Renal Autoregulation of GFR (1 of 7)

- Renal autoregulation
 - the ability of the nephrons to adjust blood flow and GFR without external control (nervous or hormonal)
 - enables nephron to maintain a relatively stable GFR in spite of changes in systemic arterial blood pressure
 - two methods of autoregulation
 - myogenic mechanism
 - tubuloglomerular feedback



Renal Autoregulation of GFR by Myogenic Mechanism

- **Myogenic mechanism** // based on the tendency of smooth muscle to contract when stretched
 - increased arterial blood pressure /// the afferent arteriole stretches this causes a response
 - arteriole constricts and prevents blood flow into the glomerulus /// this prevents change in filtration rate
 - but when blood pressure falls /// the afferent arteriole relaxes this causes a response
 - arterioles dilate /// allows blood to flow more easily into glomerulus // more filtration
 - **overall – the GFR remains stable**

Renal Autoregulation of GFR by Tubuloglomerular Feedback Mechanism

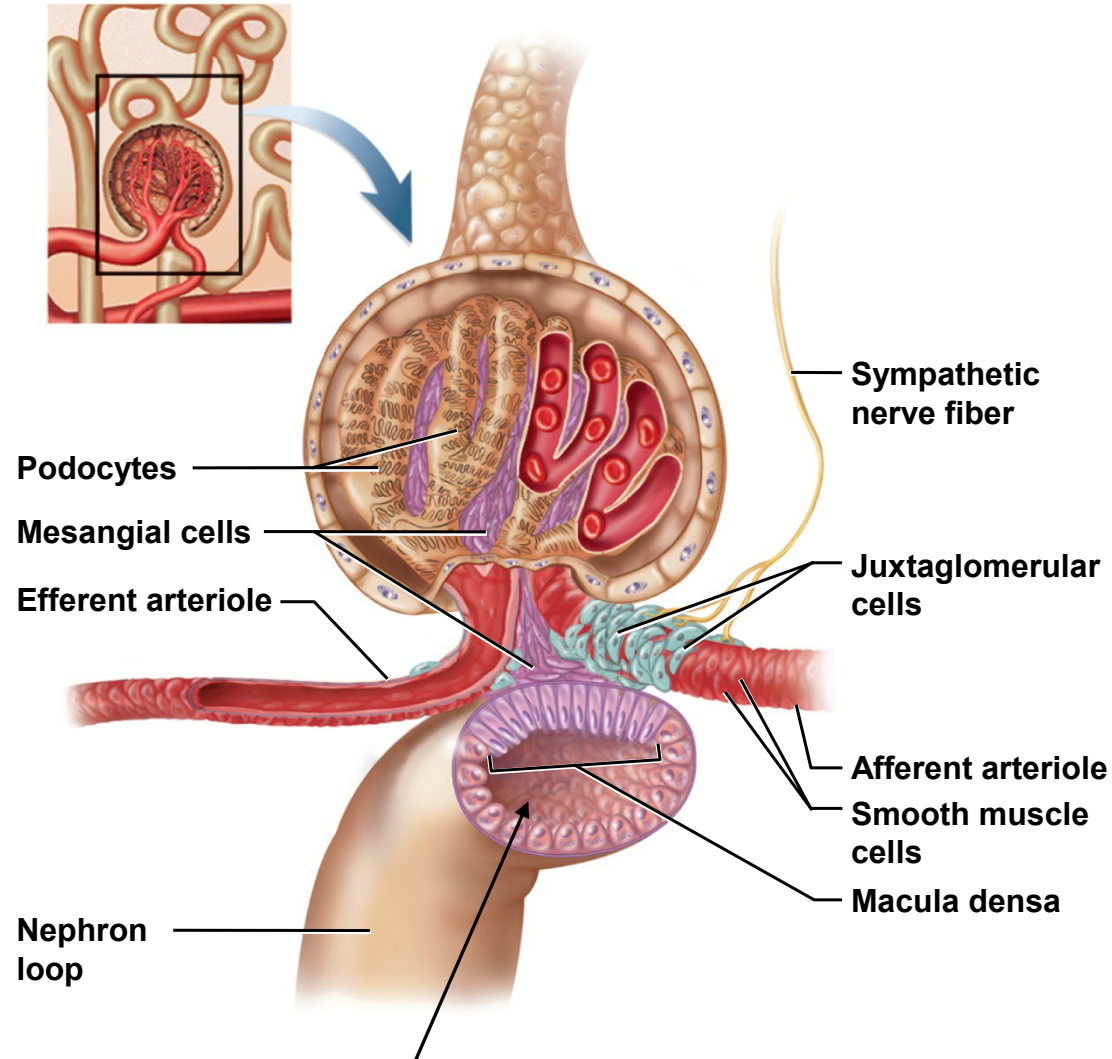


- Tubuloglomerular feedback
 - mechanism to signal **glomerulus about status of the downstream tubular fluid** /// allows for appropriate adjustments to be made to filtration rate
 - **juxtaglomerular apparatus** – complex structure that surround afferent arteriole /// proximal end of the DCT touches both the afferent and efferent arterioles as the DCT emerges from the medulla
 - *Significance: Distal end of the loop of Henle now comes in contact with the afferent and efferent arterioles at the vascular pole of the renal corpuscle // able to sample outcome of filtrate near end of nephron!*

Renal Autoregulation of GFR by Tubuloglomerular Feedback Mechanism

Three special cells occur in the juxtaglomerular apparatus

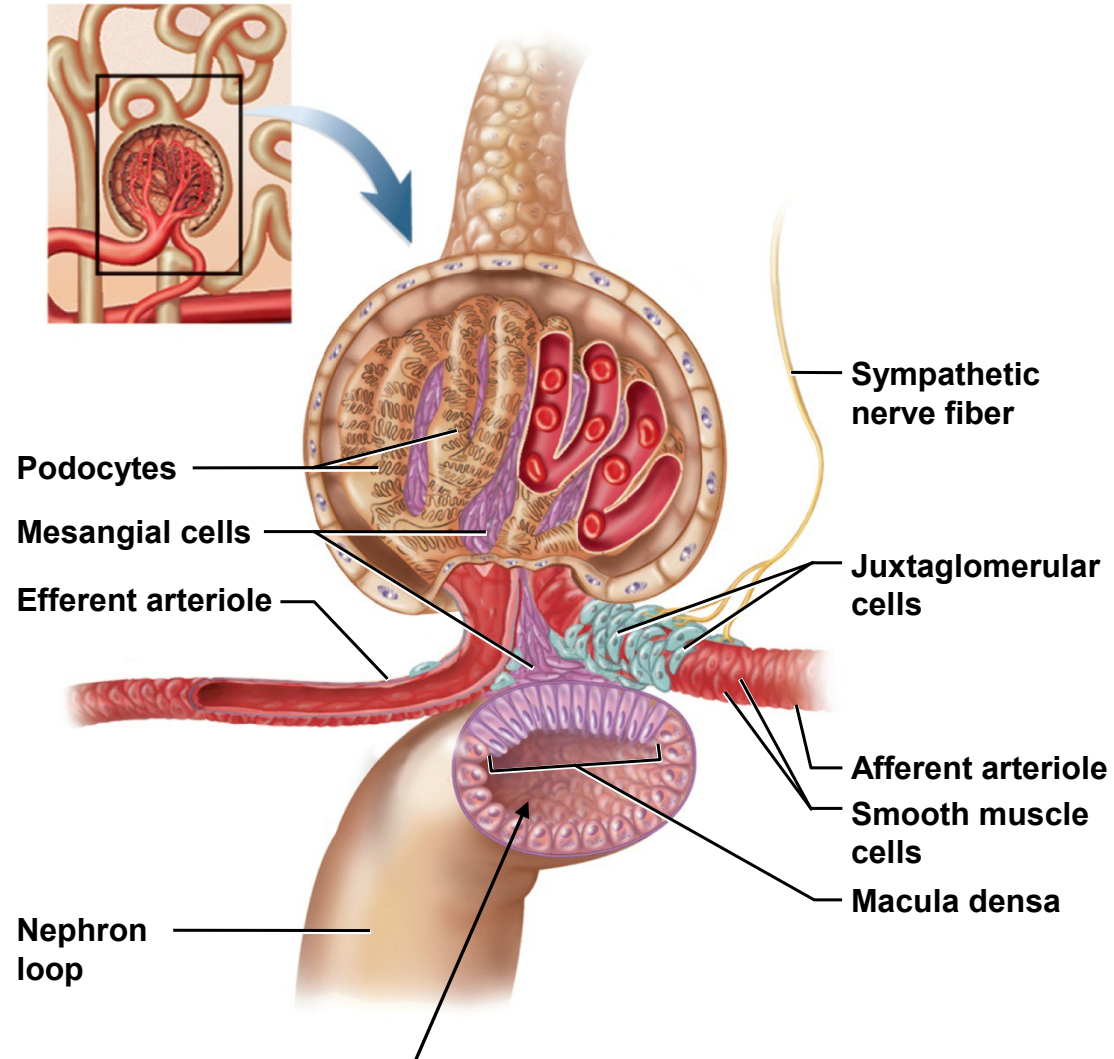
- #1 // **macula densa** = patch of slender, closely spaced epithelial cells at end of the nephron loop on the side of the tubules facing the arterioles
- senses variations in flow or fluid composition and secretes a paracrine that stimulates JG cells



Note: proximal portion
Of distal convoluted tubule

Renal Autoregulation of GFR by Tubuloglomerular Feedback Mechanism

- #2 // **juxtaglomerular (JG) cells** are enlarged smooth muscle cells located in the afferent arteriole - directly across from macula densa
 - when signaled by the macula densa
 - JGC cause afferent arterioles to dilate or constrict the arterioles
 - JGC also contain granules of **renin** /// renin secrete in response to drop in blood pressure

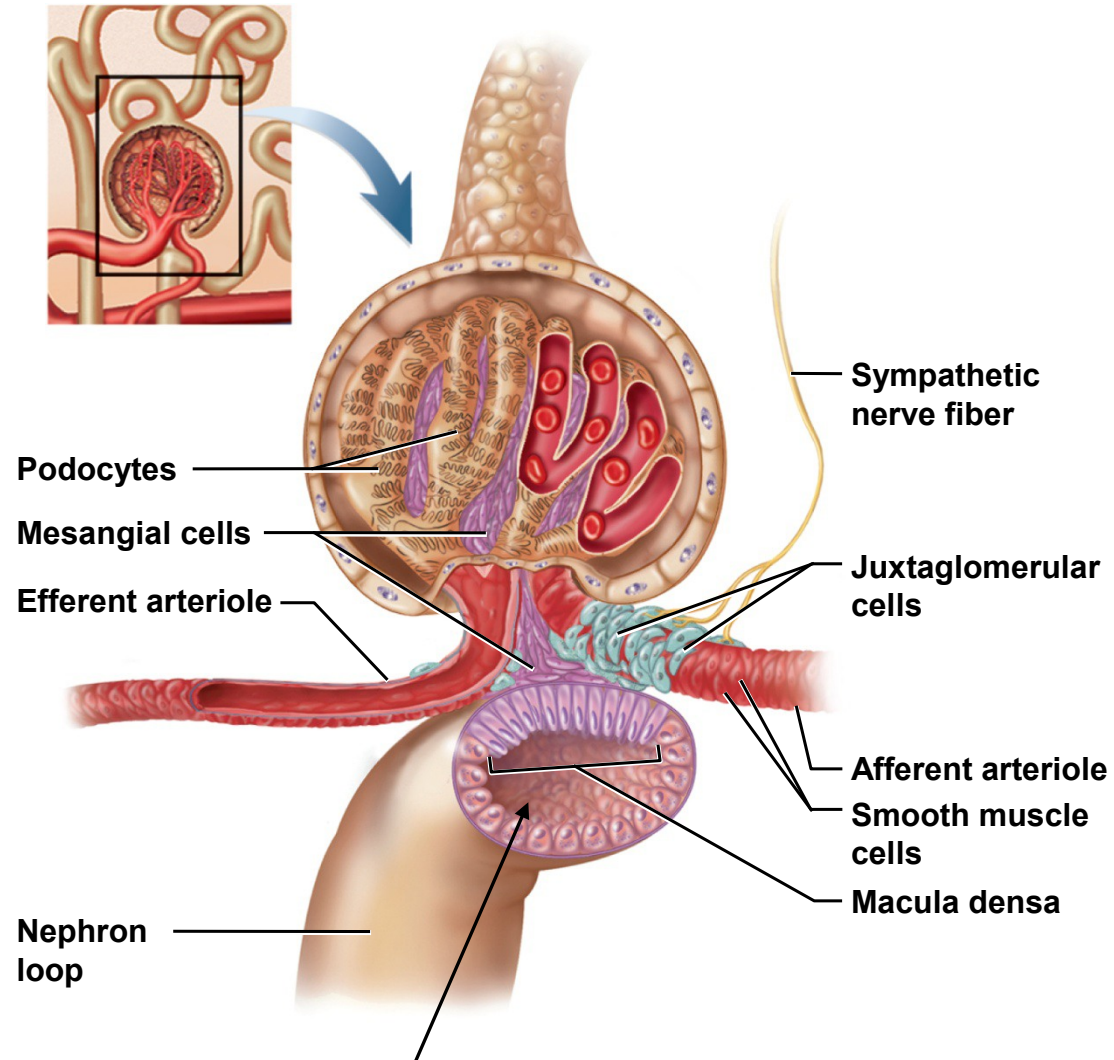


Note: proximal portion
Of distal convoluted tubule

Renal Autoregulation of GFR by Tubuloglomerular Feedback Mechanism

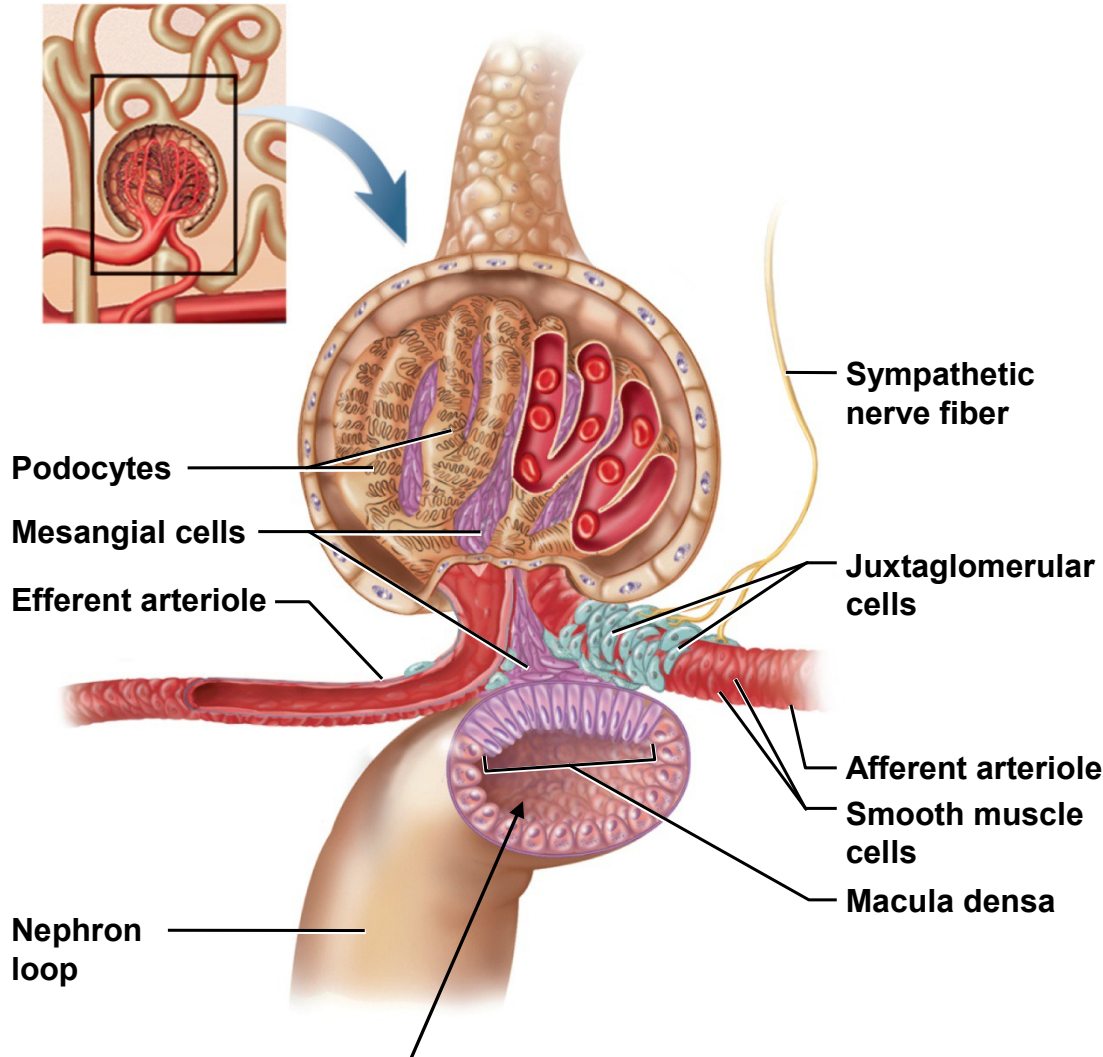
#3 // **Mesangial cells** – in the cleft between the afferent - efferent arterioles and among the capillaries of the glomerulus >>

