RENAL PHYSIOLOGY

Danil Hammoudi.MD

Functions

- Regulating blood ionic composition
- Regulating blood pH
- Regulating blood volume
- Regulating blood pressure
- Produce calcitrol and erythropoietin
- Regulating blood glucose
- Excreting wastes

Urine production maintains homeostasis

- Regulating blood volume and composition
- Excreting waste products
  - Urea
  - Creatinine
  - Uric acid

Basic processes of urine formation

- Filtration
  - Blood pressure
  - Water and solutes across glomerular capillaries
- Reabsorption
  - The removal of water and solutes from the filtrate
- Secretion
  - Transport of solutes from the peritubular fluid into the tubular fluid

Carrier Mediated Transport

- Filtration in the kidneys modified by carrier mediated transport
  - Facilitated diffusion
  - Active transport
  - Cotransport
  - Countertransport
- Carrier proteins have a transport maximum (T_m)
  - Determines renal threshold

Reabsorption and secretion

- Accomplished via diffusion, osmosis, and carrier-mediated transport
- T_m determines renal threshold for reabsorption of substances in tubular fluid

An Overview of Urine Formation

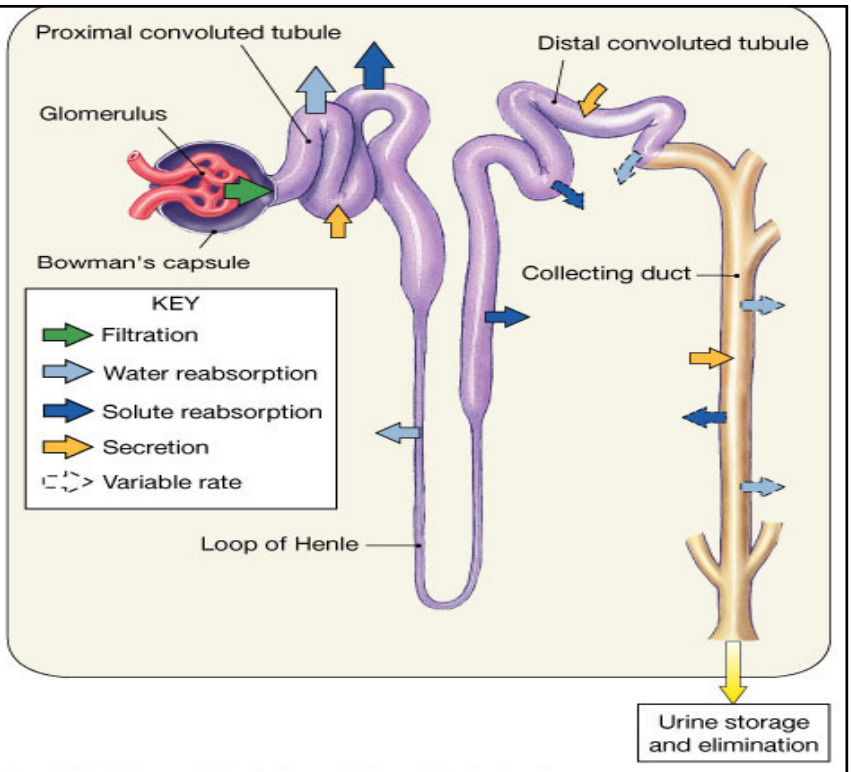


Figure 26.10 Glomerular Filtration

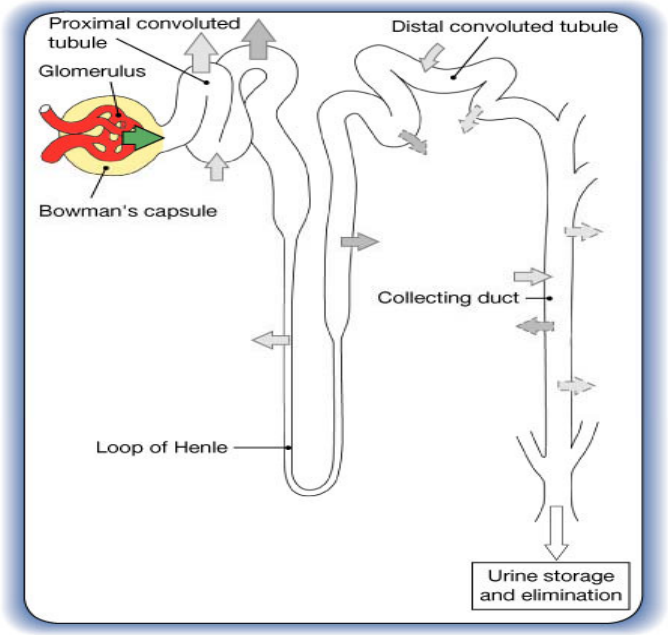


Figure 26.10

Figure 26.10 Glomerular Filtration

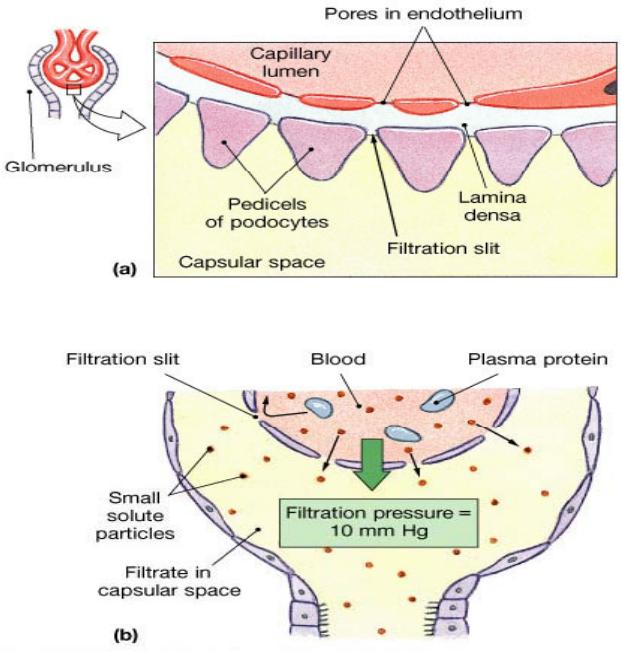


Figure 26.10a, b

Glomerular filtration rate (GFR)

- Amount of filtrate produced in the kidneys each minute
- Factors that alter filtration pressure change GFR

Factors controlling the GFR

- A drop in filtration pressure stimulates Juxtaglomerular apparatus (JGA)
  - Releases renin and erythropoietin

The Response to a Reduction in the GFR

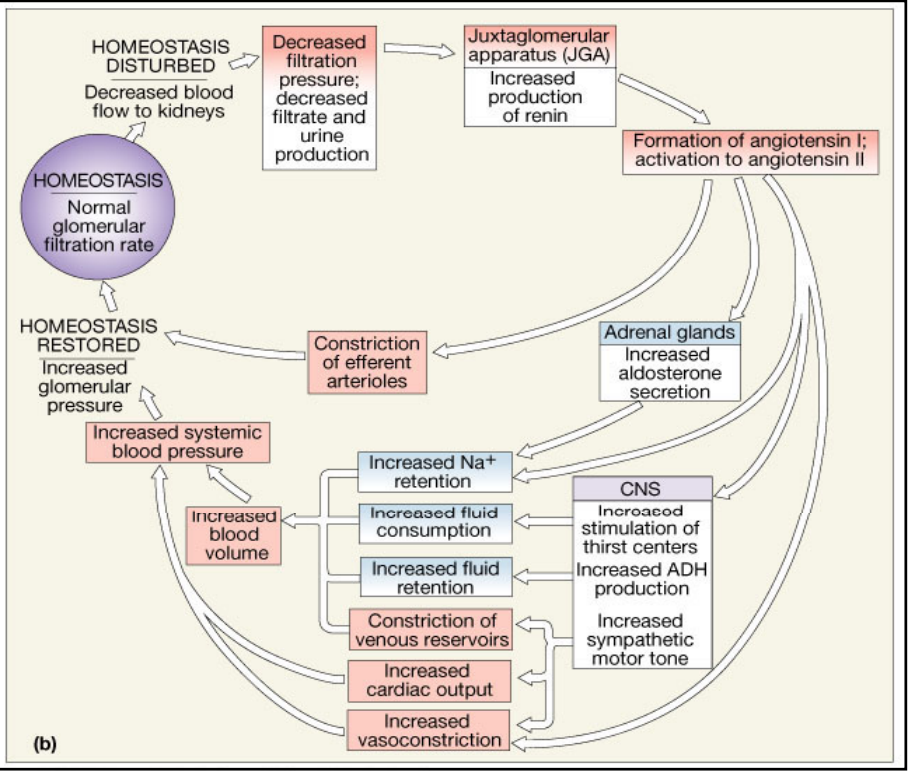


Figure 26.11 The Response to a Reduction in th

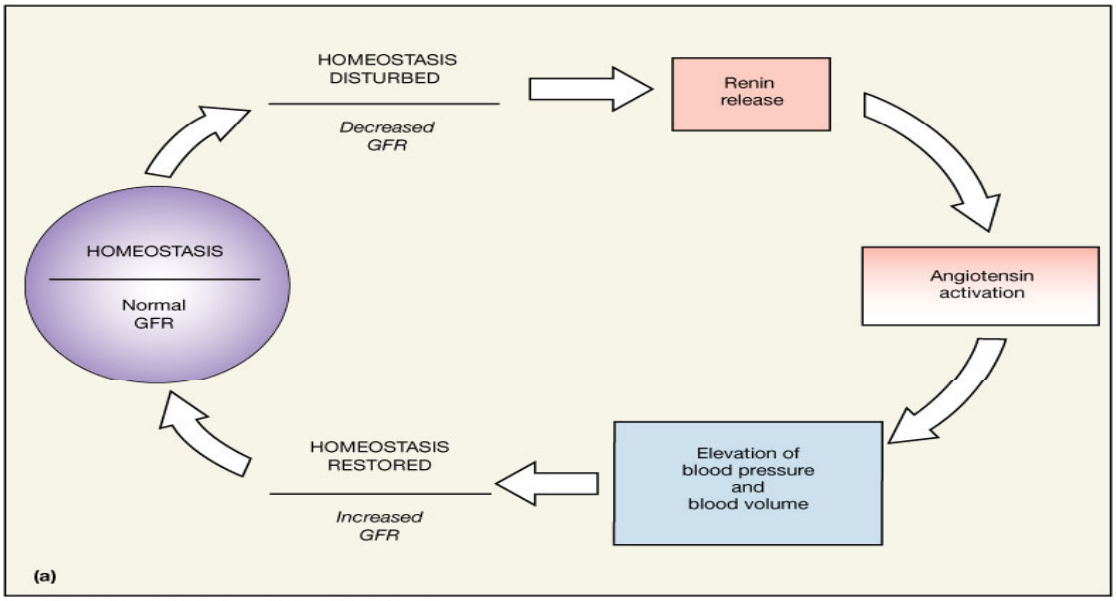


Figure 26.11a

Sympathetic activation

- Produces powerful vasoconstriction of afferent arterioles
  - Decreases GFR and slows production of filtrate
- Changes the regional pattern of blood flow
  - Alters GFR
- Stimulates release of renin by JGA

