The Respiratory System -Physiology

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LEARNING OUTCOMES

As a result of the lesson you will be able to:

- *Describe the process by which the kidney filters the blood plasma;*
- *Describe how the sympathetic nervous system, hormones, and the kidney itself regulate filtration.*
- *Describe how the renal tubules reabsorb water and useful solutes from the glomerular filtrate and return them to the blood;*
- *Describe how the tubules secrete solutes from the blood into the tubular fluid.*
- *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;*
- *Describe the hormonal mechanism for adjusting the body's rate of water loss to its state of hydration or dehydration.*

Overview of Urine Formation

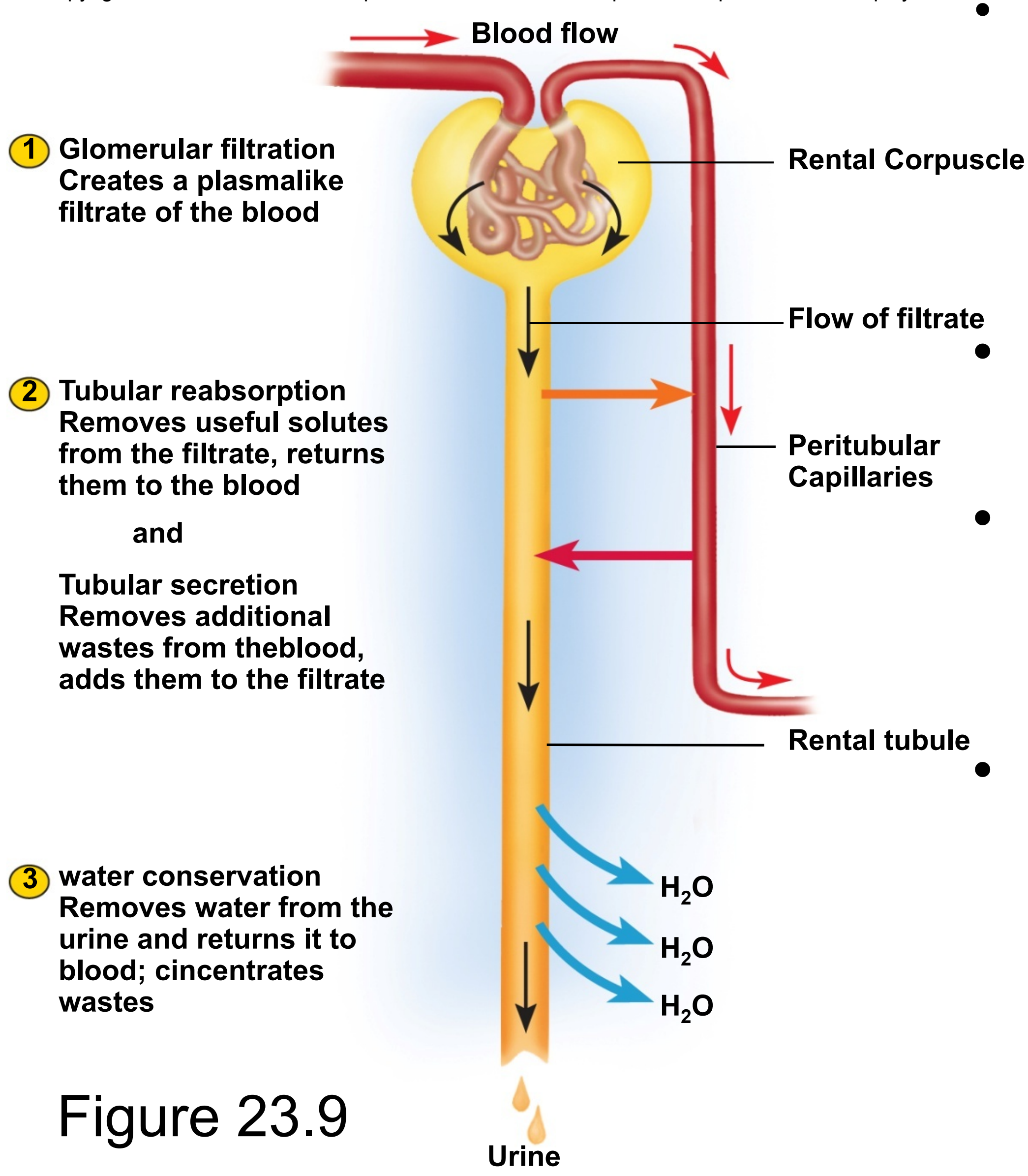


Figure 23.9

- kidneys convert blood plasma to urine in three stages
  - **glomerular filtration**
  - **tubular reabsorption and secretion**
  - **water conservation**
- **glomerular filtrate**
  - fluid in capsular space
  - blood plasma without protein
- **tubular fluid**
  - fluid in renal tubule
  - similar to above except tubular cells have removed and added substances
- **urine**
  - once it enters the collecting duct
  - only remaining change is water content

Urine Formation I: Glomerular Filtration

- kidneys convert blood plasma to urine in three stages
  - **glomerular filtration**
  - **tubular reabsorption and secretion**
  - **water conservation**
- **glomerular filtrate** – the fluid in the capsular space
  - similar to blood plasma except that is 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 Glomerulus