- connected to macula densa and JG cells by gap junctions /// communicate by means of paracrines
- build supportive matrix in glomerulus // constrict or relax capillaries to regulate flow



Note: proximal portion
Of distal convoluted tubule

Renal Autoregulation of GFR by Tubuloglomerular Feedback Mechanism



Note: proximal portion
Of distal convoluted tubule

If GFR rises

- the flow of tubular fluid increases and more sodium is reabsorbed
- macula densa stimulates JG cells with a paracrine
- JG cells contract which **constricts afferent arteriole**, reducing GFR to normal
- OR
- mesangial cells may contract, constricting the capillaries and reducing filtration

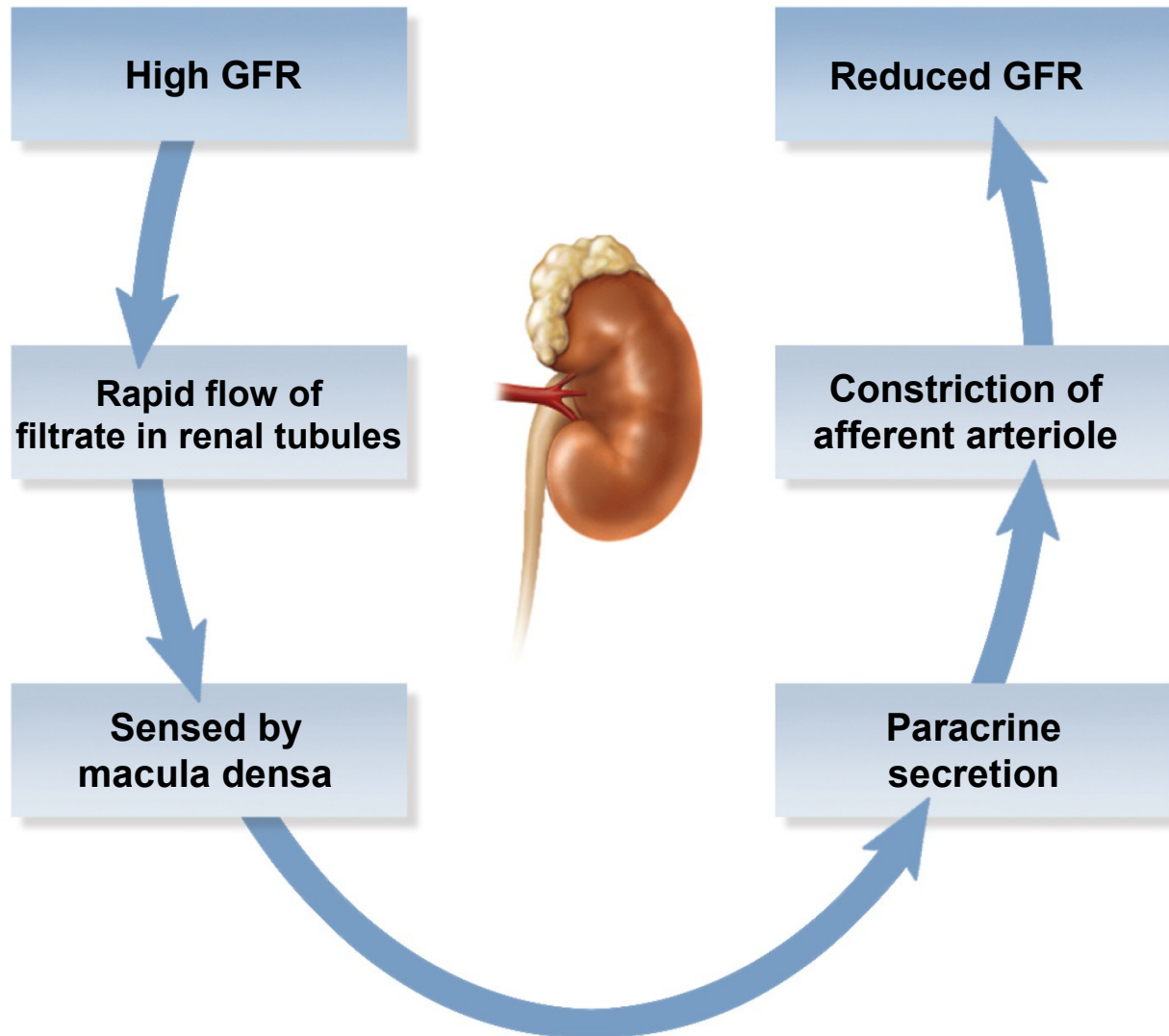
If GFR falls

- macula densa **relaxes afferent arterioles** and mesangial cells
- blood flow increases and GFR rises back to normal.



Negative Feedback Control of GFR

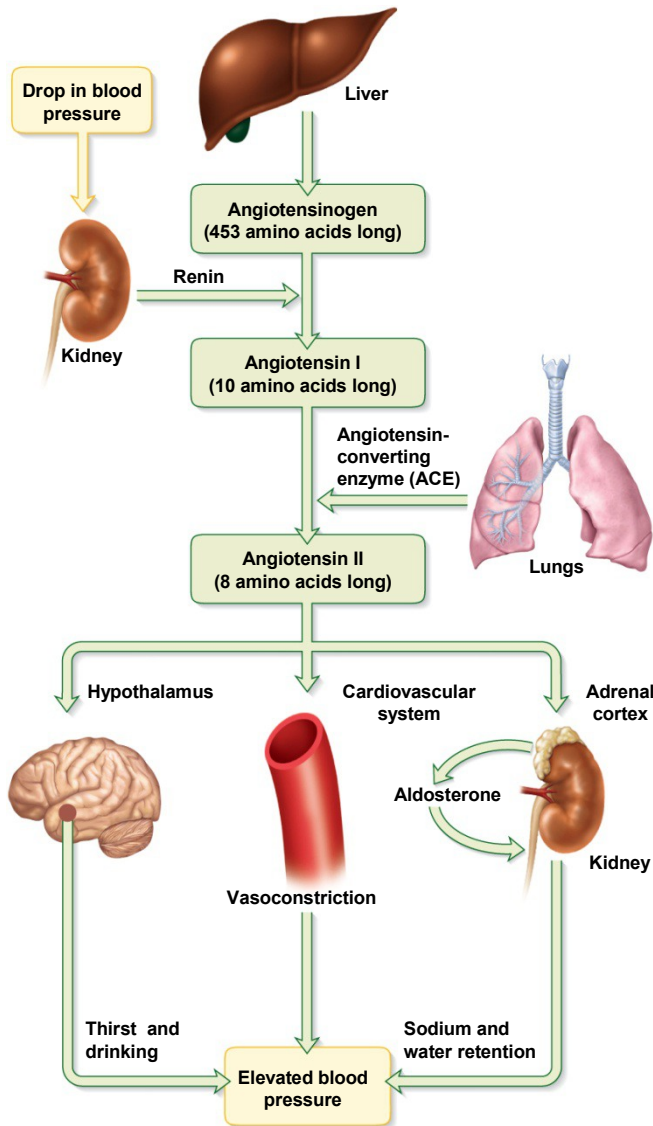
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Sympathetic Control of GFR

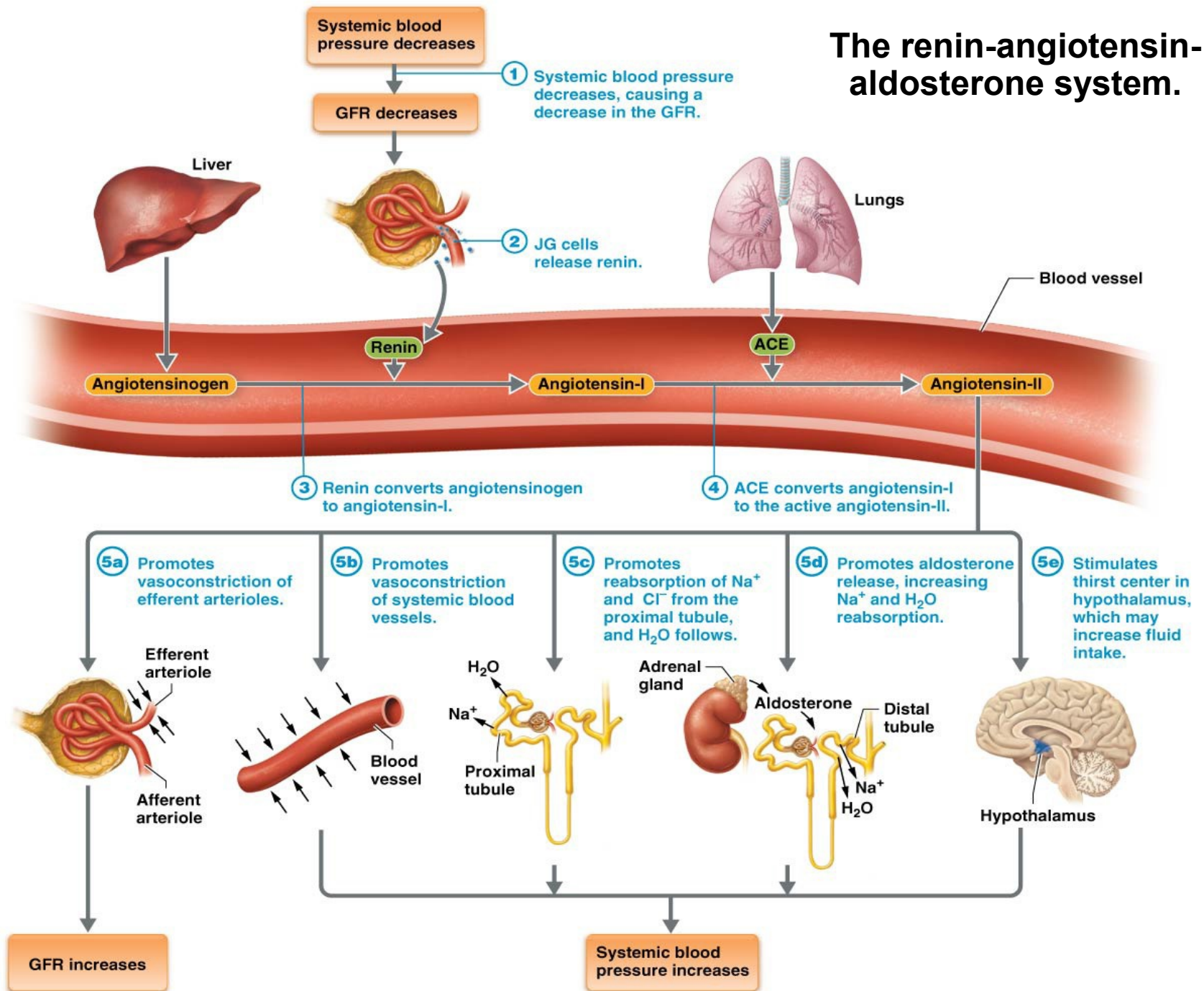
- Sympathetic nerve fibers richly innervate the renal blood vessels
- Sympathetic nervous system and adrenal epinephrine **constrict the afferent arterioles** /// experienced in strenuous exercise or acute conditions like circulatory shock
 - reduce GFR to reduce urine output
 - redirects blood from the kidneys to the heart, brain, and skeletal muscles
 - GFR may be as low as a few milliliters per minute

Hormone Control: Renin-Angiotensin-Aldosterone Mechanism

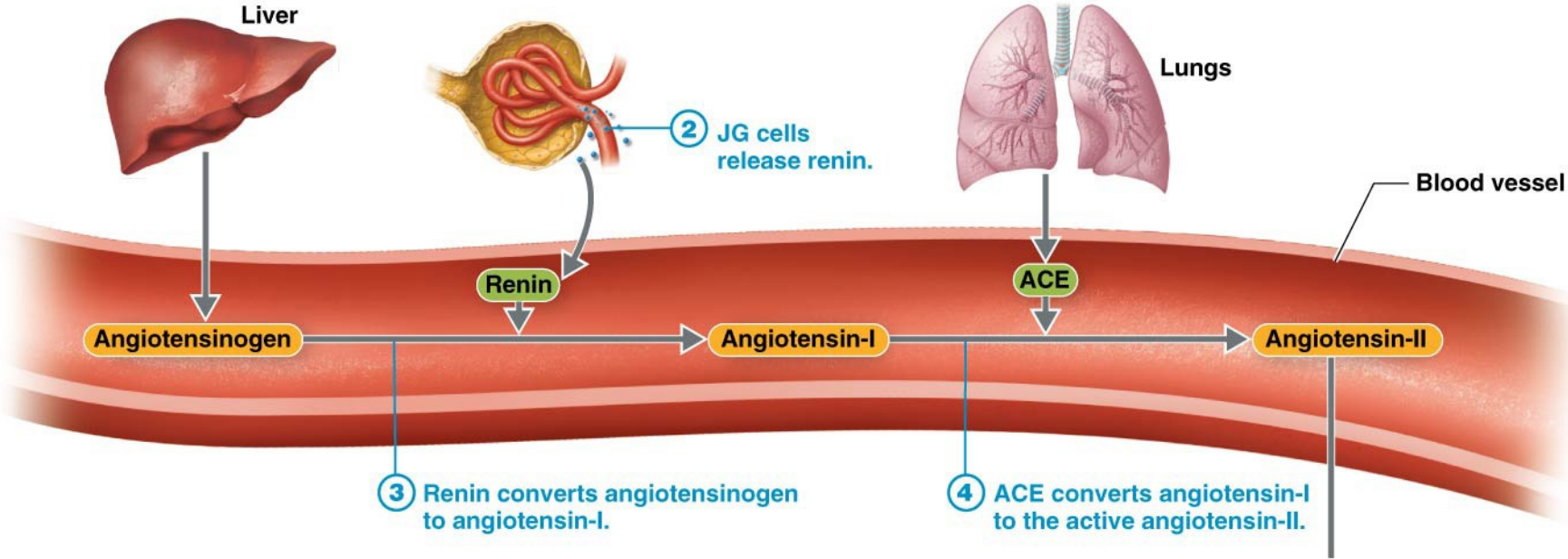


- *renin* secreted by juxtaglomerular cells when BP drops
- renin converts the blood plasma protein angiotensinogen into angiotensin-I /// angiotensinogen made by liver
- Angiotensinogen-I transported to the lungs where **angiotensin-converting enzyme (ACE)** converts angiotensin I to angiotensin II
- Angiotensin-II is an active hormone // vasopressor to peripheral arterioles
- helps to restore fluid volume and BP through several mechanisms
- *If you have high blood pressure, your doctor may give you a drug to inhibit ACE, why?*