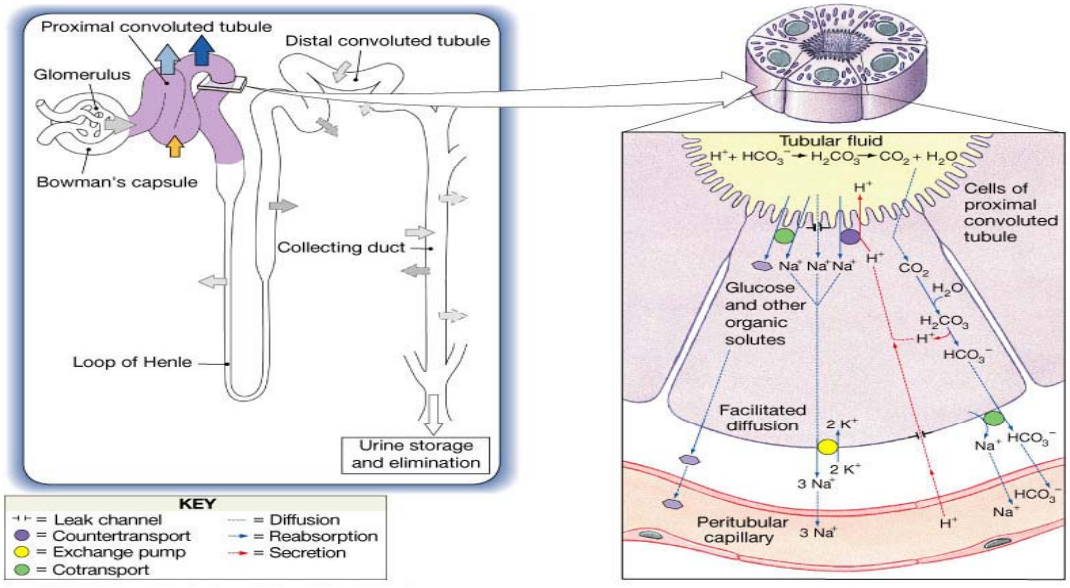
Reabsorption and secretion at the PCT

- Glomerular filtration produces fluid similar to plasma without proteins
- The PCT reabsorbs 60-70% of the filtrate produced
  - Reabsorption of most organic nutrients
  - Active and passive reabsorption of sodium and other ions
  - Reabsorption of water
- Secretion also occurs in the PCT

PLAY Animation: Early Filtrate Processing

PLAY Animation: Glomerular filtration

Figure 26.12 Transport Activities of the PCT



PLAY Animation: Proximal Convoluted Tubule

Figure 26.12

multiplication

- Countercurrent multiplication
  - Between ascending and descending limbs of loop
  - Creates osmotic gradient in medulla
  - Facilitates reabsorption of water and solutes before the DCT
  - Permits passive reabsorption of water from tubular fluid

and Concentration of Urine

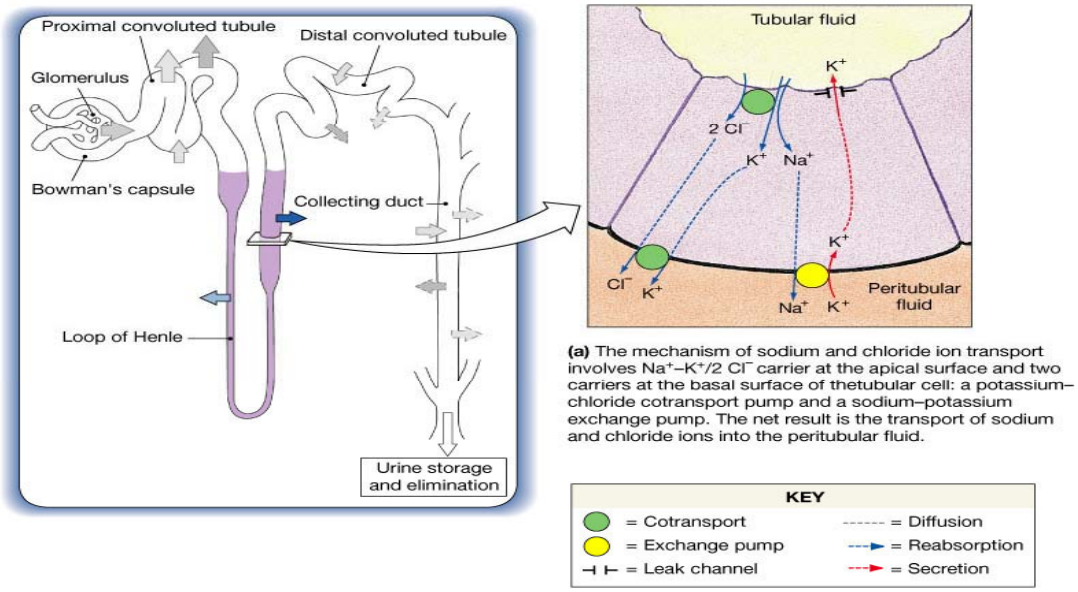
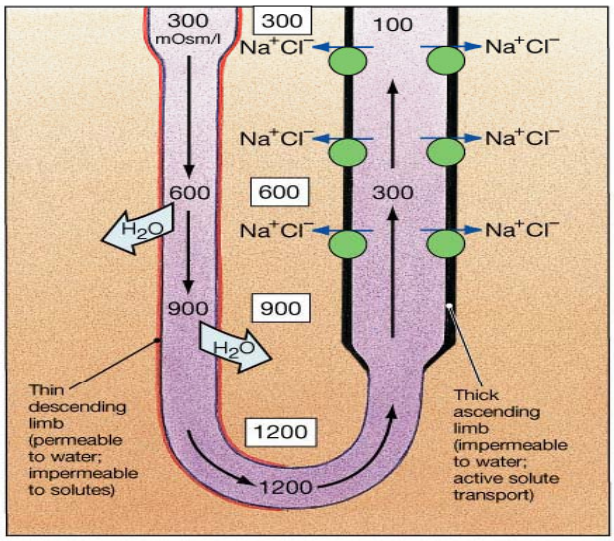


Figure 26.13a

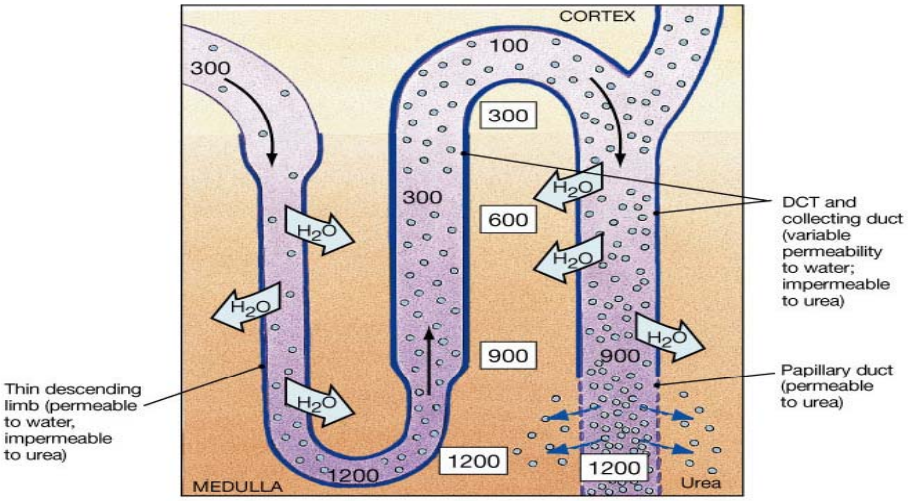
and Concentration of Urine



(b) Active transport of NaCl along the ascending thick limb results in the movement of water from the descending limb.

Figure 26.13b

and Concentration of Urine



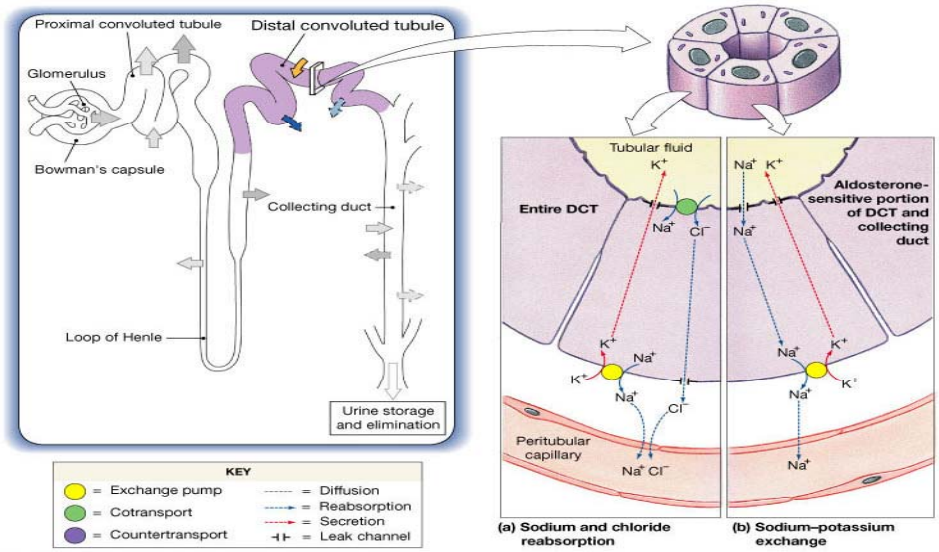
(c) The permeability characteristics of both the loop and the collecting duct tend to concentrate urea in the tubular fluid and in the medulla. The loop of Henle, DCT, and collecting duct are impermeable to urea. As water reabsorption occurs, the urea concentration rises. The papillary ducts' permeability to urea accounts for roughly one-third of the solutes in the deepest portions of the medulla.

Figure 26.13c

Reabsorption and secretion at the DCT

- DCT performs final adjustment of urine
  - Active secretion or absorption
- Absorption
  - Tubular cells actively resorb Na^+ and Cl^-
  - In exchange for potassium or hydrogen ions (secreted)

Reabsorption at the DCT



PLAY Animation: Distal Convoluted Tubule

Figure 26.14

Reabsorption at the DCT

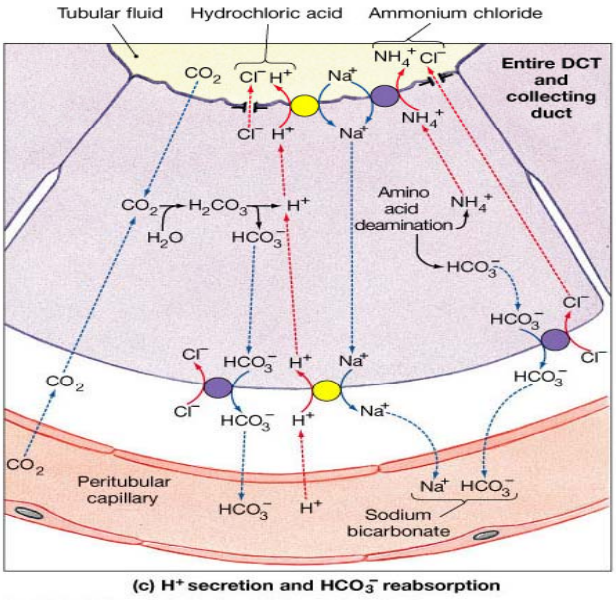


Figure 26.14c

collecting system

- Water and solute loss is regulated by aldosterone and ADH
- Reabsorption
  - Sodium ion, bicarbonate, and urea are resorbed
- Secretion
  - pH is controlled by secretion of hydrogen or bicarbonate ions

concentration

- Urine volume and osmotic concentration are regulated by controlling water reabsorption
  - Precise control allowed via facultative water reabsorption

