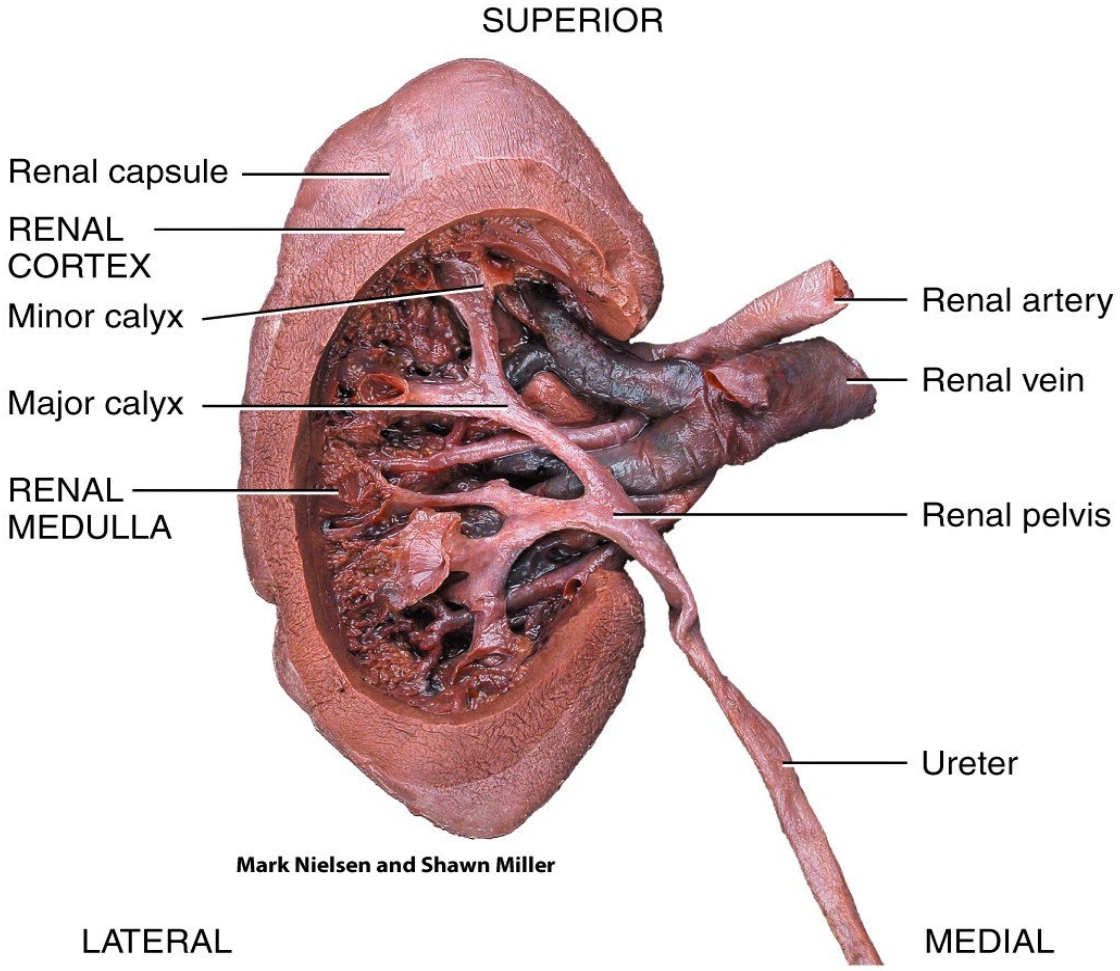
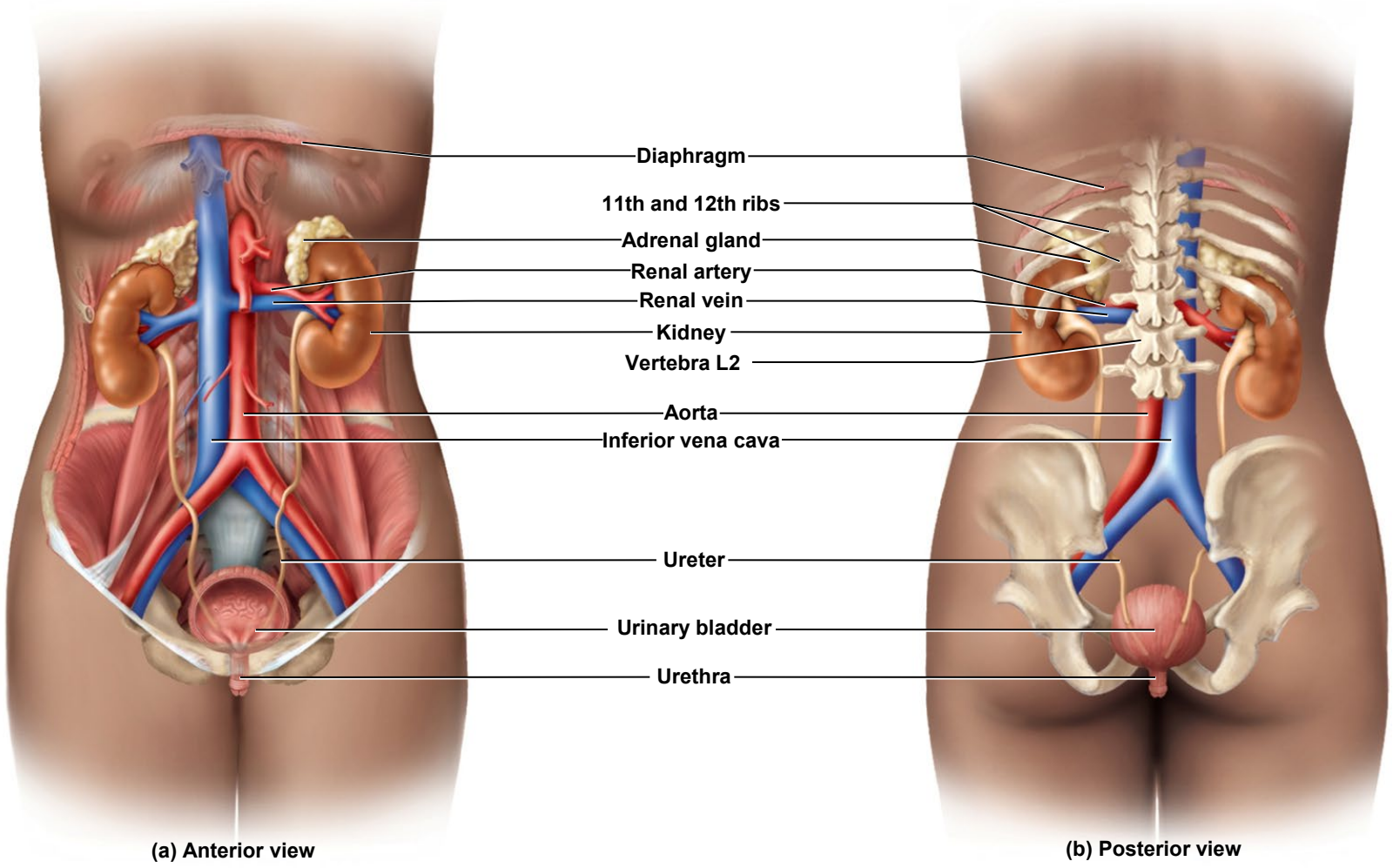
C23

Urinary System



(b) Posterior view of dissection of left kidney

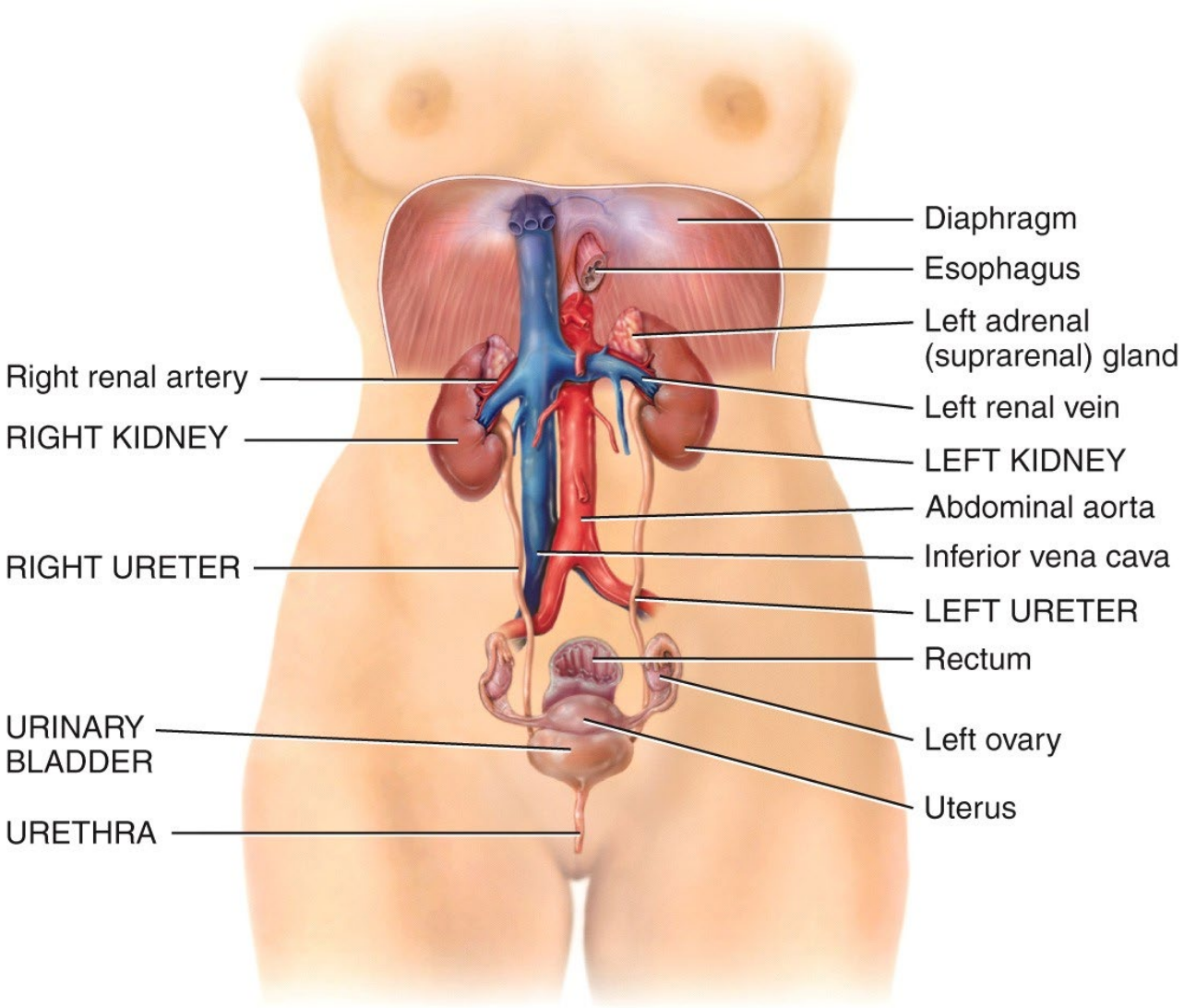
Urinary System



urinary system consists of 6 organs:

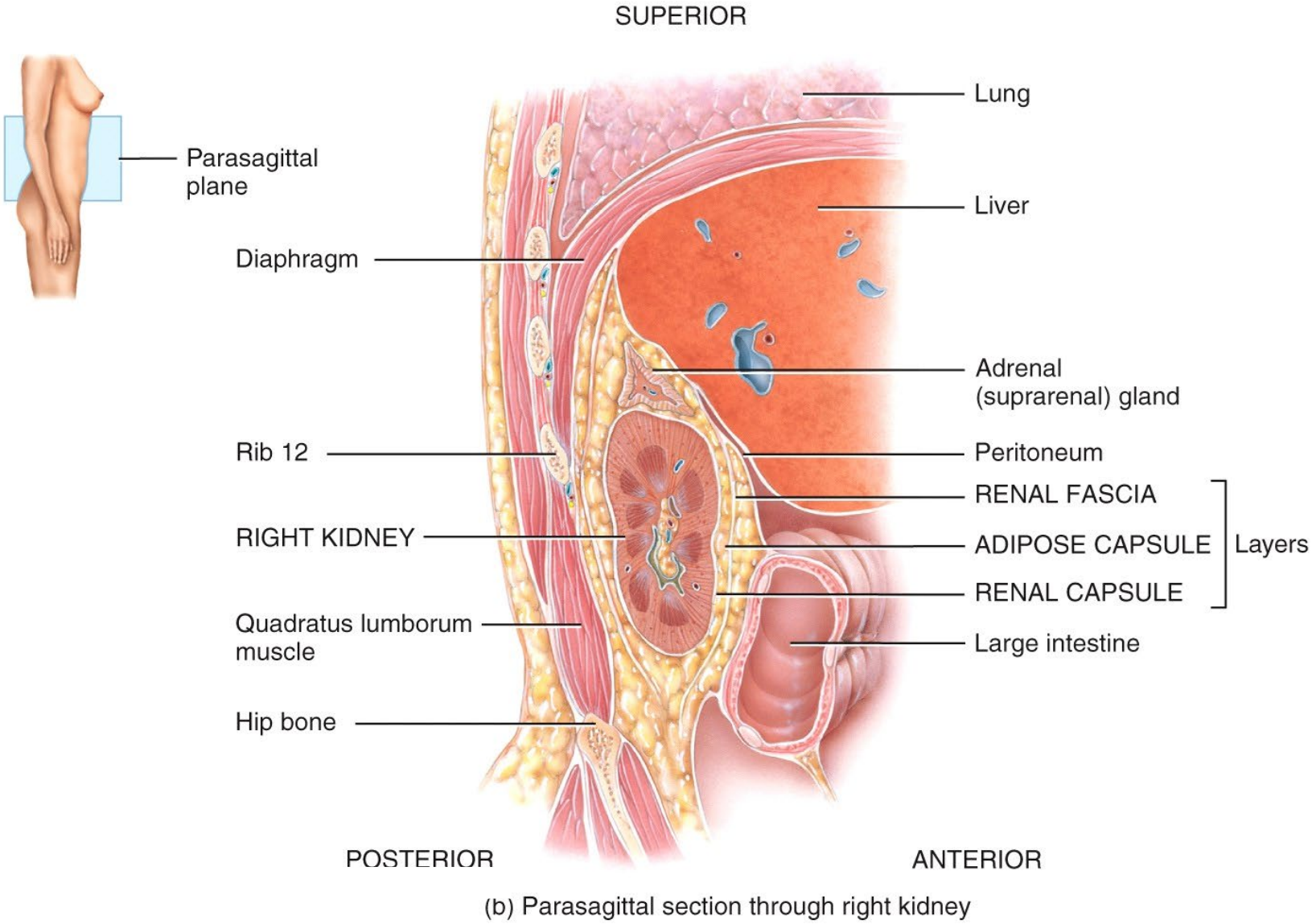
2 kidneys, 2 ureters, 1 urinary bladder, and 1 urethra

Anatomy of Urinary System



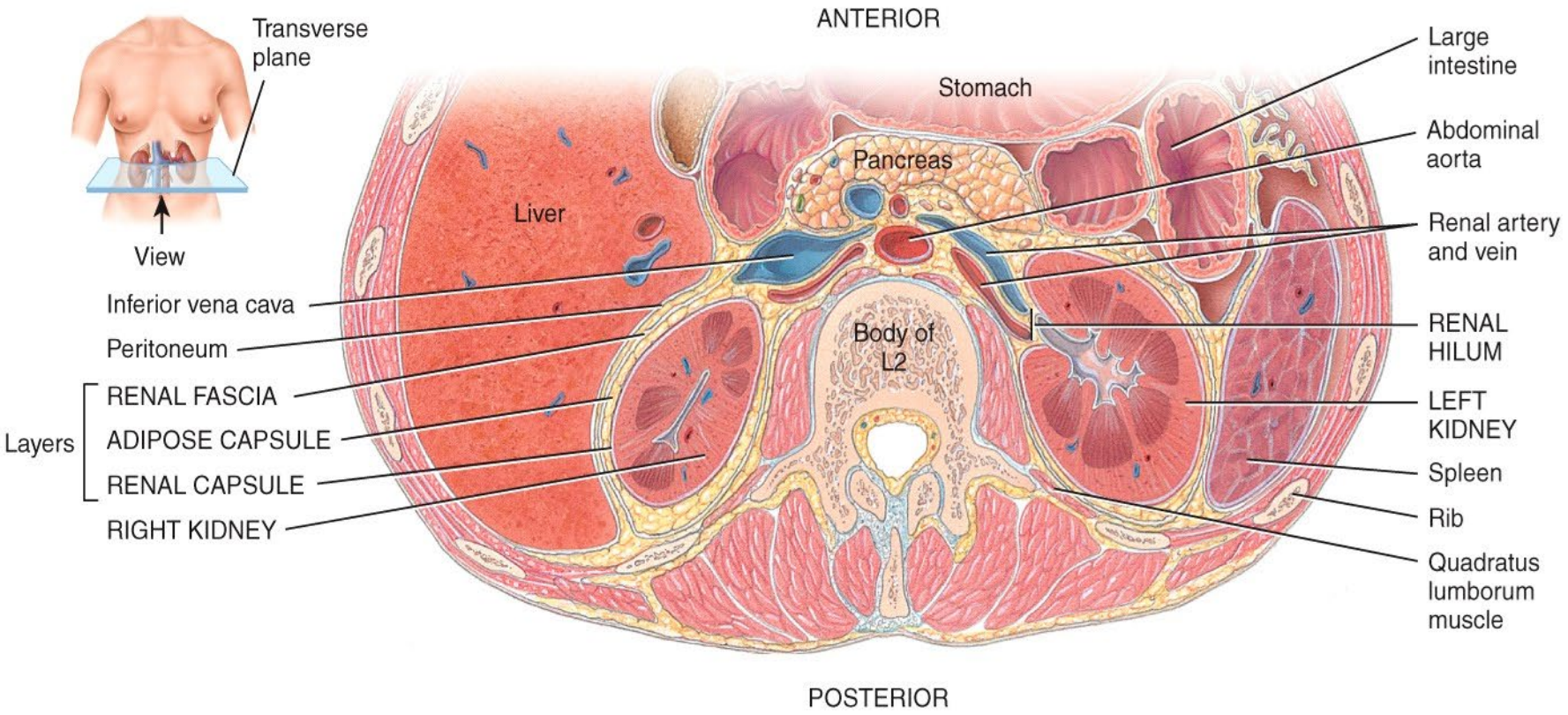
(a) Anterior view of urinary system

What layers surround the kidneys?



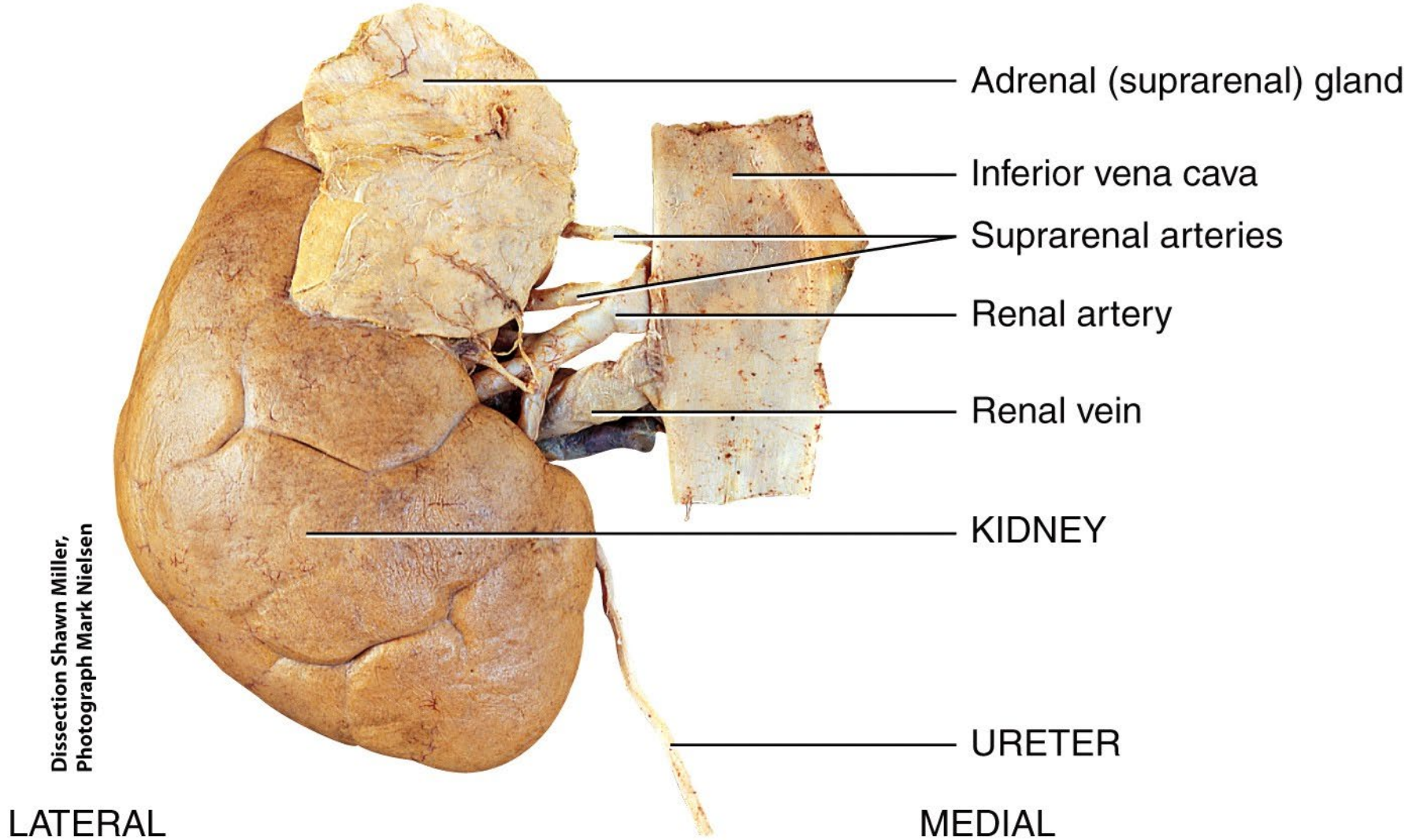
(b) Parasagittal section through right kidney

Copyright © 2014 John Wiley & Sons, Inc. All rights reserved.



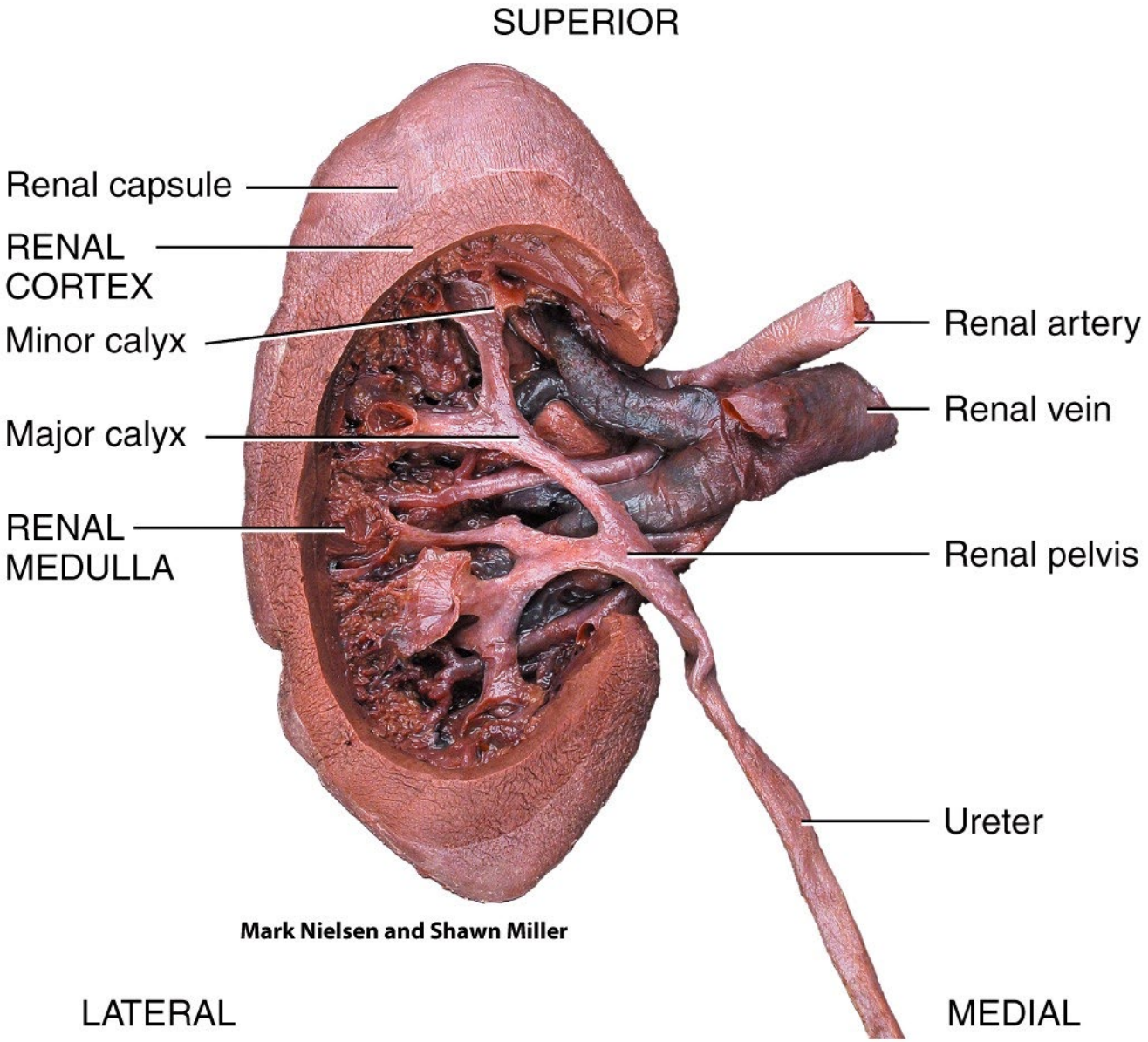
(a) Inferior view of transverse section of abdomen (L2)

What does retroperitoneal mean?

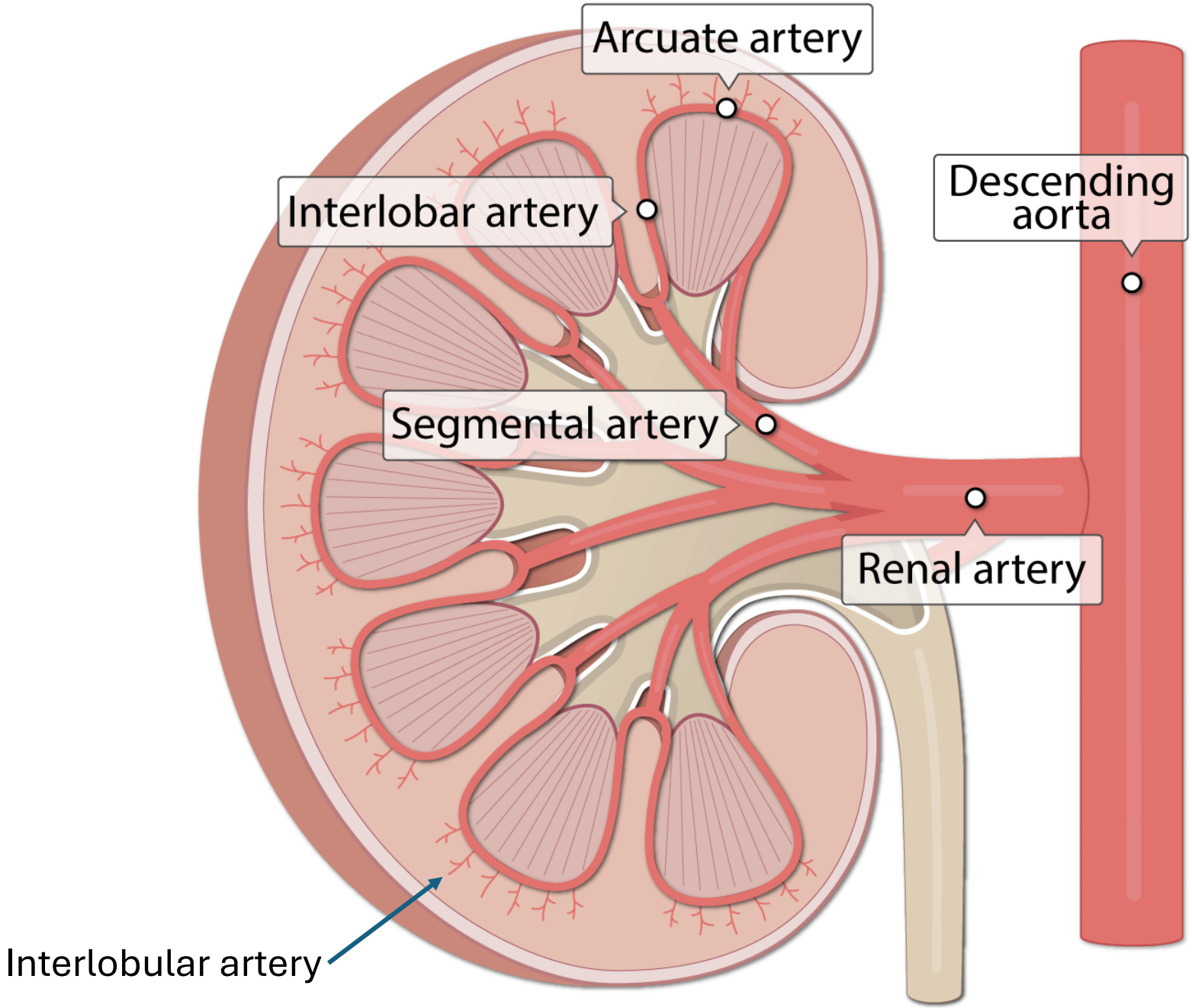


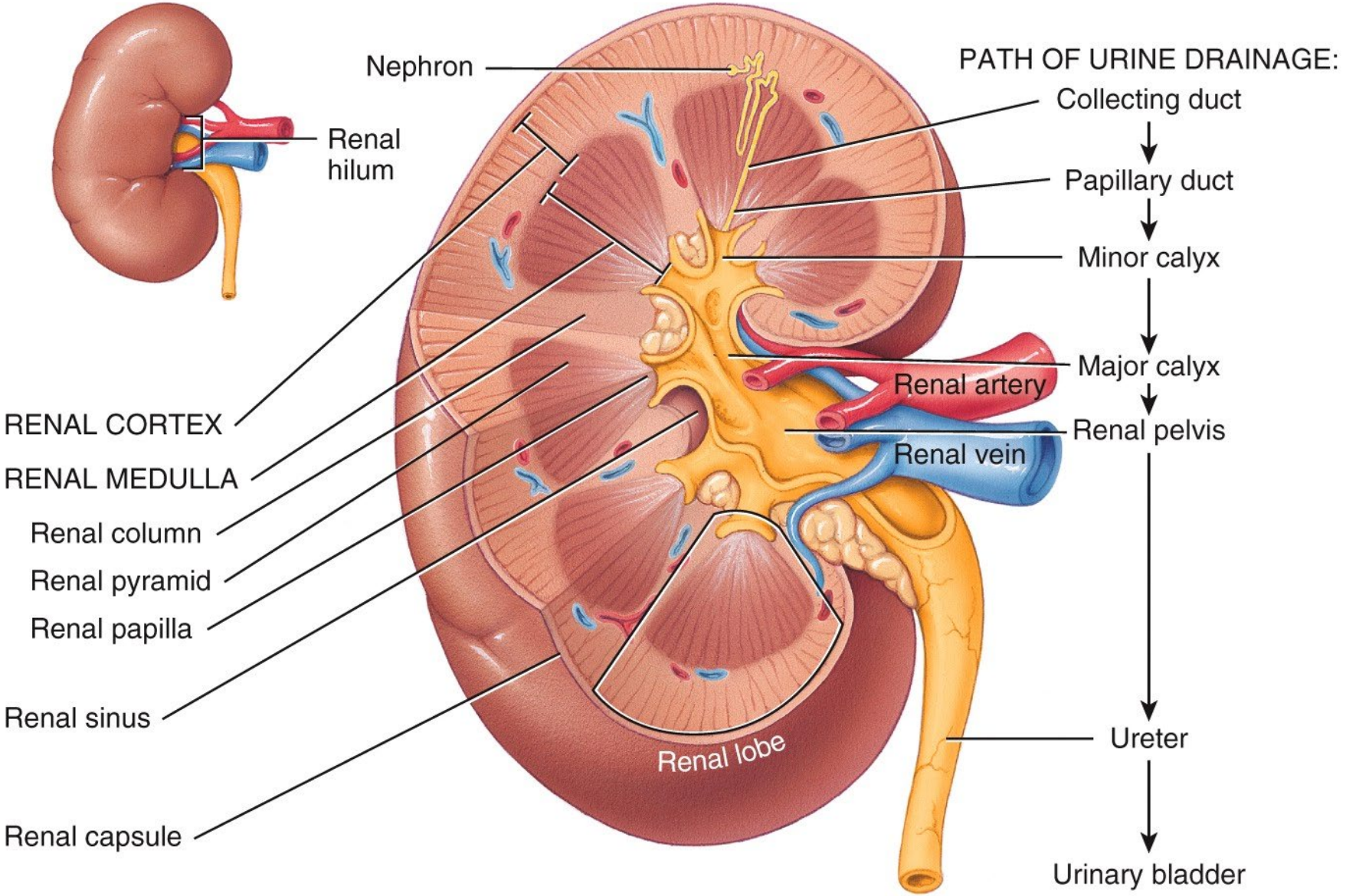
(b) Anterior view of right kidney

What is secreted from the adrenal gland? When?



(b) Posterior view of dissection of left kidney

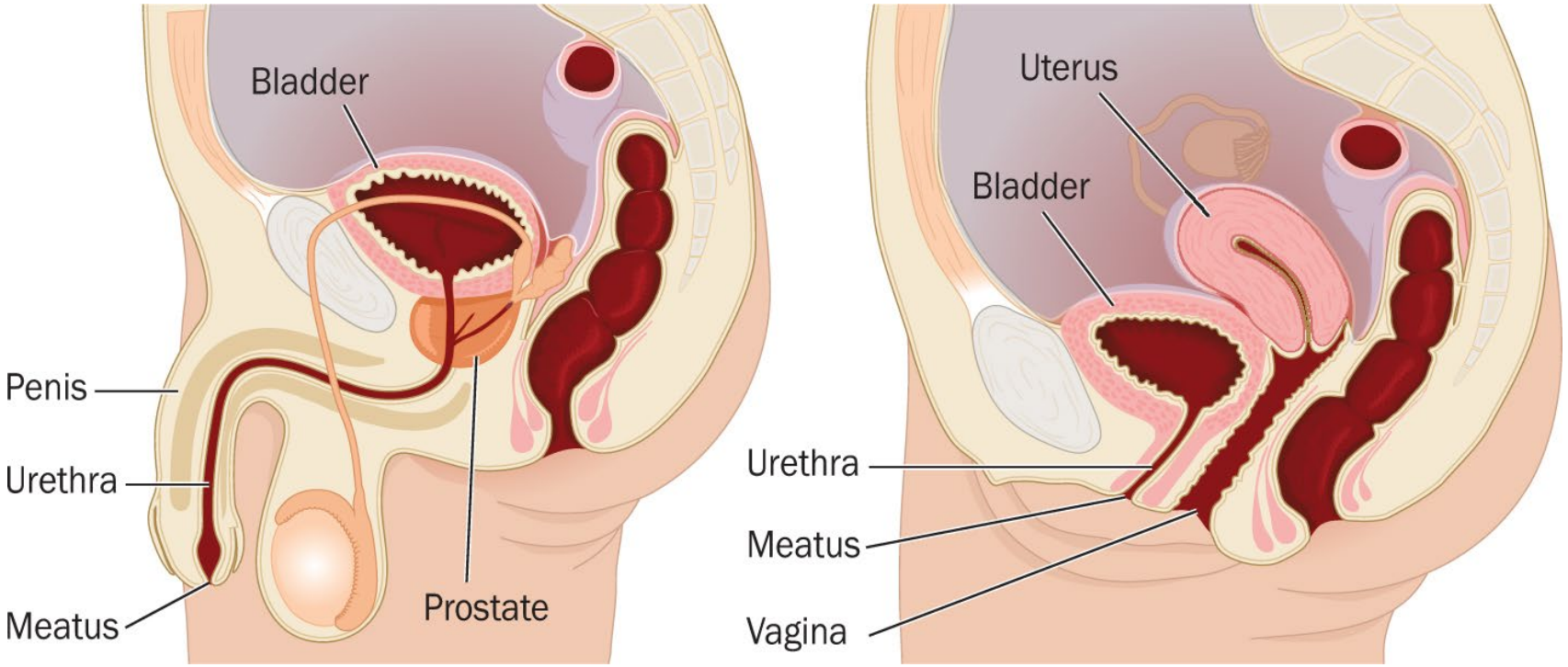

Arcuate artery
Interlobar artery
Descending aorta
Segmental artery
Renal artery
Interlobular artery



(a) Anterior view of dissection of right kidney

Copyright © 2014 John Wiley & Sons, Inc. All rights reserved.

