An Introduction to Fluid, Electrolyte, and Acid–Base Balance

• 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
27-1 Fluid, Electrolyte, and Acid–Base Balance

• 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

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
• Electrolyte 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
27-1 Fluid, Electrolyte, and Acid–Base Balance

• **Acid–Base Balance**
  
  • Precisely balances production and loss of hydrogen ions (pH)
  
  • The body generates acids during normal metabolism
    • Tends to reduce pH
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
27-2 Fluid Compartments

- Fluid in the Body
  - Water accounts for roughly:
    - 60% of male body weight
    - 50% of female body weight
    - Mostly in intracellular fluid
27-2 Fluid Compartments

- Water Exchange
  - Water exchange between ICF and ECF occurs across plasma membranes by:
    - Osmosis
    - Diffusion
    - Carrier-mediated transport
27-2 Fluid Compartments

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

- **Minor Subdivisions of ECF**
  - Lymph, perilymph, and endolymph
  - Cerebrospinal fluid (CSF)
  - Synovial fluid
  - Serous fluids (pleural, pericardial, and peritoneal)
  - Aqueous humor
27-2 Fluid Compartments

- 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
The body composition (by weight, averaged for both sexes) and major body fluid compartments of a 70-kg individual.
The body composition (by weight, averaged for both sexes) and major body fluid compartments of a 70-kg individual.
A comparison of the body compositions of adult males and females, ages 18–40 years.

**Figure 27-1b  The Composition of the Human Body**

- **WATER 60%**
  - Intracellular fluid 33%
  - Interstitial fluid 21.5%
  - Solids 40% (organic and inorganic materials)
  - Plasma 4.5%
  - Other body fluids (≤1%)

**Adult males**
A comparison of the body compositions of adult males and females, ages 18–40 years.
27-2 Fluid Compartments

- The ECF and the ICF
  - ECF Solute Content
    - Types and amounts vary regionally
      - Electrolytes
      - Proteins
      - Nutrients
      - Waste products
27-2 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

• 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

CATIONS

ECF | ICF
--- | ---

**KEY**

- **Cations**
  - Na⁺
  - K⁺
  - Ca²⁺
  - Mg²⁺

<table>
<thead>
<tr>
<th>Fluid Type</th>
<th>Na⁺</th>
<th>K⁺</th>
<th>Ca²⁺</th>
<th>Mg²⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>150</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interstitial</td>
<td>150</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intracellular</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Milliequivalents per liter (mEq/L)
Figure 27-2  Cations and Anions in Body Fluids

KEY

Anions
- $\text{HCO}_3^-$
- $\text{Cl}^-$
- $\text{HPO}_4^{2-}$
- $\text{SO}_4^{2-}$

Organic acid

Proteins

<table>
<thead>
<tr>
<th>ECF</th>
<th>ICF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma</strong></td>
<td><strong>Interstitial fluid</strong></td>
</tr>
<tr>
<td>$\text{HCO}_3^-$</td>
<td>$\text{HCO}_3^-$</td>
</tr>
<tr>
<td>$\text{Cl}^-$</td>
<td>$\text{Cl}^-$</td>
</tr>
<tr>
<td>$\text{HPO}_4^{2-}$</td>
<td>$\text{HPO}_4^{2-}$</td>
</tr>
<tr>
<td>$\text{HCO}_3^-$</td>
<td>$\text{HCO}_3^-$</td>
</tr>
<tr>
<td>$\text{Cl}^-$</td>
<td>$\text{Cl}^-$</td>
</tr>
<tr>
<td>$\text{HPO}_4^{2-}$</td>
<td>$\text{HPO}_4^{2-}$</td>
</tr>
<tr>
<td>$\text{SO}_4^{2-}$</td>
<td>$\text{SO}_4^{2-}$</td>
</tr>
<tr>
<td>Proteins</td>
<td>Proteins</td>
</tr>
</tbody>
</table>
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
27-2 Fluid Compartments

• The Osmotic Concentration of ICF and ECF
  • Is identical
  • Osmosis eliminates minor differences in concentration
    • Because plasma membranes are permeable to water
27-2 Fluid Compartments

- Basic Concepts in the Regulation of Fluids and Electrolytes

1. All homeostatic mechanisms that monitor and adjust body fluid composition respond to changes in the ECF, not in the ICF

2. No receptors directly monitor fluid or electrolyte balance

3. Cells cannot move water molecules by active transport

4. The body’s water or electrolyte content will rise if dietary gains exceed environmental losses, and will fall if losses exceed gains
27-2 Fluid Compartments