DCT and Collecting Ducts

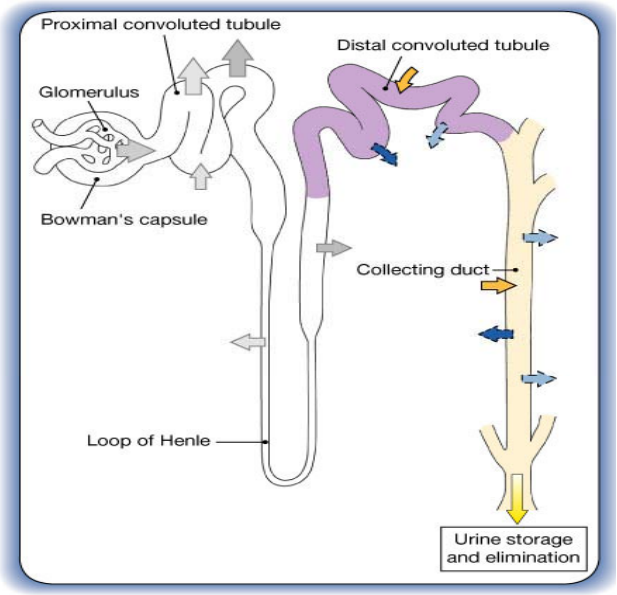


Figure 26.15

DCT and Collecting Ducts

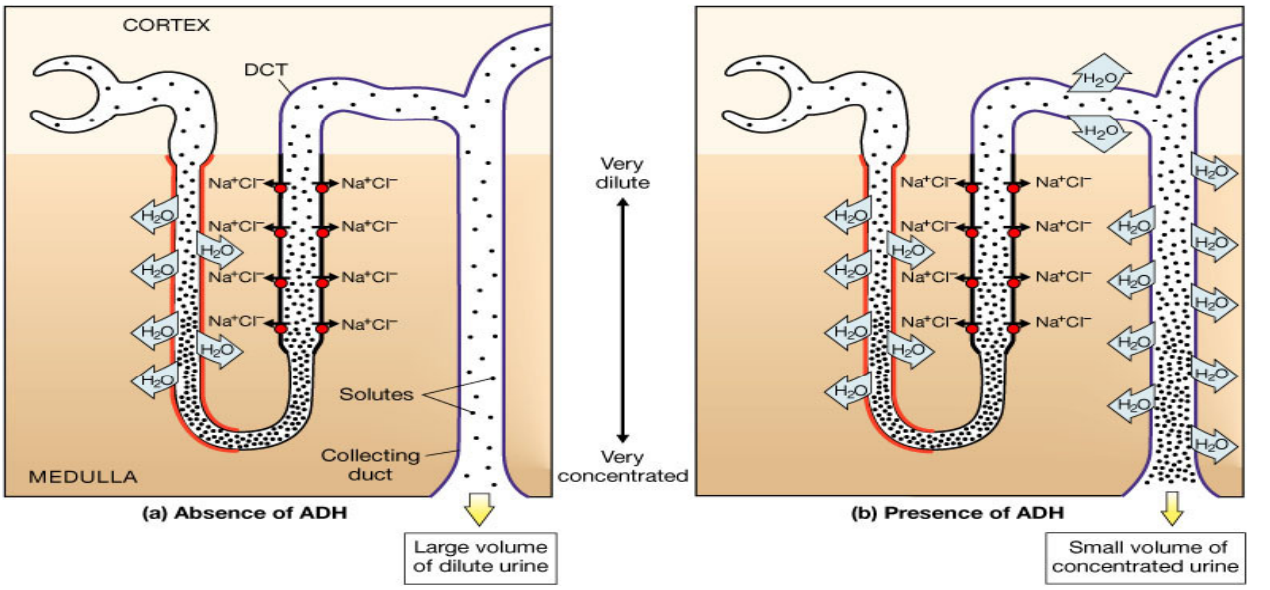


Figure 26.15a, b

Function of the vasa recta

- Removes solutes and water
  - Balances solute reabsorption and osmosis in the medulla