Male VS Female Urinary System



Functions of the Kidney (1 of 2)

Filters blood plasma, separates toxic waste, retains and conserves useful molecules // process of urine Formation eliminates toxic molecules and recovers essential ions and

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 the enzyme renin // 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 formed in the liver and circulates in the blood as an inactive molecule // is converted to *calcitriol in kidney* // *calcitriol is active form of Vit D* / contributes to calcium homeostasis

Gluconeogenesis // kidney's ability to form new glucose from amino acids – only used in extreme starvation (gluconeogenesis is also function of liver)

How do we eliminate waste from our body?

To live is to metabolize.

Catabolic metabolism creates toxic waste products (e.g. nitrogen and organic acids)

The waste products of metabolism must be removed from the body. These systems remove end catabolic waste products.

- Respiratory
- Digestive
- Sweat glands
- Urinary system

The nephron is the "structural unit" of a kidney

The nephron start at the renal capsule (also called Bowman's capsule) and ends at the distal end of the collection duct (at the renal papilla // tip of the pyramid)

Divided into five regions

Renal corpuscle (*1)*

> *Two parts = Outer glomerular capsule also called Bowman's capsule*

> *Inside is the glomerular capillaries also called the glomerulus)*

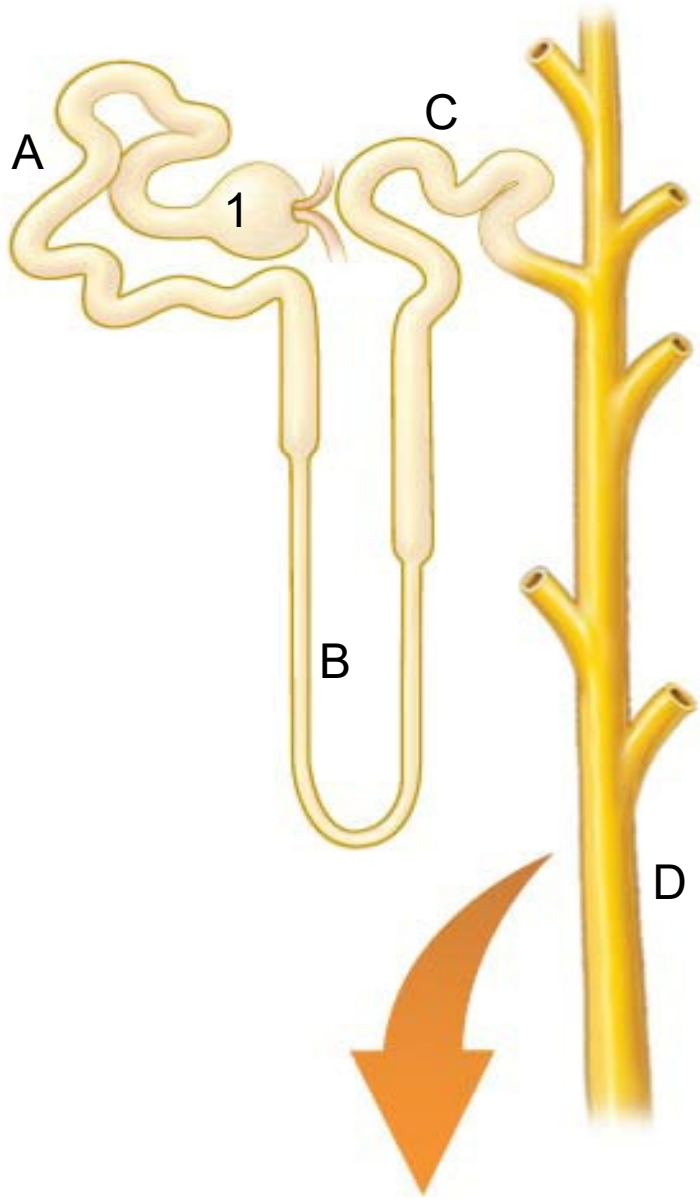
Proximal convoluted tubule A

Nephron loop B

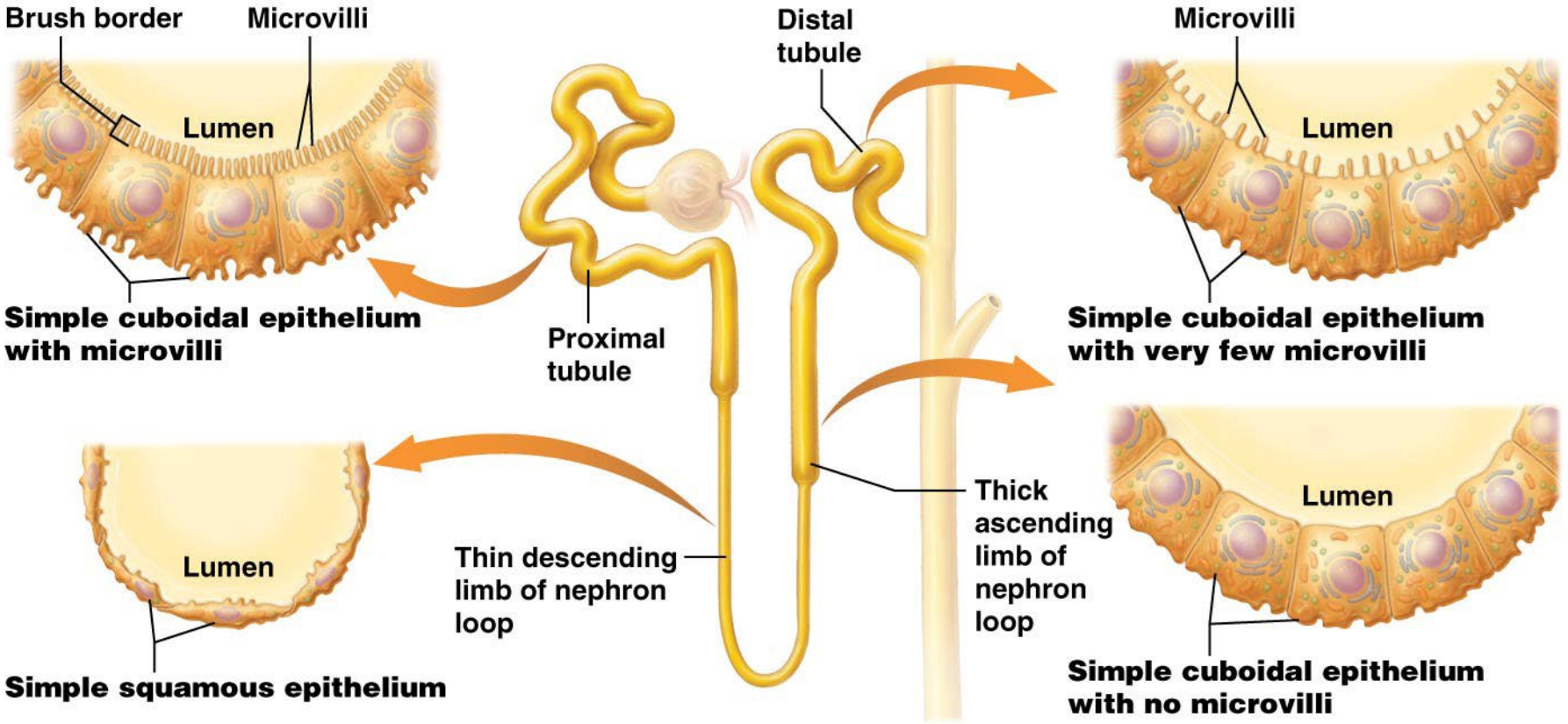
Distal convoluted tubule C

Collecting duct D

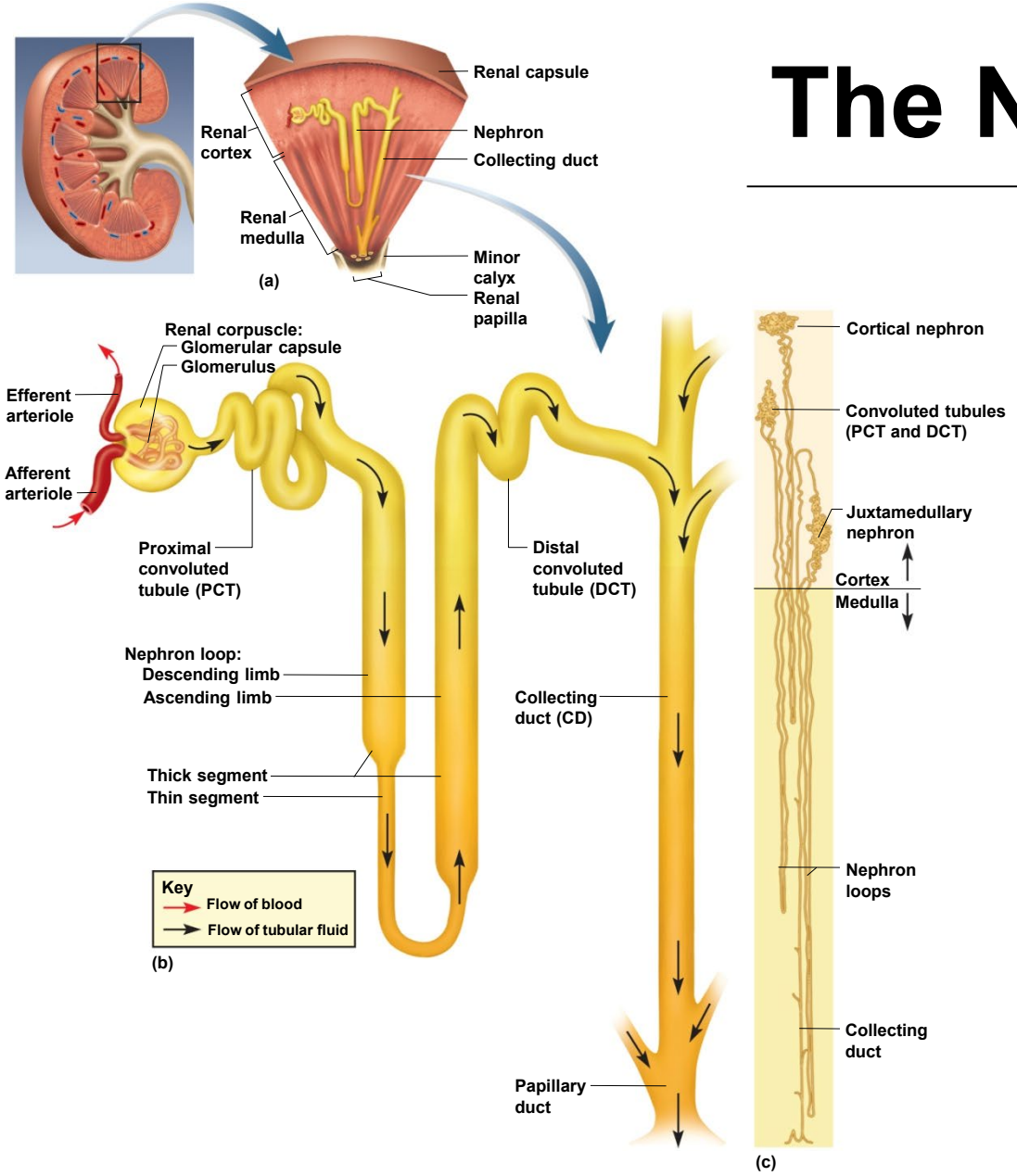
Tubules of the Nephron



Along the tubular nephron the cell's morphology and function change. Different types of transmembrane protein ion pumps modify the tubular fluid as it makes it way to the collecting duct.



The Nephron



Each kidney has approximately 1.2 million nephrons

May survive with as few as 25%

The nephron has <u>two parts:</u>

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

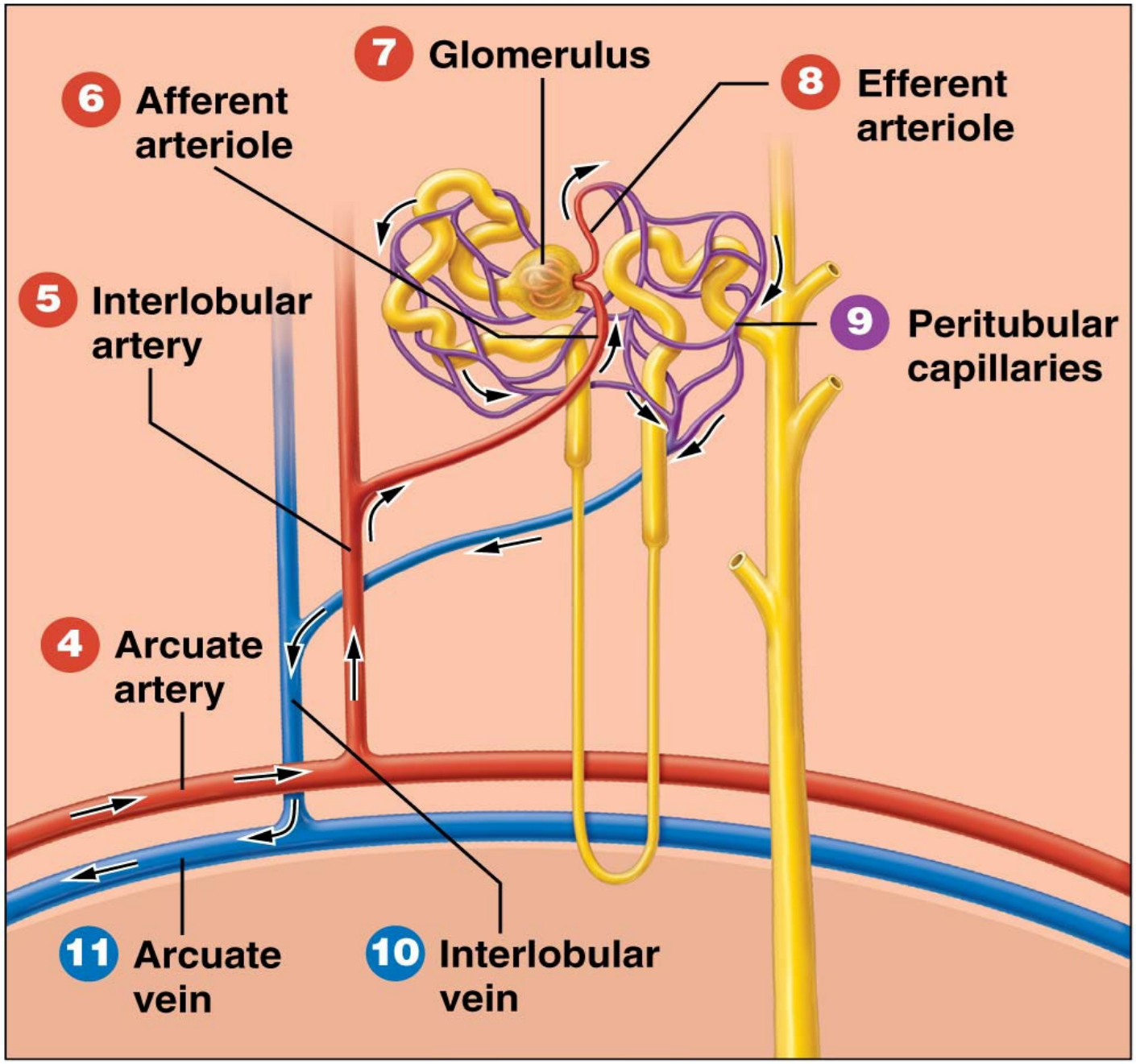
renal tubules – long coiled tubes that converts the filtrate into urine

The functional nephron requires a system of blood vessels to make urine. These blood vessels are closely associated with the tubular nephron.

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)***

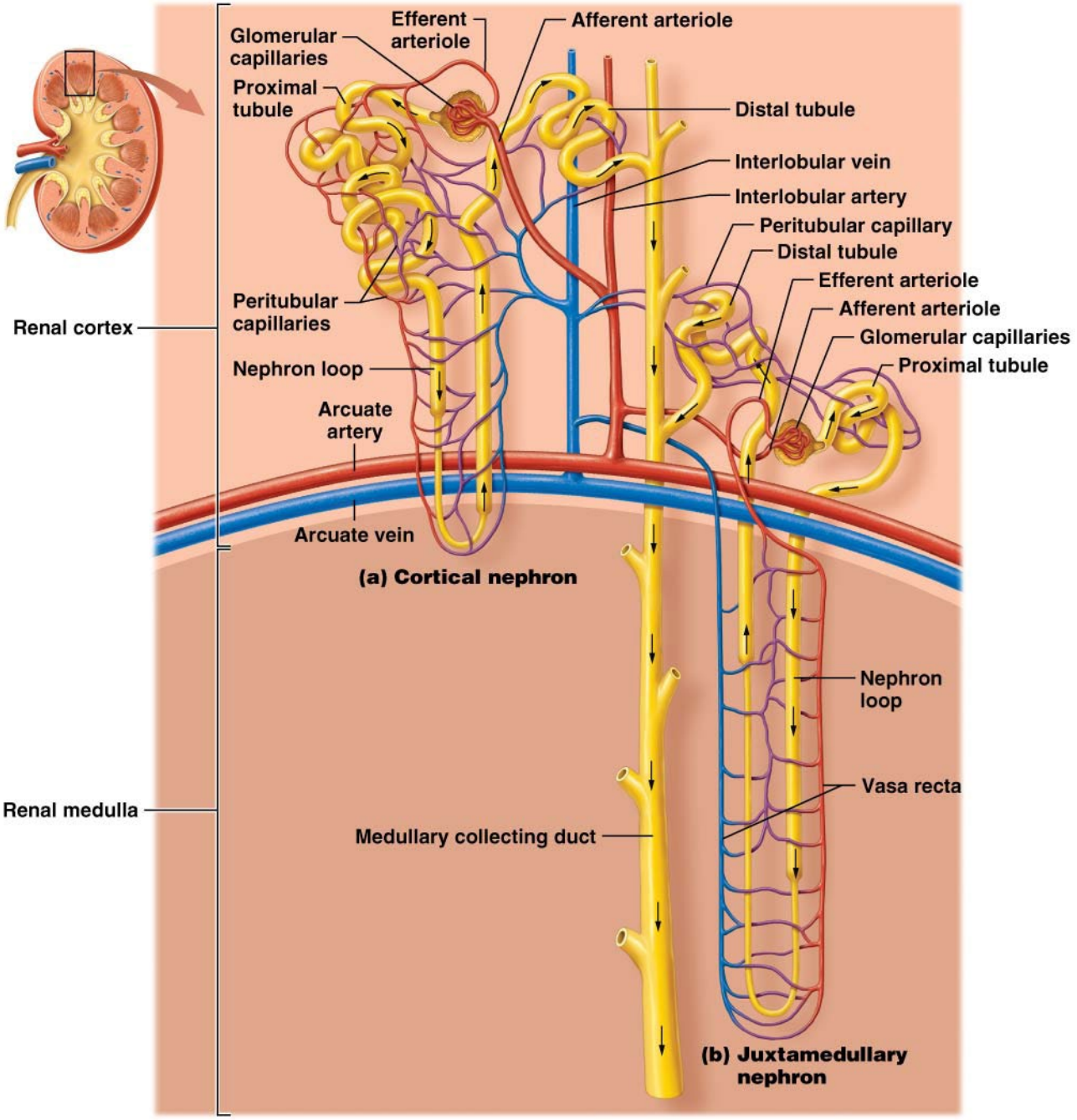


(b) Blood flow around nephron

Two different structural and functional nephrons

Cortical nephron // receives 85% of blood /// responsible for producing most of the filtration volume /// produces the urine

Juxtamedullary nephron // responsible for making the deep medulla hypertonic // makes it possible to recover water and concentrate the urine

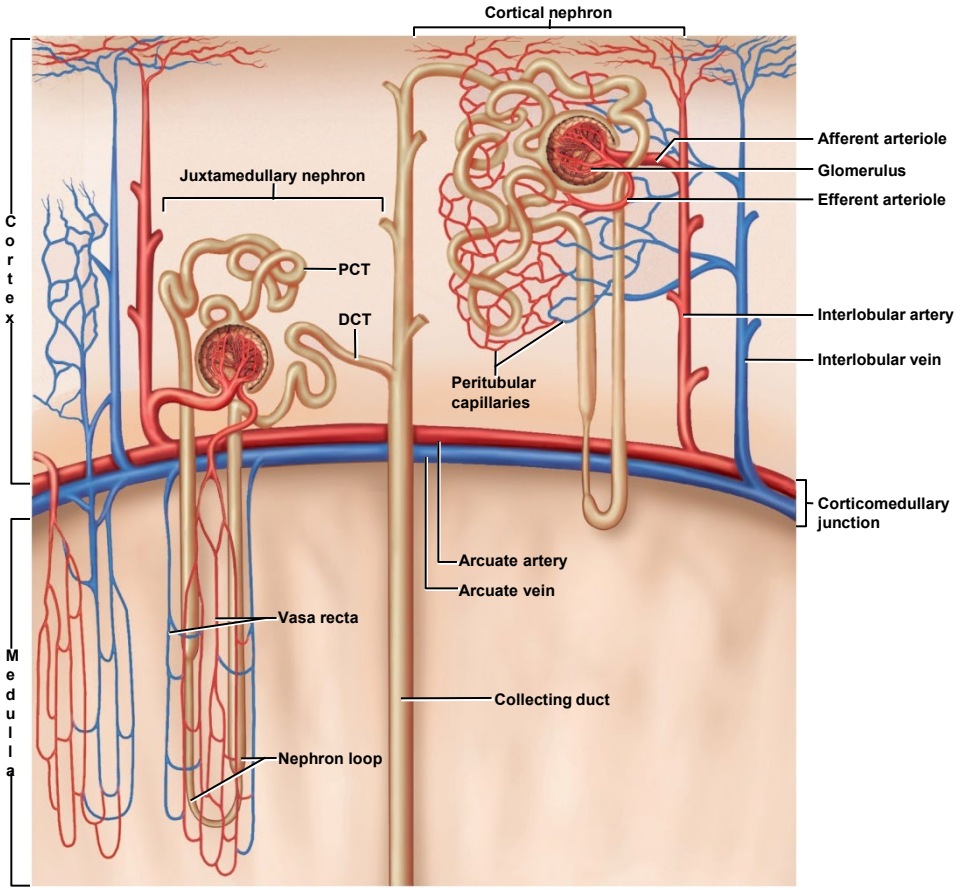


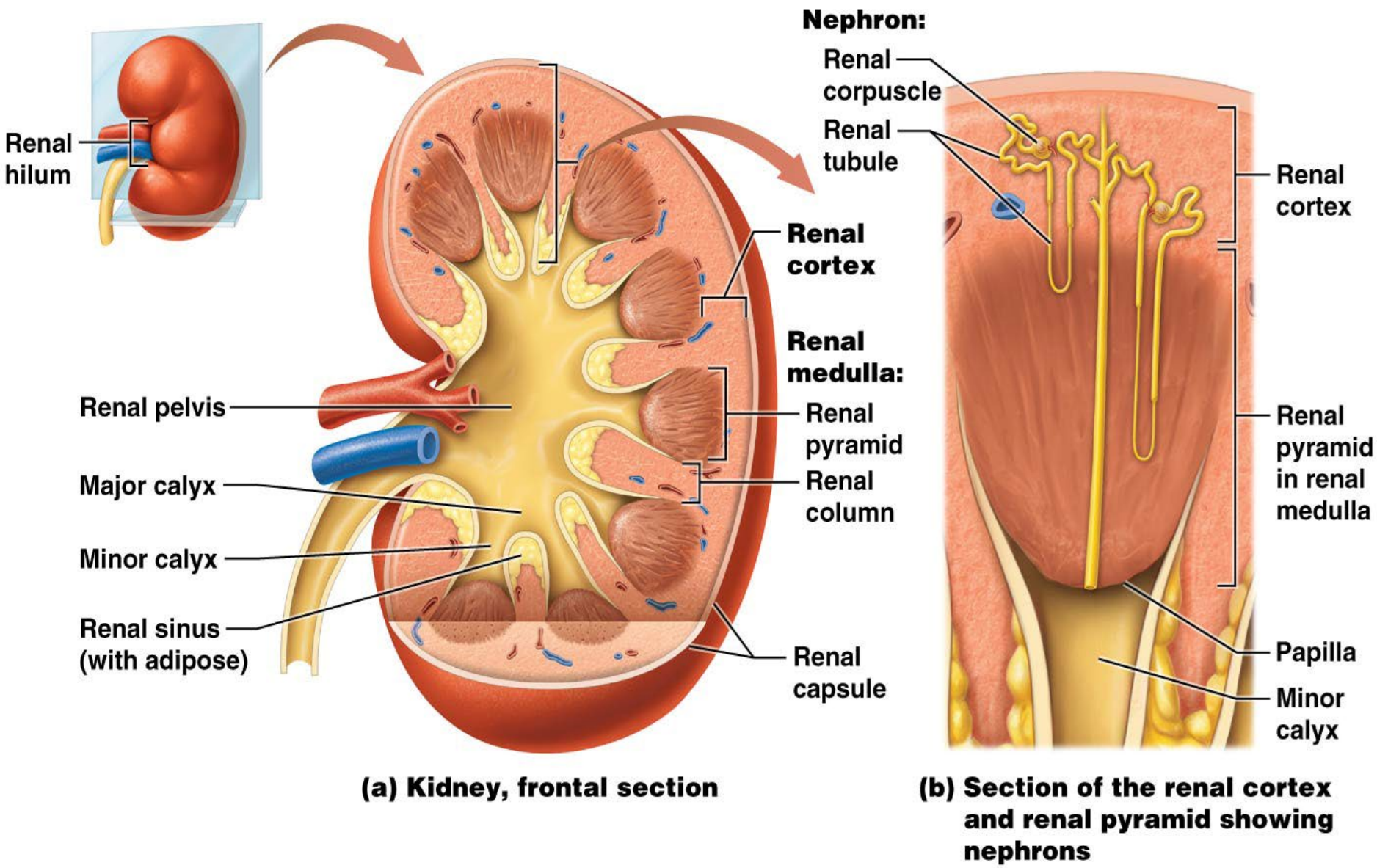
What is the structure and function of the two capillary beds surrounding the nephron's tubules?

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).

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.





(a) Kidney, frontal section

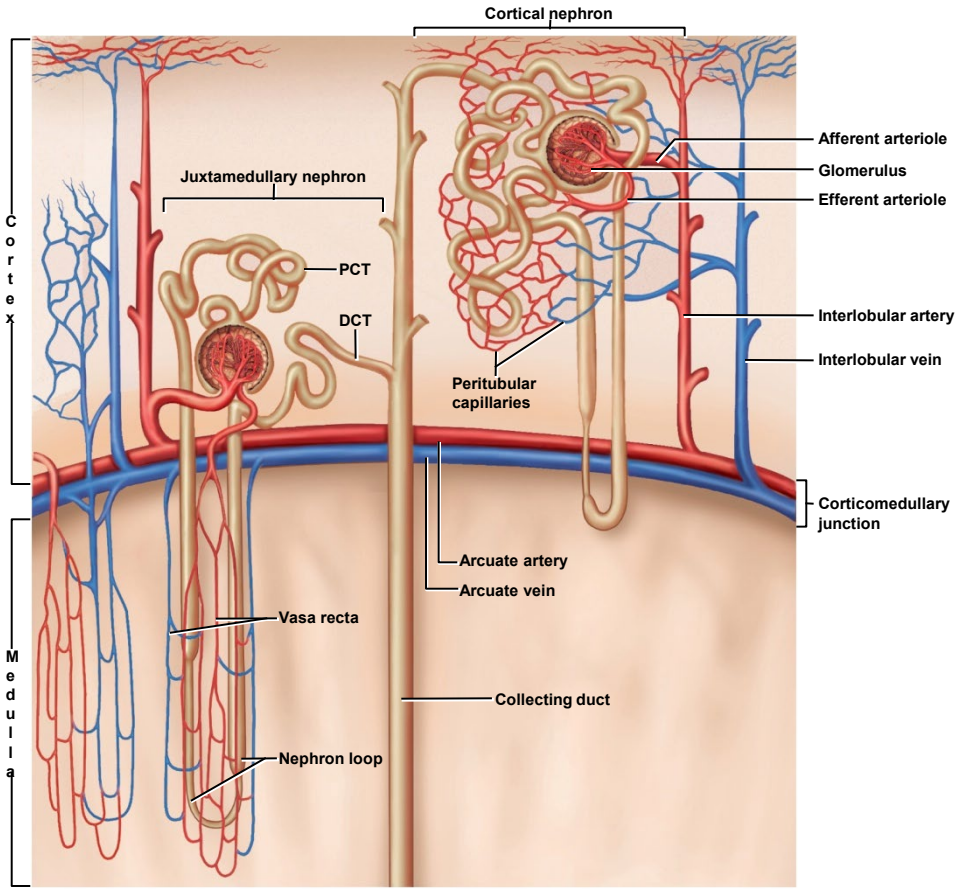
(b) Section of the renal cortex and renal pyramid showing nephrons

Renal Corpuscle Has Two Poles (sides)

Vascular pole = side where afferent and efferent arterioles enter and exit the renal corpuscle

Tubular pole – side where filtrate made inside renal corpuscle enters proximal convoluted tubule

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

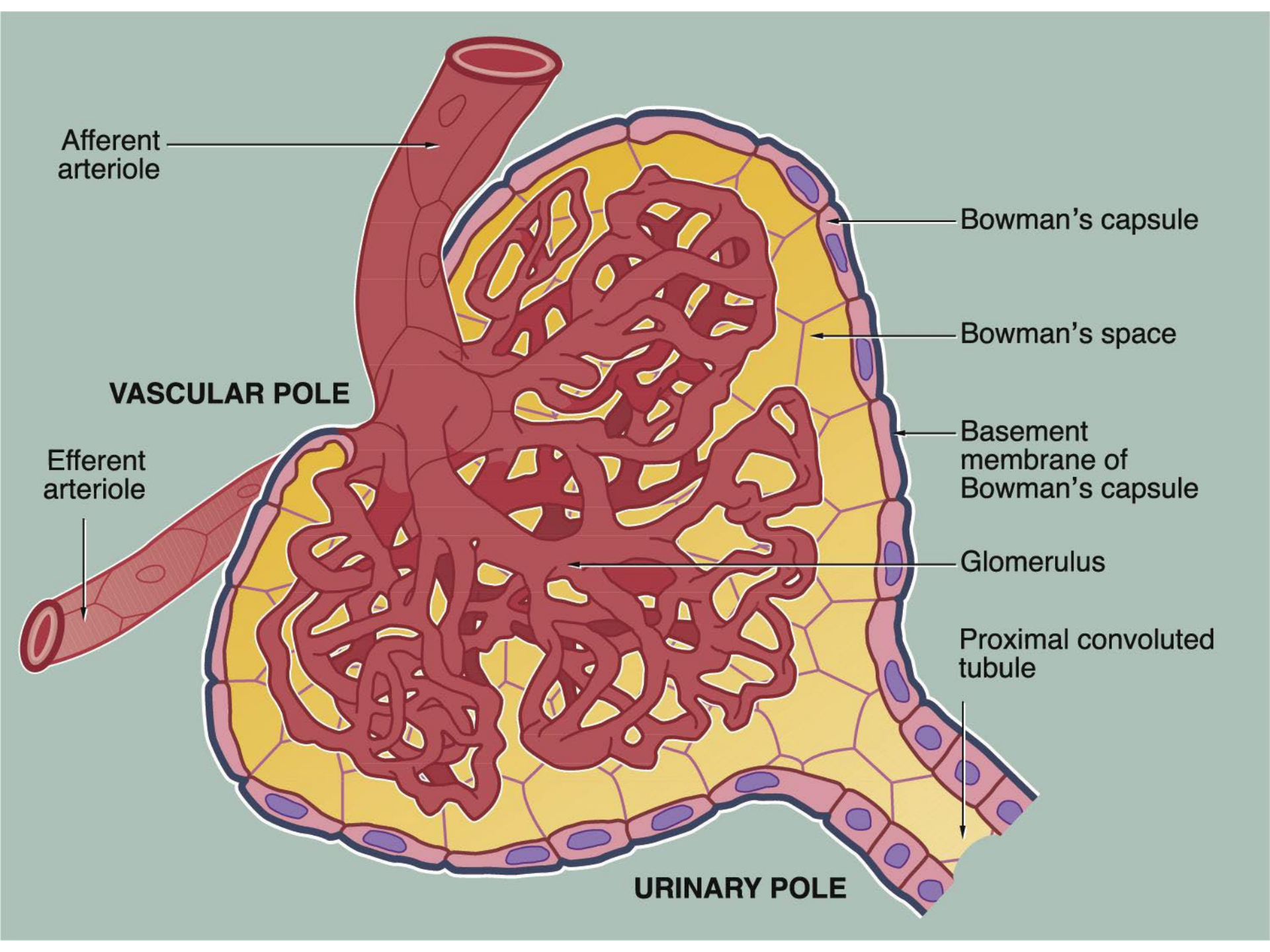


Fluid changes its name as it passes through nephron

(1) filtrate in renal corpuscle

(2) tubular fluid in PCT–LH-DCT

(3) urine in CD


Afferent arteriole
Bowman's capsule
Bowman's space
VASCULAR POLE
Efferent arteriole
Basement membrane of Bowman's capsule
Glomerulus
Proximal convoluted tubule
URINARY POLE

Proximal convoluted tubule (PCT)

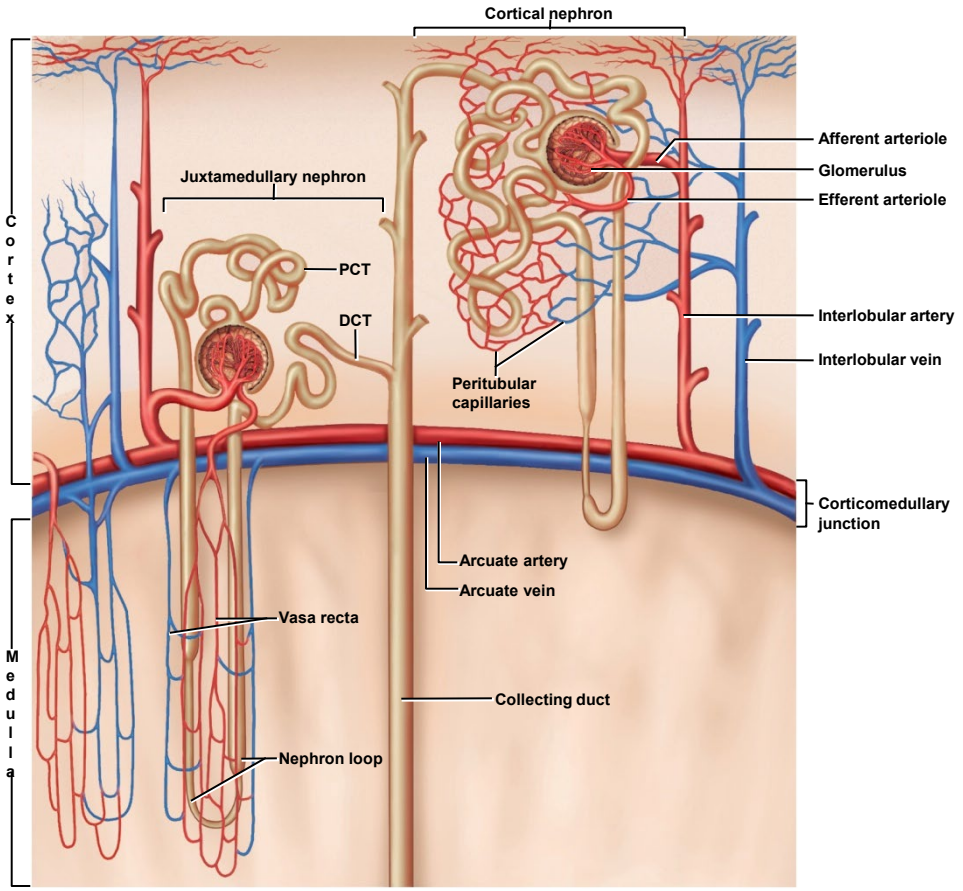
starts at the glomerular capsule

longest and most coiled region

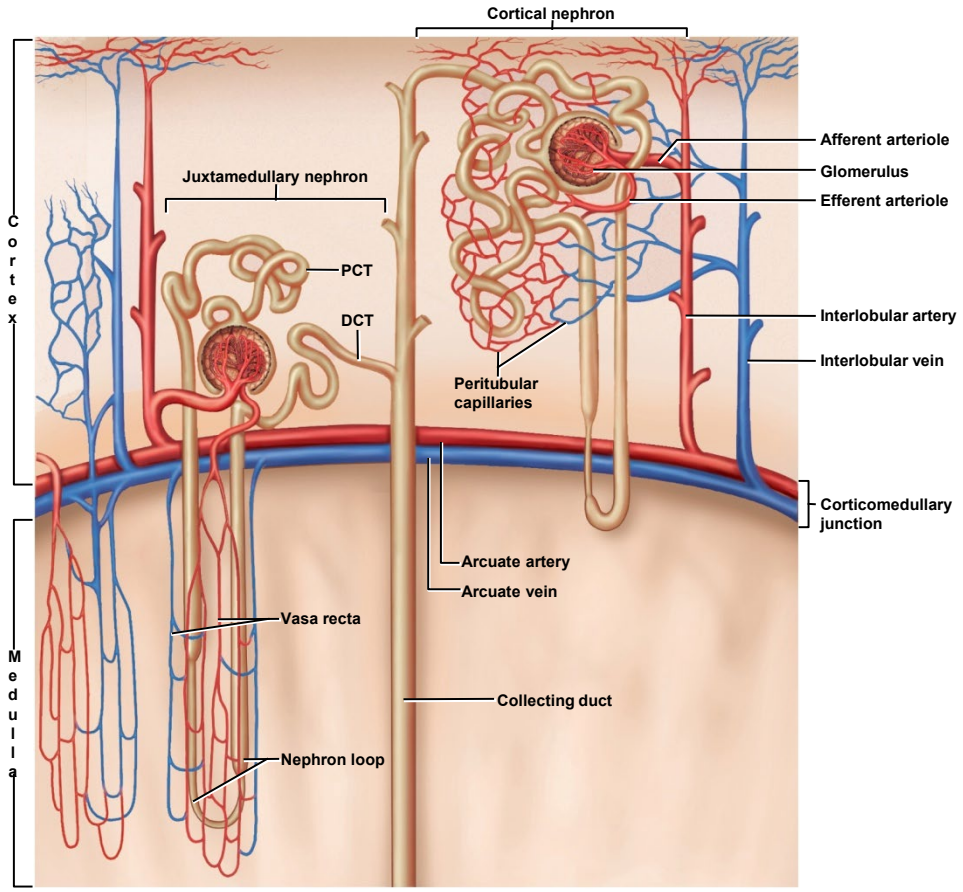
simple cuboidal epithelium with prominent microvilli for reabsorption