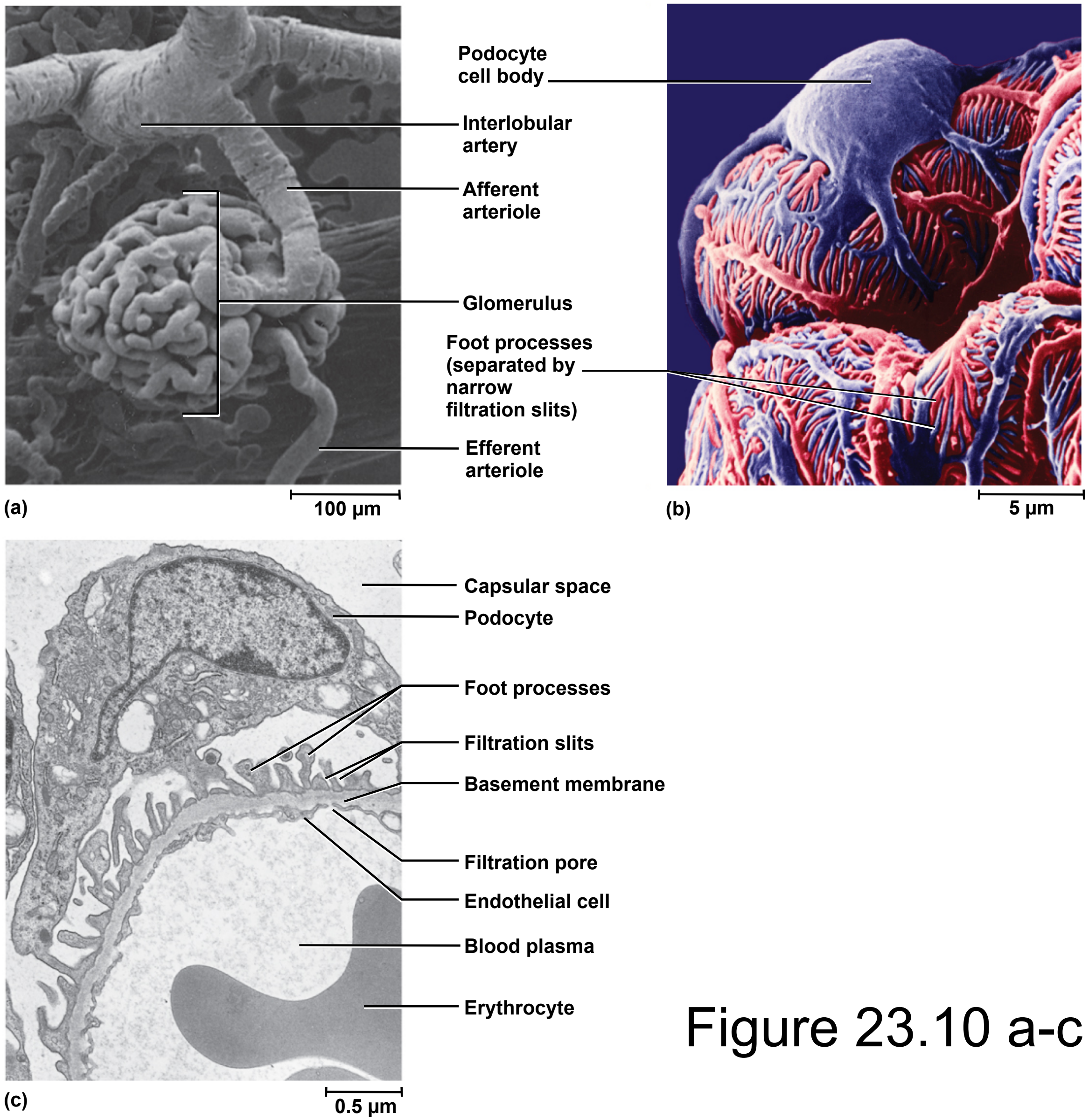


Figure 23.10 a-c

Filtration Pores and Slits

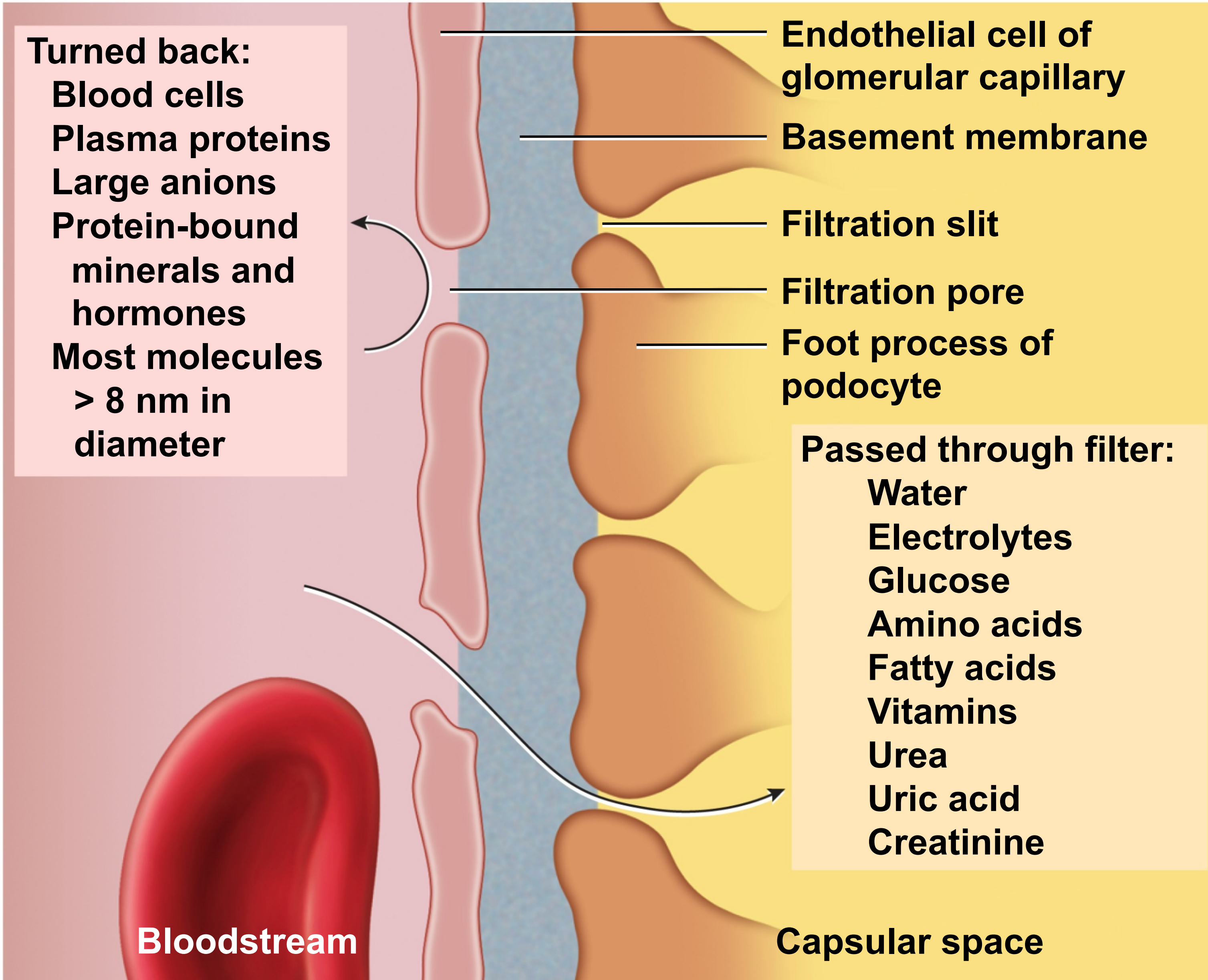


Figure 23.11

Filtration Membrane

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

- **filtration membrane** – three barriers through which fluid passes
  - **fenestrated endothelium of glomerular capillaries**
    - 70-90 nm filtration pores exclude blood cells
    - highly permeable
  - **basement membrane**
    - proteoglycan gel, negative charge, excludes molecules greater than 8nm
    - 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

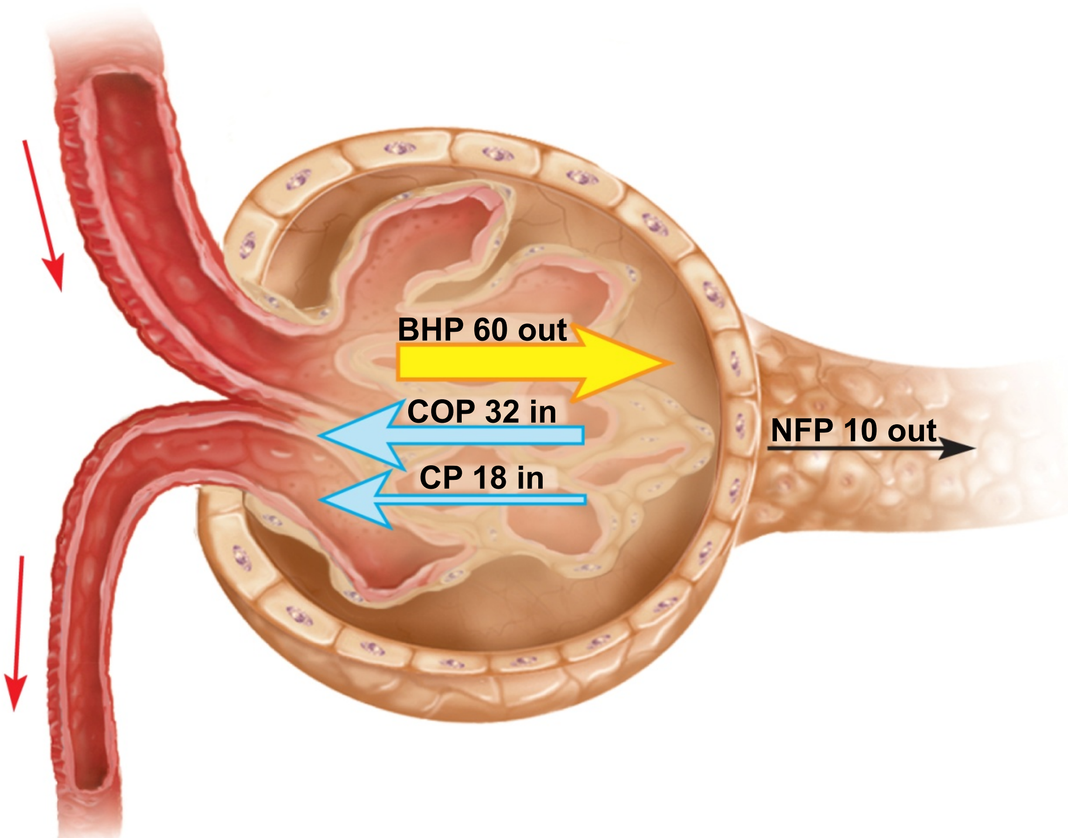
Filtration Membrane

- 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
- **kidney infections and trauma** can damage the filtration membrane and allow albumin or blood cells to filter.
  - **proteinuria (albuminuria)** – presence of protein in the urine
  - **hematuria** – presence of blood in the urine
- distance runners and swimmers often experience temporary proteinuria or hematuria
  - prolonged, strenuous exercise greatly reduces profusion of kidney
  - glomerulus deteriorates under prolonged hypoxia

Filtration Pressure

- **blood hydrostatic pressure** (BHP)
  - much higher in glomerular capillaries (60 mm Hg compared to 10 to 15 in most other capillaries)
  - because afferent arteriole is larger than efferent arteriole
  - larger inlet and smaller outlet
- **hydrostatic pressure** in capsular space
  - 18 mm Hg due to high filtration rate and continual accumulation of fluid in the capsule
- **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**$_{\mathbf{out}}$

Filtration Pressure



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 (GFR)