A Summary of Renal Function

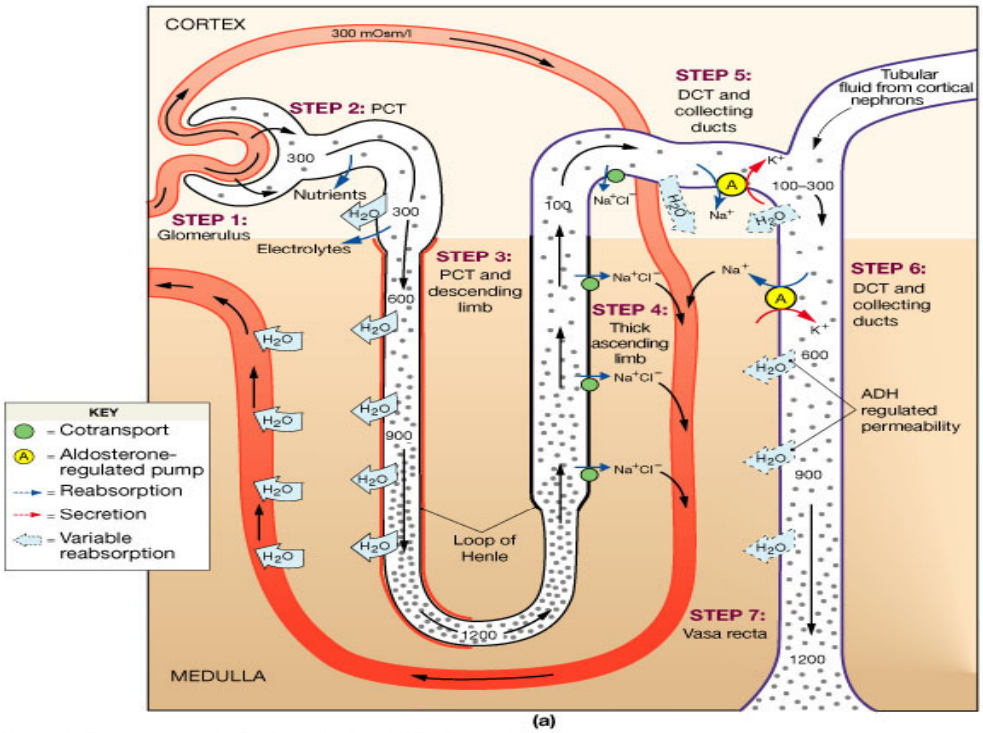


Figure 26.16a

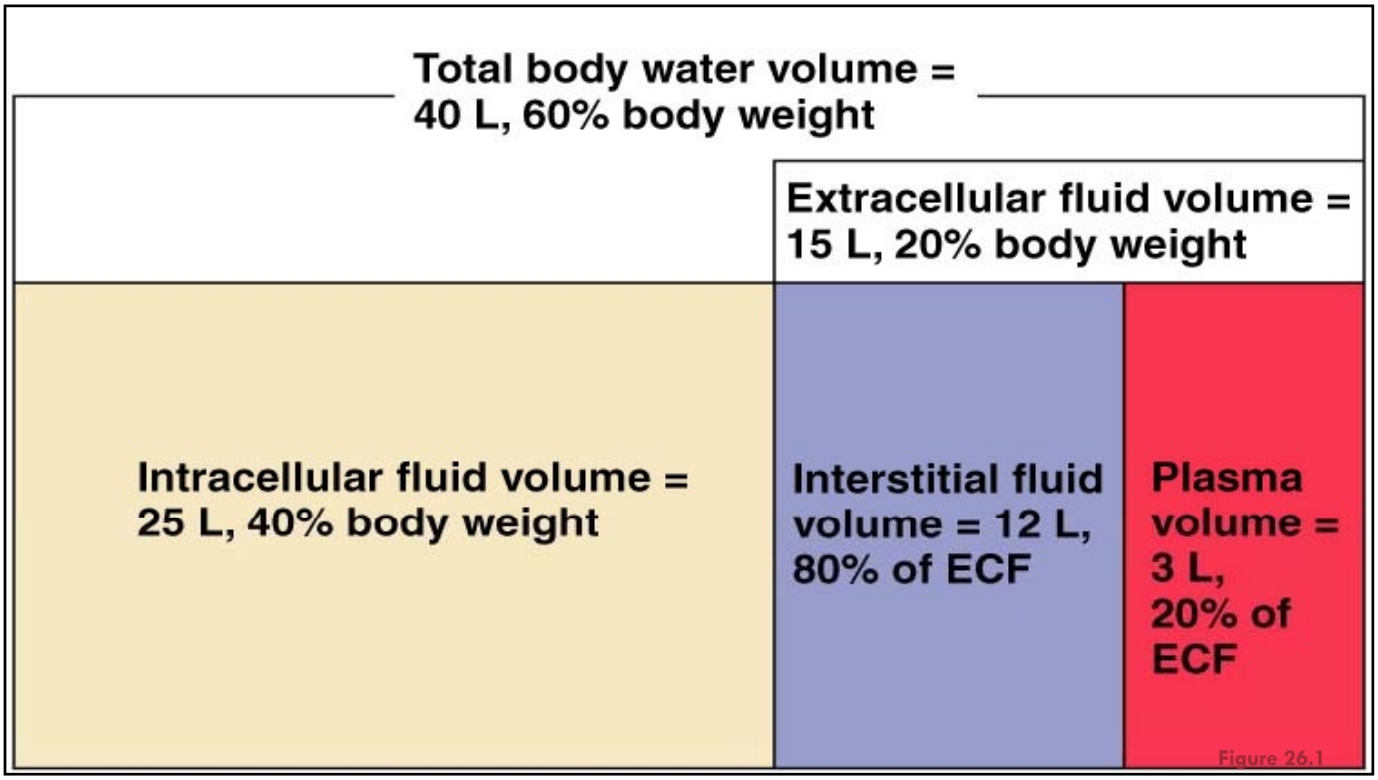


Figure 26.1

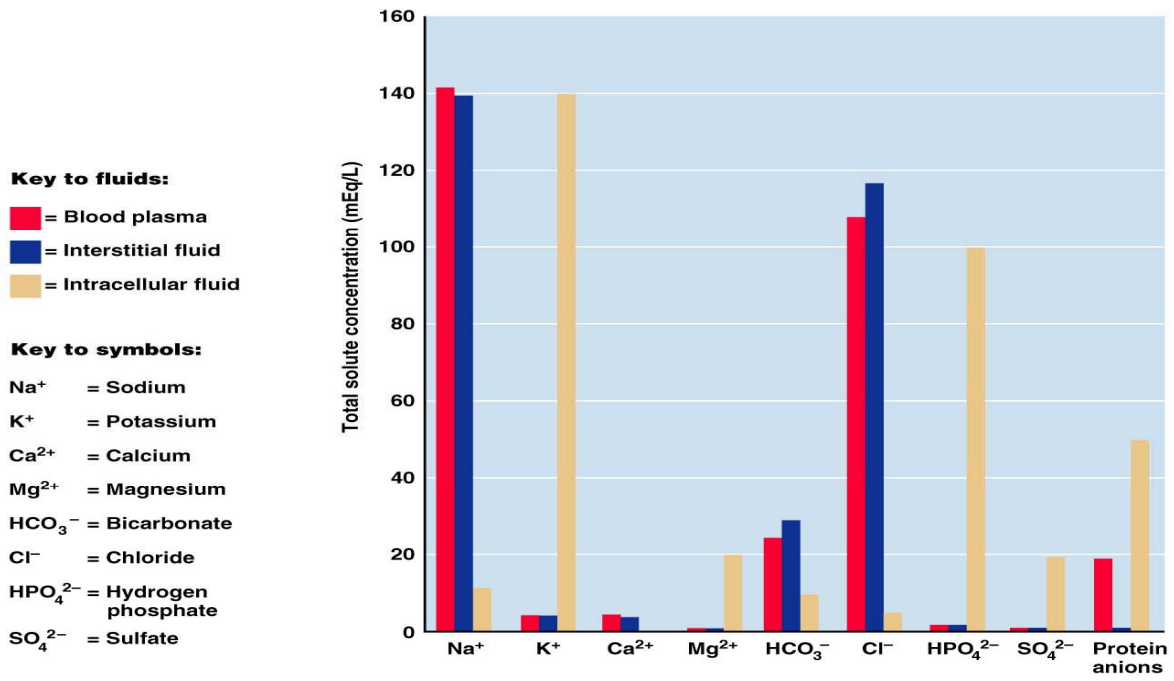


Figure 26.2

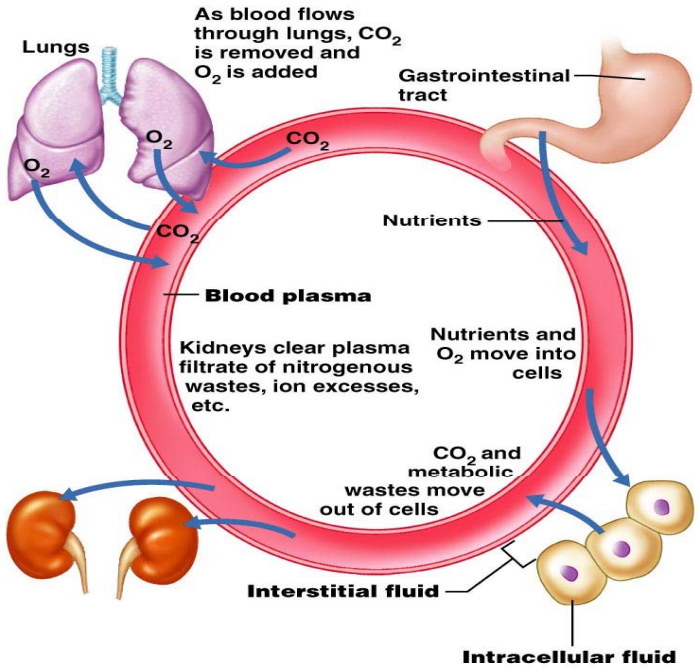


Figure 26.3

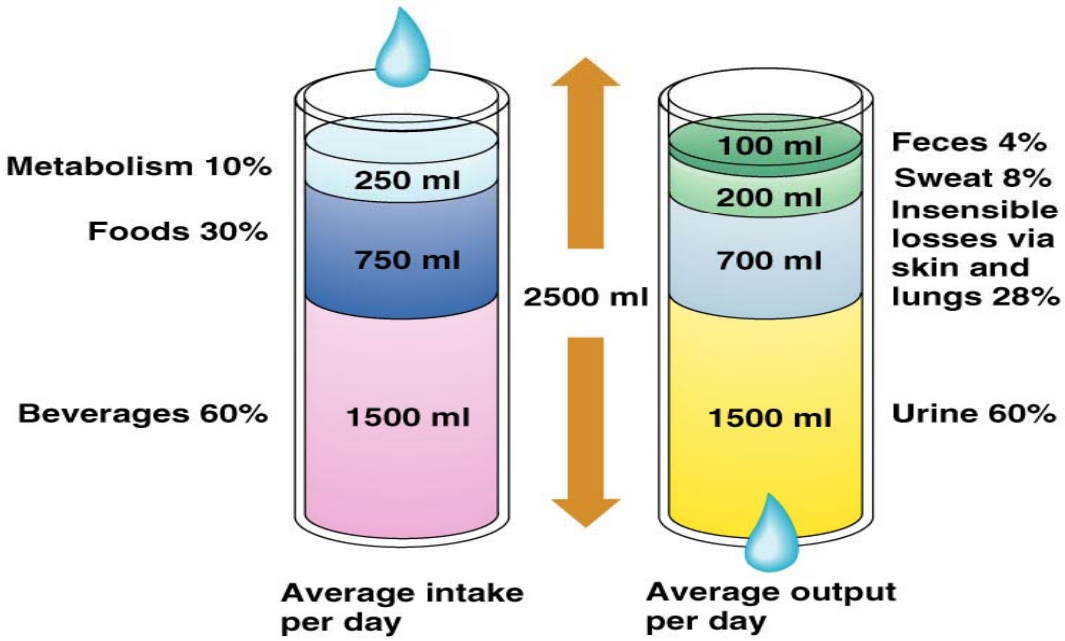


Figure 26.4

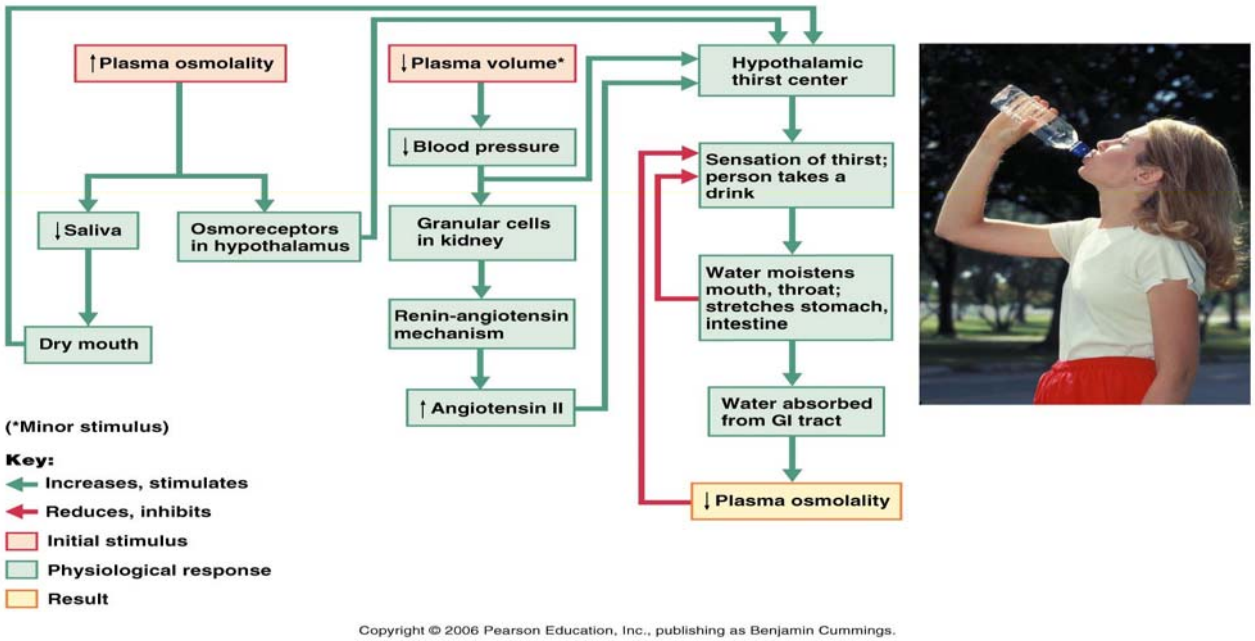


Figure 26.5

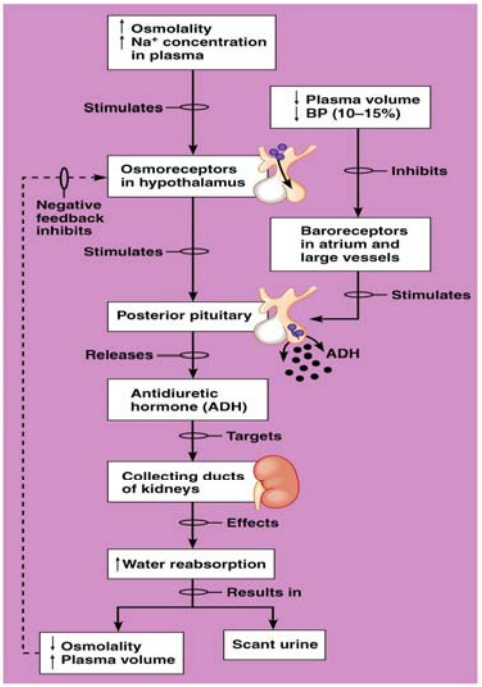


Figure 26.6

(a) Mechanism of dehydration

(b) Mechanism of hypotonic hydration

Figure 26.7

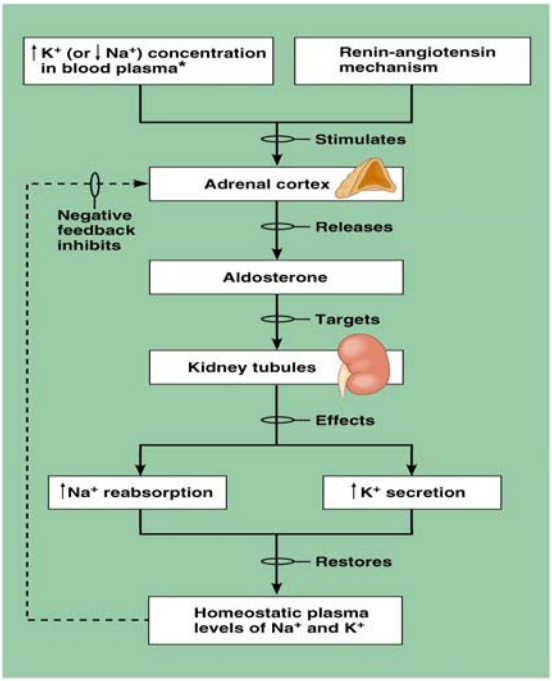


Figure 26.8

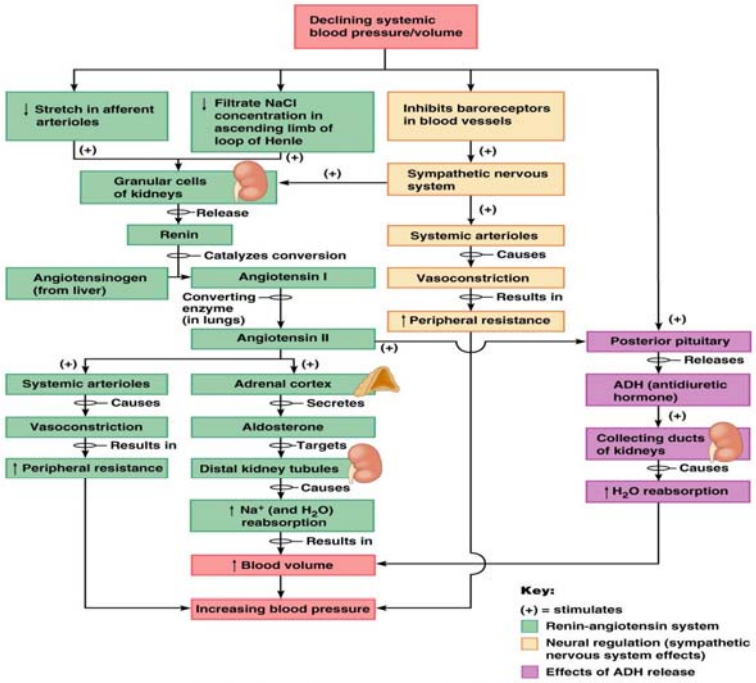


Figure 26.9

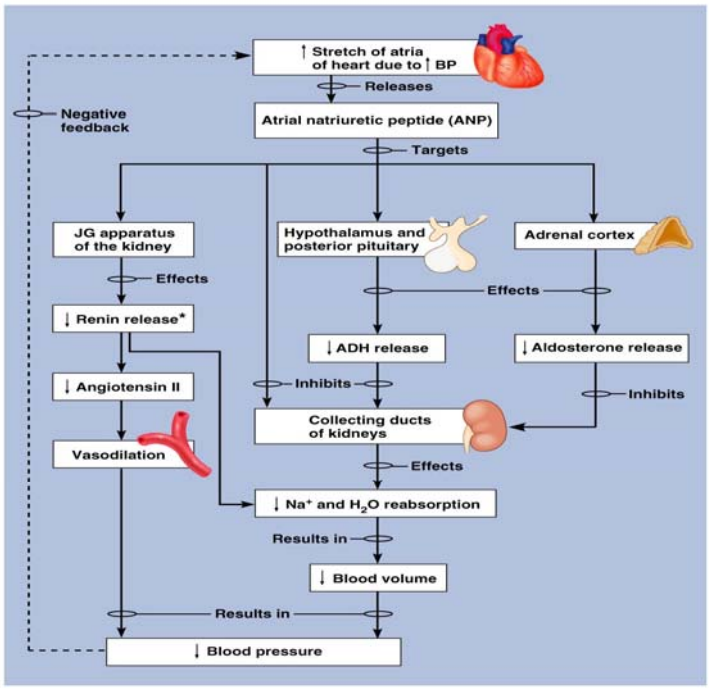


Figure 26.10

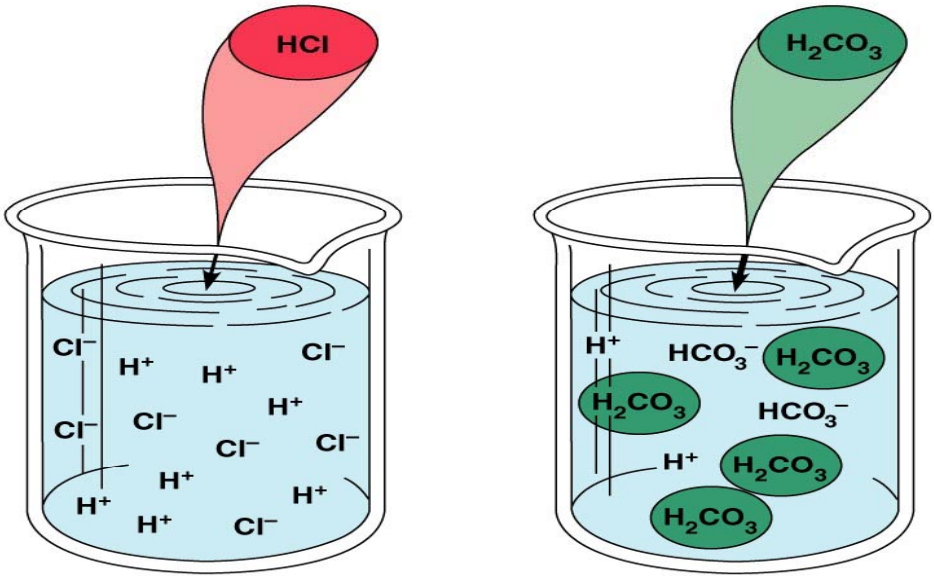


Figure 26.11

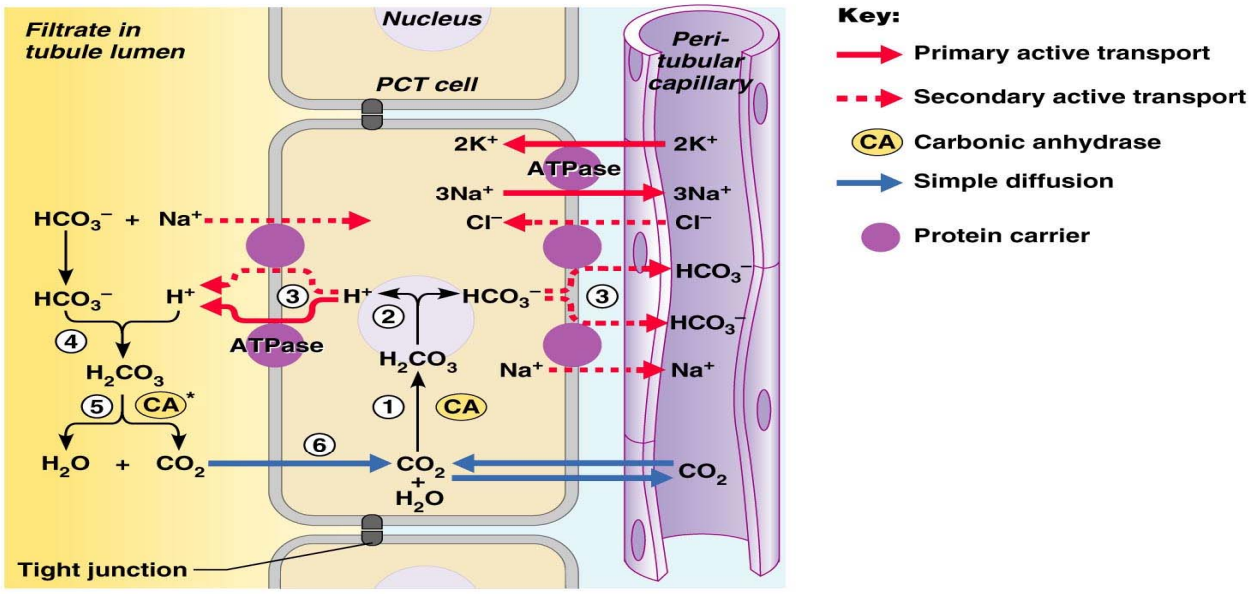


Figure 26.12

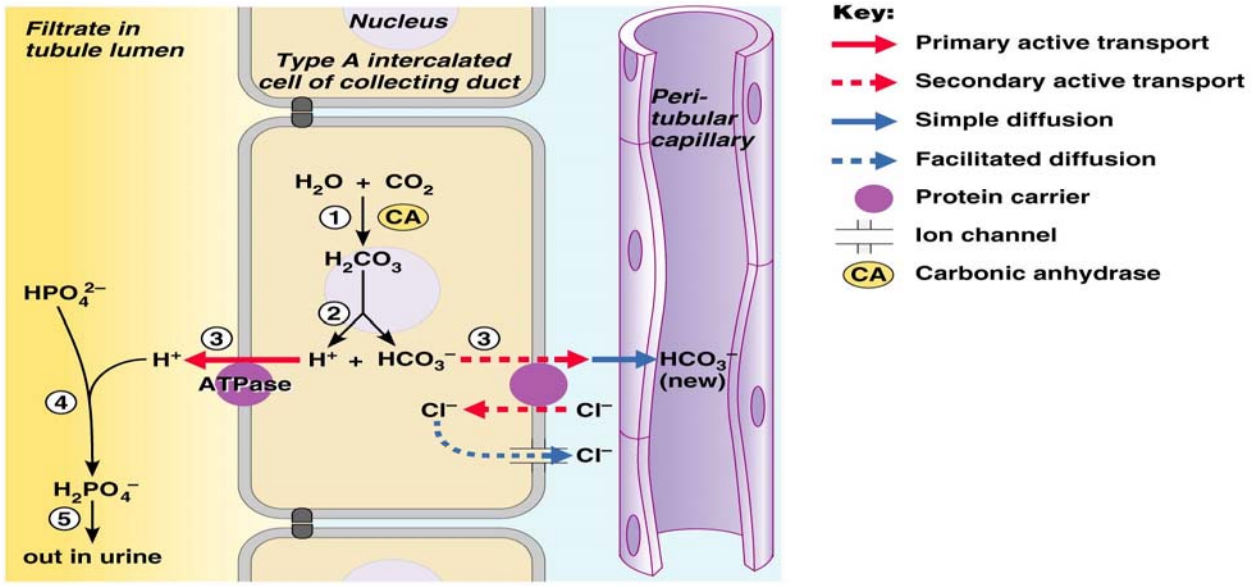


Figure 26.13

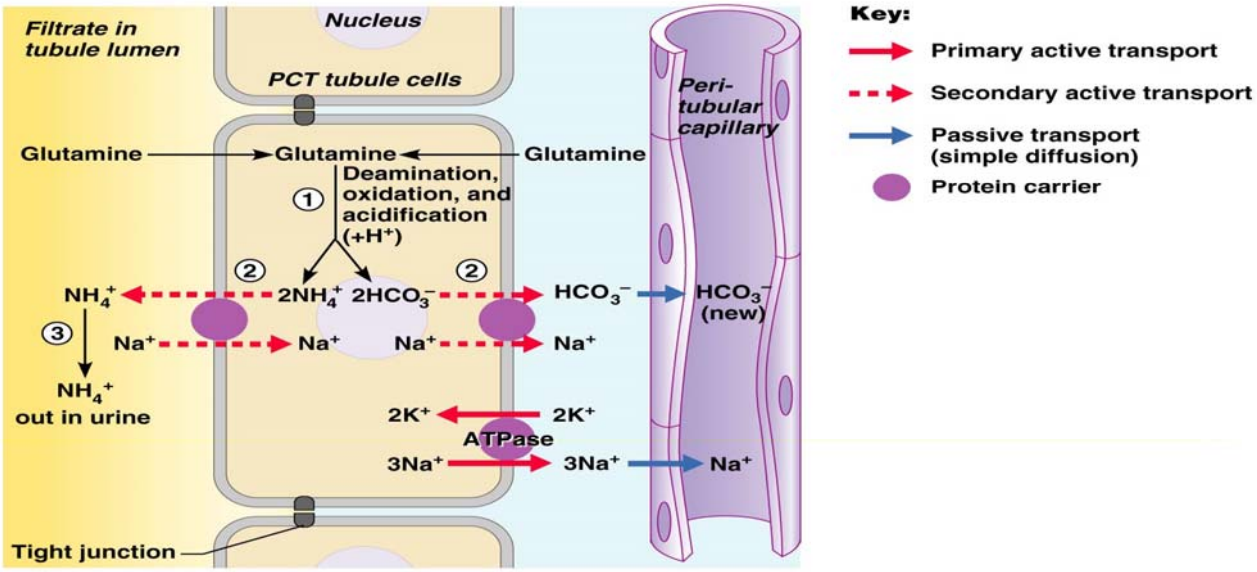


Figure 26.14

TABLE 26.1 Causes and Consequences of Electrolyte Imbalances

ION	ABNORMALITY (SERUM VALUE)	POSSIBLE CAUSES	CONSEQUENCES
Sodium	Hypernatremia (Na^+ excess: >145 mEq/L)	Dehydration; uncommon in healthy individuals; may occur in infants or the confused aged (individuals unable to indicate thirst) or may be a result of excessive intravenous NaCl administration	Thirst: CNS dehydration leads to confusion and lethargy progressing to coma; increased neuromuscular irritability evidenced by twitching and convulsions