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

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



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)

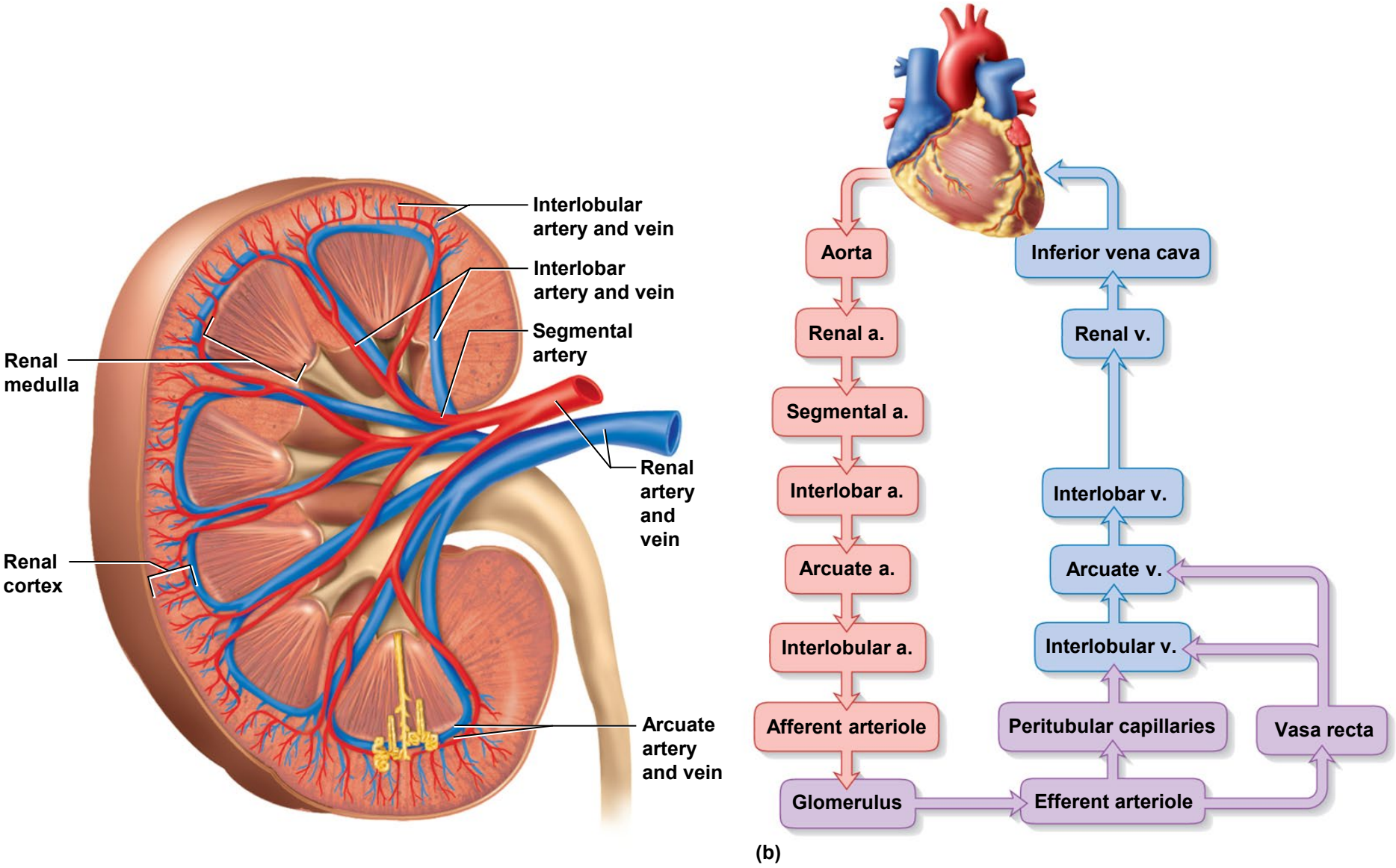
efferent arteriole

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

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

Blood start to leave kidney via interlobular vein or arcuate vein

Blood Supply Diagram



kidneys receive 21% of cardiac output

Distal Convoluted 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 convoluted tubules of cortical nephrons

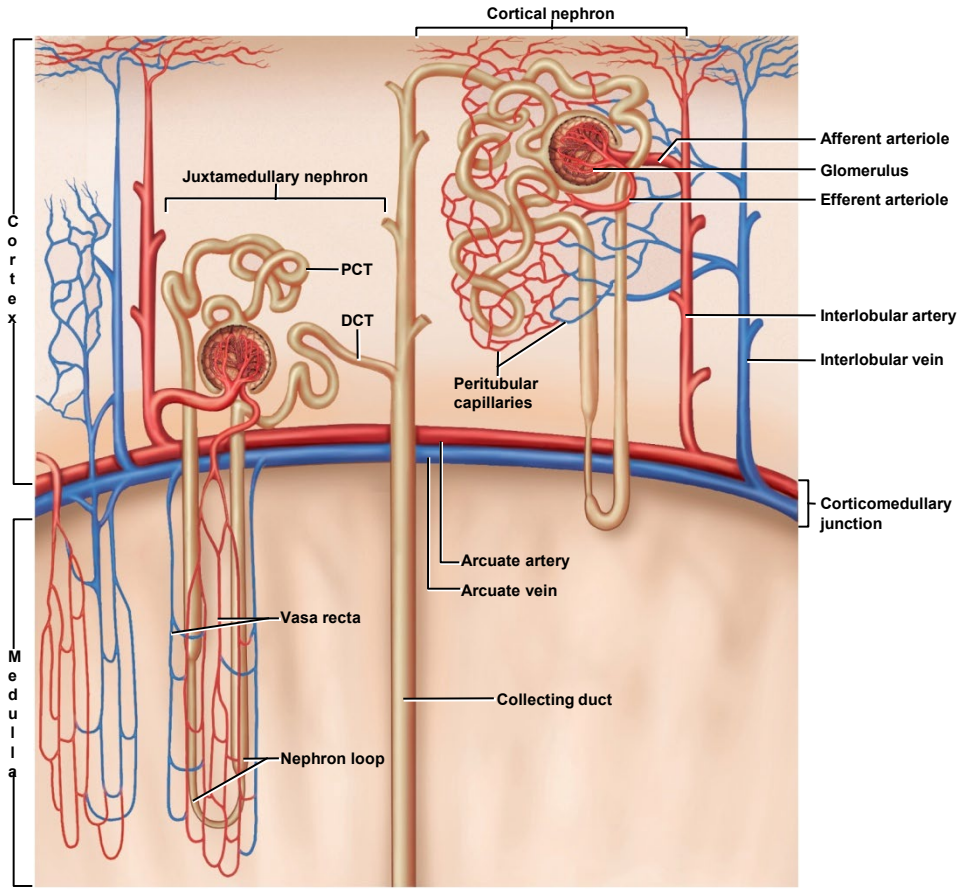
Collecting Duct

- hormone receptors are located in tubular collecting duct of cortical nephron

- primary function is to conserve water // antidieuretic hormone uses aquaporins to recover water // aldosterone recovers water by reabsorbing sodium ions

Loop of Henle

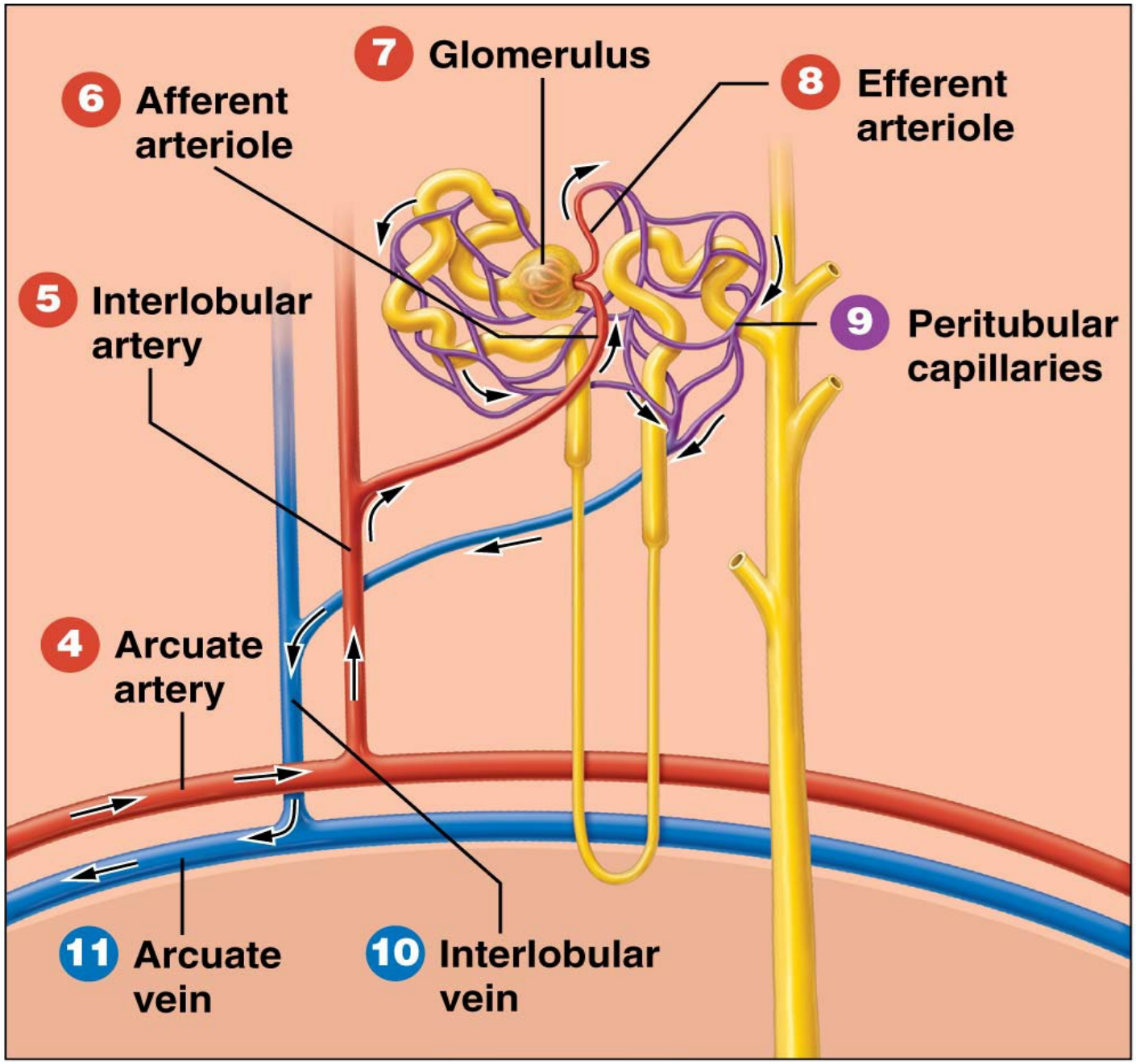
- counter current mechanisms in medulla recovers water from collecting duct and uses vasa recta capilaries to return water to systemic circuit.



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

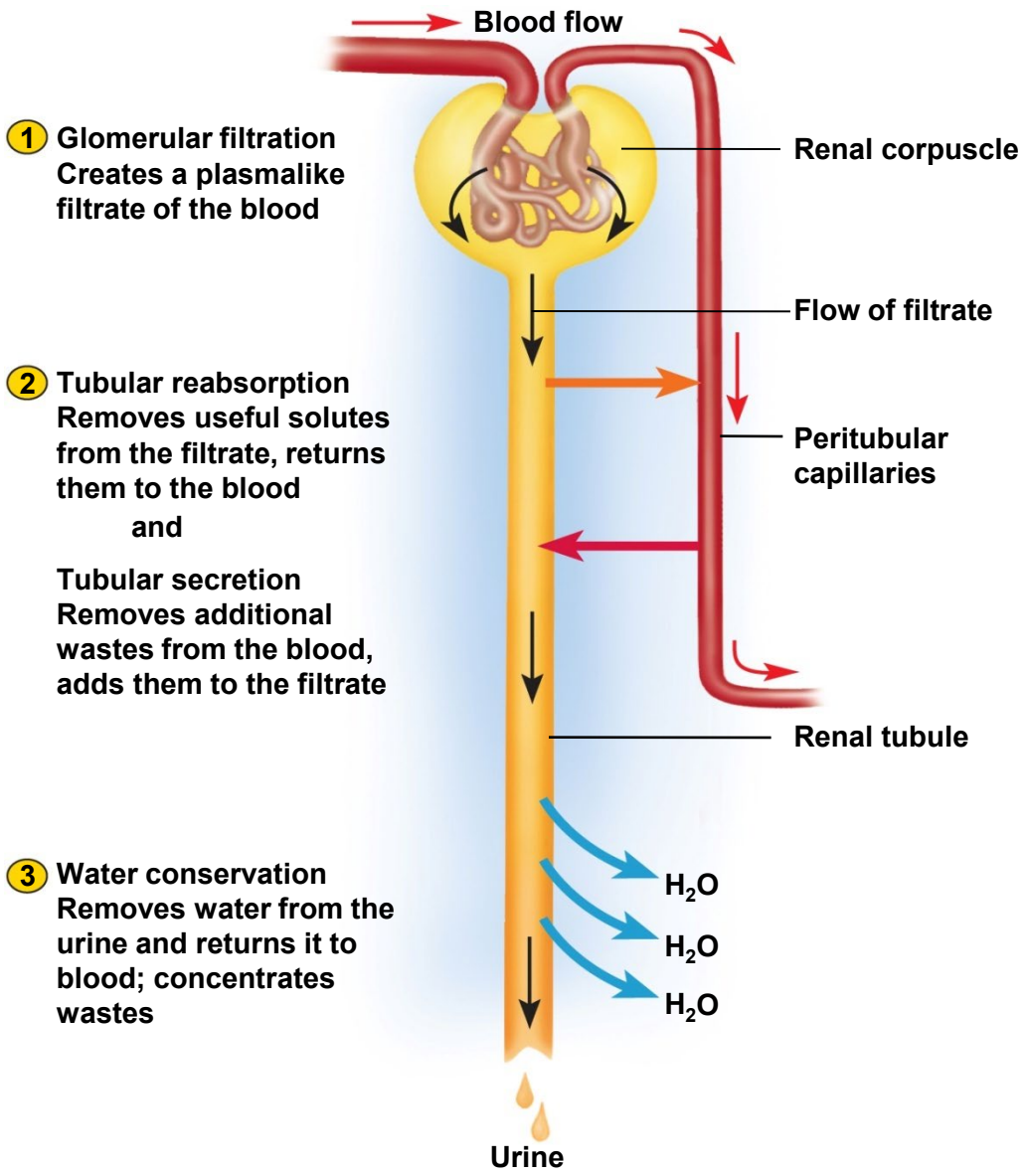
Why is this significant?

Think about why water may move across a plasma membranes!



(b) Blood flow around nephron

Overview of Urine Formation



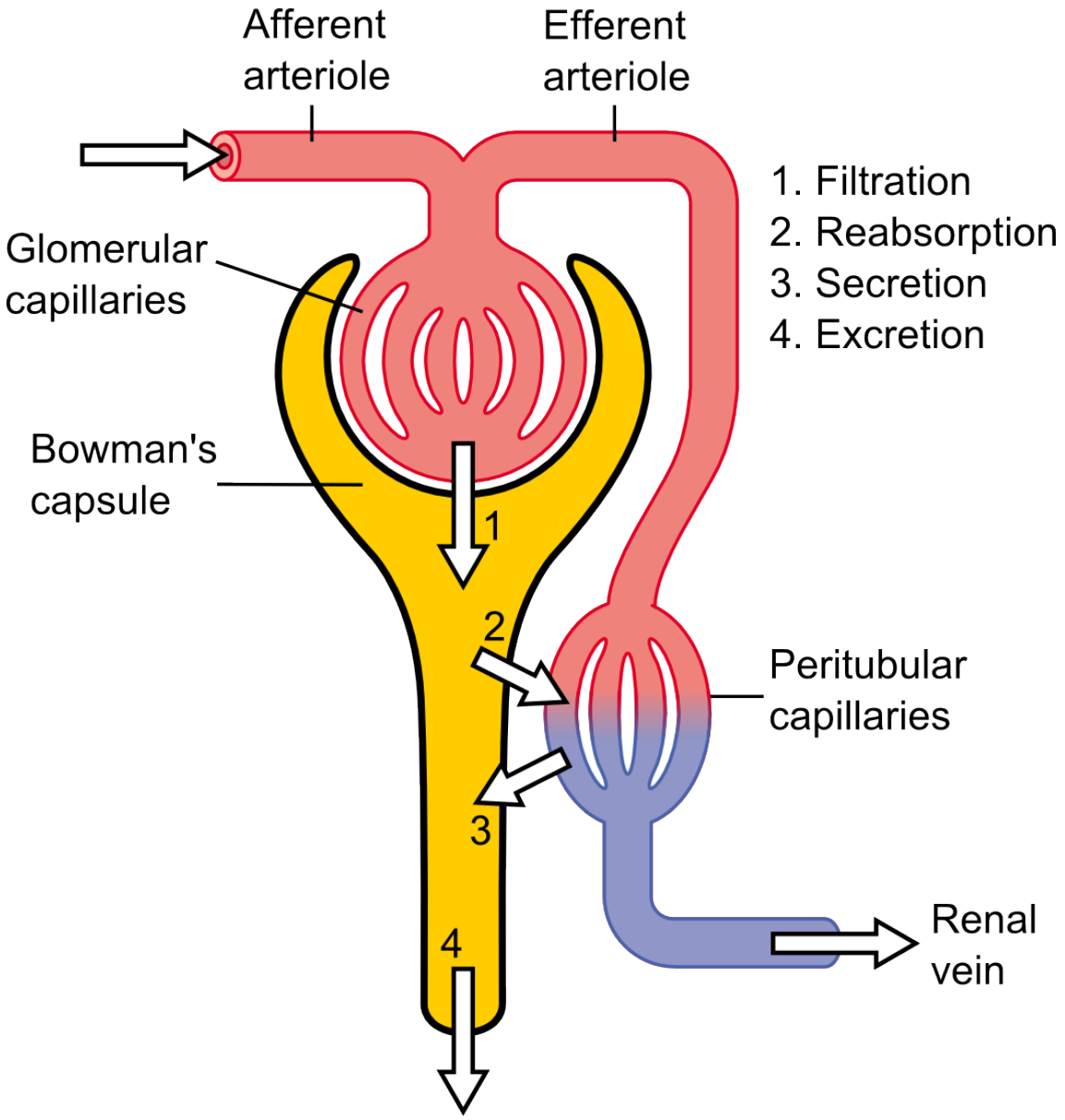
Kidneys convert's filtrate of blood plasma into urine in four stages

- –glomerular filtration
- –tubular reabsorption
- –tubular secretion
- –water conservation

Glomerular filtrate // fluid in capsular space // blood plasma without protein

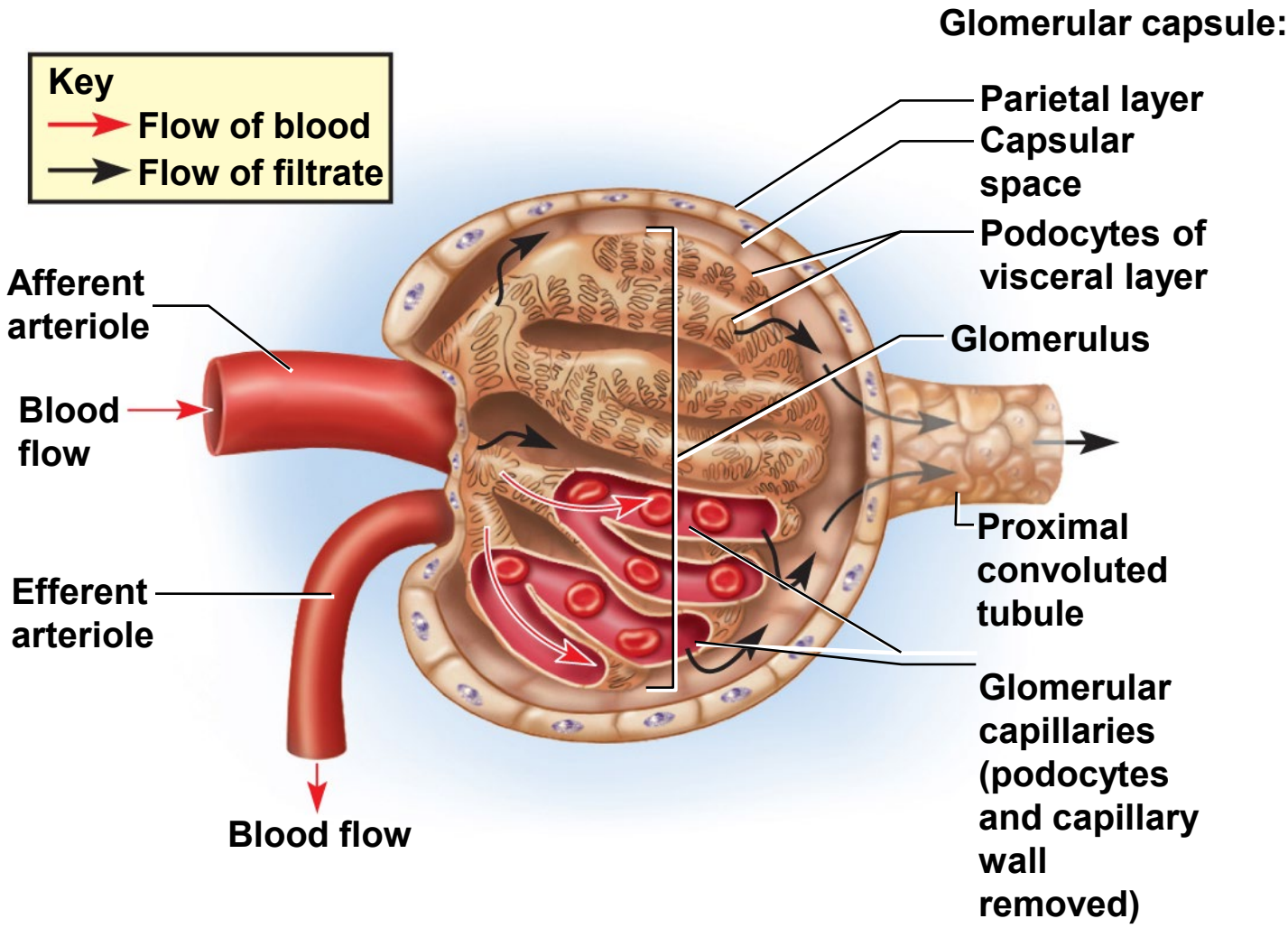
Tubular fluid // fluid in renal tubule // starts as glomerular filtrate but tubular cells remove and add substances as fluid moves through tubules

Urine // once tubular fluid enters the collecting duct it is called urine // only remaining change is water conservation



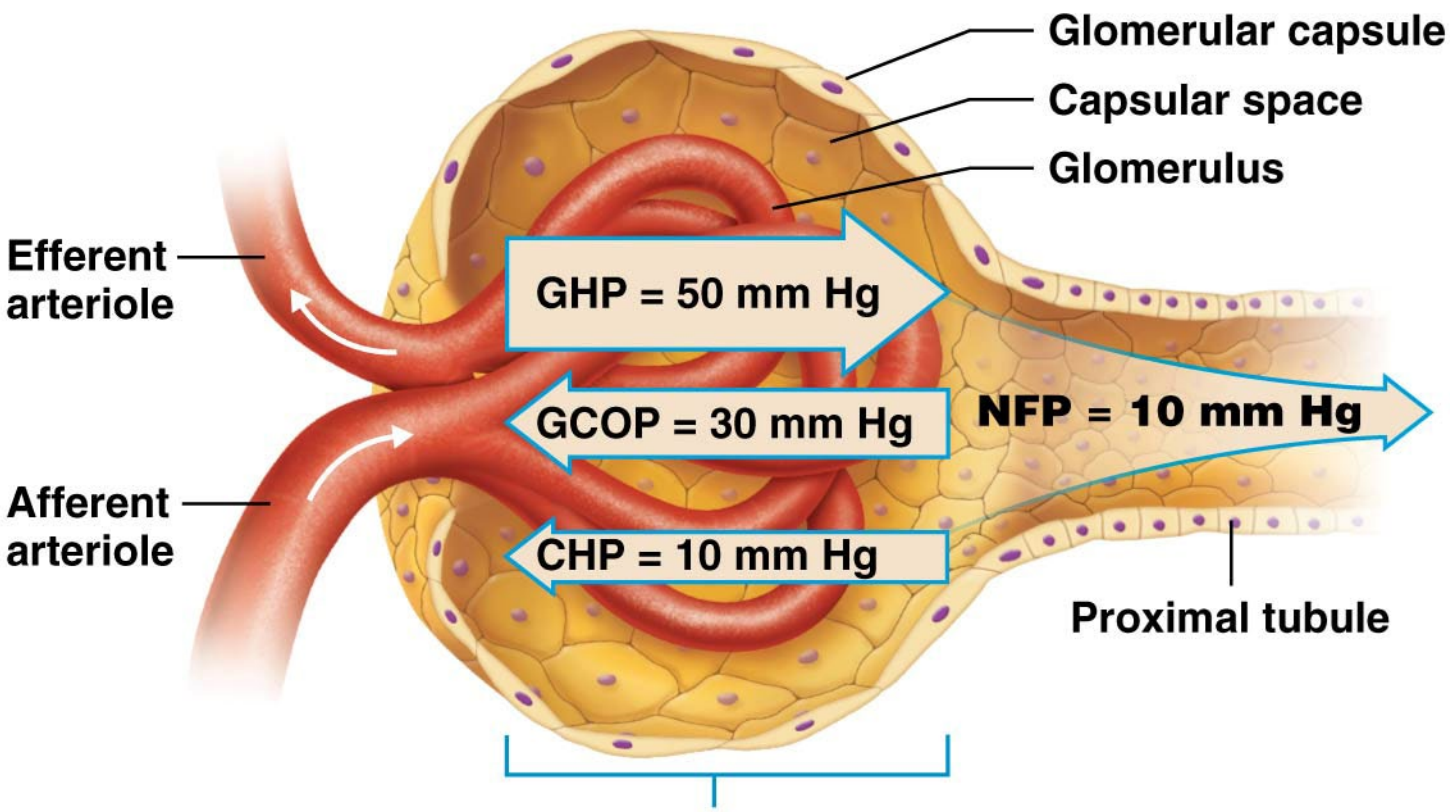
Excretion = Filtration – Reabsorption + Secretion

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.*

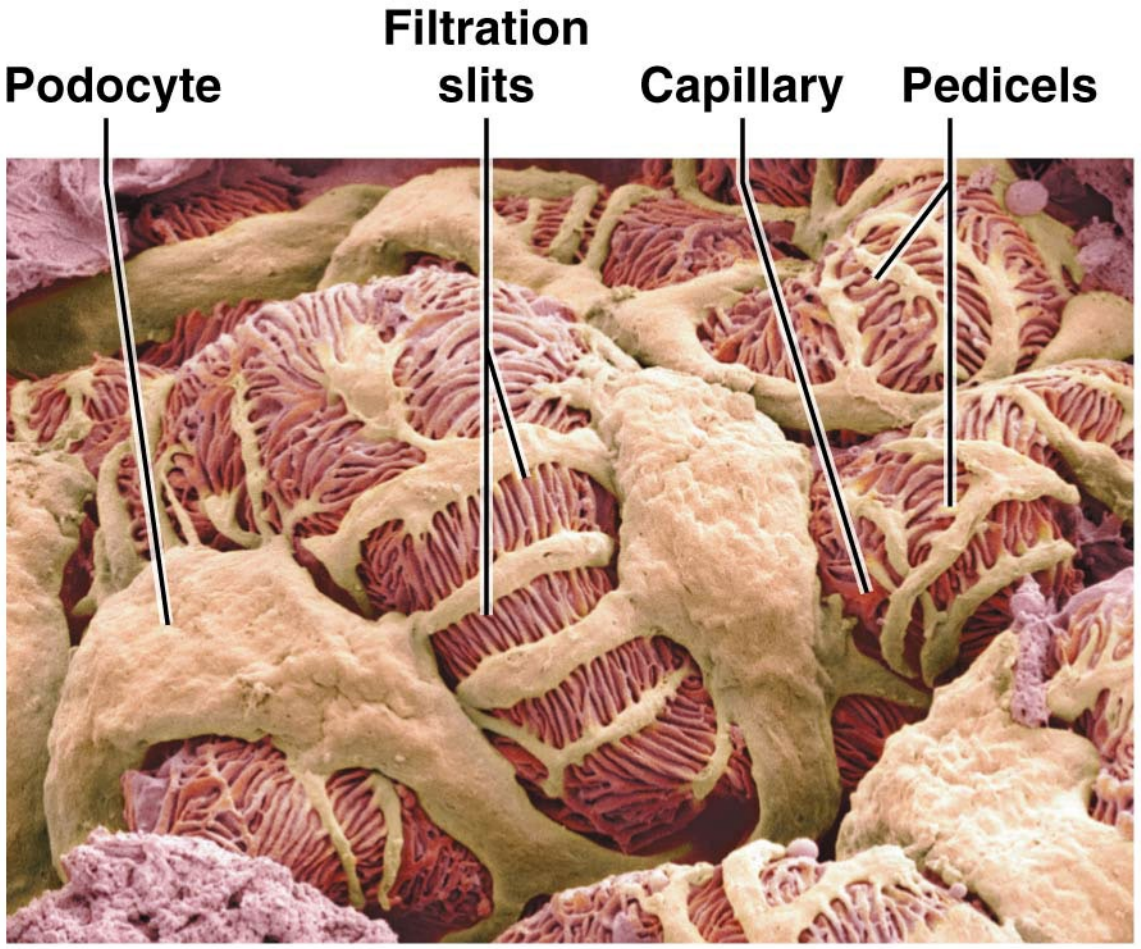
Net filtration pressure in the glomerular capillaries.



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

What is the glomerular filtration rate (GFR)? Significance?

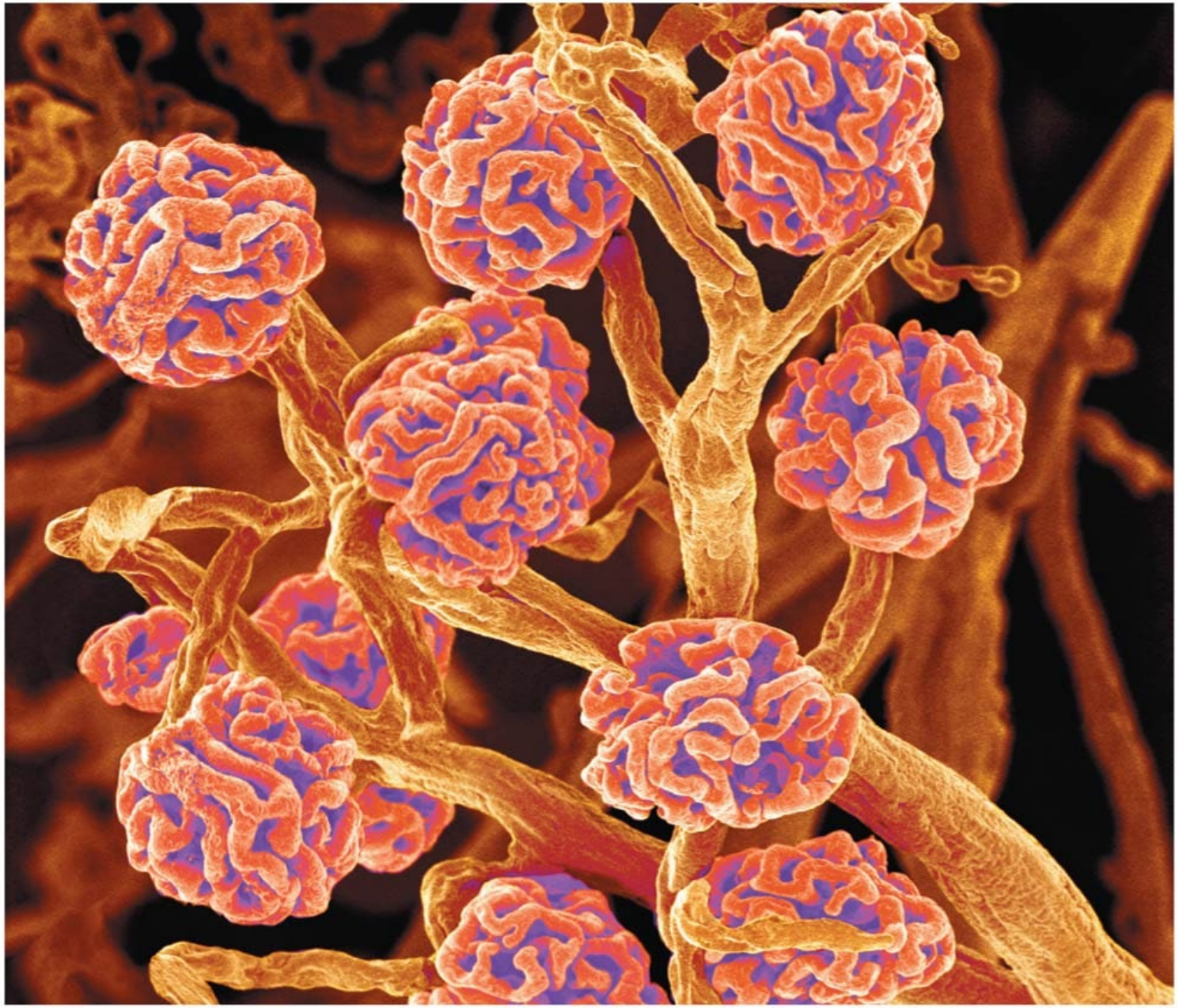
The renal corpuscle.



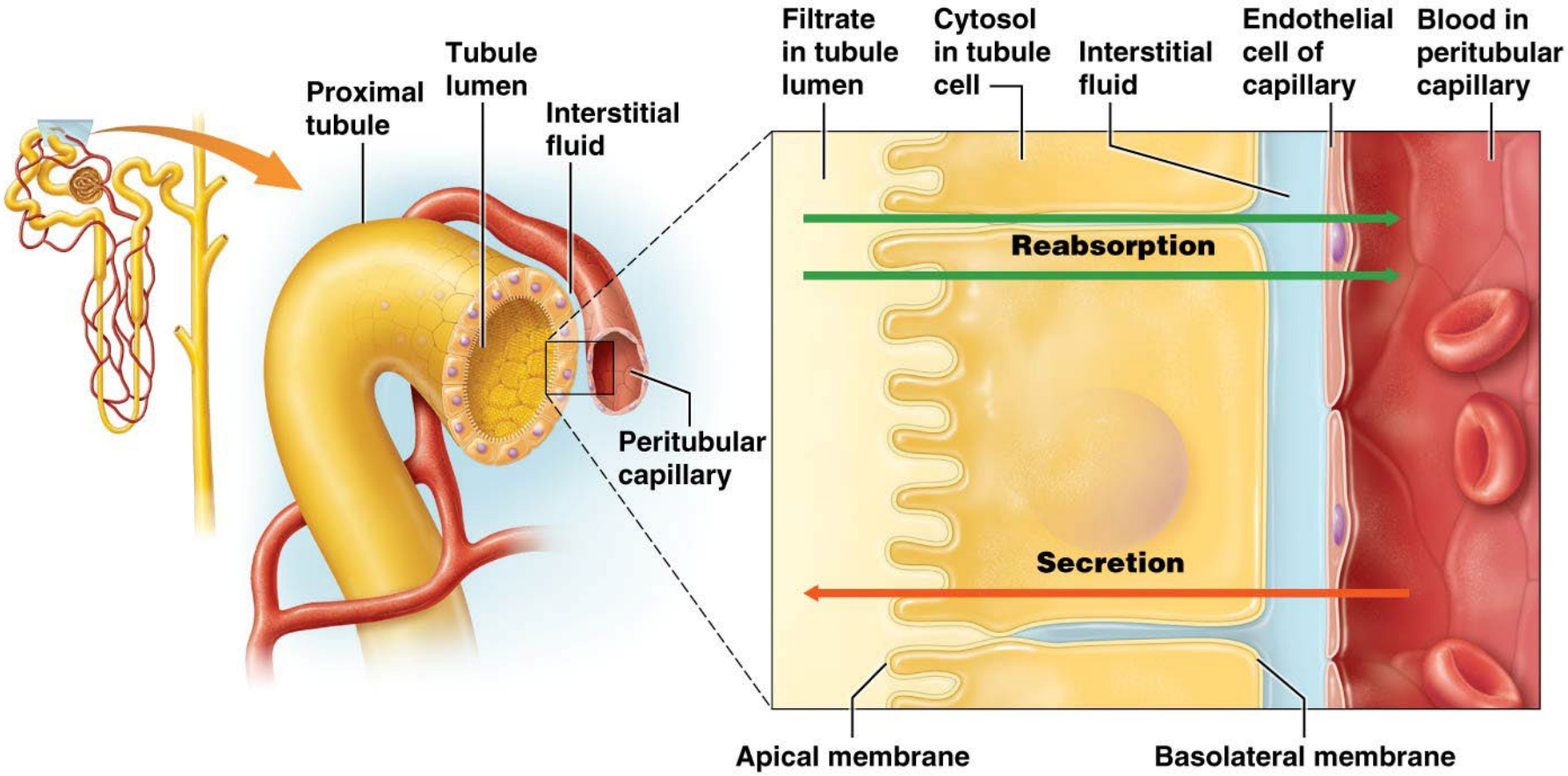
SEM (92,000×)

(b) SEM of capillary surrounded by podocytes

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



Tubular Reabsorption VS Tubular Secretion.