- **glomerular filtration rate** (GFR) – the amount of filtrate formed per minute by the 2 kidneys combined
  - $GFR = NFP \times K_f \approx 125$ mL / min or 180 L / day, male
  - $GFR = NFP \times K_f \approx 105$ 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 equals 50 to 60 times the amount of blood in the body
  - 99% of filtrate is reabsorbed since only 1 to 2 liters urine excreted / day

Regulation of Glomerular Filtration

- **GFR too high**
  - fluid flows through the renal tubules too rapidly for them to reabsorb the usual amount of water and solutes
  - urine output rises
  - chance of dehydration and electrolyte depletion
- **GFR too low**
  - wastes reabsorbed
  - azotemia may occur
- **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 of GFR

- **renal autoregulation –** the ability of the nephrons to adjust their own blood flow and GFR without external (nervous or hormonal) control

- enables them to maintain a relatively stable GFR in spite of changes in systemic arterial blood pressure

- two methods of autoregulation: **myogenic mechanism** and **tubuloglomerular feedback**

- **myogenic mechanism** – based on the tendency of smooth muscle to contract when stretched
  - increased arterial blood pressure stretches the afferent arteriole
  - arteriole constricts and prevents blood flow into the glomerulus from changing much
  - when blood pressure falls
  - the afferent arteriole relaxes
  - allows blood flow more easily into glomerulus
  - filtration remains stable

Renal Autoregulation of GFR

- **tubuloglomerular feedback** – mechanism by which glomerulus receives feedback on the status of the downstream tubular fluid and adjust filtration to regulate the composition of the fluid, stabilize its own performance, and compensate for fluctuation in systemic blood pressure
  - **juxtaglomerular apparatus** – complex structure found at the very 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 of GFR

- **three special kind of cells** occur in the juxtaglomerular apparatus:
  - **macula densa** – patch of slender, closely spaced epithelial cells at end of the nephron loop on the side of the tubules facing the arterioles
    - senses variations in flow or fluid composition and secretes a paracrine that stimulates JG cells
  - **juxtaglomerular (JG) cells** – enlarged smooth muscle cells in the afferent arteriole directly across from macula densa
    - when stimulated by the macula
    - they dilate or constrict the arterioles
    - they also contain granules of renin, which they secrete in response to drop in blood pressure
  - **mesangial cells** – in the cleft between the afferent and efferent arterioles and among the capillaries of the glomerulus
    - connected to macula densa and JG cells by gap junctions and communicate by means of paracrines
    - build supportive matrix for glomerulus, constrict or relax capillaries to regulate flow

Juxtaglomerular Apparatus

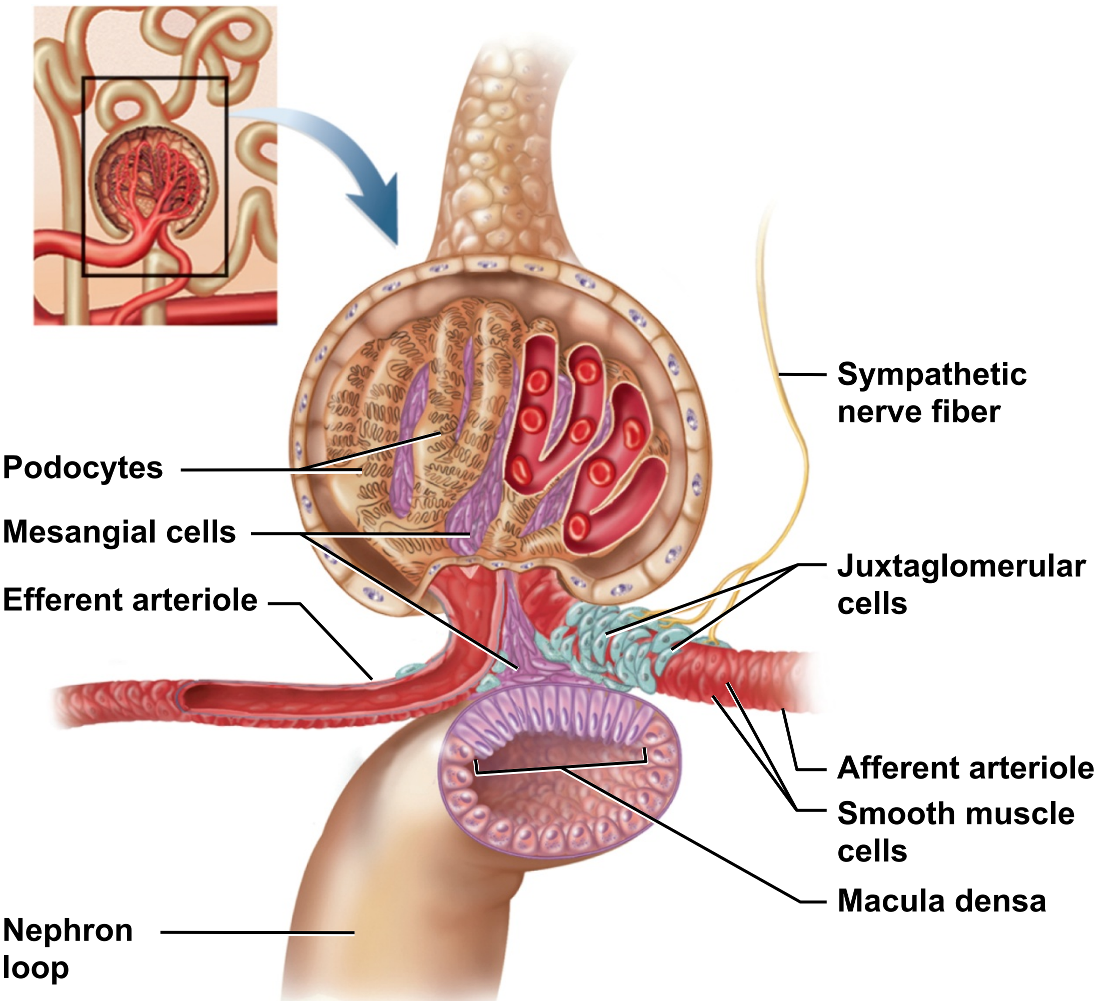


Figure 23.13

- **if GFR rises**
  - the flow of tubular fluid increases and more NaCl is reabsorbed
  - macula densa stimulates JG cells with a paracrine
  - JG cells contract which constricts afferent arteriole, reducing GFR to normal OR
  - mesangial cells may contract, constricting the capillaries and reducing filtration
- **if GFR falls**
  - macula relaxes afferent arterioles and mesangial cells
  - blood flow increases and GFR rises back to normal.

Effectiveness of Autoregulation

- maintains a dynamic equilibrium - GFR fluctuates within narrow limits only
  - blood pressure changes do affect GFR and urine output somewhat

- 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
  - occurs in hypovolemic shock