- An Overview of the Primary Regulatory Hormones
  - Affecting fluid and electrolyte balance
    1. Antidiuretic hormone
    2. Aldosterone
    3. Natriuretic peptides
27-2 Fluid Compartments

- Antidiuretic Hormone (ADH)
  - Stimulates water conservation at kidneys
    - Reducing urinary water loss
    - Concentrating urine
  - Stimulates thirst center
    - Promoting fluid intake
27-2 Fluid Compartments

- ADH Production
  - **Osmoreceptors** in hypothalamus
    - Monitor osmotic concentration of ECF
  - Change in osmotic concentration
    - Alters osmoreceptor activity
  - Osmoreceptor neurons secrete ADH
27-2 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 adrenal 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
27-2 Fluid Compartments

• “Water Follows Salt”
  • High aldosterone plasma concentration
    • Causes kidneys to conserve salt
  • Conservation of Na⁺ by aldosterone
    • Also stimulates water retention
27-2 Fluid Compartments

• 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
27-3 Fluid Movement

• Movement of Water and Electrolytes
  • 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
27-3 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
27-3 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
27-3 Fluid Movement

- Fluid Movement within the ECF
  - ECF fluid volume is redistributed
    - From lymphatic 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
27-3 Fluid Movement

- **Edema**
  - The movement of abnormal amounts of water from plasma into interstitial fluid

- **Lymphedema**
  - Edema caused by blockage of lymphatic drainage
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).
27-3 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

- Water absorbed across digestive epithelium (2000 mL)
- Water vapor lost in respiration and evaporation from moist surfaces (1150 mL)
- Water lost in feces (150 mL)
- Water secreted by sweat glands (variable)
- Water lost in urine (1000 mL)

ECF

ICF

Metabolic water (300 mL)

Plasma membranes
### 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>

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27-3 Fluid Movement

- Metabolic Generation of Water
  - Is produced within cells
  - Results from oxidative phosphorylation in mitochondria
27-3 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
  - *If ECF osmotic concentration decreases:*
    - Fluid becomes hypotonic to ICF
    - Water moves from ECF to cells
Fluid Movement

- Fluid Shifts
  - ICF volume is much greater than ECF volume
    - ICF acts as water reserve
    - Prevents large osmotic changes in ECF
27-3 Fluid Movement

- Allocation of Water Losses

- **Dehydration** (*Water Depletion*)
  - Develops when water loss is greater than gain
  - 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)
27-3 Fluid Movement

**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** (*water excess*)
    - Occurs when excess water shifts into ICF
      - Distorting cells
      - Changing solute concentrations around enzymes
      - Disrupting normal cell functions
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
27-3 Fluid Movement

• Signs of Overhydration
  • Abnormally low Na\(^+\) concentrations (*hyponatremia*)
  • Effects on CNS function (*water intoxication*)
Figure 27-4 Fluid Shifts between the ICF and ECF

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

The ECF and ICF are in balance, with the two solutions isotonic.

Water loss from ECF reduces volume and makes this solution hypertonic with respect to the ICF.

Decreased ECF volume

Decreased ICF volume

Increased ECF volume

An osmotic water shift from the ICF into the ECF restores osmotic equilibrium but reduces the ICF volume.
27-4 Electrolyte Balance

• 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*
27-4 Electrolyte Balance

• Sodium
  • Is the dominant cation in ECF
  • Sodium salts provide 90% of ECF osmotic concentration
    • Sodium chloride (NaCl)
    • Sodium bicarbonate (NaHCO₃)
27-4 Electrolyte Balance

• Normal Sodium Concentrations
  • In ECF
    • About 140 mEq/L
  • In ICF
    • Is 10 mEq/L or less
27-4 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
• 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
27-4 Electrolyte Balance

• Sodium Balance

• Total amount of sodium in ECF represents a balance between two factors

  1. Sodium ion uptake across digestive epithelium
  2. Sodium ion excretion in urine and perspiration
27-4 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
27-4 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
  - Na\(^+\) regulatory mechanism changes ECF volume
    - Keeps concentration stable
  - When Na\(^+\) losses exceed gains:
    - ECF volume decreases (increased water loss)
    - Maintaining osmotic concentration
27-4 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
Figure 27-5 The Homeostatic Regulation of Normal Sodium Ion Concentrations in Body Fluids

ADH Secretion Increases
The secretion of ADH restricts water loss and stimulates thirst, promoting additional water consumption.

Osmoreceptors in hypothalamus stimulated

HOMEOSTASIS DISTURBED
Increased Na\(^+\) levels in ECF

Recall of Fluids
Because the ECF osmolarity increases, water shifts out of the ICF, increasing ECF volume and lowering Na\(^+\) concentrations.

