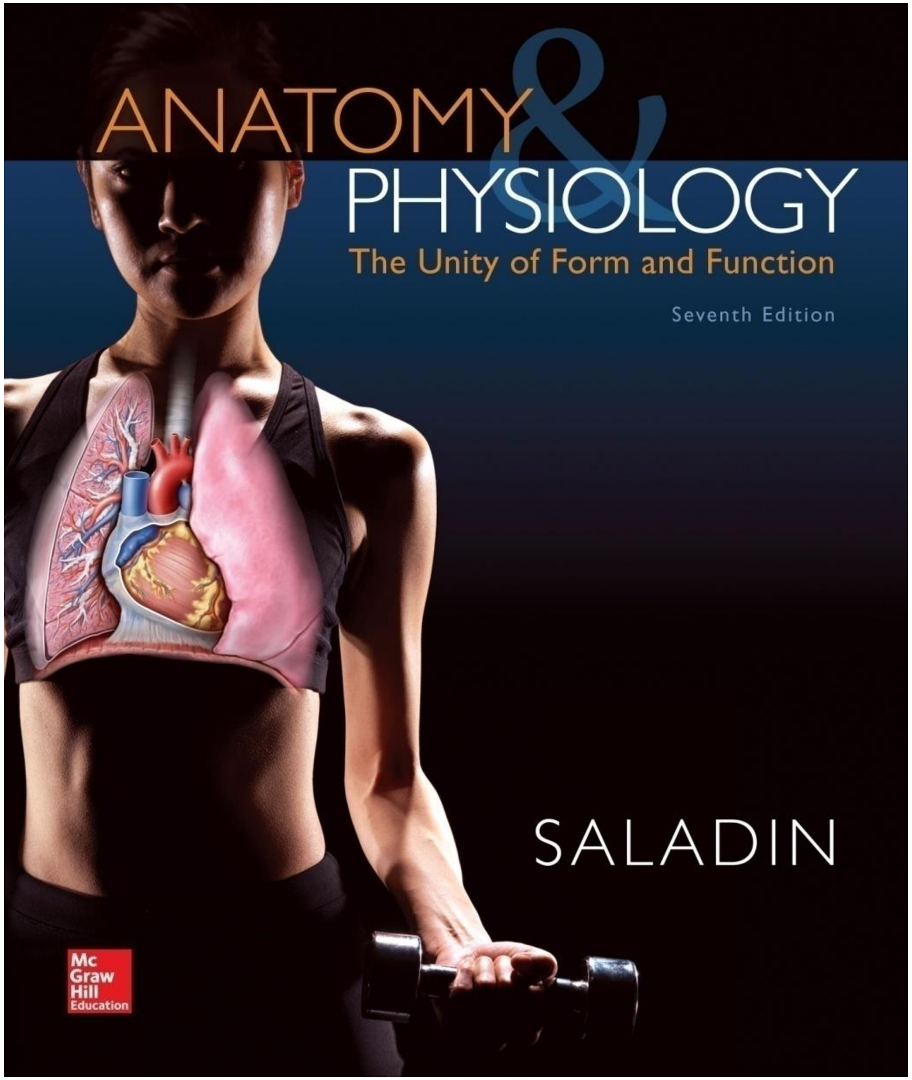
Chapter 23
Lecture Outline

See separate PowerPoint slides for all figures and tables pre-inserted into PowerPoint without notes.



Introduction

- **Urinary system rids the body of waste products**
- **Kidneys also play important roles in blood volume, pressure, and composition**
- **The urinary system is closely associated with the reproductive system**
  - Shared embryonic development and adult anatomical relationship
  - Collectively called the urogenital (UG) system

Functions of the Urinary System

- **Expected Learning Outcomes**
  - Name and locate the organs of the urinary system.
  - List several functions of the kidneys in addition to urine formation.
  - Name the major nitrogenous wastes and identify their sources.
  - Define *excretion* and identify the systems that excrete wastes.

Functions of the Urinary System

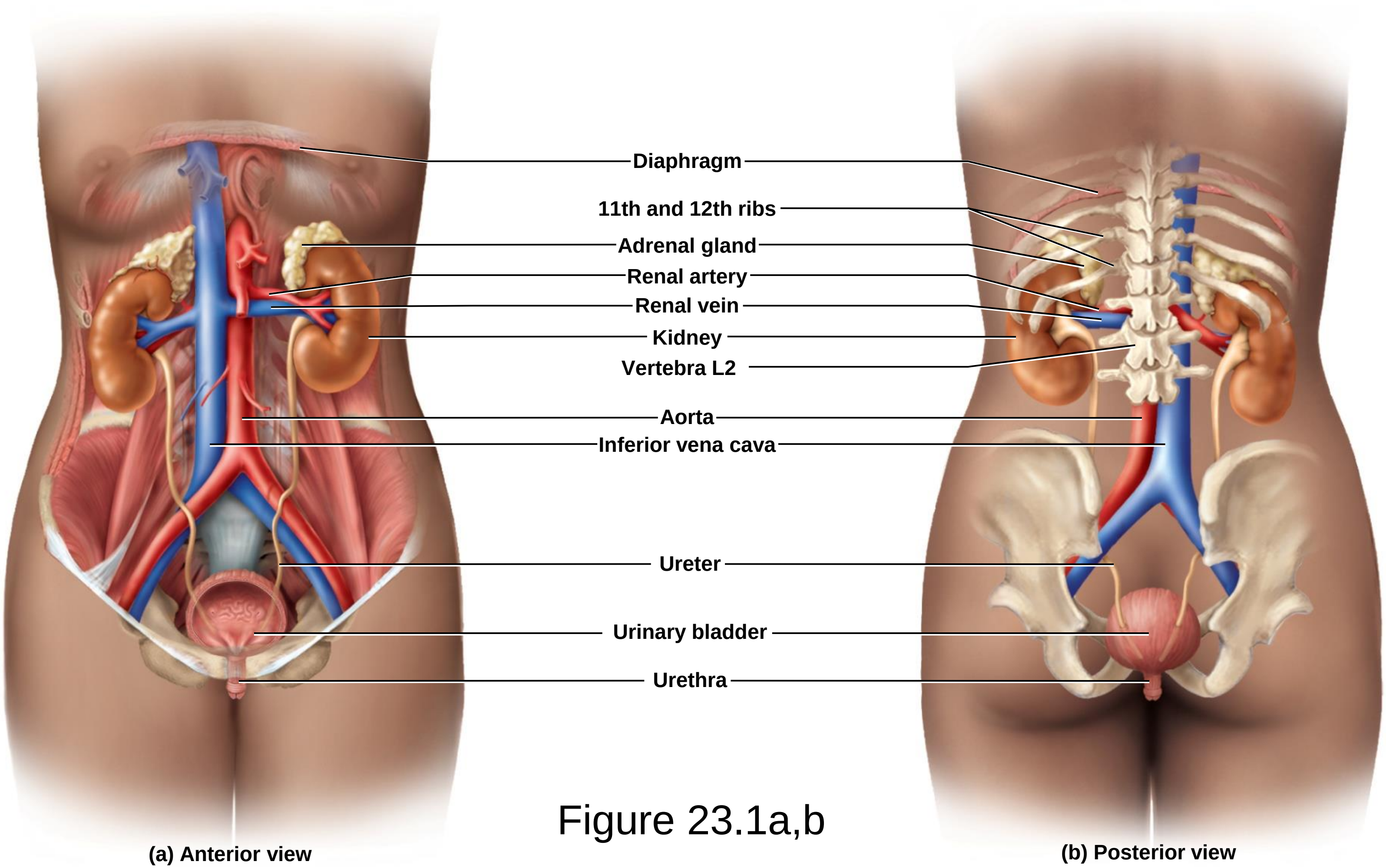


Figure 23.1a,b

- **Urinary system** consists of six organs: two kidneys, two ureters, urinary bladder, and urethra

Functions of the Kidneys

- **Filter** blood plasma, **excrete** toxic wastes
- Regulate **blood volume, pressure,** and **osmolarity**
- Regulate **electrolytes** and **acid-base** balance
- Secrete **erythropoietin,** which stimulates the production of **red blood cells**
- Help regulate **calcium** levels by participating in calcitriol synthesis
- Clear **hormones** from blood
- Detoxify **free radicals**
- In starvation, they synthesize **glucose** from amino acids

Retroperitoneal Position of the Kidney

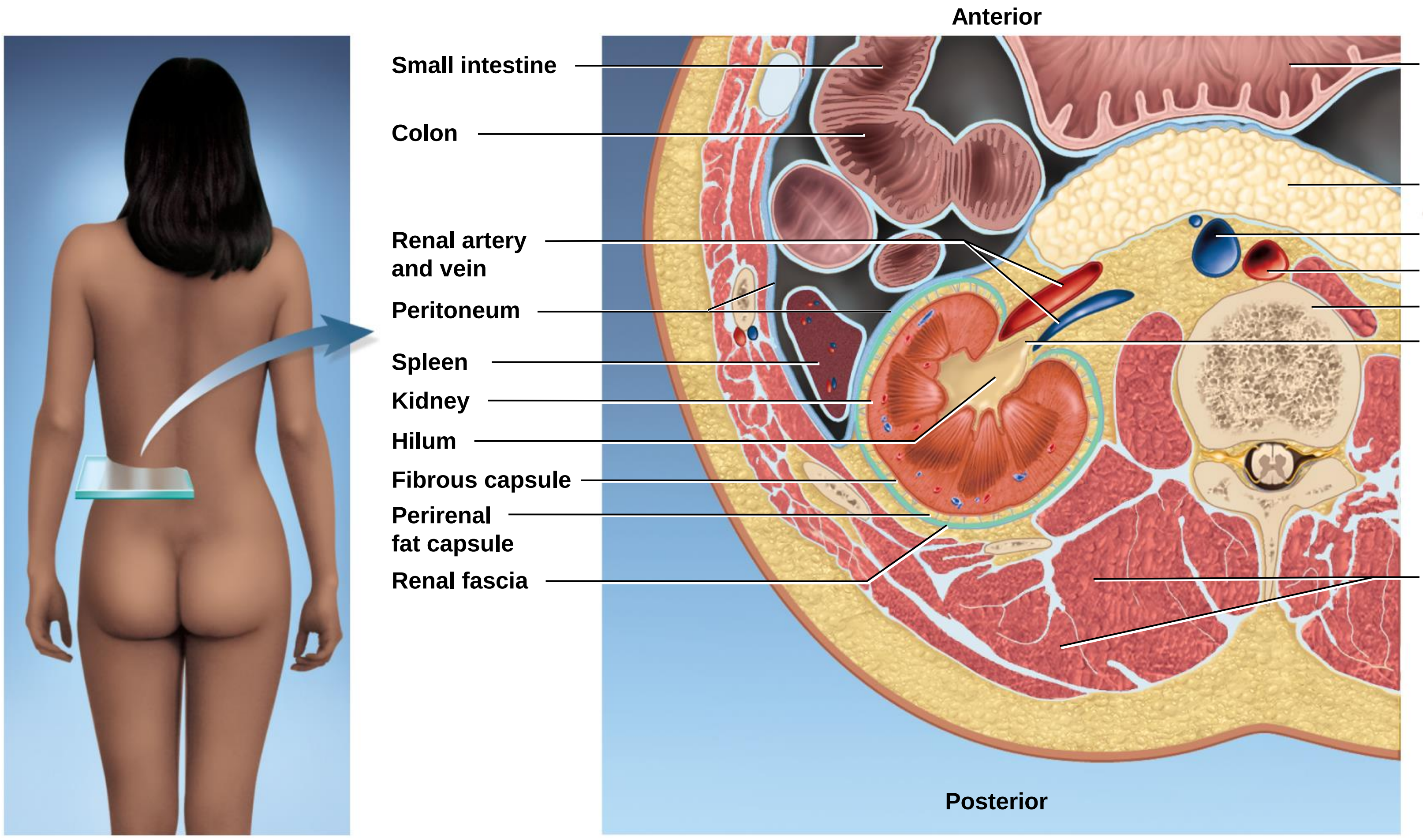


Figure 23.3

Nitrogenous Wastes

- **Waste—**any substance that is useless to the body or present in excess of the body's needs
- **Metabolic waste—**waste substance produced by the body
- **Urea formation**
  - Proteins→ amino acids → NH_2 removed → forms **ammonia,**
  - Liver converts ammonia to urea
- **Uric acid**
  - Product of nucleic acid catabolism
- **Creatinine**
  - Product of creatine phosphate catabolism

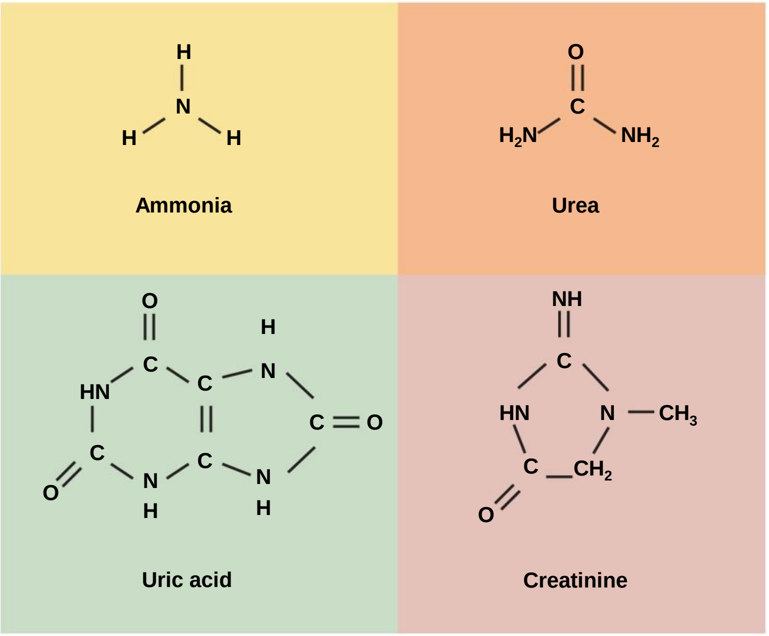


Figure 23.2

Nitrogenous Wastes

- **Blood urea nitrogen (BUN)—** level of nitrogenous waste in blood
  - Normal concentration of blood urea is 10 to 20 mg/dL
  - **Azotemia:** elevated BUN
    - May indicate renal insufficiency
  - **Uremia:** syndrome of diarrhea, vomiting, dyspnea, and cardiac arrhythmia stemming from the toxicity of nitrogenous waste
    - Treatment—hemodialysis or organ transplant

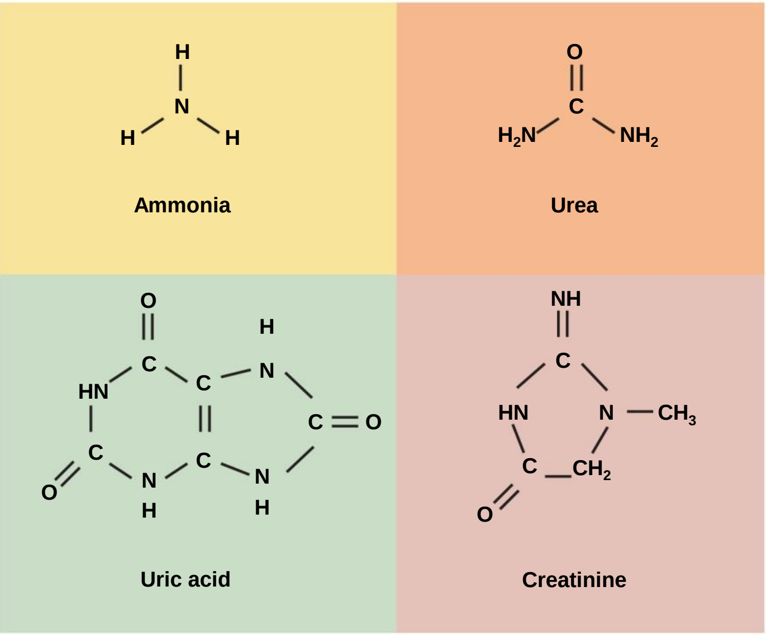


Figure 23.2

Excretion

- **Excretion**—separating wastes from body fluids and eliminating them
- **Four body systems** carry out excretion
  - **Respiratory system**
    - CO_2, small amounts of other gases, and water
  - **Integumentary system**
    - Water, inorganic salts, lactic acid, urea in sweat
  - **Digestive system**
    - Water, salts, CO_2, lipids, bile pigments, cholesterol, and other metabolic waste
  - **Urinary system**
    - Many metabolic wastes, toxins, drugs, hormones, salts, H^+, and water

Anatomy of the Kidney

- **Expected Learning Outcomes**
  - Describe the location and general appearance of the kidney.
  - Identify the external and internal features of the kidney.
  - Trace the flow of blood through the kidney.
  - Trace the flow of fluid through the renal tubules.
  - Describe the nerve supply to the kidney.