Negative Feedback Control of GFR

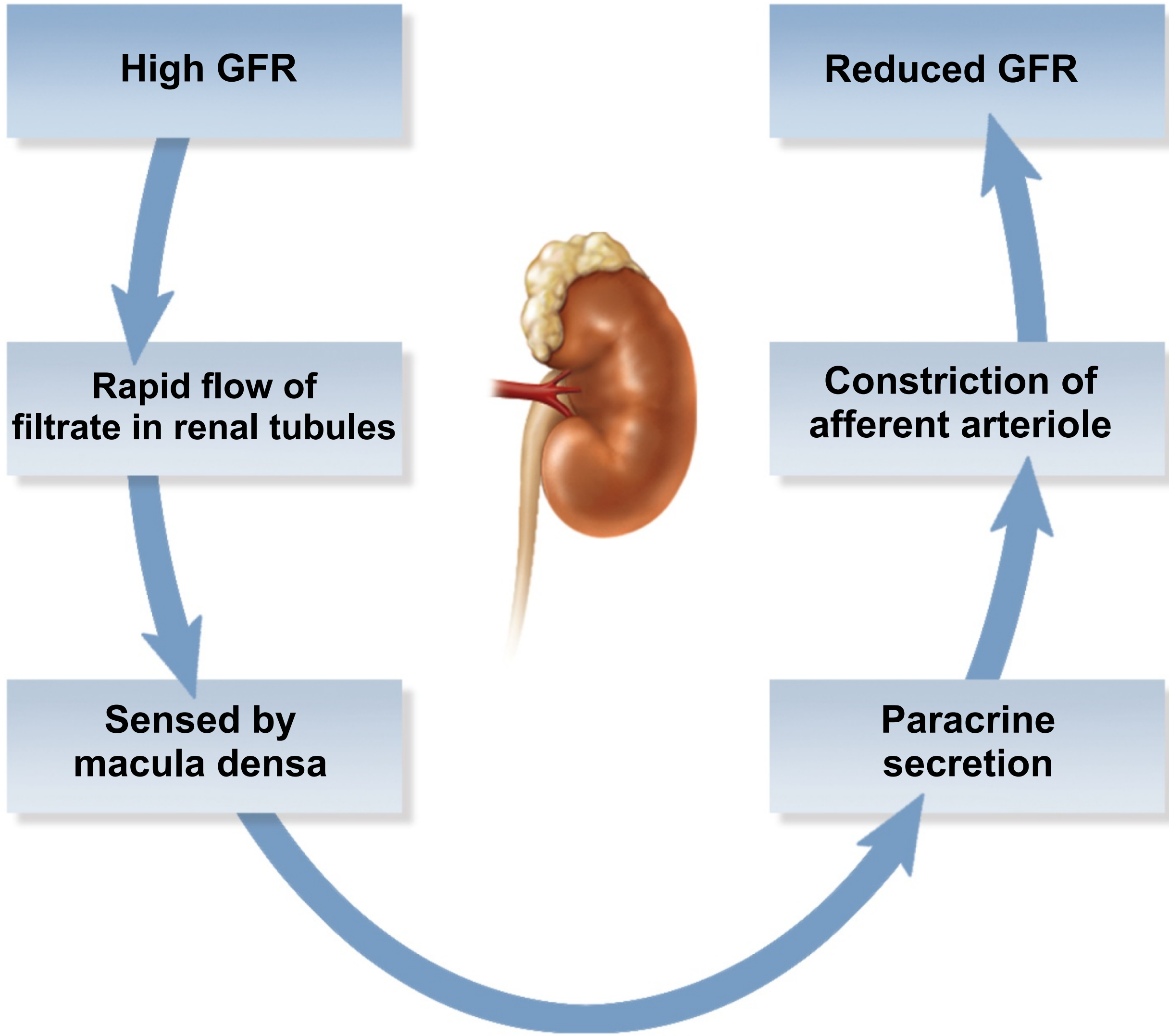


Figure 23.14

Sympathetic Control of GFR

- 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

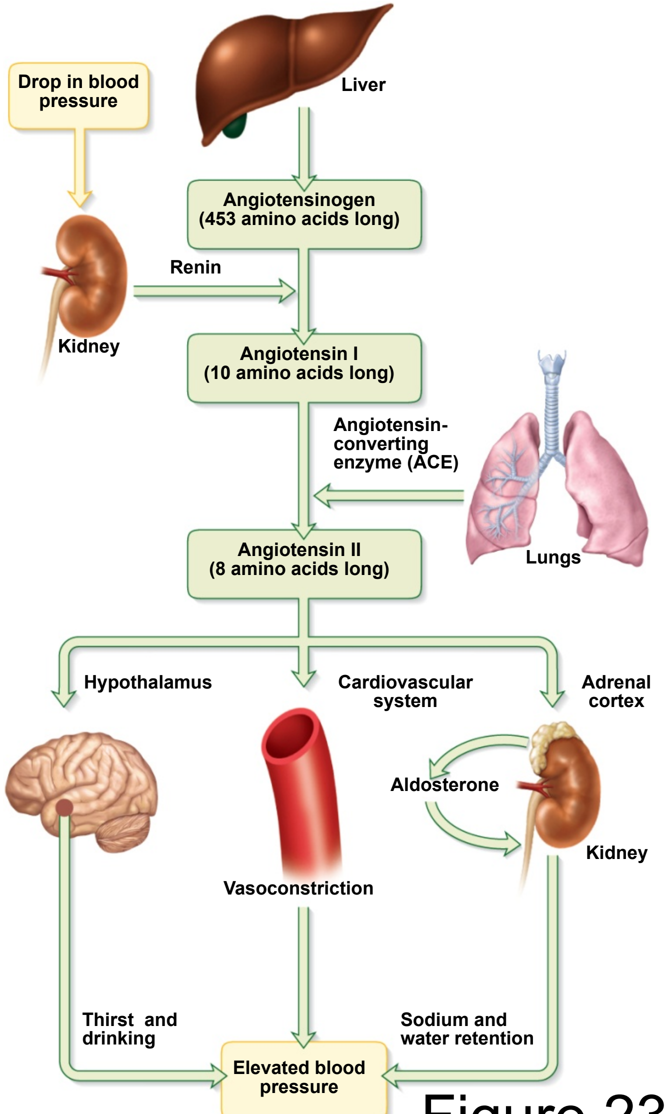


Figure 23.15

- ***renin*** secreted by juxtaglomerular cells if BP drops dramatically
- renin converts **angiotensinogen**, a blood protein, into **angiotensin I**
- in the **lungs and kidneys**, **angiotensin-converting enzyme (ACE)** converts angiotensin I to **angiotensin II**, the active hormone
  - works in several ways to restore fluid volume and BP

Falling BP & Angiotensin II

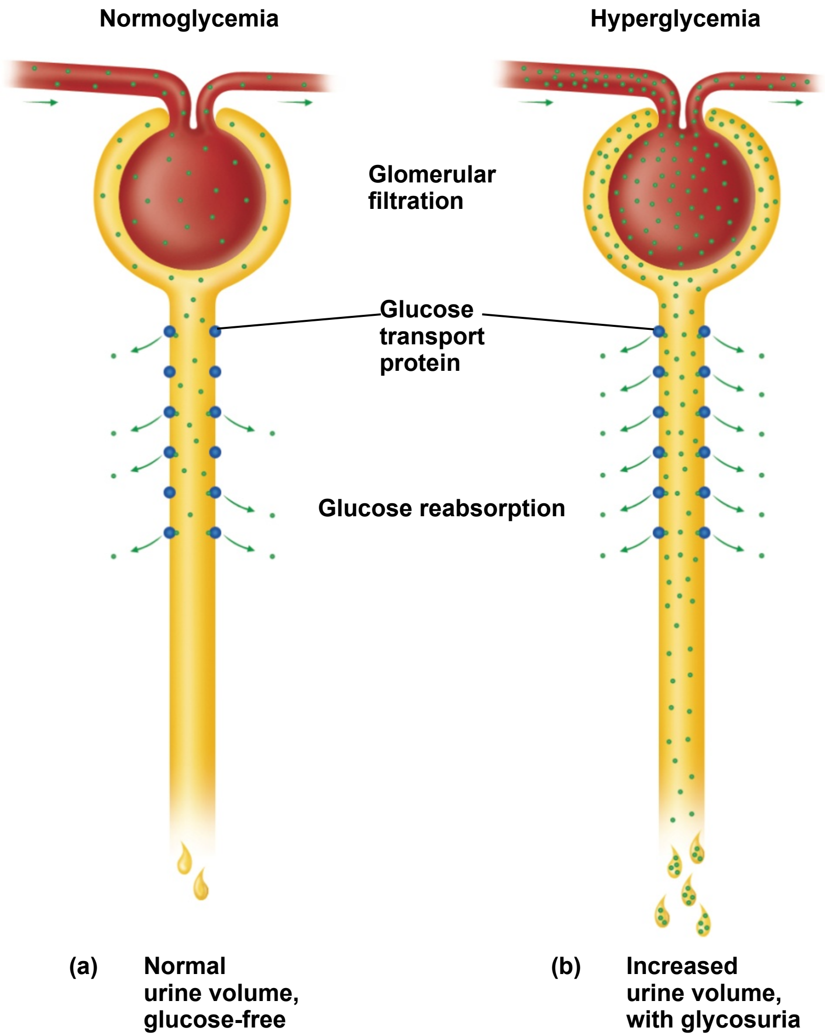


Figure 23.18

- 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 promoting Na^+ and H_2O reabsorption in DCT and collecting duct
- stimulates posterior pituitary to secrete ADH which promotes water reabsorption by collecting duct
- stimulates thirst & H_2O intake