HOMEOSTASIS RESTORED
Decreased Na\(^+\) levels in ECF

HOMESTASIS
Normal Na\(^+\) concentration in ECF

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HOMEOSTASIS
Normal Na⁺ concentration in ECF

HOMEOSTASIS DISTURBED
Decreased Na⁺ levels in ECF

Osmoreceptors in hypothalamus inhibited

ADH Secretion Decreases
As soon as the osmotic concentration of the ECF drops by 2 percent or more, ADH secretion decreases, so thirst is suppressed and water losses at the kidneys increase.

HOMEOSTASIS RESTORED
Increased Na⁺ levels in ECF

Water loss reduces ECF volume, concentrates ions
27-4 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
27-4 Electrolyte Balance

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

- **Hypernatremia**
  - Body water content declines (dehydration)
  - ECF $\text{Na}^+$ concentration $>$145 mEq/L
27-4 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
27-4 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 27-6 The Integration of Fluid Volume Regulation and Sodium Ion Concentrations in Body Fluids

Rising blood pressure and volume

Natriuretic peptides released by cardiac muscle cells

Increased blood volume and atrial distension

HOMEOSTASIS DISTURBED
Rising ECF volume by fluid gain or fluid and Na⁺ gain

Responses to Natriuretic Peptides

- Increased Na⁺ loss in urine
- Increased water loss in urine
- Reduced thirst
- Inhibition of ADH, aldosterone, epinephrine, and norepinephrine release

Combined Effects

- Reduced blood volume
- Reduced blood pressure

HOMEOSTASIS RESTORED
Falling ECF volume

HOMEOSTASIS
Normal ECF volume

Start
Figure 27-6  The Integration of Fluid Volume Regulation and Sodium Ion Concentrations in Body Fluids

HOMEOSTASIS

Normal ECF volume

Start

HOMEOSTASIS DISTURBED
Falling ECF volume by fluid loss or fluid and Na⁺ loss

Decreased blood volume and blood pressure

Endocrine Responses
Increased renin secretion and angiotensin II activation
Increased aldosterone release
Increased ADH release

Combined Effects
Increased urinary Na⁺ retention
Decreased urinary water loss
Increased thirst
Increased water intake

HOMEOSTASIS RESTORED
Rising ECF volume

Falling blood pressure and volume
Potassium Balance
- 98% of potassium in the human body is in ICF
- Cells expend energy to recover potassium ions diffused from cytoplasm into ECF

Processes of Potassium Balance
1. Rate of gain across digestive epithelium
2. Rate of loss into urine
27-4 Electrolyte Balance

• Potassium Loss in Urine
  • Is regulated by activities of ion pumps
    • Along distal portions of nephron and collecting system
    • Na\(^+\) from tubular fluid is exchanged for 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)
27-4 Electrolyte Balance

• Factors in Tubular Secretion of K$^+$
  1. Changes in $K^+$ concentration of ECF
  2. Changes in pH
  3. Aldosterone levels
27-4 Electrolyte Balance

• **Changes in Concentration of $K^+$ in ECF**
  - Higher ECF concentration increases rate of secretion

• **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
• **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
When the plasma concentration of potassium falls below 2 mEq/L, extensive muscular weakness develops, followed by eventual paralysis. This condition, called hypokalemia (kalium, potassium), is potentially lethal due to its effects on the heart.

Factors Promoting Hypokalemia

- Several diuretics, including Lasix, can produce hypokalemia by increasing the volume of urine produced.
- The endocrine disorder called aldosteronism, characterized by excessive aldosterone secretion, results in hypokalemia by overstimulating sodium retention and potassium loss.

Factors Promoting Hyperkalemia

- Chronically low body fluid pH promotes hyperkalemia by interfering with K⁺ excretion at the kidneys.
- Kidney failure due to damage or disease will prevent normal K⁺ secretion and thereby produce hyperkalemia.
- Several drugs promote diuresis by blocking Na⁺ reabsorption at the kidneys. When sodium reabsorption slows down, so does potassium secretion, and hyperkalemia can result.