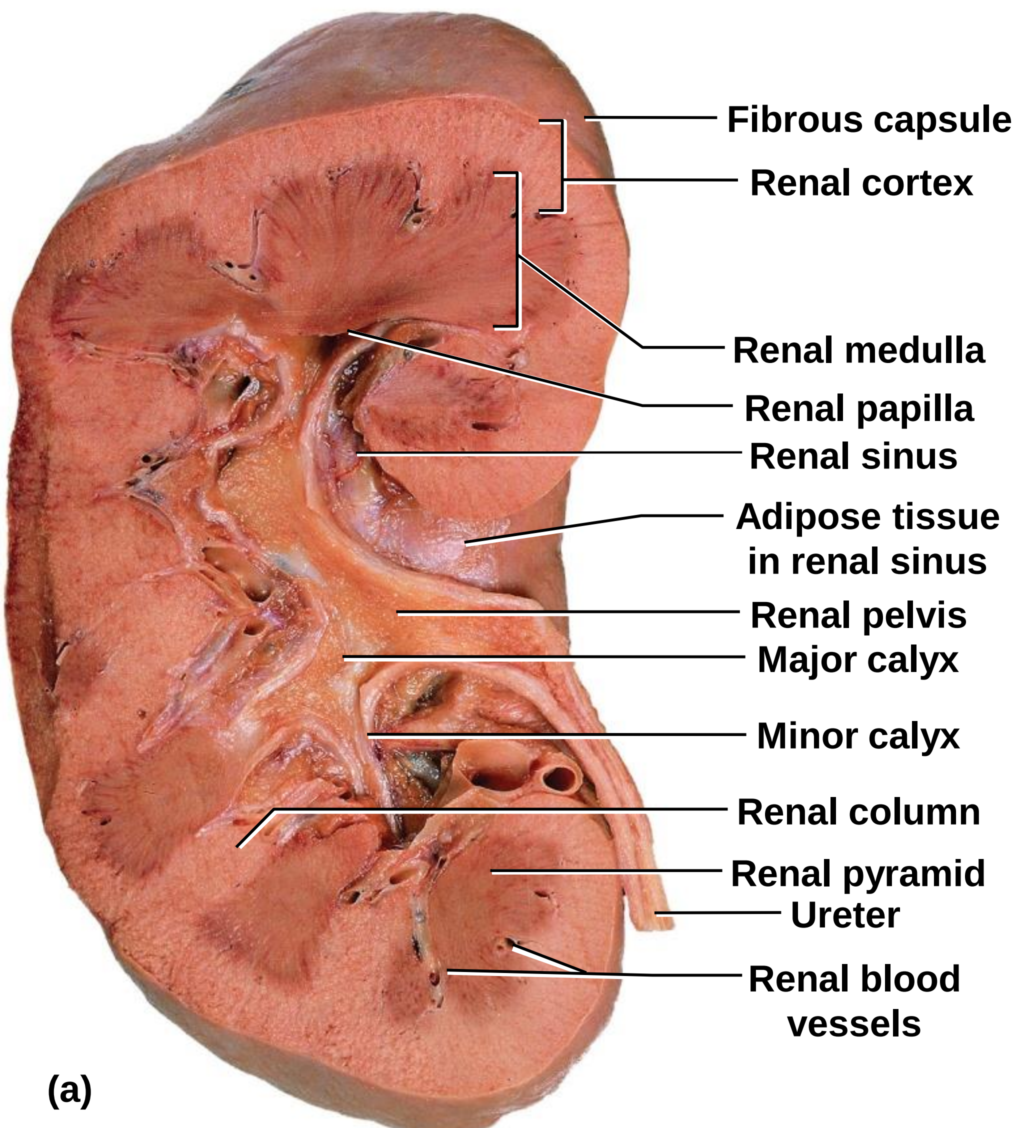
Kidney Position and Associated Structures

- **Position, weight, and size**
  - Lie against posterior abdominal wall at level of T12 to L3
  - Right kidney is slightly lower due to large right lobe of liver
  - Rib 12 crosses the middle of the left kidney
  - **Retroperitoneal** along with ureters, urinary bladder, renal artery and vein, and adrenal glands

Gross Anatomy of the Kidney

- **Shape and size**
  - About the size of a bar of bath soap
  - Lateral surface is convex, and medial is concave with a slit, called the **hilum**
    - Receives renal nerves, blood vessels, lymphatics, and ureter
- **Three protective connective tissue coverings**
  - **Renal fascia** immediately deep to parietal peritoneum
    - Binds it to abdominal wall
  - **Perirenal fat capsule:** cushions kidney and holds it into place
  - **Fibrous capsule** encloses kidney protecting it from trauma and infection
    - Collagen fibers extend from fibrous capsule to renal fascia
    - Still drop about 3 cm when going from lying down to standing up

Gross Anatomy of the Kidney



Ralph Hutchings/Visuals Unlimited

Figure 23.4a

Gross Anatomy of the Kidney

- **Renal parenchyma—**glandular tissue that forms urine
  - Appears C-shaped in frontal section
  - Encircles renal sinus
  - **Renal sinus:** cavity that contains blood and lymphatic vessels, nerves, and urine-collecting structures
    - Adipose fills the remaining cavity and holds structures in place

Gross Anatomy of the Kidney

- **Two zones of renal parenchyma**
  - Outer **renal cortex**
  - Inner **renal medulla**
    - **Renal columns—**extensions of the cortex that project inward toward sinus
    - **Renal pyramids—**6 to 10 with broad base facing cortex and renal papilla facing sinus
  - **Lobe of kidney:** one pyramid and its overlying cortex
  - **Minor calyx:** cup that nestles the papilla of each pyramid; collects its urine
  - **Major calyces:** formed by convergence of 2 or 3 minor calyces
  - **Renal pelvis:** formed by convergence of 2 or 3 major calyces
  - **Ureter:** a tubular continuation of the pelvis that drains urine down to the urinary bladder

Gross Anatomy of the Kidney

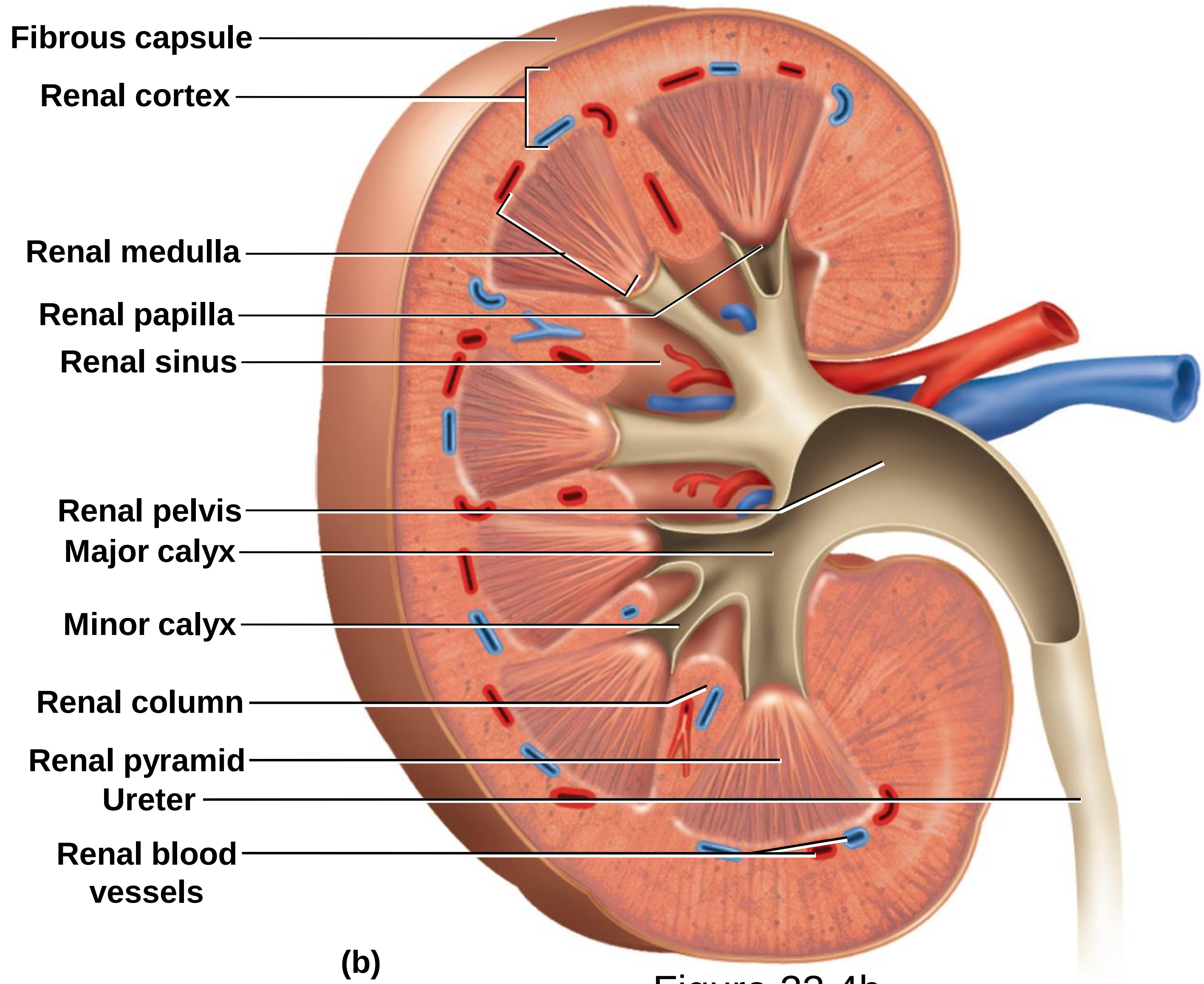


Figure 23.4b

Renal Circulation

- Kidneys are only 0.4% of body weight, but receive about 21% of cardiac output **(renal fraction)**
- **Renal artery** divides into **segmental arteries** that give rise to:
  - **Interlobar arteries:** up renal columns, between pyramids
  - **Arcuate arteries:** over pyramids
  - **Cortical radiate arteries:** up into cortex
  - Branch into **afferent arterioles:** each supplying **one nephron**
    - Leads to a ball of capillaries—**glomerulus**

Renal Circulation

(Continued)

- Blood is drained from the glomerulus by **efferent arterioles**
- Most efferent arterioles lead to **peritubular capillaries**
  - Some efferents lead to **vasa recta**—a network of blood vessels within renal medulla
- Capillaries then lead to **cortical radiate veins** or directly into **arcuate veins**
- Arcuate veins lead to **interlobar veins** which lead to the renal vein

• **Renal vein** empties into **inferior vena cava**

Renal Circulation

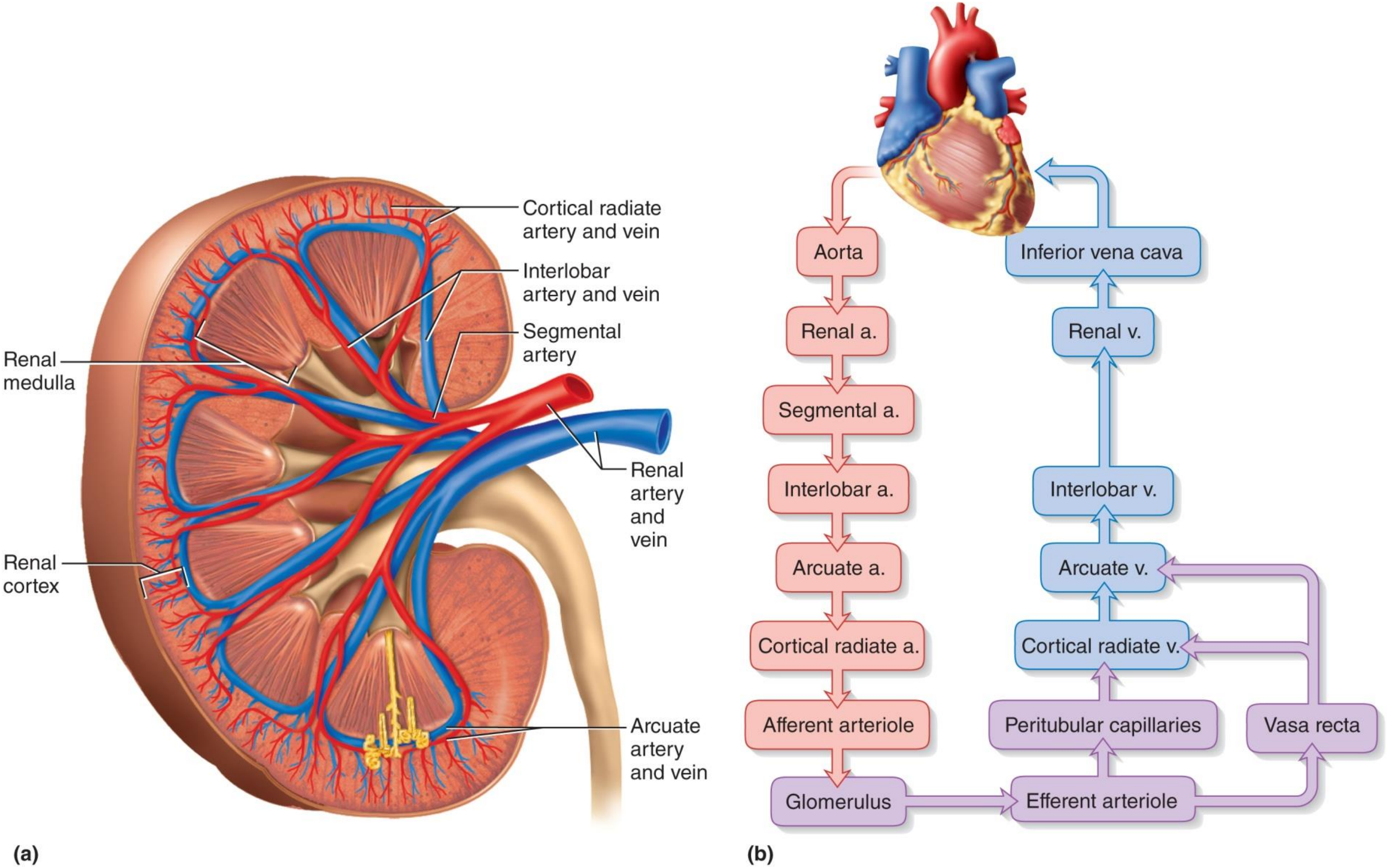


Figure 23.5a,b

- **Kidneys receive 21% of cardiac output**

Renal Circulation

- In the cortex, **peritubular capillaries** branch off of the efferent arterioles supplying the tissue near the glomerulus, the proximal and distal convoluted tubules
- In the medulla, the efferent arterioles give rise to the **vasa recta,** supplying the nephron loop portion of the nephron

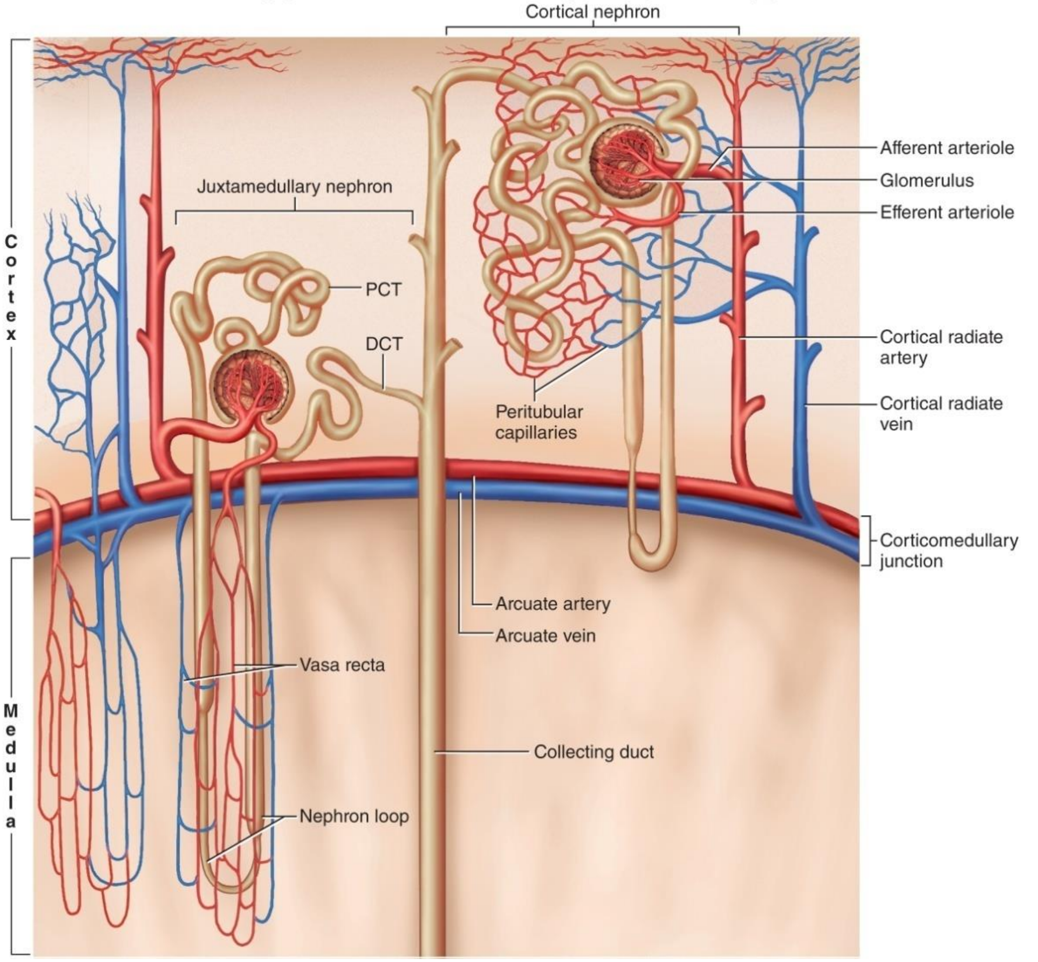


Figure 23.6

The Nephron

- **Each kidney has about 1.2 million nephrons**
- **Each composed of two principal parts**
  - **Renal corpuscle:** filters the blood plasma
  - **Renal tubule:** long, coiled tube that converts the filtrate into urine
- **Renal corpuscle** consists of the **glomerulus** and a two-layered **glomerular capsule** that encloses glomerulus
  - **Parietal (outer) layer of glomerular capsule** is simple squamous epithelium
  - **Visceral (inner) layer of glomerular capsule** consists of elaborate cells called **podocytes** that wrap around the capillaries of the glomerulus
  - **Capsular space** separates the two layers of **glomerular** capsule

The Renal Corpuscle

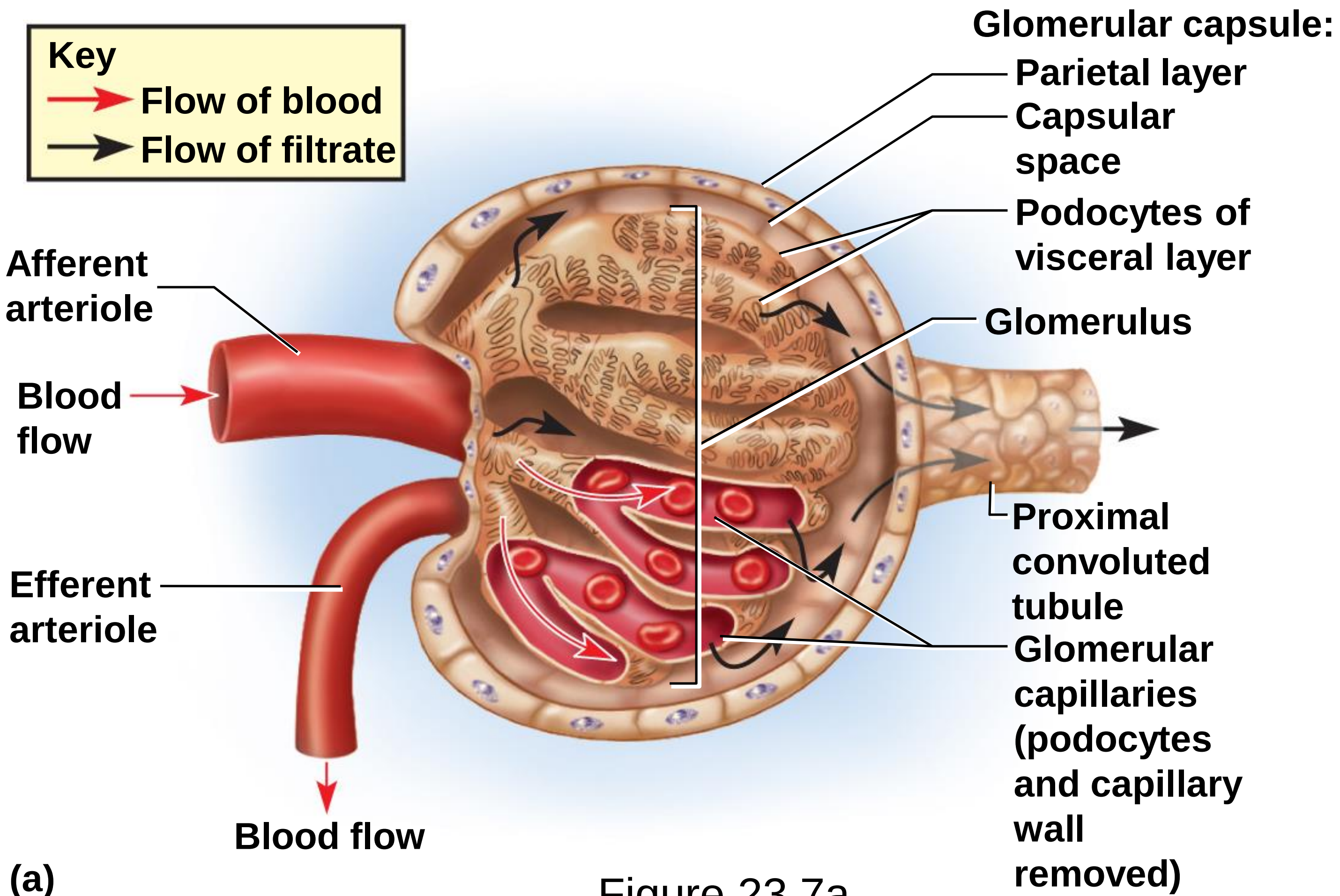


Figure 23.7a

- 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.