Urine Formation II: Tubular Reabsorption and Secretion

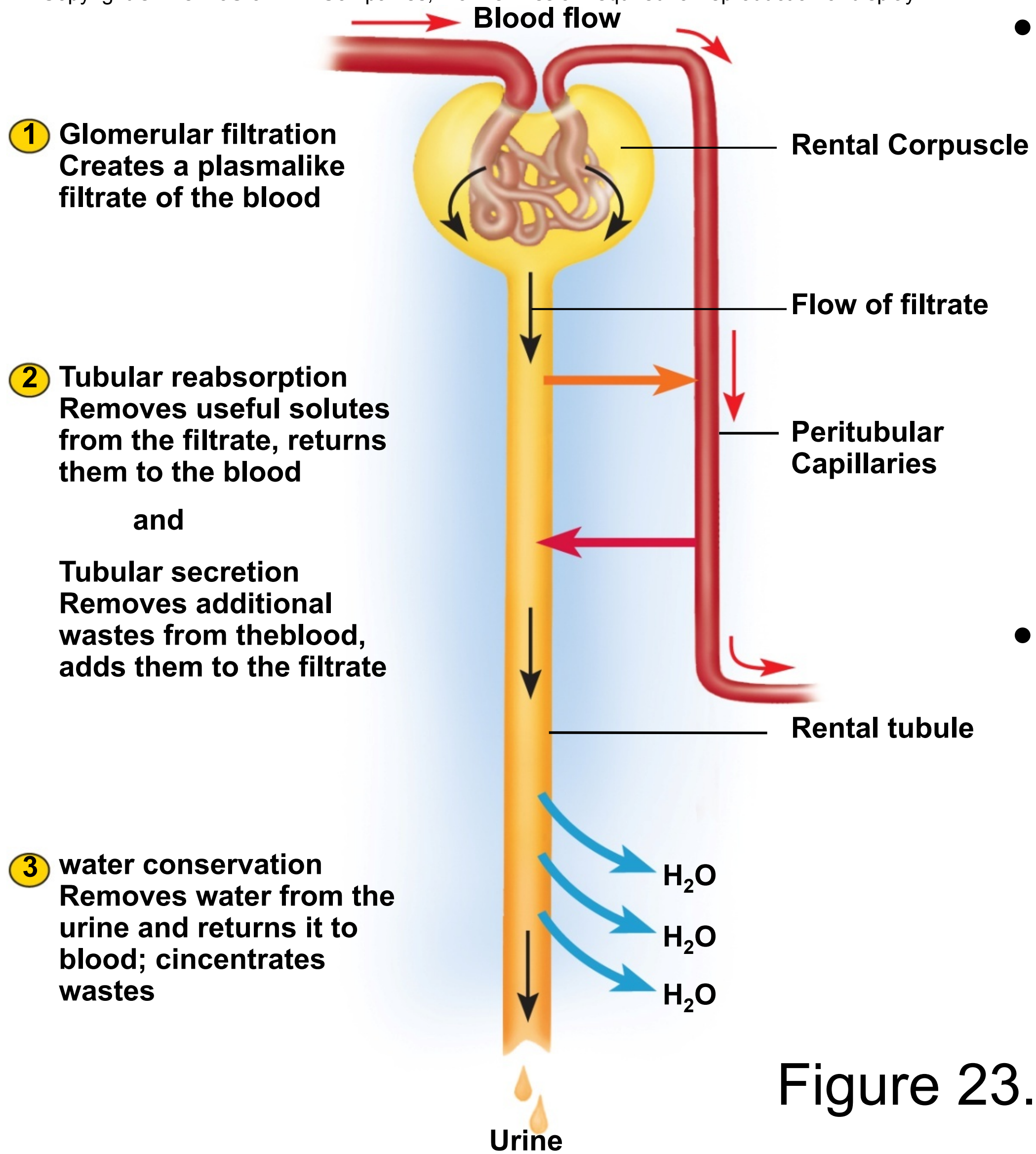


Figure 23.9

- 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

Proximal Convoluted Tubule

- **PCT reabsorbs about 65% of glomerular filtrate**, removes some substances from the blood, and **secretes** them into the 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 the tubular fluid and returning them to the blood
- **two routes of reabsorption**
  - **transcellular route**
    - substances pass through the cytoplasm of the PCT epithelial cells and out their base
  - **paracellular route**
    - substances pass between PCT cells
    - junctions between epithelial cells are quite leaky and allow significant amounts of water to pass through
    - **solvent drag** – water carries with it a variety of dissolved solutes
- taken up by **peritubular capillaries**

Sodium Chloride

- **sodium reabsorption** is the key to everything else
  - creates an osmotic and electrical gradient that drives the reabsorption of water and other solutes
  - most abundant cation in filtrate
  - creates steep concentration gradient that favors its diffusion into the 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
  - a Na^+ - H^+ antiport that pulls Na^+ into the cell while pumping out H^+ into tubular fluid

- sodium is prevented from accumulating in the epithelial cells by **Na^+ - K^+ pumps** in the basal surface of the epithelium
  - pumps Na^+ out into the extracellular fluid
  - picked up by peritubular capillaries and returned to the blood stream
  - ATP consuming active transport pumps
  - **secondary active transport** – Na^+ transporting symports in apical cell membrane do not consume ATP, are considered an example of secondary active transport for their dependence on the Na^+ - K^+ pumps at the base of the cell

- 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

Reabsorption in the PCT
Other Electrolytes

- **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} occurs later in the nephron
- **glucose** is cotransported with Na^+ by **sodium-glucose transport (SGLT) proteins.**
- **urea** diffuses through the tubule epithelium with water – reabsorbs 40 – 60% in tubular fluid
  - kidneys remove about half of the urea from the blood - creatinine is not reabsorbed at all

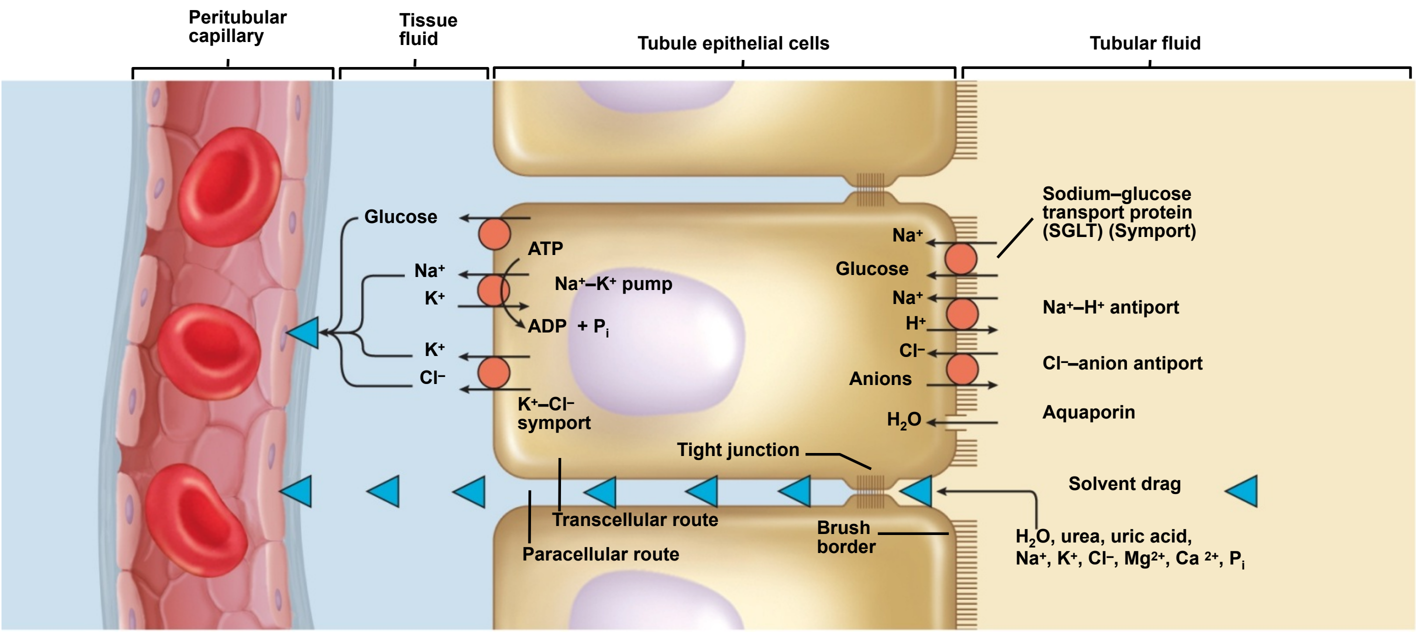


Figure 23.16

Water Reabsorption

- kidneys reduce 180 L of glomerular filtrate to 1 or 2 liters of urine each day
- two-thirds of water in filtrate is reabsorbed by the PCT
- reabsorption of all the salt and organic solutes makes the tubule cells and tissue fluid hypertonic
  - water follows solutes by osmosis through both paracellular and transcellular routes through water channels called **aquaporins**
  - in PCT, water is reabsorbed at constant rate called **obligatory water reabsorption**

