Introduction

- Water
  - Is 99% of fluid outside cells (extracellular fluid)
  - Is an essential ingredient of cytosol (intracellular fluid)
  - All cellular operations rely on water
    - As a diffusion medium for gases, nutrients, and waste products
The body must maintain normal volume and composition of

- Extracellular fluid (ECF)
- Intracellular fluid (ICF)
Fluid Balance

- Is a daily balance between
  - Amount of water gained
  - Amount of water lost to environment

- Involves regulating content and distribution of body water in ECF and ICF
Fluid, Electrolyte, and Acid–Base Balance

- The Digestive System
  - Is the primary source of water gains
    - Plus a small amount from metabolic activity
- The Urinary System
  - Is the primary route of water loss
Fluid, Electrolyte, and Acid–Base Balance

- **Electrolytes**
  - Are ions released through dissociation of inorganic compounds
  - Can conduct electrical current in solution
- **Electrolyte balance**
  - When the gains and losses of all electrolytes are equal
  - Primarily involves balancing rates of absorption across digestive tract with rates of loss at kidneys and sweat glands
Acid–Base Balance

- Precisely balances production and loss of hydrogen ions (pH)
- The body generates acids during normal metabolism
  - Tends to reduce pH
Fluid, Electrolyte, and Acid–Base Balance

- The Kidneys
  - Secrete hydrogen ions into urine
  - Generate buffers that enter bloodstream
    - In distal segments of distal convoluted tubule (DCT) and collecting system

- The Lungs
  - Affect pH balance through elimination of carbon dioxide
Fluid Compartments

- Water Accounts for Roughly
  - 60% percent of male body weight
  - 50% percent of female body weight
  - Mostly in intracellular fluid
Fluid Compartments

- Water Exchange
  - Water exchange between ICF and ECF occurs across plasma membranes by
    - Osmosis
    - Diffusion
    - Carrier-mediated transport
Fluid Compartments

- Major Subdivisions of ECF
  - Interstitial fluid of peripheral tissues
  - Plasma of circulating blood
Fluid Compartments

- Minor Subdivisions of ECF
  - Lymph, perilymph, and endolymph
  - Cerebrospinal fluid (CSF)
  - Synovial fluid
  - Serous fluids (pleural, pericardial, and peritoneal)
  - Aqueous humor
Exchange among Subdivisions of ECF

- Occurs primarily across endothelial lining of capillaries
- From interstitial spaces to plasma
  - Through lymphatic vessels that drain into the venous system
Figure 27–1a The Composition of the Human Body.
Figure 27–1a The Composition of the Human Body.
Figure 27–1b The Composition of the Human Body.
Figure 27–1b The Composition of the Human Body.
Fluid Compartments

- ECF: Solute Content
  - Types and amounts vary regionally
    - Electrolytes
    - Proteins
    - Nutrients
    - Waste products
Fluid Compartments

- The ECF and the ICF
  - Are called **fluid compartments** because they behave as distinct entities
  - Are separated by plasma membranes and active transport
Fluid Compartments

■ Cations and Anions
  ■ In ECF
    ■ Sodium, chloride, and bicarbonate
  ■ In ICF
    ■ Potassium, magnesium, and phosphate ions
    ■ Negatively charged proteins
Figure 27–2 Cations and Anions in Body Fluids.
Membrane Functions

- Plasma membranes are selectively permeable
- Ions enter or leave via specific membrane channels
- Carrier mechanisms move specific ions in or out of cell
The Osmotic Concentration of ICF and ECF

- Is identical
- Osmosis eliminates minor differences in concentration
  - Because plasma membranes are permeable to water
Fluid Compartments

- Basic Concepts in the Regulation of Fluids and Electrolytes
  - All homeostatic mechanisms that monitor and adjust body fluid composition respond to changes in the ECF, not in the ICF
  - No receptors directly monitor fluid or electrolyte balance
  - Cells cannot move water molecules by active transport
  - The body’s water or electrolyte content will rise if dietary gains exceed environmental losses, and will fall if losses exceed gains
Fluid Compartments

- An Overview of the Primary Regulatory Hormones
  - Affecting fluid and electrolyte balance:
    1. Antidiuretic hormone
    2. Aldosterone
    3. Natriuretic peptides
Fluid Compartments

- Antidiuretic Hormone (ADH)
  - Stimulates water conservation at kidneys
    - Reducing urinary water loss
    - Concentrating urine
  - Stimulates thirst center
    - Promoting fluid intake
Fluid Compartments

- ADH Production
  - Osmoreceptors in hypothalamus
    - Monitor osmotic concentration of ECF
  - Change in osmotic concentration
    - Alters osmoreceptor activity
  - Osmoreceptor neurons secrete ADH
Fluid Compartments

- ADH Release
  - Axons of neurons in anterior hypothalamus
    - Release ADH near fenestrated capillaries
    - In neurohypophysis (posterior lobe of pituitary gland)
  - Rate of release varies with osmotic concentration
    - Higher osmotic concentration increases ADH release
Aldosterone

- Is secreted by suprarenal cortex in response to
  - Rising $K^+$ or falling $Na^+$ levels in blood
  - Activation of renin–angiotensin system
- Determines rate of $Na^+$ absorption and $K^+$ loss along DCT and collecting system
Fluid Compartments

- "Water Follows Salt"
  - High aldosterone plasma concentration
    - Causes kidneys to conserve salt
  - Conservation of $\text{Na}^+$ by aldosterone
    - Also stimulates water retention
Natriuretic Peptides

