CHAPTER 7

Fluid and Electrolyte Imbalances

Learning Objectives

Upon completion of this chapter, the student will be able to:

- Differentiate between the forces of osmotic pressure and hydrostatic pressure within the bloodstream.
- Describe Starling's Laws of Capillary Forces and factors influencing fluid movement between the intracellular and extracellular fluid compartments.
- Identify causes of abnormally low or elevated levels of significant electrolytes within the bloodstream.
- Recognize complications that can occur due to abnormally low or elevated levels of electrolytes within the bloodstream.
- Discuss how different intravenous fluid solutions can be used to create changes in fluid and electrolyte levels within the bloodstream.

Key Terms

Atrial natriuretic peptide (ANP)
B-type natriuretic peptide (BNP)
Effusion
Electrolyte
Extracellular fluid (ECF)
Hydrostatic pressure
Hypercalcemia
Hyperkalemia
Hypermagnesemia
Hypernatremia
Hyperphosphatemia
Hypocalcemia
Hypokalemia
Hypomagnesemia
Hyponatremia
Hypophosphatemia
Hypovolemia
Interstitial fluid (ISF)
Intracellular fluid (ICF)
Oncotic pressure
Osmolality
Osmolarity
Osmotic pressure
Third-spacing
Tonicity

The human body is composed of approximately 60% water. It is the major constituent of the cells and bloodstream and acts as the body's solvent. **Electrolytes**, which are positively and negatively charged ions, are the body's solutes. Protein, specifically albumin, is the major solute in the bloodstream; body fluid, which is a solution largely composed of water, is the solvent. Electrolytes and protein, the solutes, have two main functions:

1. Deliver nutrients and electrolytes to cells
2. Carry away waste products from cellular metabolism

Basic Concepts of Fluid and Electrolyte Balance

Water is found in three different fluid compartments (see Fig. 7-1):

1. **Intracellular fluid (ICF)**
2. **Extracellular fluid (ECF)**
3. **Interstitial fluid (ISF)**

A constant state of fluid and electrolyte exchange occurs between the cell and its environment—mainly between the ICF and ECF. Two-thirds of the body's

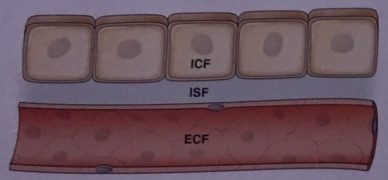


FIGURE 7-1. Water is located in the body in three basic fluid compartments. The ICF compartment is inside of the cells. The ECF compartment is within the bloodstream. The ISF compartment is between the intracellular and extracellular compartments.

water content is contained mainly within the ICF and one-third is within the ECF. Each cell is enveloped by a plasma membrane. This is a semipermeable membrane that allows passive movement of fluid and electrolytes back and forth but restricts larger particles. Table 7-1 describes the different transport mechanisms that maintain the concentration differences between ICF and ECF.

Fluid Balance

Intracellular Fluid Compartment

In the adult, 40% of total body weight is the water contained within the ICF compartment. Water can diffuse out of the ICF and cause cell shrinkage or cellular dehydration. Conversely, water can enter the ICF and cause cell swelling or cellular edema.

Extracellular Fluid Compartment

In the adult, 20% of total body weight is the water contained within the ECF compartment. Most of the ECF is found within the intravascular compartment or blood vessels. The ECF contains electrolytes, oxygen, glucose, and other nutrients to be delivered to cells, as well as cellular waste products designated for excretion.

Interstitial Fluid Compartment

ISF, which is a filtrate of the blood, is located between the cells and between the cells and capillaries. Like blood, it contains water and electrolytes, mainly sodium (Na^+). ISF lacks proteins because they are too large to diffuse out of the blood vessels into the interstitial spaces. However, during inflammation, capillary membranes become extrapermeable; the pores enlarge, allowing proteins such as white blood cells out to the tissues.

Hydrostatic Pressure

Hydrostatic pressure is the pushing force exerted by water in the bloodstream. The heart's pulsatile pumping action is the source of hydrostatic pressure, which exerts an outward force that pushes water through the capillary membrane pores into the ISF and ICF compartments (see Fig. 7-2).

TABLE 7-1. Transport Mechanisms

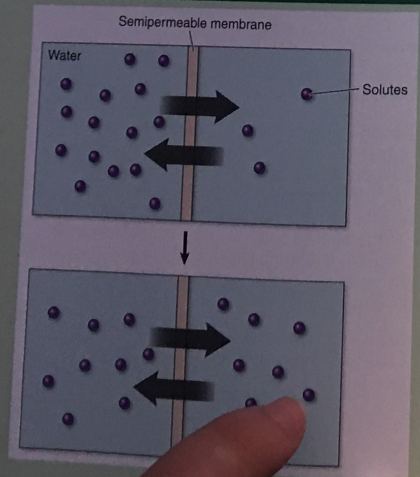
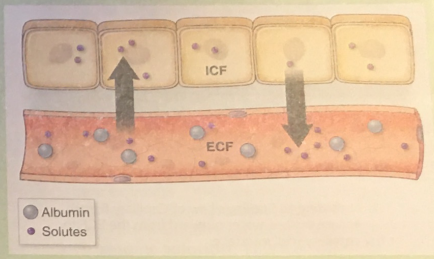
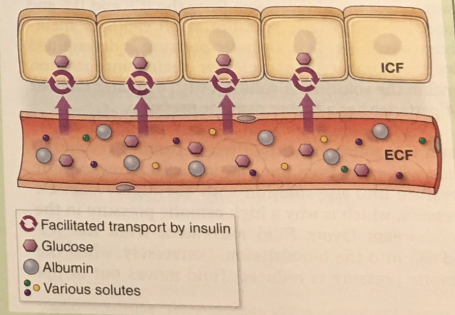
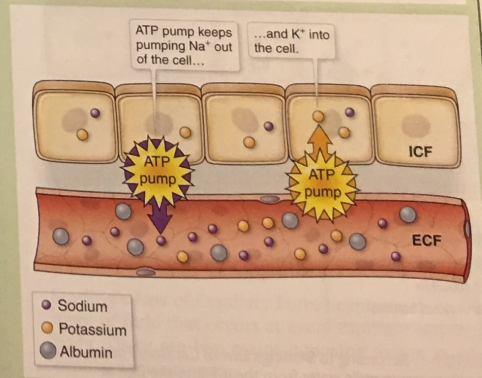
Transport Mechanism	Description	Illustration
Diffusion	The process by which molecules passively spread from areas of high concentration to areas of low concentration. Water and electrolytes diffuse from high concentration to lower concentration until an equilibrium is reached.	

TABLE 7-1. Transport Mechanisms–cont'd

Transport Mechanism	Description	Illustration
Osmosis	The tendency of molecules of a solvent to pass through a semipermeable membrane from a less concentrated solution into a more concentrated one, equalizing the concentrations on each side of the membrane. Electrolytes and water move through the cell's semi-permeable plasma membrane, but large proteins such as albumin cannot pass through the membrane. A semipermeable membrane selectively allows some molecules through its pores and obstructs others according to size.	
Facilitated transport	The passing of certain molecules through the plasma membrane with assistance from carrier proteins. Glucose undergoes facilitated transport into the cell by the carrier protein insulin.	
Active transport	Occurs when a substance requires energy to pass through a membrane against a concentration gradient. Sodium and potassium require active transport using the N^+/K^+ pump, which is within the plasma membrane to retain potassium as the major intracellular ion and sodium as the major extracellular ion. Sodium is a solute that draws water with it.	

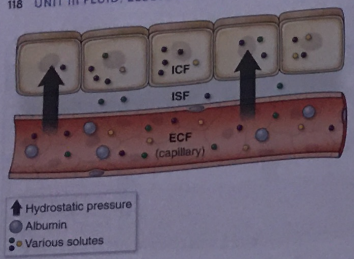


FIGURE 7-2. According to Starling's Law of Capillary Forces, hydrostatic pressure pushes water outward from the ECF to the ICF at the capillary–cell interface.

Osmotic Pressure

Osmotic pressure is the pressure exerted by the solutes in solution. In the bloodstream, osmotic pressure is exerted by electrolytes, mainly sodium ions and plasma proteins. Osmotic pressure is a force that pulls water into the bloodstream from the ICF and ISF and opposes hydrostatic pressure at all capillary membranes (see Fig. 7-3). Osmotic pressure is determined by the number of particles or their concentration within the solution. A solution with a greater number of particles has a higher osmotic pressure.

When a membrane such as a cell membrane separates two solutions with different osmotic pressures, fluid will move from the solution with lower osmotic pressure into the solution with the higher osmotic pressure, which is why a high osmotic pressure in the bloodstream favors fluid movement from the ICF and ISF into the bloodstream. Conversely, when the osmotic pressure is reduced, fluid moves out of the bloodstream and into interstitial and intracellular spaces (see Fig. 7-4).

Oncotic Pressure

Oncotic pressure, also called colloidal osmotic pressure, is a type of osmotic pressure exerted specifically by albumin in the bloodstream. Oncotic pressure and osmotic pressure exert the same type of pulling force from ICF to ECF. Albumin attracts water and helps keep it inside the blood vessel. Albumin is the main colloidal protein in the bloodstream and is essential for maintaining the oncotic pressure in the vascular system. Total albumin in the bloodstream is indicative of the body's protein nutritional status. The normal serum albumin level is 3.1 to 4.3 g/dL. Changes in this albumin level alter oncotic pressure. For example, in hypoalbuminemia (lack of sufficient albumin in the bloodstream), oncotic pressure is reduced. Hypoalbuminemia causes an imbalance in the oncotic pressure versus hydrostatic pressure forces. With reduced albumin, the oncotic pressure is low and the force exerted by hydrostatic pressure overwhelms the oncotic pressure. This causes water in the bloodstream to push outward from the capillary pores toward the ISF and ICF (see Fig. 7-5).

Osmolality

Osmolality is a measurement of the concentration of solutes per kg of solvent. It is based on 1 mole (or gram molecular weight equivalent) of a substance dissolved in 1 kilogram of water. In clinical practice, osmolality can be used to evaluate the body's hydration status based on the concentration of fluid and particles in solution. Normal plasma osmolality is 282 to 295 milliosmoles per kilogram of water. Low osmolality indicates a lesser amount of solutes in solution, whereas high osmolality indicates a greater amount of solutes. If the bloodstream is well hydrated, serum osmolality is 282 milliosmoles per kg of water or less. If the bloodstream is concentrated and has low water, the serum osmolality will be 295 milliosmoles per kg of water or greater. Serum osmolality can be calculated using the following mathematical formula: milliosmoles of solute /kg of water = 2 × serum sodium + serum glucose /18 + BUN / 2.4.

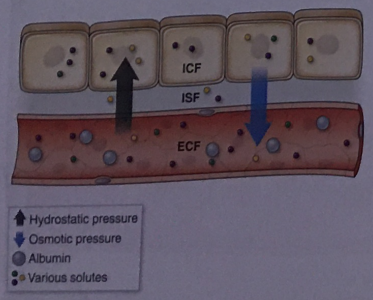


FIGURE 7-3. According to Starling's Law of Capillary Forces, osmotic pressure pulls water from the ICF into the ECF at every cell–capillary interface. The osmotic pressure opposes the hydrostatic pressure; in healthy conditions, each force balances out the other.

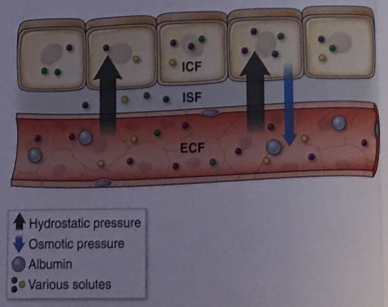


FIGURE 7-4. According to Starling's Law of Capillary Forces, when osmotic pressure is lower than hydrostatic pressure, osmotic pressure is overwhelmed and hydrostatic pressure is an unopposed force, causing water to flow from the ECF to the ICF.