Uptake by the Peritubular Capillaries

- after water and solutes leave the basal surface of the tubular epithelium, they are reabsorbed by the peritubular capillaries
  - reabsorbed by osmosis and solvent drag

- three factors promote osmosis into the capillaries
  - accumulation of reabsorbed fluid around the basolateral sides of epithelial cell creates **high interstitial fluid pressure** that drives water into the capillaries
  - narrowness of efferent arterioles **lowers blood hydrostatic pressure** in peritubular capillaries so there is less resistance to absorption
  - proteins remain in blood after filtration, which **elevates colloid osmotic pressure**
    - high COP and low BHP in the capillaries and high hydrostatic pressure in the tissue fluid, the balance of forces in the peritubular capillaries favors absorption

Transport Maximum of Glucose

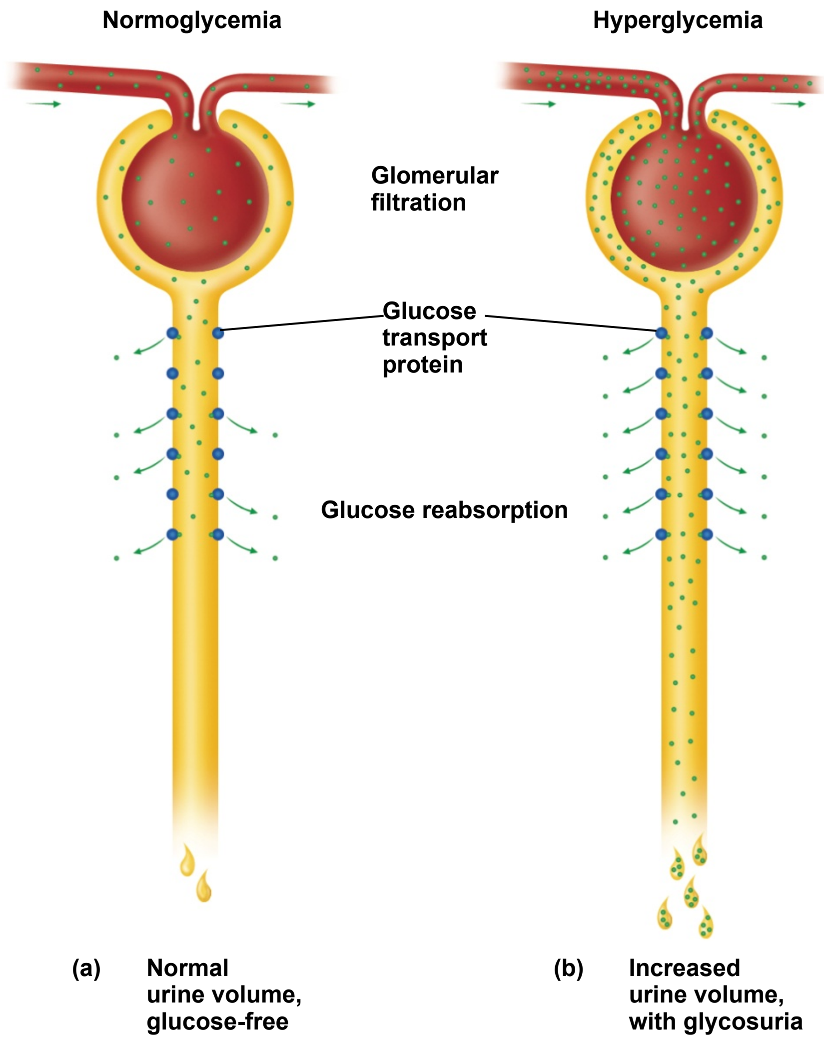


Figure 23.18

- there is a limit to the amount of solute that the renal tubules can reabsorb
- limited by the **number of transport proteins** in the plasma membrane
- if all transporters are occupied as solute molecules pass
  - excess solutes appear 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** – process in which the renal tubule extracts chemicals from the capillary blood and secretes them into tubular fluid

- two purposes in proximal convoluted tubule and nephron loop
  - **waste removal**
    - urea, uric acid, bile acids, ammonia, catecholamines, prostaglandins and a little creatinine are secreted into the tubule
    - secretion of uric acid compensates for its reabsorption earlier in PCT
    - clears blood of pollutants, morphine, penicillin, aspirin, and other drugs
      - explains need to take prescriptions 3 to 4 times/day to keep pace with the rate of clearance
  - **acid-base balance**
    - secretion of hydrogen and bicarbonate ions help regulate the pH of the body fluids

Function of 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^-
    - ions leave cells by active transport and diffusion
      - NaCl remains in the tissue fluid of renal medulla
      - water can not follow since thick segment is impermeable
  - tubular fluid very dilute as it enters distal convoluted tubule

DCT and Collecting Duct

- fluid arriving in the DCT still contains about 20% of the water and 7% of the salts from glomerular filtrate
  - if this were all passed as urine, it would amount to 36 L/day

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

- **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^+

DCT and Collecting Duct

- **aldosterone** - the "salt-retaining" hormone
  - steroid secreted by the adrenal cortex
    - when blood Na^+ concentration falls or
    - when K^+ concentration rises
    - or drop in blood pressure → renin release → angiotensin II formation → stimulates adrenal cortex to secrete aldosterone
- **functions of aldosterone**
  - acts on thick segment of nephron loop, DCT, and cortical portion of collecting duct
    - stimulates the reabsorption of more 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
    - the urine volume is reduced
    - the urine has an elevated K^+ concentration

DCT and Collecting Duct

- **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 - ↑ GFR
  - inhibits renin and aldosterone secretion
  - inhibits secretion of ADH
  - inhibits NaCl reabsorption by collecting duct

DCT and Collecting Duct

- **antidiuretic hormone** (ADH) secreted by posterior lobe of pituitary
- in response to dehydration and rising blood osmolarity
  - stimulates hypothalamus
  - hypothalamus stimulates posterior pituitary
- action - make collecting duct more permeable to water
  - water in the tubular fluid reenters the tissue fluid and bloodstream rather than being lost in urine

DCT 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, the calcium ions stay in circulation rather than precipitating into the bone tissue as calcium phosphate
  - PTH stimulates calcitriol synthesis by the epithelial cells of the PCT

Summary of Tubular Reabsorption and Secretion

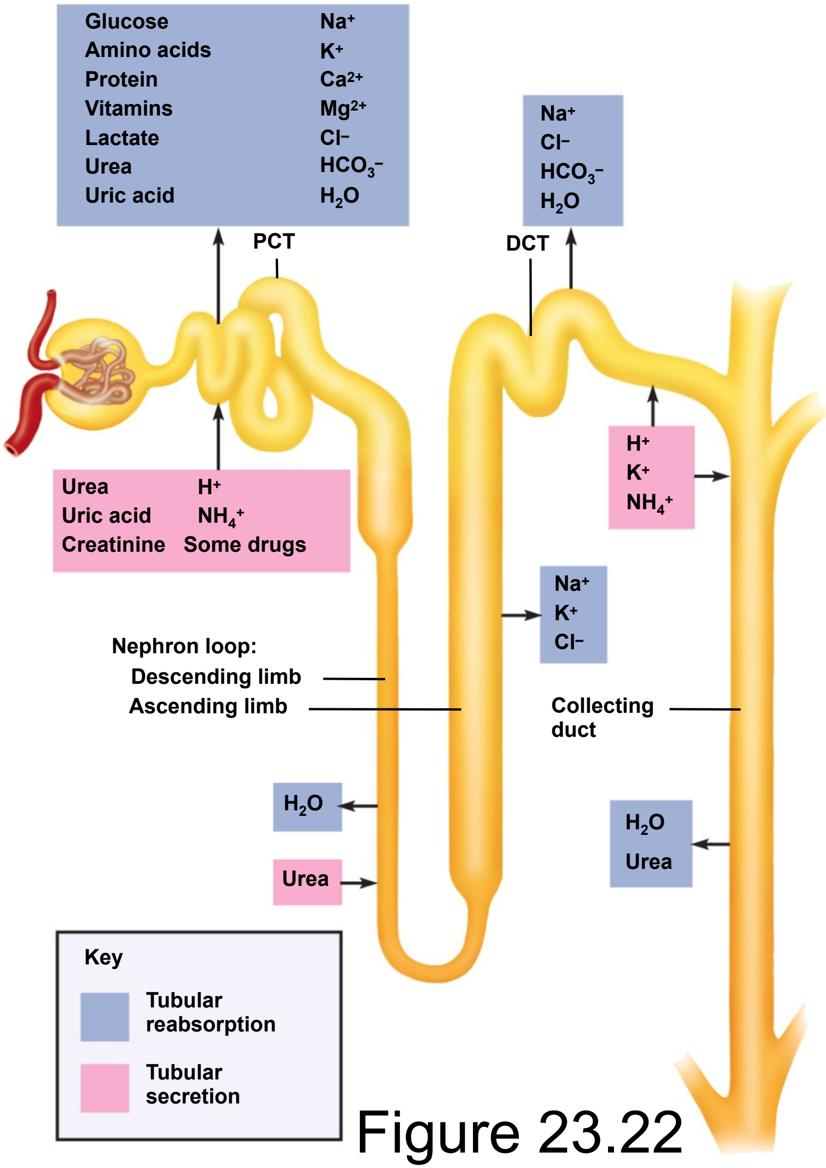


Figure 23.22

- **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

Urine Formation III: Water Conservation

- the kidney eliminates metabolic wastes from the body, but also prevents excessive water loss as well
- 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 Concentrates Urine