The Renal Corpuscle

- **Vascular pole**—the side of the corpuscle where the afferent arterial enters the corpuscle and the efferent arteriole leaves
- **Urinary pole**—the opposite side of the corpuscle where the renal tubule begins

The Renal Tubule

- **Renal (uriniferous) tubule—**duct leading away from the glomerular capsule and ending at the tip of the medullary pyramid
- **Divided into four regions**
  - **Proximal convoluted tubule, nephron loop, distal convoluted tubule:** parts of one nephron
  - **Collecting duct** receives fluid from many nephrons
- **Proximal convoluted tubule (PCT)—**arises from glomerular capsule
  - Longest and most coiled region
  - Simple cuboidal epithelium with **prominent microvilli** for majority of absorption

The Renal Tubule

- **Nephron loop** long U-shaped portion of renal tubule
  - Descending limb and ascending limb
  - **Thick segments** have simple cuboidal epithelium
    - Initial part of descending limb and part or all of ascending limb
    - Heavily engaged in the active transport of salts and have many mitochondria
  - **Thin segment** has simple squamous epithelium
    - Forms lower part of descending limb
    - Cells very permeable to water
- **Distal convoluted tubule (DCT)—**begins shortly after the ascending limb reenters the cortex
  - Shorter and less coiled than PCT
  - Cuboidal epithelium without microvilli
  - DCT is the end of the nephron

The Renal Tubule

- **Collecting duct—**receives fluid from the DCTs of several nephrons as it passes back into the medulla
  - Numerous collecting ducts converge toward the tip of the medullary pyramid
  - **Papillary duct:** formed by merger of several collecting ducts
    - 30 papillary ducts end in the tip of each papilla
    - Collecting and papillary ducts lined with simple cuboidal epithelium

- **Flow of fluid from the point where the glomerular filtrate is formed 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

Microscopic Anatomy of the Nephron

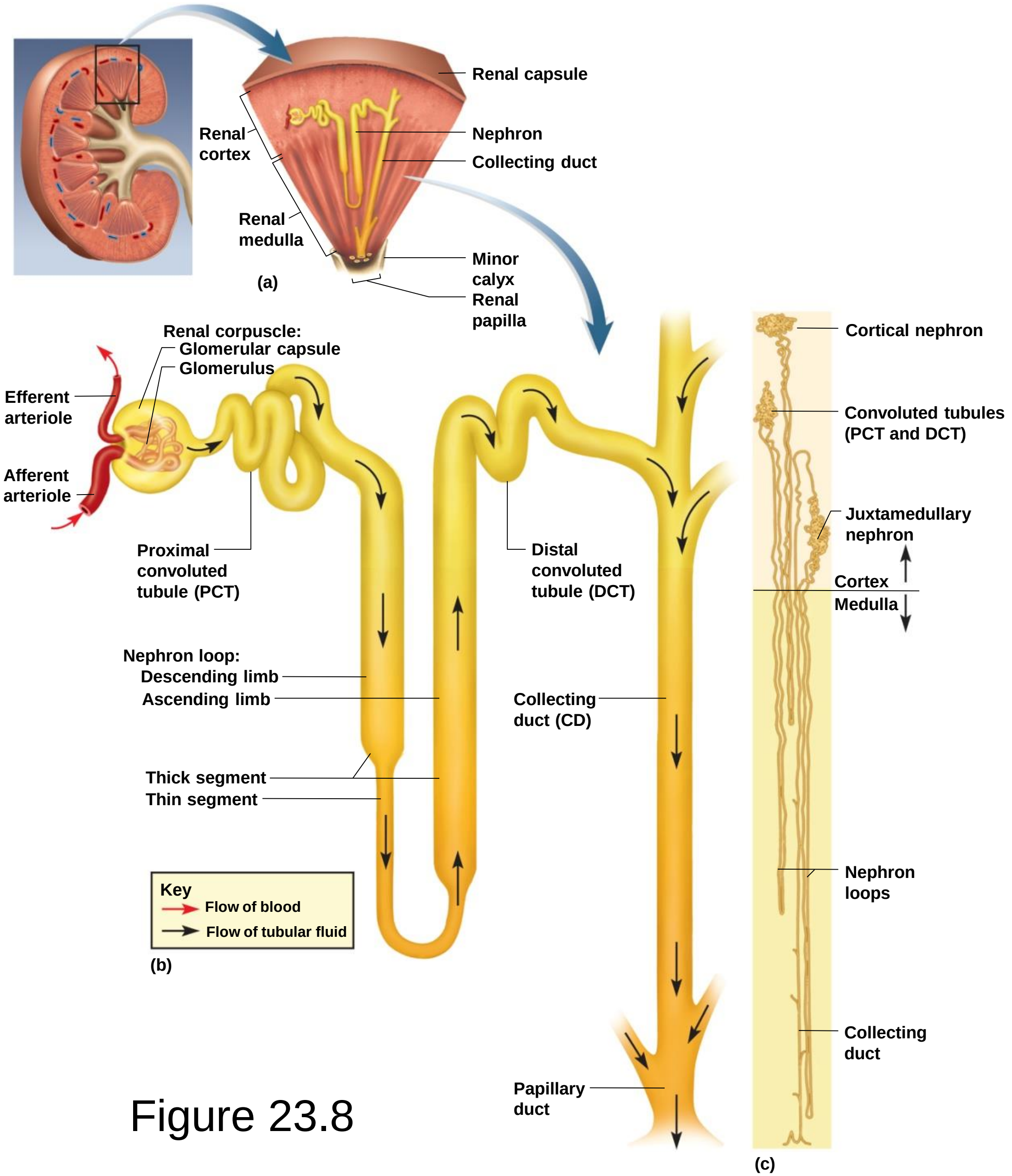


Figure 23.8

Cortical and Juxtamedullary Nephrons

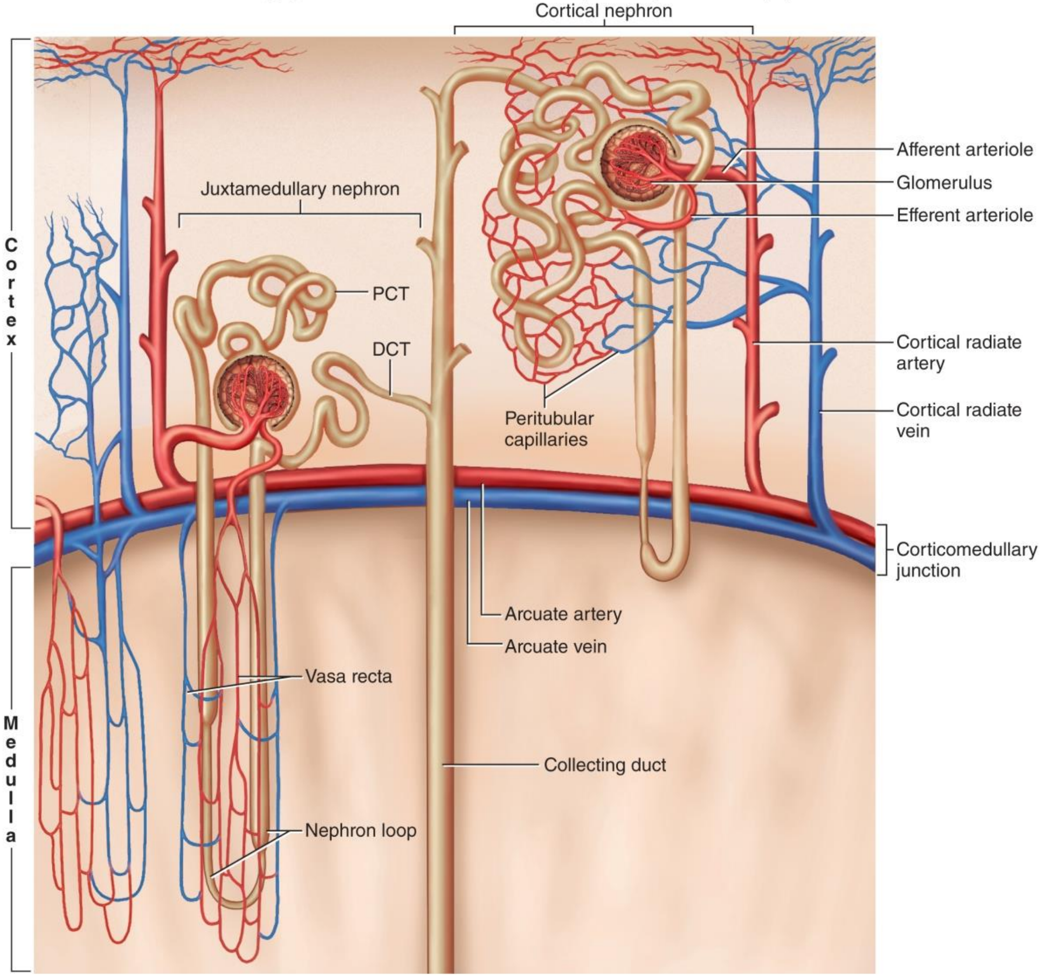


Figure 23.6

- **Cortical nephrons**
  - 85% of all nephrons
  - Short nephron loops
  - Efferent arterioles branch into **peritubular capillaries** around PCT and DCT
- **Juxtamedullary nephrons**
  - 15% of all nephrons
  - Very long nephron loops, maintain salinity gradient in the medulla and help conserve water
  - Efferent arterioles branch into **vasa recta** around long nephron loop

Renal Innervation

- **Renal plexus**—nerves and ganglia wrapped around each renal artery
  - Follows branches of renal artery into the parenchyma of the kidney
  - Issues nerve fibers to blood vessels and convoluted tubules of the nephron

Renal Innervation

Renal Plexus (Continued)

- Carries **sympathetic** innervation from the abdominal aortic plexus
  - Stimulation reduces glomerular blood flow and rate of urine production
  - Respond to falling blood pressure by stimulating the kidneys to secrete **renin,** an enzyme that activates hormonal mechanisms to restore blood pressure
- Kidneys also receive **parasympathetic** innervation of unknown function

Urine Formation I: Glomerular Filtration

- **Expected Learning Outcomes**
  - Describe the process by which the kidney filters the blood plasma, including the relevant cellular structure of the glomerulus.
  - Explain the forces that promote and oppose filtration, and calculate the filtration pressure if given the magnitude of these forces.
  - Describe how the nervous system, hormones, and the nephron itself regulate filtration.

Basic Stages of Urine Formation

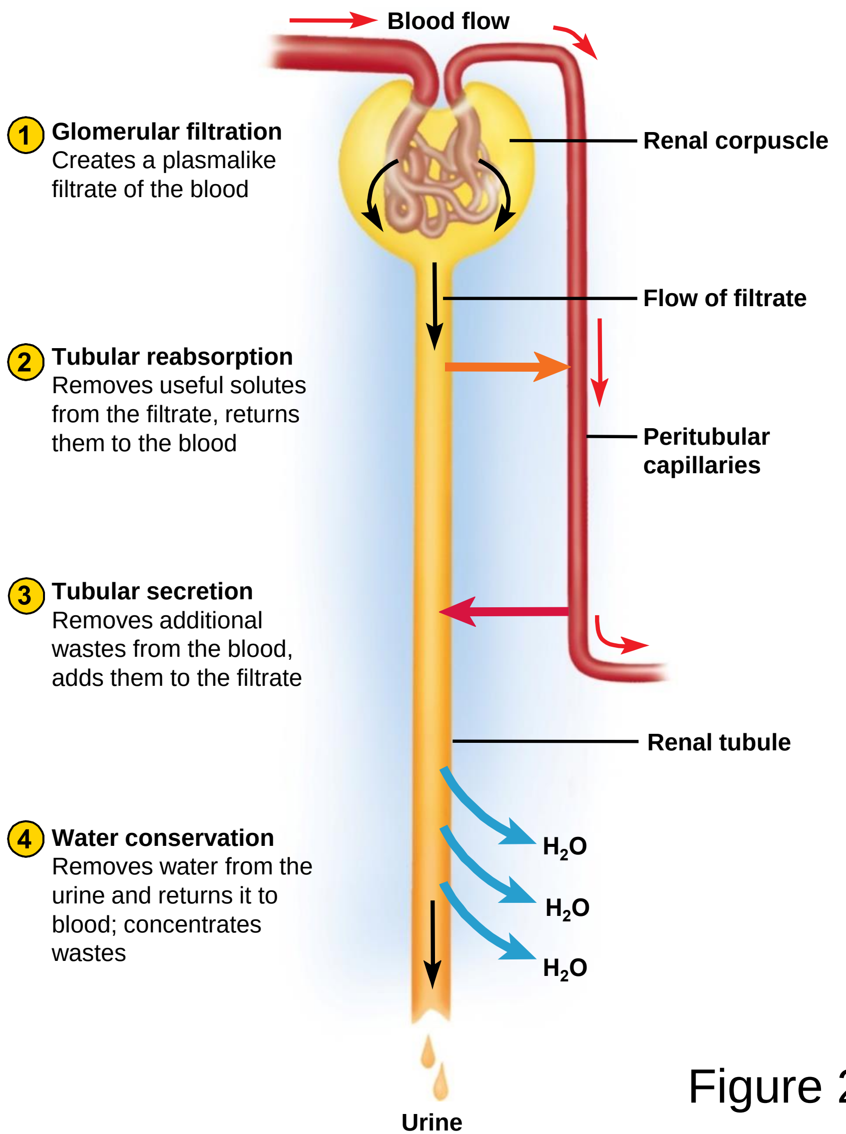


Figure 23.9

Urine Formation I: Glomerular Filtration

- **Kidneys convert blood plasma to urine in four stages**
  - **Glomerular filtration**
  - **Tubular reabsorption**
  - **Tubular secretion**
  - **Water conservation**
- **Glomerular filtrate**—the fluid in the capsular space
  - Similar to blood plasma except that it has almost no protein
- **Tubular fluid**—fluid from the proximal convoluted tubule through the distal convoluted tubule
  - Substances have been removed or added by tubular cells
- **Urine**—fluid that enters the collecting duct
  - Undergoes little alteration beyond this point except for changes in water content

