Chapter 27: Fluid, electrolyte, and acid-base homeostasis
Body Fluid Compartments

- In lean adults, body fluids constitute 55% of female and 60% of male total body mass
  - Intracellular fluid (ICF) inside cells
    - About 2/3 of body fluid
  - Extracellular fluid (ECF) outside cells
    - Interstitial fluid between cell is 80% of ECF
    - Plasma in blood is 20% of ECF
    - Also includes lymph, cerebrospinal fluid, synovial fluid, aqueous humor, vitreous body, endolymph, perilymph, and pleural, pericardial, and peritoneal fluids
Body Fluid Compartments

(a) Distribution of body solids and fluids in an average lean, adult female and male

(b) Exchange of water among body fluid compartments

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Fluid Balance

- 2 barriers separate ICF, interstitial fluid and plasma
  - Plasma membrane separates ICF from surrounding interstitial fluid
  - Blood vessel wall divide interstitial fluid from plasma
- Body is in fluid balance when required amounts of water and solutes are present and correctly proportioned among compartments
- Water is by far the largest single component of the body making up 45-75% of total body mass
- Process of filtration, reabsorption, diffusion, and osmosis all continual exchange of water and solutes among compartments
Sources of Body Water Gain and Loss

- Fluid balance related to electrolyte balance
  - Intake of water and electrolytes rarely proportional
  - Kidneys excrete excess water through dilute urine or excess electrolytes through concentrated urine

- Body can gain water by
  - Ingestion of liquids and moist foods (2300mL/day)
  - Metabolic synthesis of water during cellular respiration and dehydration synthesis (200mL/day)

- Body loses water through
  - Kidneys (1500mL/day)
  - Evaporation from skin (600mL/day)
  - Exhalation from lungs (300mL/day)
  - Feces (100mL/day)
Daily Water Gain and Loss

**WATER GAIN**
- Metabolic water (200 mL)
- Ingested foods (700 mL)
- Ingested liquids (1600 mL)

**WATER LOSS**
- GI tract (100 mL)
- Lungs (300 mL)
- Skin (600 mL)
- Kidneys (1500 mL)
Mainly by volume of water intake/how much you drink

Dehydration – when water loss is greater than gain
- Decrease in volume, increase in osmolarity of body fluids
- Stimulates thirst center in hypothalamus
Regulation of water and solute loss

- Elimination of excess body water through urine
- Extent of urinary salt (NaCl) loss is the main factor that determines body fluid volume
- Main factor that determines body fluid osmolarity is extent of urinary water loss
- 3 hormones regulate renal Na\(^+\) and Cl\(^-\) reabsorption (or not)
  - Angiotensin II and aldosterone promote urinary Na\(^+\) and Cl\(^-\) reabsorption of (and water by osmosis) when dehydrated
  - Atrial natriuretic peptide (ANP) promotes excretion of Na\(^+\) and Cl\(^-\) followed by water excretion to decrease blood volume
Hormonal Regulation of Na$^+$ and Cl$^-$

1. Increased intake of NaCl
2. Increased plasma concentrations of Na$^+$ and Cl$^-$
3. Increased osmosis of water from intracellular fluid to interstitial fluid to plasma
4. Increased blood volume
5. Increased stretching of atria of heart
6. Increased release of atrial natriuretic peptide
7. Decreased release of renin by juxtaglomerular cells
8. Decreased formation of angiotensin II
9. Increased glomerular filtration rate
10. Decreased release of aldosterone
11. Reduced reabsorption of NaCl by kidneys
12. Increased loss of Na$^+$ and Cl$^-$ in urine (natriuresis)
13. Increased loss of water in urine by osmotic
14. Decreased blood volume

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Major hormone regulating water loss is antidiuretic hormone (ADH)

- Also known as vasopressin
- Produced by hypothalamus, released from posterior pituitary
- Promotes insertion of aquaporin-2 into principal cells of collecting duct
- Permeability to water increases
- Produces concentrated urine
Movement of water between compartments

- Normally, cells neither shrink or swell because intracellular and interstitial fluids have the same osmolarity
  - Increasing osmolarity of interstitial fluid draws water out of cells and cells shrink
  - Decreasing osmolarity of interstitial fluid causes cells to swell
- Changes in osmolarity most often result from changes in Na\(^+\) concentration
- Water intoxication – drinking water faster than the kidneys can excrete it
  - Can lead to convulsions, coma or death
Series of Events in Water Intoxication

1. Excessive blood loss, sweating, vomiting, or diarrhea coupled with intake of plain water
2. Decreased Na\(^+\) concentration of interstitial fluid and plasma (hyponatremia)
3. Decreased osmolarity of interstitial fluid and plasma
4. Osmosis of water from interstitial fluid into intracellular fluid
5. Water intoxication (cells swell)
6. Convulsions, coma, and possible death
Electrolytes in body fluids

- Ions form when electrolytes dissolve and dissociate
- 4 general functions
  - Control osmosis of water between body fluid compartments
  - Help maintain the acid-base balance
  - Carry electrical current
  - Serve as cofactors
Concentrations in body fluids