Normal potassium levels in serum: (3.5–5.0 mEq/L)

High K⁺ concentrations in the ECF produce an equally dangerous condition known as hyperkalemia. Severe cardiac arrhythmias appear when the K⁺ concentration exceeds 8 mEq/L.
### 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 (135–145)</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;135)</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 (3.5–5.0)</td>
<td>Hyperkalemia (&gt;5.0)</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</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>Increase in dietary K⁺ content; ingestion of K⁺ tablets or solutions; infusion of potassium solution</td>
</tr>
</tbody>
</table>
• 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
27-4 Electrolyte Balance

- Functions of Calcium Ion (Ca$^{2+}$)
  - Muscular and neural activities
  - Blood clotting
  - Cofactors for enzymatic reactions
  - Second messengers
27-4 Electrolyte Balance

- Hormones and Calcium Homeostasis
  - Parathyroid hormone (PTH) and calcitriol
    - Raise calcium concentrations in ECF
  - Calcitonin
    - Opposes PTH and calcitriol
27-4 Electrolyte Balance

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

- 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
27-4 Electrolyte Balance

• **Hypercalcemia**
  
  • Exists if \( \text{Ca}^{2+} \) 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
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
27-4 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)
• 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
<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>Calcium (4.3–5.3)</td>
<td>Hypercalcemia (&gt;5.3)</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</td>
</tr>
<tr>
<td></td>
<td>Hypocalcemia (&lt;4.3)</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>Calcium supplements; administration of vitamin D</td>
</tr>
<tr>
<td>Magnesium (1.4–2.0)</td>
<td>Hypermagnesemia (&gt;2.0)</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</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>Intravenous infusion of solution high in Mg(^{2+})</td>
</tr>
</tbody>
</table>
Phosphate Ions \((\text{PO}_4^{3-})\)

- Are required for bone mineralization
- About 740 g \(\text{PO}_4^{3-}\) is bound in mineral salts of the skeleton
- Daily urinary and fecal losses about 30–45 mEq (0.8–1.2 g)
- In ICF, \(\text{PO}_4^{3-}\) is required for formation of high-energy compounds, activation of enzymes, and synthesis of nucleic acids
- In plasma, \(\text{PO}_4^{3-}\) is reabsorbed from tubular fluid along PCT
- Plasma concentration is 1.8–2.9 mEq/L
27-4 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)
<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>Phosphate</td>
<td>Hyperphosphatemia (&gt;3.0)</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>Chloride</td>
<td>Hyperchloremia (&gt;108)</td>
<td>Acidosis, hyperkalemia</td>
<td>Dietary excess; increased chloride retention</td>
<td>Infusion of hypotonic solution to lower plasma concentration</td>
</tr>
<tr>
<td></td>
<td>Hypochloremia (&lt;100)</td>
<td>Alkalosis, anorexia, muscle cramps, apathy</td>
<td>Vomiting; hypokalemia</td>
<td>Diuretic use and infusion of hypertonic salt solution</td>
</tr>
</tbody>
</table>
27-5 Acid–Base Balance

• Acid–Base Balance
  • pH of body fluids is altered by addition or deletion of acids or bases
  • Acids and bases may be strong or weak
    • *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
### Table 27–3  A Review of Important Terms Relating to Acid–Base Balance

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</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>
27-5 Acid–Base Balance

• Carbonic Acid
  • Is a weak acid
  • In ECF at normal pH:
    • Equilibrium state exists

\[
\text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-
\]
27-5 Acid–Base Balance

• 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
27-5 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
27-5 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
27-5 Acid–Base Balance

• Types of Acids in the Body

1. Fixed acids
2. Organic acids
3. Volatile acids
27-5 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
27-5 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
• Carbonic Acid
  • A volatile acid that can leave solution and enter the atmosphere
  • 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
27-5 Acid–Base Balance

• **Carbonic Anhydrase**
  - Enzyme that catalyzes dissociation of carbonic acid
  - Found in:
    - Cytoplasm of red blood cells
    - Liver and kidney cells
    - Parietal cells of stomach
    - Other cells
27-5 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
27-5 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
If $P_{CO_2}$ rises

When carbon dioxide levels rise, more carbonic acid forms, additional hydrogen ions and bicarbonate ions are released, and the pH goes down.
When the $P_{CO_2}$ falls, the reaction runs in reverse, and carbonic acid dissociates into carbon dioxide and water. This removes $H^+$ ions from solution and increases the pH.

$$H^+ + HCO_3^- \longrightarrow H_2CO_3 \longrightarrow H_2O + CO_2$$
Mechanisms of pH Control

To maintain acid–base balance:

- The body balances gains and losses of hydrogen ions
- And gains and losses of bicarbonate ions
27-5 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
27-5 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⁺
27-5 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

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

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

3. Phosphate buffer system
   - Buffers pH of ICF and urine
Figure 27-10 Buffer Systems in Body Fluids

Buffer Systems

Intracellular fluid (ICF)

- Phosphate Buffer System
  - The phosphate buffer system has an important role in buffering the pH of the ICF and of urine.