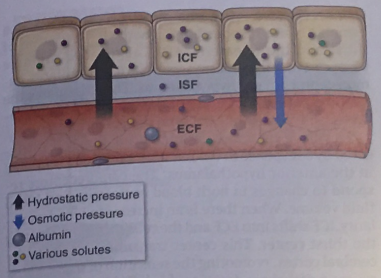


FIGURE 7-5. In hypoalbuminemia, there is a lack of sufficient albumin in the bloodstream. This causes a decrease in osmotic pressure. When osmotic pressure is lower than hydrostatic pressure, osmotic pressure is overwhelmed and hydrostatic pressure is an unopposed pushing force that pushes water from the ECF to the ICF. Cells will gain water and become edematous.

Osmolarity

Osmolarity is the number of osmoles of solute per liter of solution; it is dependent on the number of particles suspended in a solution. In the body, the major solutes are albumin, sodium (Na^+), potassium (K^+), phosphate (PO_4^-), magnesium (Mg^{++}), calcium (Ca^{++}), bicarbonate (HCO_3^-), and glucose. The major protein within the bloodstream is albumin, which is the solute in the ECF that exerts the most osmotic pressure. Sodium, the main determinant of osmolarity, is a positive ion, also called a cation; it is found mostly in the ECF and assists in the maintenance of fluid balance and osmotic pressure. Potassium is the main intracellular cation; it assists in the maintenance of neuromuscular excitability and acid–base balance. Both sodium and potassium require the cell's Na^+/K^+ pump to maintain Na^+ as the extracellular ion and K^+ as the intracellular ion. Phosphate is an intracellular negative ion, also called an anion. Magnesium plays an important role in enzymatic systems within the body. Calcium plays an important role in neuromuscular irritability, blood clotting, and bone structure. Bicarbonate is responsible for acid–base balance.

CLINICAL CONCEPT

The serum albumin level is a major protein in the bloodstream used to evaluate an individual's nutritional status.

Tonicity

Tonicity refers to the concentration of solutes in solution compared with the bloodstream. The term is also used to describe the various intravenous (IV) solutions used in the clinical setting. There are three types of IV solutions:

1. **Isotonic solution**: This has the same tonicity as blood; when infused as an IV solution, it does not cause fluid shifts or alter body cell size. It has a concentration of particles and fluid that is similar to blood and body fluids. A standard isotonic IV solution is 0.9% NaCl solution, also called normal saline. It is used frequently as a bloodstream volume expander. Often an isotonic solution is used to keep an open connection to the IV route for medication administration or a blood transfusion.
2. **Hypotonic solution**: This has fewer particles and more water than blood and body fluids. When a hypotonic solution is infused, water is added to the bloodstream and causes a fluid shift from ECF to ICF to deliver water to the body, as in dehydration treatment. A standard hypotonic solution is 0.45% NaCl and is also referred to as half normal saline.
3. **Hypertonic solution**: This contains more particles and less water than blood and body fluids. When a hypertonic solution is infused into the bloodstream, solutes are added to the bloodstream and cause fluids to shift from ICF to ECF, causing body cells to shrink. A commonly used hypertonic IV solution is mannitol. It can be used to diminish cell swelling, particularly in cerebral edema. Another hypertonic solution that is used less often is 3.0% NaCl.

CLINICAL CONCEPT

5% dextrose in water (D5W) is often added to IV normal saline to deliver some glucose to the patient to prevent hypoglycemia.

CLINICAL CONCEPT

A solution often used as a temporary replacement for blood, called Ringer's lactate (also called lactated Ringers solution), consists of similar physiologic constituents as those found in blood.

Starling's Law of Capillary Forces

Starling's Law of Capillary Forces explains the movement of fluid that occurs at every capillary bed in the body. There are two major opposing forces at every capillary membrane:

1. Hydrostatic pressure
2. Osmotic pressure (includes oncotic pressure)

Within every capillary, electrolytes and proteins within the blood exert osmotic pressure. The fluid within the capillary exerts hydrostatic pressure. These pressure forces oppose each other and attempt to balance each other out at every capillary membrane, thereby creating a state of homeostasis (see Fig. 7-6).

CLINICAL CONCEPT

Principles of Starling's Law can be applied in the clinical setting. For example, swelling can be reduced using an Epsom salt bath, which is a hypertonic magnesium salt solution. Placing a swollen finger in an Epsom salt bath will draw ICF from the finger into the Epsom salt solution, thereby reducing the finger's swelling.

Fluid Homeostasis

Various physiologic mechanisms work together in order to maintain fluid homeostasis. In terms of fluid volume, both fluid intake and output must be regulated to prevent fluid volume overload, also known as edema, and fluid volume deficit, also known as dehydration. However, in addition to fluid volume status, the relative composition of body fluids, including electrolyte and acid or base concentrations, needs to be consistent. The kidney, renin–angiotensin–aldosterone system (RAAS), osmoreceptors, thirst sensation, antidiuretic hormone (ADH), and natriuretic peptides work together to maintain fluid homeostasis in the body.

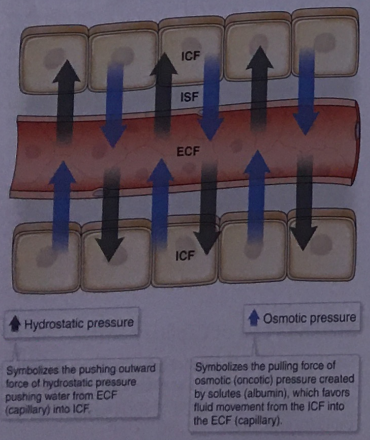


FIGURE 7-6. According to Starling's Law of Capillary Forces, homeostasis exists when hydrostatic and osmotic pressures are equal at every capillary–cell interface.

Osmoreceptors, ADH, and thirst. Changes in plasma osmolarity are responsible for both the sensation of thirst and the release of ADH, also called arginine vasopressin. High plasma osmolarity stimulates osmoreceptors in the hypothalamus. This stimulates the hypothalamic thirst center of the brain, as well as promoting the release of ADH from the posterior pituitary.

Thirst is a conscious desire to drink fluids. It is triggered by a response in the thirst center, which is located in the anterior hypothalamus. The osmoreceptors respond to changes in both blood osmolarity and blood fluid volume. When there is an increase in blood osmolarity, ICF shifts into ECF and the cells shrink, stimulating the thirst center. This center transmits signals to the cerebral cortex, promoting the sensation of thirst. Thirst causes a conscious desire to drink fluids, which brings water into the body's bloodstream to reduce osmolarity. Massive loss of blood and fluid volume, as is seen in severe trauma, will trigger the sense of thirst as well.

In a healthy person, osmoreceptors, ADH, and thirst responses work together. ADH is produced by the hypothalamus. Once the ADH is synthesized, it travels by an axonal transport mechanism to the posterior pituitary gland. When the bloodstream lacks sufficient water, plasma osmolarity is increased and the osmoreceptors shrink. This stimulates the ADH neurons to depolarize, releasing ADH from the posterior pituitary. In addition to changes in osmolarity, other factors such as pain, trauma, and medications stimulate the release of ADH.

After release into the bloodstream, ADH stimulates water reabsorption from the nephron tubule fluid at the collecting duct into the bloodstream. This raises the blood's water content and decreases the water in the tubule fluid, which eventually becomes concentrated urine. When there is enough water in the bloodstream, plasma osmolarity decreases, and ADH secretion is inhibited.

RAAS. Hypotension, hypovolemia, dehydration, and low cardiac output cause low circulation throughout the body. Reduced circulation causes low renal perfusion, which stimulates renin secretion by the kidney's juxtaglomerular apparatus. Renin initiates the RAAS, a compensatory mechanism used to replenish blood volume and raise blood pressure (see Fig. 7-7).

Renin is an enzyme released from the kidney in response to decreased renal perfusion. Renin converts angiotensinogen, a large protein produced by the liver, to angiotensin I. In the lungs, angiotensin-converting enzyme (ACE) changes angiotensin I into angiotensin II, a powerful vasoconstrictor. Angiotensin II binds to receptors in the adrenal cortex, stimulating the synthesis and secretion of aldosterone, a mineralocorticoid that increases sodium and water reabsorption into the bloodstream at the distal tubule of the nephrons. Aldosterone also stimulates the excretion of potassium into the nephron tubules, which eventually becomes urine. When blood volume decreases, aldosterone begins the reabsorption of sodium from the distal tubules into the bloodstream, bringing sodium back into the bloodstream. This causes more absorption of water and increased blood volume. When the blood volume returns to normal, aldosterone secretion is reduced.

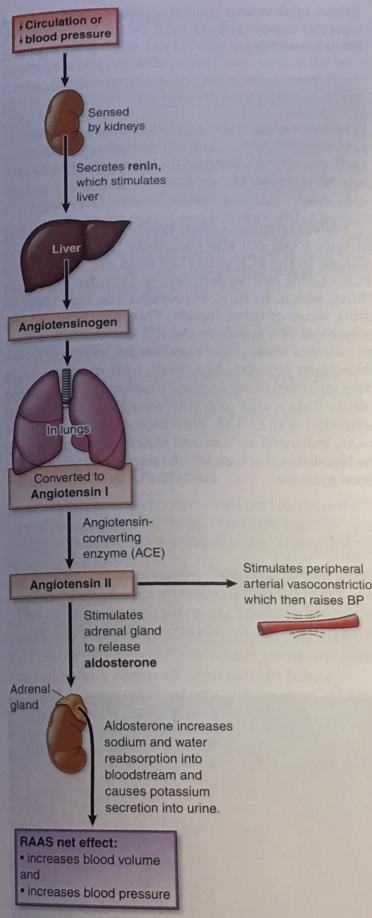


FIGURE 7-7. The RAAS. When there is a decrease in circulation or drop in blood pressure, the kidney senses decreased perfusion and releases renin. Renin stimulates the liver to release a protein called angiotensinogen. Angiotensinogen reaches the lungs and is transformed into angiotensin I. In the lungs, ACE transforms angiotensin I into angiotensin II. Angiotensin II is a potent arterial vasoconstrictor; it also stimulates the adrenal gland to release aldosterone. Aldosterone increases sodium and water reabsorption into the bloodstream at the nephron. It also causes potassium excretion from the bloodstream into the urine. The net effect of the RAAS is to raise blood volume and increase blood pressure.

CLINICAL CONCEPT

Blocking ACE in the RAAS prevents angiotensin I from becoming angiotensin II; this prevents vasoconstriction and adrenal stimulation.

Natriuretic Peptides. Natriuresis is the excretion of a large amount of both sodium and water by the kidneys in response to excess ECF volume. It is a process of natural diuresis initiated by the body.

CLINICAL CONCEPT

Diuresis is the loss of water from the body. Furosemide (Lasix) and Hydrochorthiazide (HCTZ) are commonly prescribed diuretic agents.

Three major peptides promote natriuresis: **atrial natriuretic peptide (ANP)**, **B-type natriuretic peptide) (BNP)**, and C-type natriuretic peptide (CNP). ANP is produced by the heart's atria and is secreted in response to excess ECF volume that stretches the heart's atrial chambers. CNP is produced by endothelial cells of the arteries and ventricular cells of the heart.

BNP is produced in the heart's ventricles and, to a lesser extent, in the brain. It is excreted in response to fluid volume overload stretching the heart's ventricles—the more the ventricle is stretched by blood volume, the more BNP is secreted. Both ANP and BNP promote natriuresis at the glomerulus by increasing glomerular filtration rate. CNP has limited diuretic and natriuretic effects compared with ANP and BNP, but it has only been recently identified and is not completely understood.