- ANP and BNP are released by cardiac muscle cells in response to abnormal stretching of heart walls
- Reduce thirst
- Block release of ADH and aldosterone
- Cause diuresis
- Lower blood pressure and plasma volume
Fluid Movement

- When the body loses water
  - Plasma volume decreases
  - Electrolyte concentrations rise
- When the body loses electrolytes
  - Water is lost by osmosis
- Regulatory mechanisms are different
Fluid Movement

- Fluid Balance
  - Water circulates freely in ECF compartment
  - At capillary beds, hydrostatic pressure forces water out of plasma and into interstitial spaces
  - Water is reabsorbed along distal portion of capillary bed when it enters lymphatic vessels
  - ECF and ICF are normally in osmotic equilibrium
    - No large-scale circulation between compartments
Fluid Movement

- Fluid Movement within the ECF
  - Net hydrostatic pressure
    - Pushes water out of plasma
    - Into interstitial fluid
  - Net colloid osmotic pressure
    - Draws water out of interstitial fluid
    - Into plasma
Fluid Movement

- Fluid Movement within the ECF
  - ECF fluid volume is redistributed
    - From lymphoid system to venous system (plasma)
  - Interaction between opposing forces
    - Results in continuous filtration of fluid
  - ECF volume
    - Is 80% in interstitial fluid and minor fluid compartment
    - Is 20% in plasma
Fluid Movement

- **Edema**
  - The movement of abnormal amounts of water from plasma into interstitial fluid
Fluid Gains and Losses

Water losses

- Body loses about 2500 mL of water each day through urine, feces, and insensible perspiration.
- Fever can also increase water loss.
- Sensible perspiration (sweat) varies with activities and can cause significant water loss (4 L/hr).
Fluid Movement

- Fluid Gains and Losses
  - Water gains
    - About 2500 mL/day
    - Required to balance water loss
  - Through:
    - eating (1000 mL)
    - drinking (1200 mL)
    - *metabolic generation* (300 mL)
Figure 27–3 Fluid Gains and Losses.

Absorption across digestive epithelium (2200 mL)

Respiratory losses and insensible perspiration (1150 mL)

Fecal loss (150 mL)

Sensible perspiration (variable)

Urine (1200 mL)

Plasma membranes

Metabolic generation (300 mL)

ICF
# Fluid Movement

## TABLE 27-1 Water Balance

<table>
<thead>
<tr>
<th>Source</th>
<th>Daily Input (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water content of food</td>
<td>1000</td>
</tr>
<tr>
<td>Water consumed as liquid</td>
<td>1200</td>
</tr>
<tr>
<td>Metabolic water produced during catabolism</td>
<td>300</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2500</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Method of Elimination</th>
<th>Daily Output (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urination</td>
<td>1200</td>
</tr>
<tr>
<td>Evaporation at skin</td>
<td>750</td>
</tr>
<tr>
<td>Evaporation at lungs</td>
<td>400</td>
</tr>
<tr>
<td>Loss in feces</td>
<td>150</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2500</strong></td>
</tr>
</tbody>
</table>
Fluid Movement

- Metabolic Generation of Water
  - Is produced within cells
  - Results from oxidative phosphorylation in mitochondria
Fluid Movement

**Fluid Shifts**

- Are rapid water movements between ECF and ICF
  - In response to an osmotic gradient
- If ECF osmotic concentration increases
  - Fluid becomes hypertonic to ICF
  - Water moves from cells to ECF
Fluid Movement

- **Fluid Shifts**
  - If ECF osmotic concentration decreases
    - Fluid becomes hypotonic to ICF
    - Water moves from ECF to cells
  - ICF volume is much greater than ECF volume
    - ICF acts as water reserve
    - Prevents large osmotic changes in ECF
Fluid Movement

- Dehydration
  - Also called water depletion
  - Develops when water loss is greater than gain
Fluid Movement

- Allocation of Water Losses
  - If water is lost, but electrolytes retained
    - ECF osmotic concentration rises
    - Water moves from ICF to ECF
    - Net change in ECF is small
Severe Water Loss

- Causes
  - Excessive perspiration
  - Inadequate water consumption
  - Repeated vomiting
  - Diarrhea

- Homeostatic responses
  - Physiologic mechanisms (ADH and renin secretion)
  - Behavioral changes (increasing fluid intake)
Distribution of Water Gains

- If water is gained, but electrolytes are not
  - ECF volume increases
  - ECF becomes hypotonic to ICF
  - Fluid shifts from ECF to ICF
- May result in overhydration (also called water excess):
  - occurs when excess water shifts into ICF:
    » distorting cells
    » changing solute concentrations around enzymes
    » disrupting normal cell functions
Fluid Movement

- **Causes of Overhydration**
  - Ingestion of large volume of fresh water
  - Injection of hypotonic solution into bloodstream
  - Endocrine disorders
    - Excessive ADH production
  - Inability to eliminate excess water in urine
    - Chronic renal failure
    - Heart failure
    - Cirrhosis
Fluid Movement

- Signs of Overhydration
  - Abnormally low Na⁺ concentrations (hyponatremia)
  - Effects on CNS function (water intoxication)
Electrolyte Balance

- Requires rates of gain and loss of each electrolyte in the body to be equal
- Electrolyte concentration directly affects water balance
- Concentrations of individual electrolytes affect cell functions
Electrolyte Balance

- Sodium
  - Is the dominant cation in ECF
  - Sodium salts provide 90% of ECF osmotic concentration
    - Sodium chloride (NaCl)
    - Sodium bicarbonate
Electrolyte Balance