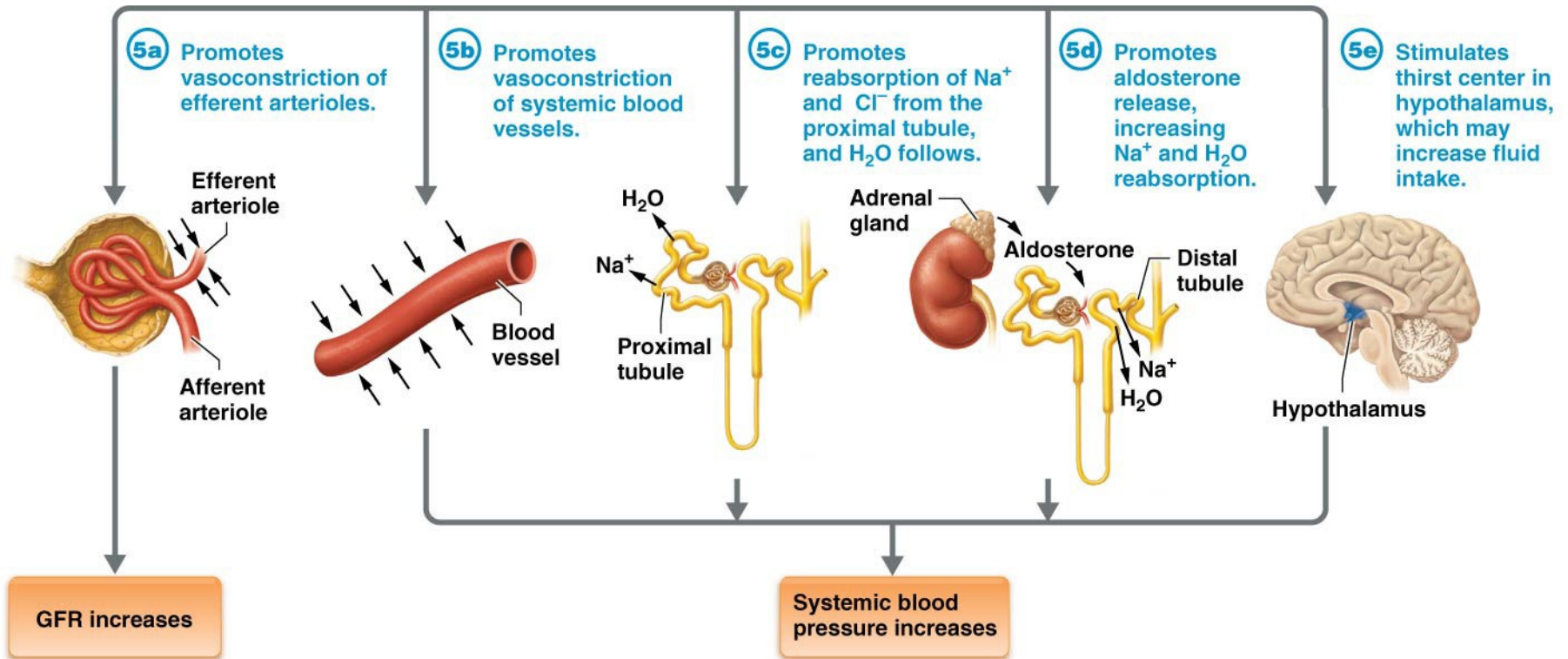
The renin-angiotensin-aldosterone system.



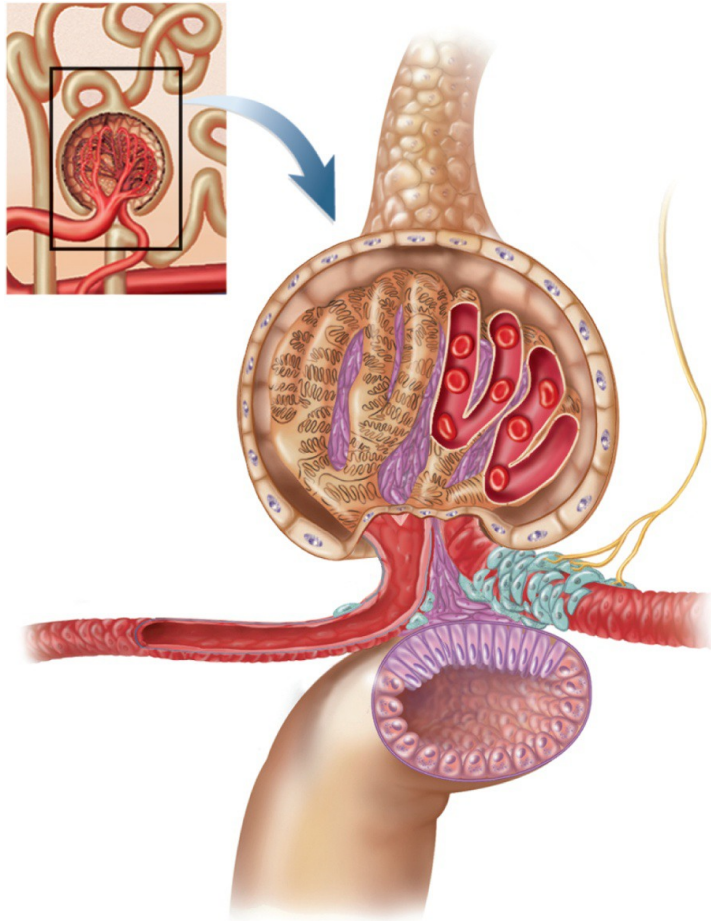
The renin-angiotensin-aldosterone system.



The renin-angiotensin-aldosterone system.



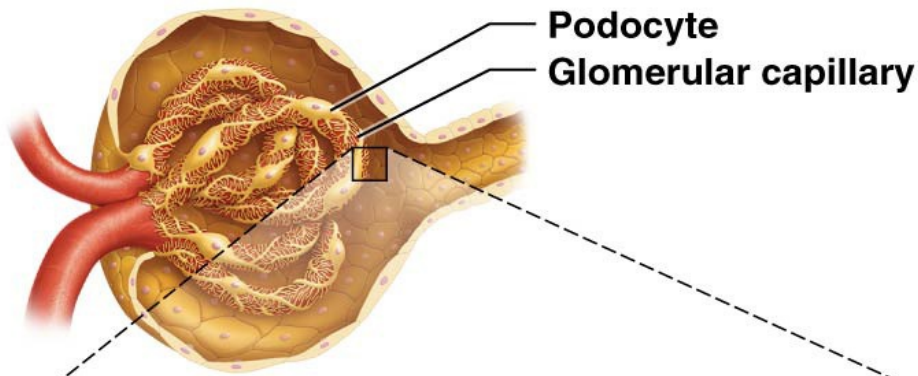
How will the activation of angiotensin-II reverse low blood pressure?



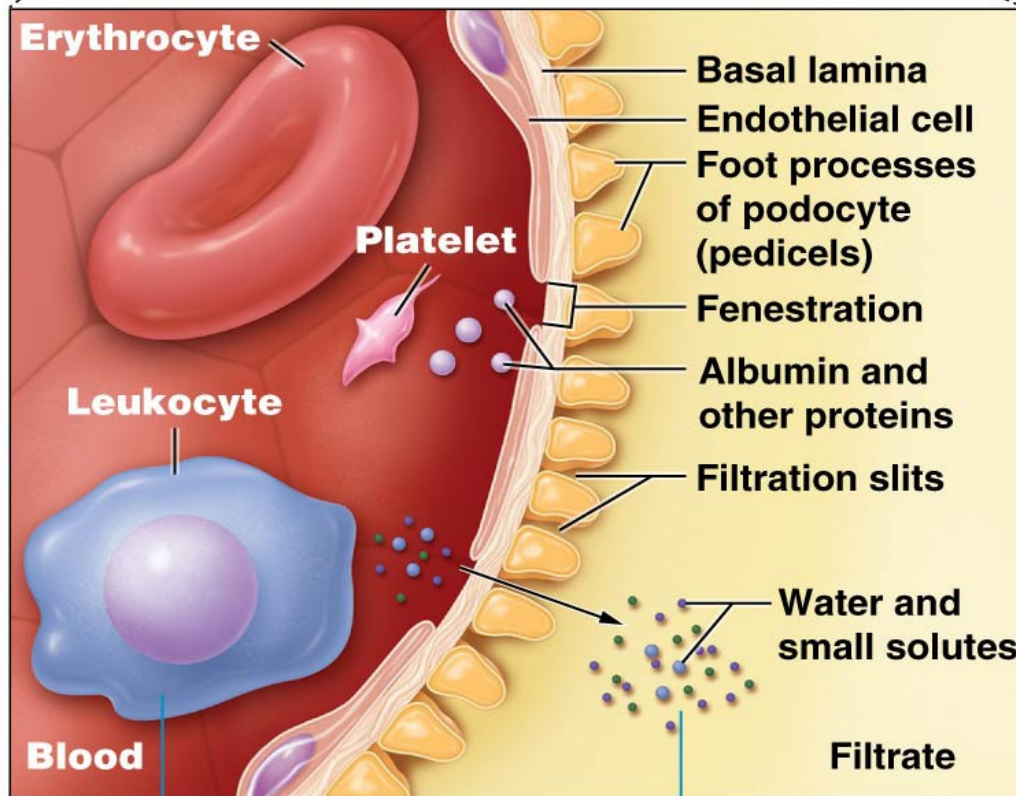
- angiotensin II = potent vasoconstrictor raising BP throughout body
- constricts efferent arteriole raising GFR despite low BP
- lowers BP in peritubular capillaries enhancing reabsorption of NaCl & H₂O
- angiotensin II stimulates adrenal cortex to secrete aldosterone /// promotes Na⁺ and H₂O reabsorption in DCT and collecting duct
- angiotensin II also stimulates posterior pituitary to secrete ADH which promotes water reabsorption by collecting duct
- angiotensin II stimulates thirst & H₂O intake

How Effective Is Autoregulation?

- Maintains a dynamic equilibrium
 - allows for GFR fluctuates within narrow range
 - system designed in conditons of normal fluctuation to the blood pressure there will be no significant change to GFR or urine output
- However, renal autoregulation **can not compensate for extreme blood pressure variation**
 - over a MAP range of 90 – 180 mm Hg, the GFR remains quite stable
 - below 70 mm Hg, glomerular filtration and urine output cease /// this occurs in hypovolemic shock



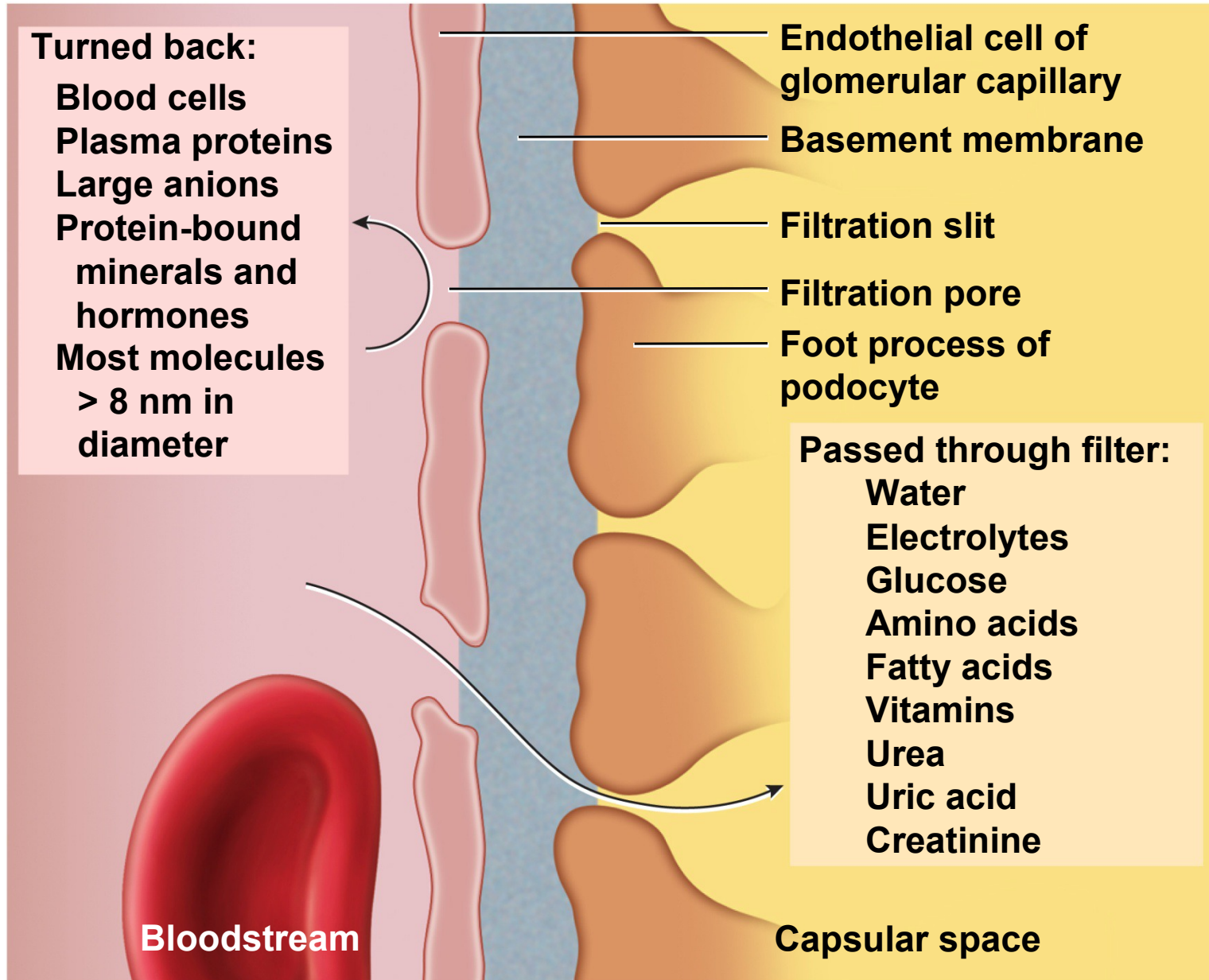
What is filtered through the glomerulus?



Formed elements and most proteins in blood are too large to fit through the filtration slits.

Water and small solutes are small enough to pass through the filtration slits and enter the filtrate.