Structure of the Glomerulus

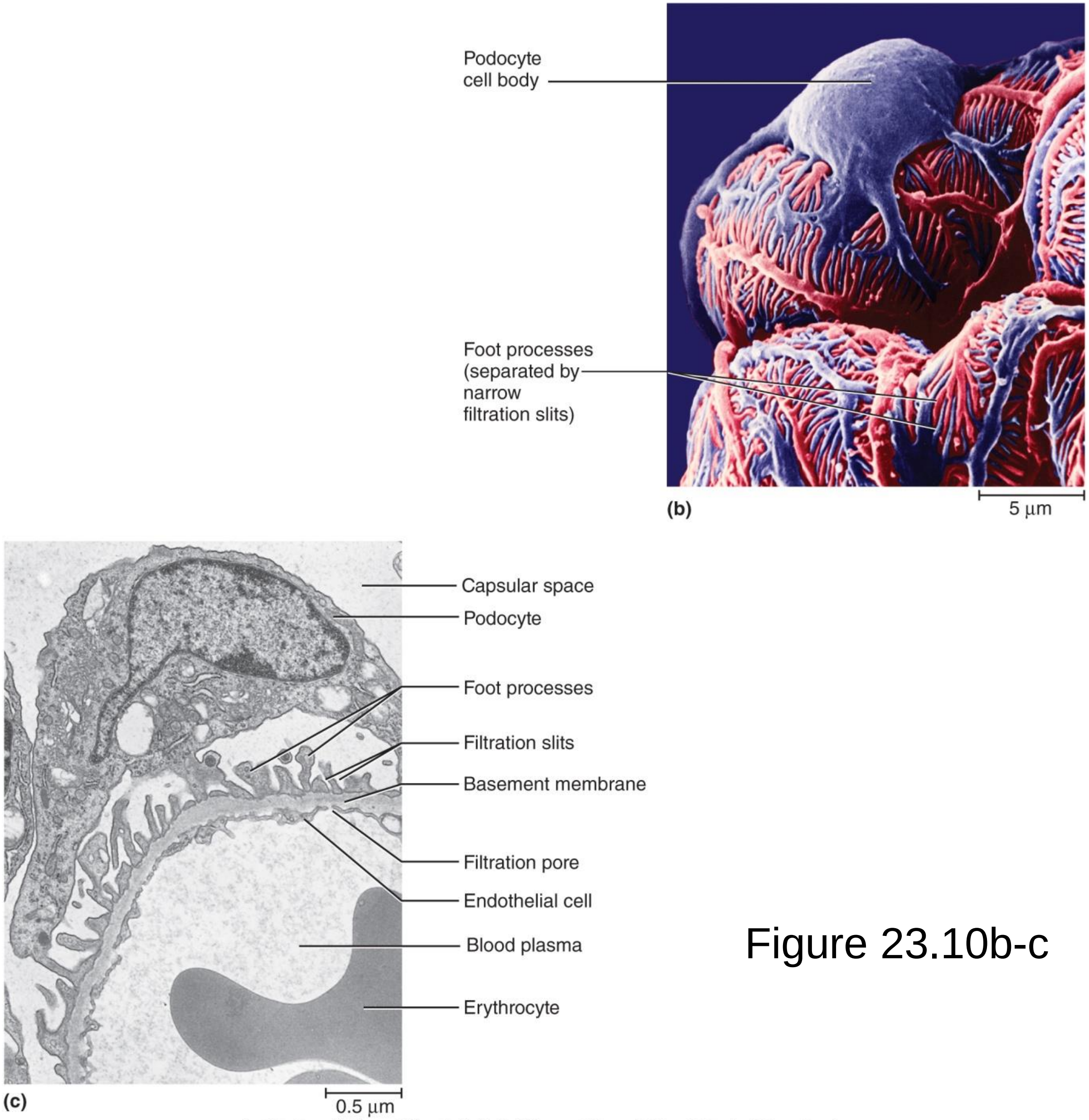


Figure 23.10b-c

The Filtration Membrane

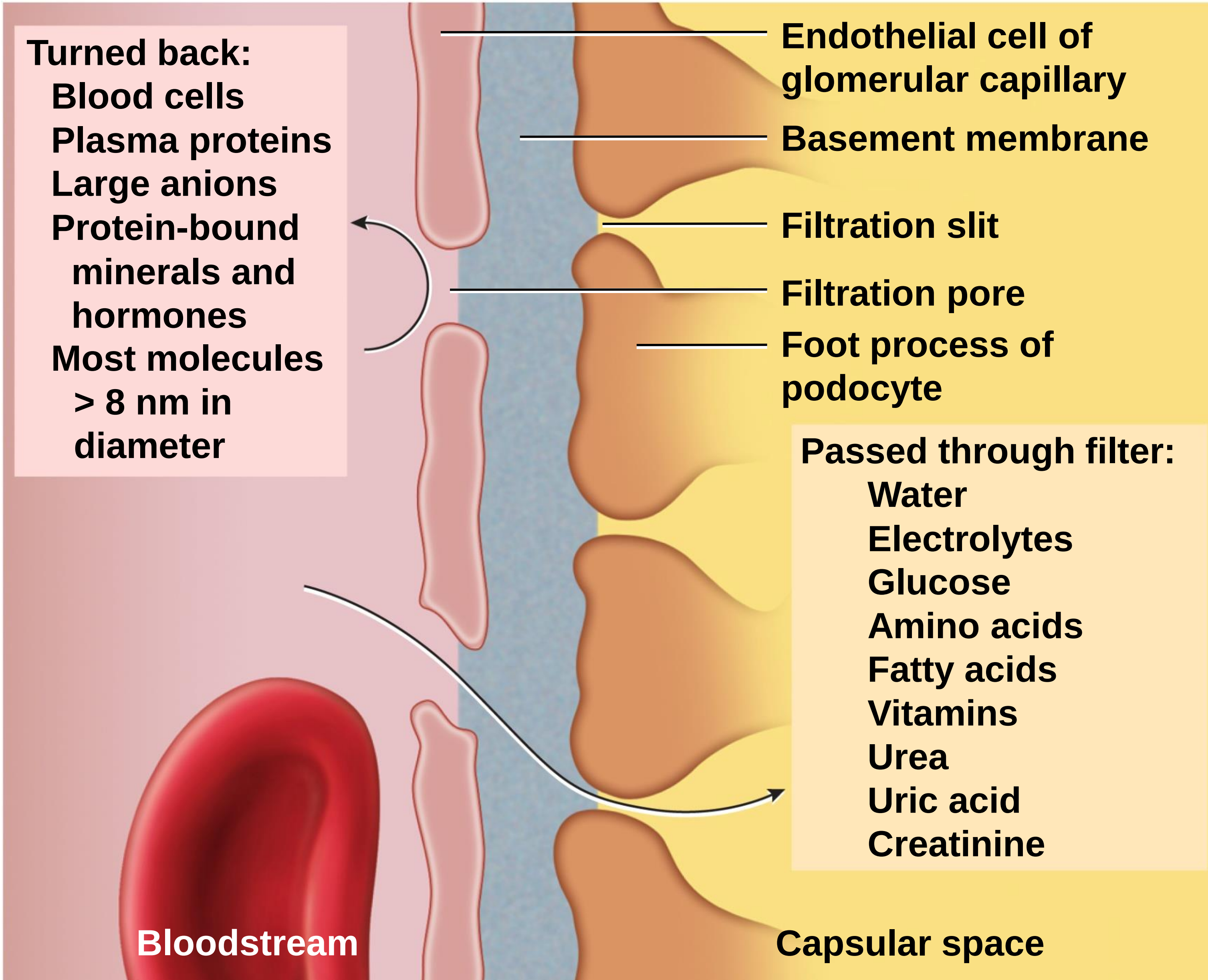


Figure 23.11

The Filtration Membrane

- **Glomerular filtration**—a special case of capillary fluid exchange in which water and some solutes in the blood plasma pass from the capillaries of the glomerulus into the capsular space of the nephron

The Filtration Membrane

- **Filtration membrane—**three barriers through which fluid passes
  - **Fenestrated endothelium of glomerular capillaries**
    - 70 to 90 nm filtration pores – small enough to exclude blood cells
    - Highly permeable
  - **Basement membrane**
    - Proteoglycan gel, negative charge, excludes molecules greater than 8 nm
    - Albumin repelled by negative charge
    - Blood plasma is 7% protein, the filtrate is only 0.03% protein
  - **Filtration slits**
    - **Podocyte** cell extensions **(pedicels)** wrap around the capillaries to form a barrier layer with 30 nm filtration slits
    - Negatively charged which is an additional obstacle for large anions

The Filtration Membrane

- **Almost any molecule smaller than 3 nm can pass freely through the filtration membrane**
  - Water, electrolytes, glucose, fatty acids, amino acids, nitrogenous wastes, and vitamins
- **Some substances of low molecular weight are bound to the plasma proteins and cannot get through the membrane**
  - Most calcium, iron, and thyroid hormone
    - Unbound fraction passes freely into the filtrate

The Filtration Membrane

- **Kidney infections and trauma** can damage the filtration membrane and allow albumin or blood cells to filter
  - **Proteinuria (albuminuria):** presence of protein in urine
  - **Hematuria:** presence of blood in the urine
- **Distance runners and swimmers often experience temporary proteinuria or hematuria**
  - Prolonged, strenuous exercise reduces profusion of kidney
  - Glomerulus deteriorates under prolonged hypoxia

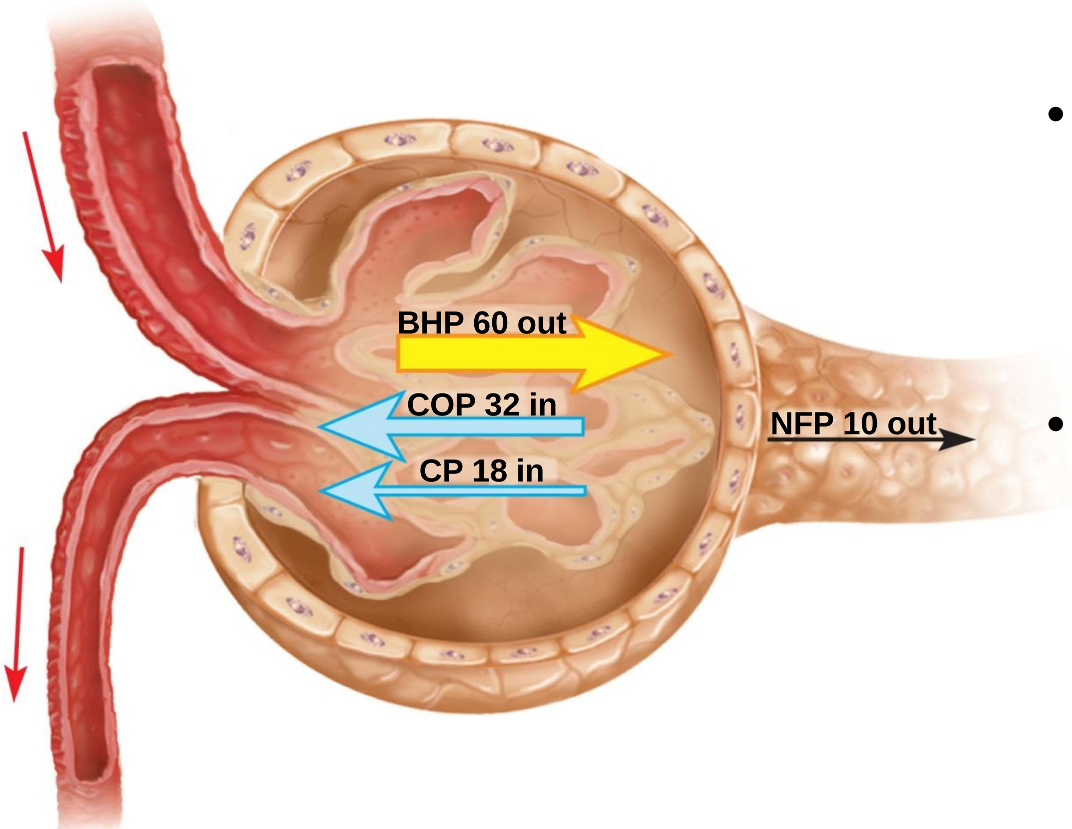
Filtration Pressure

- **Filtration pressure depends on hydrostatic and osmotic pressures on each side of the filtration membrane**
- **Blood hydrostatic pressure (BHP)**
  - High in glomerular capillaries (60 mm Hg compared to 10 to 15 in most other capillaries)
    - Because afferent arteriole is larger than efferent arteriole: a large inlet and small outlet
- **Hydrostatic pressure** in capsular space
  - 18 mm Hg due to high filtration rate and continual accumulation of fluid in the capsule

Filtration Pressure

- **Colloid osmotic pressure (COP) of blood**
  - About the same here as elsewhere: 32 mm Hg
- **Glomerular filtrate** is almost protein-free and has no significant COP
- **Higher outward pressure of 60 mm Hg,** opposed by two inward pressures of 18 mm Hg and 32 mm Hg
- **Net filtration pressure:**
  $60_{out} - 18_{in} - 32_{in} =$ **10 mm Hg_{out}**

The Forces Involved in Glomerular Filtration



Blood hydrostatic pressure (BHP)	60 mm Hg_{out}
Colloid osmotic pressure (COP)	–32 mm Hg_{in}
Capsular pressure (CP)	–18 mm Hg_{in}
Net filtration pressure (NFP)	10 mm Hg_{out}

Figure 23.12

- **High BP in glomerulus makes kidneys vulnerable to hypertension**
- **It can lead to rupture of glomerular capillaries, produce scarring of the kidneys (nephrosclerosis), and atherosclerosis of renal blood vessels, ultimately leading to renal failure**

Glomerular Filtration Rate

- **Glomerular filtration rate (GFR)**—amount of filtrate formed per minute by the two kidneys combined
  - GFR = NFP x K_f ≈ 125 mL/min. or 180 L/day (male)
  - GFR = NFP x K_f ≈ 105 mL/min. or 150 L/day (female)
    - Net filtration pressure (NFP)
    - Filtration coefficient (K_f) depends on permeability and surface area of filtration barrier
- **Total amount of filtrate produced per day equals 50 to 60 times the amount of blood in the body**
  - 99% of filtrate is reabsorbed since only 1 to 2 L urine excreted per day

Regulation of Glomerular Filtration

- **If GFR too high**
  - Fluid flows through renal tubules too rapidly for them to reabsorb the usual amount of water and solutes
  - Urine output rises
  - Chance of dehydration and electrolyte depletion
- **If GFR too low**
  - Wastes are reabsorbed
  - Azotemia may occur

Regulation of Glomerular Filtration

- **GFR controlled** by adjusting **glomerular blood pressure** from moment to moment

- **GFR control is achieved by three homeostatic mechanisms**
  - Renal autoregulation
  - Sympathetic control
  - Hormonal control

Renal Autoregulation

- **Renal autoregulation**—the ability of the nephrons to adjust their own blood flow and GFR without external (nervous or hormonal) control
- **Enables kidney to maintain a relatively stable GFR in spite of changes in systemic blood pressure**
- Two methods of autoregulation: **myogenic mechanism** and **tubuloglomerular feedback**

Renal Autoregulation

- **Myogenic mechanism**—based on the tendency of smooth muscle to contract when stretched
  - If arterial blood pressure increases
    - Afferent arteriole is stretched
    - Afferent arteriole constricts and prevents blood flow into the glomerulus from changing
  - If arterial blood pressure falls
    - Afferent arteriole relaxes
    - Afferent arteriole dilates and allows blood to flow more easily into glomerulus, so that flow rate remains similar and filtration remains stable

Renal Autoregulation

- **Tubuloglomerular feedback—**glomerulus receives feedback on the status of downstream tubular fluid and adjusts filtration rate accordingly
  - Regulates filtrate composition, stabilizes kidney performance, and compensates for fluctuations in blood pressure
  - **Juxtaglomerular apparatus:** complex structure found at the end of the nephron loop where it has just reentered the renal cortex
  - Loop comes into contact with the afferent and efferent arterioles at the vascular pole of the renal corpuscle

Renal Autoregulation

- **Tubuloglomerular feedback (Continued)**
  - **Macula densa—**patch of slender, closely spaced sensory cells in nephron loop
    - When GFR is high, filtrate contains more NaCl
    - When macula densa absorbs more NaCl, it secretes ATP
    - ATP is metabolized by nearby mesangial cells into adenosine
    - Adenosine stimulates nearby granular cells
  - **Granular (juxtaglomerular) cells:** modified smooth muscle cells wrapping around arterioles (close to macula densa)
    - Granular cells respond to adenosine by constricting afferent arterioles
      - Constriction reduces blood flow which corrects GFR
  - **Mesangial cells** might also contract, constricting capillaries and further limiting GFR

Renal Autoregulation

- **Granular cells** also contain granules of renin, which they secrete in response to drop in blood pressure
  - Participate in the renin-angiotensin-aldosterone system that works to control blood volume and pressure
- **Renal autoregulation** regulates GFR but cannot keep it entirely constant
  - Rises in blood pressure will cause a rise in GFR
  - If mean arterial pressure drops below 70 mm Hg, filtration and urine output cease

The Juxtaglomerular Apparatus

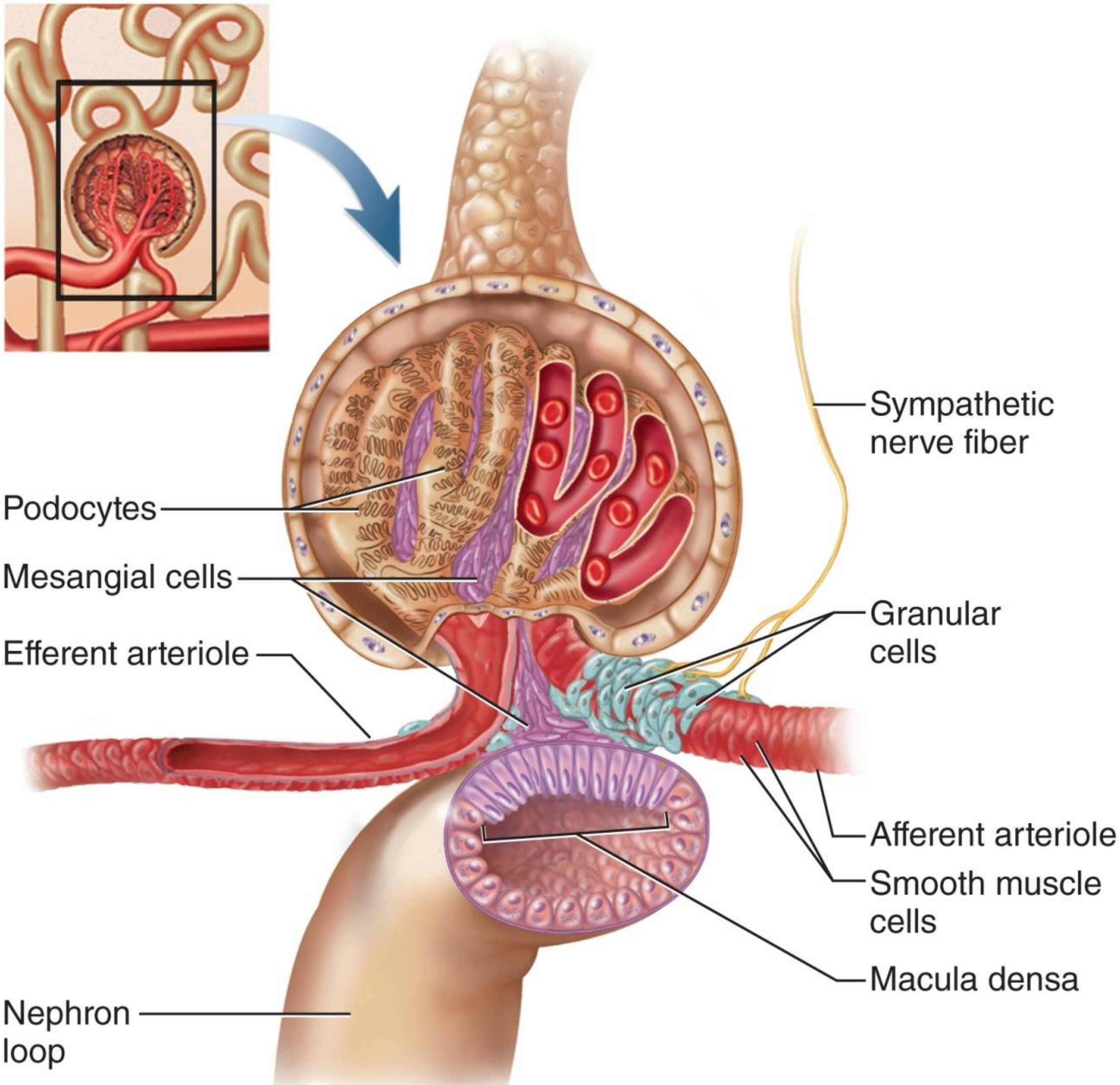


Figure 23.13

- **If GFR rises**
  - More NaCl is reabsorbed, and more adenosine is produced locally
  - Adenosine stimulates JG cells to contract which constricts afferent arteriole, reducing GFR to normal
- **If GFR falls**
  - Macula relaxes afferent arterioles and mesangial cells
  - Blood flow increases and GFR rises back to normal