- Normal Sodium Concentrations
  - In ECF
    - About 140 mEq/L
  - In ICF
    - Is 10 mEq/L or less
Electrolyte Balance

- **Potassium**
  - Is the dominant cation in ICF
  - Normal potassium concentrations
    - In ICF:
      - about 160 mEq/L
    - In ECF:
      - 3.5–5.5 mEq/L
Electrolyte Balance

- Rules of Electrolyte Balance
  1. Most common problems with electrolyte balance are caused by imbalance between gains and losses of sodium ions.
  2. Problems with potassium balance are less common, but more dangerous than sodium imbalance.
Electrolyte Balance

- Sodium Balance
  1. Sodium ion uptake across digestive epithelium
  2. Sodium ion excretion in urine and perspiration
Electrolyte Balance

- Sodium Balance
  - Typical Na\(^+\) gain and loss
    - Is 48–144 mEq (1.1–3.3 g) per day
  - If gains exceed losses
    - Total ECF content rises
  - If losses exceed gains
    - ECF content declines
Electrolyte Balance

- Sodium Balance and ECF Volume
  - Changes in ECF Na\(^+\) content
    - Do not produce change in concentration
    - Corresponding water gain or loss keeps concentration constant
Electrolyte Balance

- Sodium Balance and ECF Volume
  - $\text{Na}^+$ regulatory mechanism changes ECF volume
    - Keeps concentration stable
  - When $\text{Na}^+$ losses exceed gains
    - ECF volume decreases (increased water loss)
    - Maintaining osmotic concentration
Electrolyte Balance

- Large Changes in ECF Volume
  - Are corrected by homeostatic mechanisms that regulate blood volume and pressure
  - If ECF volume rises, blood volume goes up
  - If ECF volume drops, blood volume goes down
Electrolyte Balance

Figure 27–4 The Homeostatic Regulation of Normal Sodium Ion Concentrations in Body Fluids.
Electrolyte Balance

- **Homeostatic Mechanisms**
  - A rise in blood volume elevates blood pressure
  - A drop in blood volume lowers blood pressure
  - Monitor ECF volume indirectly by monitoring blood pressure
    - Baroreceptors at carotid sinus, aortic sinus, and right atrium
Electrolyte Balance

- **Hyponatremia**
  - Body water content rises (overhydration)
  - $\text{ECF Na}^+ \text{ concentration} < 136 \text{ mEq/L}$

- **Hypernatremia**
  - Body water content declines (dehydration)
  - $\text{ECF Na}^+ \text{ concentration} > 145 \text{ mEq/L}$
Electrolyte Balance

- **ECF Volume**

  - If ECF volume is inadequate
    - Blood volume and blood pressure decline
    - Renin–angiotensin system is activated
    - Water and Na\(^+\) losses are reduced
    - ECF volume increases
Electrolyte Balance

- Plasma Volume
  - If plasma volume is too large
    - Venous return increases:
      - stimulating release of natriuretic peptides (ANP and BNP)
      - reducing thirst
      - blocking secretion of ADH and aldosterone
    - Salt and water loss at kidneys increases
    - ECF volume declines
Figure 27–5 The Integration of Fluid Volume Regulation and Sodium Ion Concentrations in Body Fluids.
Potassium Balance

- 98% of potassium in the human body is in ICF
- Cells expend energy to recover potassium ions diffused from cytoplasm into ECF
Electrolyte Balance

- Processes of Potassium Balance
  1. Rate of gain across digestive epithelium
  2. Rate of loss into urine
Electrolyte Balance

- Potassium Loss in Urine
  - Is regulated by activities of ion pumps
    - Along distal portions of nephron and collecting system
    - \( \text{Na}^+ \) from tubular fluid is exchanged for \( \text{K}^+ \) in peritubular fluid
  - Are limited to amount gained by absorption across digestive epithelium (about 50–150 mEq or 1.9–5.8 g/day)
Electrolyte Balance

Factors in Tubular Secretion of $K^+$

1. Changes in concentration of ECF:
   - Higher ECF concentration increases rate of secretion

2. Changes in pH:
   - Low ECF pH lowers peritubular fluid pH
   - $H^+$ rather than $K^+$ is exchanged for $Na^+$ in tubular fluid
   - Rate of potassium secretion declines

3. Aldosterone levels:
   - Affect $K^+$ loss in urine
   - Ion pumps reabsorb $Na^+$ from filtrate in exchange for $K^+$ from peritubular fluid
   - High $K^+$ plasma concentrations stimulate aldosterone
Electrolyte Balance

- Calcium Balance
  - Calcium is most abundant mineral in the body
  - A typical individual has 1–2 kg (2.2–4.4 lb) of this element
  - 99% of which is deposited in skeleton
Electrolyte Balance

- Functions of Calcium Ion (Ca^{2+})
  - Muscular and neural activities
  - Blood clotting
  - Cofactors for enzymatic reactions
  - Second messengers
Electrolyte Balance

- Hormones and Calcium Homeostasis
  - Parathyroid hormone (PTH) and calcitriol
    - Raise calcium concentrations in ECF
  - Calcitonin
    - Opposes PTH and calcitriol
Electrolyte Balance

- **Calcium Absorption**
  - At digestive tract and reabsorption along DCT
    - Is stimulated by PTH and calcitriol
Electrolyte Balance

- **Calcium Ion Loss**
  - In bile, urine, or feces
    - Is very small (0.8–1.2 g/day)
    - Represents about 0.03% of calcium reserve in skeleton
Electrolyte Balance