	Hyponatremia (Na^+ deficit: <135 mEq/L)	Solute loss, water retention, or both (e.g., excessive Na^+ loss through vomiting, diarrhea, burned skin, tubal drainage of stomach, and as a result of excessive use of diuretics); deficiency of aldosterone (Addison's disease); renal disease; excess ADH release; excess H_2O ingestion	Most common signs are those of neurologic dysfunction due to brain swelling. If sodium amounts are actually normal but water is excessive, the symptoms are the same as those of water excess: mental confusion; giddiness; coma if development occurs slowly; muscular twitching, irritability, and convulsions if the condition develops rapidly. In hyponatremia accompanied by water loss, the main signs are decreased blood volume and blood pressure (circulatory shock)
Potassium	Hyperkalemia (K^+ excess: >5.5 mEq/L)	Renal failure; deficit of aldosterone; rapid intravenous infusion of KCl; burns or severe tissue injuries which cause K^+ to leave cells	Nausea, vomiting, diarrhea; bradycardia; cardiac arrhythmias, depression, and arrest; skeletal muscle weakness; flaccid paralysis
	Hypokalemia (K^+ deficit: <3.5 mEq/L)	Gastrointestinal tract disturbances (vomiting, diarrhea), gastrointestinal suction; Cushing's disease; inadequate dietary intake (starvation); hyperaldosteronism; diuretic therapy	Cardiac arrhythmias, flattened T wave; muscular weakness; metabolic alkalosis; mental confusion; nausea; vomiting
Phosphate	Hyperphosphatemia (HPO_4^{2-} excess: >2.9 mEq/L)	Decreased urinary loss due to renal failure; hypoparathyroidism; major tissue trauma; increased intestinal absorption	Clinical symptoms arise because of reciprocal changes in Ca^{2+} levels rather than directly from changes in plasma phosphate concentrations
	Hypophosphatemia (HPO_4^{2-} deficit: <1.6 mEq/L)	Decreased intestinal absorption; increased urinary output; hyperparathyroidism	