Extracellular fluid (ECF)

- Protein Buffer Systems
  - Protein buffer systems contribute to the regulation of pH in the ECF and ICF. These buffer systems interact extensively with the other two buffer systems.
    - Hemoglobin buffer system (RBCs only)
    - Amino acid buffers (All proteins)
    - Plasma protein buffers

- Carbonic Acid–Bicarbonate Buffer System
  - The carbonic acid–bicarbonate buffer system is most important in the ECF.
27-5 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
• **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
27-5 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
Figure 27-11 The Role of Amino Acids in Protein Buffer Systems

Neutral pH

If pH falls

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

If pH rises

Amino acid

In acidic medium, amino acid acts as a base and absorbs H⁺
27-5 Acid–Base Balance

• The Hemoglobin Buffer System
  • CO₂ 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
Figure 23-24 A Summary of the Primary Gas Transport Mechanisms

Systemic capillary

Cells in peripheral tissues

Cl− → Chloride shift

HCO₃⁻ → H₂CO₃

H⁺ + HCO₃⁻ → H₂CO₃

H₂CO₃ → CO₂ + H₂O

CO₂ pickup

Hb → CO₂
27-5 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
27-5 Acid–Base Balance

• The **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 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
27-5 Acid–Base Balance

• The 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 27-12a The Carbonic Acid–Bicarbonate Buffer System

Basic components of the carbonic acid–bicarbonate buffer system, and their relationships to carbon dioxide and the bicarbonate reserve.
Figure 27-12b The Carbonic Acid–Bicarbonate Buffer System

The response of the carbonic acid–bicarbonate buffer system to hydrogen ions generated by fixed or organic acids in body fluids.
The Carbonic Acid–Bicarbonate Buffer System

- Bicarbonate ion shortage is rare
- Due to large reserve of sodium bicarbonate
- Called the bicarbonate reserve
27-5 Acid–Base Balance

• The **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
27-5 Acid–Base Balance

• Limitations of Buffer Systems
  • Provide only temporary solution to acid–base imbalance
  • Do not eliminate H^+ ions
  • Supply of buffer molecules is limited
27-5 Acid–Base Balance

• Maintenance of Acid–Base Balance

  • For homeostasis to be preserved, captured H\(^+\) must:

    1. Be permanently tied up in water molecules
       • Through CO\(_2\) removal at lungs
    2. Be removed from body fluids
       • Through secretion at kidney
27-5 Acid–Base Balance

• Maintenance of Acid–Base Balance
  • Requires balancing $H^+$ gains and losses
  • Coordinates actions of buffer systems with:
    • Respiratory mechanisms
    • Renal mechanisms
27-5 Acid–Base Balance

- Respiratory and Renal Mechanisms

- Support buffer systems by:
  1. Secreting or absorbing $H^+$
  2. Controlling excretion of acids and bases
  3. Generating additional buffers
27-5 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
• 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 left
Figure 23-27a The Chemoreceptor Response to Changes in $P_{CO_2}$

- **HOMEOSTASIS RESTORED**
  - Normal arterial $P_{CO_2}$

- **HOMEOSTASIS**
  - Normal arterial $P_{CO_2}$

- Increased respiratory rate with increased elimination of CO$_2$ at alveoli

- Stimulation of CSF chemoreceptors at medulla oblongata

- Increased $P_{CO_2}$, decreased pH in CSF

- Stimulation of arterial chemoreceptors

- Increased arterial $P_{CO_2}$ (hypocapnia)

- HOMEOSTASIS DISTURBED

- Increased arterial $P_{CO_2}$
HOMEOSTASIS
Normal arterial $P_{CO_2}$

HOMEOSTASIS DISTURBED
Decreased arterial $P_{CO_2}$ (hypocapnia)

Decreased $P_{CO_2}$, increased pH in CSF
Inhibition of arterial chemoreceptors

Reduced stimulation of CSF chemoreceptors
Inhibition of respiratory muscles

Decreased respiratory rate with decreased elimination of CO$_2$ at alveoli

HOMEOSTASIS RESTORED
Normal arterial $P_{CO_2}$
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
Hydrogen Ions

- Are secreted into tubular fluid along:
  - Proximal convoluted tubule (PCT)
  - Distal convoluted tubule (DCT)
  - Collecting system
27-5 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
    • Carbonic acid–bicarbonate buffer system
    • Phosphate buffer system
    • Ammonia buffer system
27-5 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
The three major buffering systems in tubular fluid, which are essential to the secretion of hydrogen ions:

1. Carbonic acid–bicarbonate buffer system
2. Phosphate buffer system
3. Ammonia buffer system
Figure 27-13b Kidney Tubules and pH Regulation

KEY
- Countertransport
- Active transport
- Exchange pump
- Cotransport
- Reabsorption
- Secretion
- Diffusion

Production of ammonium ions and ammonia by the breakdown of glutamine.