What is moving from “where to where”?

Where does filtration, reabsorption, and secretion occur?

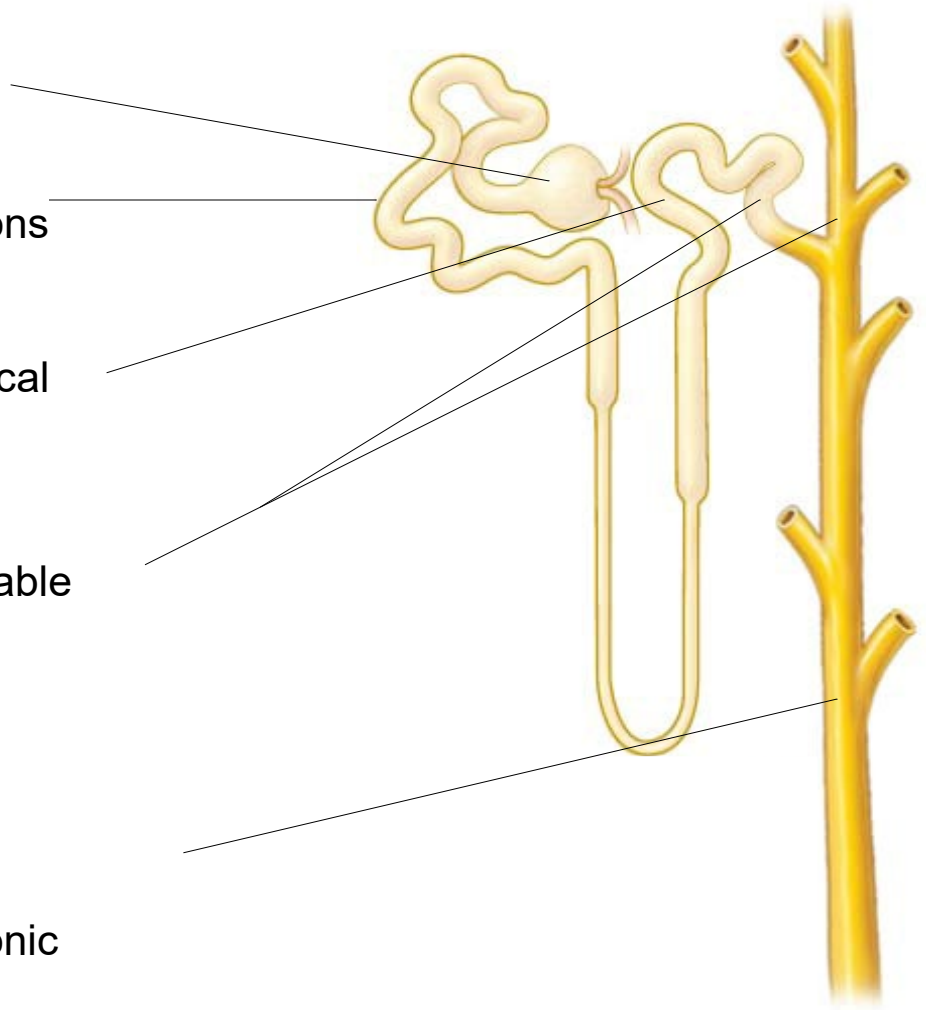
Filtration occurs in the renal corpuscle.

Most water and solute reabsorption (e.g. sodium) occur in the PCT of cortical nephrons // active co-transport mechanisms

Some secretions occurs in the DCT of cortical nephrons.

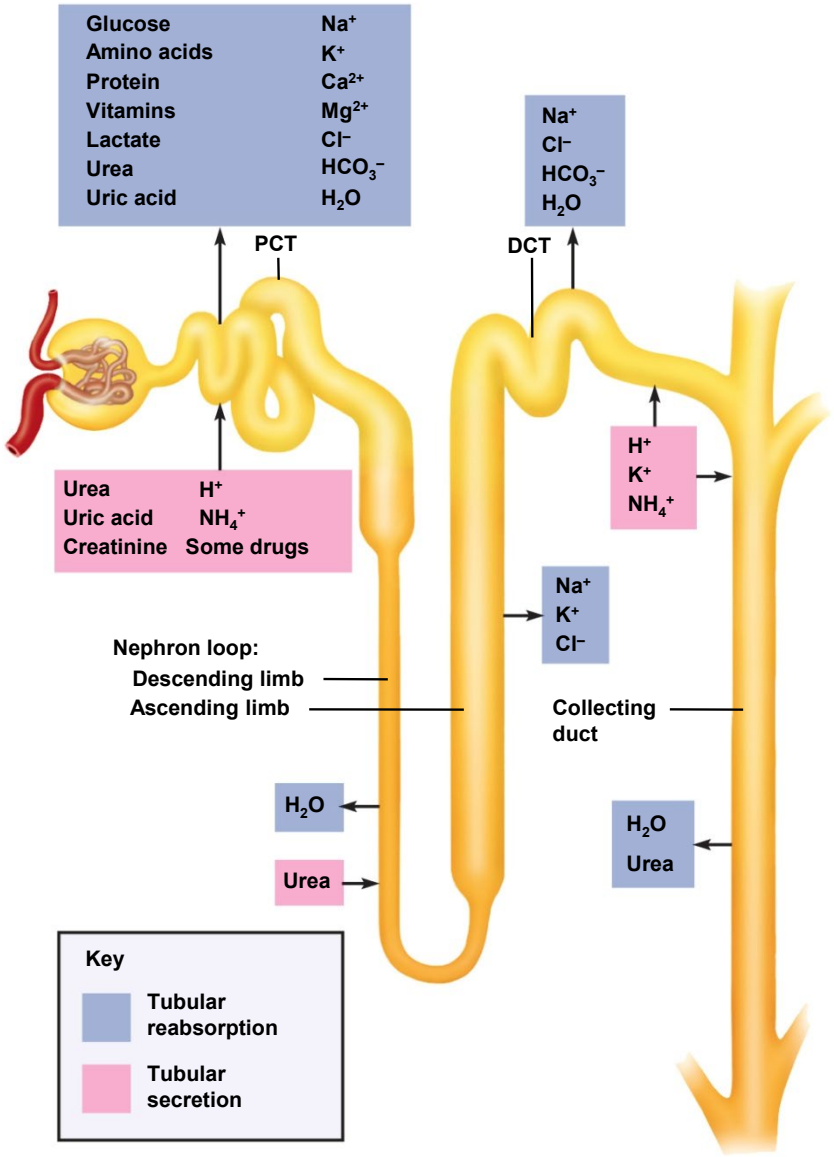
The DCT and cortical collecting duct have receptors for aldosterone /// These areas able to reabsorb sodium and water using aldosterone

ADH reabsorption of water occurs by controlling the number of aquiporins in the collecting duct's plasma membrane /// aquiporins allow water to move into hypertonic area (the deep hypertonic medulla)



Summary of Tubular Reabsorption and Secretion

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



PCT reabsorbs 65% of glomerular filtrate and returns it to peritubular capillaries

Much reabsorption by osmosis & cotransport mechanisms linked to active transport of sodium

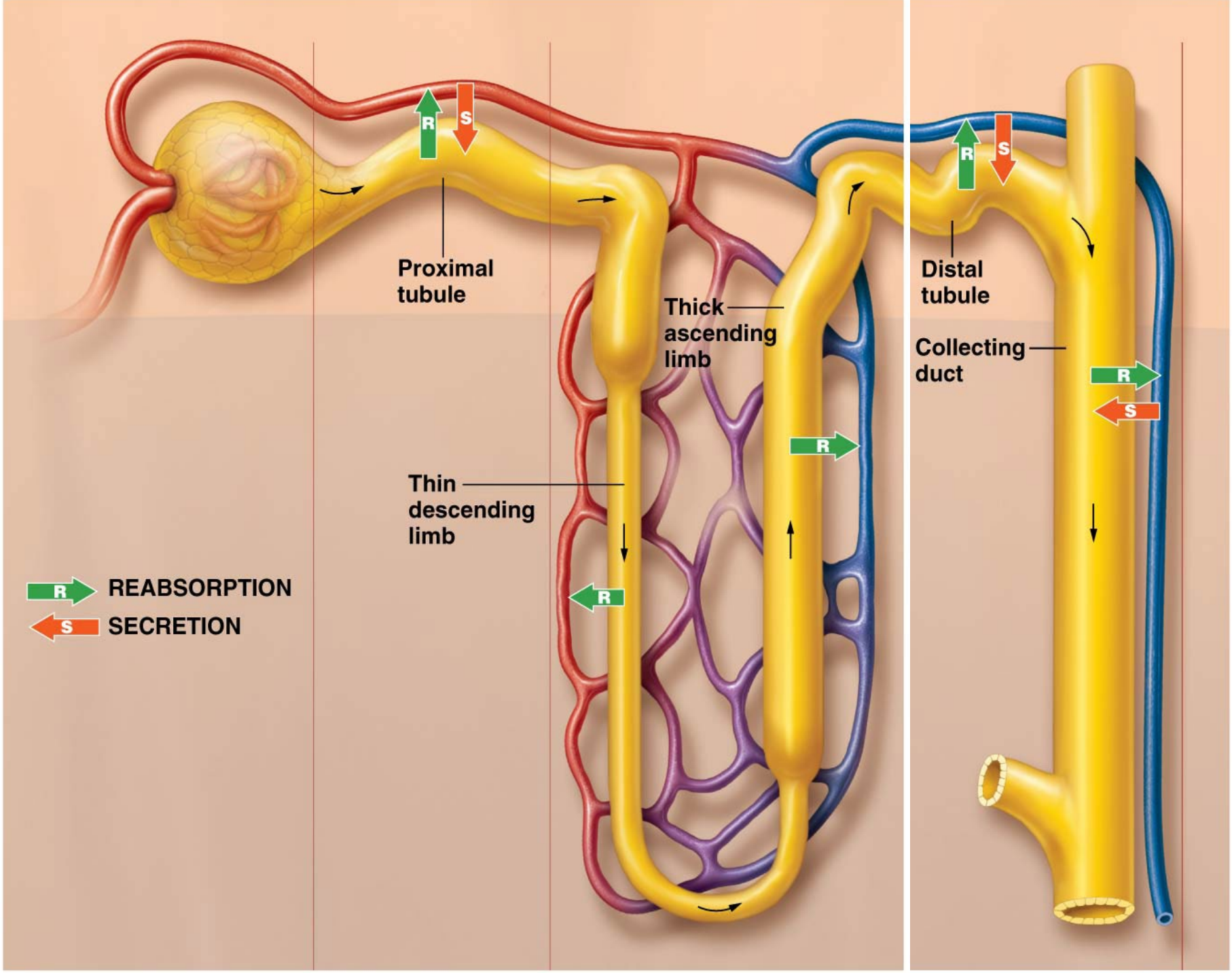
Nephron loop reabsorbs another 25% of filtrate

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

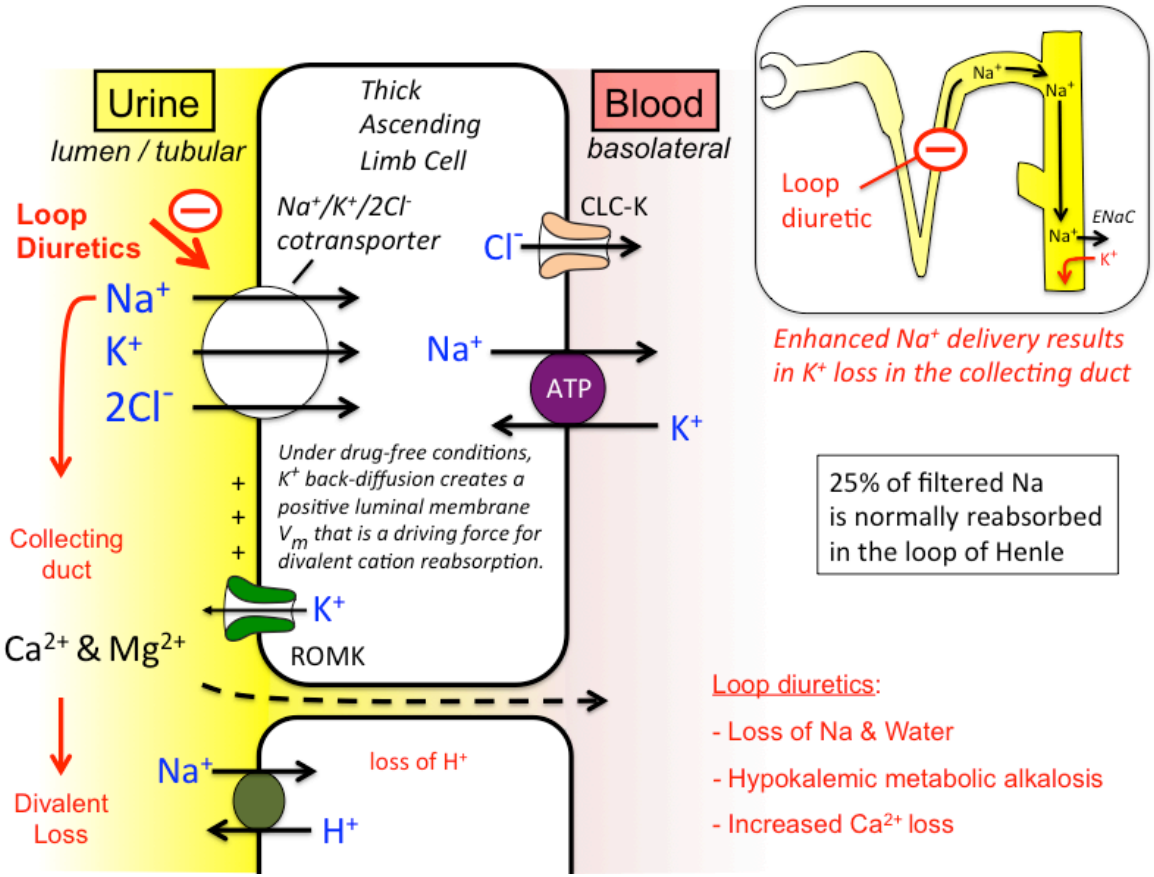
Collecting duct conserves water


R
S
Proximal tubule
Thick ascending limb
Distal tubule
Collecting duct
Thin descending limb
R
S
R
S
R
REABSORPTION
S
SECRETION

The Big Picture of Tubular Reabsorption and Secretion.

TUBULAR SEGMENTS	PROXIMAL TUBULE	NEPHRON LOOP		DISTAL TUBULE AND COLLECTING DUCT
		Thin descending limb	Thick ascending limb	
SUBSTANCES REABSORBED 	• 65% of H_2O in the filtrate • Nearly 100% of glucose, amino acids, and other organic solutes • About 90% of bicarbonate ions (HCO_3^-) • 65% or more of Na^+, K^+, Ca^{2+}, Cl^-, and Mg^{2+}	• 20% of H_2O in the filtrate	• 25% of Na^+ and Cl^-	• Most of remaining H_2O • Nearly all of the remaining Na^+, Cl^-, and Ca^{2+} • Bicarbonate ions (HCO_3^-)
SUBSTANCES SECRETED 	• Hydrogen ions (H^+) • Nitrogenous wastes such as uric acid • Some drugs			• K^+ and H^+ (regulated by hormones)

Furosemide = Potent "Loop Diuretic"



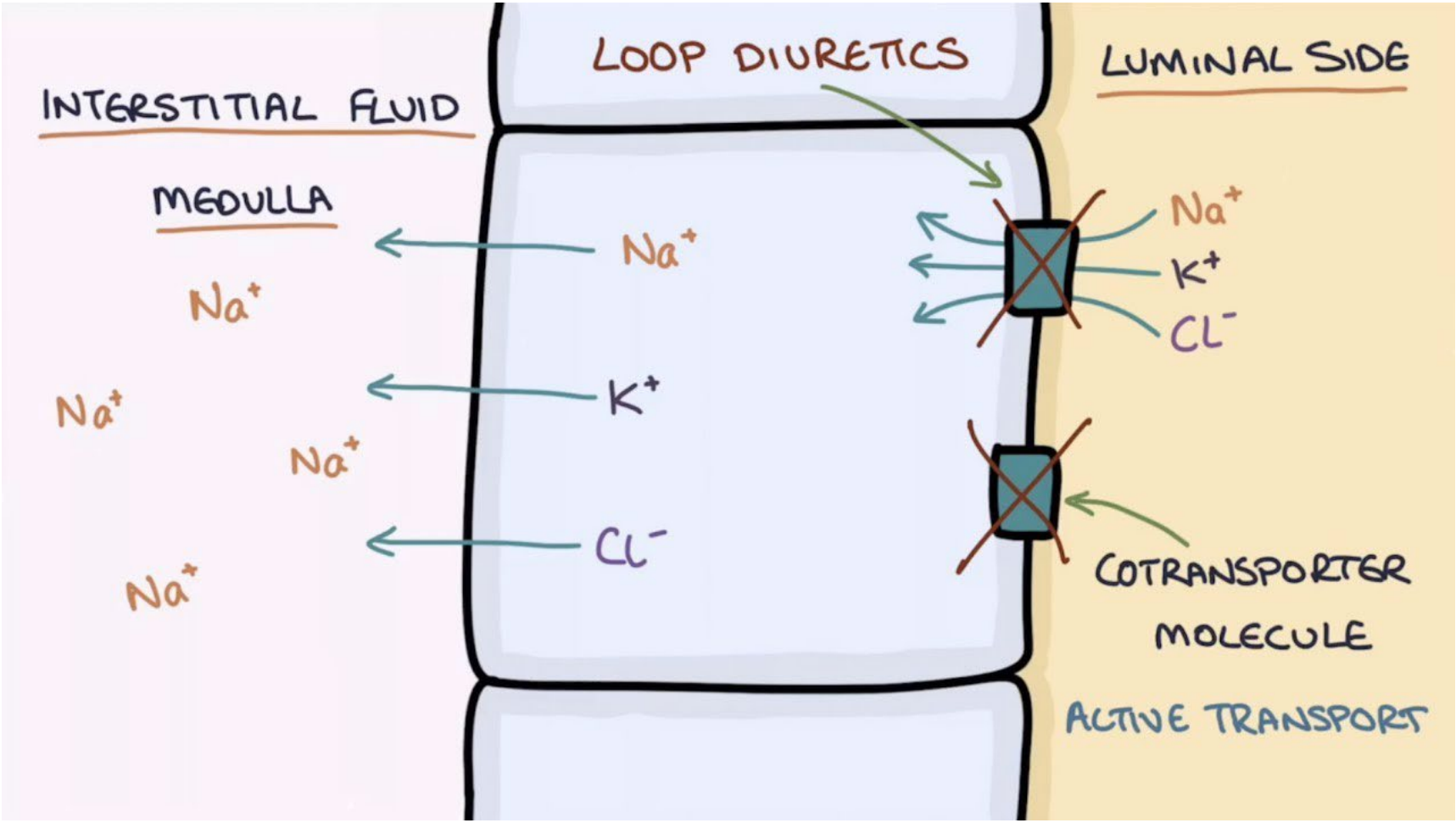
Enhanced Na^+ delivery results in K^+ loss in the collecting duct

25% of filtered Na is normally reabsorbed in the loop of Henle

Furosemide (Lasix) is a potent "loop diuretic" that treats fluid retention (edema) and high blood pressure.

It primarily works by blocking the **Na^+-K^+-$2Cl^-$ symporter** in the thick ascending limb of the loop of Henle in the kidneys, preventing the reabsorption of sodium, chloride, and potassium back into the blood.

The ions pass into the collecting duct, into the urine, and water molecules follow the ions.


LOOP DIURETICS
INTERSTITIAL FLUID
LUMINAL SIDE
MEDULLA
Na+
Na+
Na+
Na+
Na+
K+
Cl-
Na+
K+
Cl-
COTRANSPORTER MOLECULE
ACTIVE TRANSPORT

Water Reabsorption

Kidneys receive 25% of cardiac output (kidney weighs 150 g)

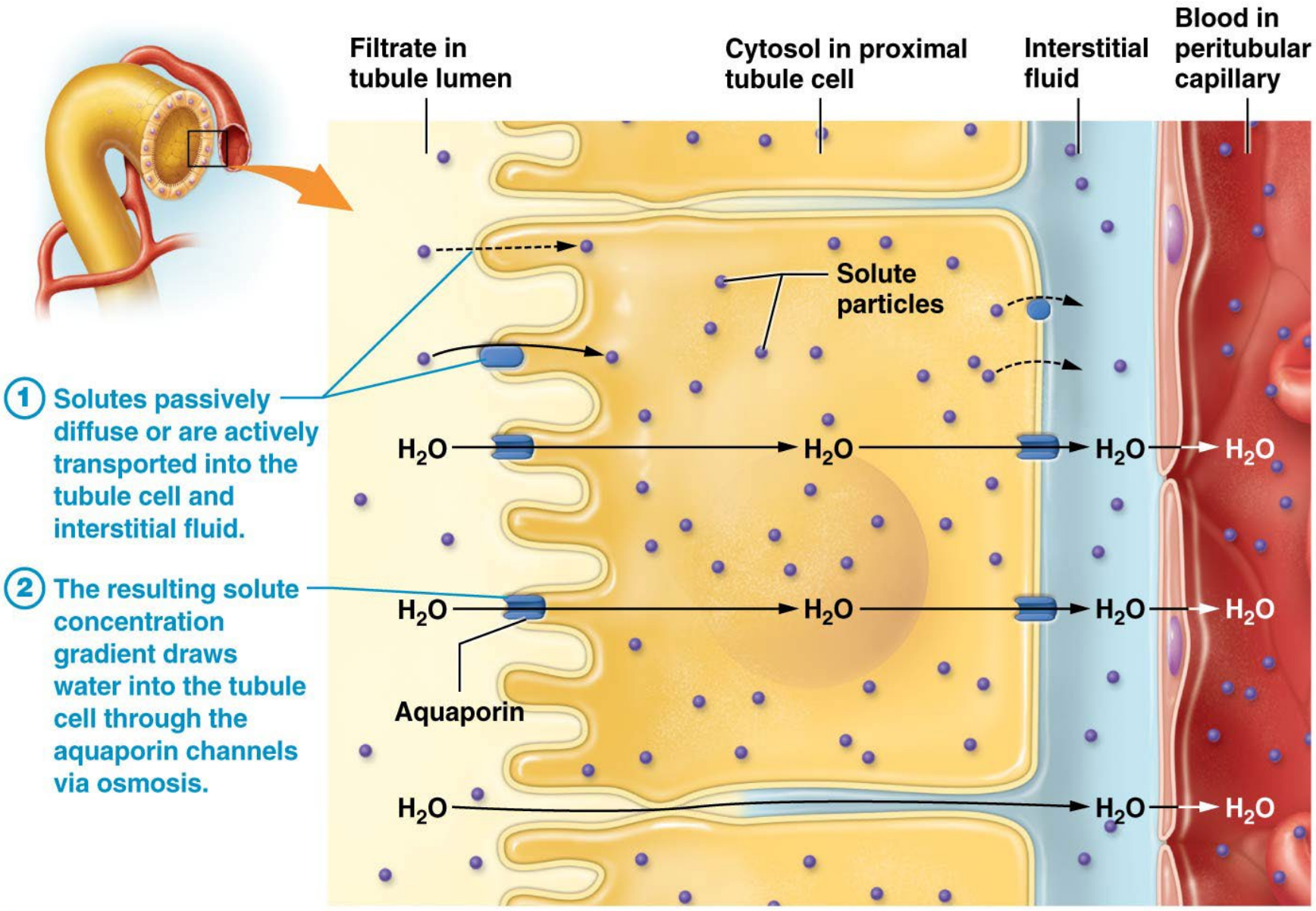
180 L of water filtered in renal corpuscle / day

1.8 L of water leaves body as urine (less than 1% of filtrate) / day

99% of filtered water is reabsorbed and much of the solute (much of the water recovery is a direct consequence of sodium active transport (over 65% 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 sodium, glucose, and amino acids are recovered, water molecules follow these slultes back into the peritubular capillaries. // obligatory water reabsorption



Obligatory water reabsorption in the proximal tubule.

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 are dehydrated, then the kidneys will produce a low volume of hypertonic urine.

Water Conservation

The kidney must eliminate 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 from the tubular fluid and collecting duct 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

Note: Aldosterone receptors in collecting duct responsible for sodium active transport mechanism to recover sodium (water follows the sodium)

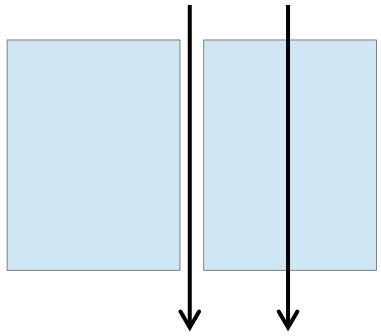
Water Reabsorption

Kidney uses active transport mechanisms to reabsorb sodium in PCT reabsorption

Water follows solutes through para-cellular and transcellular routes

Transcellular route uses water channels called aquaporins // type of transmembrane protein.

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



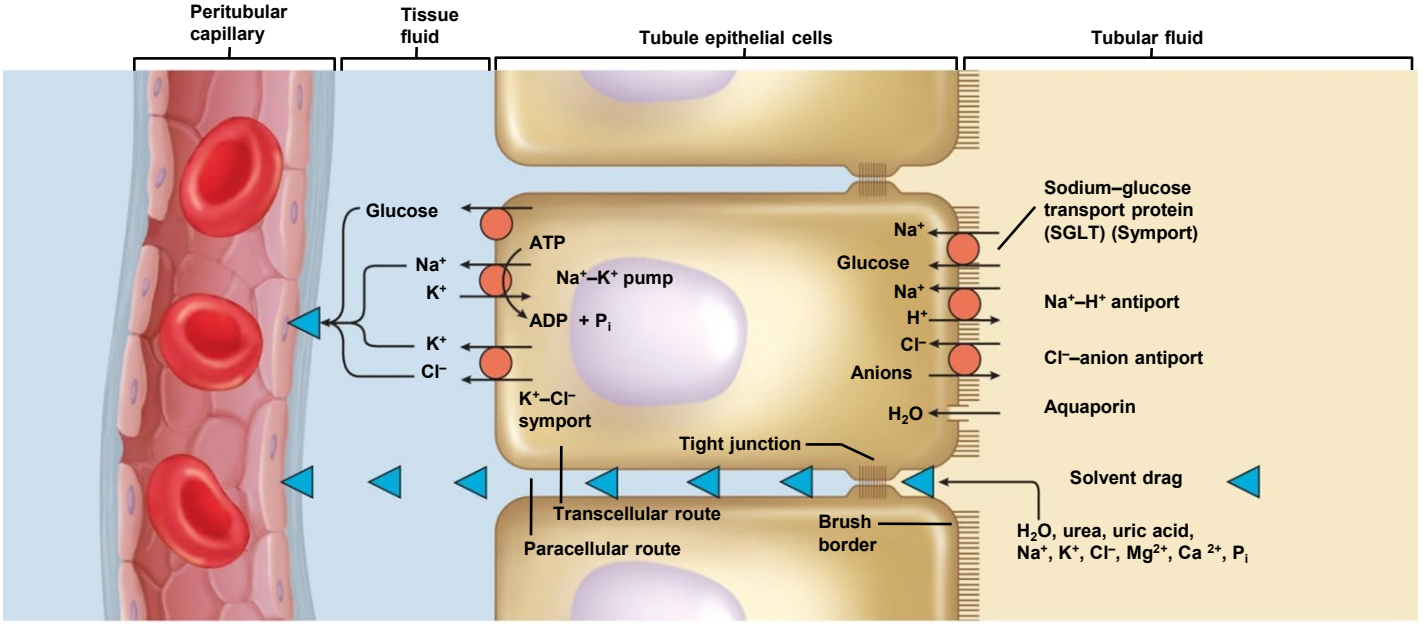
Reabsorption in the Proximal Convoluted Tublule

Potassium, magnesium, and phosphate ions diffuse through the paracellular route with water

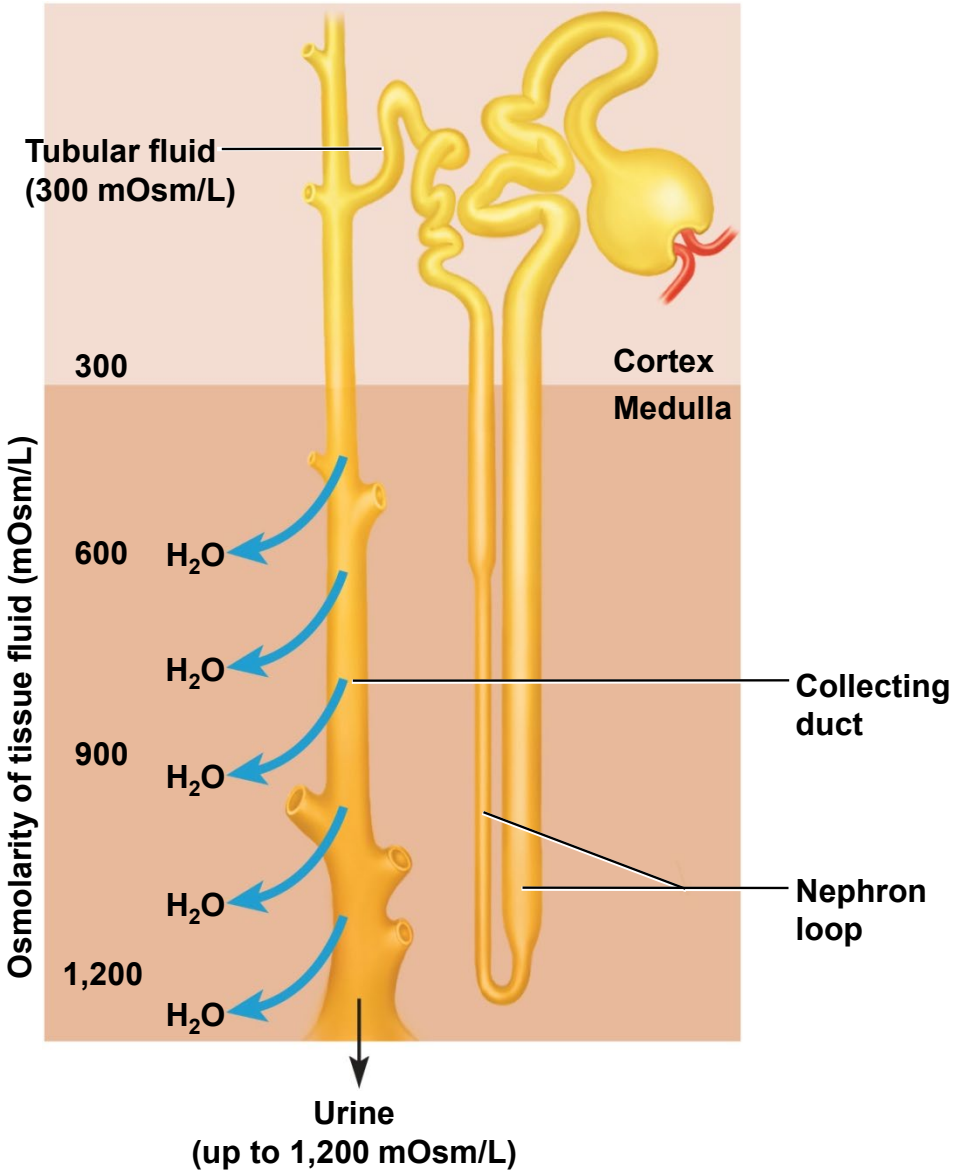
Phosphate is cotransported into the epithelial cells with Na^+

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 all nephrons

As dilute urine passes through CD into the medulla, water is reabsorbed and the 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 osmosis /// this 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

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

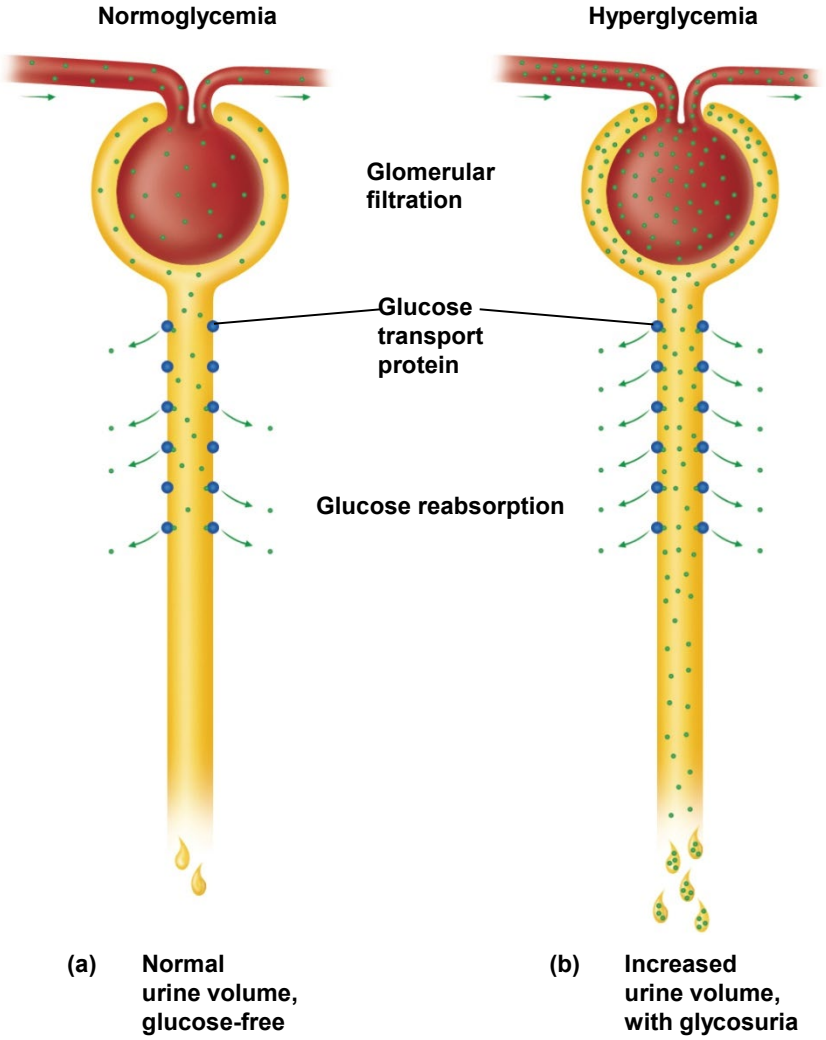
Water moves through the aquaporin channels, and the water moves from collecting duct into interstitial space /// now water continues to move from interstitial space into vasa recta /// this returns water to systemic circuit

Urine becomes more concentrated in this process

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

Lower GFR, results in more salt reabsorbed, with water following the ions /// net result is more water reabsorbed and less urine produced but urine is more concentrated (i.e. darker color)

Glucose Reabsorption and the Glucose Transport Maximum



Glucose is only "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 (Tm) then some glucose will pass PCT