Negative Feedback Control of GFR

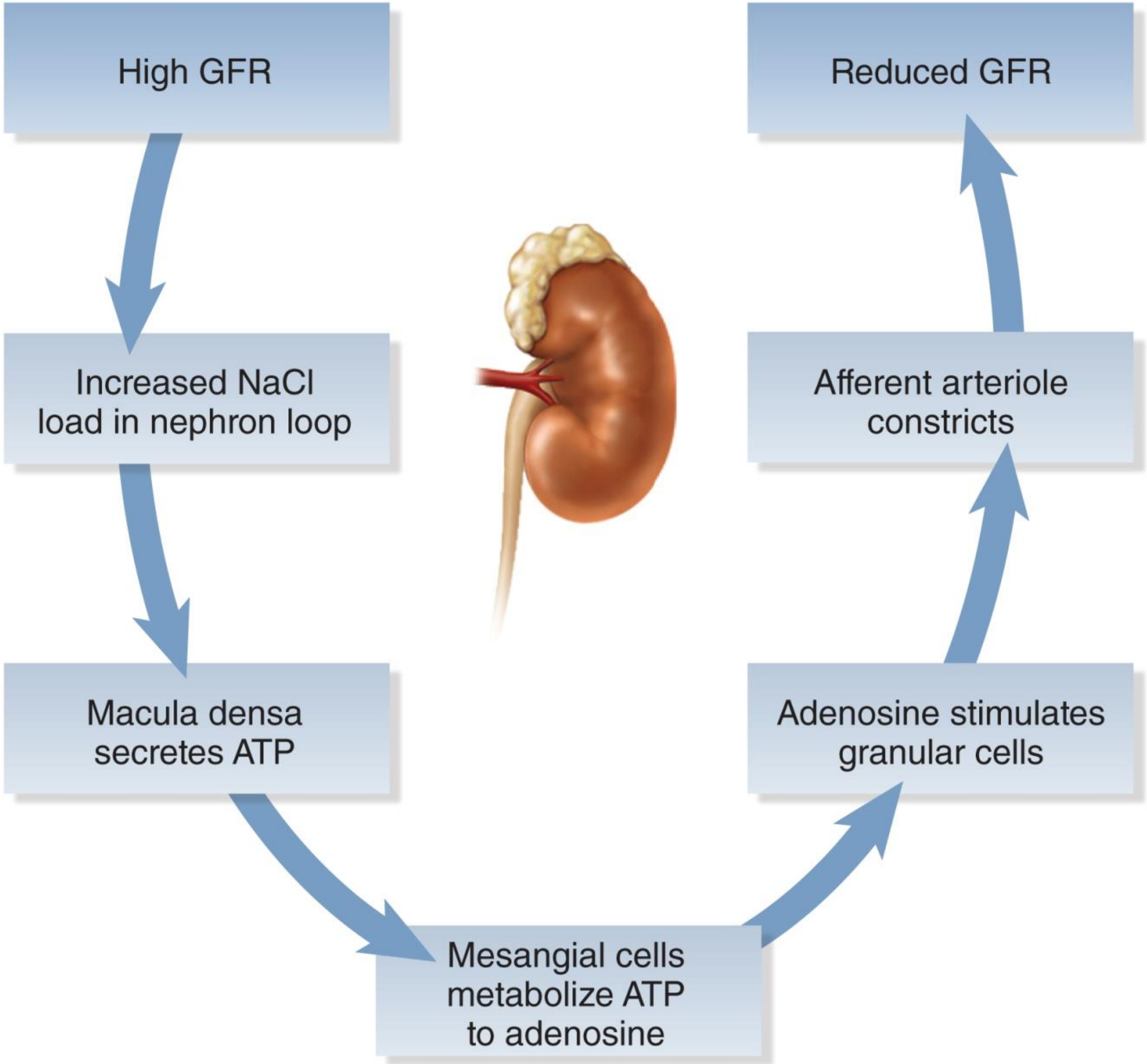


Figure 23.14

Sympathetic Control

- **Sympathetic nerve fibers richly innervate the renal blood vessels**
- Sympathetic nervous system and adrenal epinephrine **constrict the afferent arterioles** in strenuous exercise or acute conditions like circulatory shock
  - Reduces GFR and 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

Renin–Angiotensin–Aldosterone Mechanism

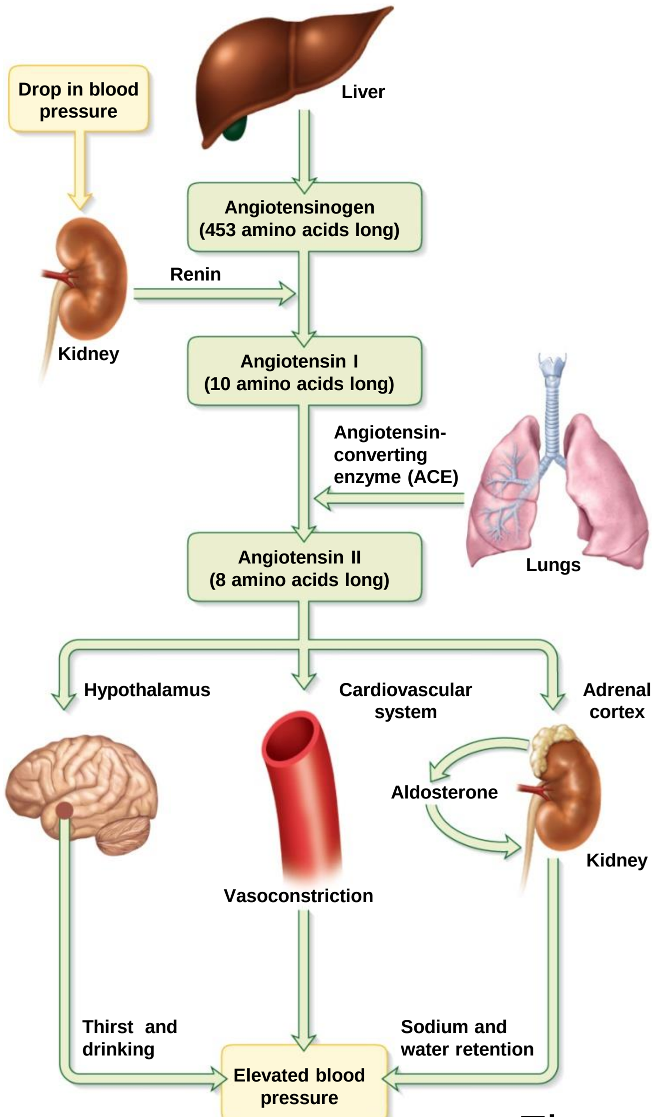


Figure 23.15

- **The renin-angiotensin-aldosterone mechanism is a system of hormones that helps control blood pressure and GFR**
- In response to a drop in blood pressure, **baroreceptors** in carotid and aorta stimulate the sympathetic nervous system
- Sympathetic fibers trigger release of **renin** by kidneys' granular cells
- Renin converts **angiotensinogen,** a blood protein, into **angiotensin I**

Renin–Angiotensin–Aldosterone Mechanism

- In lungs and kidneys, **angiotensin-converting enzyme (ACE)** converts angiotensin I to angiotensin II

- **Angiotensin II**—active hormone that increases BP
  - Potent vasoconstrictor raising BP throughout body
  - Constricts efferent arteriole raising GFR despite low BP
  - Lowers BP in peritubular capillaries enhancing reabsorption of NaCl and H_2O
  - Stimulates adrenal cortex to secrete **aldosterone**, which promotes Na^+ and H_2O reabsorption in DCT and collecting duct
  - Stimulates Na^+ and H_2O reabsorption in PCT
  - Stimulates posterior pituitary to secrete ADH which promotes water reabsorption by collecting duct
  - Stimulates thirst

Urine Formation II: Tubular Reabsorption and Secretion

- **Expected Learning Outcomes**
  - Describe how the renal tubules reabsorb useful solutes from the glomerular filtrate and return them to the blood.
  - Describe how the tubules secrete solute from the blood into the tubular fluid.
  - Describe how the nephron regulates water excretion.

Basic Stages of Urine Formation

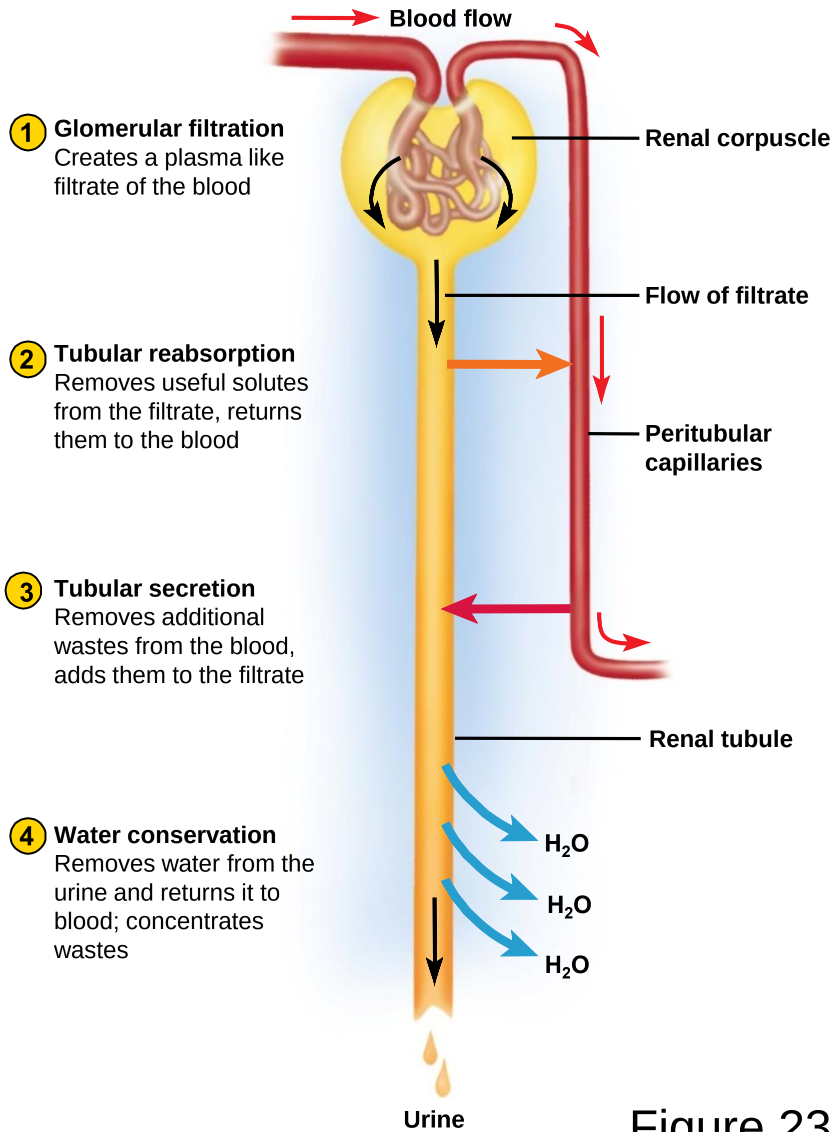


Figure 23.9

- **Conversion of glomerular filtrate to urine involves the removal and addition of chemicals by tubular reabsorption and secretion**
  - Occurs through PCT to DCT
  - Tubular fluid is modified
- **Steps involved include:**
  - Tubular reabsorption
  - Tubular secretion
  - Water conservation

The Proximal Convoluted Tubule

- **PCT reabsorbs about 65% of glomerular filtrate,** removes some substances from blood, and **secretes** them into tubular fluid for disposal in urine
  - **Prominent microvilli** and great length
  - Abundant mitochondria provide ATP for active transport
  - PCTs alone account for about 6% of one's resting ATP and calorie consumption
- **Tubular reabsorption**—process of reclaiming water and solutes from tubular fluid and returning them to blood

Tubular Reabsorption

- **Two routes of reabsorption**
  - **Transcellular route**
    - Substances pass through cytoplasm of PCT epithelial cells and out their base
  - **Paracellular route**
    - Substances pass between PCT cells
    - Junctions between epithelial cells are leaky and allow significant amounts of water to pass through
    - **Solvent drag**—water carries a variety of dissolved solutes with it
- Reabsorbed fluid is ultimately taken up by **peritubular capillaries**

Tubular Reabsorption

- **Sodium reabsorption** is key
  - Creates an osmotic and electrical gradient that drives the reabsorption of water and other solutes
  - Na^+ is most abundant cation in filtrate
  - Creates steep concentration gradient that favors its diffusion into epithelial cells
  - **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
    - Na^+–H^+ antiport that pulls Na^+ into the cell while pumping out H^+ into tubular fluid

Tubular Reabsorption

- **Sodium reabsorption (Continued)**
  - Sodium is prevented from accumulating in epithelial cells by **Na^+–K^+ pumps** in the basal surface of the epithelium
    - Pumps Na^+ out to extracellular fluid
  - Na^+ is picked up by peritubular capillaries and returned to blood
  - The Na^+–K^+ pumps (at the base) are examples of **primary active transport** – they use ATP
  - The symports on the apical surface are examples of **secondary active transport** – they do not directly consume ATP, but are dependent on the primary transport Na^+–K^+ pumps at the base of the cell to establish the sodium concentration gradient

Tubular Reabsorption

- Negative **chloride ions** follow the positive sodium ions by electrical attraction
  - Various antiports in the apical cell membrane that absorb Cl^- in exchange for other anions they eject into the tubular fluid: K^+–Cl^- symport

Tubular Reabsorption

- **Potassium, magnesium,** and **phosphate ions** diffuse through the paracellular route with water
- **Phosphate** is also cotransported into the epithelial cells with Na^+
- Some **calcium** is reabsorbed through the paracellular route in the PCT, but most Ca^{2+} reabsorption occurs later in the nephron

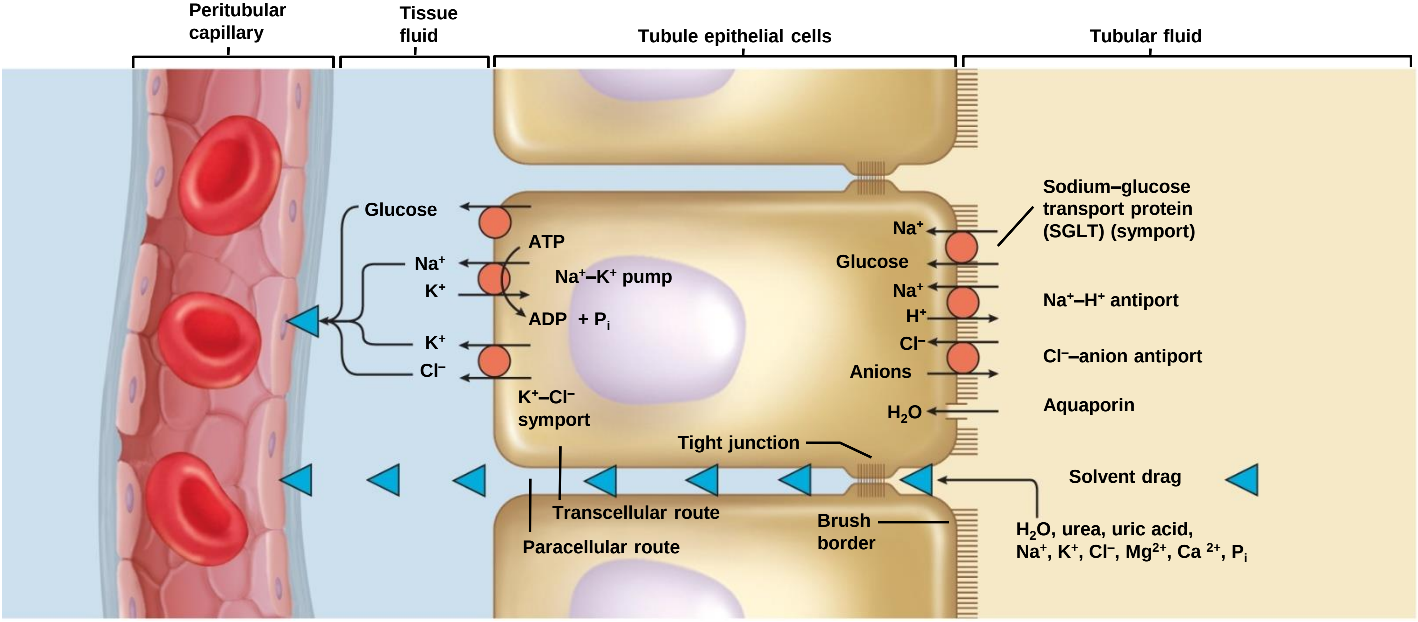


Figure 23.16

Tubular Reabsorption

- **Glucose** is cotransported with Na^+ by **sodium–glucose transport (SGLT) proteins** – normally all glucose is reabsorbed