Basic Pathophysiologic Concepts of Fluid and Electrolyte Imbalance

Regulation of fluid balance is important for maintaining the body's normal homeostatic functioning. Alterations in fluid balance occur for a variety of reasons and can be related to illness or exposure to extreme heat. Because sodium is the major extracellular ion, it has a key role in fluid balance. Fluid volume deficit or excess fluid volume has ancillary effects on different systems of the body.

Edema

Edema occurs when there is an excess of fluid in the ISF and ICF compartments. It can occur because of elevated hydrostatic pressure created by excess water

in the bloodstream or diminished osmotic force created by a low amount of solutes in the bloodstream. Edema can also occur because of inflammation, which causes increased capillary permeability; the capillary pores enlarge to allow fluid and cells out of the bloodstream to reach the site of injury. The fluid that moves into the ISF and ICF causes the edema.

When edema occurs because of high hydrostatic pressure in the bloodstream, the osmotic pressure force is overwhelmed and does not balance out the hydrostatic force. Consequently, according to Starling's Law of Capillary Forces, hydrostatic pressure pushes fluid out of the capillary membrane pores into the ISF and ICF. An example of this occurs in left-sided heart failure, where high hydrostatic pressure develops in the pulmonary bloodstream. The high hydrostatic pressure forces fluid out of the pulmonary blood vessels and into the alveolar spaces and the interstitial tissue. This is known as pulmonary edema. Edema can also occur in the peritoneal cavity as ascites, the pleural cavity as pleural effusion, and the lower extremities as ankle edema.

Edema can also occur because of a low amount of solute in the bloodstream. Low albumin in the blood, or hypoalbuminemia, causes an imbalance in capillary forces. Because albumin is the major source of oncotic pressure, hypoalbuminemia will cause low oncotic pressure in the bloodstream. According to Starling's Law of Capillary Forces, for homeostasis to occur, oncotic pressure must equal hydrostatic pressure. When oncotic pressure is low, hydrostatic pressure will be the overriding force and push fluid out of the capillary into the ISF and ICF compartments, thereby creating an edematous state.

An example of edema caused by hypoalbuminemia occurs in severe protein starvation. Without sufficient nutritional protein, blood albumin levels become extremely low and, consequently, oncotic pressure is diminished. An imbalance between oncotic pressure and hydrostatic pressure occurs at every capillary–cell interface. Hydrostatic pressure overwhelms oncotic pressure, and water is pushed out of the capillary into the ISF and ICF. Edema occurs throughout the body at every capillary–cell interface, and this is often most apparent in the peritoneal cavity as a swollen abdomen. In persons who are starving the disorder is known as kwashiorkor.

A specific kind of edema, called dependent edema, often forms in the lower extremities. Under healthy conditions, venous return to the heart from the lower extremities is assisted by venous valves and muscle contractions. A weakened venous valve system, lack of muscle contractions, and gravitational forces can allow venous blood to collect in the lower extremities. When an individual stands or sits in one position for an extended period, venous blood can pool in the lower extremities. Increased hydrostatic pressure in the veins allows fluid to flow out of the capillary into interstitial tissues. Fluid accumulates in the ankles and feet, which are the dependent parts of the body. To avoid dependent edema, brisk venous circulation back to the heart and vigorous muscle activity must be maintained in the lower extremities.

CLINICAL CONCEPT

Thromboembolic stockings (TEDS) and pneumatic compression devices that surround the lower leg attempt to enhance venous return from the lower extremities up to the heart in patients on bedrest.

Sodium retention caused by illness or consumption of salty foods can also contribute to edema. Excess sodium in the ECF pulls fluid from the ICF into the ECF, causing cellular dehydration. Dehydration causes thirst, which, in turn, encourages the individual to drink water or other liquids. This ingestion and the movement of water from the ICF into the ECF causes an excess of water in the bloodstream, which increases hydrostatic pressure. As a result, hydrostatic pressure rises and overcomes osmotic pressure with resulting edema. This is also seen whenever there is increased activation of the RAAS. With increased cycling of the RAAS, enhanced sodium and water reabsorption into the bloodstream occurs, which raises blood volume and blood pressure.

CLINICAL CONCEPT

Pitting edema occurs when pressure is applied to a small area and an indentation persists for some time after the release of the pressure. Depending on the severity, an individual can have +1, +2, or +3 pitting edema (see Fig. 7-8).

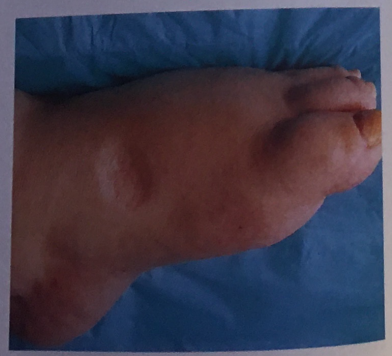


FIGURE 7-8. Pitting edema. Application of pressure over a bony area displaces the excess fluid, leaving an indentation or pit. (From Williams, L., & Hopper, P. [2019]. *Understanding medical-surgical nursing* [6th ed.]. Philadelphia, PA: F. A. Davis Company, with permission.)

Sequestered Fluids

During illness, fluids can become sequestered in body cavities that are normally free of fluids, such as the pericardial sac, peritoneal cavity, and pleural space. When this occurs, it is referred to as third-space accumulation of fluids; sometimes referred to as **third-spacing**. The fluid that accumulates in these cavities is commonly called an **effusion**. An effusion can be a transudate, which is a serous filtrate of blood, or an exudate, which contains material such as blood, lymph, proteins, pathogens, and inflammatory cells. Either type of effusion can surround organs and interfere with function. For example, a pleural effusion interferes with full lung expansion and ventilation, whereas a pericardial effusion can constrict the heart and prevent maximal filling of blood in the atria and ventricles.

CLINICAL CONCEPT

A pericardial effusion can lead to cardiac tamponade, a disorder in which the heart's pumping action is restricted because of an accumulation of fluid surrounding it.

Fluid Volume Overload

Fluid volume overload occurs when the bloodstream has an excessive amount of water. One of the most common causes of fluid volume overload is heart failure. In heart failure, the RAAS is constantly cycling, which brings an excessive amount of water into the bloodstream. Blood volume increases, which increases the hydrostatic pressure. High hydrostatic pressure overwhelms osmotic pressure at every capillary bed, leading to edema in various places in the body. Ankle edema, peritoneal edema, and pulmonary edema all occur in heart failure.

Fluid volume overload can also be seen in certain cancers that secrete ADH, causing a disorder known as syndrome of inappropriate ADH (SIADH). Other causes of ADH-related fluid volume overload include cirrhosis of the liver, polycystic kidney disease, and some forms of hypertension. Disorders that cause constant secretion of ADH promote excess water reabsorption from the collecting duct of the nephrons into the bloodstream. Water reabsorption into the blood causes fluid volume overload. The concentration of sodium in the bloodstream is highly dependent on the volume of water in the bloodstream. High water volume in the blood decreases the concentration of sodium. This is called dilutional hyponatremia.

CLINICAL CONCEPT

SIADH can occur in certain cancers, brain disorders, and after brain surgery.

Dehydration

Dehydration is a state of diminished water volume in the body. A deficit of intracellular fluid causes body cells to shrink. There is also a decreased amount of water in the extracellular fluid. Dehydration has many causes, including reduced fluid intake and excessive fluid loss caused by illness. Lack of sufficient ADH production or lack of renal stimulation by ADH can also lead to excessive fluid loss and dehydration, as can certain gastrointestinal disorders such as prolonged diarrhea. Burns, fever, and perspiration also commonly cause large fluid loss. Regardless of cause, dehydration causes **hypovolemia**, a diminished level of circulating blood volume that increases the osmolarity of the blood.

For example, in uncontrolled diabetes, glucose rises to high levels and acts as a solute in the blood. The high amount of solute in the blood raises osmotic pressure, which creates an imbalance in the capillary forces. If osmotic pressure rises to exceed hydrostatic pressure inside the capillary, then water from the ICF and ISF moves into the capillary and the cells lose water. This causes cells to shrink, a process known as cellular dehydration. The fluid shift into the circulation delivers more water to the kidneys, which is then excreted as excess urine (polyuria). Because of fluid shifts, the key symptoms of uncontrolled diabetes mellitus are thirst and polyuria.

Cellular dehydration can also occur because of hypernatremia (high sodium content of blood), which raises solute content and, in turn, raises osmotic pressure. High osmotic pressure causes water to shift from the ICF into the ECF. Cellular dehydration occurs with loss of ICF, causing the cells to shrink. The ECF gains fluid, which is excreted via the kidney; this leads to further dehydration. This situation continues until water is replenished.

ALERT! There is a risk of renal dysfunction if the adult patient develops oliguria–urine output of less than 400 mL/day or less than 20 to 30 mL/hour. The kidney needs to yield a minimum of 400 mL of fluid daily to sufficiently excrete waste products.

The physiologic response to dehydration is multifaceted. Osmoreceptors respond to the blood's high osmotic content and stimulate the thirst center in the hypothalamus. Thirst occurs, which stimulates the person to drink to replace fluid lost from the cells. The blood vessel baroreceptors sense a decreased blood pressure in dehydration. This, in turn, stimulates the sympathetic nervous system, which vasoconstricts arterial vessels and increases the heart rate to compensate. Additionally, osmoreceptors stimulate ADH secretion from the posterior pituitary gland. The ADH works at the nephron to increase water reabsorption into the bloodstream. Simultaneously, because the blood

Sequestered Fluids

During illness, fluids can become sequestered in body cavities that are normally free of fluids, such as the pericardial sac, peritoneal cavity, and pleural space. When this occurs, it is referred to as third-space accumulation of fluids; sometimes referred to as **third-spacing**. The fluid that accumulates in these cavities is commonly called an **effusion**. An effusion can be a transudate, which is a serous filtrate of blood, or an exudate, which contains material such as blood, lymph, proteins, pathogens, and inflammatory cells. Either type of effusion can surround organs and interfere with function. For example, a pleural effusion interferes with full lung expansion and ventilation, whereas a pericardial effusion can constrict the heart and prevent maximal filling of blood in the atria and ventricles.

CLINICAL CONCEPT

A pericardial effusion can lead to cardiac tamponade, a disorder in which the heart's pumping action is restricted because of an accumulation of fluid surrounding it.

Fluid Volume Overload

Fluid volume overload occurs when the bloodstream has an excessive amount of water. One of the most common causes of fluid volume overload is heart failure. In heart failure, the RAAS is constantly cycling, which brings an excessive amount of water into the bloodstream. Blood volume increases, which increases the hydrostatic pressure. High hydrostatic pressure overwhelms osmotic pressure at every capillary bed, leading to edema in various places in the body. Ankle edema, peritoneal edema, and pulmonary edema all occur in heart failure.

Fluid volume overload can also be seen in certain cancers that secrete ADH, causing a disorder known as syndrome of

Dehydration

Dehydration is a state of diminished water volume in the body. A deficit of intracellular fluid causes body cells to shrink. There is also a decreased amount of water in the extracellular fluid. Dehydration has many causes, including reduced fluid intake and excessive fluid loss caused by illness. Lack of sufficient ADH production or lack of renal stimulation by ADH can also lead to excessive fluid loss and dehydration, as can certain gastrointestinal disorders such as prolonged diarrhea. Burns, fever, and perspiration also commonly cause large fluid loss. Regardless of cause, dehydration causes **hypovolemia**, a diminished level of circulating blood volume that increases the osmolarity of the blood.

For example, in uncontrolled diabetes, glucose rises to high levels and acts as a solute in the blood. The high amount of solute in the blood raises osmotic pressure, which creates an imbalance in the capillary forces. If osmotic pressure rises to exceed hydrostatic pressure inside the capillary, then water from the ICF and ISF moves into the capillary and the cells lose water. This causes cells to shrink, a process known as cellular dehydration. The fluid shift into the circulation delivers more water to the kidneys, which is then excreted as excess urine (polyuria). Because of fluid shifts, the key symptoms of uncontrolled diabetes mellitus are thirst and polyuria.