- Hypercalcemia
  - Exists if Ca$^{2+}$ concentration in ECF is $>5.5$ mEq/L
  - Is usually caused by hyperparathyroidism
    - Resulting from oversecretion of PTH
  - Other causes
    - Malignant cancers (breast, lung, kidney, bone marrow)
    - Excessive calcium or vitamin D supplementation
Electrolyte Balance

- Hypocalcemia
  - Exists if Ca\(^{2+}\) concentration in ECF is <4.5 mEq/L
  - Is much less common than hypercalcemia
  - Is usually caused by chronic renal failure
  - May be caused by hypoparathyroidism
    - Undersecretion of PTH
    - Vitamin D deficiency
Electrolyte Balance

- **Magnesium Balance**
  - Is an important structural component of bone
  - The adult body contains about 29 g of magnesium
  - About 60% is deposited in the skeleton
  - Is a cofactor for important enzymatic reactions
    - Phosphorylation of glucose
    - Use of ATP by contracting muscle fibers
  - Is effectively reabsorbed by PCT
  - Daily dietary requirement to balance urinary loss
    - About 24–32 mEq (0.3–0.4 g)
Electrolyte Balance

- Magnesium Ions (Mg\(^{2+}\))
  - In body fluids are primarily in ICF
    - Mg\(^{2+}\) concentration in ICF is about 26 mEq/L
    - ECF concentration is much lower
Electrolyte Balance

- Phosphate Ions (PO$_4^{3-}$)
  - Are required for bone mineralization
  - About 740 g PO$_4^{3-}$ is bound in mineral salts of the skeleton
  - Daily urinary and fecal losses: about 30–45 mEq (0.8–1.2 g)
  - In ICF, PO$_4^{3-}$ is required for formation of high-energy compounds, activation of enzymes, and synthesis of nucleic acids
  - In plasma, PO$_4^{3-}$ is reabsorbed from tubular fluid along PCT
  - Plasma concentration is 1.8–2.9 mEq/L
Electrolyte Balance

- Chloride Ions (Cl\(^-\))
  - Are the most abundant anions in ECF
  - Plasma concentration is 97–107 mEq/L
  - ICF concentrations are usually low
  - Are absorbed across digestive tract with Na\(^+\)
  - Are reabsorbed with Na\(^+\) by carrier proteins along renal tubules
  - Daily loss is small: 48–146 mEq (1.7–5.1 g)
# Electrolyte Balance

## TABLE 27-2  Electrolyte Balance for Average Adult

<table>
<thead>
<tr>
<th>Ion and Normal ECF Range (mEq/L)</th>
<th>Disorder (mEq/L)</th>
<th>Signs and Symptoms</th>
<th>Causes</th>
<th>Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (136–145)</td>
<td>Hypernatremia (&gt;145)</td>
<td>Thirst, dryness and wrinkling of skin, reduced blood volume and pressure, eventual circulatory collapse</td>
<td>Dehydration; loss of hypotonic fluid</td>
<td>Ingestion of water or intravenous infusion of hypotonic solution</td>
</tr>
<tr>
<td></td>
<td>Hyponatremia (&lt;136)</td>
<td>Disturbed CNS function (water intoxication): confusion, hallucinations, convulsions, coma; death in severe cases</td>
<td>Infusion or ingestion of large volumes of hypotonic solution</td>
<td>Diuretic use and infusion of hypertonic salt solution</td>
</tr>
<tr>
<td>Potassium (3.5–5.5)</td>
<td>Hyperkalemia (&gt;5.5)</td>
<td>Severe cardiac arrhythmias; muscle spasms</td>
<td>Renal failure; use of diuretics; chronic acidosis</td>
<td>Infusion of hypotonic solution; selection of different diuretics; infusion of buffers; dietary restrictions Increase in dietary K⁺ content; ingestion of K⁺ tablets or solutions; infusion of potassium solution</td>
</tr>
<tr>
<td></td>
<td>Hypokalemia (&lt;3.5)</td>
<td>Muscular weakness and paralysis</td>
<td>Low-potassium diet; diuretics; hypersecretion of aldosterone; chronic alkalosis</td>
<td></td>
</tr>
</tbody>
</table>
# Electrolyte Balance