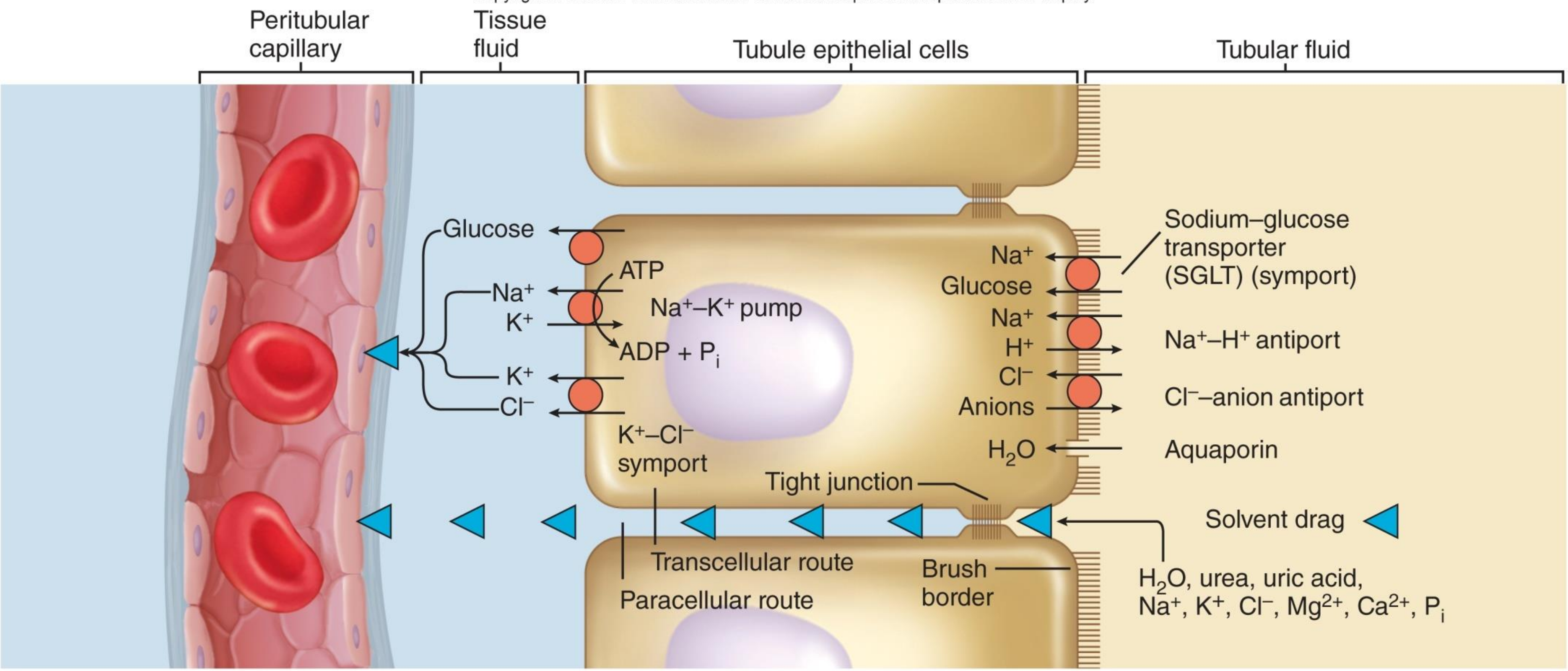


Figure 23.16

Tubular Reabsorption

- **Nitrogenous wastes**
  - Nephron reabsorbs about half of **urea** in tubular fluid
    - Concentration remaining in blood is safe
  - PCT reabsorbs **uric acid,** but later portions of the nephron secrete it
  - **Creatinine** is not reabsorbed – it is passed in urine

Tubular Reabsorption

- **Each day, kidneys reduce 180 L of glomerular filtrate to 1 or 2 L of urine**
- Two-thirds of **water** in filtrate is reabsorbed in PCT
- **Reabsorption of solutes makes the tubule cells and tissue fluid hypertonic to tubular fluid**
  - Water follows solutes by osmosis through both paracellular and transcellular routes
    - Transcellularly, water uses channels called **aquaporins**
  - In PCT, water is reabsorbed at constant rate called **obligatory water reabsorption**

Uptake by the Peritubular Capillaries

- **Peritubular capillaries reabsorb water and solutes that leave the basal surface of the tubular epithelium**
  - Reabsorption occurs by osmosis and solvent drag
- **Three factors promote osmosis into the capillaries**
  - **High interstitial fluid pressure** due to accumulation of reabsorbed fluid in extracellular space
  - **Low blood hydrostatic pressure** in peritubular capillaries due to narrowness of efferent arterioles
  - **High colloid osmotic pressure in blood** due to presence of proteins that were not filtered

The Transport Maximum

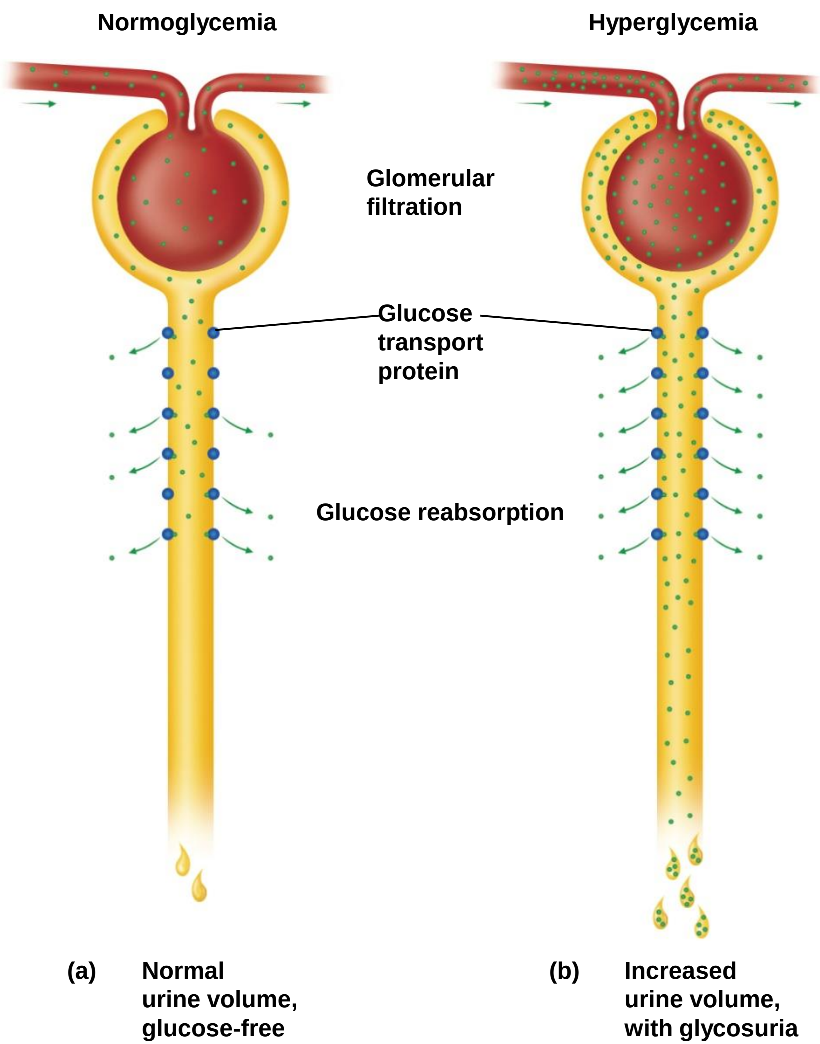


Figure 23.18

- The amount of solute that renal tubules can reabsorb is limited by the **number of transport proteins** in tubule cells' membranes
- **If all transporters are occupied, any excess solute passes by and appears in urine**
- **Transport maximum** is reached when transporters are saturated
- **Each solute has its own transport maximum**
  – Any blood glucose level above 220 mg/dL results in **glycosuria**

Tubular Secretion

- **Tubular secretion**—renal tubule extracts chemicals from capillary blood and secretes them into tubular fluid
- **Purposes of secretion in PCT and nephron loop include:**
  - **Acid–base balance**
    - Secretion of varying proportions of hydrogen and bicarbonate ions helps regulate pH of body fluids
  - **Waste removal**
    - Urea, uric acid, bile acids, ammonia, and a little creatinine are secreted into the tubule
  - **Clearance of drugs and contaminants**
    - Examples include: morphine, penicillin, and aspirin
    - Some drugs must be taken multiple times per day to keep up with renal clearance

The Nephron Loop

- **Primary function of nephron loop** is to generate salinity gradient that enables collecting duct to concentrate the urine and conserve water

- **Electrolyte reabsorption from filtrate**
  - Thick segment reabsorbs 25% of Na^+, K^+, and Cl^- in filtrate
    - Ions leave cells by active transport and diffusion
      - NaCl remains in the tissue fluid of renal medulla
      - Water cannot follow since thick segment is impermeable
  - Tubular fluid very dilute as it enters distal convoluted tubule

The Distal Convoluted Tubule 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 passed as urine, it would amount to 36 L/day

- **DCT and collecting duct reabsorb variable amounts of water and salt and are regulated by several hormones**
  - **Aldosterone, atrial natriuretic peptide, ADH,** and **parathyroid hormone**

The Distal Convoluted Tubule and Collecting Duct

- **Two kinds of cells** in the DCT and collecting duct
  - **Principal cells**
    - Most numerous
    - Have 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^+

The Distal Convoluted Tubule and Collecting Duct

- **Aldosterone**—the “salt-retaining hormone”
  - Steroid secreted by the adrenal cortex
  - Triggers for aldosterone secretion are:
    - When blood Na^+ concentration falls or
    - When K^+ concentration rises or
    - There is a drop in blood pressure $\rightarrow$ renin release $\rightarrow$ angiotensin II formation $\rightarrow$ stimulates adrenal cortex to secrete aldosterone

The Distal Convoluted Tubule and Collecting Duct

- **Functions of aldosterone**
  - Acts on thick segment of nephron loop, DCT, and cortical portion of collecting duct
    - Stimulates reabsorption of Na^+ and secretion of K^+
    - Water and Cl^- follow the Na^+
    - Net effect is that the body retains NaCl and water
      - Helps maintain blood volume and pressure
    - Urine volume is reduced
    - Urine has an elevated K^+ concentration

The Distal Convoluted Tubule and Collecting Duct

- **Natriuretic peptides**—secreted by atrial myocardium of the heart in response to high blood pressure
- **Four actions result in the excretion of more salt and water in the urine, thus reducing blood volume and pressure**
  - Dilates afferent arteriole, constricts efferent arteriole: ↑ GFR
  - Inhibits renin and aldosterone secretion
  - Inhibits secretion of ADH
  - Inhibits NaCl reabsorption by collecting duct

The Distal Convoluted Tubule and Collecting Duct

- **Antidiuretic hormone (ADH)** secreted by posterior pituitary
  - Dehydration, loss of blood volume, and rising blood osmolarity stimulate arterial baroreceptors and hypothalamic osmoreceptors
  - This triggers release of ADH from the posterior pituitary
  - ADH makes collecting duct more permeable to water
  - Water in the tubular fluid reenters the tissue fluid and bloodstream rather than being lost in urine

The Distal Convoluted Tubule and Collecting Duct

- **Parathyroid hormone (PTH)** secreted from parathyroid glands in response to calcium deficiency **(hypocalcemia)**
  - Acts on PCT to increase phosphate excretion
  - Acts on the thick segment of the ascending limb of the nephron loop, and on the DCT to increase calcium reabsorption
  - Increases phosphate content and lowers calcium content in urine
  - Because phosphate is not retained, calcium ions stay in circulation rather than precipitating into bone tissue as calcium phosphate
  - PTH stimulates calcitriol synthesis by epithelial cells of the PCT

The Distal Convoluted Tubule and Collecting Duct

- **Summary:**
- **PCT** reabsorbs 65% of glomerular filtrate and returns it to peritubular capillaries
  - Much reabsorption by osmosis and 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 making urine
- **Collecting duct conserves water**

Urine Formation III: Water Conservation

- **Expected Learning Outcomes**
  - Explain how the collecting duct and antidiuretic hormone regulate the volume and concentration of urine.
  - Explain how the kidney maintains an osmotic gradient in the renal medulla that enables the collecting duct to function.

Urine Formation III: Water Conservation

- **The kidney eliminates metabolic wastes from the body, but prevents excessive water loss**
- **As the kidney returns water to the tissue fluid and bloodstream, the fluid remaining in the renal tubules passes as urine, and becomes more concentrated**

Collecting Duct

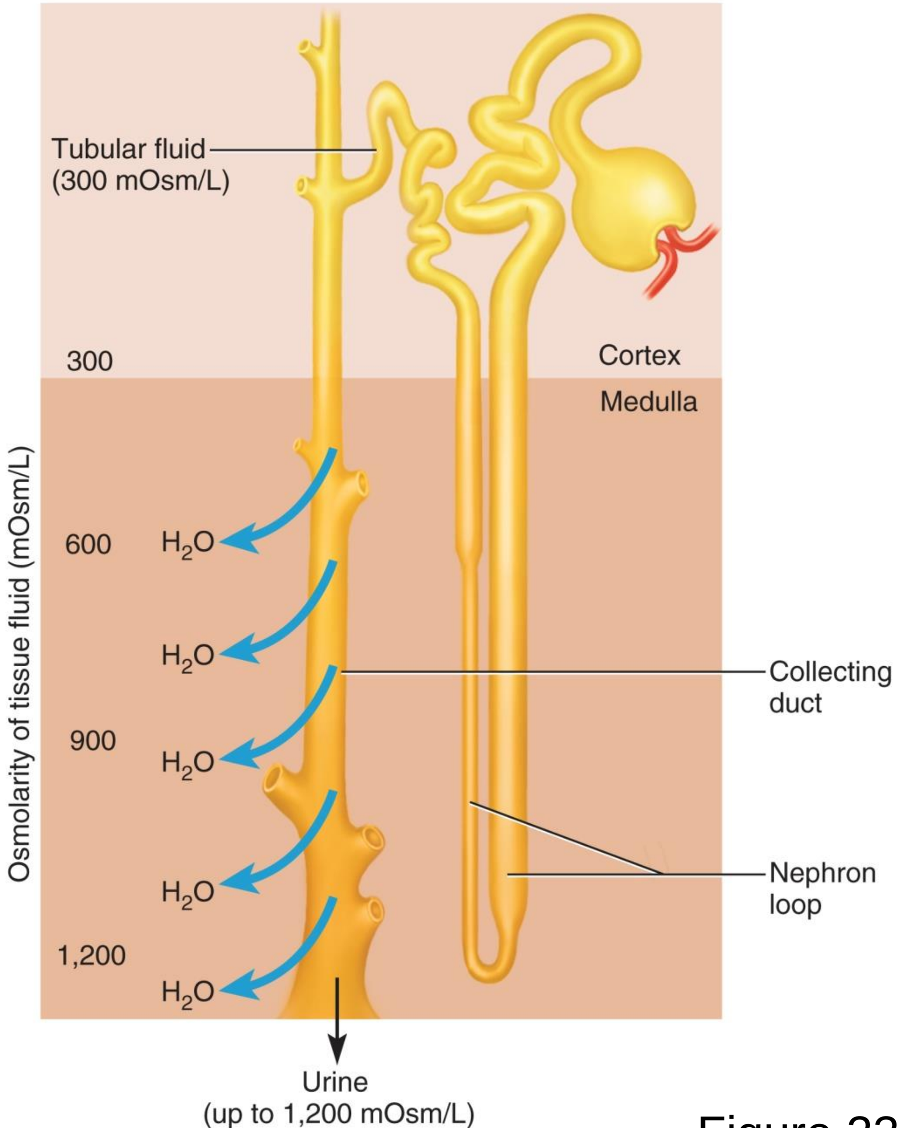


Figure 23.19

- Collecting duct (CD) begins in the cortex where it receives tubular fluid from several nephrons
- CD runs through medulla, and reabsorbs water, making urine up to four times more concentrated
- Medullary portion of CD is more permeable to water than to NaCl
- As urine passes through the increasingly salty medulla, water leaves by osmosis, concentrating urine

Control of Water Loss

- **How concentrated the urine becomes 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 NaCl, but it is impermeable to water
  - Salt is removed from the urine but water stays in
  - Urine concentration may be as low as 50 mOsm/L

Control of Water Loss

- Dehydration leads to production of **hypertonic urine**
  - Urine becomes scanty and more concentrated
  - High blood osmolarity stimulates posterior pituitary to release ADH and then an increase in synthesis of aquaporin channels by renal tubule cells
  - More water is reabsorbed by collecting duct
  - Urine is more concentrated
- If BP is low in a dehydrated person, GFR will be low
  - Filtrate moves more slowly and there is more time for reabsorption
  - More salt removed, more water reabsorbed, and less urine produced

The Countercurrent Multiplier

- **The ability of kidney to concentrate urine depends on salinity gradient in renal medulla**
  - Four times more salty in the renal medulla than the cortex

- Nephron loop acts as **countercurrent multiplier**
  - **Multiplier:** continually recaptures salt and returns it to extracellular fluid of medulla which multiplies the osmolarity of adrenal medulla
  - **Countercurrent** : because of fluid flowing in opposite directions in adjacent tubules of nephron loop

- 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

The Countercurrent Multiplier

- 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 dilute: 100 mOsm/L at top of loop
- **Recycling of urea** adds to high osmolarity of deep medulla
  - Lower end of collecting duct is permeable to urea but neither thick segment of loop nor DCT is permeable to urea
  - Urea is 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