Cellular dehydration can also occur because of hypernatremia (high sodium content of blood), which raises solute content and, in turn, raises osmotic pressure. High osmotic pressure causes water to shift from the ICF into the ECF. Cellular dehydration occurs with loss of ICF, causing the cells to shrink. The ECF gains fluid, which is excreted via the kidney; this leads to further dehydration. This situation continues until water is replenished.

volume is low, circulation to the kidneys is decreased. Decreased kidney perfusion provokes renin secretion, which activates the RAAS, resulting in increased sodium and water in the bloodstream, raising blood volume. Additionally, angiotensin II acts as a potent vasoconstrictor, which raises blood pressure. These compensatory mechanisms restore fluid balance and maintain blood pressure in states of dehydration (see Fig. 7-9).

Assessment of Fluid Volume Status

Fluid losses and gains can be clinically assessed in many ways. A basic method to clinically assess an individual's fluid volume status is daily weight. When using daily weight to assess fluid volume status, it is important to take the measurement using the same scale, at the same time of day, every day. A weight change of 2 pounds from one day to the next is likely caused by fluid gained or lost.

A record of the patient's 24-hour intake and output (I&O) is another common way to monitor fluid status. The amount of fluid intake necessary for an adult with normal heart and renal function is 1,500 mL/m² of body surface per day. On average, this is approximately 2 liters of fluid per day.

All fluids, including oral, IV, and tube feedings, are recorded as intake. All measurements should be recorded in milliliters (mL), so it is important to understand how to convert ounces to mL: *1 ounce of fluid is equal to 30 mL*. Water from ingested food can be estimated at approximately 500 to 1,000 mL/day. Output includes urine; vomitus; wound or ostomy drainage; and insensible water losses through the lungs, sweat, and feces. Wound or ostomy drainage and vomitus must be estimated. Insensible water loss is usually 1,000 mL/day, but it may be more if fever is present. Water requirements increase during specific conditions (see Box 7-1); for example, water requirements increase by 100 to 150 mL per day for each degree Celsius of body temperature elevation. I&O should be approximately equal over a 24-hour period. The daily I&O record can indicate fluid retention, which is a positive fluid balance, or fluid deficit, which is a negative fluid balance (see Fig. 7-10).

Another clinical assessment of fluid status involves the patient's vital signs. The patient who is dehydrated may have tachycardia and hypotension, particularly postural hypotension. To assess for postural hypotension, measure the blood pressure in the lying and standing positions.

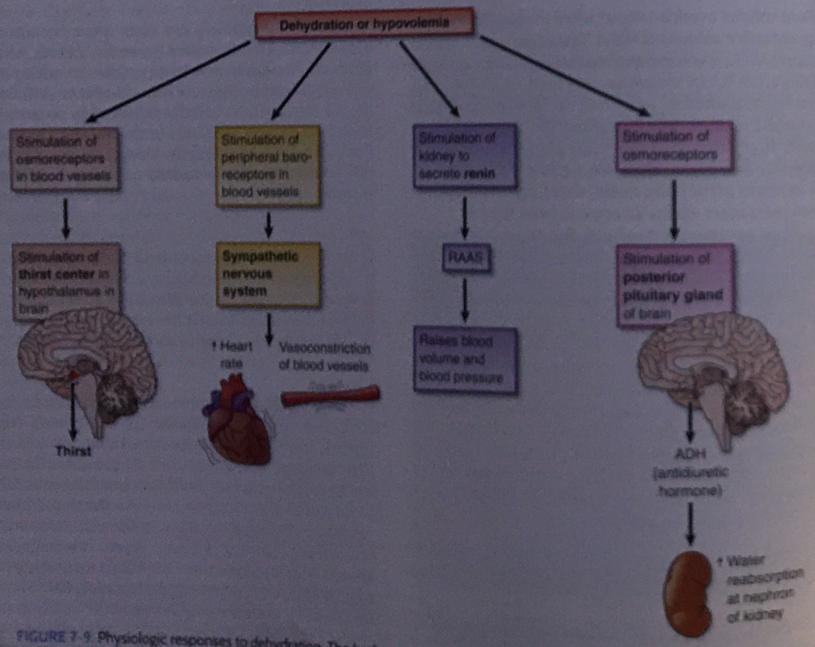


FIGURE 7-9 Physiologic responses to dehydration. The body compensates for dehydration and hypovolemia (low blood volume) in various ways.

BOX 7-1. Conditions That Cause Dehydration and Increase Water Requirements

- Bleeding
- Breastfeeding
- Burns
- Fever
- Gastrointestinal (GI) fluid loss
- Hypotension
- Nephrolithiasis
- Polyuria
- Surgical drains
- Sweating
- Tachypnea

CLINICAL CONCEPT

Orthostatic hypotension, which occurs in dehydration, is a systolic blood pressure decrease of at least 20 mm Hg or a diastolic blood pressure decrease of at least 10 mm Hg within 3 minutes when going from a lying to a standing position.

Finally, a patient with a fluid volume deficit will have a number of symptoms of dehydration, including thirst, dry mucous membranes, poor skin turgor, hypotension, low urine output, and dark-colored urine. Poor skin turgor is demonstrated through nonelasticity of the skin. When the skin is pinched, a small tent of the skin remains.

A patient who has fluid volume excess will have edema, moist mucous membranes, and may have hypertension. With fluid excess, weight gain and possibly ascites, as well as pitting edema, can occur. In severe fluid volume excess, dyspnea may also be present because of pulmonary edema. Box 7-2 presents the different signs and symptoms of fluid volume deficit and excess.

Electrolyte Imbalances

For a cell to function properly, serum electrolytes must be within normal range. Sodium is the main extracellular electrolyte, whereas potassium is the main intracellular electrolyte. The cellular Na^+/K^+ pump is constantly at work to try to retain K^+ in the intracellular compartment and move Na^+ to the extracellular environment.

Many enzymatic, hormonal, and chemically mediated mechanisms are dependent on normal levels of serum electrolytes. These include the generation of

INTAKE AND OUTPUT SHEET

Hospital # _____ Patient's name _____

Date _____ Room # _____

	INTAKE			OUTPUT			
				Urine		Gastric	
	By Mouth	Tube	Parenteral	Voided	Catheter	Emesis	Suction
Time 7–3	6 oz tea		IV 500 mL D5W in NaCl 0.9%	500 mL			
Time 3–11	6 oz tea		IV 500 mL D5W in NaCl 0.9%	500 mL			
Time 11–7	8 oz water			200 mL			
24-hour total	400 mL		1,000 mL				
24-hour grand total • **Intake**			1,400 mL	24-hour grand total • **Output**			1,200 mL

FIGURE 7-10. Sample I&O record. *Remember: 1 ounce = 30 mL.*

BOX 7-2. Signs and Symptoms of Fluid Volume Deficit and Excess

FLUID VOLUME DEFICIT
- Dark urine with high specific gravity
- Depressed fontanelles (infant)
- Dry mucous membranes
- Low urine output
- Orthostatic hypotension
- Poor skin turgor
- Thirst
- Weight loss

FLUID VOLUME EXCESS
- Ascites
- Crackles in lungs
- Dyspnea caused by pulmonary fluid accumulation
- Edema, either ankle or sacral
- Weight gain (2 lb = 1 liter of fluid)

adenosine triphosphate (ATP), transcription and translation of DNA and ribonucleic acid (RNA), neural transmission, and muscular contraction.

Alterations in sodium, potassium, and calcium ion levels have a major effect on neurotransmission and muscular contraction. Changes in nerve and muscle excitability are particularly important in cardiac muscle, where rhythm disruption and conduction disturbances can be life threatening.

Most cells maintain an electrochemical gradient because of the effect of intracellular and extracellular sodium and potassium. This is most apparent in cell-to-cell impulse propagation in neurotransmission. Without stimulation, cells maintain a resting membrane potential created by a set ratio of intracellular and extracellular sodium and potassium ions. Action potentials, the impulses generated along neuronal axons, are created by changes in sodium and potassium ions in ICF and ECF. During an action potential, sodium ion channels open in the plasma membrane, allowing the entry of sodium ions into the cell. This is followed by the opening of potassium ion channels that permit the exit of potassium ions from the cell. The inward flow of sodium ions increases the concentration of positively charged cations in the cell and causes depolarization, where the potential of the cell is higher than the cell's resting potential. The sodium channels close at the peak of the action potential, whereas potassium continues to leave the cell. The efflux of potassium ions decreases the membrane potential in the repolarization phase (see Fig. 7-11). With imbalances of sodium and potassium in the body, neural transmission in the body is widely disrupted. There is body-wide muscular weakness and changes in sensation such as paresthesias (numbness and tingling). The muscles of the gastrointestinal system dysfunction, causing nausea, constipation, and abdominal distention. Confusion and disorientation are common symptoms of central nervous system (CNS) dysfunction. Cardiac dysfunction is particularly apparent with potassium-level disruption. Electrocardiogram (ECG) changes, rhythm disturbances, and postural hypotension occur.

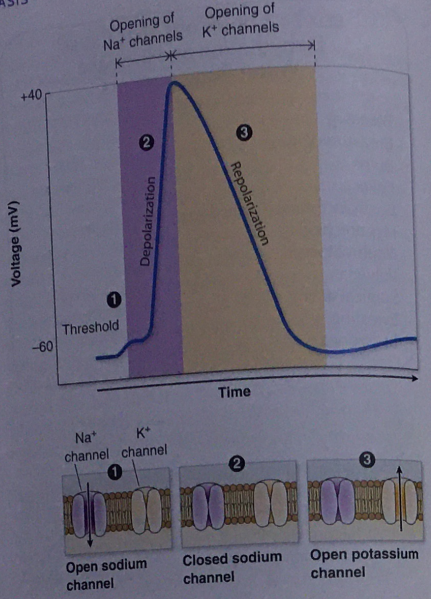


FIGURE 7-11. Nerve impulses are generated by action potentials within the neuron plasma membrane. Action potentials are generated by special types of ion channels embedded in a cell's plasma membrane. These channels are shut when the membrane potential is near the resting potential of the cell. (1) When the channels open, they allow an inward flow of sodium ions, which produces a rise in the membrane potential known as depolarization. This then causes more channels to open, and the process proceeds until all of the available sodium ion channels are open, resulting in a large upswing in the membrane potential. (2) The ion channels then close and sodium ions can no longer enter the neuron. (3). Potassium channels are then activated, and there is an outward current of potassium ions, returning the electrochemical gradient to the resting state. This is called repolarization.

Cardiac muscle contractility is largely dependent on calcium ions. Like neurons and other muscles, a given cardiac muscle cell has a resting membrane potential. A notable difference between skeletal and cardiac muscle is how each depolarizes the muscle cells. When skeletal muscle is stimulated by motor nerves, an influx of Na^+ quickly depolarizes the skeletal muscle cell. In cardiac muscle cells, calcium influx through voltage-gated calcium channels on the plasma membrane causes muscle contraction. Changes in serum calcium levels can cause hypotension, cardiac dysrhythmias, heart failure, and diminished responsiveness to cardiac drugs.

Sodium Imbalances

Sodium is the main electrolyte in the ECF and is the primary determinant of the ECF's osmolarity and volume. It must constantly be pumped out of the cell into the bloodstream. Sodium has many important physiologic roles. It controls the distribution of water, helps maintain normal fluid balance, and contributes to osmotic pressure. Sodium is also important to maintain the electrical gradient of neural membranes. However, because it is an extracellular ion, alterations in fluid balance can adversely affect its levels, which is why serum sodium levels need to be interpreted based on hydration status. Sodium is diluted by excess water in the bloodstream and concentrated when there is lack of sufficient water in the bloodstream.