Tubular fluid in lumen

NH₄⁺ NH₃

Glutamine
Glutaminase

Carbon chain

HCO₃⁻

Na⁺ HCO₃⁻
27-5 Acid–Base Balance

• Renal Responses to Acidosis
  1. Secretion of $H^+$
  2. Activity of buffers in tubular fluid
  3. Removal of $CO_2$
  4. Reabsorption of $NaHCO_3^-$
27-5 Acid–Base Balance

• 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
The response of the kidney tubule to alkalosis

Tubular fluid in lumen

\( \text{HCO}_3^- \)

\( \text{Cl}^- \)

\( \text{H}^+ \)

\( \text{H}_2\text{CO}_3 \)

\( \text{CO}_2 + \text{H}_2\text{O} \)

Carbonic anhydrase

KEY

- Countertransport
- Active transport
- Exchange pump
- Cotransport
- Reabsorption
- Secretion
- Diffusion
27-6 Acid–Base Balance Disturbances

• Acid–Base Balance Disturbances
  • Disorders
    • Circulating buffers
    • Respiratory performance
    • Renal function
  • Cardiovascular conditions
    • Heart failure
    • Hypotension
  • Conditions affecting the CNS
    • Neural damage or disease that affects respiratory and cardiovascular reflexes
27-6 Acid–Base Balance Disturbances

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

- **Compensated Phase**
  - When condition persists
  - Physiological adjustments occur
27-6 Acid–Base Balance Disturbances

• **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 27-14 Interactions among the Carbonic Acid–Bicarbonate Buffer System and Compensatory Mechanisms in the Regulation of Plasma pH

The response to acidosis caused by the addition of $H^+$

**Respiratory Response to Acidosis**
Increased respiratory rate lowers $P_{CO_2}$, effectively converting carbonic acid molecules to water.

**Other buffer systems absorb $H^+$**

**KIDNEYS**
- Secretion of $H^+$
- Kidney tubules respond by (1) secreting $H^+$ ions, (2) removing $CO_2$, and (3) reabsorbing $HCO_3^-$ to help replenish the bicarbonate reserve.

**CARBONIC ACID-BICARBONATE BUFFER SYSTEM**
- $H_2CO_3$ (carbonic acid) + $HCO_3^-$ (bicarbonate ion)

**BICARBONATE RESERVE**
- $HCO_3^- + Na^+$ (sodium bicarbonate)
Figure 27-14b Interactions among the Carbonic Acid–Bicarbonate Buffer System and Compensatory Mechanisms in the Regulation of Plasma pH

**The response to alkalosis caused by the removal of H⁺**

**Respiratory Response to Alkalosis**
- Decreased respiratory rate elevates $P_{CO_2}$, effectively converting $CO_2$ molecules to carbonic acid.

**CARBONIC ACID-BICARBONATE BUFFER SYSTEM**
- $CO_2 + H_2O \rightarrow H_2CO_3$ (carbonic acid)
- $H_2CO_3 \rightarrow H^+ + HCO_3^-$ (bicarbonate ion)
- Other buffer systems release $H^+$
- Generation of $H^+$

**BICARBONATE RESERVE**
- $HCO_3^- + Na^+ \rightarrow NaHCO_3$ (sodium bicarbonate)

**KIDNEYS**
- Secretion of $HCO_3^-$
- Kidney tubules respond by conserving $H^+$ ions and secreting $HCO_3^-$. 

**Renal Response to Alkalosis**
- Kidney tubules respond by conserving $H^+$ ions and secreting $HCO_3^-$. 

**Lungs**
- $CO_2 + H_2O \rightarrow H_2CO_3$ (carbonic acid)
- $H_2CO_3 \rightarrow H^+ + HCO_3^-$ (bicarbonate ion)

**Respiratory Response to Alkalosis**
- Decreased respiratory rate elevates $P_{CO_2}$, effectively converting $CO_2$ molecules to carbonic acid.
27-6 Acid–Base Balance Disturbances

• **Respiratory Acidosis**
  • Develops when the respiratory system cannot eliminate all CO₂ generated by peripheral tissues
  • Primary sign
    • Low plasma pH due to hypercapnia
  • Primary cause
    • Hypoventilation
Figure 27-15a Respiratory Acid–Base Regulation

**Respiratory Acidosis**
- Elevated $P_{CO_2}$ results in a fall in plasma pH

**Responses to Acidosis**
- **Respiratory compensation:** Stimulation of arterial and CSF chemoreceptors results in increased respiratory rate.
- **Renal compensation:** $H^+$ ions are secreted and $HCO_3^-$ ions are generated.
- Buffer systems other than the carbonic acid–bicarbonate system accept $H^+$ ions.