- Concentration of ions typically expressed in milliequivalents per liter (mEq/liter)
  - Na\(^+\) or Cl\(^-\) number of mEq/liter = mmol/liter
  - Ca\(^{2+}\) or HPO\(_4\)^{2-}\) number of mEq/liter = 2 x mmol/liter

- Chief difference between 2 ECF compartments (plasma and interstitial fluid) is plasma contains many more protein anions
  - Largely responsible for blood colloid osmotic pressure
ICF differs considerably from ECF

- ECF most abundant cation is Na\(^+\), anion is Cl\(^-\)
- ICF most abundant cation is K\(^+\), anion are proteins and phosphates (HPO\(_4^{2-}\))
- Na\(^+\)/K\(^+\) pumps play major role in keeping K\(^+\) high inside cells and Na\(^+\) high outside cell
Electrolyte and protein anion concentrations

![Bar chart showing concentrations of various ions in blood plasma, interstitial fluid, and intracellular fluid.]

Key:
- Red: Blood plasma
- Blue: Interstitial fluid
- Orange: Intracellular fluid

- Na⁺: 145 mEq/liter
- K⁺: 140 mEq/liter
- Ca²⁺: 117 mEq/liter
- Mg²⁺: 35 mEq/liter
- Cl⁻: 100 mEq/liter
- HCO₃⁻: 27 mEq/liter
- HPO₄²⁻ (organic): 20 mEq/liter
- SO₄²⁻: 20 mEq/liter
- Protein anions: 50 mEq/liter

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Sodium $\text{Na}^+$

- Most abundant ion in ECF
- 90% of extracellular cations
- Plays pivotal role in fluid and electrolyte balance because it accounts for almost half of the osmolarity of ECF
- Level in blood controlled by
  - Aldosterone – increases renal reabsorption
  - ADH – if sodium too low, ADH release stops
  - Atrial natriuretic peptide – increases renal excretion
Chloride Cl\(^-\)

- Most prevalent anions in ECF
- Moves relatively easily between ECF and ICF because most plasma membranes contain Cl\(^-\) leakage channels and antiporters
- Can help balance levels of anions in different fluids
  - Chloride shift in RBCs
- Regulated by
  - ADH – governs extent of water loss in urine
  - Processes that increase or decrease renal reabsorption of Na\(^+\) also affect reabsorption of Cl\(^-\)
Potassium $K^+$

- Most abundant cations in ICF
- Key role in establishing resting membrane potential in neurons and muscle fibers
- Also helps maintain normal ICF fluid volume
- Helps regulate pH of body fluids when exchanged for $H^+$
- Controlled by aldosterone – stimulates principal cells in renal collecting ducts to secrete excess $K^+$
Bicarbonate $\text{HCO}_3^-$

- Second most prevalent extracellular anion
- Concentration increases in blood passing through systemic capillaries picking up carbon dioxide
  - Carbon dioxide combines with water to form carbonic acid which dissociates
  - Drops in pulmonary capillaries when carbon dioxide exhaled
- Chloride shift helps maintain correct balance of anions in ECF and ICF
- Kidneys are main regulators of blood $\text{HCO}_3^-$
  - Can form and release $\text{HCO}_3^-$ when low or excrete excess
Calcium $Ca^{2+}$

- Most abundant mineral in body
- 98% of calcium in adults in skeleton and teeth
- In body fluids mainly an extracellular cation
- Contributes to hardness of teeth and bones
- Plays important roles in blood clotting, neurotransmitter release, muscle tone, and excitability of nervous and muscle tissue
- Regulated by parathyroid hormone
  - Stimulates osteoclasts to release calcium from bone – resorption
  - Also enhances reabsorption from glomerular filtrate
  - Increases production of calcitrol to increase absorption for GI tract
- Calcitonin lowers blood calcium levels
Phosphate

- About 85% in adults present as calcium phosphate salts in bone and teeth
- Remaining 15% ionized – H$_2$PO$_4^-$, HPO$_4^{2-}$, and PO$_4^{3-}$ are important intracellular anions
- HPO$_4^{2-}$ important buffer of H$^+$ in body fluids and urine
- Same hormones governing calcium homeostasis also regulate HPO$_4^{2-}$ in blood
  - Parathyroid hormone – stimulates resorption of bone by osteoclasts releasing calcium and phosphate but inhibits reabsorption of phosphate ions in kidneys
  - Calcitrol promotes absorption of phosphates and calcium from GI tract
Magnesium

- In adults, about 54% of total body magnesium is part of bone as magnesium salts
- Remaining 46% as Mg$^{2+}$ in ICF (45%) or ECF (1%)
- Second most common intracellular cation
- Cofactor for certain enzymes and sodium-potassium pump
- Essential for normal neuromuscular activity, synaptic transmission, and myocardial function
- Secretion of parathyroid hormone depends on Mg$^{2+}$
- Regulated in blood plasma by varying rate excreted in urine
Acid-base balance