Filtration Pores and Slits Determine Filtrate Composition





Urine Volume

- normal volume for average adult - 1 to 2 L/day
- polyuria - output in excess of 2 L/day
- oliguria – output of less than 500 mL/day
- anuria - 0 to 100 mL/day
 - low output occurs in kidney disease
 - dehydration
 - circulatory shock
 - prostate enlargement
- urine output less than 400 mL/day // the body cannot maintain safe homeostasis

Composition and Properties of Urine (1 of 2)



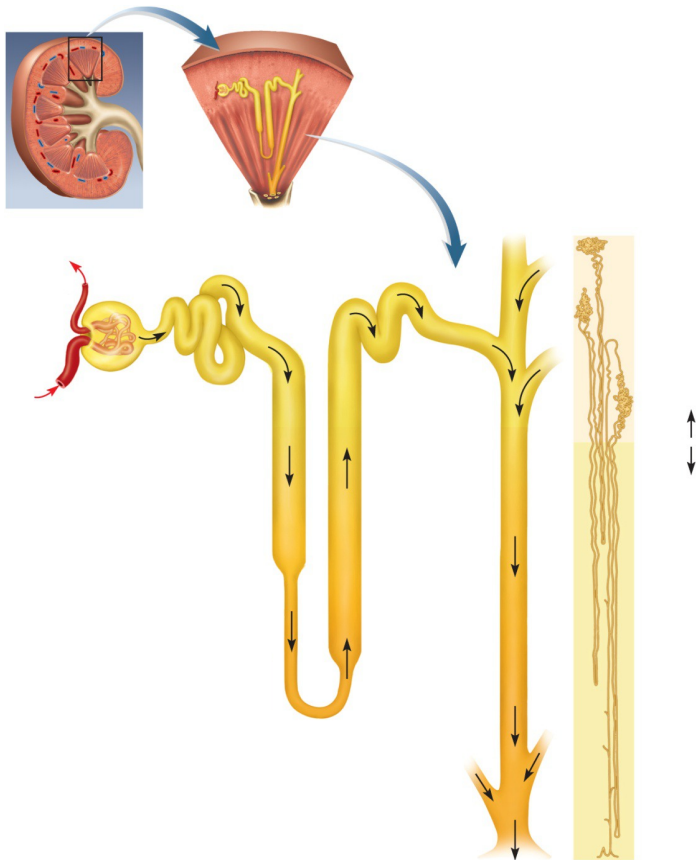
- osmolarity (blood = 300 mOsm/L) /// ranges from 50 mOsm/L to 1,200 mOsm/L within kidney
- pH - range: 4.5 to 8.2, usually 6.0 (mildly acidic)
- chemical composition: 95% water, 5% solutes
 - **Normal** to find /// urea, NaCl, KCl, creatinine, uric acid, phosphates, sulfates, traces of calcium, magnesium, and sometimes bicarbonate, urochrome and a trace of bilirubin
 - **Abnormal** to find /// glucose, free hemoglobin, albumin, ketones, bile pigments

Composition and Properties of Urine

- **urinalysis** – the examination of the physical and chemical properties of urine
 - appearance - clear, almost colorless to deep amber - yellow color due to urochrome pigment from breakdown of hemoglobin (RBCs) – other colors from foods, drugs or diseases
 - cloudiness or blood could suggest urinary tract infection, trauma or stones
 - pyuria – pus in the urine
 - hematuria – blood in urine due to urinary tract infection, trauma, or kidney stones
 - odor - bacteria degrade urea to ammonia, some foods impart aroma
 - specific gravity - compared to distilled water /// density of urine ranges from 1.001 -1.028

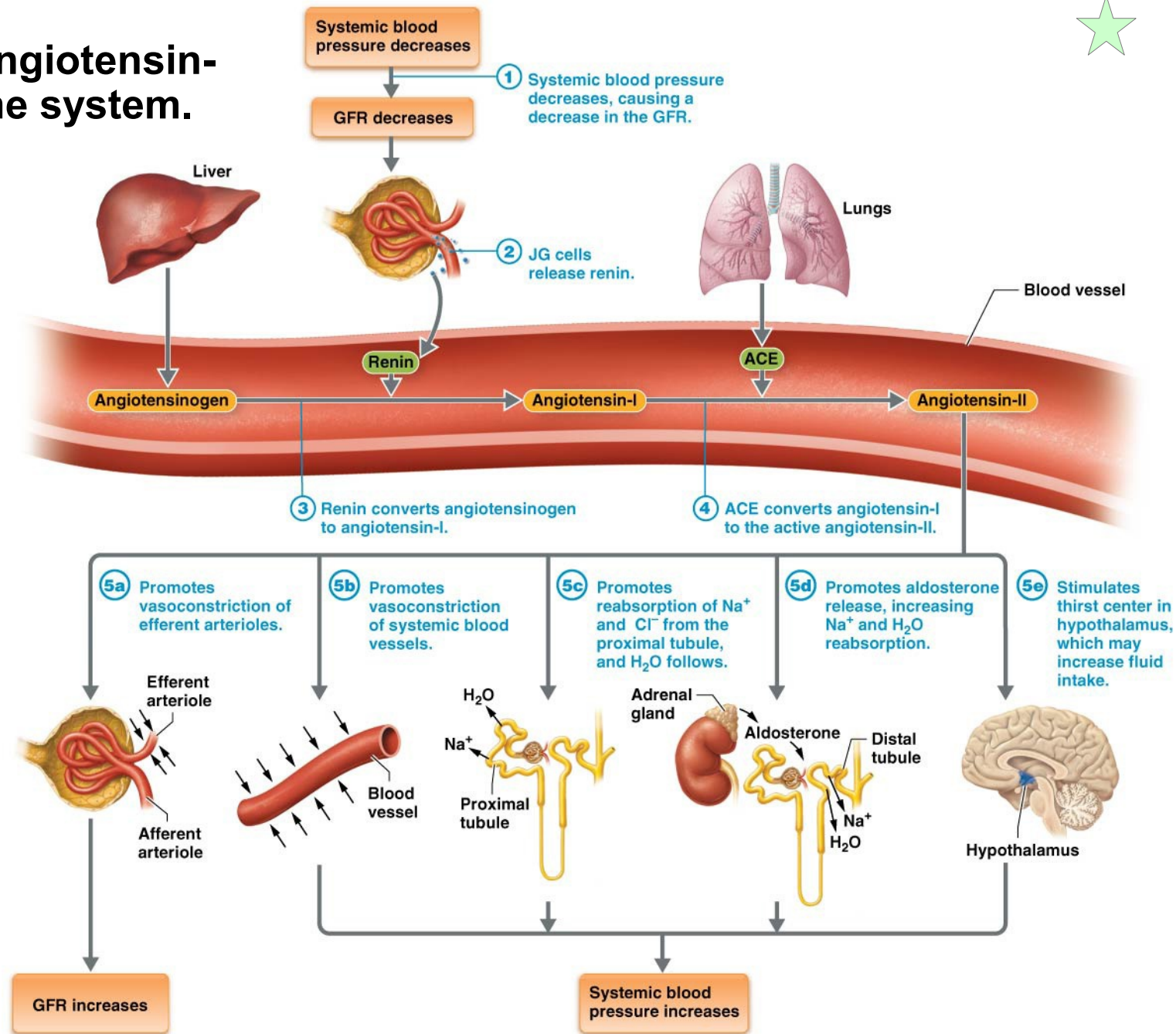


Aldosterone and Antidiuretic Hormone



- Aldosterone and antidiuretic hormone have their receptors at the end of the DCT and within the cortical region of the collecting duct.
- Each hormone is able to change the volume of urine produced.
- The hormones use different mechanisms to reduce the volume of urine produced by moving water from the collecting duct to systemic circuit. // cause change in blood volume
- Aldosterone (salt retention hormone) activates transmembrane pumps to move sodium out of collecting duct and into blood vessels. // water follows the sodium
- Antidiuretic hormone insert aquaporins into collecting duct // these water passageways allow water to move from collecting duct into blood vessels
- Which hormone will change blood tonicity? Why?

The renin-angiotensin-aldosterone system.



DCT and Collecting Duct

- fluid arriving in the **DCT** still contains about 20% of the water and 7% of the salts from glomerular filtrate /// if this were all to pass from kidneys as urine, **it would amount to 36 L/day**
- DCT and collecting duct reabsorb variable amounts of water and salt /// regulated by **several hormones**
 - **aldosterone, atrial natriuretic peptide, antidiuretic hormone, and parathyroid hormone**
- two different cells located in the DCT and first segment of collecting duct
 - **principal cells** /// most numerous with receptors for hormones /// involved in salt and water balance
 - **intercalated cells** /// involved in acid/base balance by secreting H^+ into tubule lumen and reabsorbing K^+



DCT and Collecting Duct

- Aldosterone – nickname is the “salt-retention” hormone
 - steroid secreted by the adrenal cortex when
 - blood Na^+ concentration falls
 - K^+ concentration rises
 - drop in blood pressure → renin release → angiotensin-II formation → stimulates adrenal cortex to secrete aldosterone

DCT and Collecting Duct

- Functions of aldosterone
 - acts on thick segment of nephron loop, DCT, and cortical portion of collecting duct
 - stimulates the reabsorption of Na^{\pm} and secretion of K^{\pm}
 - water and Cl^- follow the Na^+
 - net effect is that the body retains “both” NaCl and water // helps maintain blood volume and pressure
 - the urine volume is reduced
 - the urine has an elevated K^+ concentration

DCT and Collecting Duct



- **Antidiuretic hormone** (ADH) secreted by posterior lobe of pituitary
- ADH release in response to dehydration and/or rising blood osmolarity
 - Hypothalamus senses hypertonicity (high osmolarity) /// hypothalamus signals posterior pituitary to release ADH
- ADH action - make collecting duct more permeable to water // insert aquaporins into CD plasma membrane
 - water in the CD re-enters interstitial fluid and diffuse into vasa recta capillaries // less urine formed



Endocrine Function of the Heart

- **Atrial natriuretic peptide (ANP)** /// secreted by atrial myocardium of the heart in response to high blood pressure
 - has four actions that result in the excretion of more salt and water in the urine, thus reducing blood volume and pressure
 - dilates afferent arteriole, constricts efferent arteriole /// results in increase in GFR
 - inhibits renin and aldosterone secretion
 - inhibits secretion of ADH
 - inhibits NaCl reabsorption by collecting duct

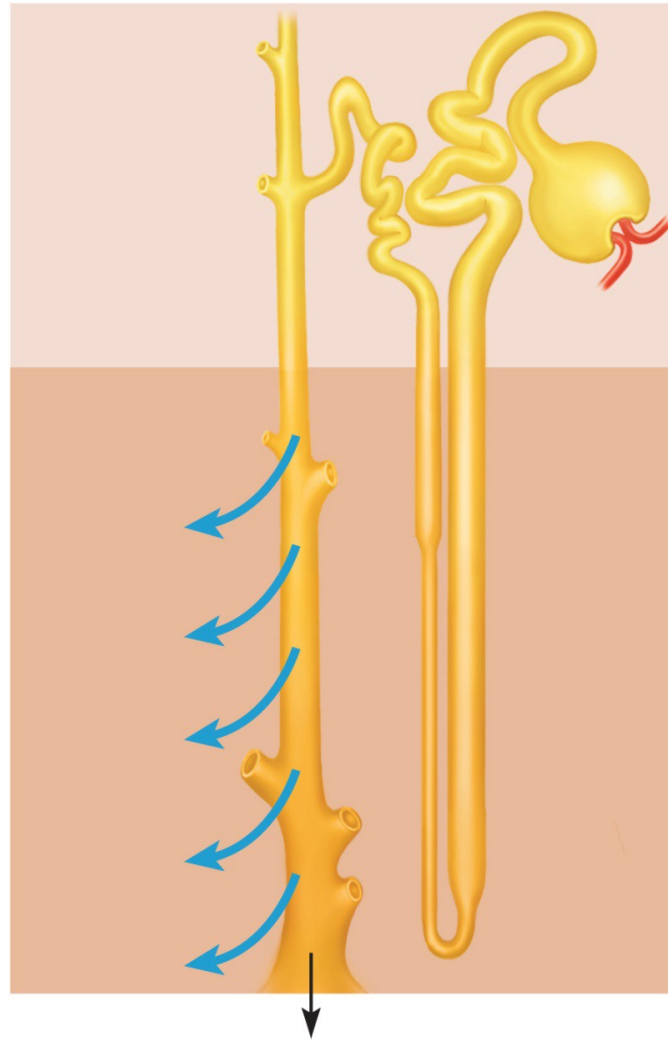
DCT and Collecting Duct



- Parathyroid hormone (PTH)
 - secreted from parathyroid glands in response to calcium deficiency (hypocalcemia)
 - acts on PCT to increase phosphate secretion
 - acts on the thick segment of the ascending limb of the nephron loop, and on the DCT to increase calcium reabsorption
 - **Net affect: more phosphate in urine and less calcium in urine**
 - because phosphate is not retained, the calcium ions stay in circulation rather than precipitating into the bone tissue as calcium phosphate
 - PTH stimulates calcitriol synthesis (Vitamin D) by the epithelial cells of the PCT – Vit D increases calcium absorption by GI tract

Water Conservation

Counter-current Multiplication & Counter-current Exchange

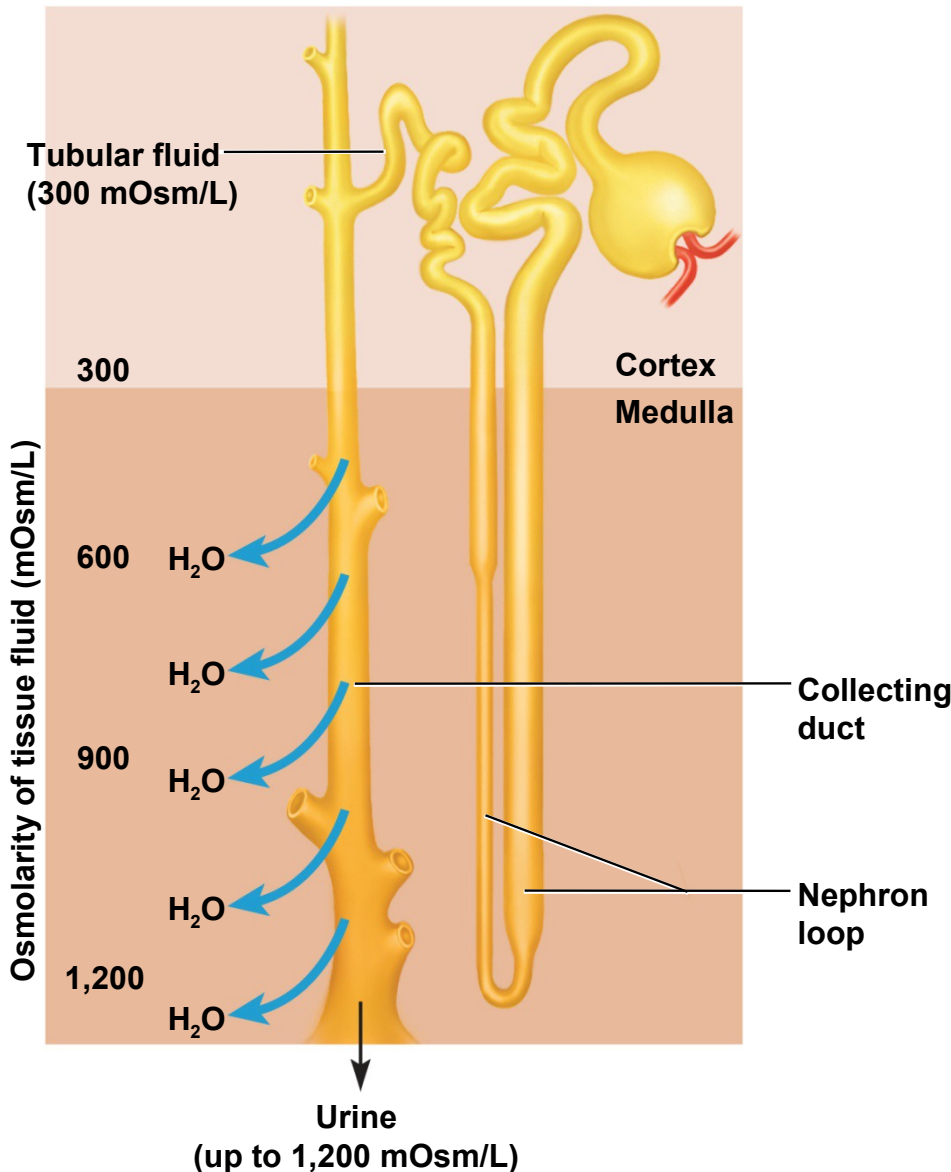


Water Conservation



- The kidney must eliminate metabolic wastes from the body
- The kidney must also **prevent excessive water loss**
- Therefore, the kidney recovers water from the collecting duct and returns it to the systemic circuit
- Any **fluid remaining in the renal tubules** will pass from body as urine
- As water is conserved the urine becomes more concentrated!
- This requires two mechanisms working together: **counter current multiplication** and **counter current exchange**