Table 23.1.1

TABLE 26.1 Causes and Consequences of Electrolyte Imbalances *(continued)*

ION	ABNORMALITY (SERUM VALUE)	POSSIBLE CAUSES	CONSEQUENCES
Chloride	Hyperchloremia (Cl^- excess: >105 mEq/L)	Dehydration; increased retention or intake; metabolic acidosis; hyperparathyroidism	No direct clinical symptoms; symptoms generally associated with the underlying cause, which is often related to pH abnormalities
	Hypochloremia (Cl^- deficit: <95 mEq/L)	Metabolic alkalosis (e.g., due to vomiting or excessive ingestion of alkaline substances); aldosterone deficiency	
Calcium	Hypercalcemia (Ca^{2+} excess: >5.2 mEq/L or 10.5 mg%)*	Hyperparathyroidism; excessive vitamin D; prolonged immobilization; renal disease (decreased excretion); malignancy	Decreased neuromuscular excitability leading to cardiac arrhythmias and arrest, skeletal muscle weakness, confusion, stupor, and coma; kidney stones; nausea and vomiting
	Hypocalcemia (Ca^{2+} deficit: <4.5 mEq/L or 9 mg%)*	Burns (calcium trapped in damaged tissues); hypoparathyroidism; vitamin D deficiency; renal tubular disease; renal failure; hyperphosphatemia; diarrhea; alkalosis	Increased neuromuscular excitability leading to tingling of fingers, tremors, skeletal muscle cramps, tetany, convulsions; depressed excitability of the heart; osteomalacia; fractures
Magnesium	Hypermagnesemia (Mg^{2+} excess: >2.2 mEq/L)	Rare; occurs in renal failure when Mg is not excreted normally; excessive ingestion of Mg^{2+}-containing antacids	Lethargy; impaired CNS functioning, coma, respiratory depression; cardiac arrest
	Hypomagnesemia (Mg^{2+} deficit: <1.4 mEq/L)	Alcoholism; loss of intestinal contents, severe malnutrition; diuretic therapy	Tremors, increased neuromuscular excitability, tetany, convulsions

*1 mg% = 1 mg/100 ml

Table 26.1.2

TABLE 26.2 Causes and Consequences of Acid-Base Imbalances

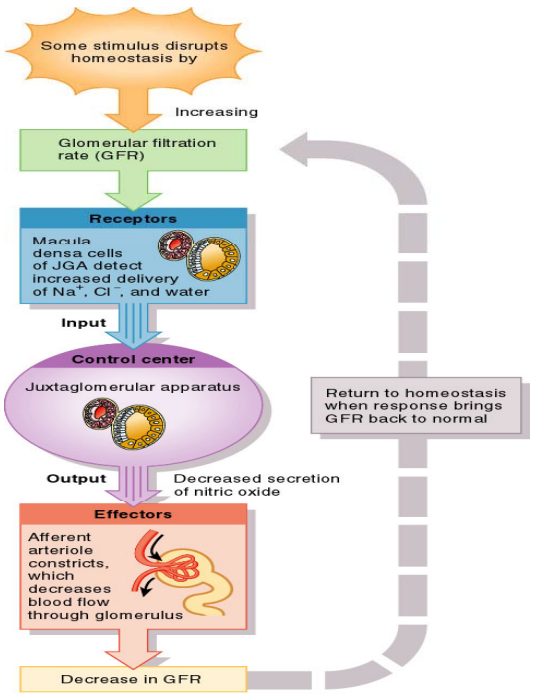
CONDITION AND HALLMARK	POSSIBLE CAUSES; COMMENTS
METABOLIC ACIDOSIS	
uncompensated (uncorrected) (HCO_3^- <22 mEq/L; pH <7.35)	**Severe diarrhea:** bicarbonate-rich intestinal (and pancreatic) secretions rushed through digestive tract before their solutes can be reabsorbed; bicarbonate ions are replaced by renal mechanisms that generate new bicarbonate ions **Renal disease:** failure of kidneys to rid body of acids formed by normal metabolic processes **Untreated diabetes mellitus:** lack of insulin or inability of tissue cells to respond to insulin, resulting in inability to use glucose; fats are used as primary energy fuel, and ketoacidosis occurs **Starvation:** lack of dietary nutrients for cellular fuels; body proteins and fat reserves are used for energy—both yield acidic metabolites as they are broken down for energy **Excess alcohol ingestion:** results in excess acids in blood **High ECF potassium concentrations:** potassium ions compete with H^+ for secretion in renal tubules; when ECF levels of K^+ are high, H^+ secretion is inhibited
METABOLIC ALKALOSIS	
uncompensated (HCO_3^- >26 mEq/L; pH >7.45)	**Vomiting or gastric suctioning:** loss of stomach HCl requires that H^+ be withdrawn from blood to replace stomach acid; thus H^+ decreases and HCO_3^- increases proportionately **Selected diuretics:** cause K^+ depletion and H_2O loss. Low K^+ directly stimulates the tubule cells to secrete H^+. Reduced blood volume elicits the renin-angiotensin mechanism, which stimulates Na^+ reabsorption and H^+ secretion. **Ingestion of excessive sodium bicarbonate (antacid):** bicarbonate moves easily into ECF, where it enhances natural alkaline reserve **Excess aldosterone** (e.g., adrenal tumors): promotes excessive reabsorption of Na^+, which pulls increased amount of H^+ into urine. Hypovolemia promotes the same relative effect because aldosterone secretion is increased to enhance Na^+ (and H_2O) reabsorption. ►

Table 26.2.1

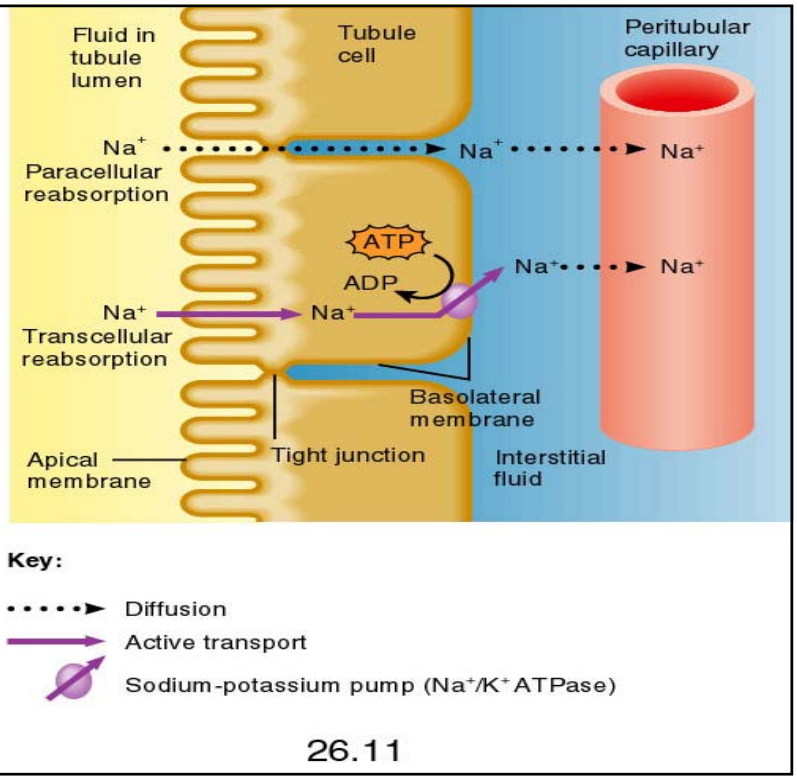
TABLE 26.2 Causes and Consequences of Acid-Base Imbalances *(continued)*

CONDITION AND HALLMARK	POSSIBLE CAUSES; COMMENTS
RESPIRATORY ACIDOSIS (HYPOVENTILATION)	
uncompensated (>45 mm Hg; pH <7.35)	**Impaired lung function** (e.g., in chronic bronchitis, cystic fibrosis, emphysema): impaired gas exchange or alveolar PCO_2 ventilation
	Impaired ventilatory movement: paralysis of respiratory muscles, chest injury, extreme obesity
	Narcotic or barbiturate overdose or injury to brain stem: depression of respiratory centers, resulting in hypoventilation and respiratory arrest
RESPIRATORY ALKALOSIS (HYPERVENTILATION)	
uncompensated (P_{CO_2} <35 mm Hg; pH >7.45)	**Strong emotions**: pain, anxiety, fear, panic attack
	Hypoxia: asthma, pneumonia, high altitude; represents effort to raise P_{O_2} at the expense of excessive CO_2 excretion
	Brain tumor or injury: abnormality of respiratory controls