- Major homeostatic challenge is keeping $H^+$ concentration (pH) of body fluids at appropriate level
- 3D shape of proteins sensitive to pH
- Diets with large amounts of proteins produce more acids than bases which acidifies blood
- Several mechanisms help maintain pH of arterial blood between 7.35 and 7.45
  - Buffer systems, exhalation of $CO_2$, and kidney excretion of $H^+$
Buffer systems

- Act to quickly temporarily bind $H^+$
- Raise pH but do not remove $H^+$
- Most consist of weak acid and salt of that acid functioning as weak base

- Protein buffer system
  - Most abundant buffer in ICF and blood plasma
  - Hemoglobin in RBCs
  - Albumin in blood plasma
  - Free carboxyl group acts like an acid by releasing $H^+$
  - Free amino group acts as a base to combine with $H^+$
  - Side chain groups on 7 of 20 amino acids also can buffer $H^+$
Buffer Systems

- **Carbonic acid-bicarbonate buffer system**
  - Based on bicarbonate ion ($\text{HCO}_3^-$) acting as weak base and carbonic acid ($\text{H}_2\text{CO}_3$) acting as weak acid
  - $\text{HCO}_3^-$ is a significant anion in both ICF and ECF
  - Because CO$_2$ and H$_2$O combine to form this buffer system cannot protect against pH changes due to respiratory problems in which there is an excess or shortage of CO$_2$

- **Phosphate buffer system**
  - Dihydrogen phosphate ($\text{H}_2\text{PO}_4^-$) and monohydrogen phosphate ($\text{HPO}_4^{2-}$)
  - Phosphates are major anions in ICF and minor ones in ECF
  - Important regulator of pH in cytosol
Exhalation of carbon dioxide

- Increase in carbon dioxide in body fluids lowers pH of body fluids
- Because $\text{H}_2\text{CO}_3$ can be eliminated by exhaling $\text{CO}_2$ it is called a volatile acid
- Changes in the rate and depth of breathing can alter pH of body fluids within minutes
  - Negative feedback loop
Regulation of blood pH by the respiratory system

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Kidney excretion of H⁺

- Metabolic reactions produce nonvolatile acids
- One way to eliminate this huge load is to excrete H⁺ in urine
- In the proximal convoluted tubule, Na⁺ /H⁺ antiporters secrete H⁺ as they reabsorb Na⁺
- Intercalated cells of collecting duct include proton pumps that secrete H⁺ into tubule fluid
- Urine can be up to 1000 times more acidic than blood
- 2 other buffers can combine with H⁺ in collecting duct
  - HPO₄²⁻ and NH₃
Secretion of H⁺ by intercalated cells in the collecting duct
Acid-base imbalances

- Normal pH range of arterial blood 7.35-7.45
  - Acidosis – blood pH below 7.35
  - Alkalosis – blood pH above 7.45
- Major physiological effect of
  - Acidosis – depression of synaptic transmission in CNS
  - Alkalosis – overexcitability of CNS and peripheral nerves
Physiological responses to normalize arterial blood pH

- Changes in blood pH may be countered by compensation
  - Complete – brought within normal range
  - Partial – still too low or high
  - Respiratory – hyperventilation or hypoventilation
  - Renal – secretion of $H^+$ and reabsorption of $HCO_3^-$
Respiratory acidosis/ alkalosis results from changes in partial pressure of CO$_2$ in systemic arterial blood

- Respiratory acidosis – abnormally high $P_{CO_2}$ in systemic arterial blood
  - Inadequate exhalation of CO$_2$
  - Any condition that decreases movement of CO$_2$ out – emphysema, pulmonary edema, airway obstruction
  - Kidneys can help raise blood pH
  - Goal to increase exhalation of CO$_2$ – ventilation therapy
Respiratory alkalosis

- Abnormally low $P_{CO_2}$ in systemic arterial blood
  - Cause is hyperventilation due to oxygen deficiency from high altitude or pulmonary disease, stroke or severe anxiety
  - Renal compensation can help
  - One simple treatment to breather into paper bag for short time
Metabolic acidosis/alkalosis

Results from changes in HCO$_3^-$ concentration

- Metabolic acidosis – abnormally low HCO$_3^-$ in systemic arterial blood
  - Loss of HCO$_3^-$ from severe diarrhea or renal dysfunction
  - Accumulation of an acid other than carbonic acid – ketosis
  - Failure of kidneys to excrete H$^+$ from metabolism of dietary proteins

- Hyperventilation can help
- Administer IV sodium bicarbonate and correct cause of acidosis
Metabolic alkalosis

- Abnormally high $\text{HCO}_3^-$ in systemic arterial blood
  - Nonrespiratory loss of acid - vomiting of acidic stomach contents, gastric suctioning
  - Excessive intake of alkaline drugs (antacids)
  - Use of certain diuretics
  - Severe dehydration
  - Hypoventilation can help
  - Give fluid solutions to correct $\text{Cl}^-$, $\text{K}^+$ and other electrolyte deficiencies and correct cause of alkalosis
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