Collecting Duct Concentrates Urine



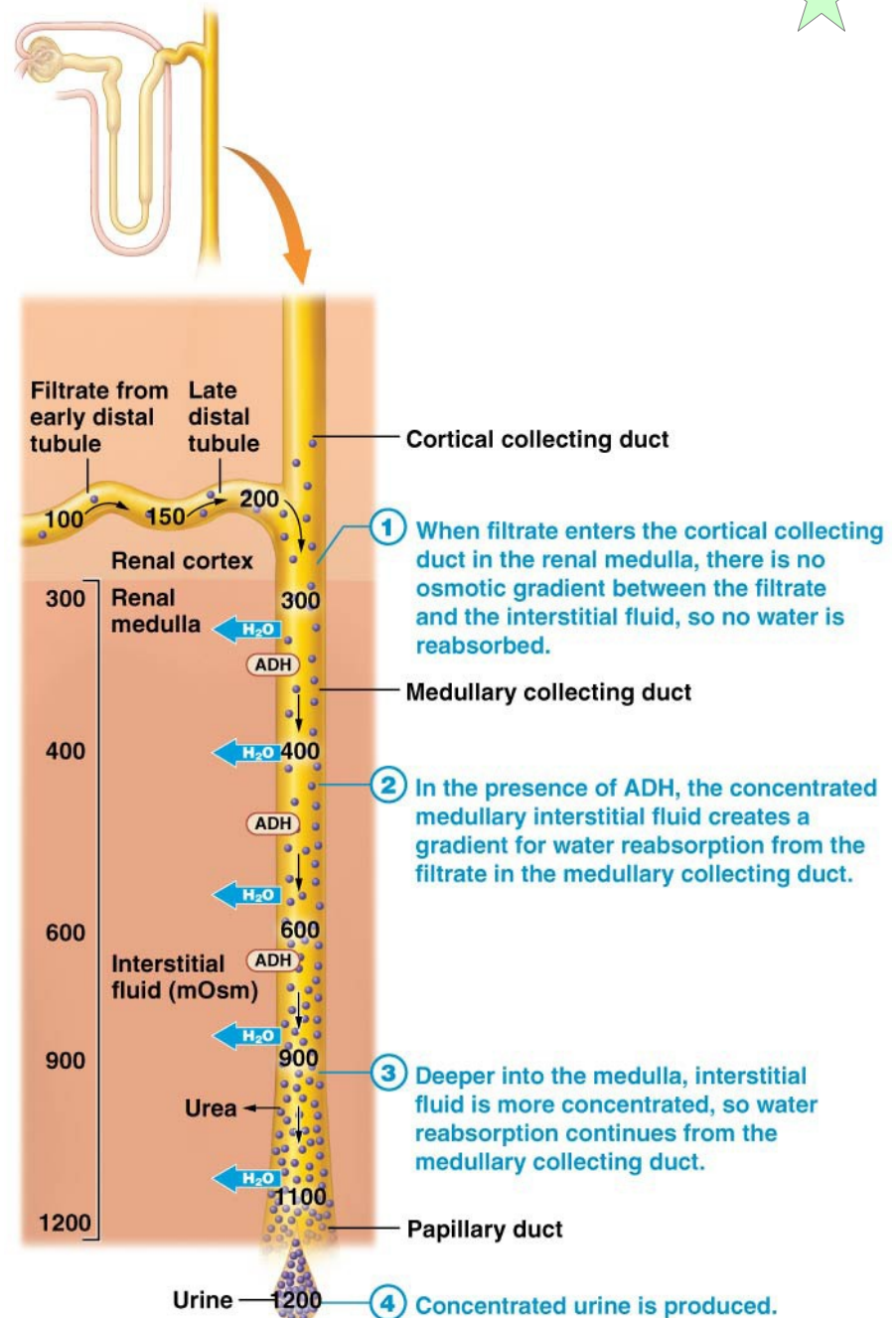
- collecting duct (CD) begins in the cortex where it **receives tubular fluid from several nephrons**
- as CD passes through the medulla, water is **reabsorbed and concentrates urine in CD up to four times**
- medullary portion of CD is more permeable to water than to NaCl
- as urine passes through the increasingly salty medulla, water may leave by osmosis if aquaporins are placed into plasma membrane of CD



Formation of concentrated urine.

For water to diffuse from the CD to the interstitial space, it requires the interstitial space to be hypertonic

How is the deep medulla made hypertonic (1200 mOsm)?





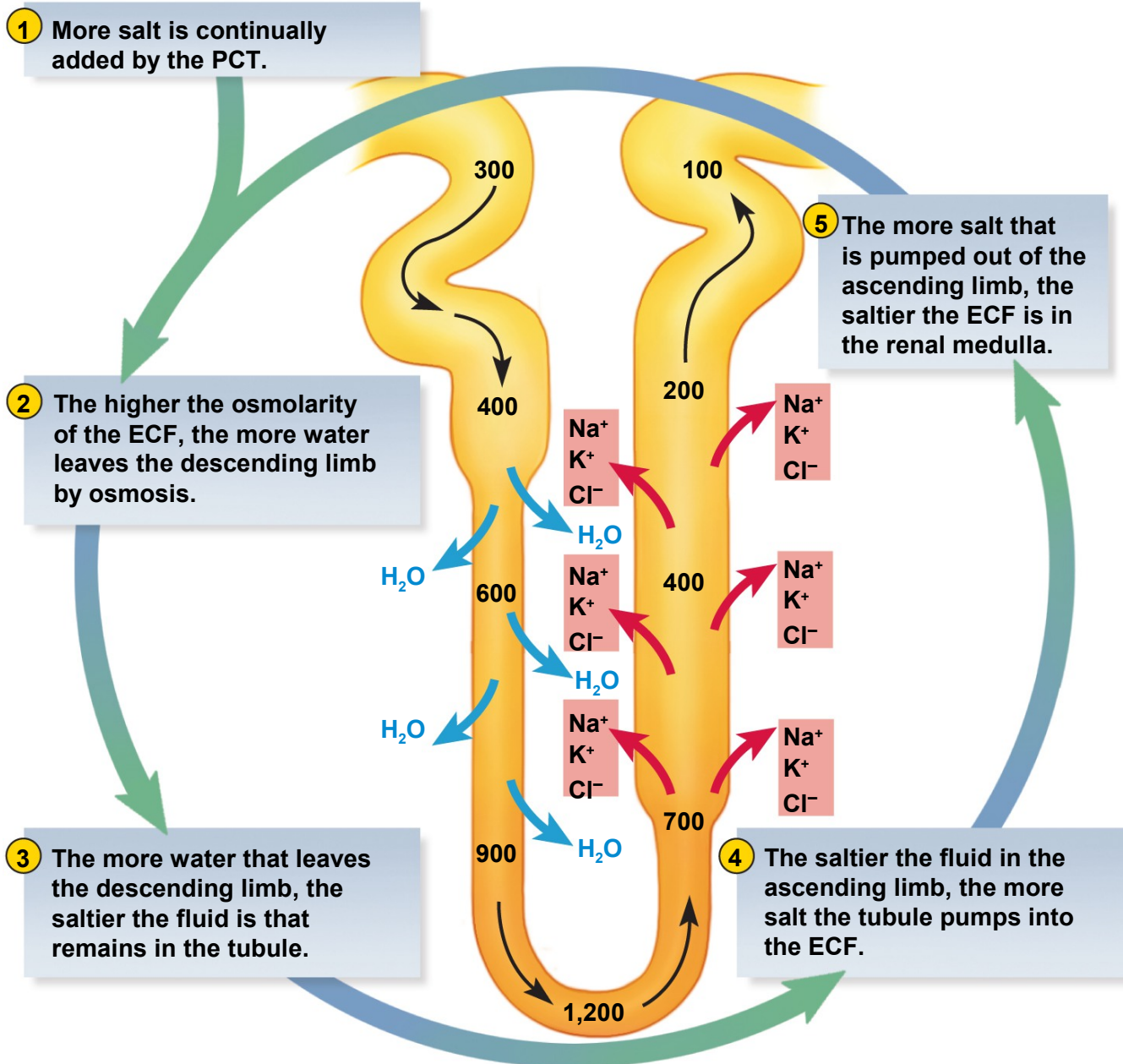
Countercurrent Multiplier = Loop of Henle

- the ability of kidney to concentrate urine in the CD depends on creating a gradient between the CD and the deep renal medulla
 - Deep medulla four times as salty in the renal medulla than the cortex
- nephron loop acts as countercurrent multiplier
 - multiplier - continually recaptures salt and returns it to interstitial space fluid of medulla /// this multiplies the salinity in renal medulla
 - called countercurrent because of fluid flowing in opposite directions in adjacent tubules of nephron loop

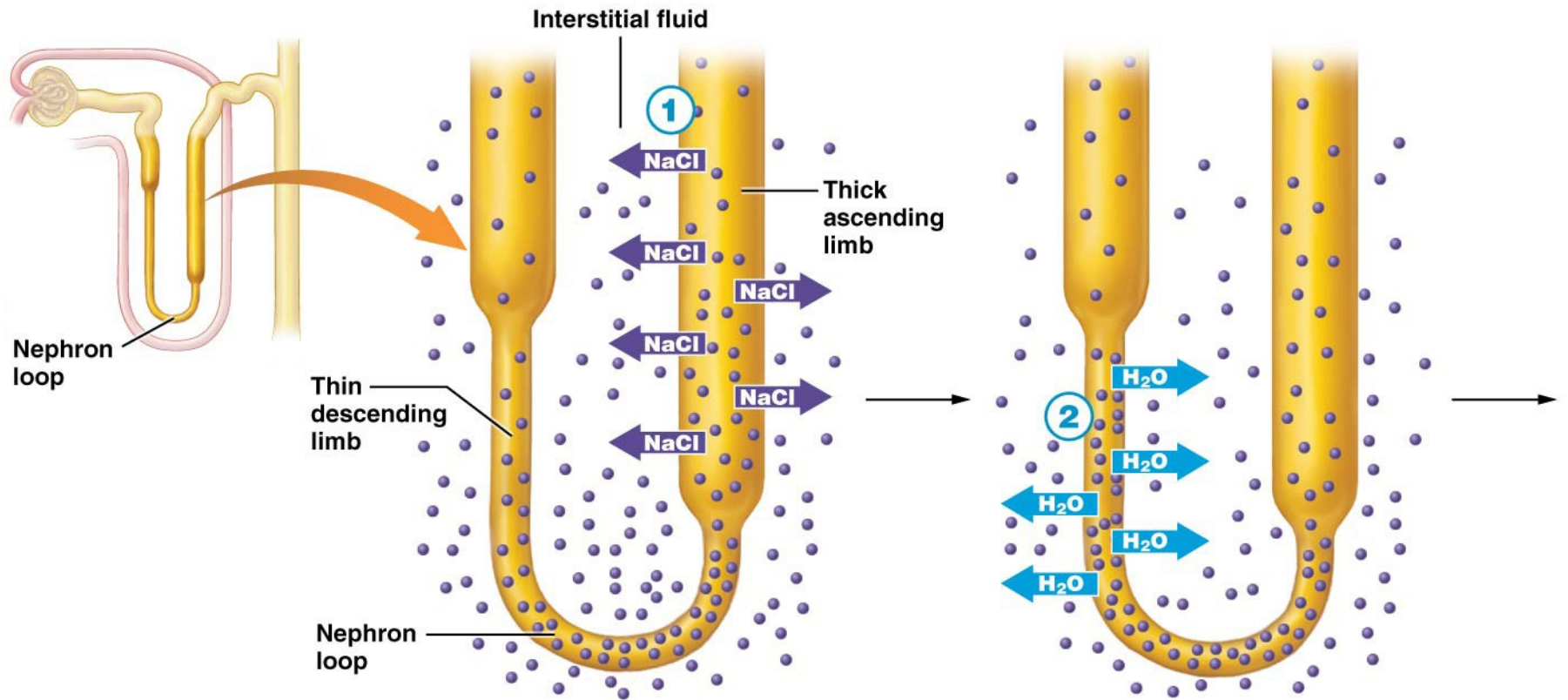
Countercurrent Multiplier = Loop of Henle

- fluid flowing downward in descending limb
 - passes through environment of increasing osmolarity
 - most of descending limb very permeable to water but not to NaCl
 - water passes from tubule into the ECF leaving salt behind
 - concentrates tubular fluid to 1,200 mOsm/L at lower end of loop
- fluid flowing upward in ascending limb
 - impermeable to water
 - reabsorbs Na⁺, K⁺, and Cl⁻ by active transport pumps into ECF
 - maintains high osmolarity of renal medulla
 - tubular fluid becomes hypotonic – 100 mOsm/L at top of loop
- recycling of urea: lower end of CD permeable to urea
 - urea contributes to the osmolarity of deep medullary tissue
 - continually cycled from collecting duct to the nephron loop and back
 - urea remains concentrated in the collecting duct and some of it always diffuses out into the medulla adding to osmolarity

Countercurrent Multiplier of Nephron Loop



The countercurrent multiplier in the nephron loop.



① NaCl is actively transported from the filtrate in the thick ascending limb into the interstitial fluid, raising its NaCl concentration.

② The NaCl pumped into the interstitial fluid draws water out of the filtrate in the thin descending limb into the interstitial fluid by osmosis.

(a) The process of the countercurrent multiplier system



Countercurrent Exchange = Vasa Recta

- **vasa recta** – capillary branching off efferent arteriole in medulla /// it surrounds loop of Henle of juxamedullary nephons
 - provides blood supply to medulla and concentrates NaCl and urea deep in medulla's interstitial space
- countercurrent system - formed by blood flowing in opposite directions in parallel capillaries
- **Net result: As water leaves CD and moves into the interstitial space, the water must be immediately moved into the vasa recta capillaries so the tonicity is not reduced**
- If tonicity was reduced then water molecules would not have the gradient to leave CD



Countercurrent Exchange System = Vasa Recta

Descending capillaries /// exchanges water for salt
water diffuses out of capillaries and salt diffuses in

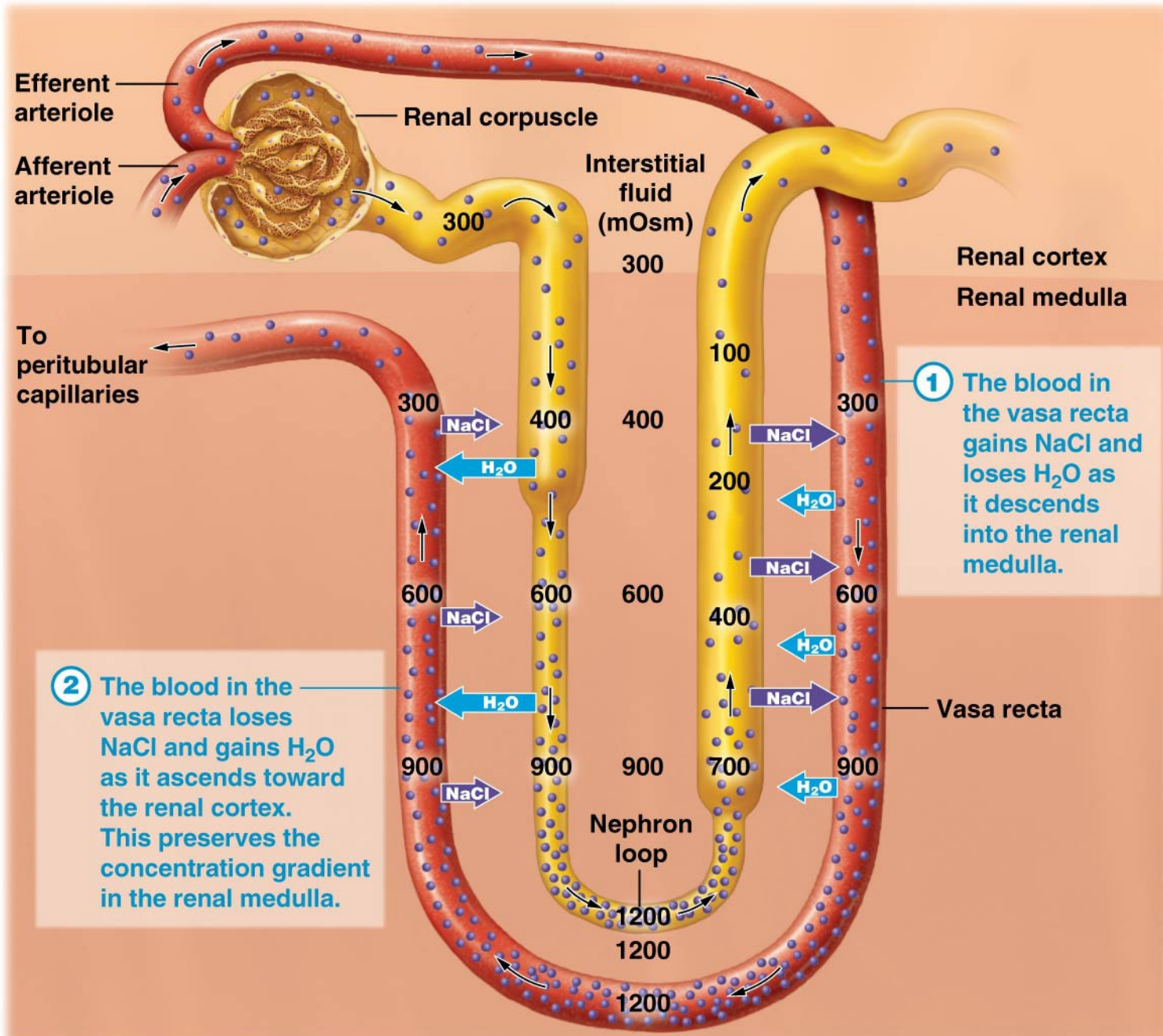
Ascending capillaries // / exchanges salt for water

- water diffuses into and NaCl diffuses out of blood
- the vasa recta gives the salt back and does not subtract from the osmolarity of the medulla

Absorb more water on way out than the way in, /// carry away water reabsorbed from the urine by collecting duct and nephron loop

Must remove water in the interstitial space from CD in order to maintain osmolarity of the interstitial space! This is the “exchange”.