CLINICAL CONCEPT

The average diet contains 1 to 3 grams of sodium per day. A low-sodium diet consists of less than 1,500 mg of sodium per day. Low-sodium diets are recommended in hypertension and heart failure.

Hyponatremia

Hyponatremia is a sodium serum level of less than 135 mEq/L. The clinical picture of hyponatremia centers around water. When dehydration occurs because the body has lost sodium and fluid together, it is known as hypovolemic hyponatremia. This primarily happens due to losses from the kidney (renal) or GI tract (nonrenal).

The causes of renal hypovolemic hyponatremia include adrenal insufficiency, osmotic diuresis, diuretic use, and salt-losing nephritis. The causes of nonrenal hypovolemic hyponatremia include diarrhea, vomiting, excessive sweating, cystic fibrosis, gastric lavage, fistulas, burns, and wounds. In cases of dehydration caused by hypovolemic hyponatremia, the symptoms are thirst, dry mouth, orthostatic hypotension, tachycardia, azotemia (high blood urea nitrogen concentration), and oliguria. In the older adult, electrolyte imbalances, particularly hyponatremia, can occur due to side effects of medications, insensitivity of the thirst center, or inadequate hydration.

CLINICAL CONCEPT

Neurological deficits, confusion, and behavioral changes are common effects of hyponatremia in the older adult. These CNS changes can lead to patient falls, which may be the first apparent sign of electrolyte imbalance.

Conversely, hyponatremia can occur in the presence of hypervolemia, or excess water. In this case, hyponatremia develops because sodium is diluted within an excess of water, which is why it is a dilutional hyponatremia. Symptoms include headache, lethargy, apathy, confusion, nausea, vomiting, diarrhea, muscle cramps, and muscle spasms.

Hyponatremia most commonly occurs when water excretion is impaired and sodium is diluted within a large volume of water in the bloodstream. This is clinically significant when hyponatremia is part of a drop in the serum total osmolality, which is measured by the calculation: 2(Na) mEq/L + serum glucose (mg/dL) / 18 + BUN (mg/dL) / 2.8.

When there is an acute drop in the serum osmolality, neuronal cell swelling occurs because of the water shift from the extracellular space to the intracellular space. Swelling of the brain cells results in two consequences:

- It inhibits ADH secretion from neurons in the hypothalamus and hypothalamic thirst center, which leads to excess water elimination as dilute urine.
- There is an immediate cellular adaptation with loss of electrolytes, and over the next few days there is a more gradual loss of organic intracellular solutes.

Severe hyponatremia can cause seizures, coma, and irreversible neurological damage because of brain swelling.

Treatment of hyponatremia is based on its etiology. If the patient is dehydrated, slow replacement of sodium with adequate fluid intake is the easiest method. Slow treatment is necessary, as rapid correction of serum sodium can precipitate severe neurological complications. If that does not help, more aggressive measures will be needed, such as replacement with normal saline or hypertonic saline solution.

CLINICAL CONCEPT

A patient who receives normal saline needs to be watched carefully for edema, particularly for pulmonary edema or other signs of fluid overload.

If the etiology of hyponatremia is Syndrome of Inappropriate ADH (SIADH), treatment requires restriction of water intake and investigating the source of ADH. If the etiology is fluid overload, diuretics will be used to remove excess water.

CLINICAL CONCEPT

Severe hyponatremia (less than 125 mEq/L) has a high mortality rate. In instances when the serum sodium level is lower than 105 mEq/L, the mortality is over 50%. Post-operative and elderly patients have the highest incidence of hyponatremia.

Hypernatremia

Hypernatremia is a sodium level greater than 145 mEq/L. It can occur with an excess of sodium or decrease in body water (see Box 7-3). Most commonly, it

BOX 7-3. Causes of Hyponatremia and Hypernatremia

CAUSES OF HYPONATREMIA
- Adrenal insufficiency
- Burns
- Cirrhosis
- Congestive heart failure
- Diaphoresis with more salt lost than water
- Diarrhea
- Diuretic therapy
- Excess hypotonic fluid administration (called *dilutional hyponatremia*)
- Hyperglycemia
- Hypoaldosteronism
- Laxatives
- Nasogastric suction
- Psychogenic polydipsia
- Renal disease
- SIADH, which causes excess reabsorption of water into the bloodstream at the nephron

CAUSES OF HYPERNATREMIA
- Certain medications such as osmotic diuretics, sodium bicarbonate, and sodium chloride
- Cushing's syndrome
- Diabetes insipidus (lack of antidiuretic hormone)
- Diarrhea
- Excess sodium administration
- Excessive adrenocortical secretion
- Hypercalcemia
- Impaired thirst
- Increased aldosterone
- Potassium depletion
- Profuse diaphoresis
- Tube feedings with lack of adequate water administration
- Uncontrolled diabetes mellitus
- Water deprivation

is caused by water loss, although it can be caused by salt loading. With kidney dysfunction, other factors may be involved, such as the inability of the renal tubule to react to ADH, causing the kidneys to not reabsorb water. With an inadequate amount of water in the blood, sodium is more concentrated and presents as a high serum level. Also, if the kidneys' glomerular filtration rate is decreased, sodium and water reabsorption into the bloodstream is low, which stimulates the adrenal gland's secretion of aldosterone. Aldosterone causes reabsorption of sodium and water from the nephron tubule fluid into the circulation, raising the sodium level.

When hypernatremia of any etiology occurs, cells become dehydrated. The high osmotic load of the increased sodium acts to extract water from the cells. Dehydrated cells shrink from water extraction. In mild hypernatremia, individuals usually can drink water to lower the sodium level in the blood and the body regains equilibrium. However, severe hypernatremia often occurs in ill patients who cannot take oral fluids. The CNS is particularly sensitive to changes in sodium concentrations in the bloodstream. In severe hypernatremia, water is lost from brain cells. The brain cells then compensate by moving water from cerebrospinal fluid (CSF) into the brain cells. This also brings in solutes such as amino acids and other organic solutes from the CSF into the brain cells. These changes keep the brain cells from severely dehydrating. During the treatment of the hypernatremic patient, usually clinicians will use intravenous hypotonic solutions which are high in water content. During treatment, if this water is infused too rapidly, it will move into the brain cells which are hypertonic compared to the hypotonic intravenous fluid. This can cause cerebral edema, leading to seizures, coma, and death. In treating severe hypernatremia, clinicians need to precisely calculate the free water deficit and replace water intravenously slowly over several hours to prevent cerebral edema from occurring.

The clinical manifestations of hypernatremia can be divided into two distinct patterns, one with fluid overload and one without fluid overload. If hypernatremia causes water retention, then the picture is one of an edematous state: weight gain and hypertension. With severe edematous states, there may also be mental changes and pulmonary edema causing dyspnea. If the hypernatremia is that of sodium retention and water loss, the patient will appear to be dehydrated and demonstrate thirst, irritability, tachycardia, flushed skin, dry mucous membranes, and oliguria.

CLINICAL CONCEPT

Hypernatremia risk is highest in breastfed infants and the elderly.

Treatment of hypernatremia depends on the underlying cause. Replacement fluids can be given orally or parenterally if it is caused by fluid depletion. Oral glucose–electrolyte replacement solutions are available for infants and children. If excess water is present, diuretic therapy may be necessary.

The mortality rate from hypernatremia is high, especially among elderly patients. Mortality rates of 42% to 75% have been reported for acute changes and 10% to 60% for chronic hypernatremia.

Potassium Imbalances

Potassium is the main electrolyte of the ICF; adults require 40 to 60 mEq/L/day of K^+. Potassium is involved in a wide range of body functions, including conduction of nerve impulses in skeletal, cardiac, and smooth muscle; acid–base balance; synthesis of adenosine-5'-triphosphate (ATP); osmotic balance; and the kidney's ability to concentrate urine. The nephron regulates potassium because of the action of aldosterone, which absorbs sodium and water and excretes potassium at the distal tubule.

Muscle contains the bulk of the body's potassium, and alterations in potassium levels have neuromuscular effects. A decrease in serum potassium causes decreased neuromuscular excitability, resulting in muscle weakness. An increase in potassium causes increased neuromuscular excitability, resulting in muscle spasms. Changes in neuromuscular excitability are particularly important in the heart, where alterations in serum potassium can produce serious cardiac arrhythmias.

Fluid shifts between the ICF and ECF can cause temporary changes in plasma potassium levels. Additionally, potassium levels should be assessed in relation to acid–base balance. Potassium will move from the ICF to the ECF based on changes in the hydrogen ion (H^+) concentration in the bloodstream. When H^+ is high in the bloodstream, H^+ excretion takes precedence over K^+ excretion at the kidney. In acidosis, aldosterone stimulates excretion of H^+ ions from the bloodstream instead of K^+ ions. As a result, K^+ remains in the bloodstream, making it appear as though there is an excess of K^+ in the blood, but this is not true hyperkalemia. When the acidosis is treated, K^+ will move into the ICF compartment, which will demonstrate that K^+ is actually low in the bloodstream. In diabetic ketoacidosis, when treatment is instituted using insulin, K^+ moves into the intracellular compartment. This movement of K^+ into the cells leaves an actual low K^+ level in the blood, thereby requiring administration of supplemental potassium.

Hypokalemia

Hypokalemia refers to a plasma concentration of potassium below 3.5 mEq/L. Diuretic therapy is the most common cause of hypokalemia; it is present in 20% to 50% of patients on non–potassium-sparing diuretics. African Americans and females are more susceptible. Risk is enhanced by concomitant illness such as heart failure or nephrotic syndrome. Both thiazide and loop diuretics increase the loss of K^+ in the urine.

Inadequate intake is also a frequent cause of hypokalemia. Patients who are nothing-by-mouth status (NPO), alcoholics, patients who have undergone bariatric surgery, and those who suffer from eating disorders are at greatest risk. A daily potassium intake of at least 40 to 50 mEq is required for optimal cell function.

The body can also lose approximately 80% to 90% of potassium via the kidneys, with the remainder lost through sweat and feces. Renal losses are increased by stress, trauma, metabolic alkalosis, and increased levels of aldosterone. Skin and gastrointestinal losses of K^+ can become excessive in burns, vomiting, nasogastric suctioning, and diarrhea. Severe diarrheal illness can cause a loss of potassium of 40 to 60 mEq/L.

The major signs and symptoms associated with hypokalemia include anorexia, nausea, vomiting, sluggish bowel, cardiac arrhythmias, postural hypotension, muscle fatigue, and weakness. Leg cramps are particularly common. Also, respiratory muscles can be weakened in severe hypokalemia. Deep tendon reflexes may be decreased or absent on physical examination. On ECG, there is a prolonged PR interval, flattened T wave, and prominent U wave (see Fig. 7-12).

Some specific clinical conditions can decrease potassium levels in the bloodstream. When large amounts of IV dextrose solution are administered to patients, the pancreas secretes excessive amounts of insulin; this can cause hypokalemia. The administration of adrenergic agents, such as epinephrine or albuterol, can also cause a drop in blood potassium levels. Commonly, diuretics also cause a loss of potassium from the bloodstream.

Digitalis toxicity often occurs when the patient is in the state of hypokalemia. Digitalis is a drug used when a patient is in heart failure. Heart failure often causes a loss of potassium because of the cycling of the RAAS when the heart is weakened. When digitalis is administered to a patient, potassium and digitalis compete for binding sites in the heart. In hypokalemia, there are open binding sites for potassium in the heart, and digitalis binds to these sites. When a high number of binding sites become occupied by digitalis, the potential for digitalis toxicity increases.

CLINICAL CONCEPT

Diuretics and digitalis are often prescribed together in heart failure. Diuretics commonly cause urinary loss of potassium, leading to hypokalemia. Hypokalemia causes increased binding of digitalis in the heart, which increases susceptibility of digitalis toxicity, commonly demonstrated as arrhythmias. Potassium blood level and digitalis level need to be frequently monitored in heart failure.