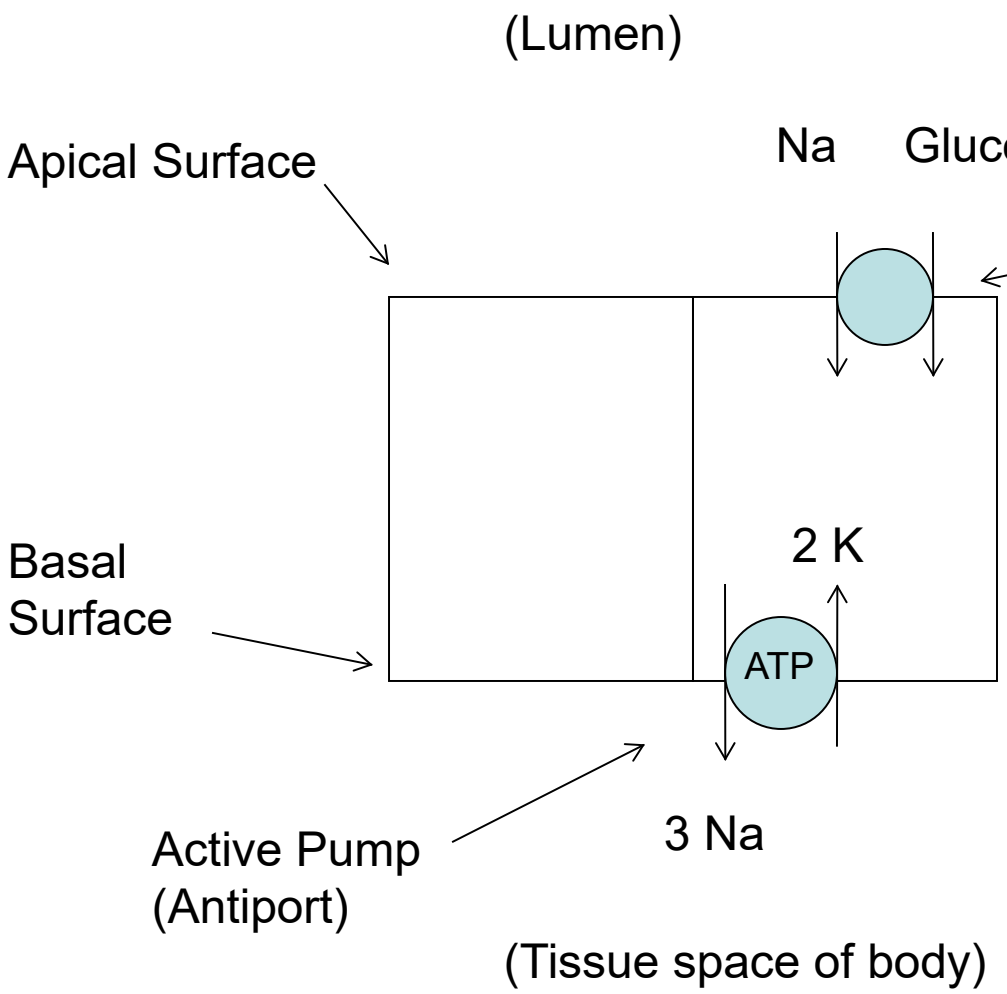
Now glucose becomes an osmotic diuretic // explain

Blood glucose concentrations above 220 mg/dL causes glucosuria

Doctor's use to taste urine to see if patients were diabetic

Secondary Co-Transport

(Powered by the Sodium Potassium ATP Pump)

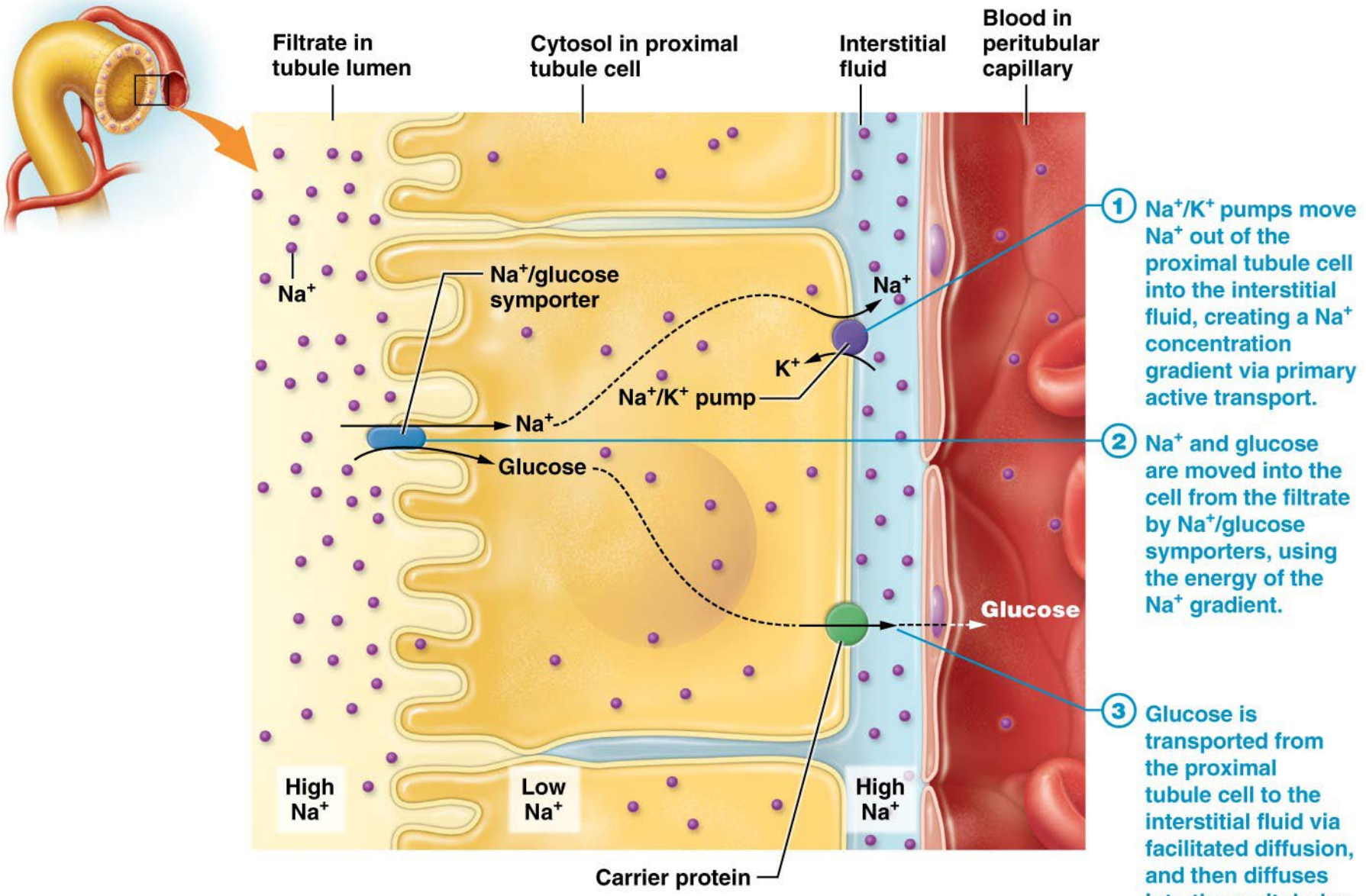


the antiport (active pump) uses ATP to lower the intracellular concentration of Na

this creates a concentration gradient that favors the movement of sodium from the lumen into the cell (passive – no ATP required)

then glucose is co-transported passively with the sodium using a symport pump

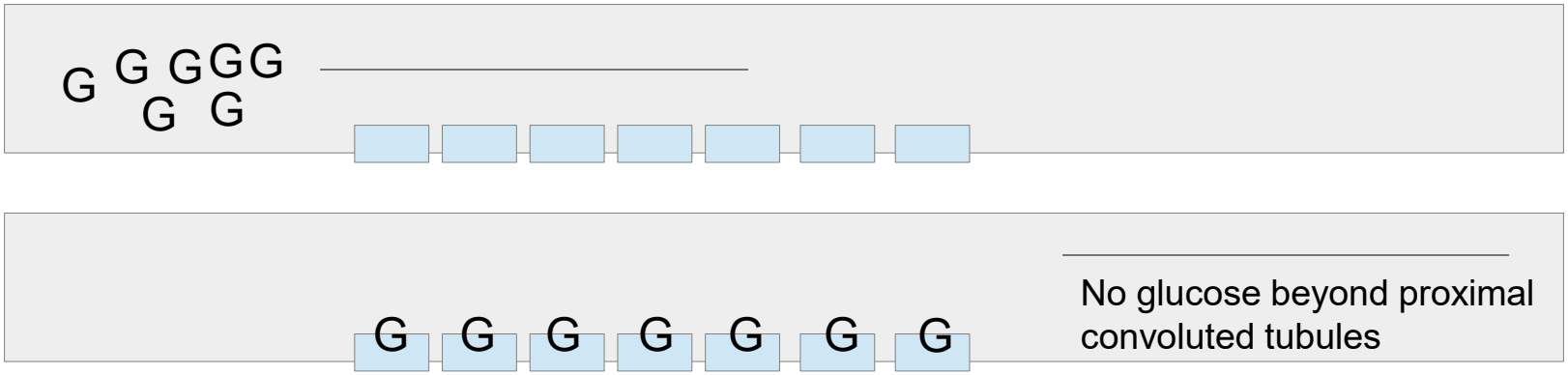
Glucose reabsorption in the proximal tubule.



Facilitated diffusion

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

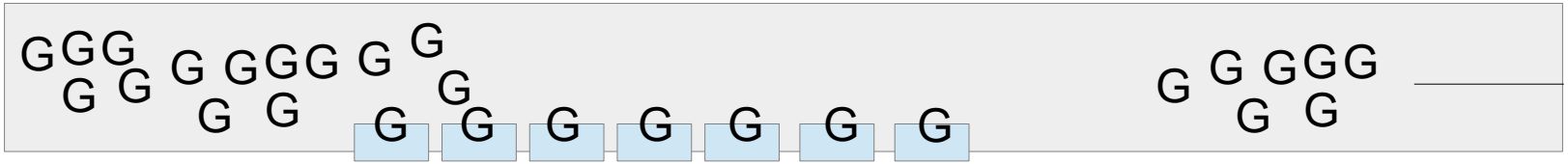
Enough transporters to capture all glucose // These glucose transporters only in PCT



All glucose reabsorbed

Blood glucose concentration exceeds Tm

Glucose not captured now pass proximal convoluted tubules



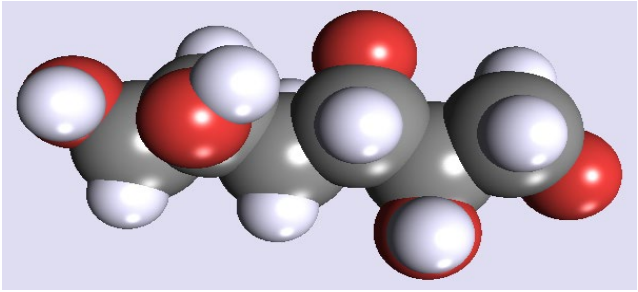
Some glucose reabsorbed

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

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)



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

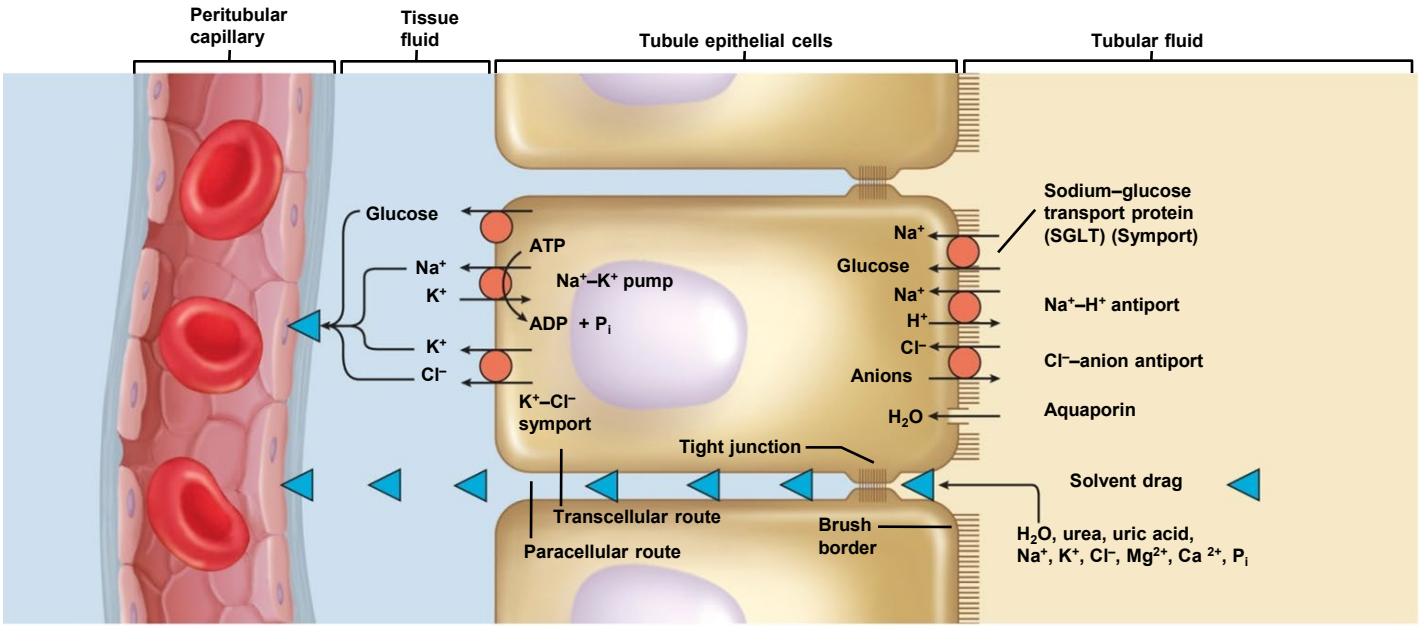
Other Ions, and Urea Reabsorption in the PCT

Potassium, magnesium, and phosphate ions diffuse through the paracellular route with water

Phosphate is co-transported 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)

GFR is regulated by autoregulation, autonomic nervous system, and hormones

GFR is important because this volume is necessary 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

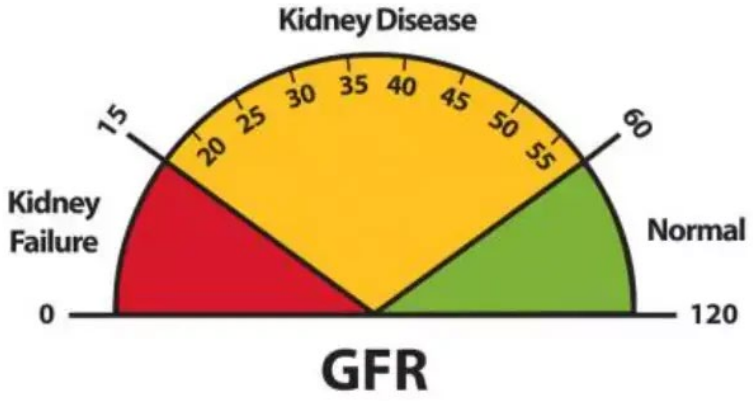
–urine output rises

–greater chance of dehydration and electrolyte depletion

Urine Volume Is Influenced By Glomerular Filtration Rate

If GFR too low // wastes not filtered // wastes stay in plasma // azotemia may occur (i.e. high nitrogen concentration in blood)

If GFR too high // not able to reabsorb ions and other need molecules // increase urine volume // dehydration occurs



- ***This is why we need to regulate GFR!***
- ***Blood creatinine is used to determine GFR rate and assess kidney function.***
- ***Can you explain a similar logic about cardiac output and tidal volume?***

Creatine and **creatinine** are not the same; they are related but distinct compounds with opposite roles. Creatine is a nutrient that supplies energy to muscles, while creatinine is a metabolic waste product generated from the breakdown of creatine.

Key Differences:

Creatine (The Fuel): Produced in the liver, kidneys, and pancreas (or consumed in diet) to help generate energy (ATP) for muscle contractions. It is often used as a workout supplement to improve strength.

Creatinine (The Waste): Produced when muscle creatine breaks down naturally. It is filtered out of the blood by the kidneys, making it a key biomarker for kidney function

Relationship:
Because creatinine is a breakdown product of creatine, high dietary intake or supplementation of creatine can cause a temporary rise in creatinine levels. This increase often does not indicate kidney damage but simply higher metabolic turnover, though it should be monitored.

High creatinine levels on a lab report may suggest the kidneys are not filtering waste efficiently.

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 (without nervous or hormonal regulation)

enables nephron to maintain a relatively stable GFR despite 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 dialate /// 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

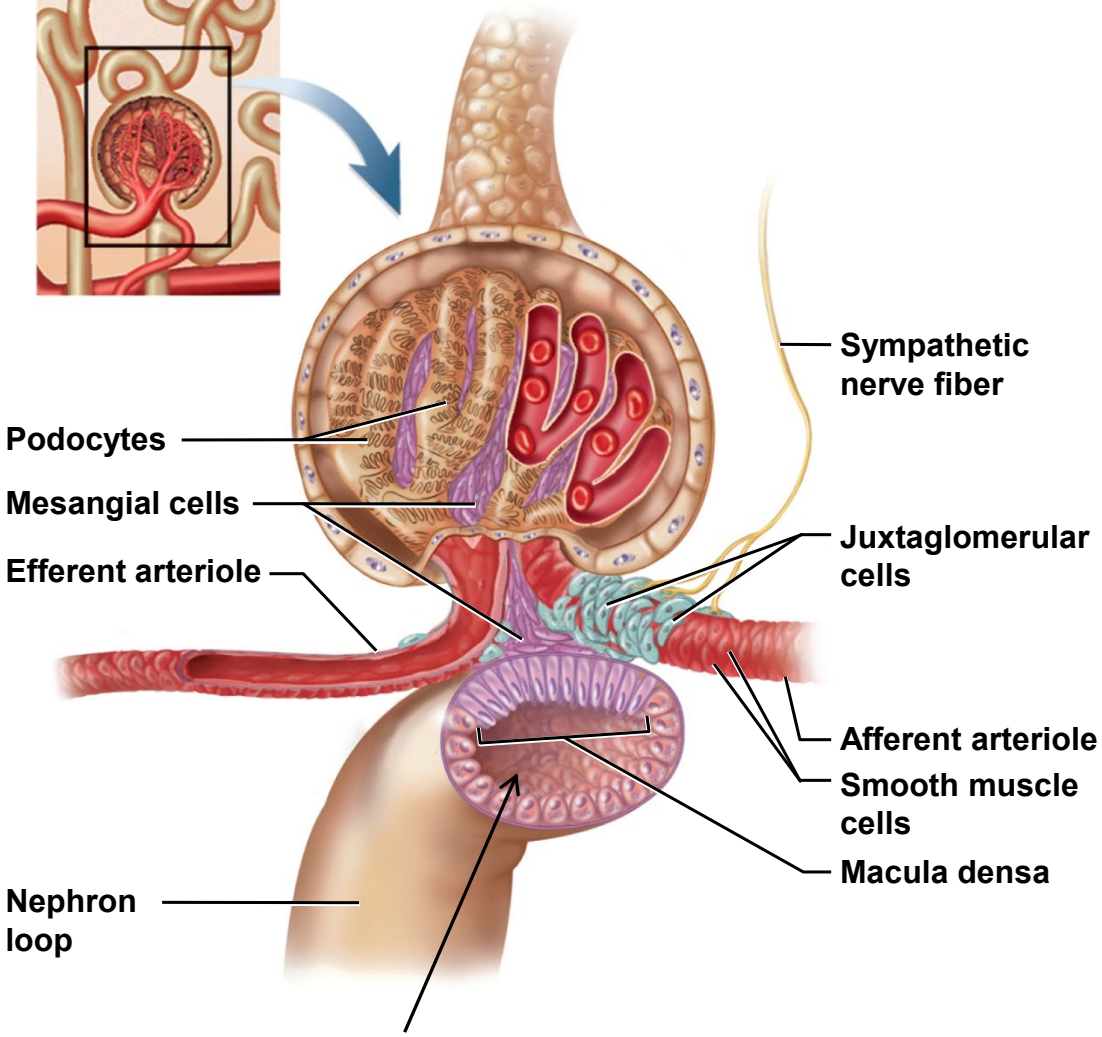
Significance: Distal end of the loop of Henle now comes in contact with the afferent and efferent arterioles at the vascular pole of the renal corpuscle // able to sample outcome of filtrate near end of nephron!

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 ascending nephron loop on the side of the tubules that face the arterioles

senses variations in flow or fluid composition and secretes a paracrine that stimulates JG cells



Note: proximal portion
Of distal convoluted tubule

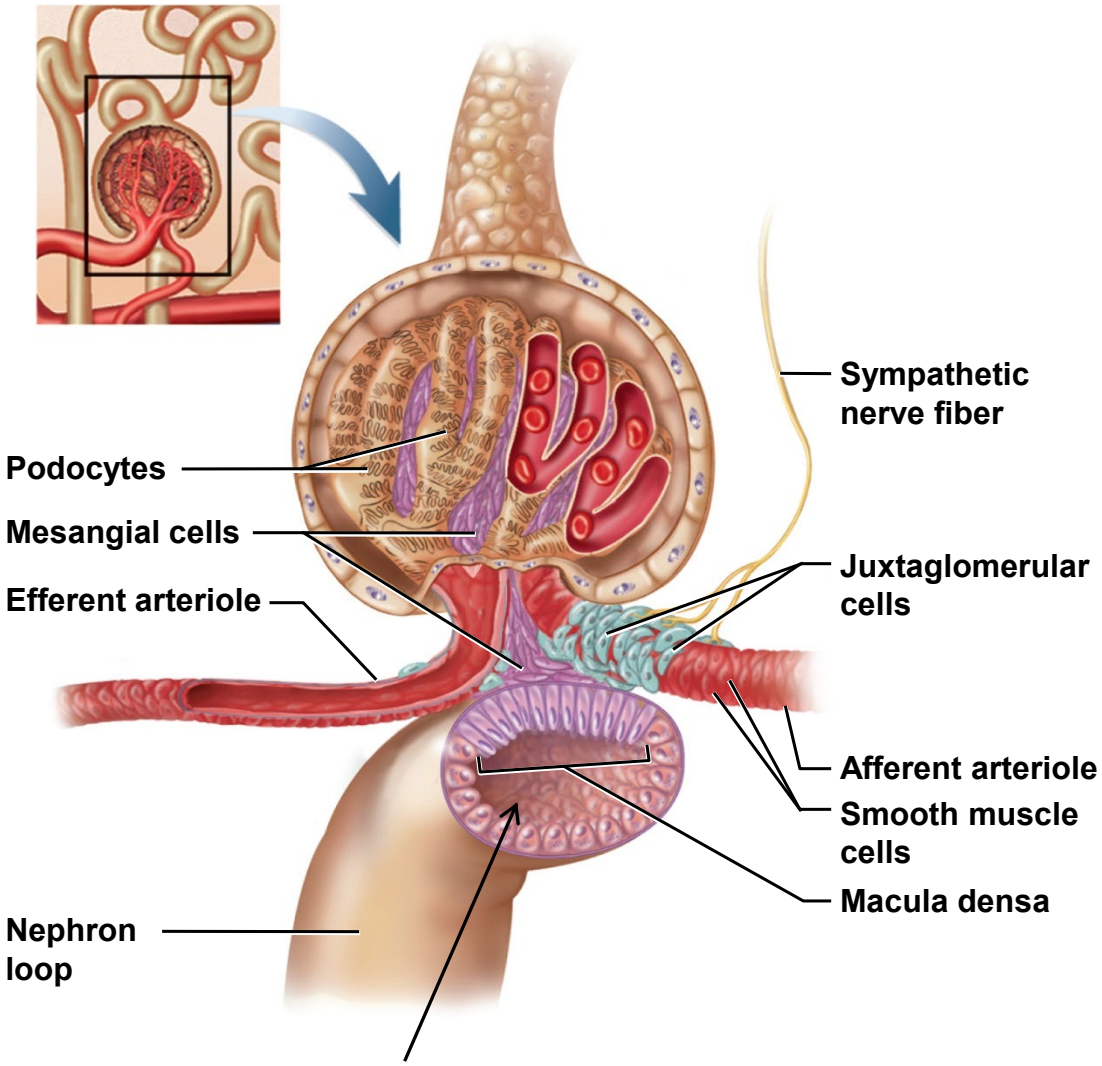
Renal Autoregulation of GFR by Tubuloglomerular Feedback Mechanism

#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



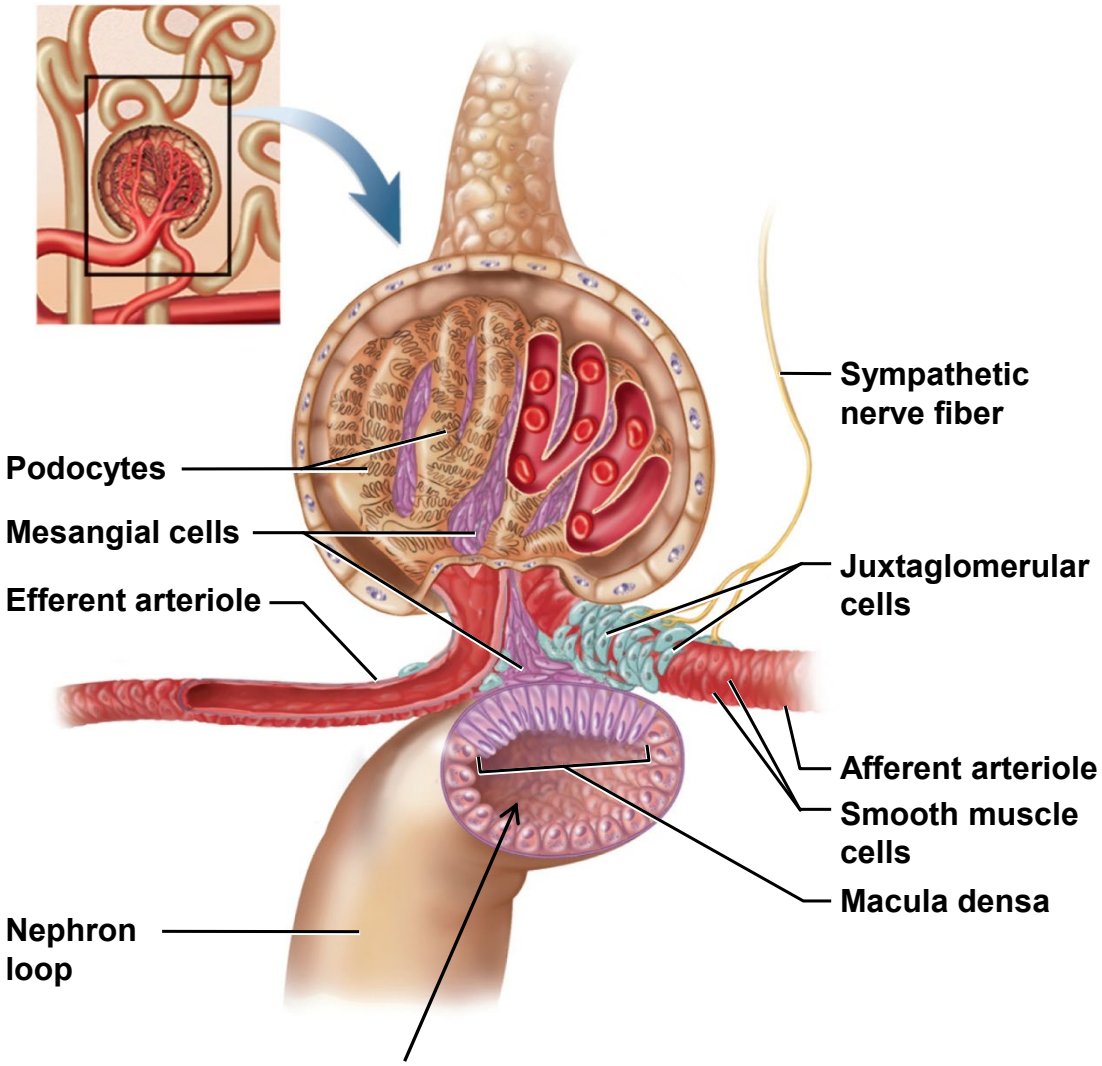
Note: proximal portion
Of distal convoluted tubule

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 >>

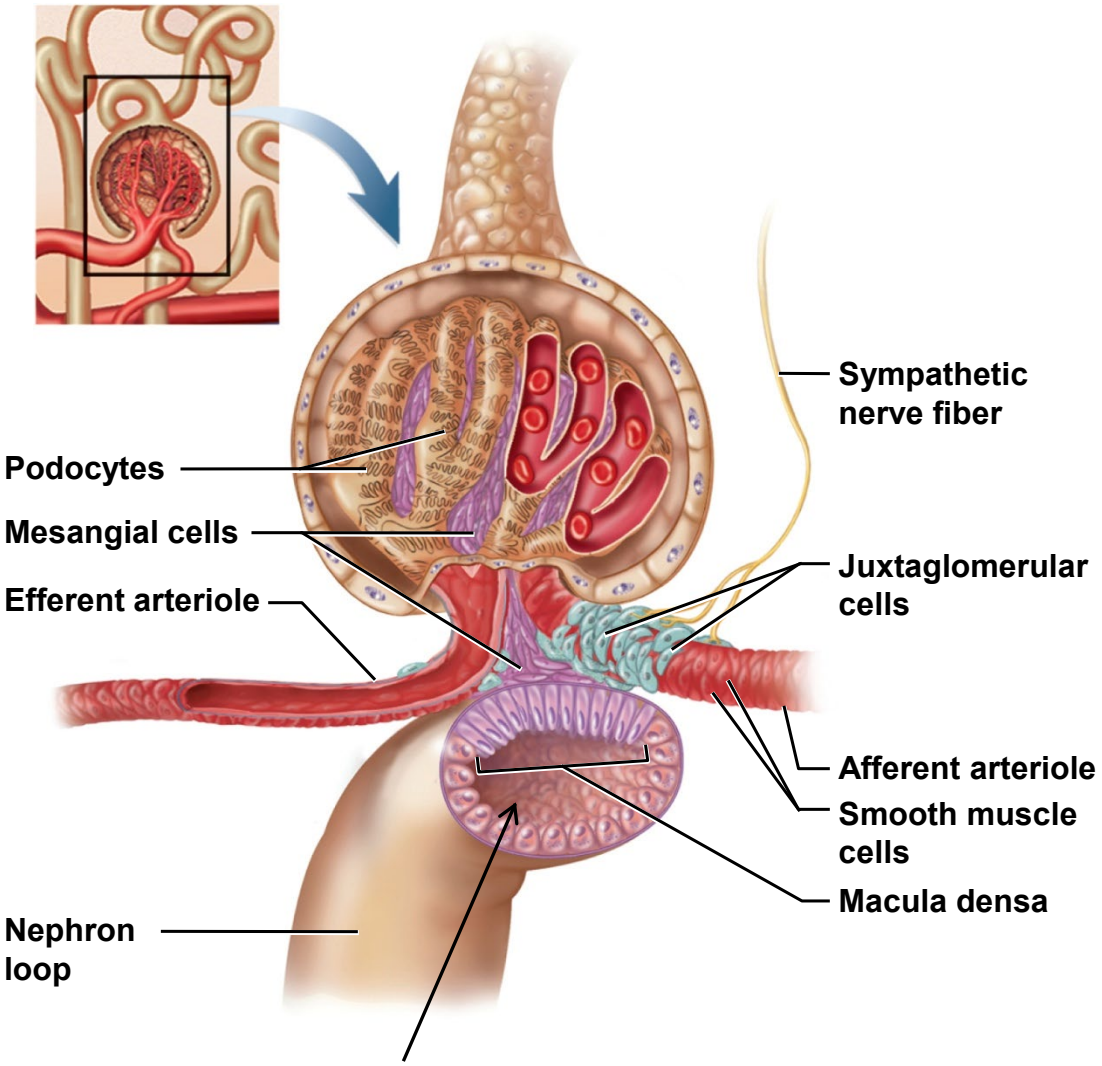
connected to macula densa and JG cells by gap junctions /// communicate by means of paracrines

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

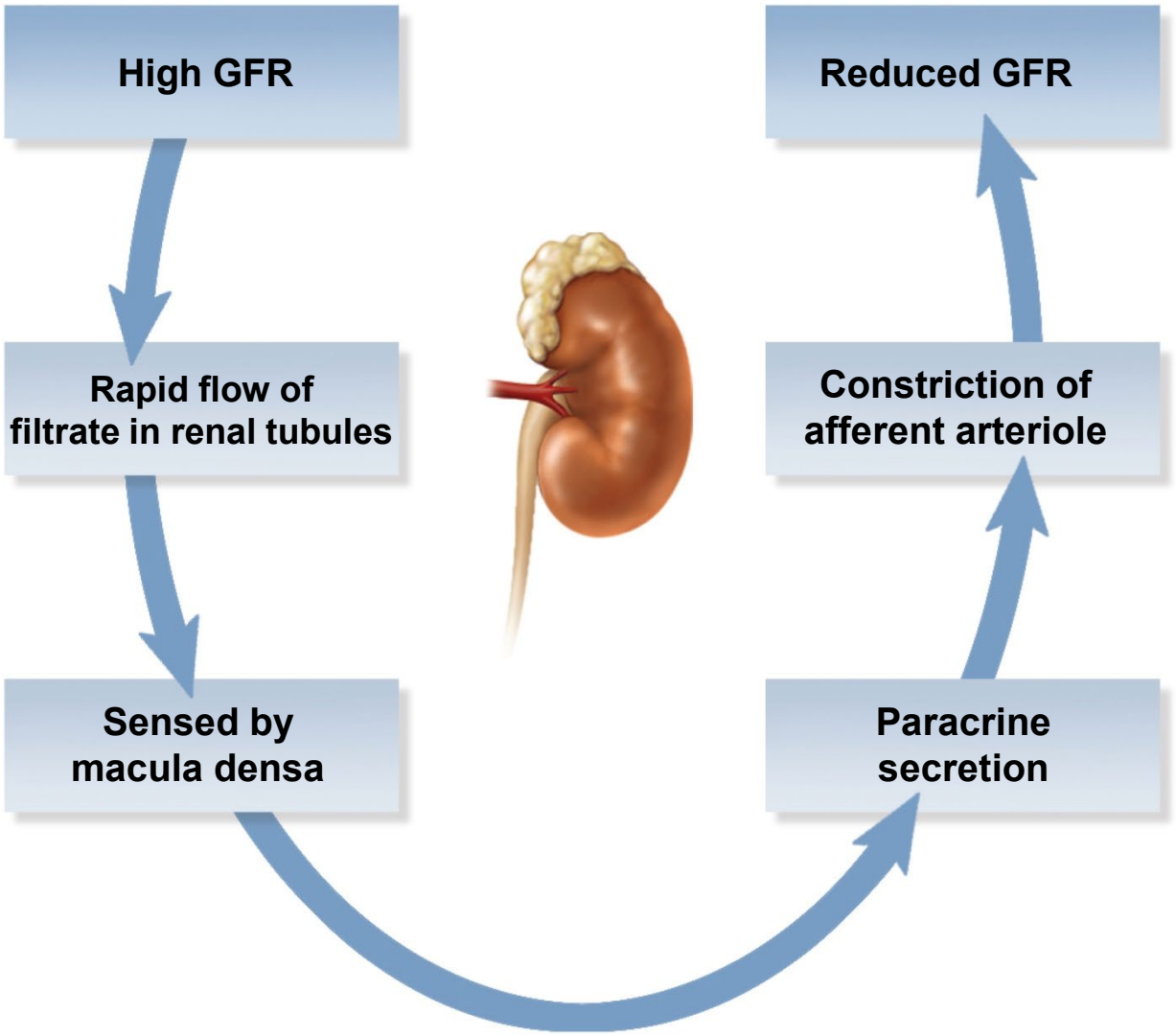
–mesangial cells may contract, constricting the capillaries and reducing filtration

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



Sympathetic Control of GFR

Sympathetic nerve fibers richly innervate the renal blood vessels

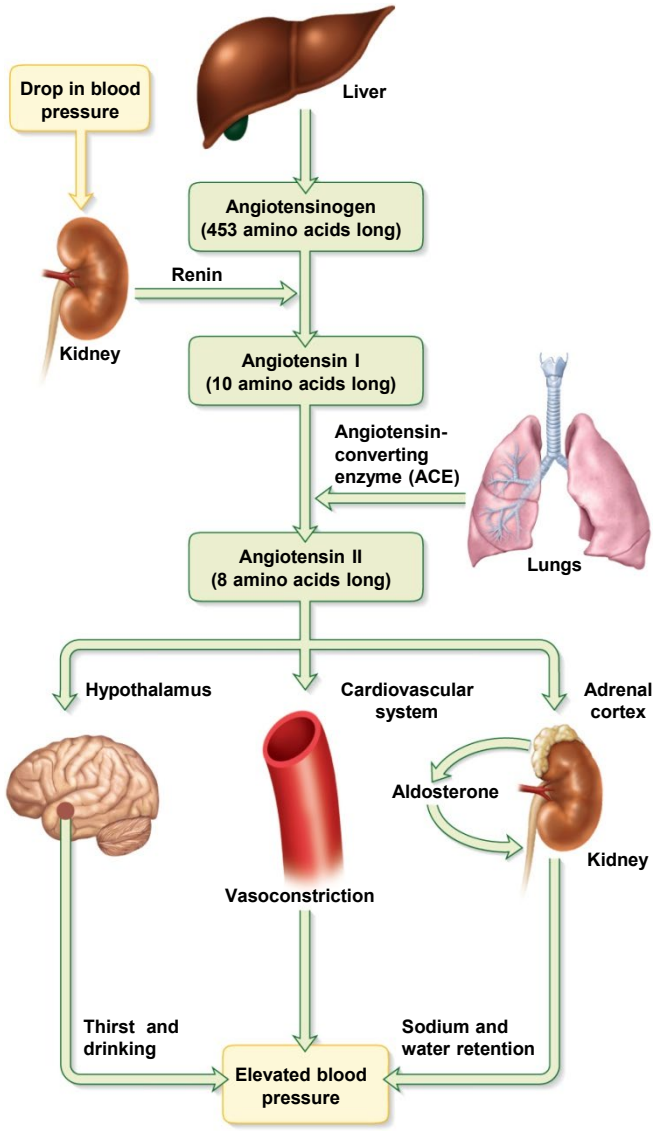
Sympathetic nervous system and adrenal epinephrine constrict the afferent arterioles /// experienced in strenuous exercise or acute conditions like circulatory shock