The countercurrent exchanger in the vasa recta.

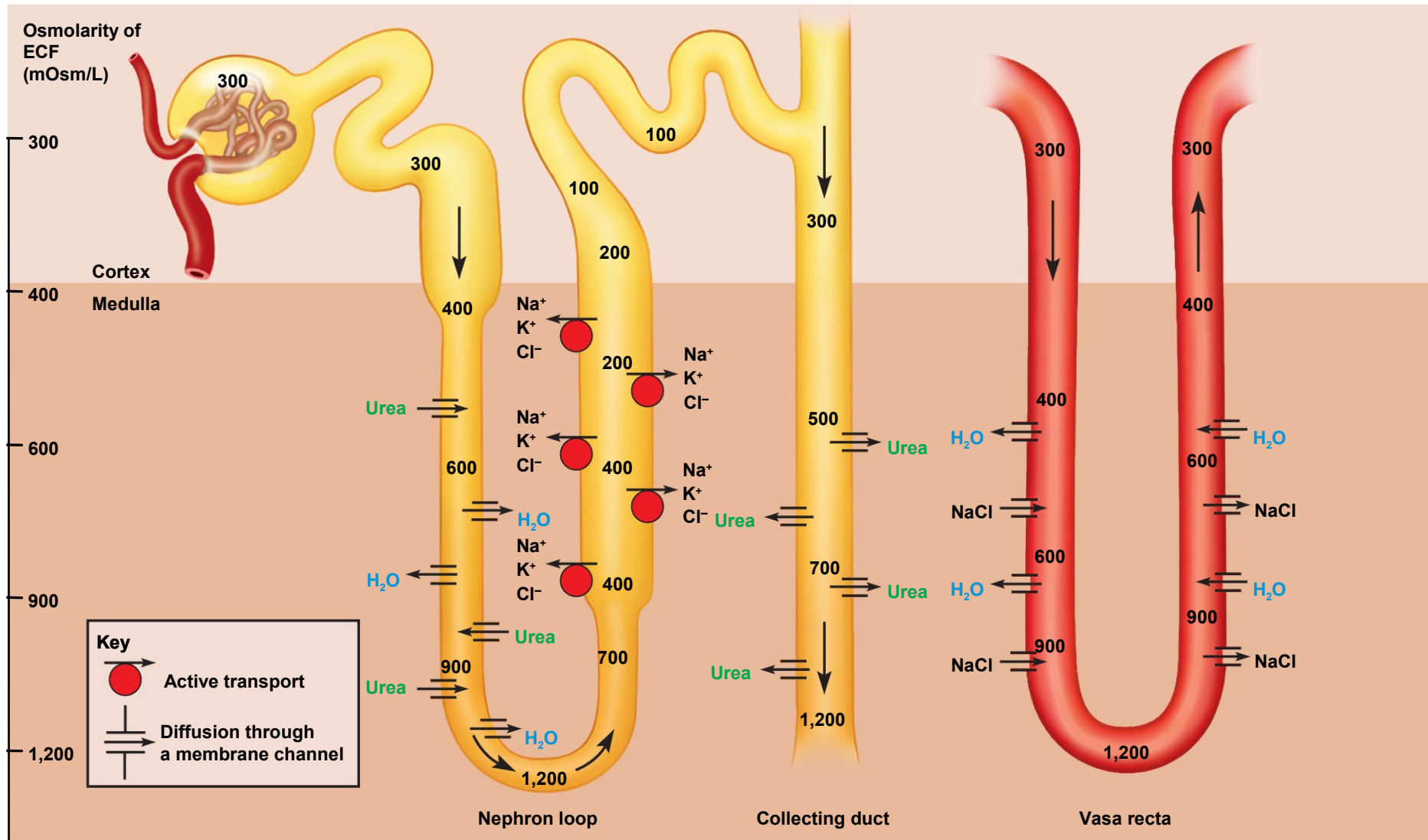




Maintenance of Osmolarity in Renal Medulla

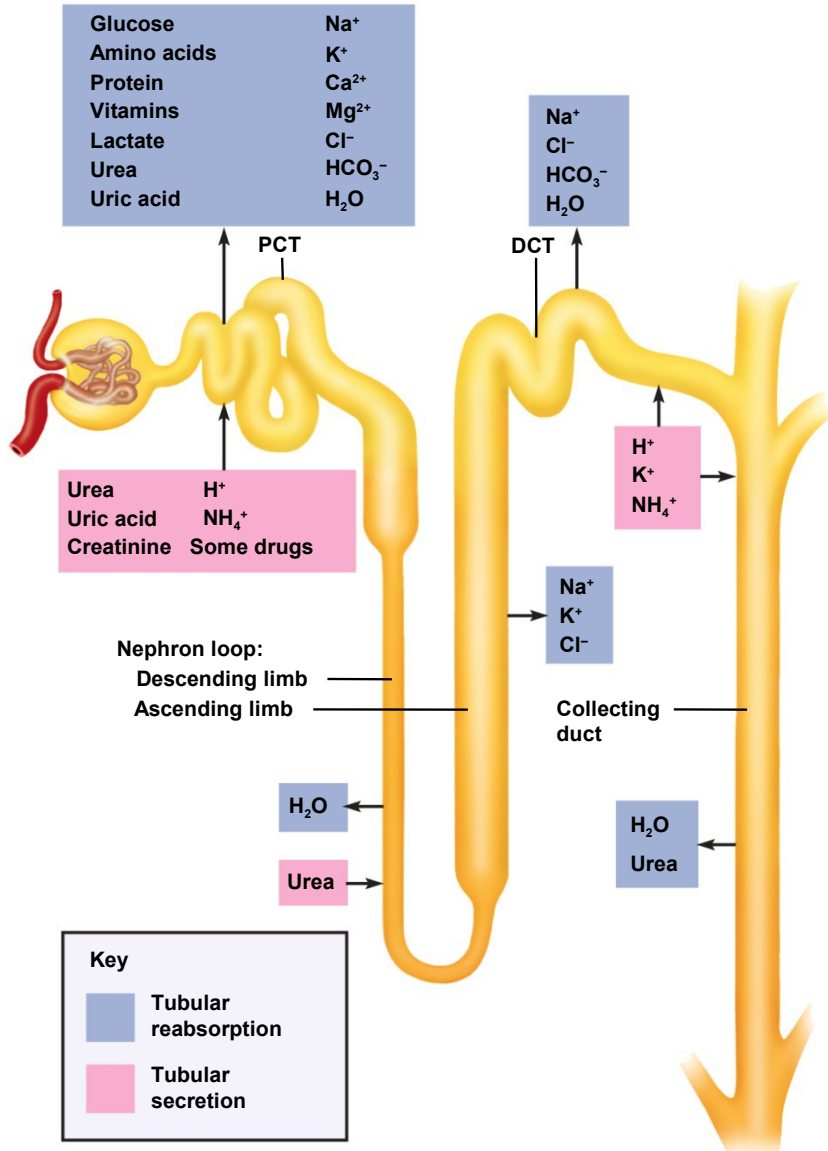
Countercurrent Multiplier Loop of Henle

Countercurrent Exchange Vasa Recta



Summary of Tubular Reabsorption and Secretion

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- PCT reabsorbs 65% of glomerular filtrate and returns it to peritubular capillaries
 - much reabsorption by osmosis & cotransport mechanisms linked to active transport of sodium
- nephron loop reabsorbs another 25% of filtrate
- DCT reabsorbs Na^+ , Cl^- and water under hormonal control, especially aldosterone and ANP
- the tubules also extract drugs, wastes, and some solutes from the blood and secrete them into the tubular fluid
- DCT completes the process of determining the chemical composition of urine
- collecting duct conserves water

Urinary Bladder

- urinary bladder - muscular sac located on floor of pelvic cavity
 - inferior to peritoneum and posterior to pubic symphysis
- **3 layers**
 - parietal peritoneum, superior, fibrous adventitia other areas
 - muscularis /// detrusor muscle /// 3 layers of smooth muscle
 - mucosa - transitional epithelium
 - rugae - conspicuous wrinkles in relaxed bladder

What is the volume capacity of the urinary bladder?



trigone – smooth-surfaced triangular area marked with openings of ureters and urethra

capacity when full is **500 ml** (max. is 700 - 800 ml)

highly distensible

as it fills, it expands superiorly

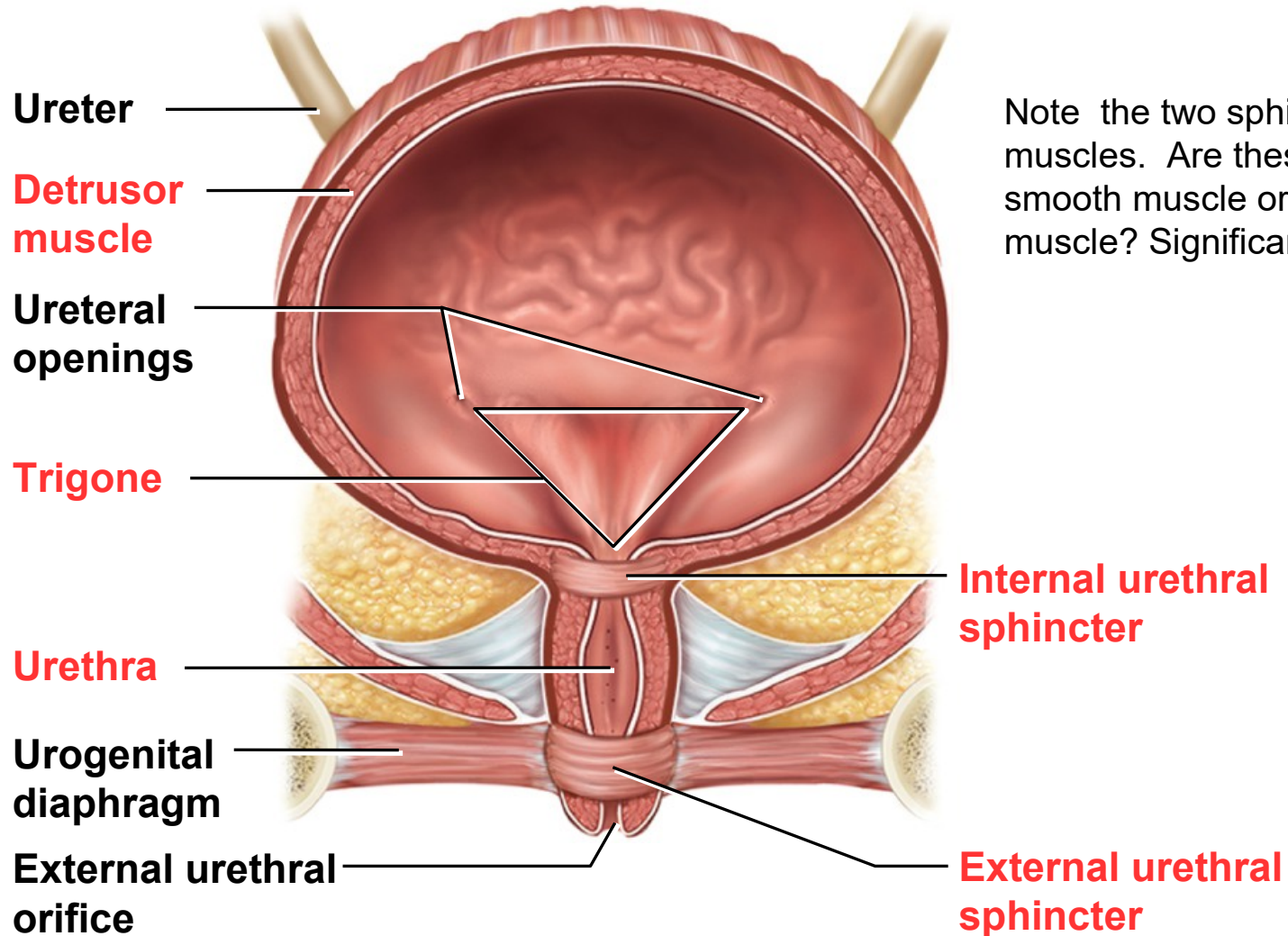
rugae flatten as bladder fills

epithelium thins from five or six layers to two or three (i.e. transitional epithelium)

The Ureter

- retroperitoneal, muscular tube that extends from the kidney to the urinary bladder
 - about 25 cm long
 - passes posterior to bladder and enters it from below
 - flap of mucosa acts as a valve into bladder
 - keeps urine from moving back up into the ureter when bladder contracts

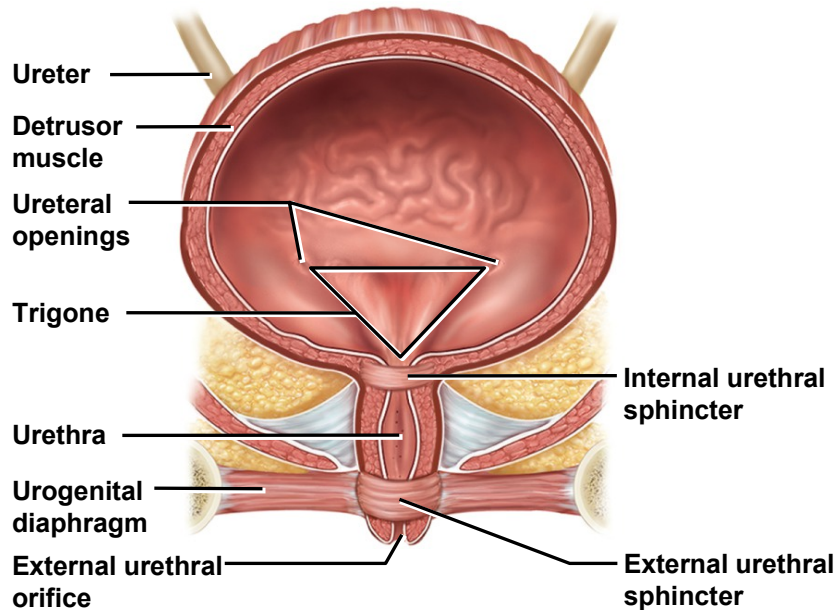
Urinary Bladder



Note the two sphincter muscles. Are these muscles smooth muscle or skeletal muscle? Significance?