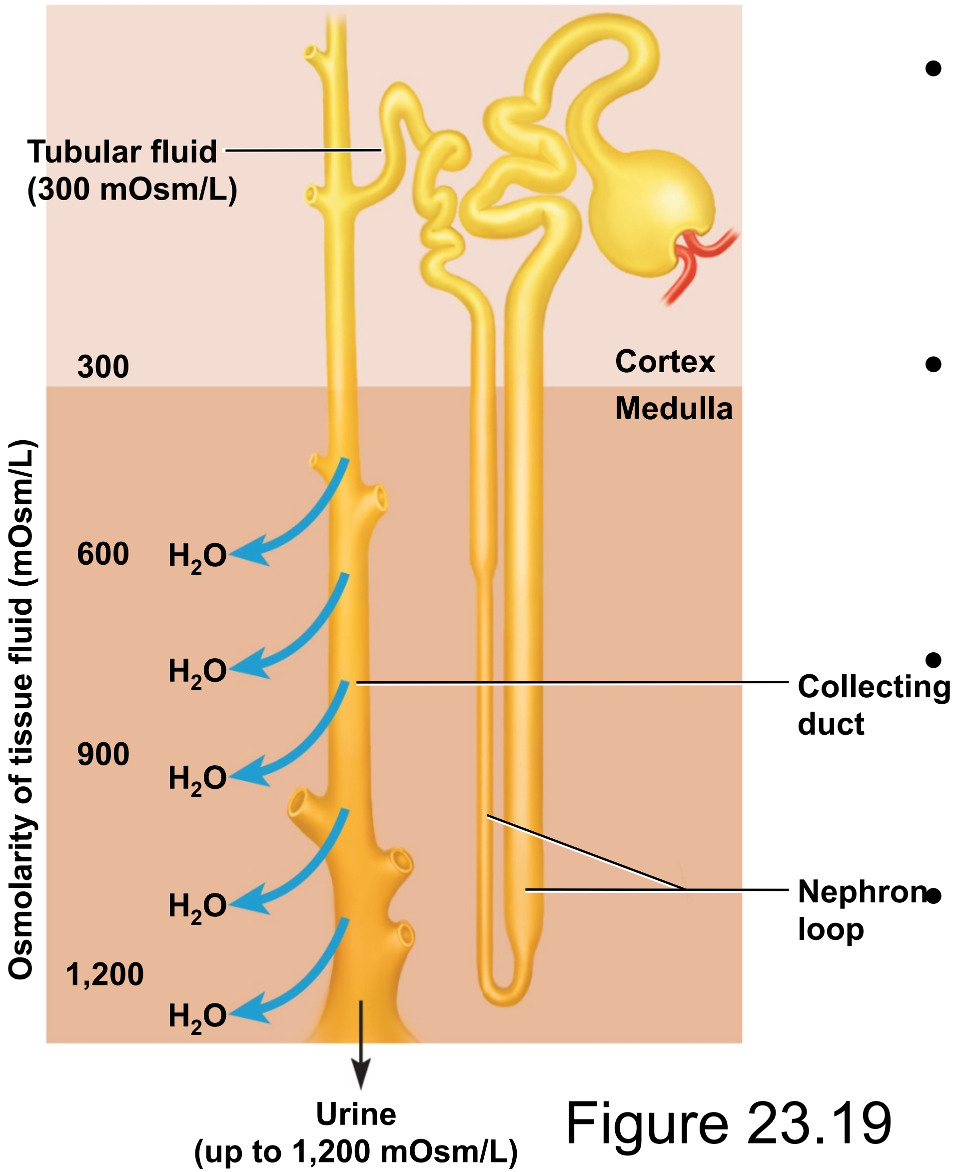


Figure 23.19

- collecting duct (CD) begins in the cortex where it receives tubular fluid from several nephrons
- as CD passes through the medulla, it reabsorbs water and concentrates urine 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 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 removed from the urine stays in the CD
  - urine concentration may be as low as 50 mOsm/L
- producing **hypertonic urine**
  - dehydration causes the urine to become 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 more time for reabsorption –
  - more salt removed, more water reabsorbed and less urine produced

Countercurrent Multiplier

- the ability of kidney to concentrate urine depends on salinity gradient in renal 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 extracellular fluid of medulla which multiplies the salinity in 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
- 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