**Combined Effects**
- Decreased $P_{CO_2}$
- Decreased $H^+$ and increased $HCO_3^-$

**HOMEOSTASIS**
- Normal acid–base balance

**HOMEOSTASIS DISTURBED**
- Hypoventilation causing increased $P_{CO_2}$

**HOMEOSTASIS RESTORED**
- Plasma pH returns to normal
Respiratory Alkalosis

- Primary sign
  - High plasma pH due to hypcapnia
- Primary cause
  - Hyperventilation
Figure 27-15b Respiratory Acid–Base Regulation

**HOMEOSTASIS DISTURBED**

Hyperventilation causing decreased $P_{CO_2}$

**Responses to Alkalosis**

Respiratory compensation:
Inhibition of arterial and CSF chemoreceptors results in a decreased respiratory rate.

Renal compensation:
$H^+$ ions are generated and $HCO_3^-$ ions are secreted.

Buffer systems other than the carbonic acid–bicarbonate system release $H^+$ ions.

**Combined Effects**

- Increased $P_{CO_2}$
- Increased $H^+$ and decreased $HCO_3^-$

**HOMEOSTASIS RESTORED**

Plasma pH returns to normal

**b** Respiratory alkalosis
• **Metabolic Acidosis**

  • Three major causes

    1. Production of large numbers of fixed or organic acids
       • $\text{H}^+$ overloads buffer system
       • **Lactic acidosis**
          • Produced by anaerobic cellular respiration
       • **Ketoacidosis**
          • Produced by excess ketone bodies

    2. Impaired $\text{H}^+$ excretion at kidneys

    3. Severe bicarbonate loss
Figure 27-16a Responses to Metabolic Acidosis

Metabolic Acidosis
- Elevated $H^+$ results in a fall in plasma pH

Responses to Metabolic Acidosis
- Respiratory compensation: Stimulation of arterial and CSF chemoreceptors results in increased respiratory rate.
- Renal compensation: $H^+$ ions are secreted and $HCO_3^-$ ions are generated.
- Buffer systems accept $H^+$ ions.

Combined Effects
- Decreased $H^+$ and increased $HCO_3^-$
- Decreased $P_{CO_2}$

HOMEOSTASIS DISTURBED
- Increased $H^+$ production or decreased $H^+$ excretion

Normal acid–base balance

HOMEOSTASIS
- Plasma pH returns to normal

Metabolic acidosis can result from increased acid production or decreased acid excretion, leading to a buildup of $H^+$ in body fluids.
Figure 27-16b Responses to Metabolic Acidosis

**Homeostasis Disturbed**
- Bicarbonate loss; depletion of bicarbonate reserve

**Metabolic Acidosis**
- Plasma pH falls because bicarbonate ions are unavailable to accept $\text{H}^+$

**Responses to Metabolic Acidosis**
- **Respiratory compensation:** Stimulation of arterial and CSF chemoreceptors results in increased respiratory rate.
- **Renal compensation:** $\text{H}^+$ ions are secreted and $\text{HCO}_3^-$ ions are generated.
- **Buffer systems other than the carbonic acid–bicarbonate system accept $\text{H}^+$ ions.**

**Combined Effects**
- Decreased $\text{P}_{\text{CO}_2}$
- Decreased $\text{H}^+$ and increased $\text{HCO}_3^-$

**Homeostasis Restored**
- Plasma pH returns to normal

**Homeostasis**
- Normal acid-base balance

Metabolic acidosis can result from a loss of bicarbonate ions that makes the carbonic acid–bicarbonate buffer system incapable of preventing a fall in pH.
• Combined Respiratory and Metabolic Acidosis
  • Respiratory and metabolic acidosis are typically linked
    • Low $O_2$ generates lactic acid
    • Hypoventilation leads to low $P_{O_2}$
• **Metabolic Alkalosis**
  
  • Is caused by elevated HCO$_3^-$ concentrations
  
  • Bicarbonate ions interact with H$^+$ in solution
    
    • Forming H$_2$CO$_3$
  
  • Reduced H$^+$ causes alkalosis
Figure 27-17  Metabolic Alkalosis

**HOMEOSTASIS DISTURBED**

- Loss of $\text{H}^+$; gain of $\text{HCO}_3^-$

**Metabolic Acidosis**

- Elevated $\text{HCO}_3^-$ results in a rise in plasma pH

**Responses to Metabolic Alkalosis**

- **Respiratory compensation:**
  - Stimulation of arterial and CSF chemoreceptors results in decreased respiratory rate.

- **Renal compensation:**
  - $\text{H}^+$ ions are generated and $\text{HCO}_3^-$ ions are secreted.