## TABLE 27-2 Electrolyte Balance for Average Adult

<table>
<thead>
<tr>
<th>Ion and Normal ECF Range (mEq/L)</th>
<th>Disorder (mEq/L)</th>
<th>Signs and Symptoms</th>
<th>Causes</th>
<th>Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Calcium</strong>&lt;br&gt;(4.5–5.5)</td>
<td>Hypercalcemia (&lt;5.5)</td>
<td>Confusion, muscle pain, cardiac arrhythmias, kidney stones, calcification of soft tissues</td>
<td>Hyperparathyroidism; cancer; vitamin D toxicity; calcium supplement overdose</td>
<td>Infusion of hypotonic fluid to lower Ca^{2+} levels; surgery to remove parathyroid gland; administration of calcitonin Calcium supplements; administration of vitamin D</td>
</tr>
<tr>
<td></td>
<td>Hypocalcemia (&lt;4.5)</td>
<td>Muscle spasms, convulsions, intestinal cramps, weak heartbeats, cardiac arrhythmias, osteoporosis</td>
<td>Poor diet; lack of vitamin D; renal failure; hypoparathyroidism; hypomagnesemia</td>
<td></td>
</tr>
<tr>
<td><strong>Magnesium</strong>&lt;br&gt;(1.4–2.1)</td>
<td>Hypermagnesemia (&gt;2.1)</td>
<td>Confusion, lethargy, respiratory depression, hypotension</td>
<td>Overdose of magnesium supplements or antacids (rare)</td>
<td>Infusion of hypotonic solution to lower plasma concentration Intravenous infusion of solution high in Mg^{2+}</td>
</tr>
<tr>
<td></td>
<td>Hypomagnesemia (&lt;1.4)</td>
<td>Hypocalcemia, muscle weakness, cramps, cardiac arrhythmias, hypertension</td>
<td>Poor diet; alcoholism; severe diarrhea; kidney disease; malabsorption syndrome; ketoacidosis</td>
<td></td>
</tr>
<tr>
<td><strong>Phosphate</strong>&lt;br&gt;(1.8–2.9)</td>
<td>Hyperphosphatemia (&gt;2.9)</td>
<td>No immediate symptoms; chronic elevation leads to calcification of soft tissues</td>
<td>High dietary phosphate intake; hypoparathyroidism</td>
<td>Dietary reduction; PTH supplementation</td>
</tr>
<tr>
<td></td>
<td>Hypophosphatemia (&lt;1.8)</td>
<td>Anorexia, dizziness, muscle weakness, cardiomyopathy, osteoporosis</td>
<td>Poor diet; kidney disease; malabsorption syndrome; hyperparathyroidism; vitamin D deficiency</td>
<td>Dietary improvement; vitamin D and/or calcitriol supplementation</td>
</tr>
<tr>
<td><strong>Chloride</strong>&lt;br&gt;(97–107)</td>
<td>Hyperchloremia (&gt;107)</td>
<td>Acidosis, hyperkalemia</td>
<td>Dietary excess; increased chloride retention Vomiting; hypokalemia</td>
<td>Infusion of hypotonic solution to lower plasma concentration Diuretic use and infusion of hypertonic salt solution</td>
</tr>
<tr>
<td></td>
<td>Hypochloremia (&lt;97)</td>
<td>Alkalosis, anorexia, muscle cramps, apathy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Acid–Base Balance

- pH of body fluids is altered by
  - Introduction of acids or bases
- Acids and bases may be strong or weak
# Acid–Base Balance

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>pH</strong></td>
<td>The negative exponent (negative logarithm) of the hydrogen ion concentration ([H^+])</td>
</tr>
<tr>
<td><strong>Neutral</strong></td>
<td>A solution with a pH of 7; the solution contains equal numbers of hydrogen ions and hydroxide ions</td>
</tr>
<tr>
<td><strong>Acidic</strong></td>
<td>A solution with a pH below 7; in this solution, hydrogen ions ([H^+]) predominate</td>
</tr>
<tr>
<td><strong>Basic, or alkaline</strong></td>
<td>A solution with a pH above 7; in this solution, hydroxide ions ([OH^-]) predominate</td>
</tr>
<tr>
<td><strong>Acid</strong></td>
<td>A substance that dissociates to release hydrogen ions, decreasing pH</td>
</tr>
<tr>
<td><strong>Base</strong></td>
<td>A substance that dissociates to release hydroxide ions or to tie up hydrogen ions, increasing pH</td>
</tr>
<tr>
<td><strong>Salt</strong></td>
<td>An ionic compound consisting of a cation other than hydrogen and an anion other than a hydroxide ion</td>
</tr>
<tr>
<td><strong>Buffer</strong></td>
<td>A substance that tends to oppose changes in the pH of a solution by removing or replacing hydrogen ions; in body fluids, buffers maintain blood pH within normal limits (7.35–7.45)</td>
</tr>
</tbody>
</table>
Acid–Base Balance

- **Strong acids and strong bases**
  - Dissociate completely in solution

- **Weak acids or weak bases**
  - Do not dissociate completely in solution
  - Some molecules remain intact
  - Liberate fewer hydrogen ions
  - Have less effect on pH of solution
Acid–Base Balance

- Carbonic Acid
  - Is a weak acid
  - In ECF at normal pH
    - Equilibrium state exists
    - Is diagrammed $H_2CO_3 \leftrightarrow H^+ + HCO_3^-$
The Importance of pH Control

- pH of body fluids depends on dissolved
  - Acids
  - Bases
  - Salts

- pH of ECF
  - Is narrowly limited, usually 7.35–7.45
Acid–Base Balance

- **Acidosis**
  - Physiological state resulting from abnormally low plasma pH
  - Acidemia: plasma pH < 7.35

- **Alkalosis**
  - Physiological state resulting from abnormally high plasma pH
  - Alkalemia: plasma pH > 7.45
Acid–Base Balance

- Acidosis and Alkalosis
  - Affect all body systems
    - Particularly nervous and cardiovascular systems
  - Both are dangerous
    - But acidosis is more common
    - Because normal cellular activities generate acids
Acid–Base Balance

Types of Acids in the Body

- Volatile acids
- Fixed acids
- Organic acids
Acid–Base Balance

- Volatile Acids
  - Can leave solution and enter the atmosphere
  - **Carbonic acid** is an important volatile acid in body fluids
  - At the lungs, carbonic acid breaks down into carbon dioxide and water
    - Carbon dioxide diffuses into alveoli
Carbon Dioxide

- In solution in peripheral tissues
  - Interacts with water to form carbonic acid
- Carbonic acid dissociates to release
  - Hydrogen ions
  - Bicarbonate ions
Carbonic Anhydrase (CA)

- Enzyme that catalyzes dissociation of carbonic acid
- Found in
  - Cytoplasm of red blood cells
  - Liver and kidney cells
  - Parietal cells of stomach
  - Other cells
Acid–Base Balance