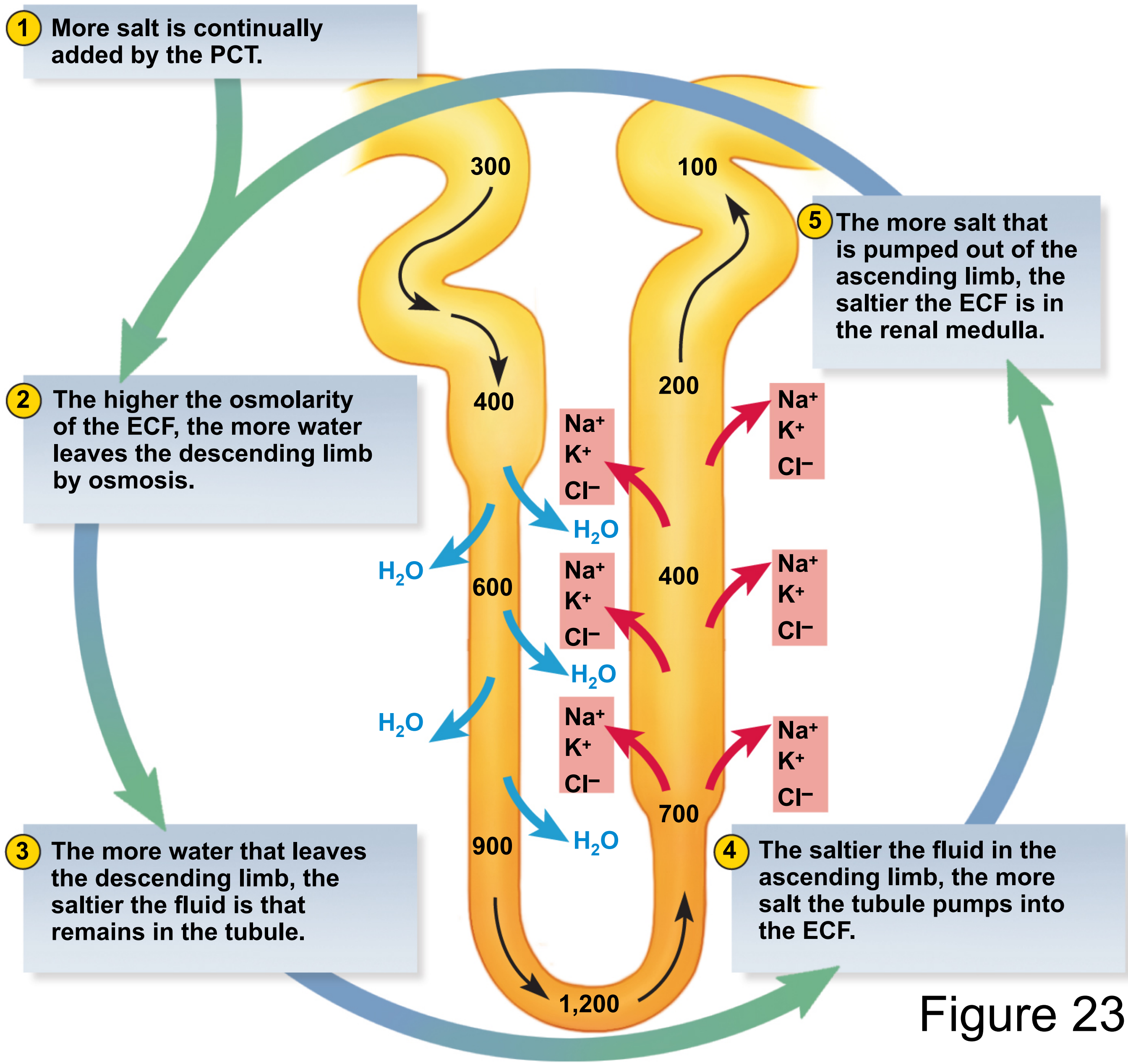


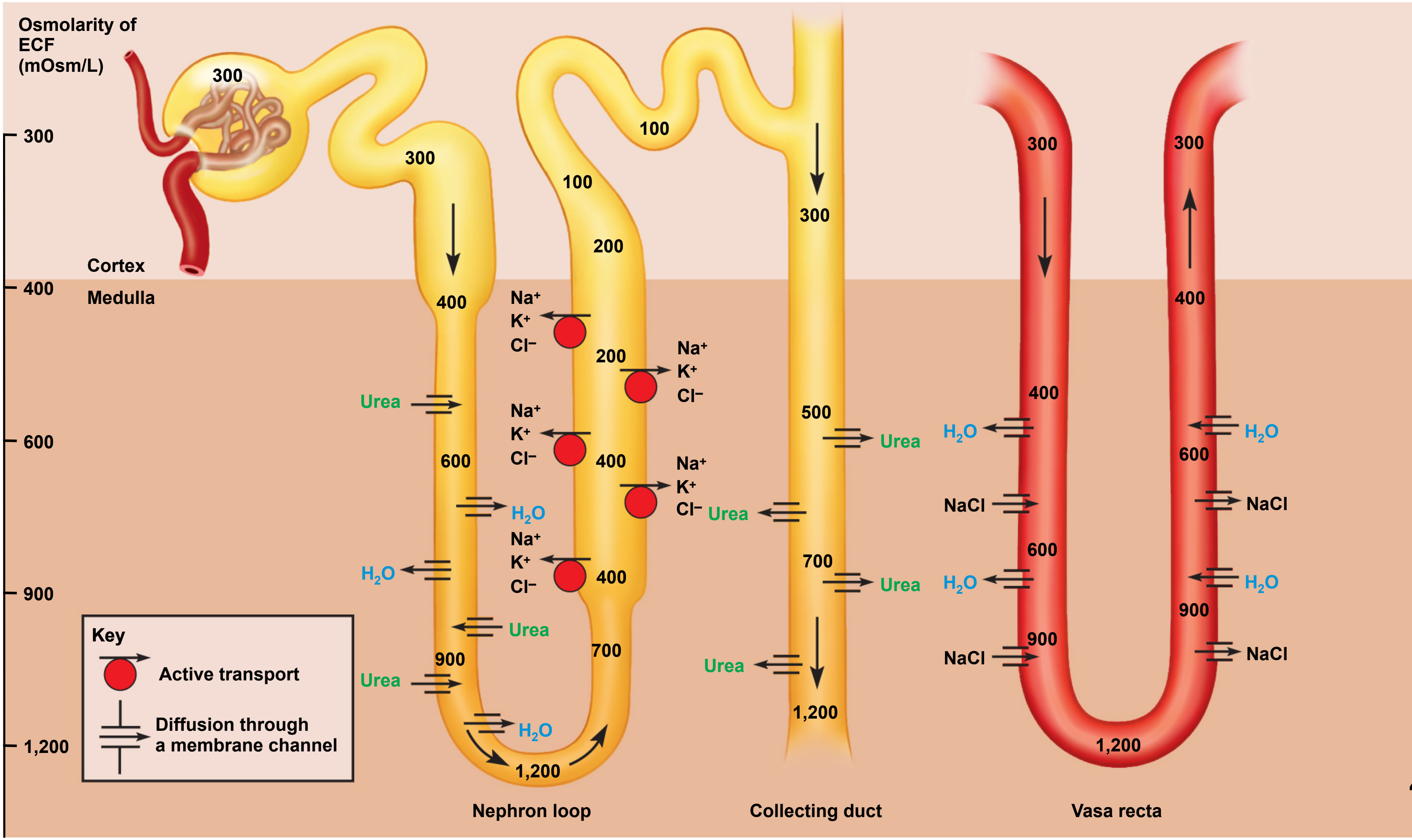
Figure 23.20

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**
  - exchanges water for salt
  - water diffuses out of capillaries and salt diffuses in
- as blood flows back up to the cortex the opposite occurs
- **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, and thus they carry away water reabsorbed from the urine by collecting duct and nephron loop

Maintenance of Osmolarity in Renal Medulla

Figure 23.21



Summary of Tubular Reabsorption and Secretion

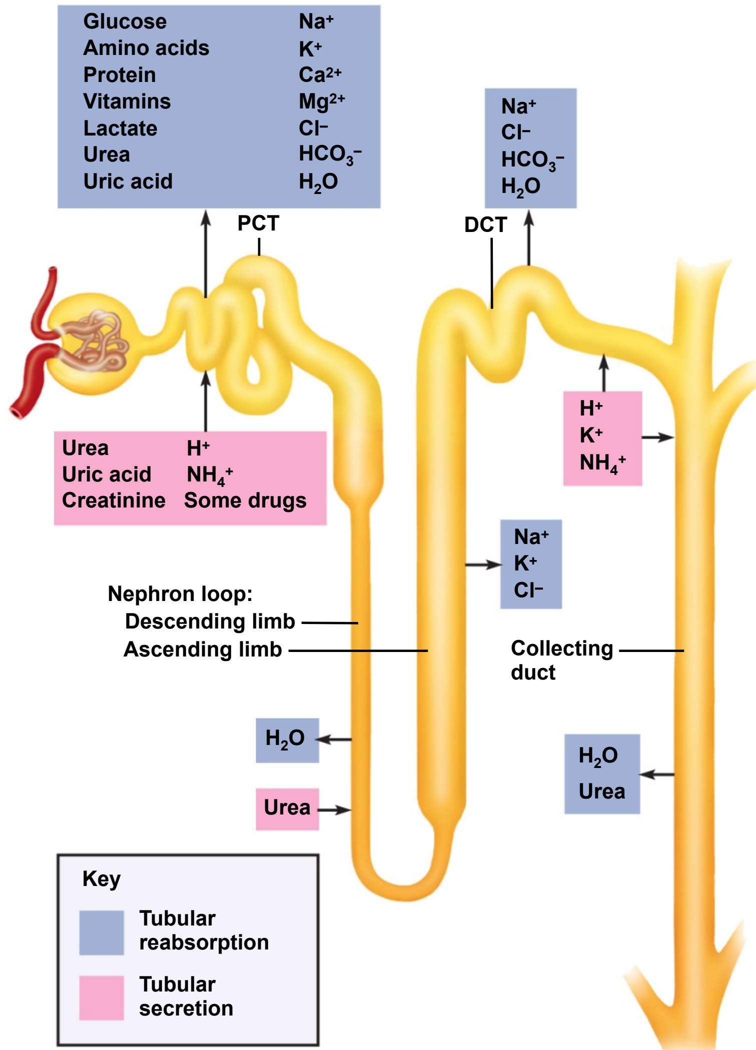


Figure 23.22

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

- **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

Diabetes

- **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** causing not enough water to be reabsorbed in the collecting duct
    - more water passes in urine

Diuretics

- **diuretics** – any chemical that increases urine volume
  - some increase GFR
    - caffeine dilates the afferent arteriole
  - reduce tubular reabsorption of water
    - alcohol inhibits ADH secretion
  - 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

- 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
- determine renal clearance
- determine glomerular filtration rate

Renal Clearance

- **renal clearance** – the volume of blood plasma from which a particular waste is completely removed in 1 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

- **determine renal clearance** (C) by collecting blood and urine samples, measuring the waste concentration in each, and measuring the rate of urine output:
  - 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
  - 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 - 48% which is normal for urea

Glomerular Filtration Rate

- kidney disease often results in lowering of GFR –need to measure patient's GFR
  - can not use clearance rate of urea
    - some urea filtered by glomerulus is reabsorbed in the tubule
    - some urea is secreted into the tubule
- need a substance that is not secreted or 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 or secreted by the renal tubule
  - inulin GFR = renal clearance on inulin
- clinically GFR is estimated from **creatinine excretion**
  - does not require injecting a substance or drawing blood to determine its blood concentration

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 of this timely release