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 is made by liver

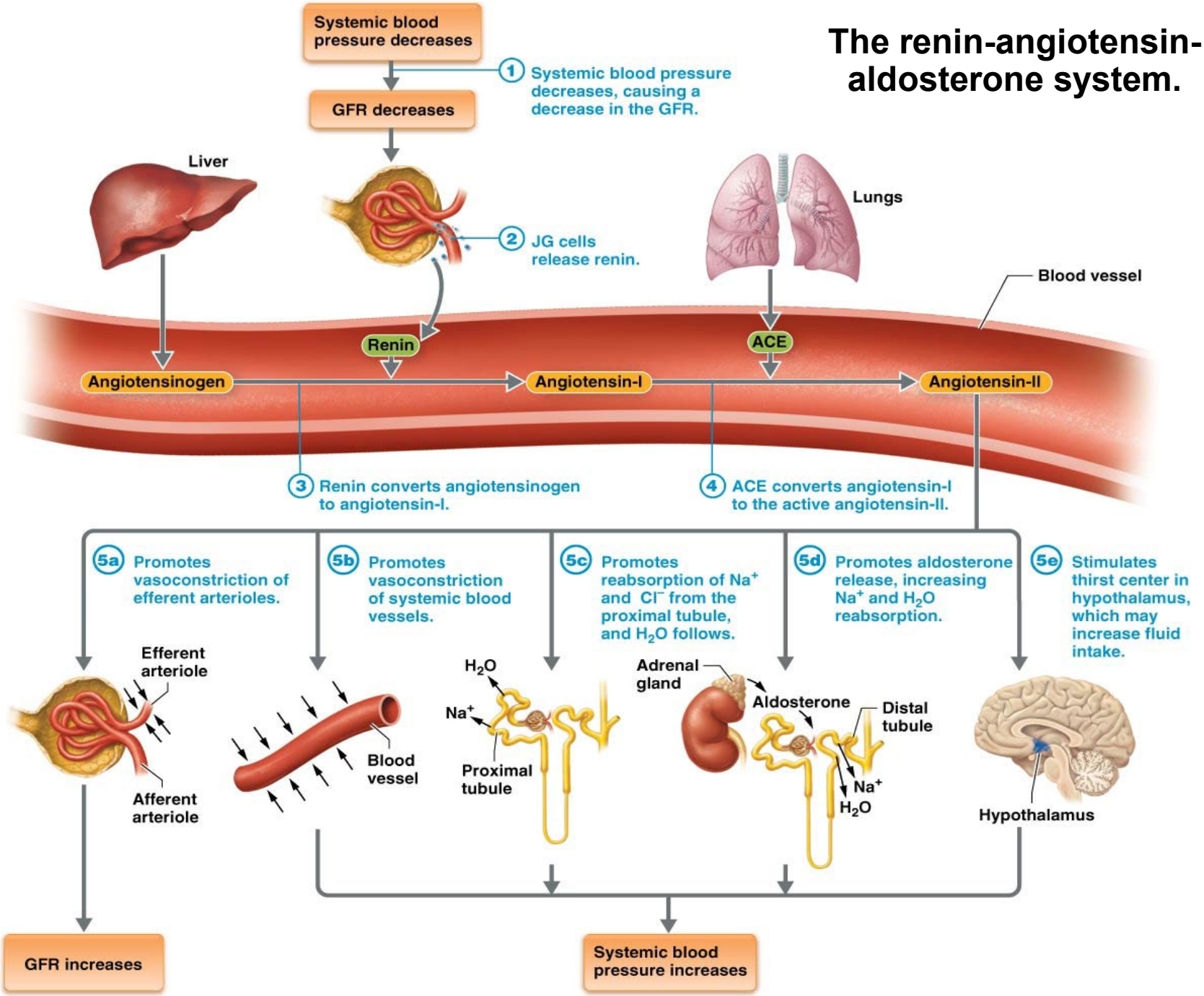
Angiotensinogen-I transported to the lungs where angiotensin-converting enzyme (ACE) converts angiotensin I to angiotensin II

Angiotensin-II is an active hormone // three functions: 1 vasopressor to peripheral arterioles // 2 targets adrenal gland to release aldosterone // 3 also receptors in brain to stimulate thirst

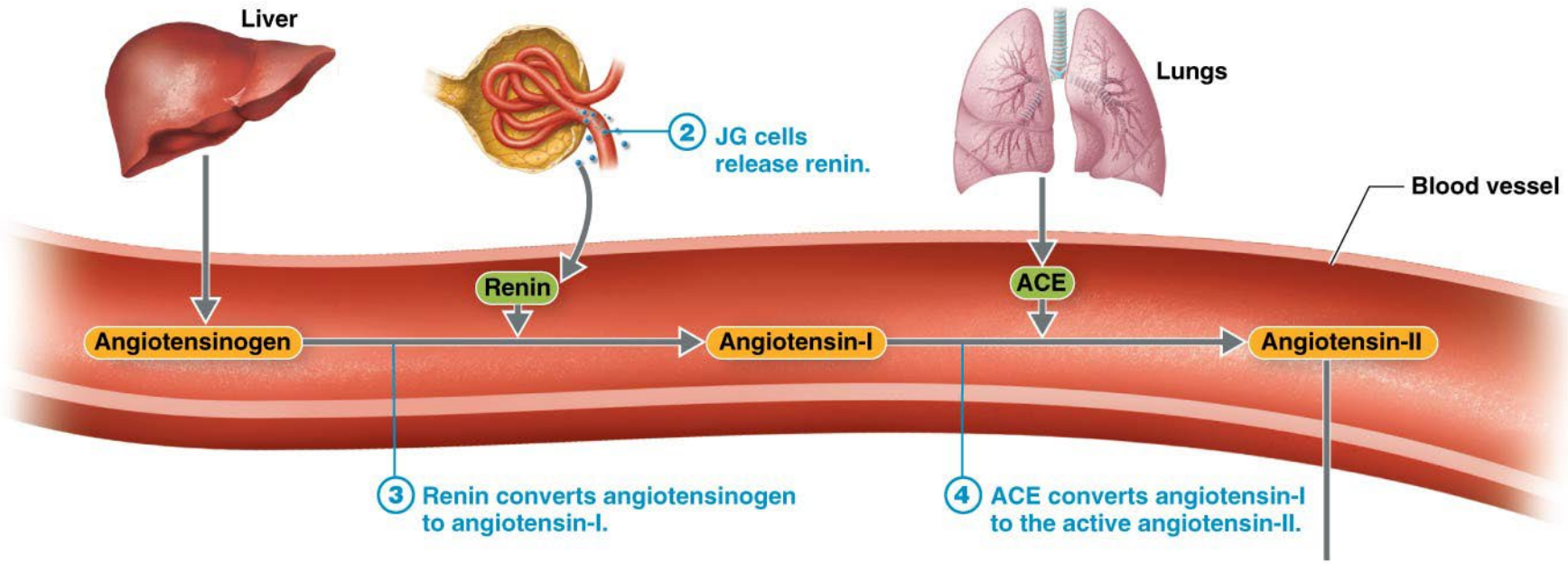
All three helps to restore fluid volume and BP through several mechanisms

If you have high blood pressure, your doctor may give you a drug to inhibit ACE, why?

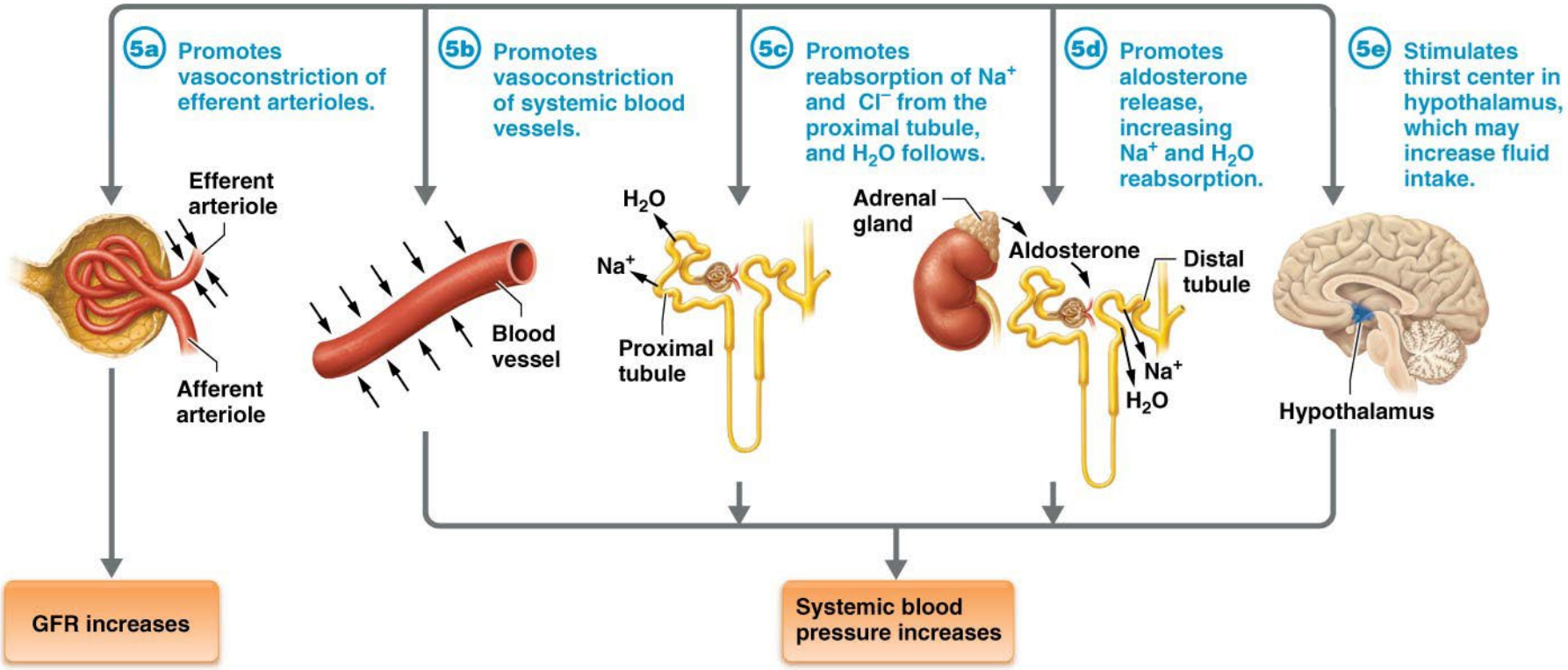
The renin-angiotensin-aldosterone system.



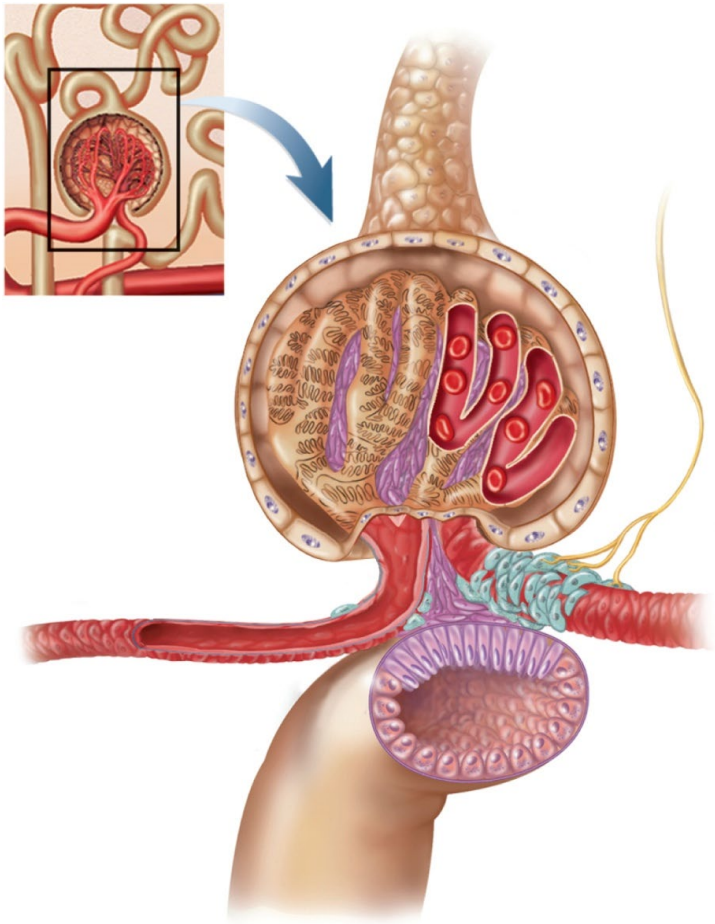
The renin-angiotensin-aldosterone system.



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 & H_2O

angiotensin II stimulates adrenal cortex to secrete aldosterone /// promotes Na^+ and H_2O 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 & H_2O intake

How Effective Is Autoregulation?

Maintains a dynamic equilibrium

Allows for GFR fluctuates within narrow range

System designed to work in normal fluctuation of blood pressure so that 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

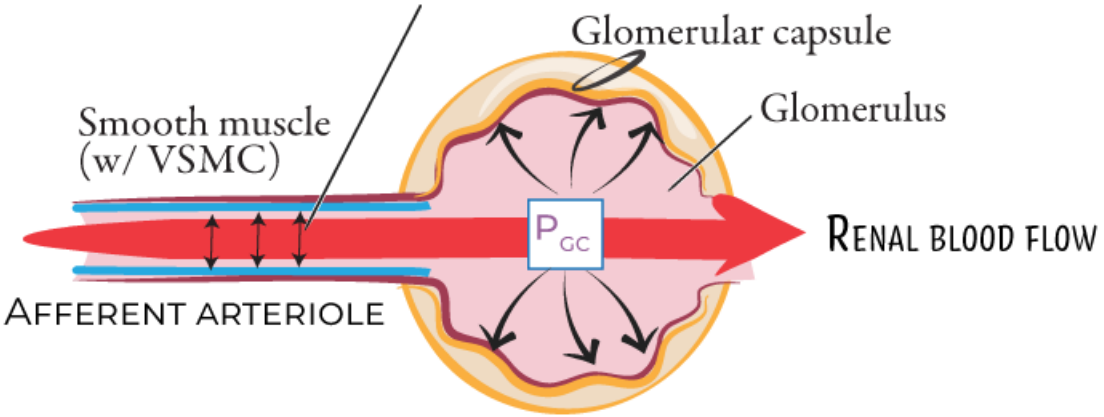
Below 70 mm Hg, glomerular filtration and urine output cease /// this occurs in hypovolemic shock

GFR: Intrinsic Regulation

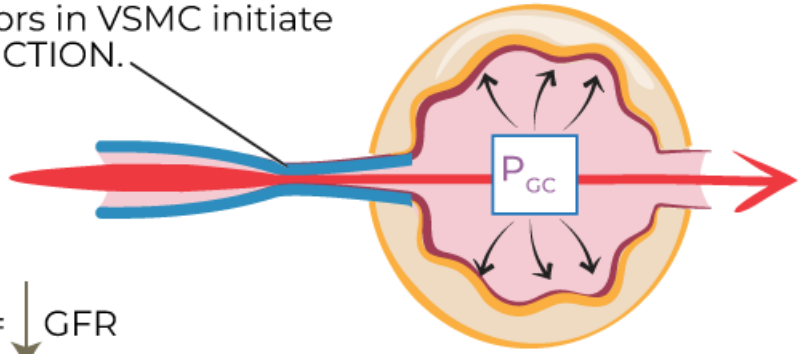
Myogenic Mechanism

Relies on inherent properties of the arterioles.

1. ↑ RBF = ↑ Hydrostatic pressure against the walls of the afferent arteriole.

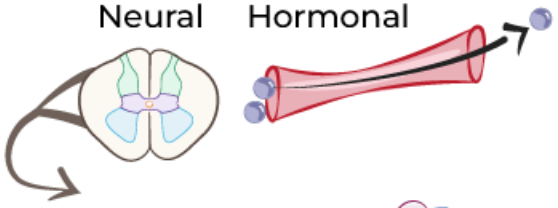


2. Stretch receptors in VSMC initiate VASOCONSTRICTION.



3. ↓ RBF = ↓ PGC = ↓ GFR

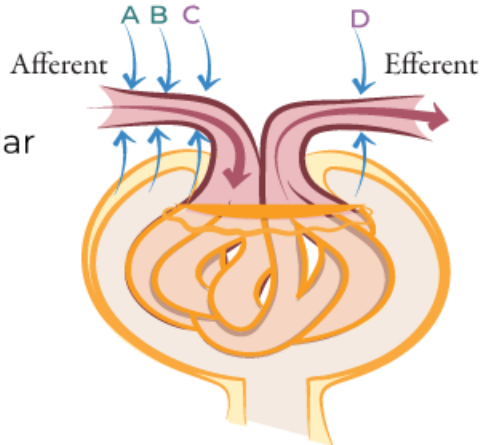
GFR Regulation - Overview

	INTRINSIC Intra-Renal	EXTRINSIC Extra-Renal
	Kidney 	Neural Hormonal 
Location:	Local, kidney 	System-wide, requires transport in bloodstream. 
Active MAP range:	80-180 mmHg	<80 mmHg
Goal:	Maintain constant **GFR** over a wide range of MAP.	Maintain **blood volume and pressure**; regulation of GFR is one facet of this.

Mechanisms:

A. Myogenic response

B. Tubuloglomerular feedback

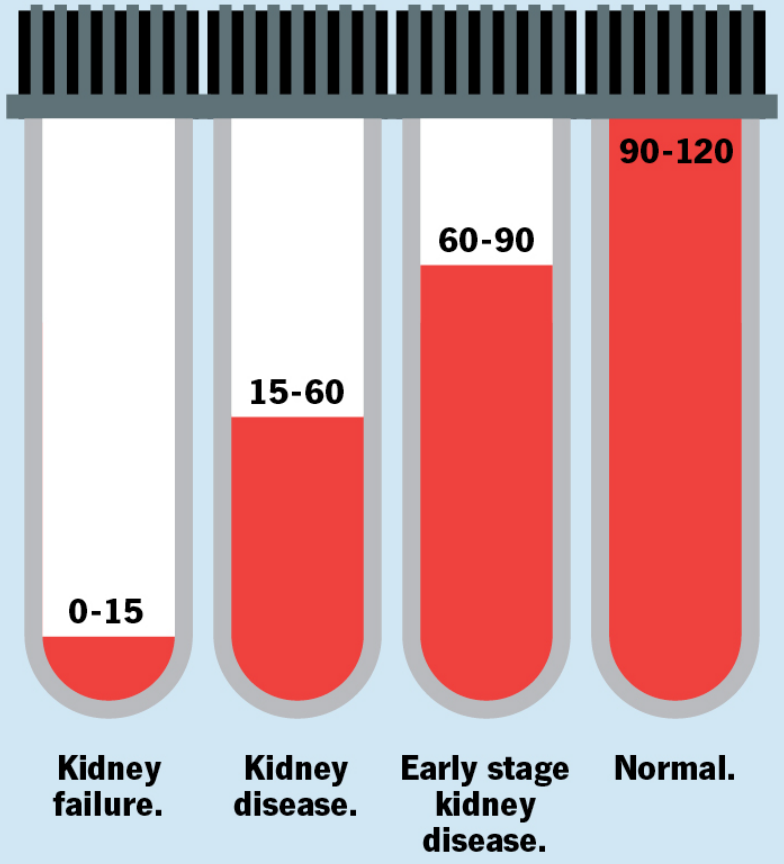


C. Neural: Sympathetic

D. Hormonal: angiotensin II

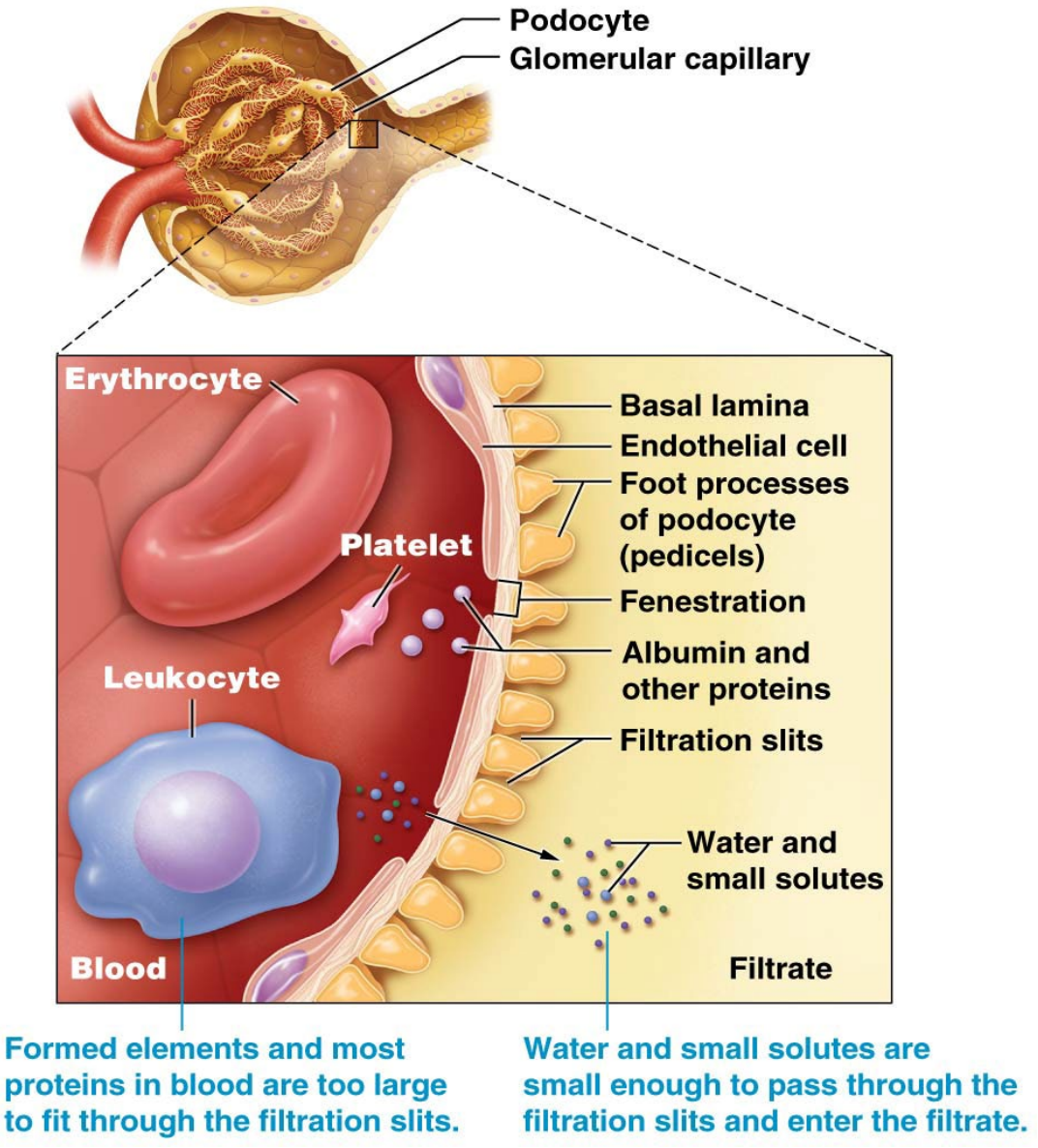
eGFR and Chronic Kidney Disease

eGFR is a type of blood test that measures how well your kidneys filter your blood and helps healthcare providers stage chronic kidney disease.

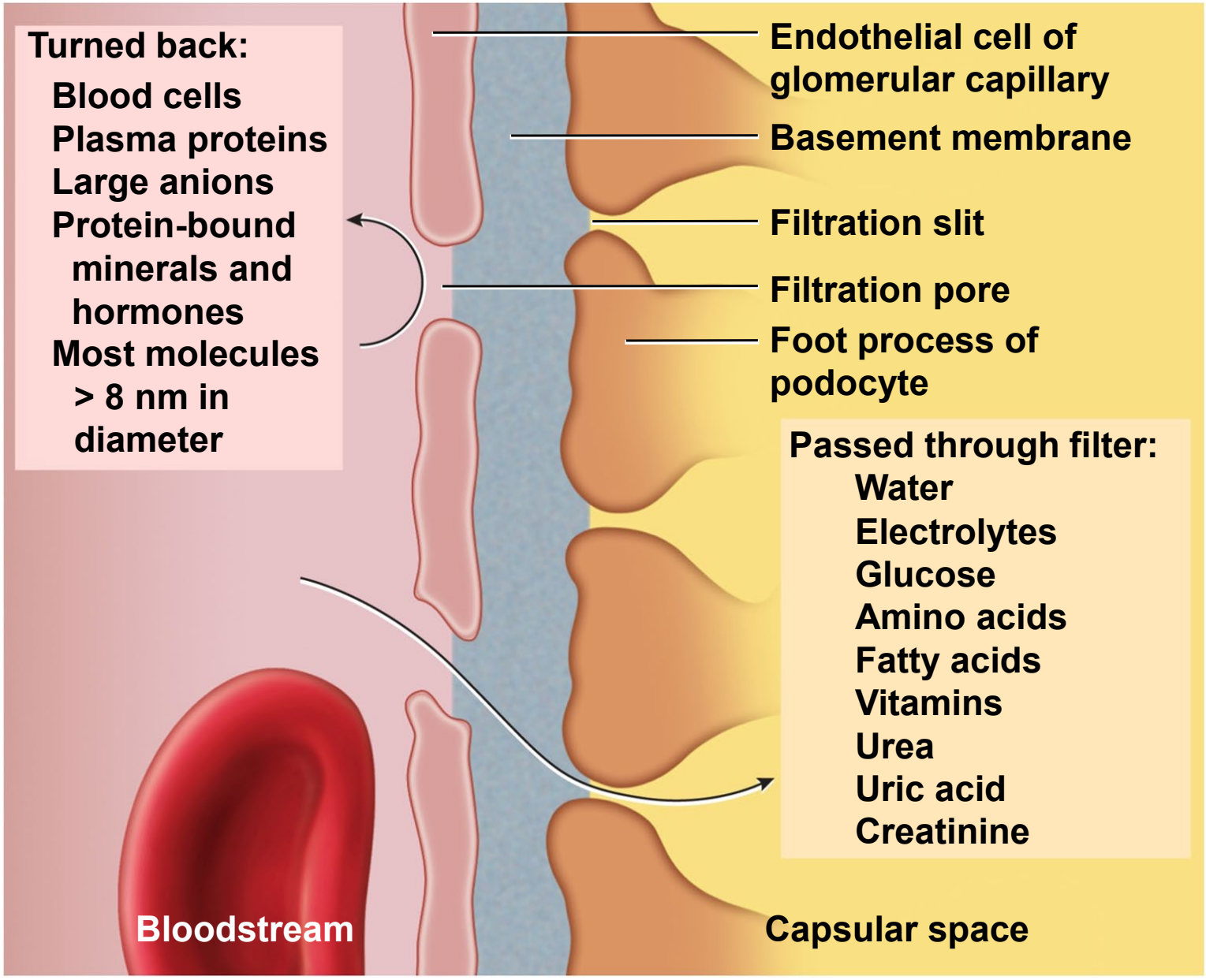


Cleveland Clinic

What is filtered through the glomerulus?



Filtration Pores and Slits Determine Filtrate Composition



Urine Volume

GFR is 180 liters per day (almost 55 gallons)

Normal volume for average adult - 1 to 2 L per 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)

Normal osmolarity (blood = 300 mOsm/L)

Ranges from 50 mOsm/L to 1,200 mOsm/L within kidney

pH urine 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

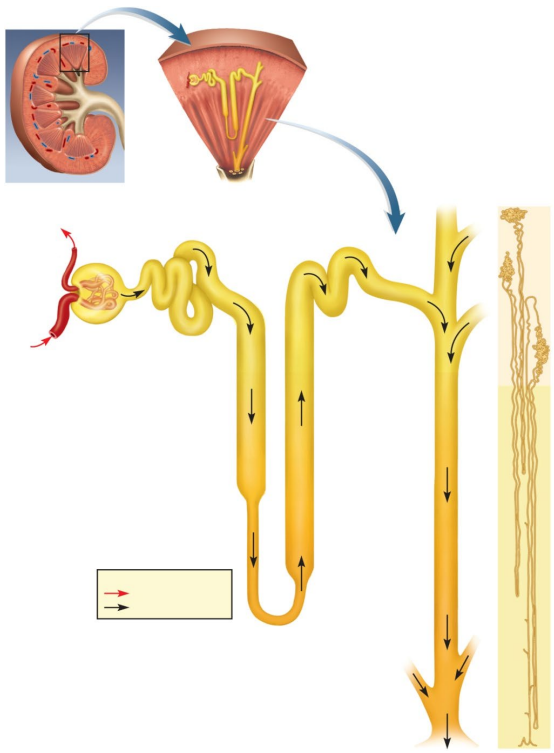
Pyuria – pus in the urine

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

Hormone Regulation: Aldosterone and Antidiuretic Hormone



Aldosterone and antidiuretic hormone have their <u>receptors at the end of the DCT and within the cortical region of the collecting duct.</u>

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

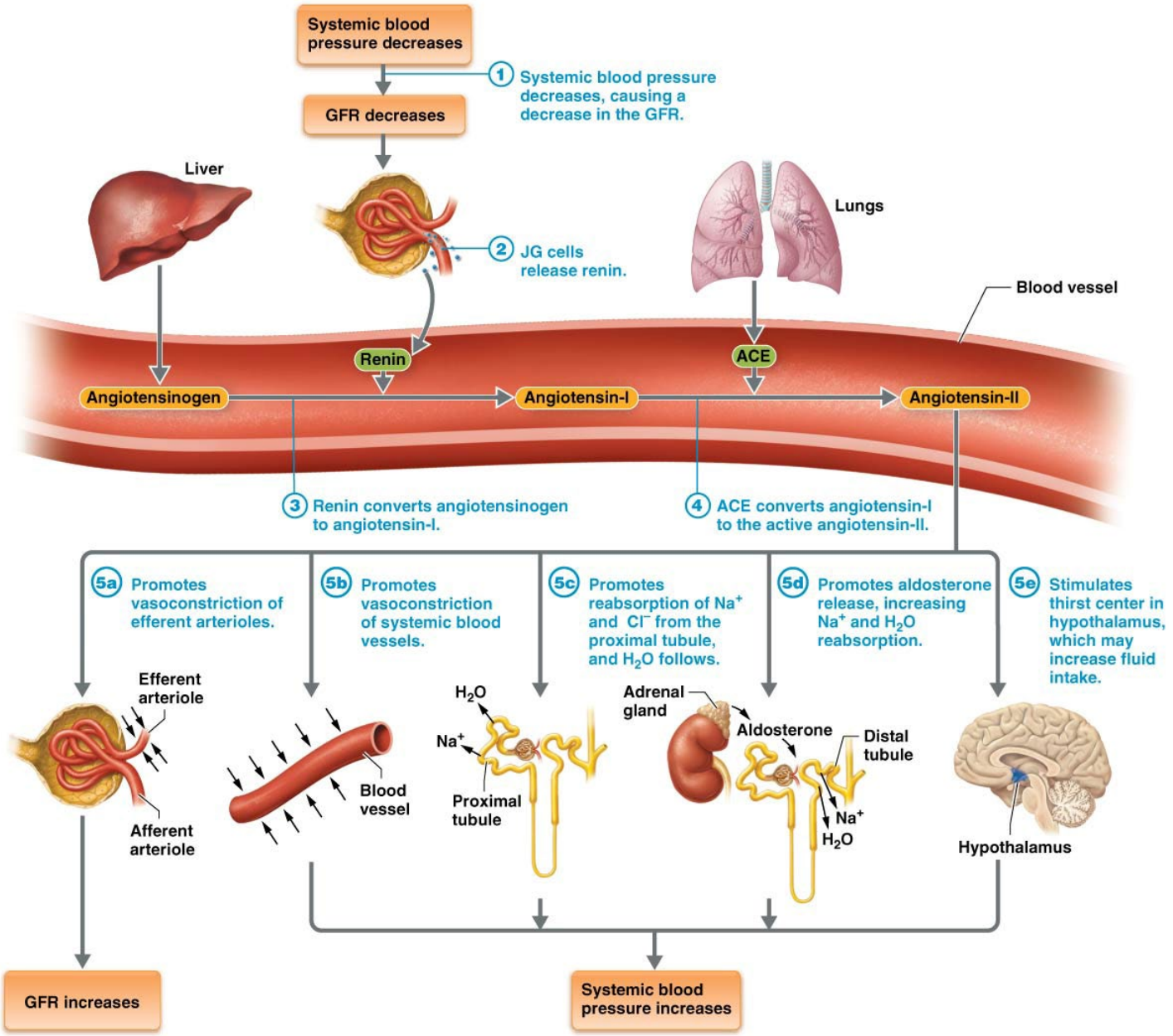
Aldosterone (salt retention hormone) activates transmembrane pumps to move sodium out of collecting duct and into blood vessels. // water follows the sodium

Antidiuretic hormone insert aquiporins into collecting duct // these water passageways allow water to move from collecting duct into blood vessels

Each hormone can change the volume of urine produced.