- Buffer systems other than the carbonic acid–bicarbonate system donate $\text{H}^+$ ions.

**Combined Effects**

- Increased $\text{H}^+$ and decreased $\text{HCO}_3^-$

**HOMEOSTASIS RESTORED**

- Plasma pH returns to normal
27-6 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
Figure 27-18 A Diagnostic Chart for Suspected Acid–Base Disorders

Suspected Acid–Base Disorder

Check pH

Acidosis pH < 7.35 (acidemia)

Check $P_{CO_2}$

Metabolic Acidosis

- $P_{CO_2}$ normal or decreased

Respiratory Acidosis

- $P_{CO_2}$ increased (> 50 mm Hg)
  - Primary cause is hypoventilation

Check $HCO_3^-$

Acute Metabolic Acidosis

- $P_{CO_2}$ normal
  - Reduction due to respiratory compensation
  - Examples: respiratory failure, CNS damage, pneumothorax

Chronic (compensated) Metabolic Acidosis

- $P_{CO_2}$ decreased (> 35 mm Hg)
  - Examples: emphysema, asthma

Chronic (compensated) Respiratory Acidosis

- $HCO_3^-$ increased (> 28 mEq/L)
  - Examples: lactic acidosis, ketoacidosis, chronic renal failure

Acute Respiratory Acidosis

- $HCO_3^-$ normal
  - Examples: respiratory failure, CNS damage, pneumothorax

Check anion gap

Normal

- Due to loss of $HCO_3^-$ or to generation or ingestion of HCl
  - Examples: diarrhea

Increased

- Due to generation or retention of organic or fixed acids
  - Examples: lactic acidosis, ketoacidosis, chronic renal failure

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Figure 27-18 A Diagnostic Chart for Suspected Acid–Base Disorders

Suspected Acid–Base Disorder

Check pH

Alkalosis  pH > 7.45 (alkalemia)

Check \( P_{CO_2} \)

Metabolic Alkalosis  \( P_{CO_2} \) increased (>45 mm Hg)

- \( (HCO_3^-) \) will be elevated
- Examples:
  - vomiting
  - loss of gastric acid

Respiratory Alkalosis  \( P_{CO_2} \) decreased (<35 mm Hg)

- Primary cause is hyperventilation

Check \( HCO_3^- \)

Acute Respiratory Alkalosis  Normal or slight decrease in \( HCO_3^- \)

- Examples:
  - fever
  - panic attacks

Chronic (compensated) Respiratory Alkalosis  Decreased \( HCO_3^- \) (<24 mEq/L)

- Examples:
  - anemia
  - CNS damage
<table>
<thead>
<tr>
<th>Disorder</th>
<th>pH (normal 7.35–7.45)</th>
<th>HCO₃⁻ (normal 21–28 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 Compensated: increased (above 28)</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>Metabolic acidosis</td>
<td>Decreased (below 7.35)</td>
<td>Decreased (below 24)</td>
<td>Acute: normal Compensated: decreased (below 35)</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>Respiratory alkalosis</td>
<td>Increased (above 7.45)</td>
<td>Acute: normal Compensated: decreased (below 24)</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>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>
</tr>
</tbody>
</table>
27-7 Age and Fluid, Electrolyte, and Acid–Base Balance

• Fluid, Electrolyte, and Acid–Base Balance in Fetuses and Newborns
  • Fetal pH Control
    • Buffers in fetal bloodstream provide short-term pH control
    • Maternal kidneys eliminate generated $\text{H}^+$
  • Newborn Electrolyte Balance
    • Body water content is high
      • 75% of body weight
    • Basic electrolyte balance is same as adult’s
• Aging and Fluid Balance

• Body water content, ages 40–60
  • Males 55%
  • Females 47%

• After age 60
  • Males 50%
  • Females 45%
27-7 Age and Fluid, Electrolyte, and Acid–Base Balance

• 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
  • Insensible perspiration increases as skin becomes thinner
27-7 Age and Fluid, Electrolyte, and Acid–Base Balance

- Aging and Fluid Balance
  - Maintaining fluid balance requires higher daily water intake
  - Reduction in ADH and aldosterone sensitivity
    - Reduces body water conservation when losses exceed gains
  - Muscle mass and skeletal mass decrease
    - Cause net loss in body mineral content
27-7 Age and Fluid, Electrolyte, and Acid–Base Balance

- Aging and Acid–Base Balance
  - Loss is partially compensated by:
    - Exercise
    - Dietary mineral supplement
  - Reduction in vital capacity
    - Reduces respiratory compensation
    - Increases risk of respiratory acidosis
    - Aggravated by arthritis and emphysema
  - Disorders affecting major systems increase