- CO₂ and pH
  - Most CO₂ in solution converts to carbonic acid
    - Most carbonic acid dissociates
  - P_{CO₂} is the most important factor affecting pH in body tissues
    - P_{CO₂} and pH are inversely related
Acid–Base Balance

- CO₂ and pH
  - When CO₂ levels rise
    - H⁺ and bicarbonate ions are released
    - pH goes down
  - At alveoli
    - CO₂ diffuses into atmosphere
    - H⁺ and bicarbonate ions in alveolar capillaries drop
    - Blood pH rises
Acid–Base Balance

Figure 27–6 The Basic Relationship between PCO$_2$ and Plasma pH.
Acid–Base Balance

- **Fixed Acids**
  - Are acids that do not leave solution
  - Once produced they remain in body fluids
    - Until eliminated by kidneys
  - Sulfuric acid and phosphoric acid
    - Are most important fixed acids in the body
    - Are generated during catabolism of:
      - amino acids
      - phospholipids
      - nucleic acids
Acid–Base Balance

- **Organic Acids**
  - Produced by aerobic metabolism
    - Are metabolized rapidly
    - Do not accumulate
  - Produced by anaerobic metabolism (e.g., lactic acid)
    - Build up rapidly
Acid–Base Balance

- Mechanisms of pH Control
  - To maintain acid–base balance
    - The body balances gains and losses of hydrogen ions
Acid–Base Balance

- **Hydrogen Ions (H⁺)**
  - Are gained
    - At digestive tract
    - Through cellular metabolic activities
  - Are eliminated
    - At kidneys and in urine
    - At lungs
  - Must be neutralized to avoid tissue damage
  - Acids produced in normal metabolic activity
    - Are temporarily neutralized by buffers in body fluids
Acid–Base Balance

- Buffers
  - Are dissolved compounds that stabilize pH
    - By providing or removing H⁺
  - Weak acids
    - Can donate H⁺
  - Weak bases
    - Can absorb H⁺
Acid–Base Balance

- **Buffer System**
  - Consists of a combination of
    - A weak acid
    - And the anion released by its dissociation
  - The anion functions as a weak base
  - In solution, molecules of weak acid exist in equilibrium with its dissociation products
Three Major Buffer Systems

- **Protein buffer systems**: Help regulate pH in ECF and ICF. Interact extensively with other buffer systems.

- **Carbonic acid–bicarbonate buffer system**: Most important in ECF.

- **Phosphate buffer system**: Buffers pH of ICF and urine.
Figure 27–7 Buffer Systems in Body Fluids.
acid–base balance

- **Protein Buffer Systems**
  - Depend on amino acids
  - Respond to pH changes by accepting or releasing $H^+$
  - If pH rises
    - Carboxyl group of amino acid dissociates
    - Acting as weak acid, releasing a hydrogen ion
    - Carboxyl group becomes carboxylate ion
### Acid–Base Balance

- **Protein Buffer Systems**
  - At normal pH (7.35–7.45)
    - Carboxyl groups of most amino acids have already given up their $\text{H}^+$
  - If pH drops
    - Carboxylate ion and amino group act as weak bases
    - Accept $\text{H}^+$
    - Form carboxyl group and amino ion
Acid–Base Balance

- **Protein Buffer Systems**
  - Carboxyl and amino groups in peptide bonds cannot function as buffers
  - Other proteins contribute to buffering capabilities
    - Plasma proteins
    - Proteins in interstitial fluid
    - Proteins in ICF
Acid–Base Balance

In alkaline medium, amino acid acts as an acid and releases $H^+$

Amino acid

If pH rises

If pH falls

In acidic medium, amino acid acts as a base and absorbs $H^+$

Neutral pH

Figure 27–8 The Role of Amino Acids in Protein Buffer Systems.
Acid–Base Balance

- The Hemoglobin Buffer System
  - CO$_2$ diffuses across RBC membrane
    - No transport mechanism required
  - As carbonic acid dissociates
    - Bicarbonate ions diffuse into plasma
    - In exchange for chloride ions (chloride shift)
  - Hydrogen ions are buffered by hemoglobin molecules
Acid–Base Balance

- The Hemoglobin Buffer System
  - Is the only intracellular buffer system with an immediate effect on ECF pH
  - Helps prevent major changes in pH when plasma $P_{CO_2}$ is rising or falling
Acid–Base Balance

- Carbonic Acid–Bicarbonate Buffer System
  - Carbon Dioxide
    - Most body cells constantly generate carbon dioxide
    - Most carbon dioxide is converted to carbonic acid, which dissociates into $\text{H}^+$ and a bicarbonate ion
  - Is formed by carbonic acid and its dissociation products
  - Prevents changes in pH caused by organic acids and fixed acids in ECF


Carbonic Acid–Bicarbonate Buffer System

1. Cannot protect ECF from changes in pH that result from elevated or depressed levels of CO$_2$
2. Functions only when respiratory system and respiratory control centers are working normally
3. Ability to buffer acids is limited by availability of bicarbonate ions
Figure 27–9 The Carbonic Acid–Bicarbonate Buffer System

(a) Carbonic acid–bicarbonate buffer system

(b) Bicarbonate reserve

Fixed acids or organic acids: add H⁺
Phosphate Buffer System

- Consists of anion $\text{H}_2\text{PO}_4^-$ (a weak acid)
- Works like the carbonic acid–bicarbonate buffer system
- Is important in buffering pH of ICF
Acid–Base Balance