Treatment of hypokalemia is accomplished by replacement of potassium with foods such as orange juice, bananas, dried fruits, meats, and oral or parenteral K^+

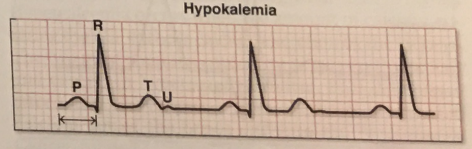


FIGURE 7-12. Electrocardiogram changes indicative of hypokalemia.

preparations. Potassium can also be prescribed intravenously; commonly 20 mEq of potassium chloride (KCl) per liter of IV solution is administered to NPO patients, not to exceed a total of 60 mEq/ day.

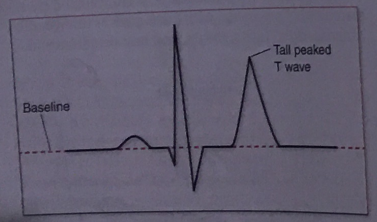
ALERT! Rapid administration of K^+ can cause cardiac arrest. IV potassium must always be diluted and never given as an IV bolus. It is excoriating to the skin and blood vessels in large doses. In emergency cases, up to 40 mEq of potassium can be administered through a central venous line.

Hyperkalemia

Hyperkalemia is a blood K^+ level greater than 5.2 mEq/dL. Normal kidney function is important in the regulation of potassium. Renal failure is a major cause of hyperkalemia because the kidneys lose the ability to excrete K^+. Any decrease in renal perfusion, such as decreased cardiac output, will diminish the kidney's ability to excrete K^+, thus increasing the amount of potassium in the body. Hyperkalemia can also occur in major muscle trauma such as a crushing injury because potassium is released rapidly from muscle cells.

The clinical presentation of a patient with hyperkalemia will depend on the level of the potassium imbalance and if it is chronically or acutely elevated. Early symptoms of hyperkalemia include numbness or tingling of the extremities, muscle cramping, diarrhea, apathy, and mental confusion. The ECG will show wide QRS complexes and tall, peaked T waves (see Fig. 7-13); as the potassium level rises, the ECG will show bradycardia, irregular pulse rate, and, ultimately, cardiac arrest.

Treatment of hyperkalemia is dependent on the cause. If hyperkalemia is severe (greater than 7.0 mEq/L), rapid treatment is needed to move K^+ from ECF to ICF. Continuous ECG monitoring is necessary. An infusion of 50% dextrose, 10 units of regular insulin, and 75 mEq of sodium bicarbonate can be administered. If K^+ levels continue to be elevated and the patient has normal renal function, a diuretic such as furosemide (Lasix®) can be administered. Calcium chloride or calcium gluconate (Kalcinate®) can also be administered. Albuterol and diuretics can be used to reduce high blood potassium. Another option for treatment is to give sodium polystyrene sulfonate (Kayexalate®), which acts at the bowel to capture potassium and excrete it via feces. An oral suspension, called Patiromer (Veltassa), can enhance potassium excretion from the intestine into the feces. Alternatively, hemodialysis or renal replacement therapy can reduce K^+ (see Box 7-4).



URE 7-13. Electrocardiogram changes indicative of rkalemia.

Calcium Imbalances

Calcium and phosphorus are the major mineral contents of bone. Small amounts of these electrolytes, which are regulated by vitamin D and parathyroid hormone (PTH), are found in the circulation. The major function of vitamin D is to facilitate the absorption of calcium from the gastrointestinal tract into the bloodstream; once in the bloodstream, PTH controls calcium levels. When the plasma calcium level is low, PTH is stimulated; when the plasma calcium level is high, PTH is inhibited.

PTH acts on bone to mobilize calcium and raise blood levels. Calcitonin, a hormone produced by the thyroid, acts at the bone and kidneys to remove calcium from the circulation.

Calcium is an important element in the body because of its role in the formation and function of bones and teeth, normal clotting, and regulation of neuromuscular irritability. It is stored in the bone, bound to plasma proteins, and bound with organic ions such as citrate. A small amount of calcium also remains free. This free, or ionized, calcium interacts in normal physiologic functions. The ionized form participates in cellular activities such as enzymatic reactions; neuron excitability; muscle contraction; release of hormones, neurotransmitters, and other chemical messengers; blood vessel contractility; cardiac contractility and automaticity; and blood clotting. Calcium is found in both ECF and ICF.

Because calcium is highly protein bound, interpretation of calcium levels is based on serum albumin levels. About half of the calcium in the body is bound to albumin. Hypoalbuminemia can cause the appearance of low calcium levels called pseudohypocalcemia. In pseudohypocalcemia, there is a normal level of body calcium with more in the ionized state than in the bound state because there is a diminished amount of albumin able to carry calcium. It is important to recognize that calcium and phosphate PO_4^- have an inverse relationship in the bloodstream. Both are bone-derived ions; when Ca^{++} rises in the bloodstream, PO_4^- diminishes in the bloodstream. When PO_4^- rises in the bloodstream, Ca^{++} diminishes in the bloodstream.

Hypocalcemia

Hypocalcemia consists of a blood calcium level of less than 8.7 mg/dL in adults. It is most commonly caused by lack of sufficient Ca^{++} in the diet, vitamin D deficiency, renal disease, or hypoparathyroidism.

BOX 7-4. Causes of Hypokalemia and Hyperkalemia

CAUSES OF HYPOKALEMIA
- Alkalosis
- Diuretic therapy
- Elevated glucocorticoids
- Excessive gastrointestinal, renal, or skin losses
- Hyperaldosteronism
- Inadequate intake
- Laxative abuse
- Nasogastric suction
- Redistribution of potassium (K^+) between the intracellular and extracellular spaces

CAUSES OF HYPERKALEMIA
- Addison's disease
- Burns (can redistribute K^+ into ECF from ICF)
- Digitalis toxicity
- Excessive administration of K^+ sparing diuretics (spironolactone)
- Extreme exercise
- Hemolysis of red blood cells
- Hypoaldosteronism
- Medications: antibiotics such as sulfamethoxazole and trimethoprim (Bactrim®). ACE inhibitors, chemotherapeutic agents, and immunosuppressive agents such as cyclosporine
- Metabolic acidosis
- Na^+ depletion
- Renal failure
- Trauma (can redistribute K^+ into ECF from ICF)

Acute hypocalcemia is manifested by neuromuscular excitability, which is demonstrated in individuals as a subjective experience of paresthesias (numbness and tingling) around the mouth, hands, and feet. Chvostek's sign and Trousseau's sign are examples of neuromuscular irritability caused by chronically low calcium levels (see Fig. 7-14 and Fig. 7-15). Other signs may include muscle spasms of the face, hands, and feet; laryngeal spasm; seizures; and death. Cardiovascular effects of hypocalcemia include hypotension, arrhythmias (particularly heart block and ventricular fibrillation), and failure to respond to cardioactive drugs. Chronic hypocalcemia causes bone pain and fragility, dry skin and hair, cataracts, depression, and dementia. Because of the inverse relationship between calcium and phosphate in the blood, hypocalcemia will cause hyperphosphatemia.

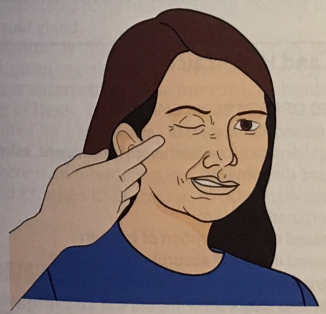


FIGURE 7-14. Chvostek's sign. (From Williams, L., & Hopper, P. [2019]. *Understanding medical-surgical nursing* [6th ed.]. Philadelphia, PA: F. A. Davis Company, with permission.)

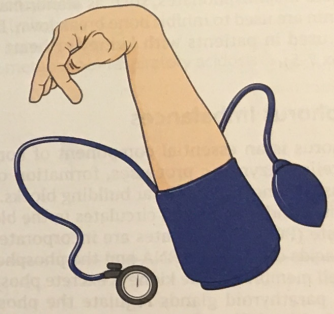


FIGURE 7-15. Trousseau's sign. (From Williams, L., & Hopper, P. [2019]. *Understanding medical-surgical nursing* [6th ed.]. Philadelphia, PA: F. A. Davis Company, with permission.)

Treatment of hypocalcemia requires calcium replacement. Oral calcium supplements with vitamin D are often used, as vitamin D is needed for calcium absorption from the intestine.

Hypercalcemia

Hypercalcemia is a calcium level greater than 10 mg/dL. Hypercalcemia occurs when the amount of calcium entering the ECF exceeds calcium excretion by the kidneys. The two most common causes are hyperparathyroidism and cancer. In hyperparathyroidism, PTH is overproduced, and the hormone pulls excessive amounts of calcium out of the bones and into the bloodstream. Cancer-related hypercalcemia is caused by malignant cells invading the bone, causing bone destruction. Cancer also releases a parathyroid-like hormone, causing an

increase in serum calcium levels. Other causes of hypercalcemia are prolonged immobility that causes calcium to leech out of bone; excess calcium or vitamin D intake; toxic levels of drugs such as lithium, thiazide diuretics, and theophylline; aluminum-induced osteomalacia; and hypophosphatemia.

The signs and symptoms of hypercalcemia involve decreased neuromuscular excitability. Muscle flaccidity, proximal muscle weakness of the lower extremities, bone tenderness, and decreased neuromuscular activity of the bowel causing constipation are the main effects. High calcium concentrations in the urine increase susceptibility to renal calculi. The heart responds to hypercalcemia with increased contractility and ventricular arrhythmias. Other non-specific effects include dulled consciousness, depression, anorexia, nausea, vomiting, and ulcers. Hyperreflexia and tongue fasciculations may also occur. Hypercalcemia also causes hypophosphatemia.

Treatment involves enhancement of urinary excretion of calcium and inhibition of bone breakdown. Increased fluids and loop diuretics enhance calcium excretion. Bisphosphonates, such as alendronate, and calcitonin are used to inhibit bone breakdown. Dialysis can be used in patients with kidney or heart failure (see Box 7-5).

Phosphorus Imbalances

Phosphorus is an essential component of bone, red blood cells, enzymatic processes, formation of ATP, acid–base balance, and cellular building blocks. Phosphorus is found in bone and circulates in the blood as phosphate (PO_4^-). Phosphates are incorporated into nucleic acids of DNA and RNA and the phospholipids of the cell membrane. The kidneys excrete phosphate, and the parathyroid glands regulate the phosphate level in the blood. Phosphate has a reciprocal relationship with calcium in the blood, meaning that when calcium is low in the bloodstream, phosphate is high and vice versa.

Hypophosphatemia

Hypophosphatemia consists of a blood level of phosphate lower than 2.5 mg/dL. There are three main causes of hypophosphatemia: decreased intestinal absorption of phosphorus, increased excretion of phosphorus by the kidneys, and an intracellular shift of phosphate. Low phosphate causes red blood cell, white blood cell, and platelet dysfunction, as well as neural dysfunction and disturbed musculoskeletal function. Lack of sufficient phosphate can cause tremors, paresthesias, hyporeflexia, anorexia, dysphagia, muscle weakness, joint stiffness, bone pain, and osteomalacia. Treatment of hypophosphatemia is replacement therapy.

Hyperphosphatemia

Hyperphosphatemia is a PO_4^- level of 4.5 mg/dL or greater in the blood. The most common cause is kidney failure, where the kidneys are unable to excrete excessive phosphorus. Hyperphosphatemia is usually accompanied by hypocalcemia, and many of its symptoms are related to low calcium levels. Treatment is directed at correcting the cause of the disorder. Calcium-based phosphate binders, such as sevelamer and lanthanum carbonate, inhibit gastrointestinal absorption of phosphate. Dialysis can also reduce hyperphosphatemia (see Box 7-6).