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 volume of tubular fluid 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 $\rightarrow$ renin release $\rightarrow$ angiotensin-II formation $\rightarrow$ 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^+ and secretion of K^+

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 aqueporins 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

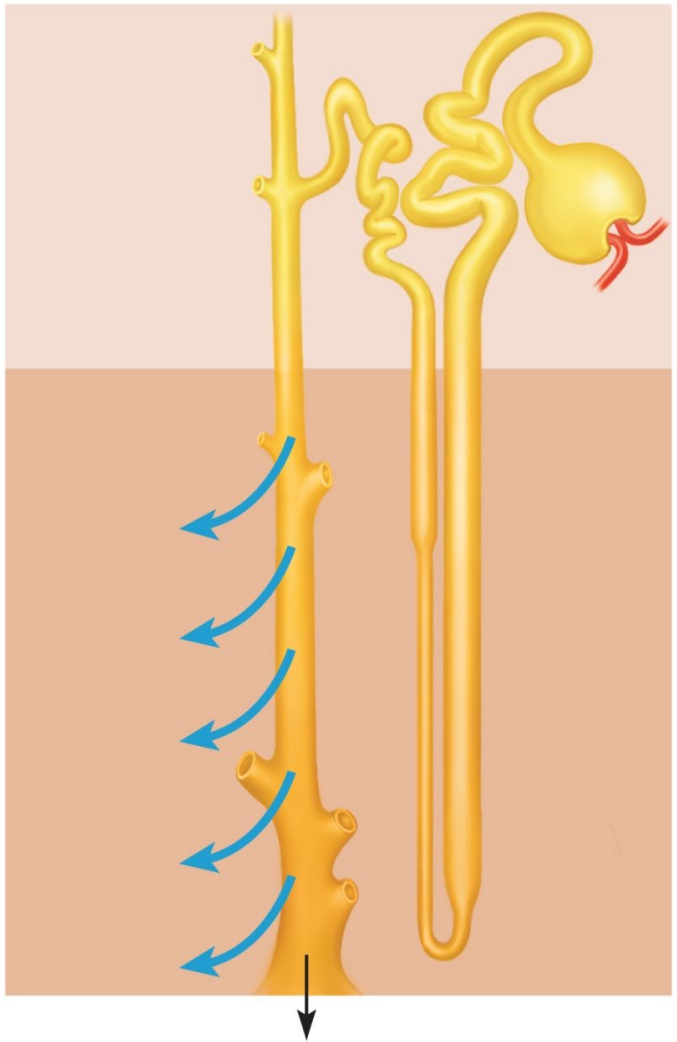
Net affect: more phosphate in urine and less calcium in urine

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 Using the

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

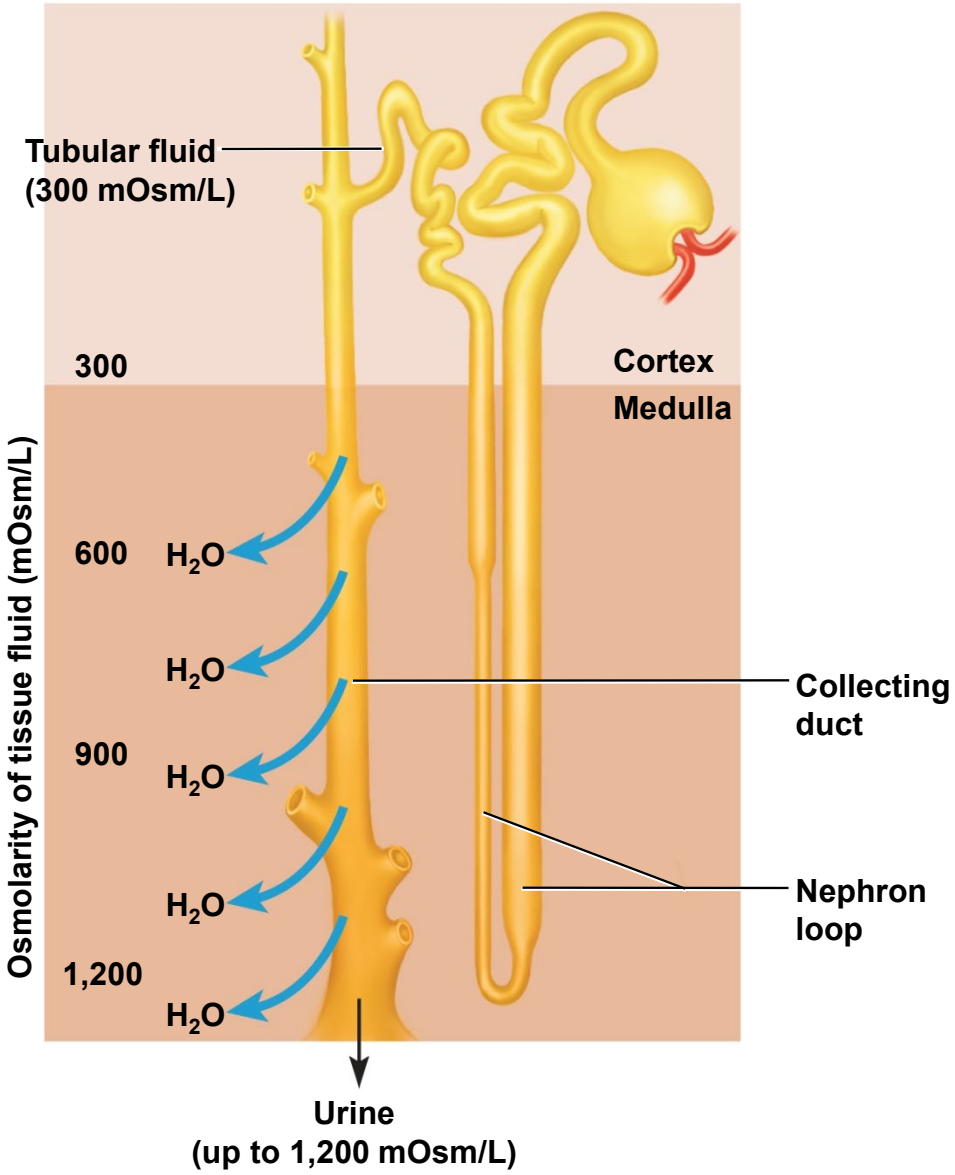
Therefore, the kidney recovers water from the collecting duct and returns it to the systemic circuit

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

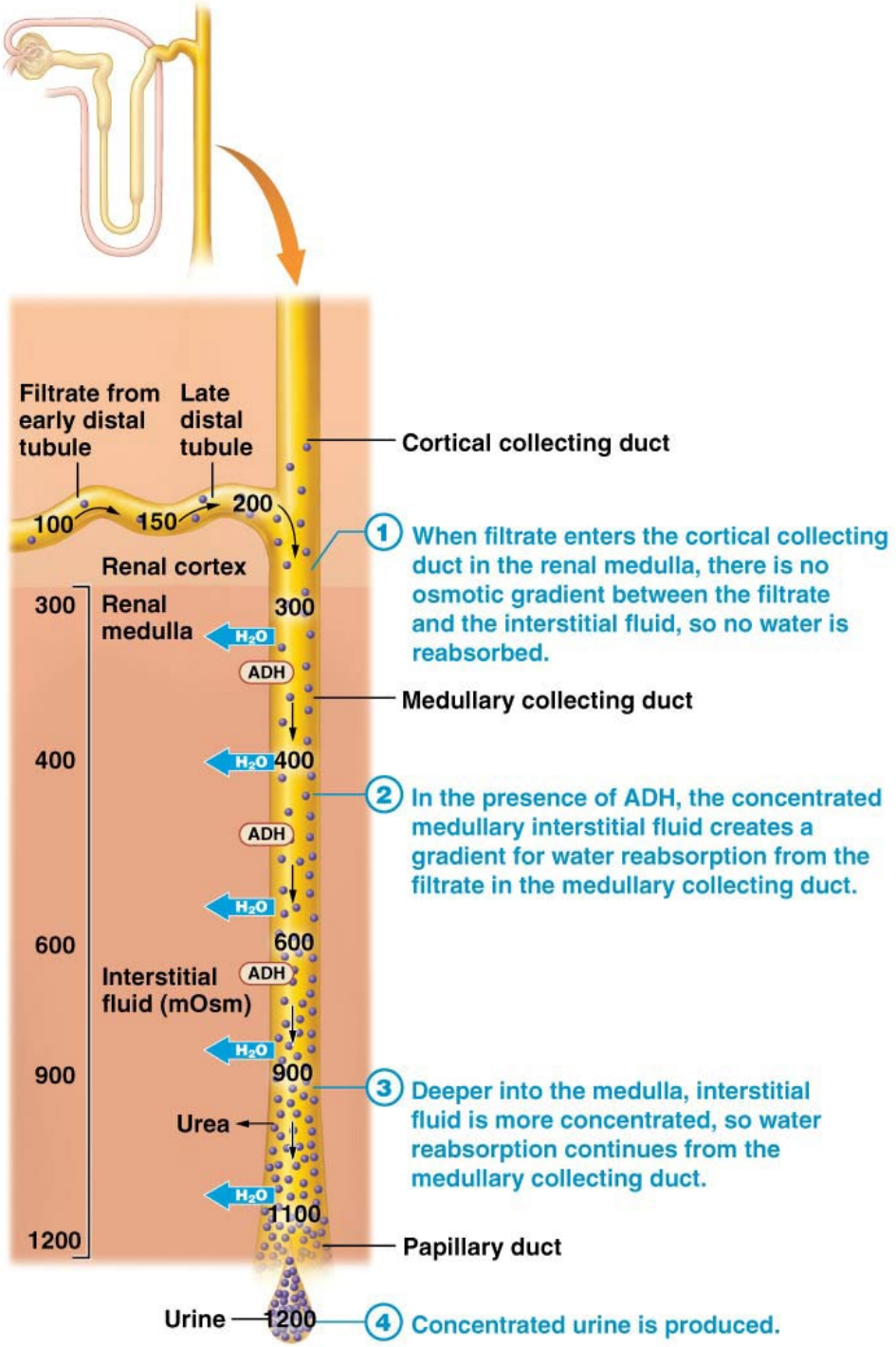
Medullary portion of CD is more permeable to water than to NaCl

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

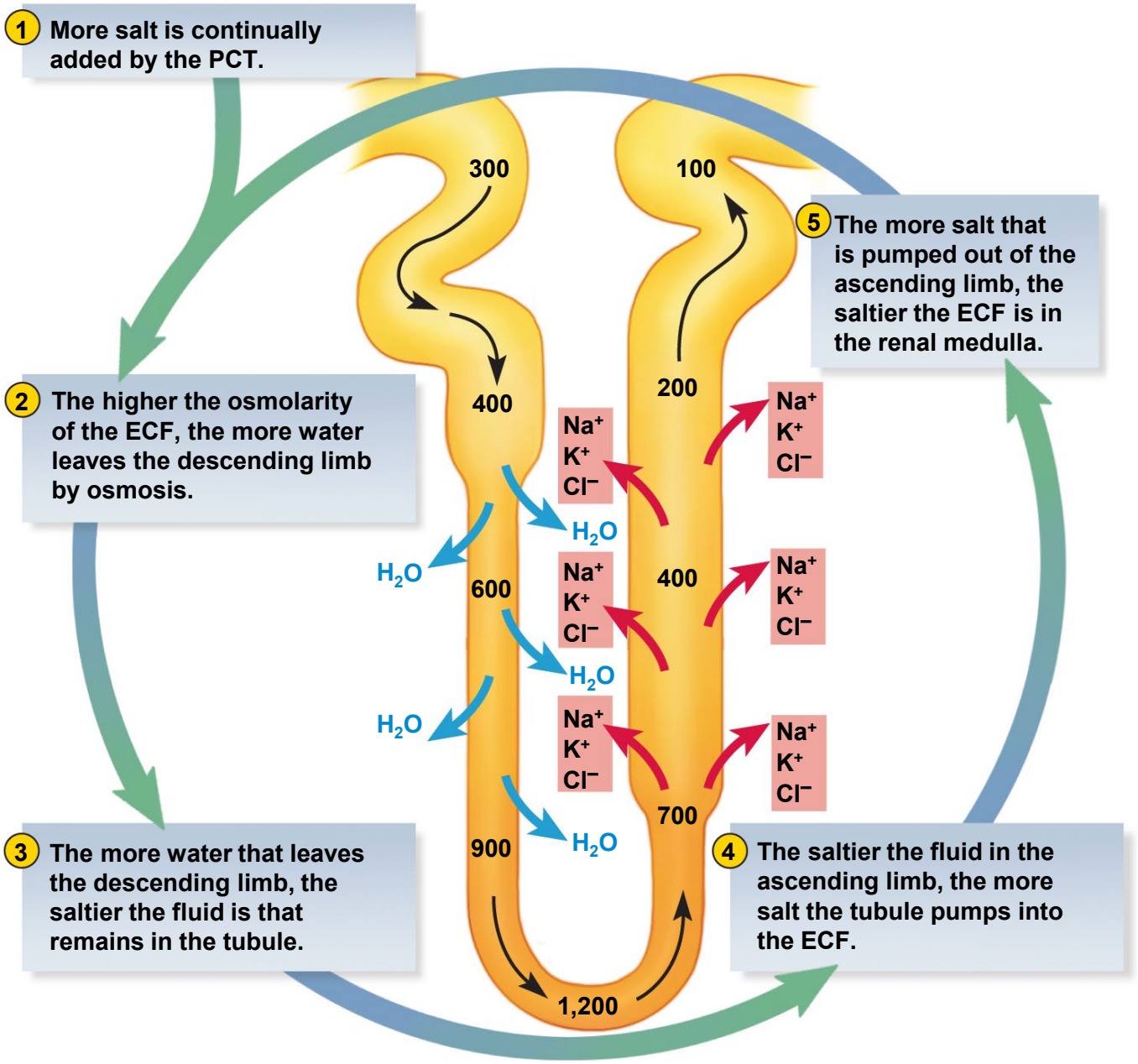
Fluid flowing upward in ascending limb

–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

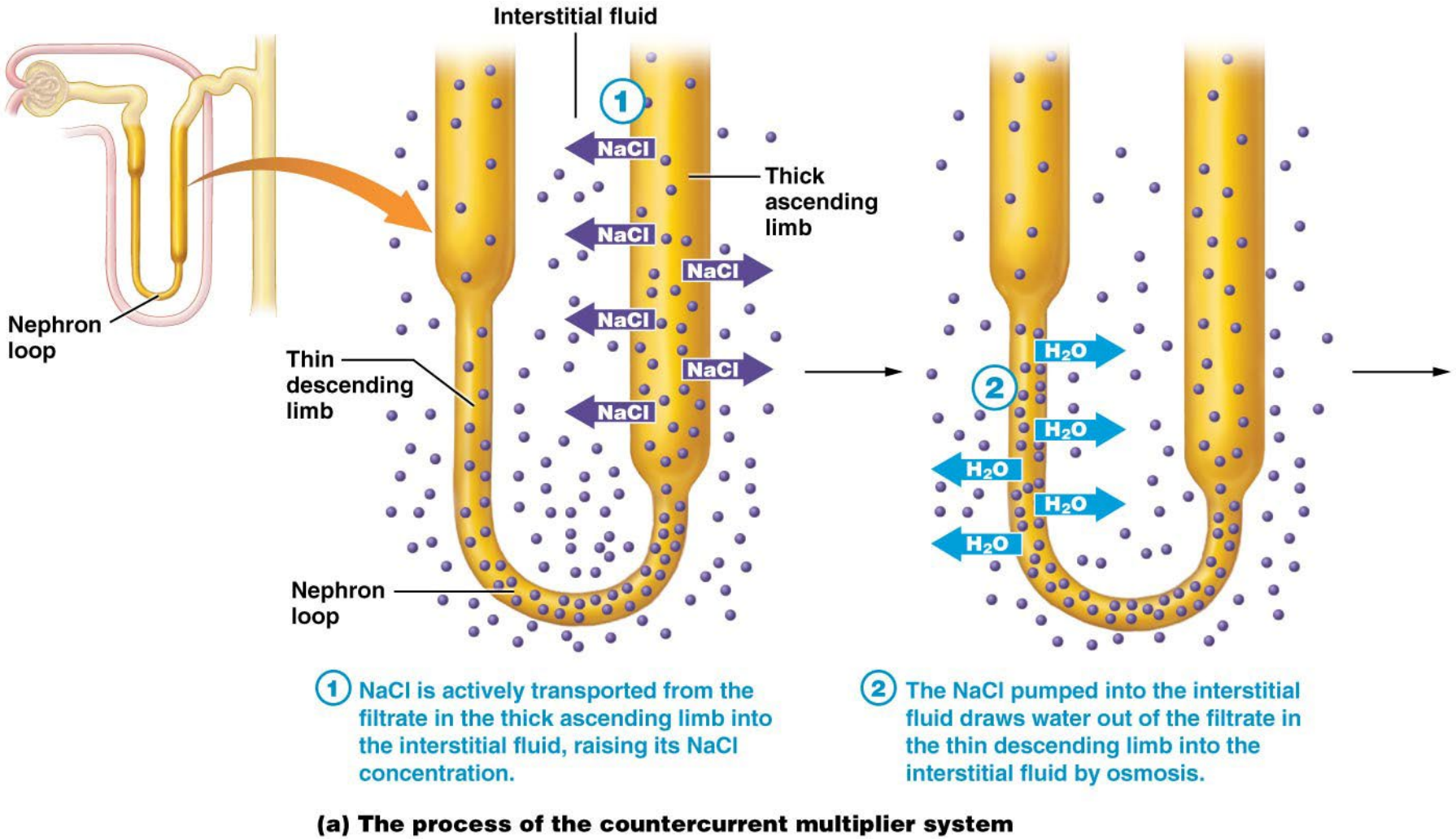
Recycling of urea: lower end of CD permeable to urea

–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.



(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 tonicty 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

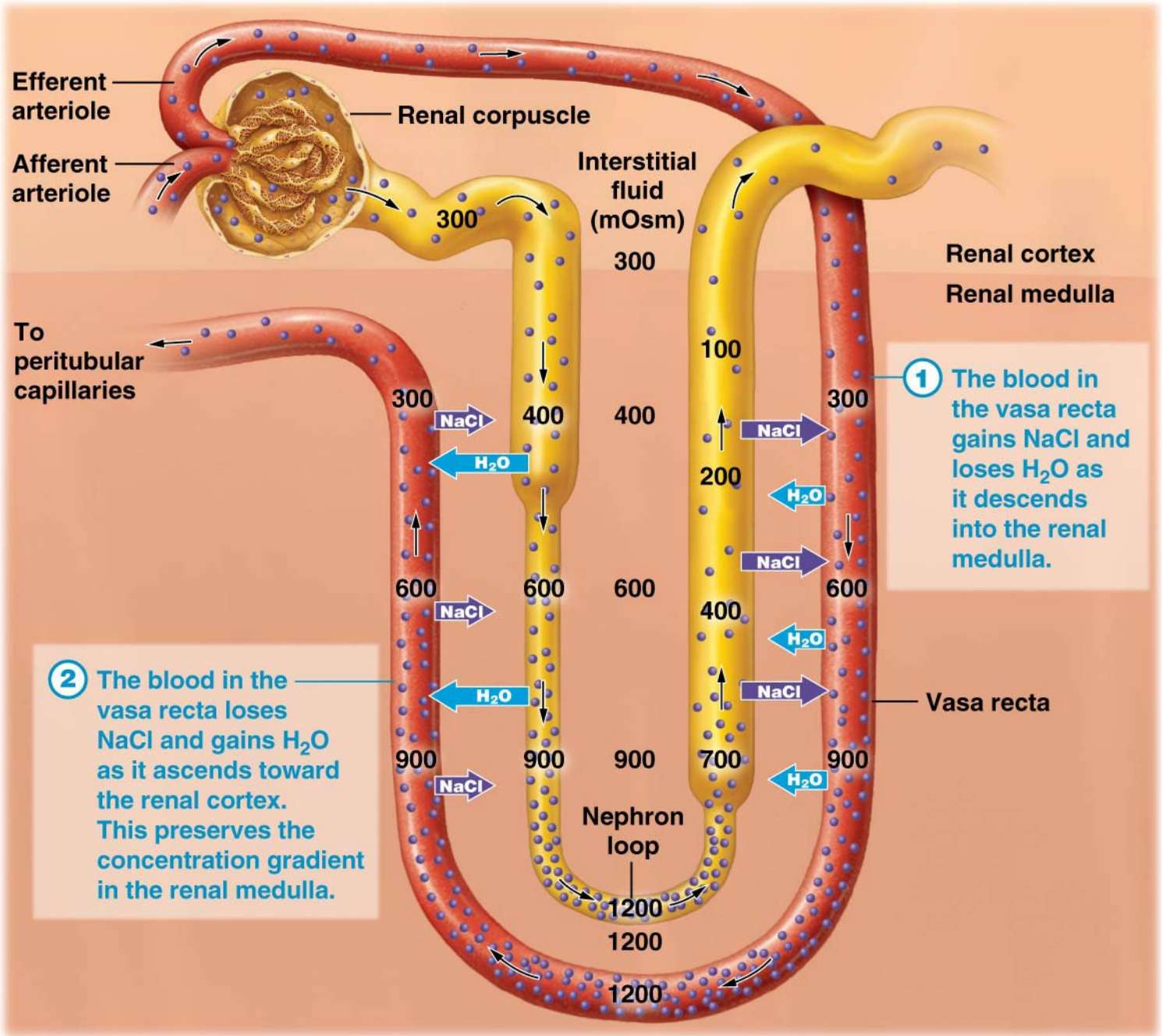
Water diffuses into and NaCl diffuses out of blood

The vasa recta gives the salt back and does not subtract from the osmolarity of the medulla

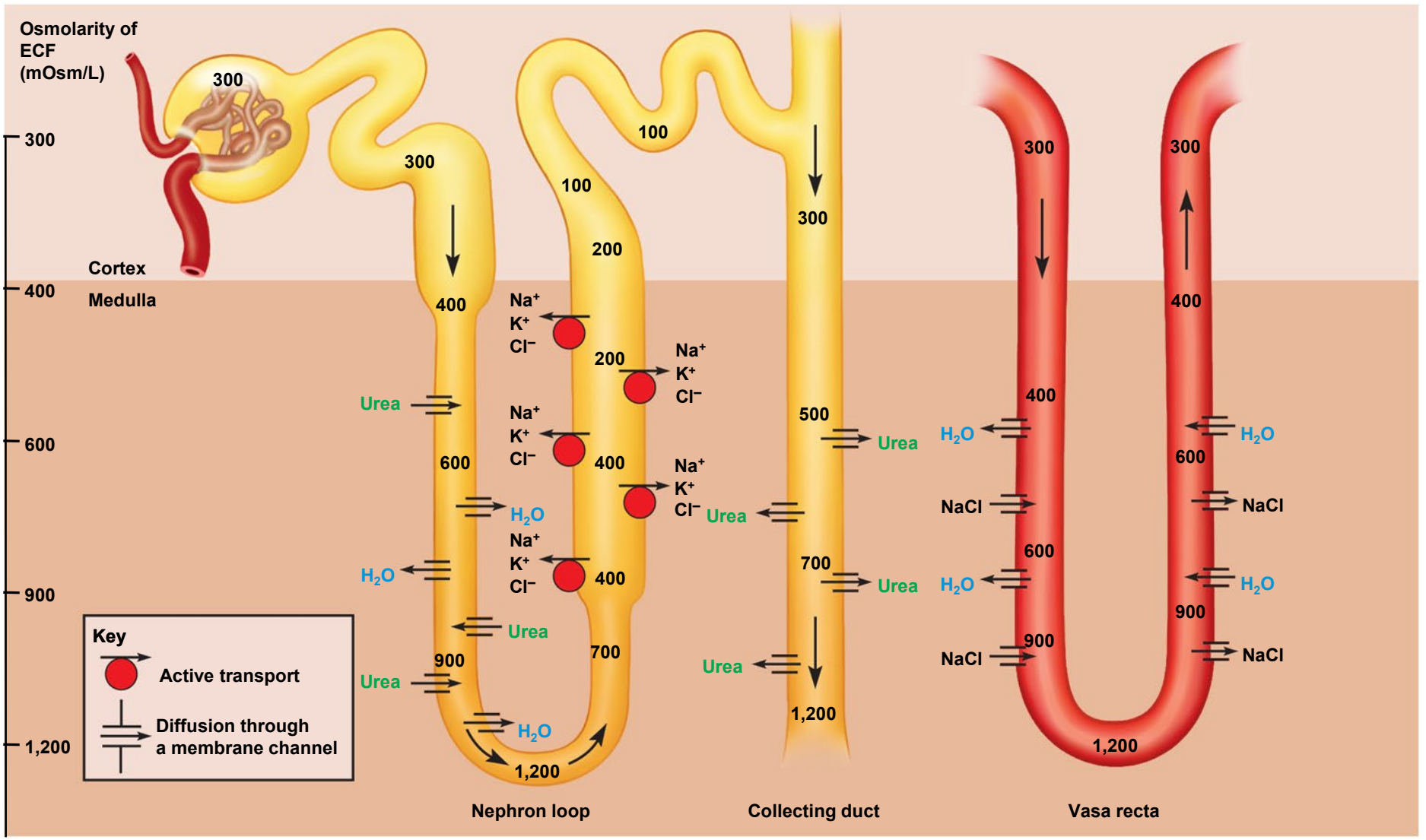
Absorb more water on way out than the way in, /// carry away water reabsorbed from the urine by collecting duct and nephron loop

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



Urinary Bladder

Urinary bladder - muscular sac located on floor of pelvic cavity

Inferior to peritoneum and posterior to pubic symphysis

Three layers

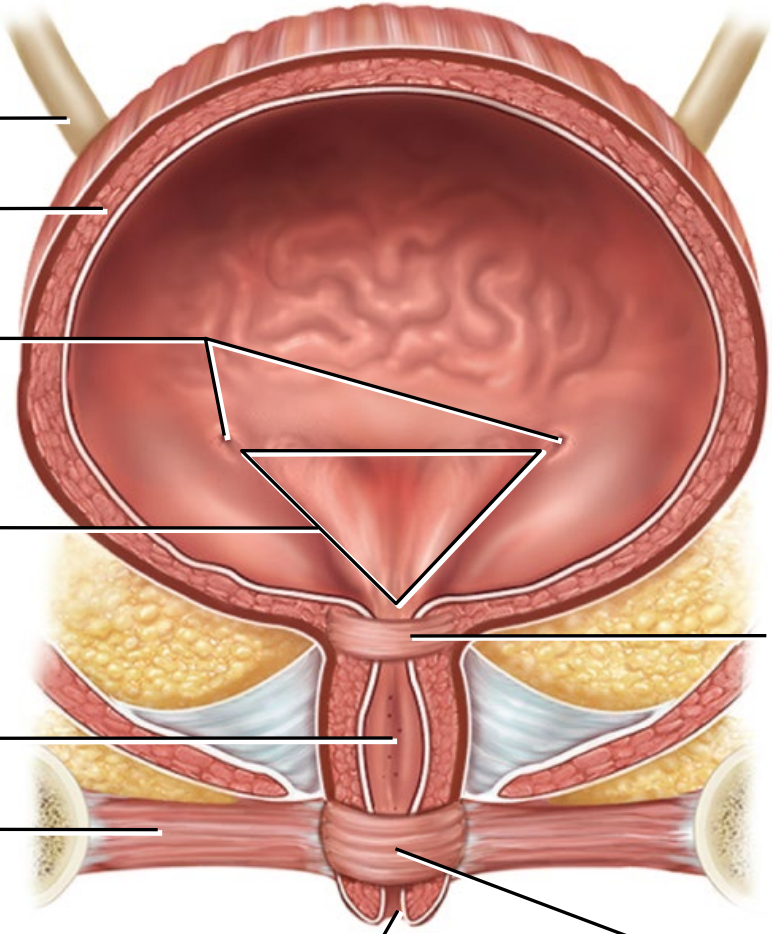
Parietal peritoneum, superior, fibrous adventitia other areas

Muscularis /// detrusor muscle /// 3 layers of smooth muscle

Mucosa - transitional epithelium

Rugae - conspicuous wrinkles in relaxed bladder

Urinary Bladder



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

Female

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 (transitional epithelium)

The Ureter

Retroperitoneal, muscular tube that extends from the kidney to the urinary bladder

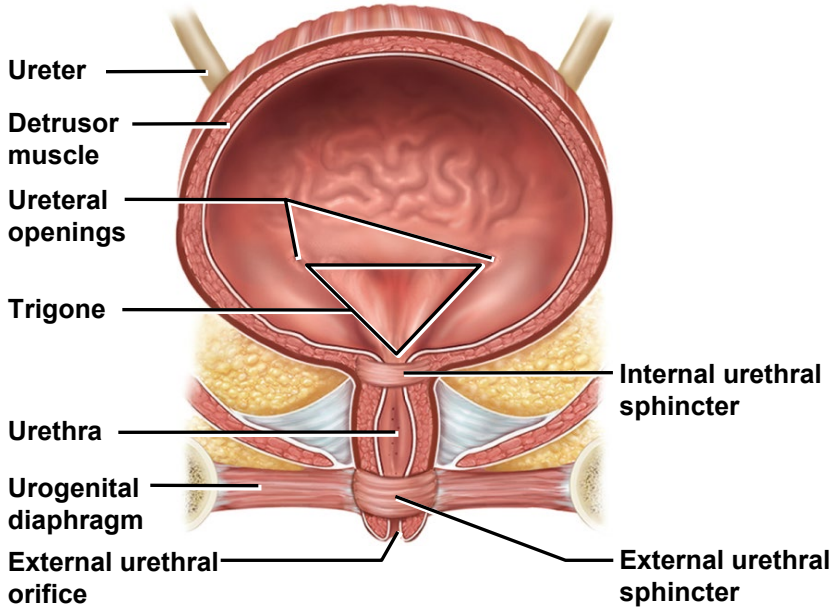
About 25 cm long

Passes posterior to bladder and enters it from below

Flap of mucosa acts as a valve into bladder

Keeps urine from moving into the ureter when bladder contracts

Female Urethra



(a) Female

3 to 4 cm long

Bound to anterior wall of vagina

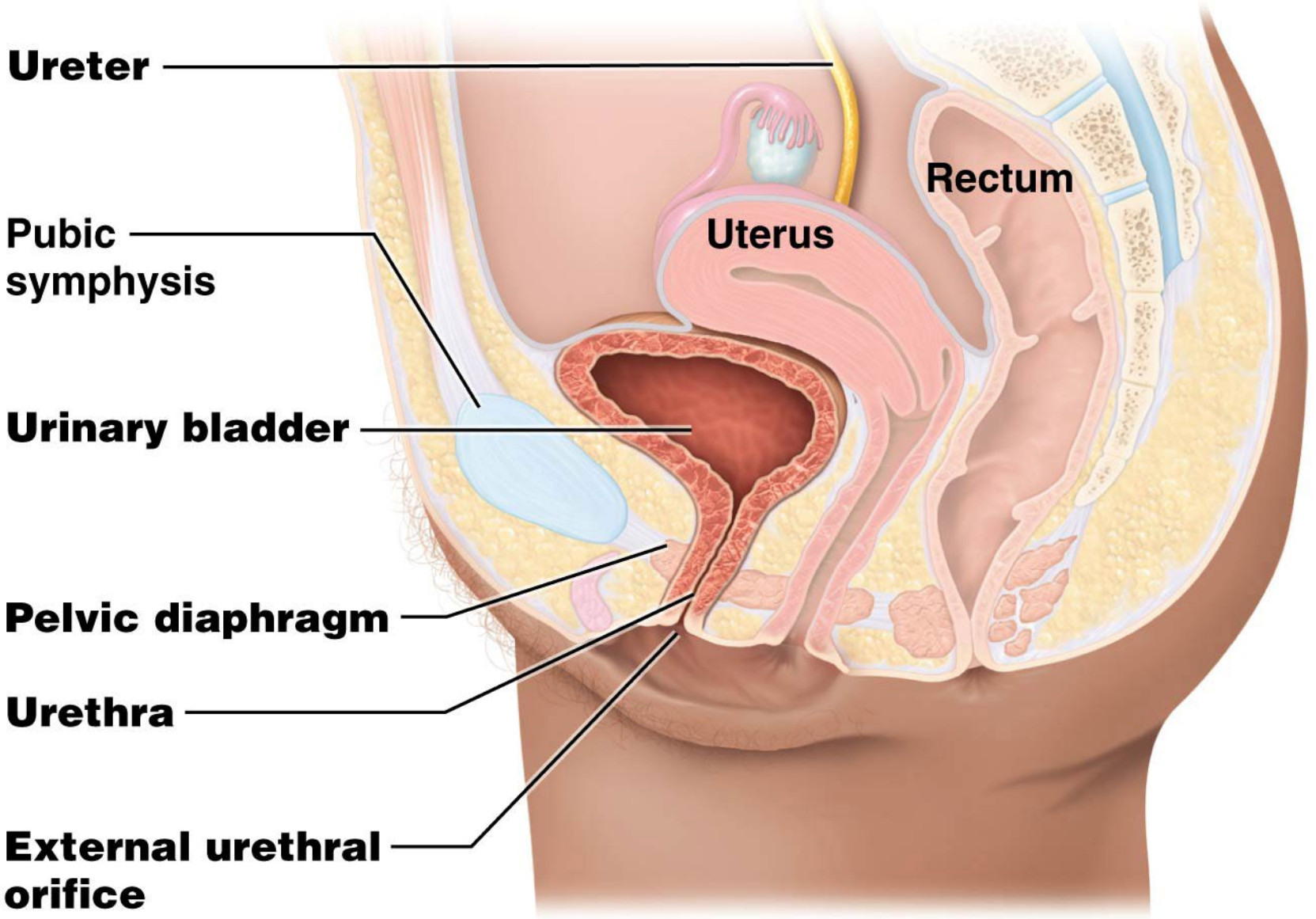
External urethral orifice

Between vaginal orifice and clitoris

Internal urethral sphincter /// detrusor muscle fascicles form sphincter // smooth muscle under involuntary control

External urethral sphincter // where the urethra passes through the pelvic floor // fascicles form sphincter // skeletal muscle under voluntary control

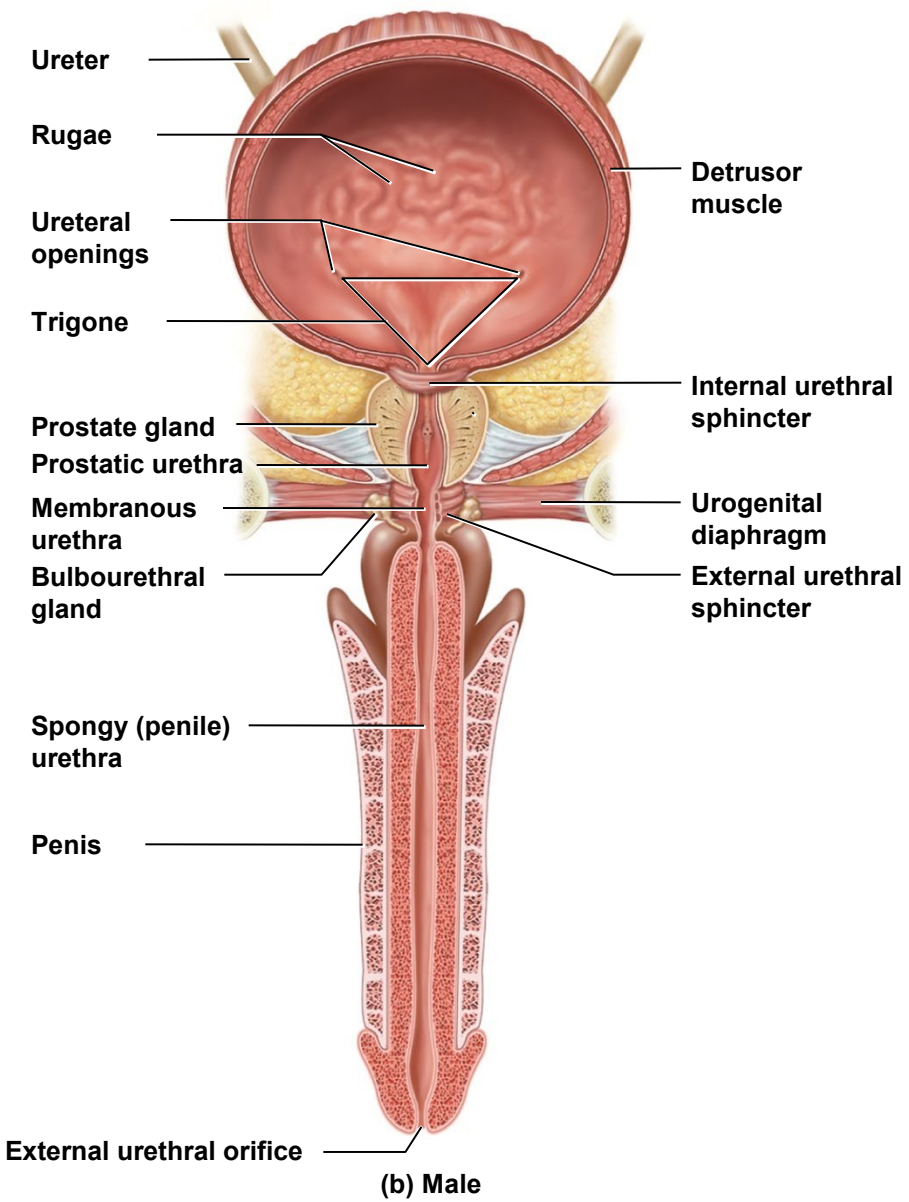
Figure 24.26b Comparison of urinary tract anatomy in the male and female.