- Limitations of Buffer Systems
  - Provide only temporary solution to acid–base imbalance
  - Do not eliminate $\text{H}^+$ ions
  - Supply of buffer molecules is limited
Maintenance of Acid–Base Balance

For homeostasis to be preserved, captured $\text{H}^+$ must:

1. Be permanently tied up in water molecules:
   - through $\text{CO}_2$ removal at lungs

2. Be removed from body fluids:
   - through secretion at kidney
Acid–Base Balance

- Maintenance of Acid–Base Balance
  - Requires balancing $H^+$ gains and losses
  - Coordinates actions of buffer systems with
    - Respiratory mechanisms
    - Renal mechanisms
Acid–Base Balance

- Respiratory and Renal Mechanisms
  - Support buffer systems by
    - Secreting or absorbing $\text{H}^+$
    - Controlling excretion of acids and bases
    - Generating additional buffers
Acid–Base Balance

- Respiratory Compensation
  - Is a change in respiratory rate
    - That helps stabilize pH of ECF
  - Occurs whenever body pH moves outside normal limits
  - Directly affects carbonic acid–bicarbonate buffer system
Acid–Base Balance

- Respiratory Compensation
  - Increasing or decreasing the rate of respiration alters pH by lowering or raising the $P_{CO_2}$
  - When $P_{CO_2}$ rises
    - pH falls
    - Addition of CO$_2$ drives buffer system to the right
  - When $P_{CO_2}$ falls
    - pH rises
    - Removal of CO$_2$ drives buffer system to the right
Acid–Base Balance

- **Renal Compensation**
  - Is a change in rates of $H^+$ and $HCO_3^-$ secretion or reabsorption by kidneys in response to changes in plasma pH.
  - The body normally generates enough organic and fixed acids each day to add 100 mEq of $H^+$ to ECF.
  - Kidneys assist lungs by eliminating any $CO_2$ that
    - Enters renal tubules during filtration.
    - Diffuses into tubular fluid en route to renal pelvis.
Acid–Base Balance

- Hydrogen Ions
  - Are secreted into tubular fluid along
    - Proximal convoluted tubule (PCT)
    - Distal convoluted tubule (DCT)
    - Collecting system
Acid–Base Balance

- Buffers in Urine
  - The ability to eliminate large numbers of $\text{H}^+$ in a normal volume of urine depends on the presence of buffers in urine:
    1. Carbonic acid–bicarbonate buffer system
    2. Phosphate buffer system
    3. Ammonia buffer system
Acid–Base Balance

- Major Buffers in Urine
  - Glomerular filtration provides components of
    - Carbonic acid–bicarbonate buffer system
    - Phosphate buffer system
  - Tubule cells of PCT
    - Generate ammonia
Acid–Base Balance

Figure 27–10a Kidney Tubules and pH Regulation.
Acid–Base Balance

Figure 27–10b Kidney Tubules and pH Regulation: The Production of Ammonium Ions and Ammonia by the Breakdown of Glutamine.
Figure 27–10c Kidney Tubules and pH Regulation: The Response of the Kidney Tubules to Alkalosis.
- **Renal Responses to Acidosis**
  1. Secretion of $\text{H}^+$
  2. Activity of buffers in tubular fluid
  3. Removal of $\text{CO}_2$
  4. Reabsorption of $\text{NaHCO}_3$
Renal Responses to Alkalosis

1. Rate of secretion at kidneys declines
2. Tubule cells do not reclaim bicarbonates in tubular fluid
3. Collecting system transports $\text{HCO}_3^-$ into tubular fluid while releasing strong acid (HCl) into peritubular fluid
1. Disorders:
   - Circulating buffers
   - Respiratory performance
   - Renal function

2. Cardiovascular conditions:
   - Heart failure
   - Hypotension

3. Conditions affecting the CNS:
   - Neural damage or disease that affects respiratory and cardiovascular reflexes
Acid–Base Balance Disturbances

- **Acute phase**
  - The initial phase
  - pH moves rapidly out of normal range

- **Compensated phase**
  - When condition persists
  - Physiological adjustments occur
Respiratory Acid–Base Disorders

- Result from imbalance between
  - $\text{CO}_2$ generation in peripheral tissues
  - $\text{CO}_2$ excretion at lungs
- Cause abnormal $\text{CO}_2$ levels in ECF
Metabolic Acid–Base Disorders

Result from

- Generation of organic or fixed acids
- Conditions affecting $\text{HCO}_3^-$ concentration in ECF
Figure 27–11a Interactions among the Carbonic Acid–Bicarbonate Buffer System and Compensatory Mechanisms in the Regulation of Plasma pH.
Figure 27–11b Interactions among the Carbonic Acid–Bicarbonate Buffer System and Compensatory Mechanisms in the Regulation of Plasma pH.
Acid–Base Balance Disturbances

- **Respiratory Acidosis**
  - Develops when the respiratory system cannot eliminate all CO$_2$ generated by peripheral tissues
  - Primary sign
    - Low plasma pH due to hypercapnia
  - Primary cause
    - Hypoventilation
Respiratory Alkalosis

- Primary sign
  - High plasma pH due to hypocapnia

- Primary cause
  - Hyperventilation
Acid–Base Balance Disturbances

Figure 27–12a Respiratory Acid–Base Regulation.
Acid–Base Balance Disturbances

Figure 27–12b Respiratory Acid–Base Regulation.