Female

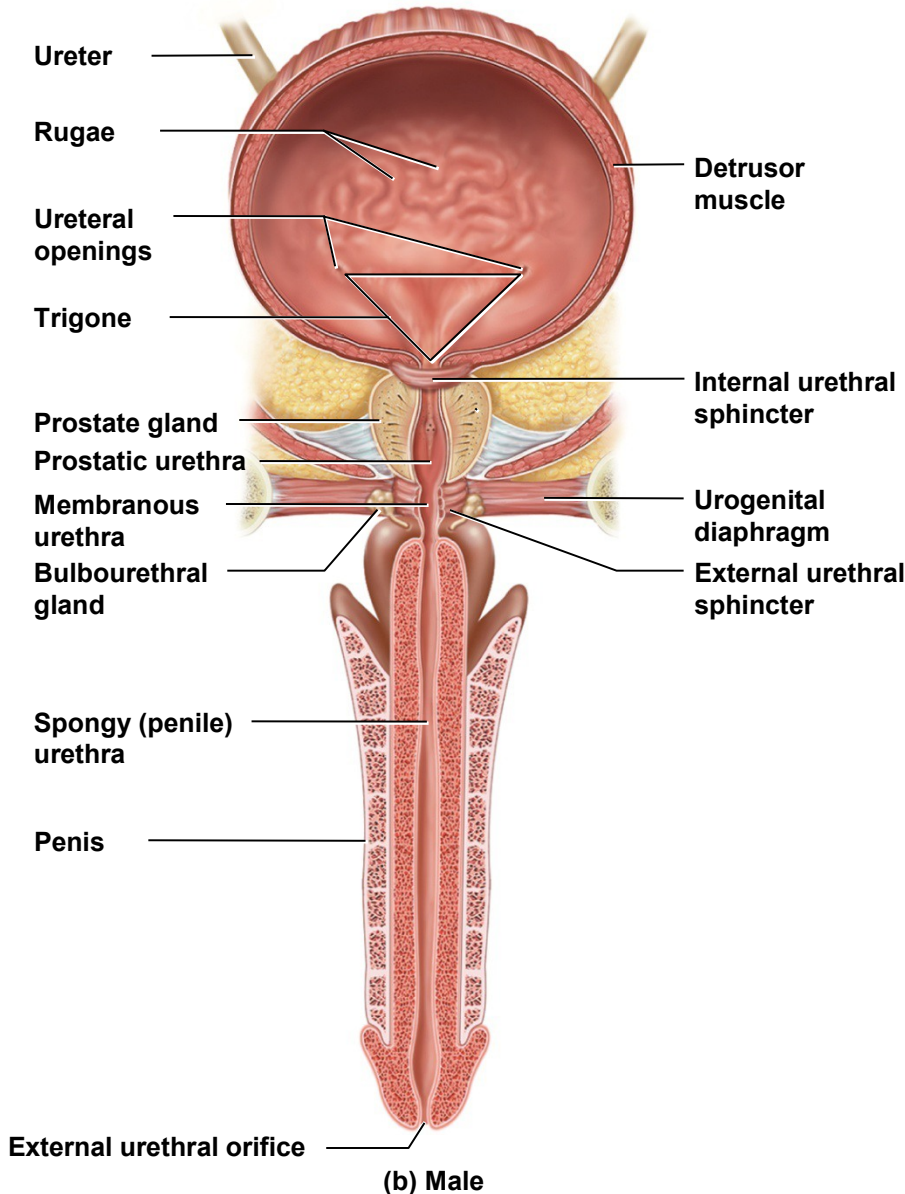
Female Urethra



(a) Female

- 3 to 4 cm long
- bound to anterior wall of vagina
- external urethral orifice
 - between vaginal orifice and clitoris
- internal urethral sphincter
 - detrusor muscle thickening
 - smooth muscle under involuntary control
- external urethral sphincter
 - where the urethra passes through the pelvic floor
 - skeletal muscle under voluntary control

Male Urethra



- 18 cm long
- 3 regions of male urethra
 - prostatic urethra (2.5 cm) // passes through prostate gland
 - membranous urethra (.5 cm) // passes through muscular floor of pelvic cavity
 - spongy (penile) urethra (15 cm) // passes through penis in corpus spongiosum
- internal urethral sphincter // detrusor muscle thickening
- external urethral sphincter // part of skeletal muscle of pelvic floor

Micturition

Involuntary reflex:

Voluntary control:

① Urine fills the bladder and stretches its wall.

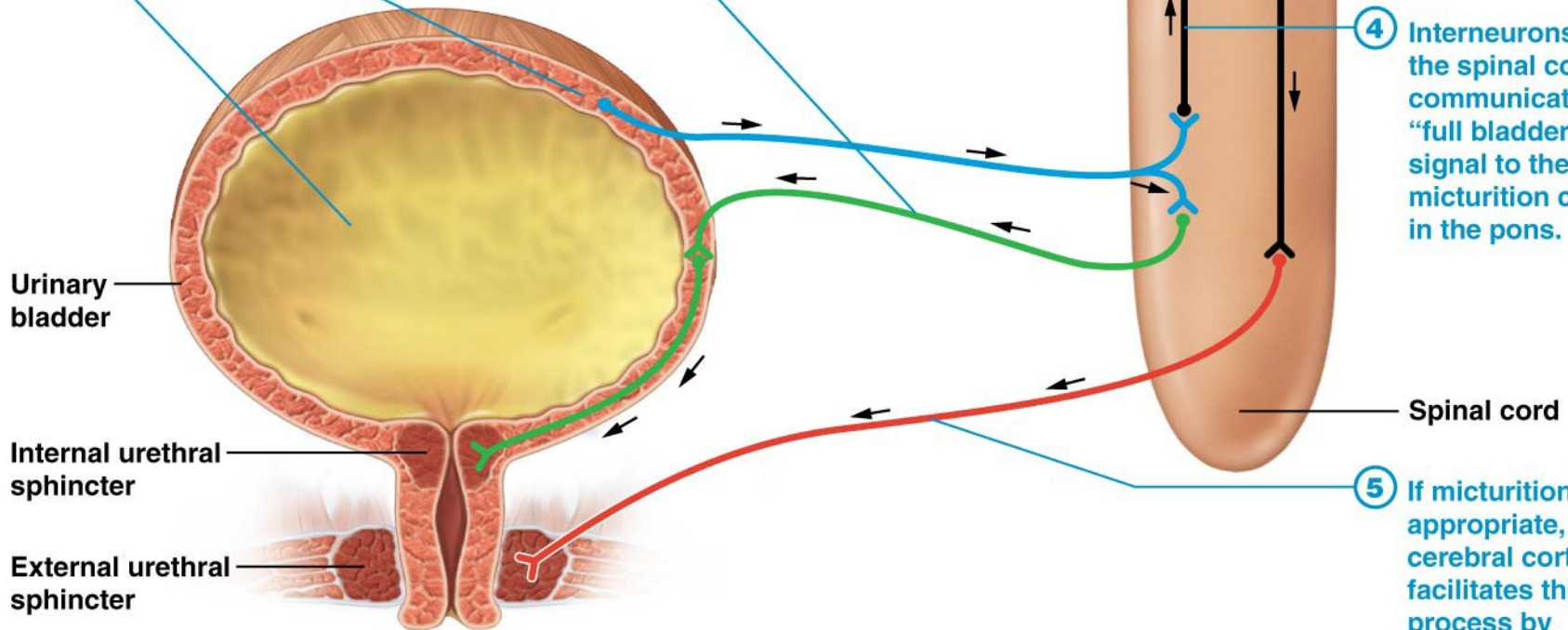
② Stretch receptors send a signal via sensory afferent fibers to the sacral portion of the spinal cord.

③ Parasympathetic efferent fibers stimulate the detrusor muscle to contract and the internal urethral sphincter to relax, causing micturition.

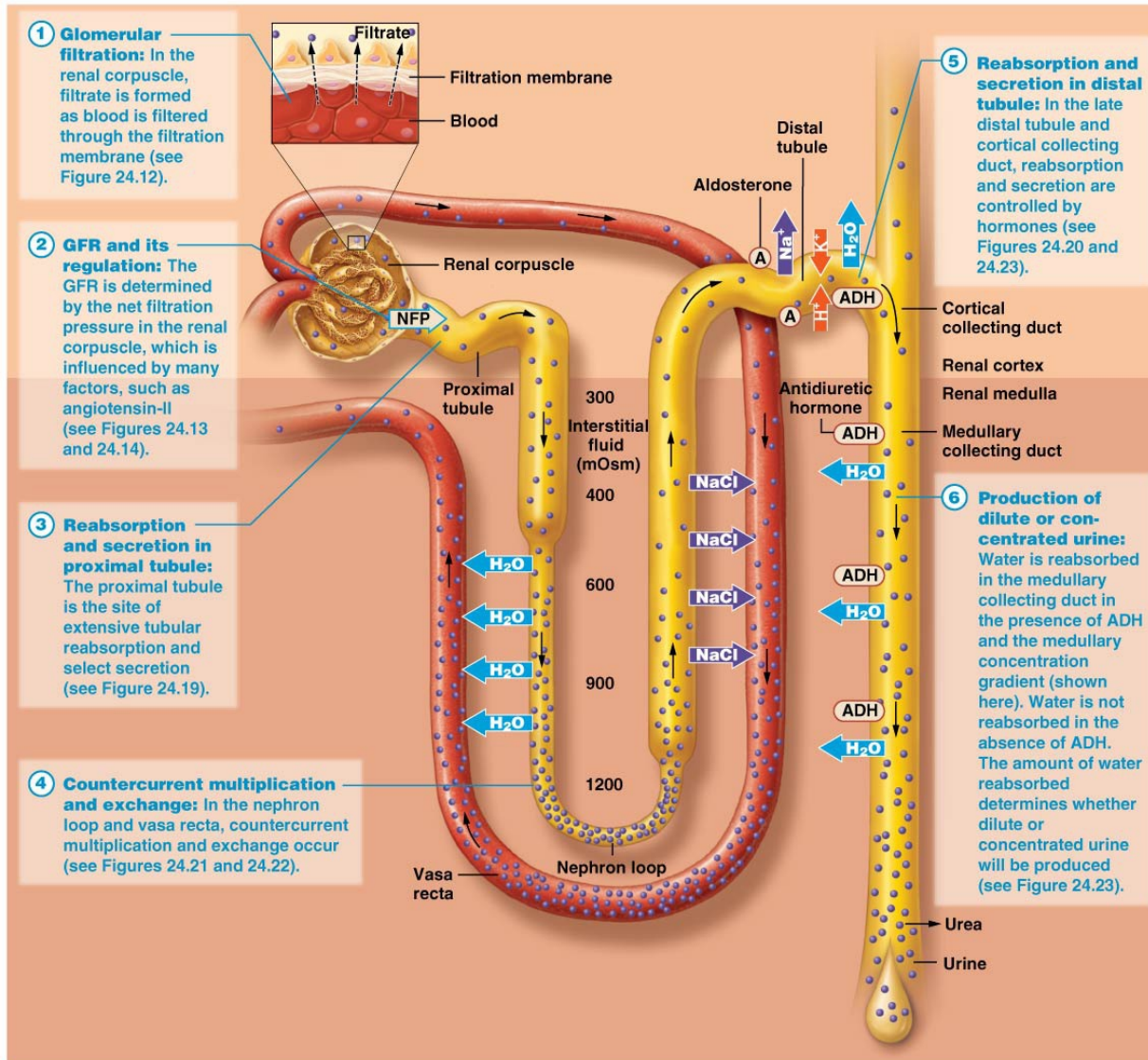
To pons
From brain centers

④ Interneurons in the spinal cord communicate the "full bladder" signal to the micturition center in the pons.

⑤ If micturition is appropriate, the cerebral cortex facilitates this process by allowing the external urethral sphincter to relax, and urine is voided.

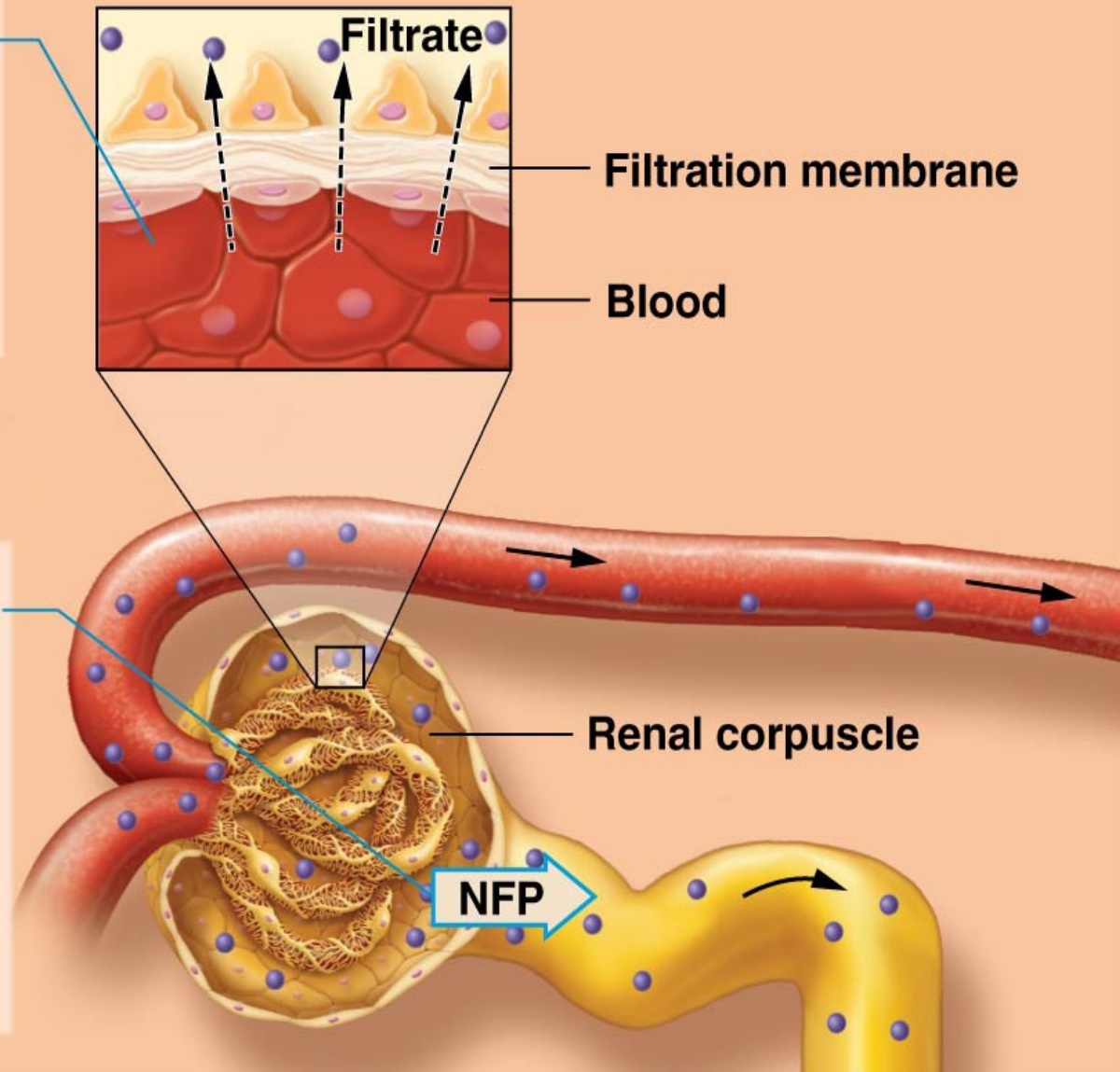


The Big Picture of Renal Physiology.