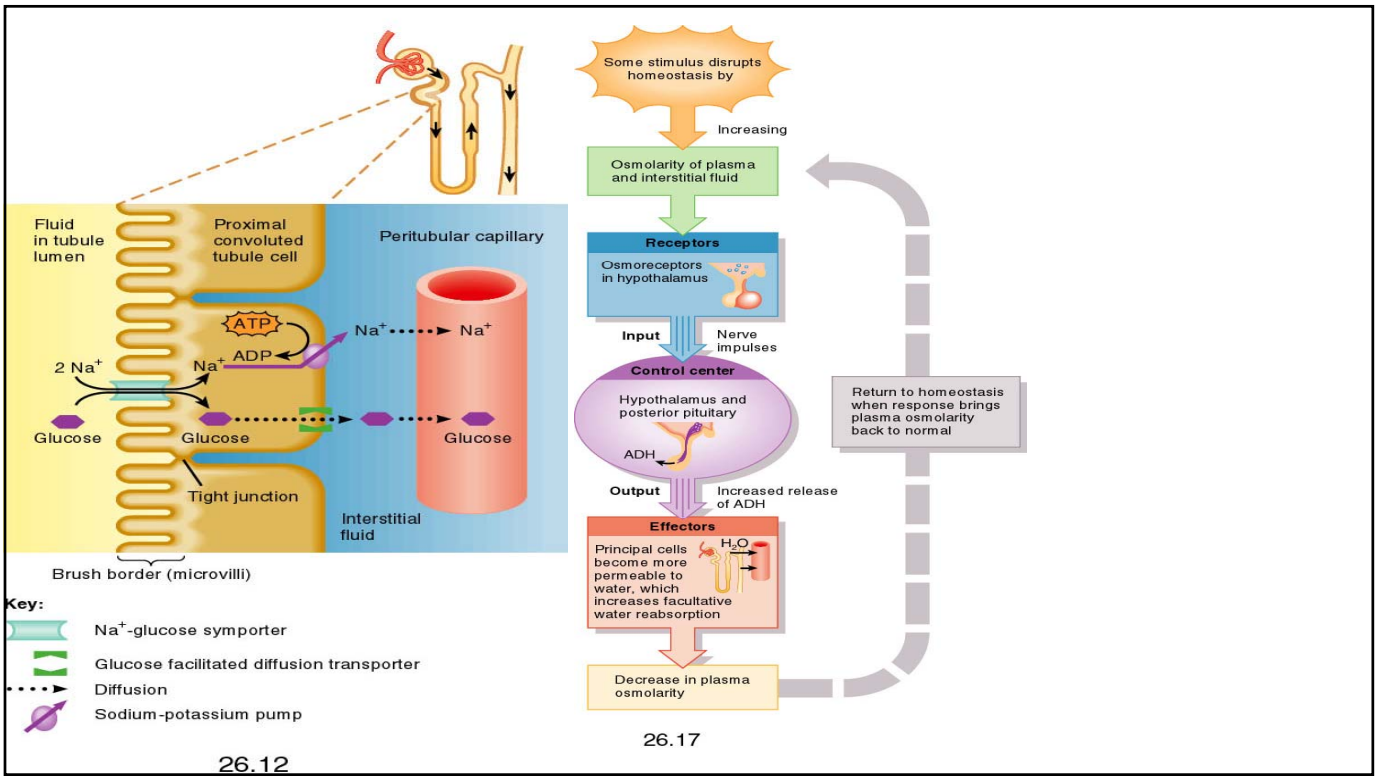
Table 26.2.2

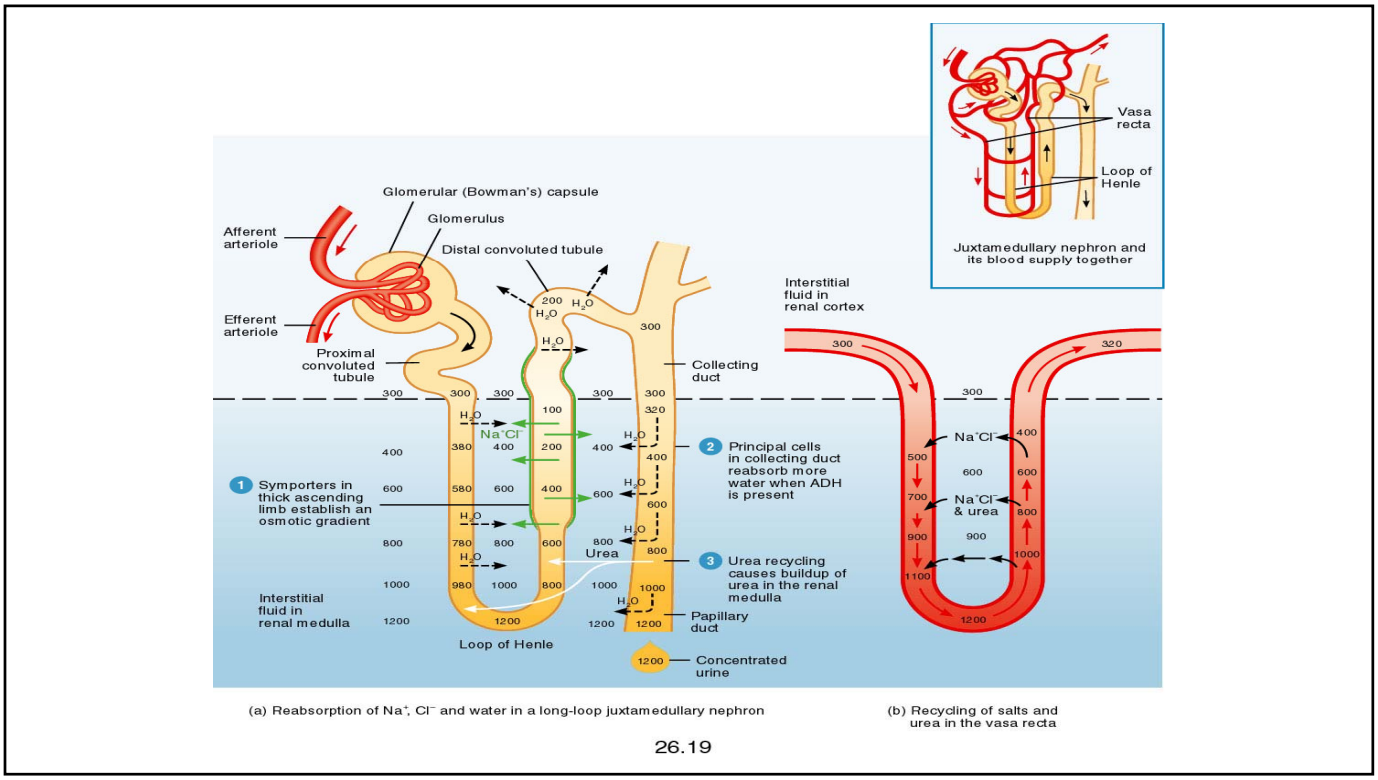


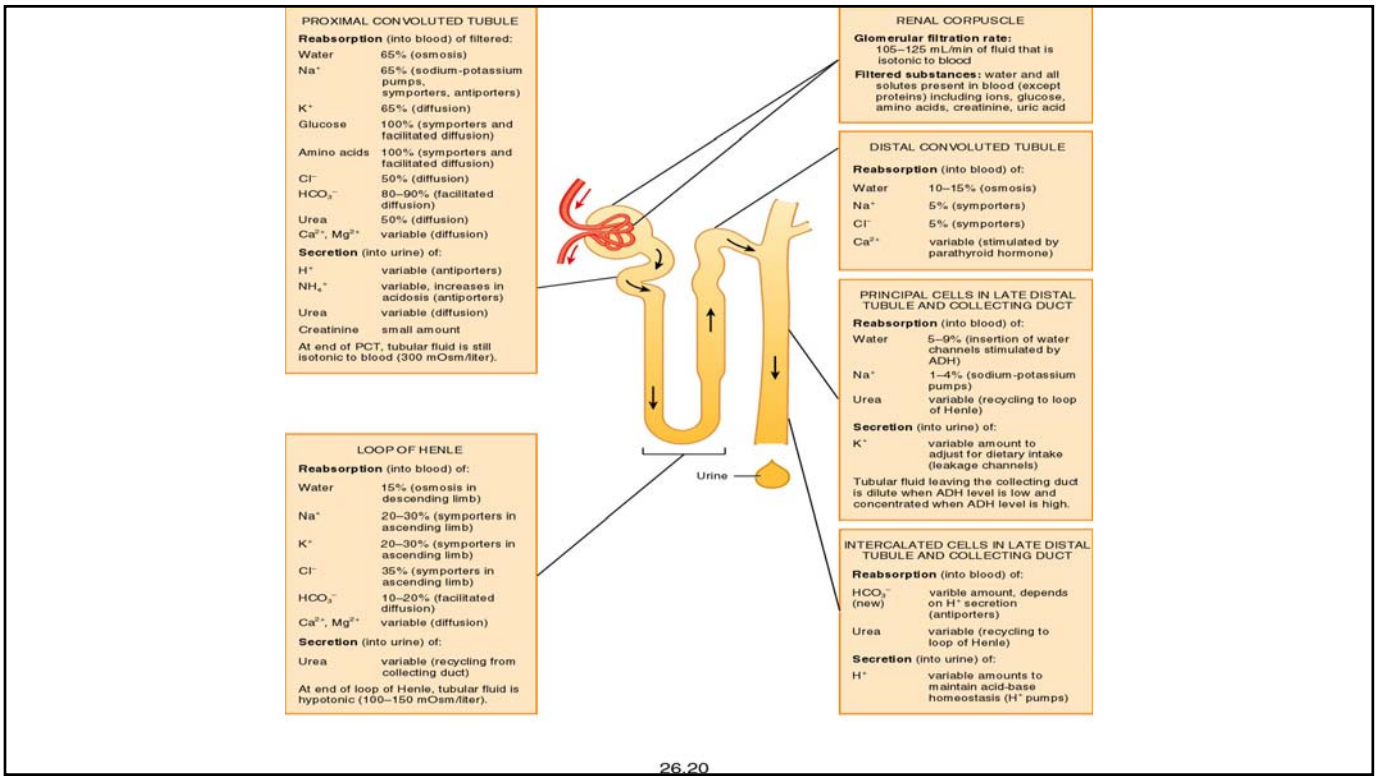
26.10

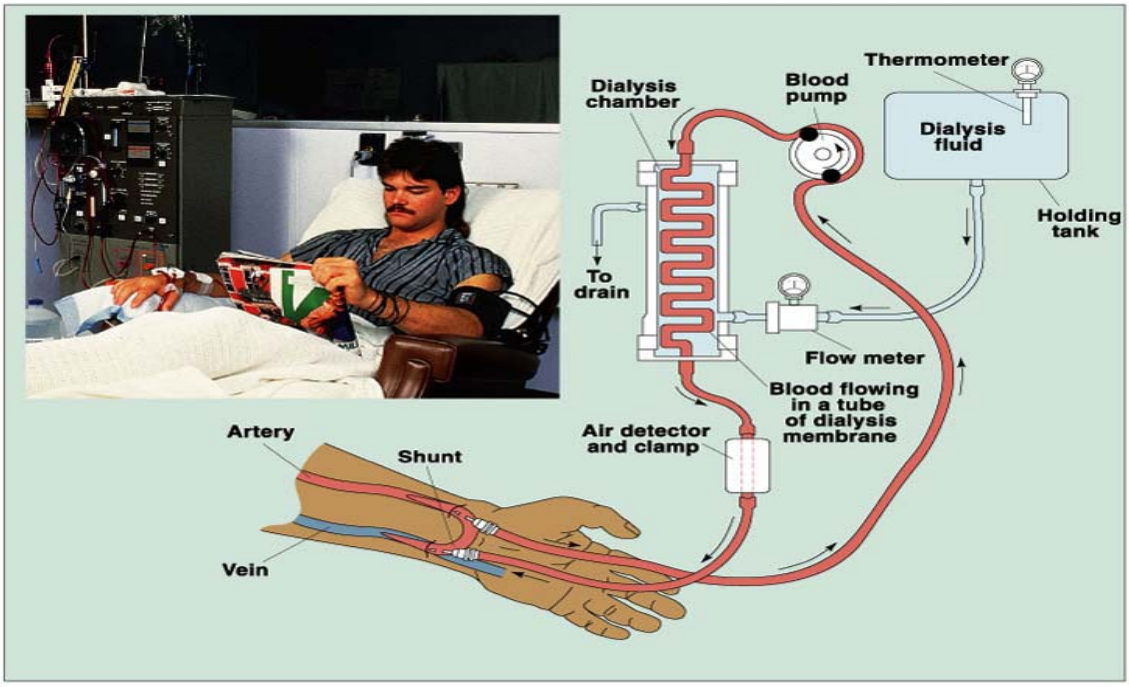


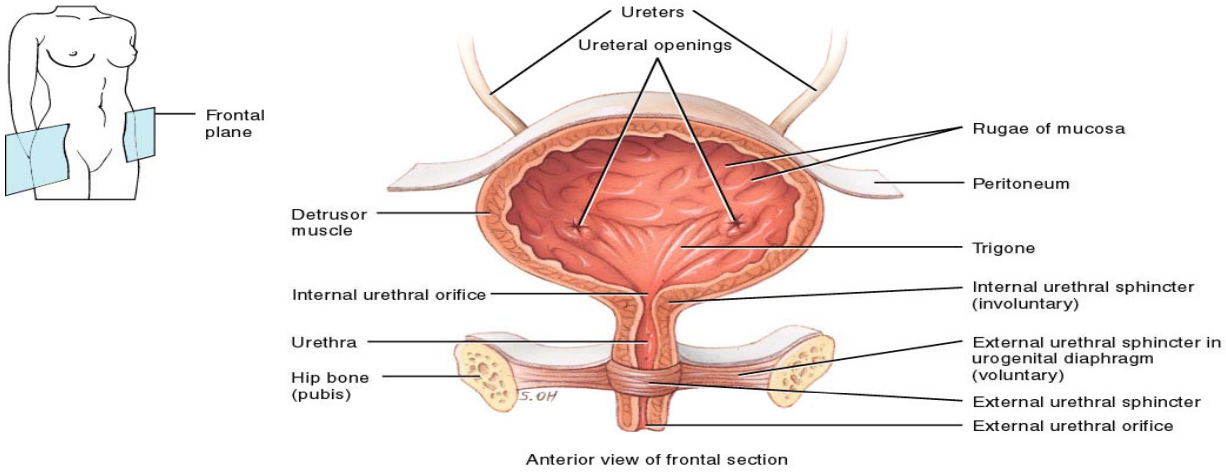
26.11


Fluid in tubule lumen
Proximal convoluted tubule cell
Peritubular capillary
ATP
Na+
ADP
2 Na+
Glucose
Glucose
Glucose
Tight junction
Interstitial fluid
Brush border (microvilli)
Key:
Na+-glucose symporter
Glucose facilitated diffusion transporter
Diffusion
Sodium-potassium pump
26.12
Some stimulus disrupts homeostasis by
Increasing
Osmolarity of plasma and interstitial fluid
Receptors
Osmoreceptors in hypothalamus
Input
Nerve impulses
Control center
Hypothalamus and posterior pituitary
ADH
Output
Increased release of ADH
Effectors
Principal cells become more permeable to water, which increases facultative water reabsorption
H2O
Decrease in plasma osmolarity
Return to homeostasis when response brings plasma osmolarity back to normal
26.17


Glomerular (Bowman's) capsule
Glomerulus
Afferent arteriole
Efferent arteriole
Distal convoluted tubule
Proximal convoluted tubule
Collecting duct
Loop of Henle
Interstitial fluid in renal medulla
Interstitial fluid in renal cortex
Na+Cl−
Urea
1 Symporters in thick ascending limb establish an osmotic gradient
2 Principal cells in collecting duct reabsorb more water when ADH is present
3 Urea recycling causes buildup of urea in the renal medulla
Papillary duct
Concentrated urine
Na+Cl− & urea
Vasa recta
Loop of Henle
Juxtamedullary nephron and its blood supply together
(a) Reabsorption of Na+, Cl− and water in a long-loop juxtamedullary nephron
(b) Recycling of salts and urea in the vasa recta
26.19


PROXIMAL CONVOLUTED TUBULE
Reabsorption (into blood) of filtered:
Water 65% (osmosis)
Na+ 65% (sodium-potassium pumps, symporters, antiporters)
K+ 65% (diffusion)
Glucose 100% (symporters and facilitated diffusion)
Amino acids 100% (symporters and facilitated diffusion)
Cl− 50% (diffusion)
HCO3− 80–90% (facilitated diffusion)
Urea 50% (diffusion)
Ca2+, Mg2+ variable (diffusion)
Secretion (into urine) of:
H+ variable (antiporters)
NH4+ variable, increases in acidosis (antiporters)
Urea variable (diffusion)
Creatinine small amount
At end of PCT, tubular fluid is still isotonic to blood (300 mOsm/liter).
LOOP OF HENLE
Reabsorption (into blood) of:
Water 15% (osmosis in descending limb)
Na+ 20–30% (symporters in ascending limb)
K+ 20–30% (symporters in ascending limb)
Cl− 35% (symporters in ascending limb)
HCO3− 10–20% (facilitated diffusion)
Ca2+, Mg2+ variable (diffusion)
Secretion (into urine) of:
Urea variable (recycling from collecting duct)
At end of loop of Henle, tubular fluid is hypotonic (100–150 mOsm/liter).
Urine
RENAL CORPUSCLE
Glomerular filtration rate: 105–125 mL/min of fluid that is isotonic to blood