- HOMEOSTASIS
  - Normal acid–base balance
  - HOMEOSTASIS RESTORED
    - Buffer systems other than carbonic acid–bicarbonate system release H⁺ ions
    - Increased $P_{CO_2}$

- HOMEOSTASIS DISTURBED
  - Hyperventilation causing decreased $P_{CO_2}$
  - RESPIRATORY ALKALOSIS
    - Inhibition of arterial and CSF chemoreceptors
    - Renal compensation
      - $H^+$ generation; $HCO_3^-$ secretion
    - Respiratory compensation
      - Decreased respiratory rate

(b)
Acid–Base Balance Disturbances

- **Metabolic Acidosis**
  1. Production of large numbers of fixed or organic acids:
     - \( \text{H}^+ \) overloads buffer system
  2. Impaired \( \text{H}^+ \) excretion at kidneys
  3. Severe bicarbonate loss
Acid–Base Balance Disturbances

- Two Types of Metabolic Acidosis
  - Lactic acidosis
    - Produced by anaerobic cellular respiration
  - Ketoacidosis
    - Produced by excess ketone bodies
Acid–Base Balance Disturbances

Figure 27–13 Responses to Metabolic Acidosis.
Acid–Base Balance Disturbances

- Combined Respiratory and Metabolic Acidosis
  - Respiratory and metabolic acidosis are typically linked
    - Low $O_2$ generates lactic acid
    - Hypoventilation leads to low $PO_2$
Acid–Base Balance Disturbances

- **Metabolic Alkalosis**
  - Is caused by elevated $\text{HCO}_3^-$ concentrations
  - Bicarbonate ions interact with $\text{H}^+$ in solution
    - Forming $\text{H}_2\text{CO}_3$
  - Reduced $\text{H}^+$ causes alkalosis
Figure 27–14 Metabolic Alkalosis.
Acid–Base Balance Disturbances

- The Detection of Acidosis and Alkalosis
  - Includes blood tests for pH, $P_{CO_2}$ and $HCO_3^-$ levels
    - Recognition of acidosis or alkalosis
    - Classification as respiratory or metabolic
Acid–Base Balance Disturbances

Figure 27–15 A Diagnostic Chart for Acid–Base Disorders.
# Acid–Base Balance Disturbances

## TABLE 27–4 Changes in Blood Chemistry Associated with the Major Classes of Acid–Base Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>pH (normal 7.35–7.45)</th>
<th>HCO₃⁻ (normal 24–28 mEq/L)</th>
<th>P&lt;sub&gt;CO₂&lt;/sub&gt; (mm Hg) (normal = 35–45)</th>
<th>Remarks</th>
<th>Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory acidosis</td>
<td>Decreased (below 7.35)</td>
<td>Acute: normal</td>
<td>Increased (above 45)</td>
<td>Generally caused by hypoventilation and CO₂ buildup in tissues and blood</td>
<td>Improve ventilation; in some cases, with bronchodilation and mechanical assistance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compensated: increased</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>(above 28)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>Decreased (below 7.35)</td>
<td>Decreased (below 24)</td>
<td>Acute: normal</td>
<td>Caused by buildup of organic or fixed acid, impaired H⁺ elimination at kidneys, or HCO₃⁻ loss in urine or feces</td>
<td>Administration of bicarbonate (gradual), with other steps as needed to correct primary cause</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Compensated: decreased (below 35)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory alkalosis</td>
<td>Increased (above 7.45)</td>
<td>Acute: normal</td>
<td>Decreased (below 35)</td>
<td>Generally caused by hyperventilation and reduction in plasma CO₂ levels</td>
<td>Reduce respiratory rate, allow rise in P&lt;sub&gt;CO₂&lt;/sub&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compensated: decreased</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(below 35)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>Increased (above 7.45)</td>
<td>Increased (above 28)</td>
<td>Increased (above 45)</td>
<td>Generally caused by prolonged vomiting and associated acid loss</td>
<td>pH below 7.55: no treatment; pH above 7.55: may require administration of NH₄Cl</td>
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</tbody>
</table>
Fetal pH Control

- Buffers in fetal bloodstream provide short-term pH control
- Maternal kidneys eliminate generated H⁺
Newborn Electrolyte Balance

- Body water content is high
  - 75% of body weight
- Basic electrolyte balance is same as adult’s
Age and Fluid, Electrolyte, and Acid–Base Balance

- Aging and Fluid Balance
  - Body water content, ages 40–60
    - Males 55%
    - Females 47%
  - After age 60
    - Males 50%
    - Females 45%
Aging and Fluid Balance

- Decreased body water content reduces dilution of waste products, toxins, and drugs
- Reduction in glomerular filtration rate and number of functional nephrons
  - Reduces pH regulation by renal compensation
- Ability to concentrate urine declines
  - More water is lost in urine
Aging and Fluid Balance

- Insensible perspiration increases as skin becomes thinner
- Maintaining fluid balance requires higher daily water intake
- Reduction in ADH and aldosterone sensitivity
  - Reduces body water conservation when losses exceed gains
Age and Fluid, Electrolyte, and Acid–Base Balance

- Aging and Electrolyte Balance
  - Muscle mass and skeletal mass decrease
    - Cause net loss in body mineral content
  - Loss is partially compensated by
    - Exercise
    - Dietary mineral supplement
Aging and Acid–Base Balance

- Reduction in vital capacity
  - Reduces respiratory compensation
  - Increases risk of respiratory acidosis
  - Aggravated by arthritis and emphysema
Aging and Major Systems

- Disorders affecting major systems increase
  - Affecting fluid, electrolyte, and/or acid–base balance