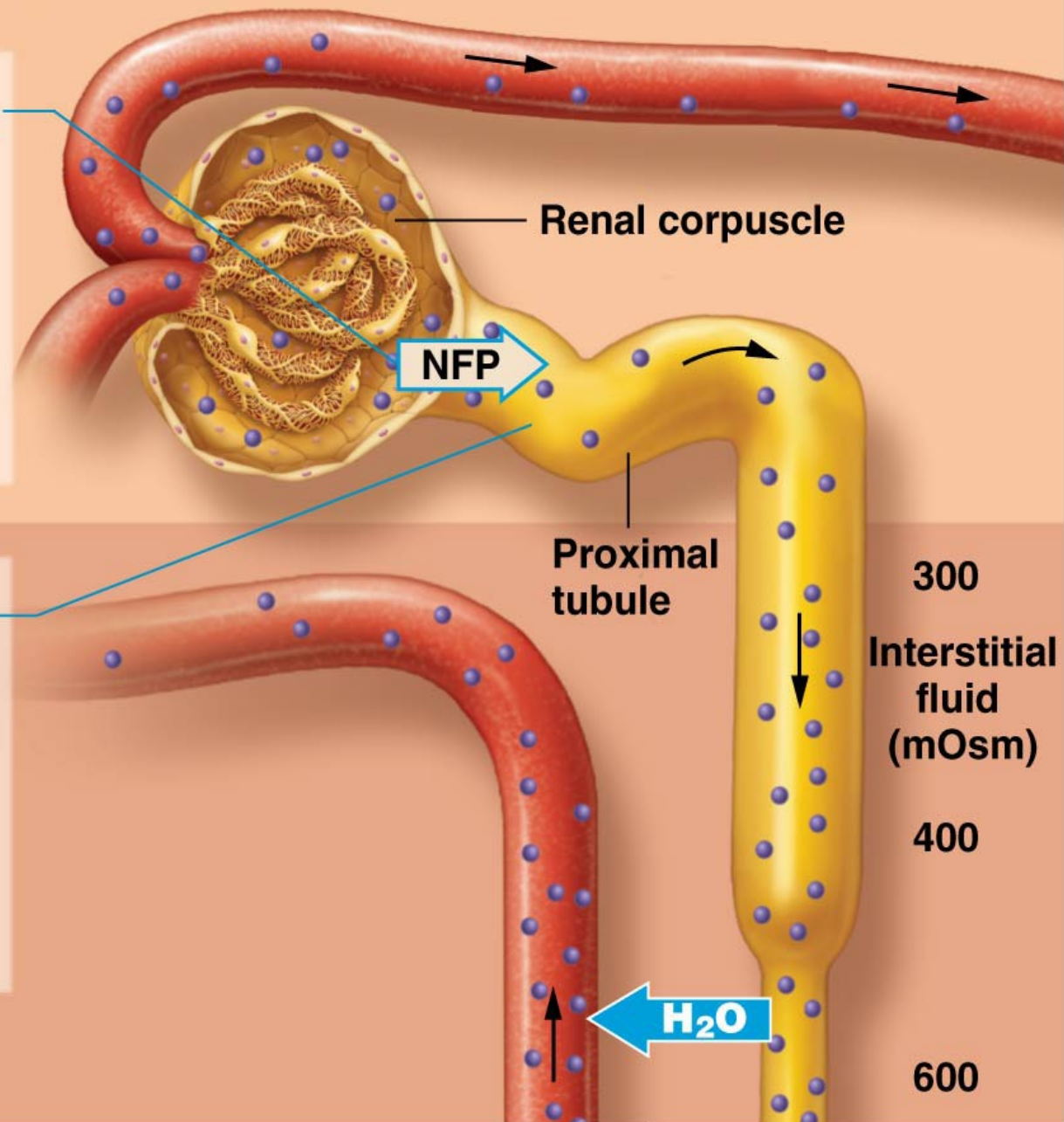
1 Glomerular filtration:
In the renal corpuscle, filtrate is formed as blood is filtered through the filtration membrane (see Figure 24.12).

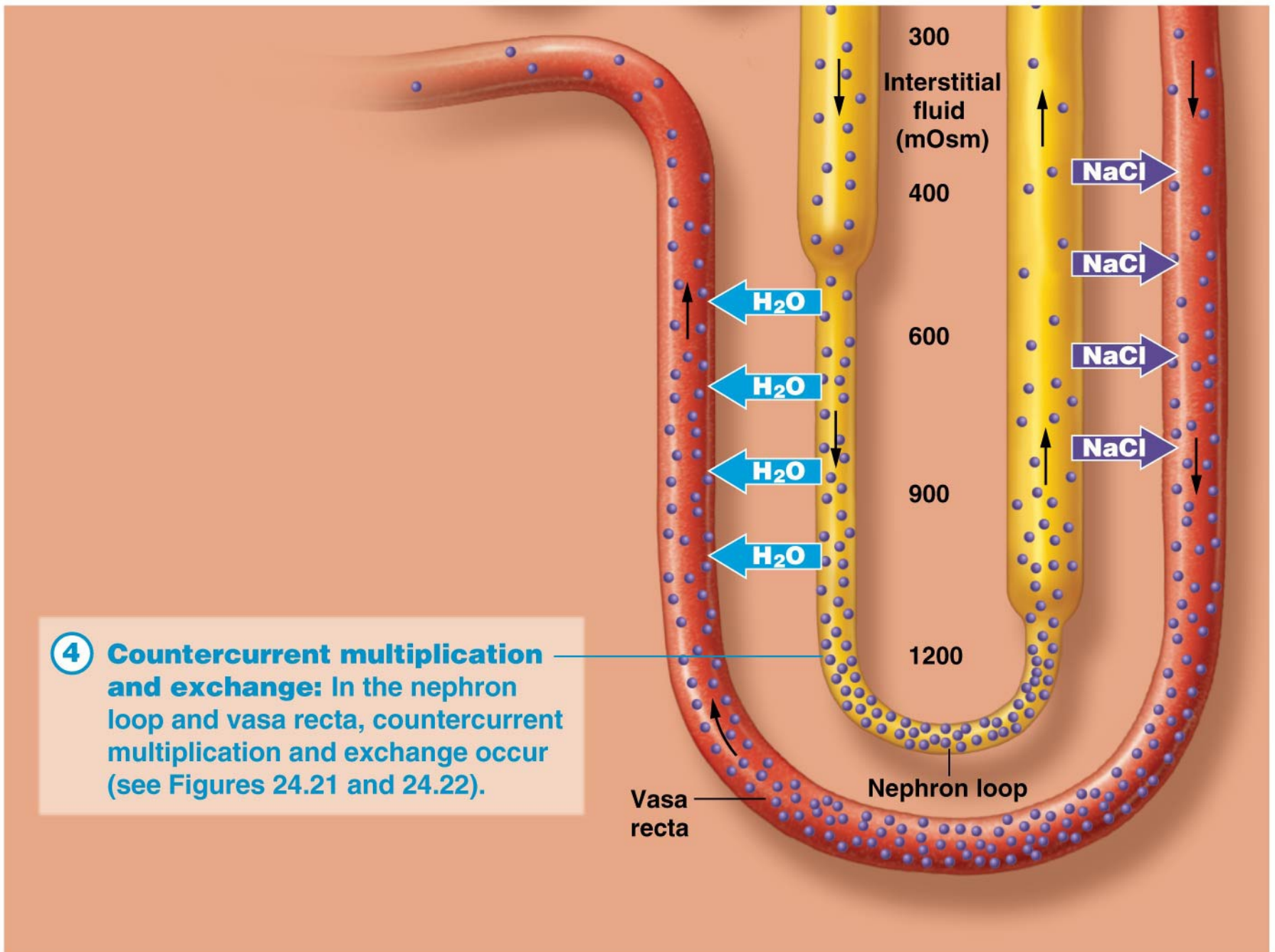
2 GFR and its regulation:
The GFR is determined by the net filtration pressure in the renal corpuscle, which is influenced by many factors, such as angiotensin-II (see Figures 24.13 and 24.14).



2 GFR and its regulation: The GFR is determined by the net filtration pressure in the renal corpuscle, which is influenced by many factors, such as angiotensin-II (see Figures 24.13 and 24.14).

3 Reabsorption and secretion in proximal tubule: The proximal tubule is the site of extensive tubular reabsorption and select secretion (see Figure 24.19).

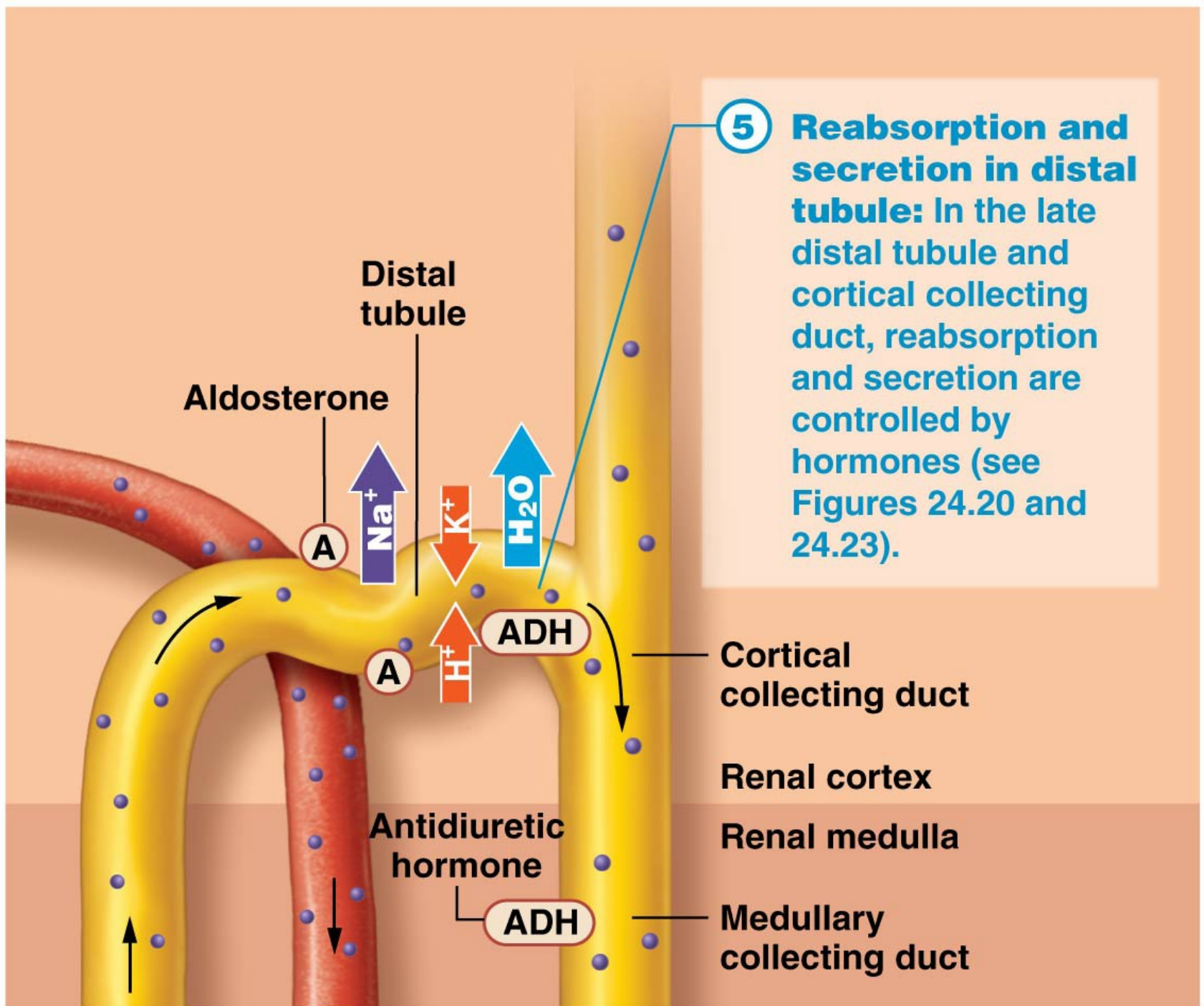


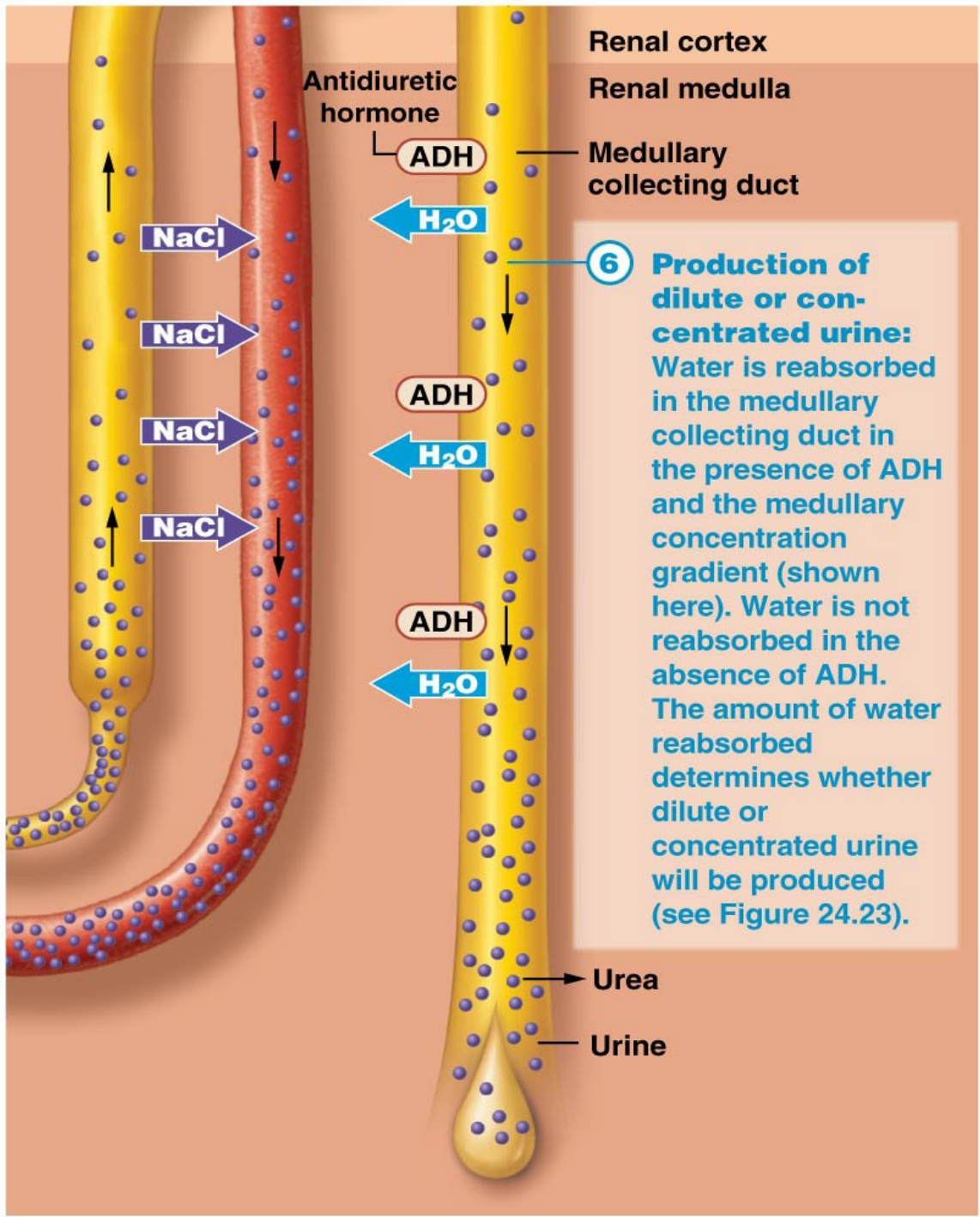


4 Countercurrent multiplication and exchange: In the nephron loop and vasa recta, countercurrent multiplication and exchange occur (see Figures 24.21 and 24.22).

Vasa recta

Nephron loop

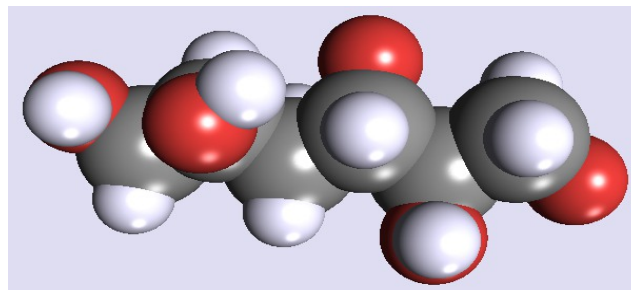




Why is manitol an osmotic diuretic?

Osmotic diuretics have their major effect in the proximal convoluted tubule. Any osmotic active agent that is filtered by the glomerulus but not reabsorbed causes water to be retained in PCT and promotes a water diuresis. Such agents can be used to reduce intracranial pressure and to promote prompt removal of renal toxins. The prototypical osmotic diuretic is mannitol.

The presence of a non-reabsorb solute such as mannitol prevents the normal absorption of water by interposing a countervailing osmotic force. As a result, urine volume increases. The increase in urine flow rate decreases the contact time between fluid and the tubular epithelium, thus also reducing sodium reabsorption. (Wiki)



Mannitol is a sugar alcohol. It is filtered by glomerulus but not reabsorbed.