Filtered substances: water and all solutes present in blood (except proteins) including ions, glucose, amino acids, creatinine, uric acid
DISTAL CONVOLUTED TUBULE
Reabsorption (into blood) of:
Water 10–15% (osmosis)
Na+ 5% (symporters)
Cl− 5% (symporters)
Ca2+ variable (stimulated by parathyroid hormone)
PRINCIPAL CELLS IN LATE DISTAL TUBULE AND COLLECTING DUCT
Reabsorption (into blood) of:
Water 5–9% (insertion of water channels stimulated by ADH)
Na+ 1–4% (sodium-potassium pumps)
Urea variable (recycling to loop of Henle)
Secretion (into urine) of:
K+ variable amount to adjust for dietary intake (leakage channels)
Tubular fluid leaving the collecting duct is dilute when ADH level is low and concentrated when ADH level is high.
INTERCALATED CELLS IN LATE DISTAL TUBULE AND COLLECTING DUCT
Reabsorption (into blood) of:
HCO3− (new) varible amount, depends on H+ secretion (antiporters)
Urea variable (recycling to loop of Henle)
Secretion (into urine) of:
H+ variable amounts to maintain acid-base homeostasis (H+ pumps)
26.20


Thermometer
Dialysis chamber
Blood pump
Dialysis fluid
Holding tank
To drain
Flow meter
Blood flowing in a tube of dialysis membrane
Air detector and clamp
Artery
Shunt
Vein



26.21

Characteristics of Urine

- Volume = 1 to 2 liters / day
- Color = yellow or amber (red from beets)
- Turbidity = Transparent
- Odor = aromatic (asparagus gives another distinct odor)
- pH = 4.6 to 8.0
- Specific gravity (density) – more dense with solutes.

Filtered or Reabsorbed

Substance	Plasma	Urine
Proteins	200 g	0.1 g
Bicarbonate	4.6 g	0
Glucose	3 g	0
Urea	4.8 g	25 g
Uric acid	0.15 g	0.8 g
Creatinine	0.03 g	1.6 g

Normal Constituents of Urine

- Urea – from metabolism of amino acids
- Creatinine – from creatine metabolism
- Uric acid – from catabolism of nucleic acids
- Urobilinogen – breakdown of hemoglobin
- Hippuric acid, indican, and ketone bodies
- Other substances and inorganic molecules

Abnormal Constituents of Urine

- **Albuminuria**
- **Glucosuria**
- **Hematuria**
- **Pyuria**
- **Ketonuria (Ketosis)**
- **Bilirubinuria**
- **Casts**
- **Renal calculi**
- **Microbes**

Words

- Glomerulonephritis (*Steptococcus)*
- Pyelonephritis
- Cystitis
- Polycystic disease
- Renal failure
- UTI's
- Azotemia

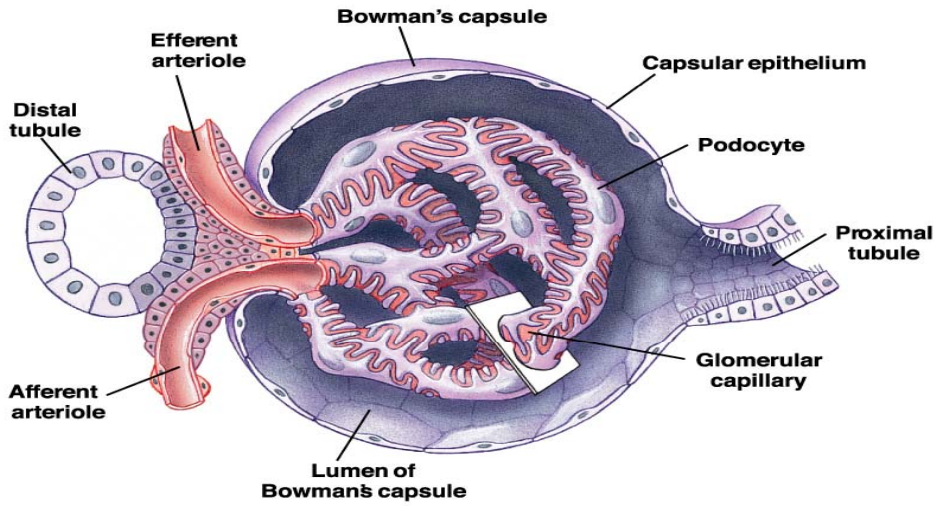
More Words

- Intravenous Pyelogram (IVP)
- Uremia
- Urethritis
- Enuresis
- Nocturnal enuresis
- Micturition
- Incontinence

More Words

- Lithotripsy
- Dysuria
- Polyuria
- Nocturia
- Anuria
- Oliguria

Regulation-Mineralocorticoids

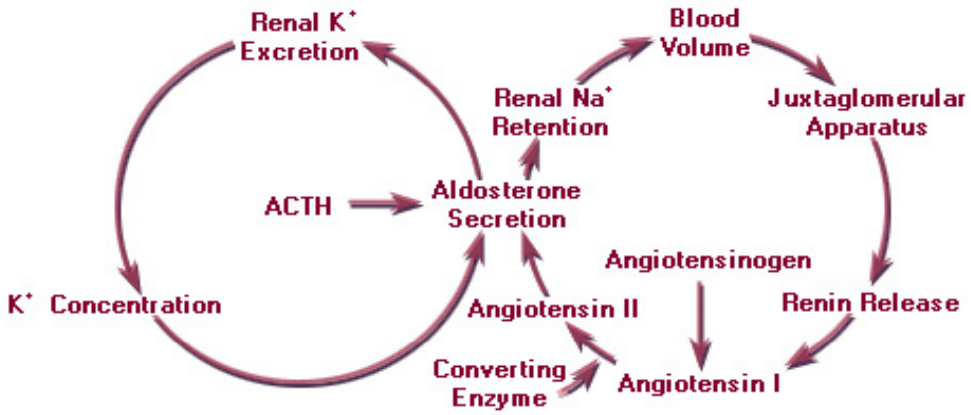


Regulation-Mineralocorticoids

Stimuli for Renin Secretion

1. ⇩ blood pressure
2. ⇩ serum Na
3. ⇩ blood volume
4. ANS stimulation

Regulation-Mineralocorticoids



Regulation-Mineralocorticoids

Actions of Angiotensin II

1. Direct arteriolar vasoconstrictor
2. Stimulus to aldosterone secretion


11th and 12th ribs
Minor calyx
Major calyx
Urinary bladder
Ureter
Renal pelvis
Kidney