(b) Sagittal section through female pelvis

© 2016 Pearson Education,

Male Urethra



(b) Male

18 cm long

Three regions of male urethra

Prostatic urethra (2.5 cm) // passes through prostate gland

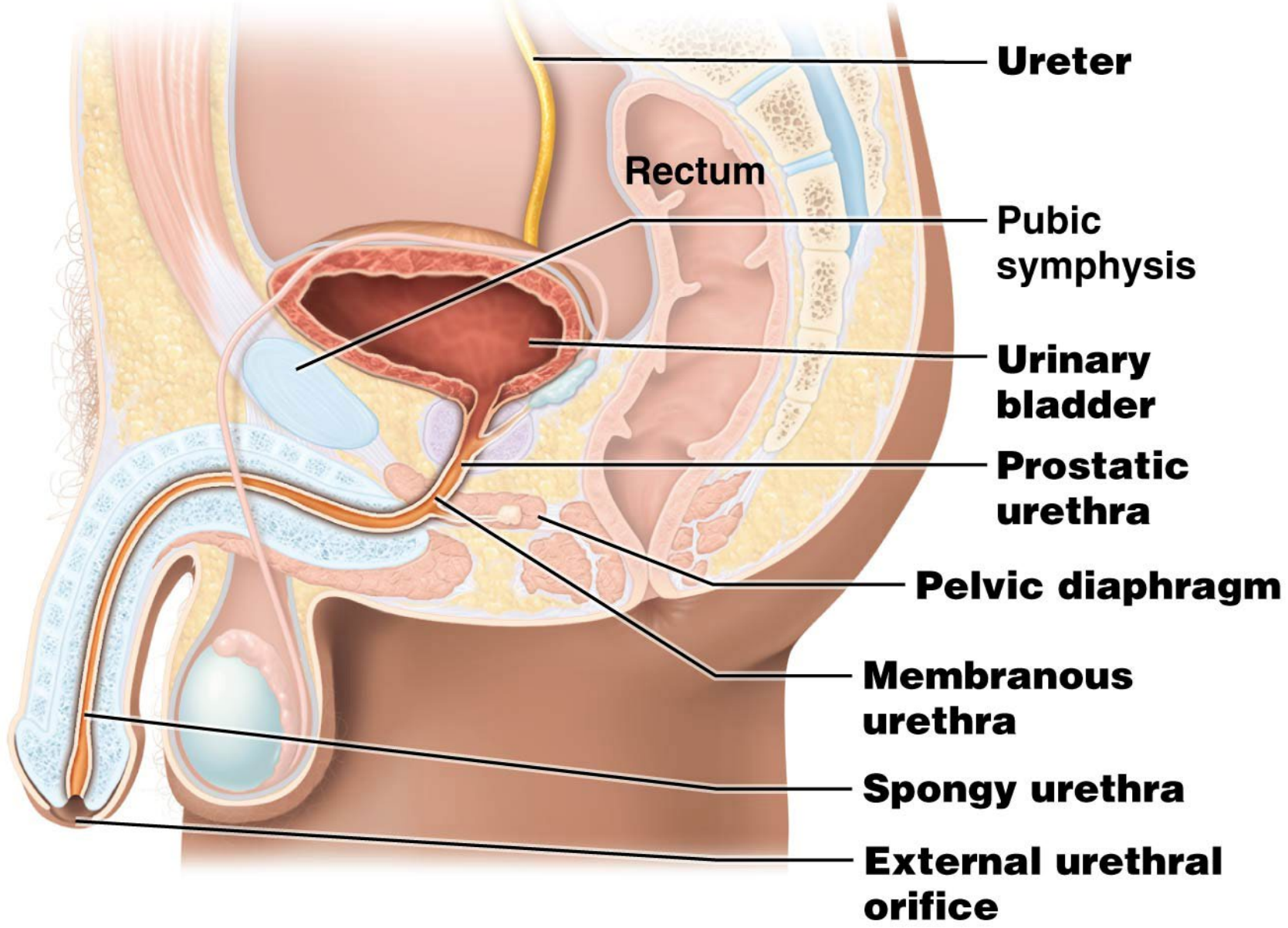
Membranous urethra (.5 cm) // passes through muscular floor of pelvic cavity

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

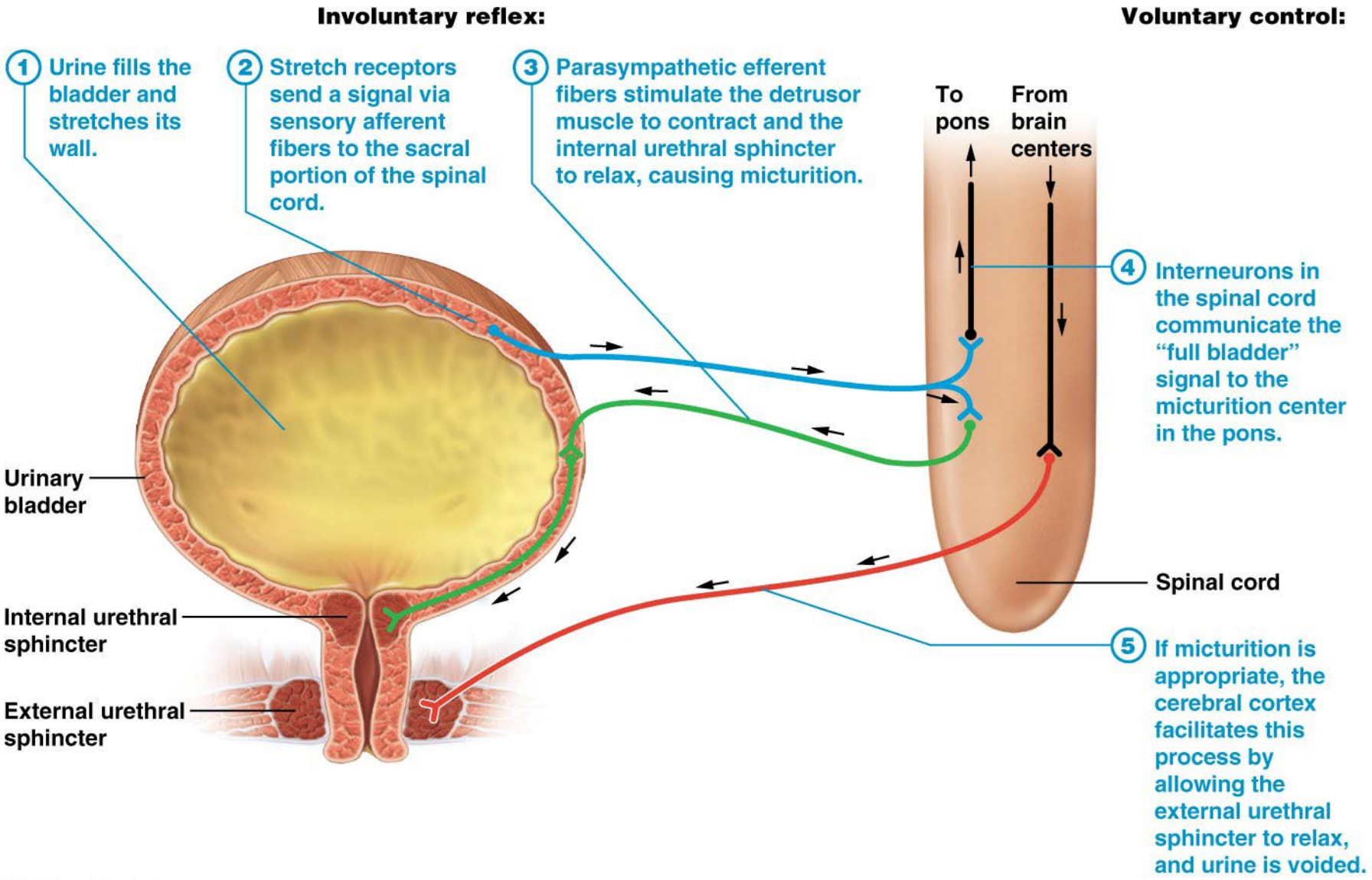
Figure 24.26a Comparison of urinary tract anatomy in the male and female.



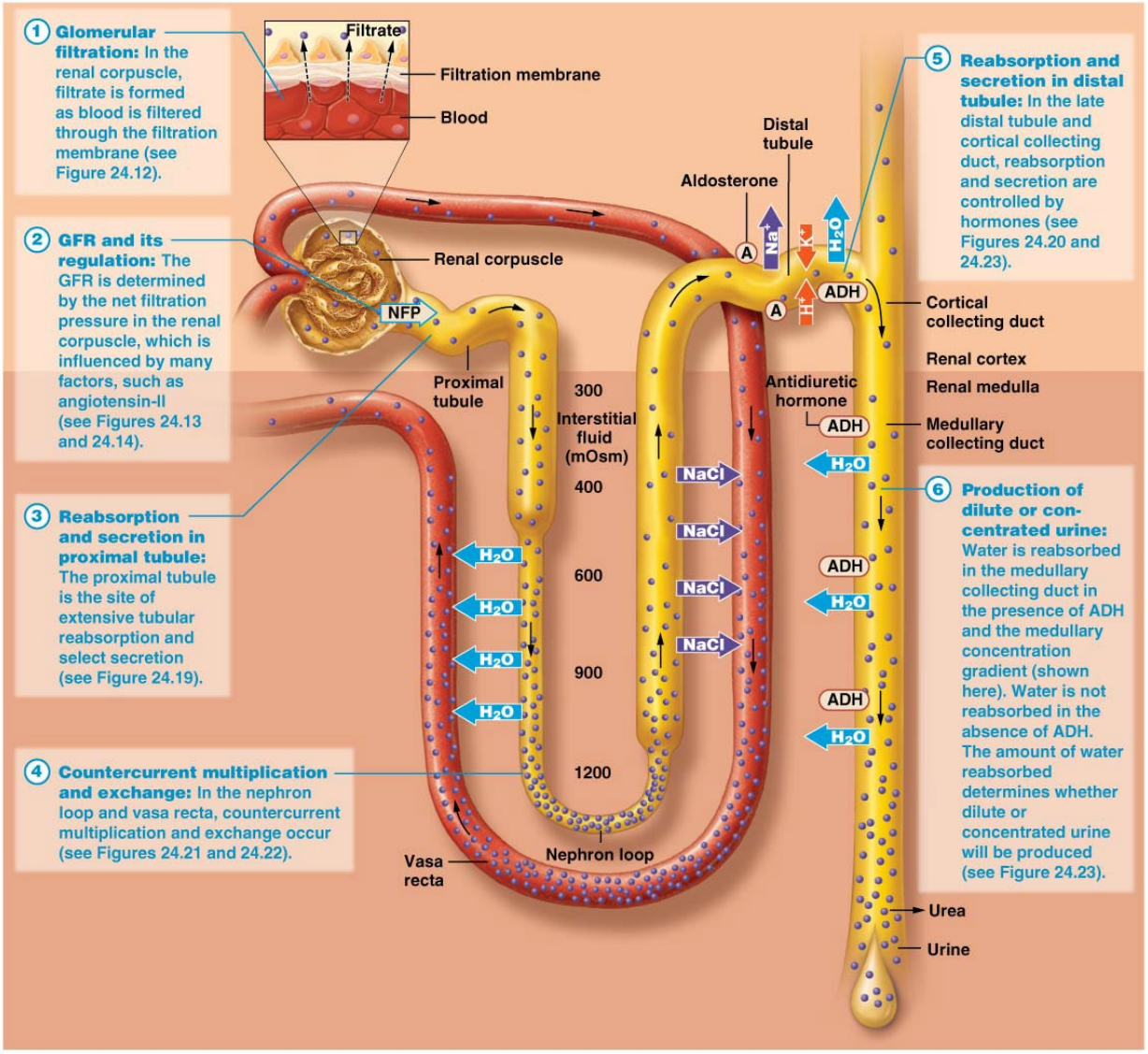
(a) Sagittal section through male pelvis

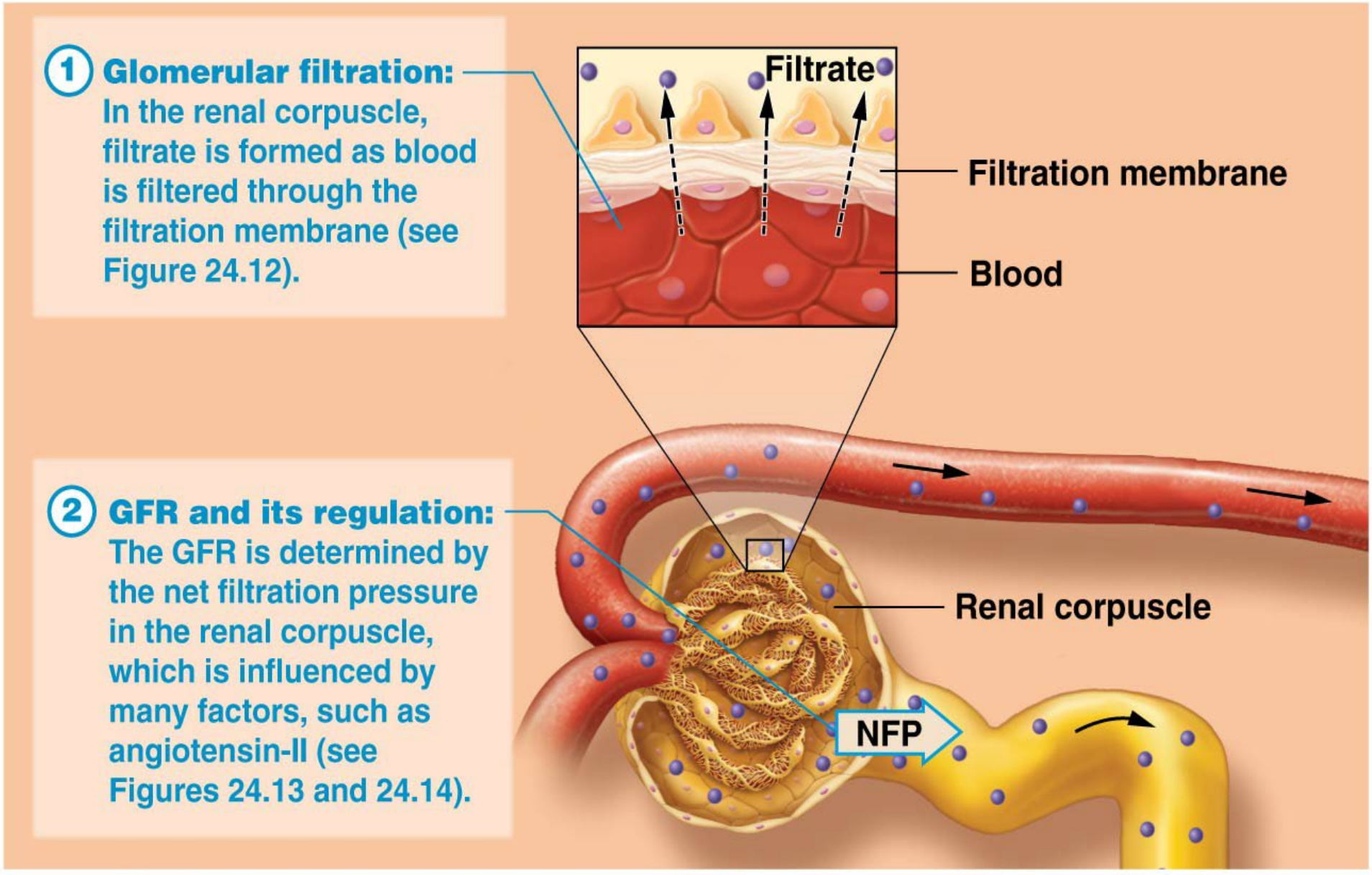
© 2016 Pearson Education,

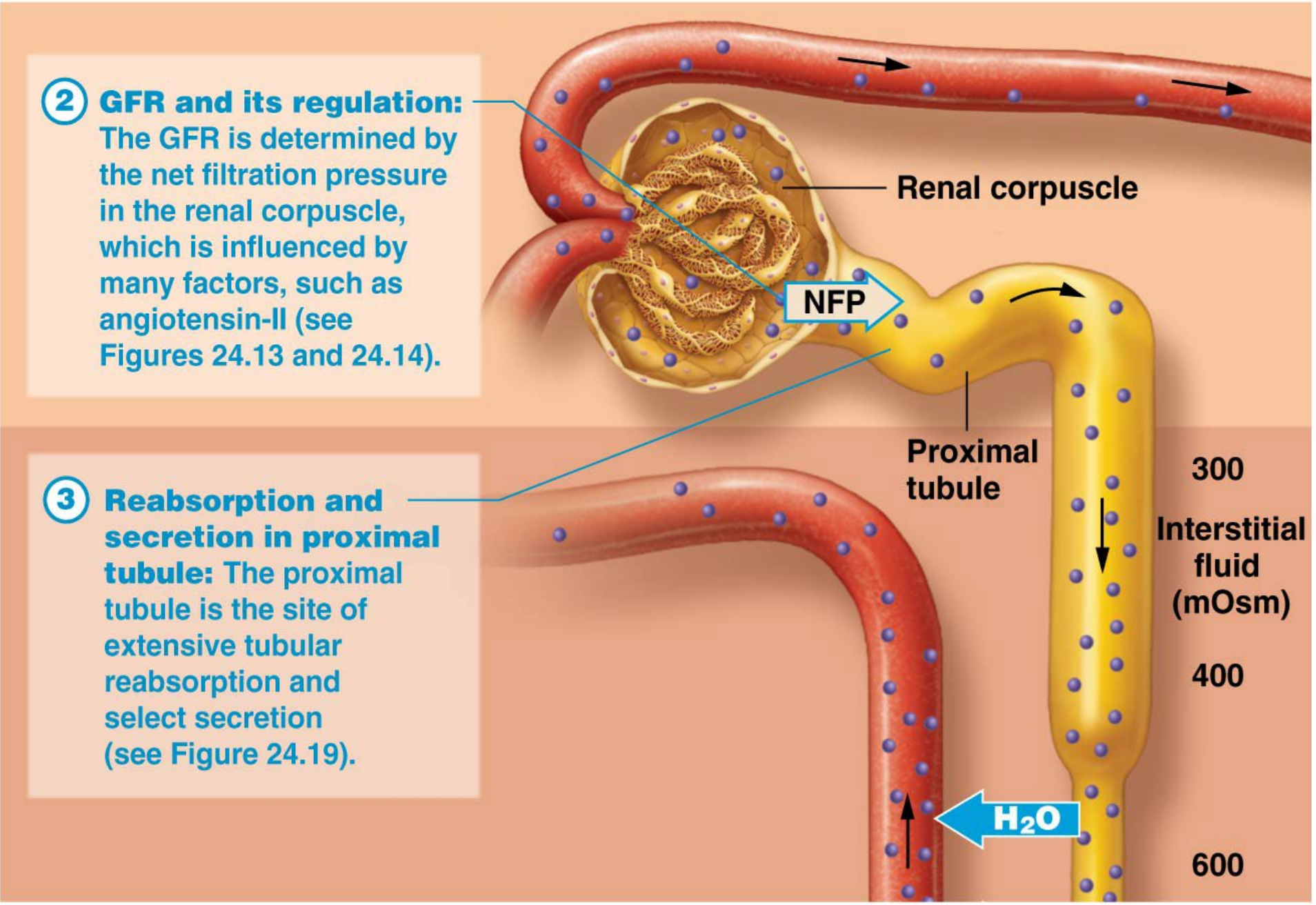
Micturition

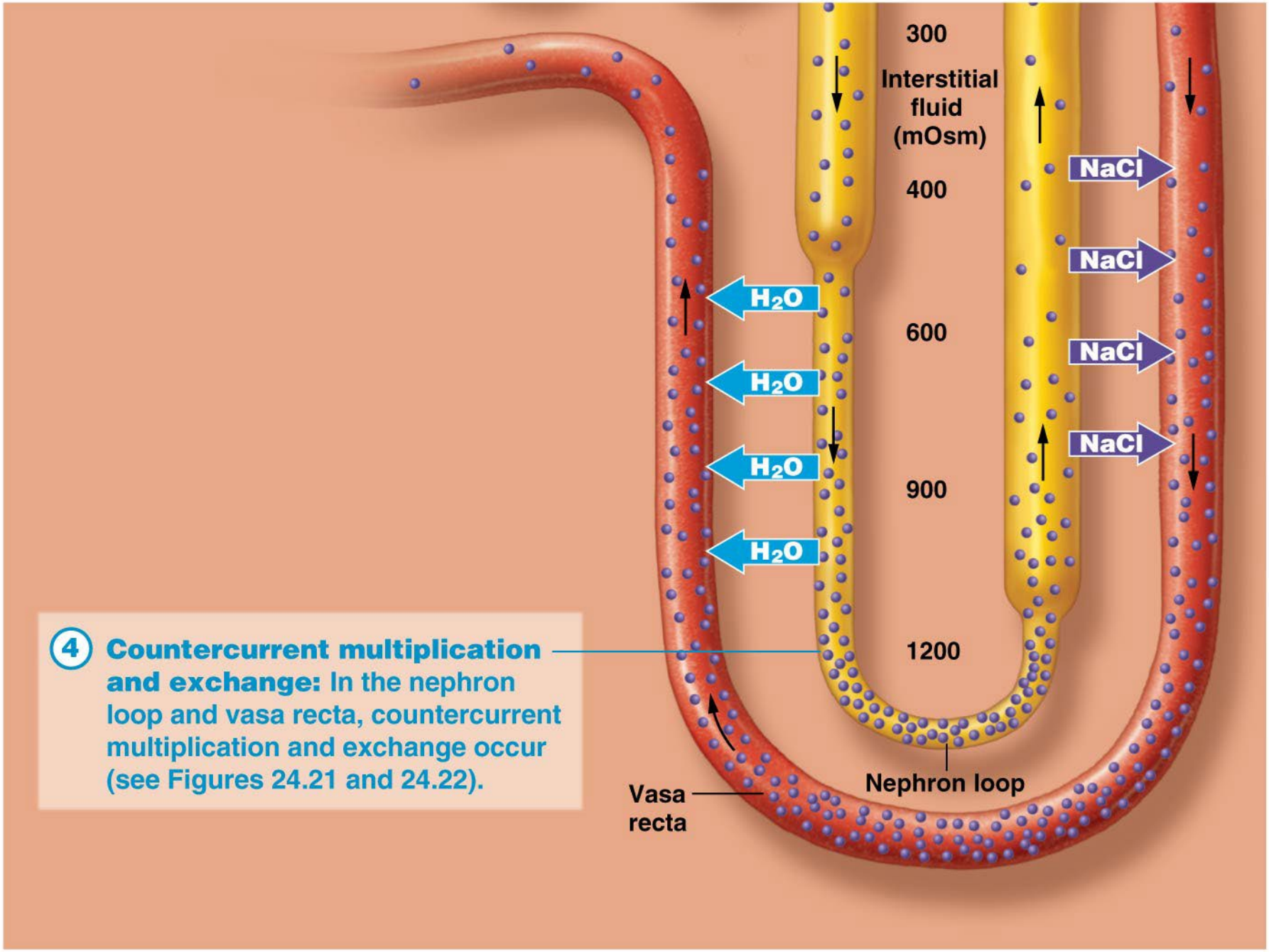


The Big Picture of Renal Physiology.

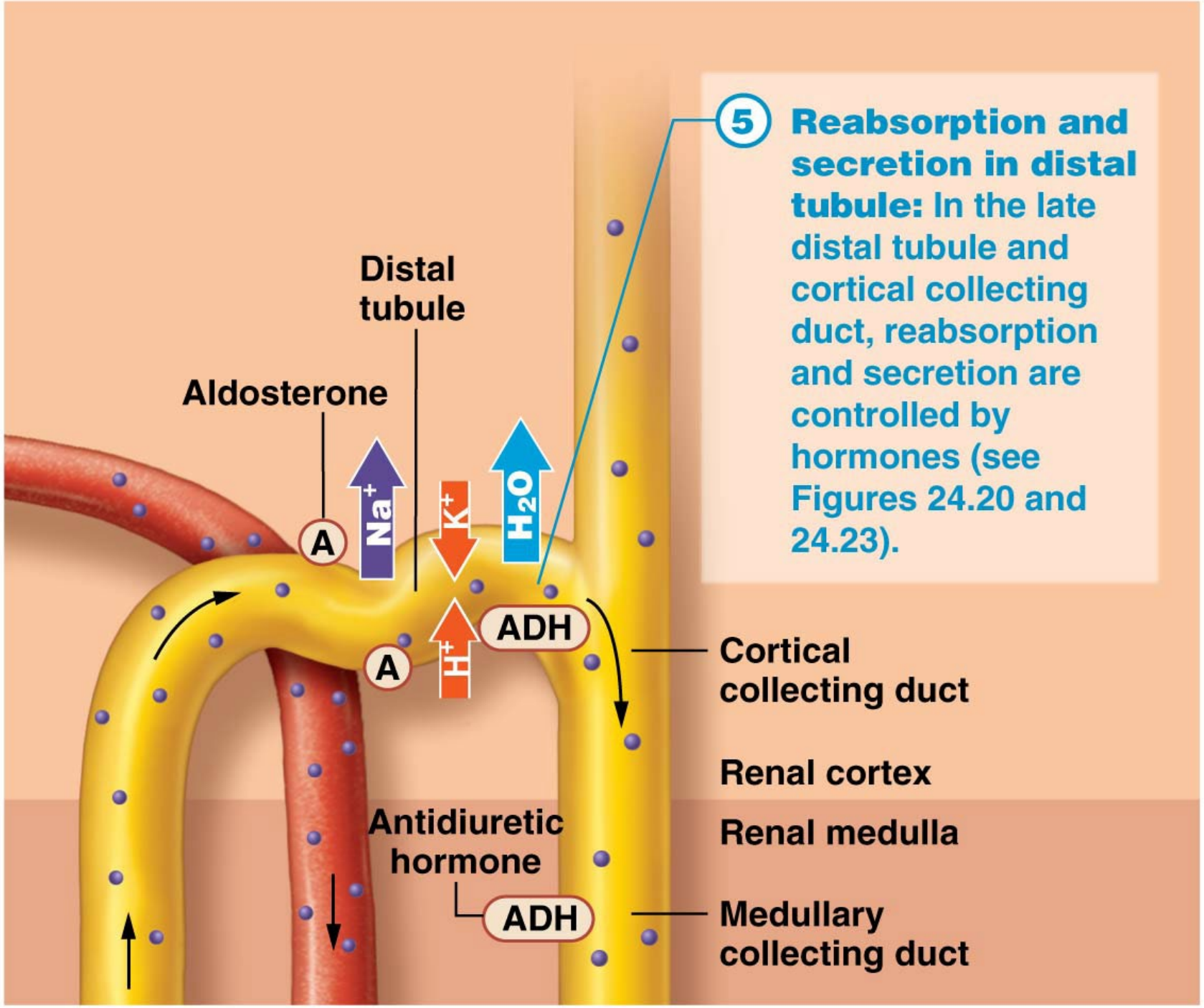


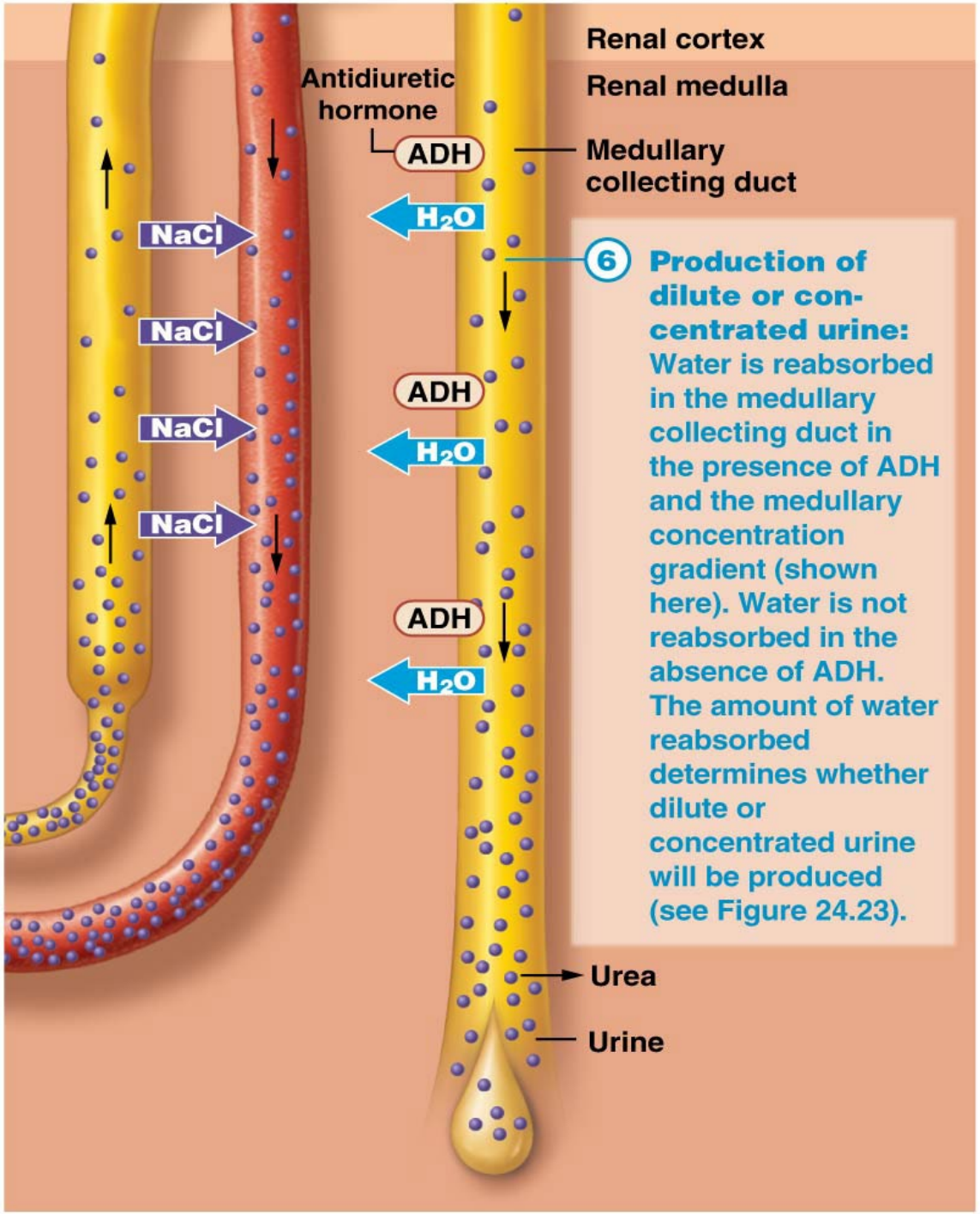

1 Glomerular filtration:
In the renal corpuscle, filtrate is formed as blood is filtered through the filtration membrane (see Figure 24.12).
2 GFR and its regulation:
The GFR is determined by the net filtration pressure in the renal corpuscle, which is influenced by many factors, such as angiotensin-II (see Figures 24.13 and 24.14).
Filtrate
Filtration membrane
Blood
Renal corpuscle
NFP


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).
Renal corpuscle
NFP
Proximal tubule
300
Interstitial fluid (mOsm)
400
H2O
600



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


5 Reabsorption and secretion in distal tubule: In the late distal tubule and cortical collecting duct, reabsorption and secretion are controlled by hormones (see Figures 24.20 and 24.23).
Distal tubule
Aldosterone
A
Na^+
K^+
H_2O
A
H^+
ADH
Cortical collecting duct
Renal cortex
Renal medulla
Antidiuretic hormone
ADH
Medullary collecting duct


Renal cortex
Renal medulla
Antidiuretic hormone
ADH
Medullary collecting duct
H_2O
NaCl
NaCl
NaCl
NaCl
ADH
H_2O
ADH
H_2O
6
Production of dilute or concentrated urine: Water is reabsorbed in the medullary collecting duct in the presence of ADH and the medullary concentration gradient (shown here). Water is not reabsorbed in the absence of ADH. The amount of water reabsorbed determines whether dilute or concentrated urine will be produced (see Figure 24.23).
Urea
Urine

Chronic KIDNEY DISEASE

Kidney diseases are a leading cause of death in the United States.

1/7



More than 1 in 7 (**15%**) of U.S. adults may have chronic kidney disease. That's **37 million** people.



But **90%** of those people don't know they have it.

Every day, more than **360** people begin treatment for kidney failure (dialysis or a kidney transplant).



Having chronic kidney disease increases one's risk of **heart disease**, heart failure, **stroke** and early death.

INDIANA UNIVERSITY
SCHOOL OF MEDICINE

Source: U.S. Centers for Disease Control and Prevention, 2021

STAGE 1
Some damage. Kidneys function normally.

STAGE 2
Mild damage. Kidneys are still functioning well.

STAGE 3
Moderate damage. Kidneys are not functioning as well as they should.

STAGE 4
Significant damage. Kidney function is limited.

STAGE 5
Severe damage. Kidneys are close to failure or have failed.

In early stages, there are often few to no signs of disease.

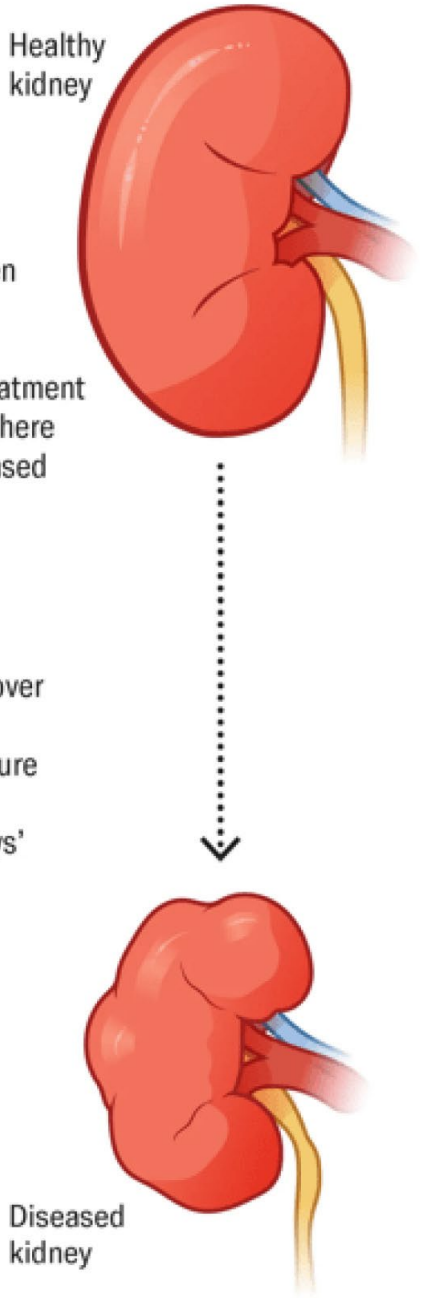


Symptoms usually begin around stage 4 and include nausea, appetite loss, vomiting, fatigue, sleep problems, decreased mental acuity and shortness of breath.



By stage 5, patients are seriously unwell. Kidneys are working at less than 15 percent capacity. Symptoms and signs include those listed in stage 4, plus less frequent urination, dry itchy skin, numb or swollen appendages, and aching muscles.





SHORT-TERM DAMAGE

Acute kidney injury is a sudden, often temporary drop in kidney function caused by illness, injury, infection, dehydration or blockage. Prompt treatment can restore function, but without it there can be lasting damage and an increased risk of chronic kidney disease.

GRADUAL LONG-TERM DAMAGE

Chronic kidney disease is a slow, progressive loss of kidney function over months or years, often driven by conditions such as high blood pressure or diabetes. Ongoing inflammation causes scarring, reducing the kidneys' ability to repair themselves.

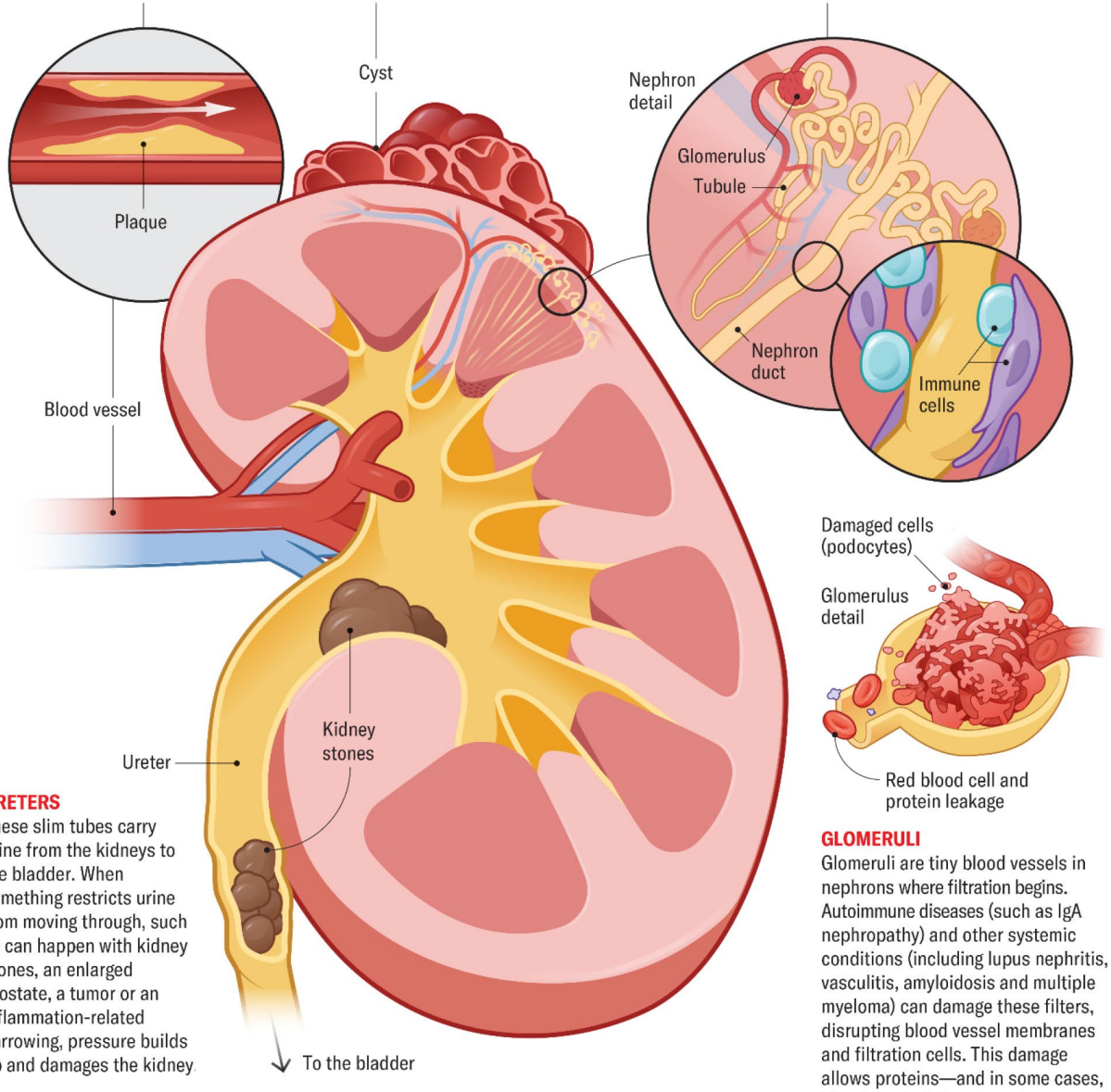
ADVANCED KIDNEY FAILURE

End-stage kidney disease occurs when the kidneys can no longer sufficiently filter toxins or balance fluid and electrolytes. Depending on the cause, early diagnosis and ongoing care can help slow progression toward this stage.

BLOOD VESSELS
High blood pressure, diabetes, and other conditions can damage vessels that supply the kidneys with blood. Over time plaque buildup and vessel narrowing can reduce blood flow, impairing kidney function.

MAIN KIDNEY TISSUE
The body of the kidney can be affected by genetic conditions, such as polycystic kidney disease (PKD), where progressive cyst formation gradually replaces healthy tissue and reduces kidney function.

NEPHRONS
These functional units of the kidney filter waste from the blood. When the tissue between nephrons becomes inflamed and scarred, known as interstitial nephritis, immune cells and excess fluid can compress and distort the tubules, leading to structural damage. This condition can be caused by medications (such as NSAIDs), toxins or infections, among other things.



URETERS
These slim tubes carry urine from the kidneys to the bladder. When something restricts urine from moving through, such as can happen with kidney stones, an enlarged prostate, a tumor or an inflammation-related narrowing, pressure builds up and damages the kidney.

GLOMERULI
Glomeruli are tiny blood vessels in nephrons where filtration begins. Autoimmune diseases (such as IgA nephropathy) and other systemic conditions (including lupus nephritis, vasculitis, amyloidosis and multiple myeloma) can damage these filters, disrupting blood vessel membranes and filtration cells. This damage allows proteins—and in some cases, blood—to leak into the urine.