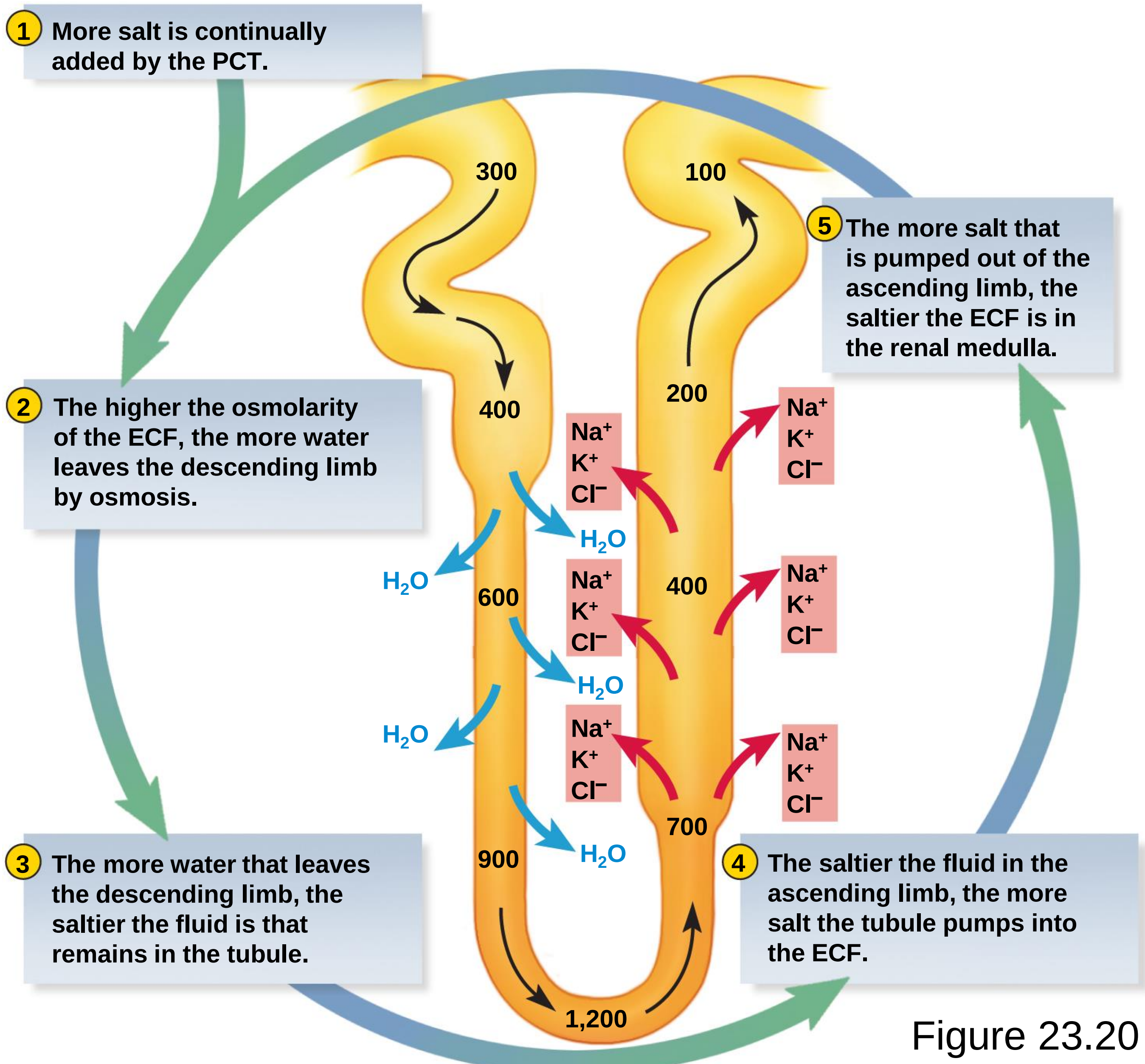


Figure 23.20

The Countercurrent Exchange System

- **Vasa recta**—capillary branching off efferent arteriole in medulla
  - Provides blood supply to medulla and does not remove NaCl and urea from medullary ECF
- **Countercurrent system**—formed by blood flowing in opposite directions in adjacent parallel capillaries
- **Descending capillaries of vasa recta**
  - Exchanges water for salt
  - Water diffuses out of capillaries and salt diffuses in

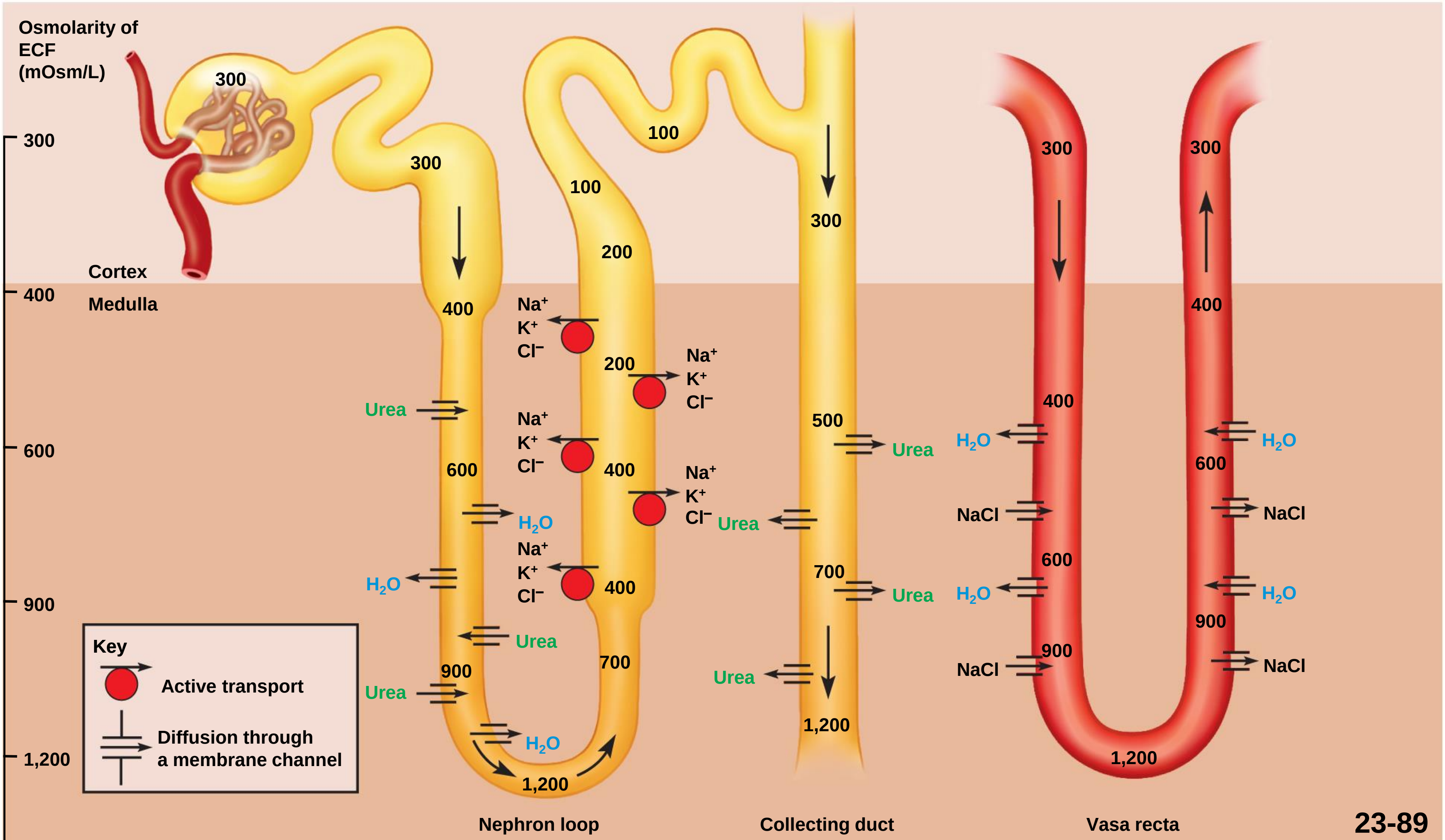
The Countercurrent Exchange System

- **As blood flows back up to the cortex, the opposite occurs**

- **Ascending capillaries of vasa recta**
  - Exchanges salt for water
  - Water diffuses into and NaCl diffuses out of blood
  - Vasa recta gives the salt back and does not subtract from the osmolarity of the medulla

Functional Relationship of the Nephron Loop

Figure 23.21



Summary of Reabsorption and Secretion

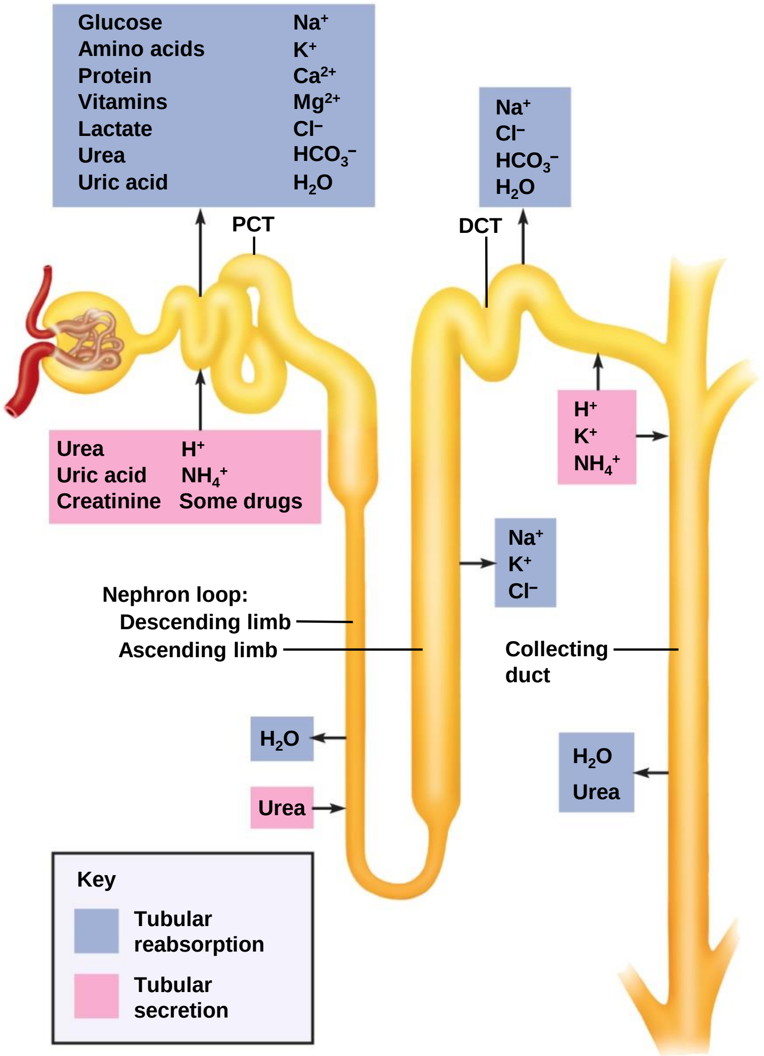


Figure 23.22

Urine and Renal Function Tests

- **Expected Learning Outcomes**
  - Describe the composition and properties of urine.
  - Carry out some calculations to evaluate renal function.

Composition and Properties of Urine

- **Urinalysis—**examination of physical and chemical properties of urine
- **Appearance—**varies from clear to deep amber depending on state of hydration
  - Yellow color due to urochrome pigment from breakdown of hemoglobin (RBCs)
  - Cloudiness or blood could suggest urinary tract infection, trauma, or stones; or might just be contamination with other fluids
  - **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 and diseases impart particular aromas

Composition and Properties of Urine

- **Specific gravity—**compares urine sample's density to that of distilled water
  – Density of urine ranges from 1.001 to1.028 g/mL
- **Osmolarity** (blood = 300 mOsm/L)
  – Ranges from 50 mOsm/L to 1,200 mOsm/L in dehydrated person
- **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

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 from kidney disease, dehydration, circulatory shock, prostate enlargement
  - Low urine output of less than **400 mL/day,** the body cannot maintain a safe, low concentration of waste in the plasma (leads to azotemia)

Urine Volume

- **Diabetes—**any metabolic disorder resulting in chronic polyuria
- **At least four forms of diabetes**
  - **Diabetes mellitus type 1, type 2,** and **gestational diabetes**
    - High concentration of glucose in renal tubule
    - Glucose opposes the osmotic reabsorption of water
    - More water passes in urine (osmotic diuresis)
    - Glycosuria—glucose in the urine
  - **Diabetes insipidus**
    - **ADH hyposecretion** causes not enough water to be reabsorbed in the collecting duct
    - More water passes in urine

Urine Volume

- **Diuretics—**any chemical that increases urine volume
  - Some increase GFR
    - Caffeine dilates the afferent arteriole
  - Some reduce tubular reabsorption of water
    - Alcohol inhibits ADH secretion
  - Some act on nephron loop (loop diuretic): inhibit Na^+–K^+–Cl^- symport
    - Impairs countercurrent multiplier reducing the osmotic gradient in the renal medulla
    - Collecting duct unable to reabsorb as much water as usual
  - Diuretics are commonly used to treat hypertension and congestive heart failure by reducing the body's fluid volume and blood pressure

Renal Function Tests

- Tests for diagnosing kidney disease
- Evaluating their severity
- Monitoring their progress
- Determining renal clearance
- Determining glomerular filtration rate

Renal Clearance

- **Renal clearance**—the volume of blood plasma from which a particular waste is completely removed in one minute

- **Represents the net effect of three processes**

  Glomerular filtration of the waste
+ Amount added by **tubular secretion**
– Amount removed by **tubular reabsorption**
  Renal clearance

Renal Clearance

- **Determine renal clearance (C)** by collecting blood and urine samples, measuring the waste concentration in each, and measuring the rate of urine output
- If…
  - U: waste concentration in urine: 6.0 mg/mL (urea example)
  - V: rate of urine output: 2 mL/min.
  - P: waste concentration in plasma: 0.2 mg/mL
  - C: renal clearance in mL/min. of waste cleared
- Then…
  - C = UV/P = 60 mL/min (60 mL of blood plasma is completely cleared of urea per minute)

- **Compare C to normal GFR of 125 mL/min. to see if normal rate of clearance is occurring**
  - In above example 48%, which is normal clearance for urea

Glomerular Filtration Rate

- **Often need to measure GFR to assess kidney disease**
  - Cannot use clearance rate of urea, because reabsorption and secretion of urea influence its clearance

- **Need a substance that is not secreted nor reabsorbed at all so that all of it in the urine gets there by glomerular filtration**

- Use **inulin,** a plant polysaccharide to determine GFR
  - Neither reabsorbed nor secreted by the renal tubule
  - A known concentration of inulin can be injected in the blood and its output in the urine can be measure
  - Inulin clearance = GFR
- Clinically GFR is estimated from **creatinine excretion**
  - Does not require injecting a substance and has a small, acceptable amount of error

Urine Storage and Elimination

- **Expected Learning Outcomes**
  - Describe the functional anatomy of the ureters, urinary bladder, and male and female urethra.
  - Explain how the nervous system and urethral sphincters control the voiding of urine.

Urine Storage and Elimination

- Urine is produced continually
- Does not drain continually from the body
- Urination is episodic—occurring when we allow it
- Made possible by storage apparatus and neural controls for timely release

The Ureters

- **Ureters—**retroperitoneal, muscular tubes that extend from each **kidney to the urinary bladder**
  - About 25 cm long
  - Pass posterior to bladder and enter it from below
  - Flap of mucosa at entrance of each ureter acts as a valve into bladder
    - Keeps urine from backing up into ureter when bladder contracts

The Ureters

Ureters (Continued)

- Three layers of ureter
  - **Adventitia**—connective tissue layer that connects ureter to surrounding structures
  - **Muscularis**—two layers of smooth muscle with third layer in lower ureter
    - Urine enters, it stretches and contracts in peristaltic wave
  - **Mucosa**—transitional epithelium
    - Begins at minor calyces and extends through the bladder
- Lumen very narrow, easily obstructed by kidney stones

The Urinary Bladder

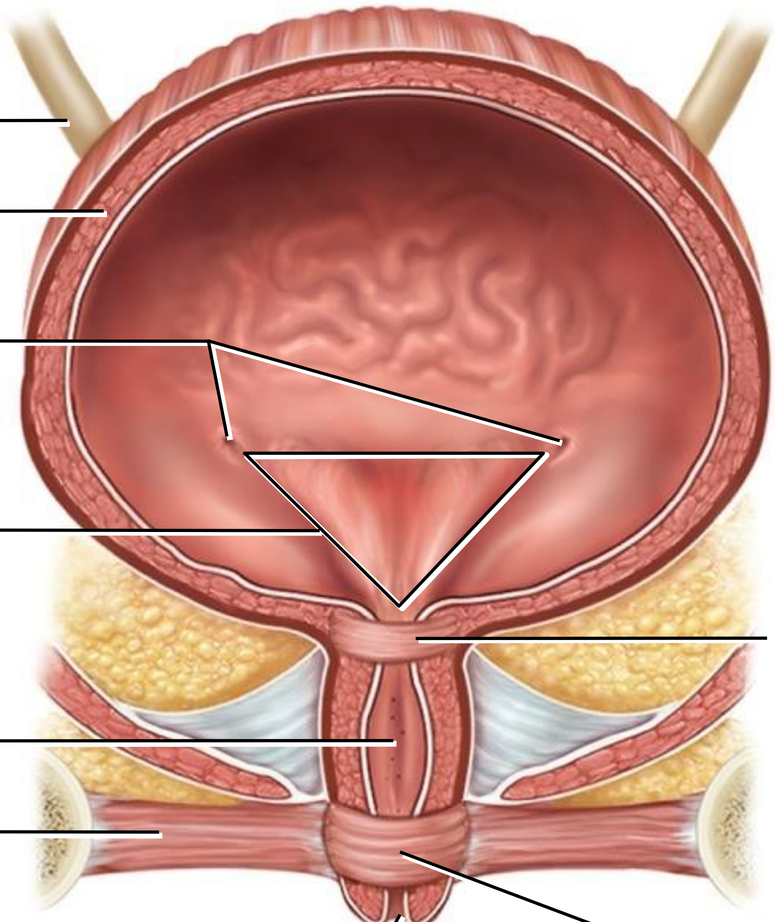
- **Urinary bladder—**muscular sac located on floor of the pelvic cavity
  - Inferior to peritoneum and posterior to pubic symphysis
- **Three layers**
  - Covered by parietal peritoneum, superiorly, and by fibrous adventitia elsewhere
  - Muscularis: **detrusor:** three layers of smooth muscle
  - Mucosa: transitional epithelium
    - Umbrella cells on surface of epithelium protect it from the hypertonic, acidic urine
    - **Rugae**—conspicuous wrinkles in empty bladder

The Urinary Bladder

- **Trigone**—smooth-surfaced triangular area on bladder floor that is marked with openings of ureters and urethra

- **Capacity—moderate fullness is 500 mL, maximum fullness is 700 to 800 mL**
  - Highly distensible
  - As it fills, it expands superiorly
  - Rugae flatten
  - Epithelium thins from five or six layers to two or three