Magnesium Imbalances

Magnesium (Mg^{++}) is largely stored in bone and, like calcium, is protein bound within the bloodstream. About 60% of the body's magnesium is found in the bones. It is required for many cellular metabolic processes, such as functioning of nerve conduction, replication and transcription of DNA, translation of RNA, intracellular enzyme reactions, and all processes that require ATP. The cardiovascular system requires magnesium for vasodilation and normal functioning.

BOX 7-5. Causes of Hypocalcemia and Hypercalcemia

CAUSES OF HYPOCALCEMIA

- Alcohol abuse
- Drugs: loop diuretics, anticonvulsants, calcitonin, gentamicin, phosphates
- Hyperphosphatemia
- Hypoalbuminemia
- Hypomagnesemia
- Hypoparathyroidism
- Inadequate dietary intake or inadequate vitamin D
- Malabsorption
- Pancreatitis
- Sepsis

CAUSES OF HYPERCALCEMIA

- Decreased elimination of calcium
- Drugs: diuretics, chemotherapy, androgens, estrogen, lithium, theophylline
- Excess vitamin D
- Hyperparathyroidism
- Increased bone resorption of calcium
- Increased intestinal absorption of calcium
- Malignancy such as bone, multiple myeloma, blood, breast, and lung cancer
- Prolonged immobility
- Renal insufficiency

BOX 7-6. Causes of Hypophosphatemia and Hyperphosphatemia

CAUSES OF HYPOPHOSPHATEMIA

- Recovery phase of diabetic ketoacidosis
- Acute alcoholism
- Severe burns
- Receiving total parenteral nutrition (TPN)
- Refeeding after prolonged undernutrition
- Severe respiratory alkalosis

Acute severe hypophosphatemia with serum phosphate < 1 mg/dL (< 0.32 mmol/L) is most often caused by transcellular shifts of phosphate often superimposed on chronic phosphate depletion.

Chronic hypophosphatemia usually is the result of decreased renal phosphate reabsorption. Causes include the following:

- Increased parathyroid hormone levels, as in primary and secondary hyperparathyroidism
- Other hormonal disturbances, such as Cushing's syndrome and hypothyroidism
- Vitamin D deficiency
- Electrolyte disorders, such as hypomagnesemia and hypokalemia
- Theophylline intoxication
- Long-term diuretic use

Severe chronic hypophosphatemia usually results from a prolonged negative phosphate balance. Causes include:

- Chronic starvation or malabsorption, often in patients with alcoholism, especially when combined with vomiting or copious diarrhea
- Long-term ingestion of large amounts of phosphate-binding aluminum, usually in the form of antacids

CAUSES OF HYPERPHOSPHATEMIA

Increased intake of PO_4^-

This can result from the following:

- Excessive oral or rectal use of an oral phosphate–saline laxative (Phospho-soda®)
- Excessive parenteral administration of phosphate
- Milk-alkali syndrome
- Vitamin D intoxication

Decreased excretion of PO_4^-

This can result from the following:

- Renal failure, acute or chronic
- Hypoparathyroidism
- Pseudohypoparathyroidism
- Severe hypomagnesemia
- Tumoral calcinosis
- Bisphosphonate therapy

Shift of phosphate from intracellular to extracellular space

This can result from the following:

- Rhabdomyolysis
- Tumor lysis
- Acute hemolysis
- Acute metabolic or respiratory acidosis

Magnesium also affects sodium and potassium levels both inside and outside the cell membrane. In addition, magnesium can compete with and exert effects on calcium-mediated processes because of its effect on the parathyroid gland.

Magnesium is ingested from the diet in meats, seafood, green vegetables, and some sources of ground water. It is absorbed from the intestine, reabsorbed in the loop of Henle, and then excreted by the kidney. It is inhibited by high plasma calcium levels and high PTH levels. Magnesium also assists in the release of PTH. There is an interdependent relationship between Mg^{++} and K^+: when K^+ decreases, so does Mg^{++} and vice versa.

Hypomagnesemia

Hypomagnesemia is a magnesium blood level of less than 1.5 mEq/L. It occurs when Mg^{++} ions are released from bone in exchange for increased uptake of calcium. It usually occurs in conjunction with hypocalcemia and hypokalemia. Causes of hypomagnesemia are prolonged diarrhea, laxative abuse, increased renal excretion of magnesium, sepsis, burns, and serious wounds requiring débridement. Signs and symptoms of low Mg^{++} are similar to those of low Ca^{++} and K^+ levels. These include neuromuscular manifestations such as tetany, Chvostek's sign, Trousseau's sign, tremors, muscle spasms, Babinski's sign, and cardiac arrhythmias. ECG changes similar to those of hypokalemia may be seen. More serious manifestations may be respiratory muscle paralysis, complete heart block, ventricular dysrhythmias, tachycardia, hypertension, and coma. Treatment of hypomagnesemia is replacement therapy, commonly with magnesium sulfate.

Hypermagnesemia

Hypermagnesemia is a magnesium blood level of greater than 2.5 mEq/L. Magnesium is often used to treat cardiac disorders and pregnancy-related

eclampsia, and levels must be carefully monitored. The most common cause of hypermagnesemia is renal dysfunction. High Mg^{++} inhibits acetylcholine release and can cause diminished neuromuscular function, demonstrated by hyporeflexia and muscle weakness. Magnesium also blocks calcium channels and can cause cardiovascular effects such as hypotension and arrhythmias. Severely high Mg^{++} levels (greater than 10 mEq/L) can cause cardiac arrest. Sedation, confusion, coma, and respiratory paralysis can occur. To counteract hypermagnesemia, IV calcium or dialysis can be used (see Box 7-7).

BOX 7-7. Causes of Hypermagnesemia and Hypomagnesemia

CAUSES OF HYPERMAGNESEMIA

- Renal failure
- Excessive intake
- Lithium therapy
- Hypothyroidism
- Addison disease
- Familial hypocalciuric hypercalcemia
- Milk-alkali syndrome
- Hyperparathyroidism
- Excessive Mg^{++} containing cathartics or laxatives
- Excessive M^{++} treatment for eclampsia
- Tumor lysis syndrome in chemotherapy
- Rhabdomyolysis

CAUSES OF HYPOMAGNESEMIA

Causes related to decreased magnesium intake include the following:

- Starvation
- Alcohol dependence and withdrawal
- Total parenteral nutrition

Causes related to the redistribution of magnesium from extracellular to intracellular space include the following:

- Hungry bone syndrome
- Treatment of diabetic ketoacidosis
- Refeeding syndrome
- Acute pancreatitis

Causes related to gastrointestinal magnesium loss include the following:

- Diarrhea
- Vomiting and nasogastric suction
- Gastrointestinal fistulas and ostomies
- Hypomagnesemia with secondary hypocalcemia (HSH)

Causes related to renal magnesium loss include the following:

- Renal tubular defects
- Gitelman's syndrome
- Classic Bartter's syndrome (type III Bartter's syndrome)
- Diuretics
- Antimicrobials: amphotericin B, aminoglycosides, pentamidine, capreomycin, viomycin, foscarnet
- Chemotherapeutic agents: cisplatin, cetuximab
- Immunosuppressants: tacrolimus, cyclosporine
- Proton pump inhibitors
- Primary hyperaldosteronism

Chapter Summary

- The human body is 60% water, and it is contained in three different compartments: intracellular, interstitial, and extracellular.
- The extracellular compartment is within the bloodstream, the intracellular compartment is within each cell, and the interstitial compartment is in the tissue between the cells and bloodstream.
- Hypovolemia, hypotension, or low perfusion of the kidney stimulates the RAAS.
- Signs of dehydration include thirst, dry mucous membranes, hypotension, poor skin turgor, dark-colored urine, and low urine volume.
- Hypovolemia or dehydration can cause oliguria (lack of adequate urine output), defined as less than 400 mL urine/day or less than 20 mL/urine per hour.
- Hypovolemia causes hypotension, which stimulates the baroreceptors to trigger the sympathetic nervous system to increase heart rate and arterial vasoconstriction.
- Blocking ACE inhibits the conversion of angiotensin I to angiotensin II in the RAAS.
- Angiotensin II is a potent vasoconstrictor and stimulates the adrenal gland to secrete aldosterone.
- ACE inhibitors and angiotensin receptor blockers are drugs that are commonly used to lower blood pressure and treat heart failure.
- Aldosterone increases sodium and water reabsorption into the bloodstream and excretes potassium into the urine.
- The RAAS is a compensatory mechanism of the body that will raise blood volume and stimulate arterial vasoconstriction, leading to an increase in blood pressure.
- The posterior pituitary can sense low blood volume and in response releases ADH, which causes water reabsorption into the bloodstream and raises water volume of blood.
- SIADH causes excess secretion of ADH and excess water reabsorption, which results in hypervolemia and dilutional hyponatremia.
- When the body has excessive water in the bloodstream, natriuretic peptides, ANP and BNP are released by the heart tissue to increase water output into the urine.
- Diuresis means water loss from the body. The body contains natural diuretics, and many drugs act as diuretics. Major pharmacological diuretics include furosemide and hydrochlorothiazide.
- Starling's Law of Capillary Forces explains that there are two major forces at every capillary–cell interface in the body: hydrostatic and osmotic pressure. Hydrostatic pressure forces fluid out of the capillary pores into the tissues, and osmotic pressure pulls water from the tissues into the bloodstream.
- There are three types of IV solution: isotonic, hypotonic, and hypertonic. The loss of body water, whether acute or chronic, can cause a range of problems from mild lightheadedness to convulsions and coma. Conversely, the administration of excess water can be lethal to the patient.
- The electrolytes Na^+, K^+, Ca^{++}, Mg^{++}, and PO_4^- are the main ionic solutes in the blood.
- Sodium and water have a major influence on hydration status. Hydration status influences sodium concentration. Water follows sodium with fluid shifts.
- Hyponatremia can be due either to lack of sufficient sodium in the bloodstream or to excessive water in the bloodstream that dilutes the sodium content.
- Electrolyte imbalances, particularly hyponatremia, can cause behavioral changes such as disorientation and confusion in the older adult.
- Hypernatremia is associated with dehydration as a decrease in water level increases the sodium concentration.
- Potassium is one of the most important electrolytes to monitor in the body, particularly in patients with cardiac disease.
- Loop diuretics, often used in heart failure or edema, can cause hypokalemia.
- Hypokalemia can cause cardiac dysrhythmias and can cause digitalis toxicity.
- IV potassium must always be diluted because it is excoriating to skin and blood vessels. Commonly 20 mEq of K^+ is added to a liter of IV fluid and administered over 8 hours.
- In emergency cases, up to 40 mEq of potassium can be administered through a central venous line.
- Hyperkalemia can cause cardiac arrest.
- Hypocalcemia can cause neuromuscular excitability, muscle cramping, and muscle spasms.
- Chvostek's and Trousseau's signs, both apparent muscle spasms, are indicative of hypocalcemia.
- Hypocalcemia and hypercalcemia can cause cardiac dysrhythmias (arrhythmias).
- Hypercalcemia causes sluggishness of muscles and can cause constipation due to slowed peristalsis and hardened stool. Hypercalcemia can also precipitate in the urine and cause kidney stones.
- Many types of cancers can secrete a parathyroid-like hormone that raises Ca^{++} levels in blood.
- Phosphate and calcium blood levels have an inverse relationship. When PO_4^- is high in bloodstream, calcium is low. When PO_4^- is low in bloodstream, calcium is high.
- Hypomagnesemia or hypermagnesemia can cause cardiac dysrhythmias (arrhythmias).