The Urinary Bladder



(a) Female

Figure 23.23a

Kidney Stones

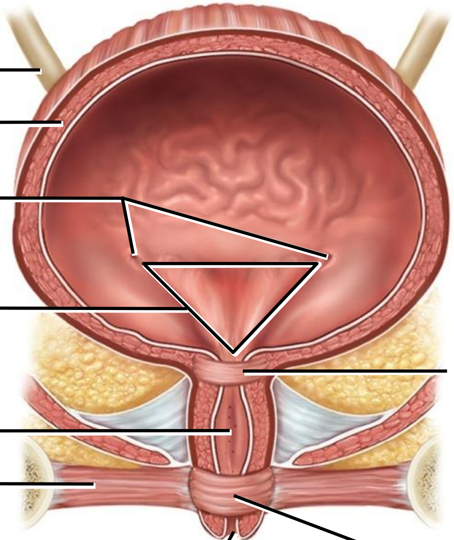
- **Renal calculus (kidney stone)**—hard granule of calcium phosphate, calcium oxalate, uric acid, or a magnesium salt called **struvite**
- **Form in the renal pelvis**
- **Usually small enough to pass unnoticed in the urine flow**
  - Large stones might block renal pelvis or ureter and can cause pressure buildup in kidney which destroys nephrons
    - Passage of large jagged stones is excruciatingly painful and may damage ureter causing hematuria

Kidney Stones

- **Causes** include hypercalcemia, dehydration, pH imbalances, frequent urinary tract infections, or enlarged prostate gland causing urine retention

- **Treatment** includes stone-dissolving drugs, often surgery, or **lithotripsy (nonsurgical technique that pulverizes stones with ultrasound)**

The Urethra



(a) Female

Figure 23.23a

- **Urethra is tube that conveys urine out of body**
- **Female urethra:**
  - 3 to 4 cm long, bound to anterior wall of vagina
  - **External urethral orifice** is between vaginal orifice and clitoris
- **Internal urethral sphincter**
  - Detrusor muscle thickening
  - Smooth muscle - involuntary
- **External urethral sphincter**
  - Where urethra passes through the pelvic floor
  - Skeletal muscle - voluntary control

The Urethra

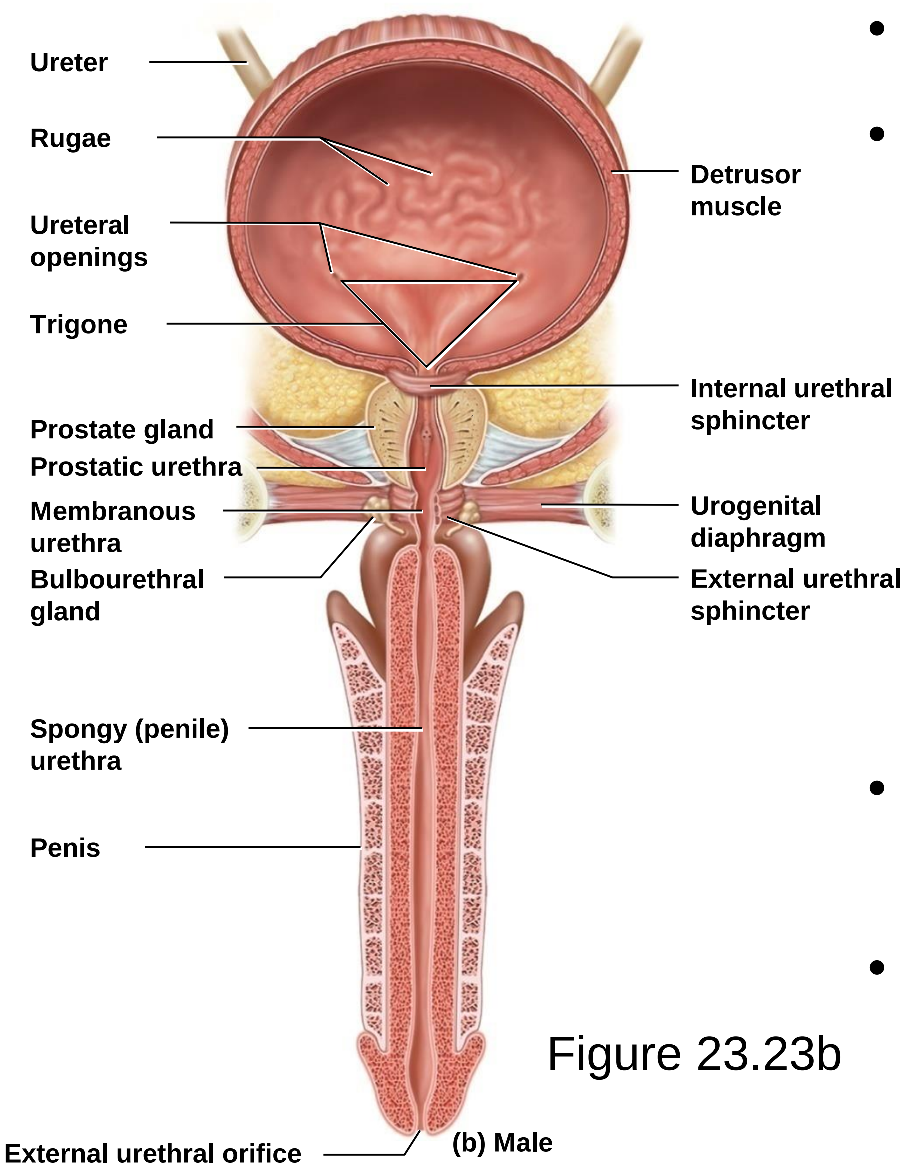


Figure 23.23b

- **Male urethra: 18 cm long**
- **Three regions**
  – **Prostatic urethra** (2.5 cm)
    - Passes through prostate gland
  – **Membranous urethra** (0.5 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**
  – Skeletal muscle of pelvic floor

Urinary Tract Infection (UTI)

- **Cystitis**—infection of the urinary bladder
  - Especially common in females due to short urethra
  - Frequently triggered by sexual intercourse
  - Can spread up the ureter causing pyelitis
- **Pyelitis**—infection of the renal pelvis
- **Pyelonephritis**—infection that reaches the cortex and the nephrons
  - Can result from blood-borne bacteria

Voiding Urine

- **Between acts of urination, the bladder fills**
  - **Detrusor** muscle relaxes
  - **Urethral sphincters** are tightly closed
    - Sympathetic activity in upper lumbar spinal cord stimulates postganglionic fibers to the detrusor muscle (relax it) and internal urethral sphincter (excite it)
    - **Somatic motor fibers** from upper sacral spinal cord travel through pudendal nerve to supply the **external sphincter** to allow voluntary control

Voiding Urine

- **Micturition**—the act of urinating
- **Micturition reflex**—involuntary spinal reflex that partly controls urination (steps 1–4)
  - Stretch receptors detect filing of bladder, transmit afferent signals to the spinal cord
  - Signals return to bladder from spinal cord (S2 or S3) via parasympathetic fibers in the pelvic nerve
  - Efferent signals excite detrusor muscle
  - Efferent signals relax internal urethral sphincter; urine is involuntary voided if not inhibited by the brain

Voiding Urine

Mictruition (Continued)

- **Voluntary control** (steps 5–8)
  - For voluntary control, the micturition center in the pons receives signals from stretch receptors
  - If it is timely to urinate, the pons returns signals to spinal interneurons that excite detrusor and relax internal urethral sphincter; urine is voided
  - If it is untimely to urinate, signals from the pons excite spinal interneurons that keep external urethral sphincter contracted; urine is retained in the bladder
  - If it is timely to urinate, signals from the pons cease, and external urethral sphincter relaxes; urine is voided

Neural Control of Micturition

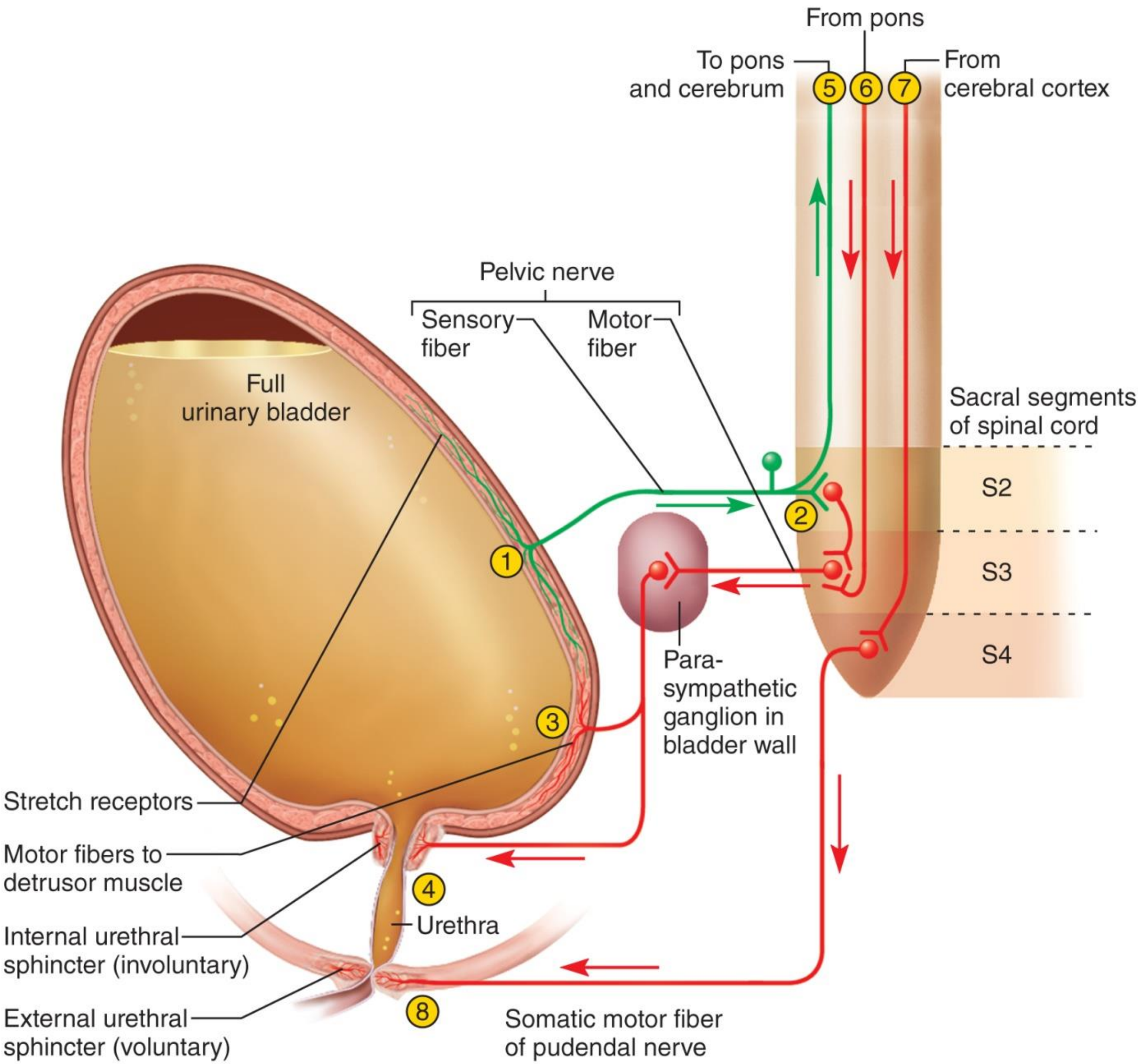


Figure 23.24

Involuntary micturition reflex

1. Stretch receptors detect filling of bladder, transmit afferent signals to spinal cord.
2. Signals return to bladder from spinal cord segments S2 and S3 via parasympathetic fibers in pelvic nerve.
3. Efferent signals excite detrusor muscle.
4. Efferent signals relax internal urethral sphincter. Urine is involuntarily voided if not inhibited by brain.

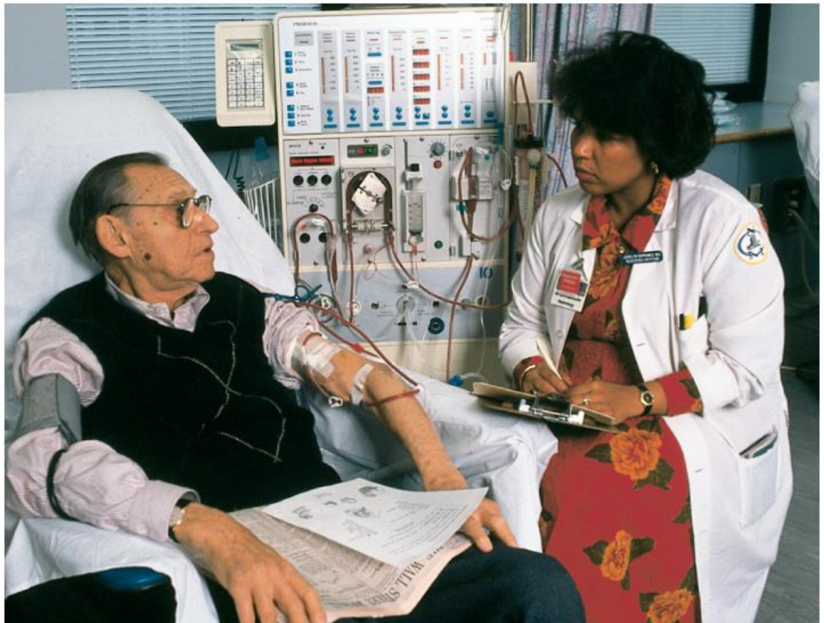
Voluntary control

5. For voluntary control, micturition center in pons receives signals from stretch receptors.
6. If it is timely to urinate, pons returns signals to spinal interneurons that excite detrusor and relax internal urethral sphincter. Urine is voided.
7. If it is untimely to urinate, signals from cerebrum excite spinal interneurons that keep external urethral sphincter contracted. Urine is retained in bladder.
8. If it is timely to urinate, signals from cerebrum inhibit sacral neurons that keep external sphincter closed. External urethral sphincter relaxes and urine is voided.

Voiding Urine

- **There are times when the bladder is not full enough to trigger the micturition reflex but one wishes to “go” anyway**
  - **Valsalva maneuver** used to compress bladder
  - Excites stretch receptors early to get the reflex started

Renal Insufficiency and Hemodialysis



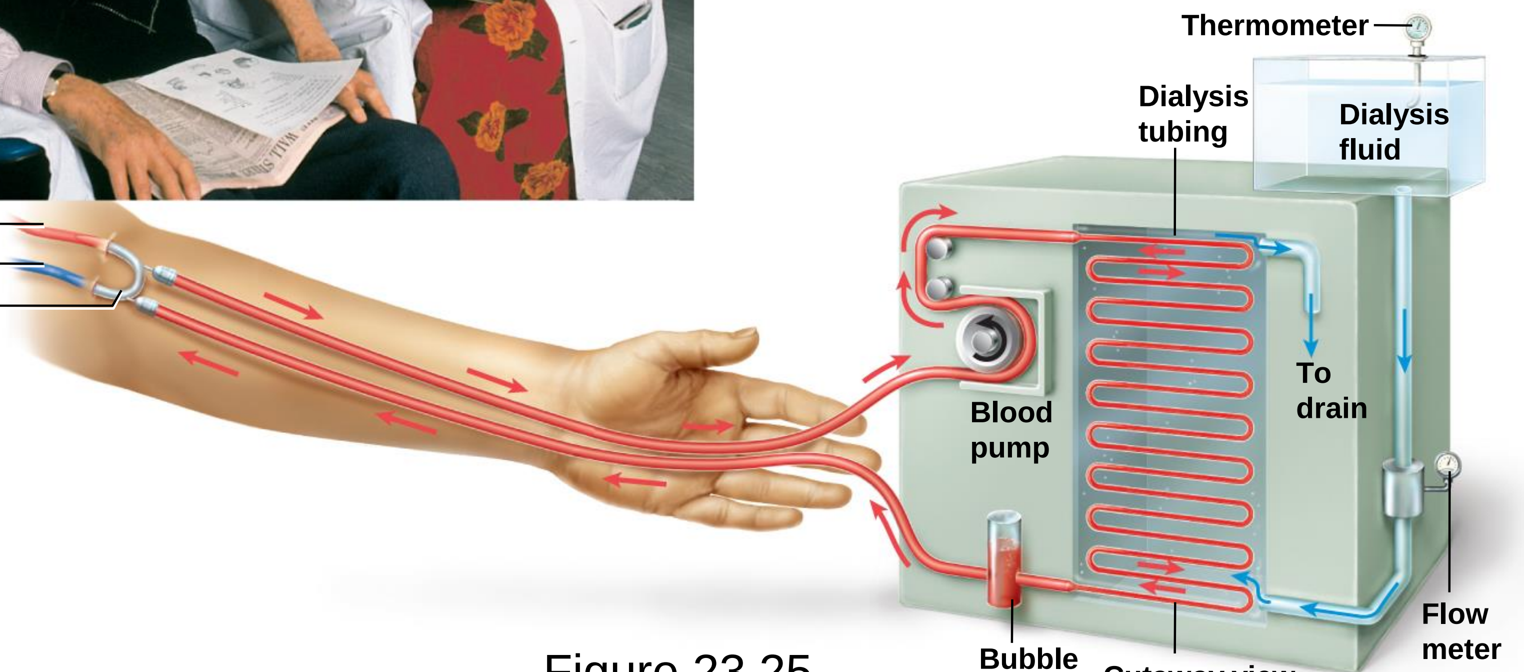


Figure 23.25

Hank Morgan/Photo Researchers, Inc.

Renal Insufficiency and Hemodialysis

- **Renal insufficiency—**a state in which the kidneys cannot maintain homeostasis due to extensive destruction of their nephrons
- **Causes of nephron destruction**
  – Hypertension, chronic kidney infections, trauma, prolonged ischemia and hypoxia, poisoning by heavy metals or solvents, blockage of renal tubules in transfusion reaction, atherosclerosis, or glomerulonephritis
- **Nephrons can regenerate and restore kidney function after short-term injuries**
  – Other nephrons hypertrophy to compensate for lost kidney function

Renal Insufficiency and Hemodialysis

- **Can survive with one-third of one kidney**
- **When 75% of nephrons are lost, urine output of 30 mL/hr is insufficient (normal 50 to 60 mL/hr) to maintain homeostasis**
  - Causes azotemia, acidosis, and uremia develops, also anemia
- **Hemodialysis—**procedure for artificially clearing wastes from the blood
  - Wastes leave bloodstream and enter dialysis fluid as blood flows through a semipermeable cellophane tube; also removes excess body water