Making the Connections

Pathophysiology Signs and Symptoms	Physical Assessment Findings	Diagnostic Testing	Treatment
Dehydration | Lack of body water in intracellular and extracellular fluid.			
Thirst. Dry mucous membranes. Weakness.	Low urine output. Dark urine. Poor skin turgor. Dry mucous membranes. Hypotension. In infants, depressed fontanelle.	High blood urea nitrogen (BUN). Oliguria. Hypernatremia caused by low water in blood.	Oral fluids. IV 0.45% NaCl.
Overhydration | Excess of body water in ICF and ECF.			
Edema. Weight gain.	Dyspnea caused by pulmonary fluid accumulation. Crackles in lungs. Edema, either ankle or sacral. Weight gain. Ascites.	Dilutional hyponatremia (excess water in the bloodstream causes a low sodium concentration in the bloodstream).	Diuretic.
Hyponatremia | Serum sodium lower than 135 mEq/L. Commonly caused by heart failure, diuretic therapy, cirrhosis, nephrosis, excess water intake, SIADH.			
Muscle cramps. Weakness. Headache. Depression. Anxiety. Lethargy. Confusion. Anorexia Nausea. Vomiting.	Weakness. Depression. Anxiety. Lethargy. Confusion. Vomiting.	Serum sodium less than 135 mEq/L.	Depends on cause of low sodium. Slow replacement of sodium if true hyponatremia. Restriction of water intake if caused by dilutional hyponatremia.
Hypernatremia | Serum sodium greater than 145 mEq/L. Commonly caused by loss of water, fluid restriction, hypertonic IV fluids, diaphoresis with more water loss than sodium, tube feedings without adequate free water, Cushing's syndrome, diabetes insipidus.			
Decreased salivation. Thirst. Headache. Agitation. Seizures.	Decreased skin turgor if low water volume. Decreased reflexes. Tachycardia. Weak, thready pulse. Hypertension or hypotension depending on water volume.	Serum sodium greater than 145.	If caused by inadequate water: Replace with IV fluid 0.45% NaCl.
Hypokalemia | Serum potassium level less than 3.5 mEq/L. Commonly caused by dietary deficiency, diuretics, vomiting, diarrhea, nasogastric (NG) suction, hyperaldosteronism, salt wasting kidney disease, gastrointestinal (GI) surgery, alkalosis, laxative abuse.			
Anorexia, nausea, vomiting. Muscle weakness. Muscle cramps. Paresthesias. Confusion.	Postural hypotension. Increased sensitivity to digitalis toxicity. Muscle weakness.	Serum potassium level less than 3.5 mEq/L. ECG dysrhythmias ECG: U wave.	Oral or parenteral K^+.

Making the Connections–cont'd

Signs and Symptoms	Physical Assessment Findings	Diagnostic Testing	Treatment
Hyperkalemia | Serum potassium level greater than 5.2 mEq/L. Commonly caused by excessive intake, aldosterone deficiency, Na^+ depletion, acidosis, tissue trauma, burns, extreme exercise, renal failure, Addison's disease (lack of cortisol), hemolysis, potassium-sparing diuretics, ACE inhibitors.			
Nausea, vomiting. Intestinal cramping. Diarrhea. Paresthesias. Muscle weakness. Muscle cramping. Dizziness.	Muscle weakness. Dizziness.	Serum potassium level greater than 5.2 mEq/L. ECG changes, including peaked T wave. Risk of cardiac arrest with severe K^+ excess.	An infusion of 50% dextrose, 10 units of regular insulin, and 75 mEq of sodium bicarbonate. Furosemide (Lasix®). Albuterol. Calcium chloride or calcium gluconate (Kalcinate®). Sodium polystyrene sulfonate (Kayexalate®). Patiromer.
Hypocalcemia | Serum calcium level less than 8.7 mg/dL. Commonly caused by hypoparathyroidism, malabsorption syndrome, hypomagnesemia, hyperphosphatemia, renal failure, insufficient vitamin D, hypoalbuminemia, diuretic therapy, diarrhea, acute pancreatitis, gastric surgery, massive blood transfusion.			
Body-wide muscle cramps (tetany). Laryngeal spasm. Paresthesias. Bone pain, deformities, fracture. Dry skin, hair. Confusion. Seizure.	Increased neuromuscular excitability (tetany). Hyperactive reflexes. Positive Chvostek's and Trousseau's sign. Hypotension. Seizure. Dementia possible.	Serum calcium level less than 8.7 mg/dL. Arrhythmias. Heart block. Ventricular fibrillation.	Administration of Ca^{++} and vitamin D.
Hypercalcemia | Serum calcium level greater than 10.0 mg/dL. Commonly caused by excessive calcium in diet, excessive vitamin D, immobility, bone breakdown, hyperparathyroidism, hypophosphatemia, diuretics, ACE inhibitors, lithium therapy, prolonged immobility, malignancy of bone or blood. Many types of cancer release a parathyroid-like substance that raises blood Ca^{++}.			
Anorexia. Nausea, vomiting. Constipation. Muscle weakness. Bone fracture possible.	Decreased neuromuscular excitability. Ataxia. Loss of muscle tone. Hypertension.	Serum calcium level greater than 10.0 mg/dL. Urine hematuria/calcium. Kidney stone possible. Bone breakdown may be apparent as source of high calcium in the bloodstream. Hypertension. Heart block.	Increased fluids and loop diuretics enhance calcium excretion. Bisphosphonates and calcitonin are used to inhibit bone breakdown. Dialysis may be necessary.
Hypophosphatemia | Serum phosphorus level less than 2.5 mg/dL. Can be caused by ingestion of excess antacids (aluminum and calcium), severe diarrhea, lack of vitamin D, hypercalcemia, alkalosis, hyperparathyroidism, diabetic ketoacidosis, alcoholism.			
Tremor. Lack of coordination. Paresthesias. Confusion. Seizures. Muscle weakness. Joint stiffness. Bone pain.	Tremor. Ataxia. Muscle weakness. Decreased reflexes.	Serum phosphorus level less than 2.5 mg/dL. Complete blood count; low hemoglobin, hematocrit, hemolytic anemia. Platelet dysfunction; bruising. White blood cell dysfunction; infections. Low bone density Osteomalacia.	Replacement of PO_4^-.

Continued

Making the Connections–cont'd

Signs and Symptoms	Physical Assessment Findings	Diagnostic Testing	Treatment
Hyperphosphatemia | Serum phosphorus level greater than 4.5 mg/dL. Can be caused by laxatives, enemas containing phosphate, massive trauma, heat stroke, rhabdomyolysis, tumor lysis syndrome, potassium deficiency, hypocalcemia, kidney failure, hypoparathyroidism.			
Paresthesias. Muscle cramps.	Tetany. Hypotension.	Serum phosphorus level greater than 4.5 mg/dL. Cardiac arrhythmias.	Calcium-based phosphate binders and dialysis reduce hyperphosphatemia.
Hypomagnesemia | Serum magnesium level less than 1.5 mg/dL. Can be caused by malnutrition/malabsorption, excessive loss of GI fluids, alcoholism/cirrhosis, diuretic therapy, hyperparathyroidism, hyperaldosteronism, diabetic ketoacidosis, thyroid malfunction, pancreatitis, NG suction, fistulas, renal diseases, proton pump inhibitors (PPIs), and certain antibiotic, immunosuppressive, and chemotherapeutic agents.			
Muscle cramps. Personality change. Uncontrollable movements.	Positive Chvostek's and Trousseau's sign. Nystagmus. Positive Babinski's sign. Hypertension.	Serum magnesium level less than 1.5 mg/dL. ECG: tachycardia, arrhythmias.	Replacement Mg^{++} therapy.
Hypermagnesemia | Serum magnesium level greater than 2.5 mg/dL. Can be caused by excessive use of Mg-containing antacids and laxatives, untreated diabetic ketoacidosis, excessive Mg infusion as in treatment of eclampsia of pregnancy, renal failure.			
Lethargy. Confusion. Weakness.	Decreased reflexes (hyporeflexia). Hypotension. Weak muscles.	Serum magnesium level greater than 2.5 mg/dL. ECG: Arrhythmias. Cardiac arrest possible.	IV calcium or dialysis.

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CHAPTER 8

Acid–Base Imbalances

Learning Objectives

Upon completion of this chapter, the student will be able to:

- List the four primary types of acid–base disturbances.
- Name and describe the three primary buffer systems in the body.
- Explain how the lungs and kidneys compensate for acid–base disturbances.
- Describe how pH abnormalities may cause alterations in electrolyte levels.
- Interpret arterial blood gas values to identify acid–base disturbances.

Key Terms

Acid
Acidic
Acidosis
Acidemia
Alkaline
Alkalosis
Alkalemia
Anion gap (AG)
Arterial blood gas (ABG)
Base
Basic
Blood pH
Buffer
$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$
Carbonic acid–bicarbonate system
Compensation
Metabolic acidosis
Metabolic alkalosis
Nonvolatile acid
Saturation of hemoglobin with oxygen (SaO_2)
Partial pressure of carbon dioxide (Pco_2)
Partial pressure of oxygen (Po_2)
pH
Pulse oximetry
Respiratory acidosis
Respiratory alkalosis
Volatile acid

Every second, a multitude of physiologic and biochemical reactions occur within the body. As cells require sufficient oxygen and nutrients to function normally, they also require a suitable acid–base environment. The proteins within the body contain many acidic and basic groups; thus any alteration in pH disrupts protein structure and function. To prevent such changes in pH, the body employs **buffer** systems. The body utilizes three buffer systems: proteins, phosphates, and the carbonic acid–bicarbonate system. Although all of these systems are important, the majority of this chapter focuses on the carbonic acid–bicarbonate buffer system.

Basic Concepts of Acid–Base Balance

Knowing the chemistry of acids, bases, and buffers provides a means for understanding disturbances in the body.

Acids, Bases, and Buffers

An **acid** is any compound that donates hydrogen ions (H^+) in solution. When H^+ ions predominate in a solution, the solution is **acidic**. In the body, acids are present in two forms: volatile and nonvolatile. When CO_2, a volatile gas, combines with water, the **volatile acid**, carbonic acid (H_2CO_3), forms. Carbonic anhydrase, an enzyme present in large amounts in erythrocytes, helps to catalyze this reaction. H_2CO_3 can also dissociate into CO_2 and H_2O, with the CO_2 then being exhaled by the lungs. Other acids are not converted to CO_2 and thus are referred to as **nonvolatile** (or fixed) acids.

A **base** is a compound that accepts H^+ ions in solution. When basic ions predominate in a solution, the solution is **alkaline** or **basic**.

Metabolism and Acid–Base Levels

Various compounds in the body are acidic or basic. For example, cellular metabolism of fats and carbohydrates

produces large quantities of CO_2. The CO_2 combines with H_2O in the bloodstream, forming the volatile acid, carbonic acid (H_2CO_3). Acidic products also form during hypoxic states when pyruvate converts to lactic acid during anaerobic metabolism. Metabolism of positively charged amino acids and hydrolysis of phosphates also produce acidic compounds. Most basic compounds form from the metabolism of negatively charged amino acids. By using buffers, the body counteracts potential pH changes brought on by these metabolic products.

pH Values

The H^+ ion is a very strong acid. In body fluids, however, the concentration of H^+ ions compared with other ions is extremely low. Because the hydrogen ion concentration is so small, it is expressed in terms of **pH**. The values for pH are calculated as the negative logarithm (p) of the H^+ ion concentration in mEq/L. For example, a pH value of 4 indicates that the H^+ concentration of a solution is 10^{-4} (0.00001 mEq/L). pH values and H^+ ion concentration are inversely related. A lower pH value indicates a higher concentration of H^+ ions and a more acidic solution, whereas a higher pH value represents a lower concentration of H^+ ions and a more alkaline solution (see Fig. 8-1).

Buffers

The normal range for **blood pH** is slightly basic at **7.35 to 7.45**. Deviations outside this normal range affect cellular function profoundly and are potentially life threatening. To prevent such large swings in blood pH, three buffer systems (protein, phosphate, and carbonic acid–bicarbonate) absorb excess H^+ ions or donate H^+ ions as needed.

Protein Buffering System

Because of their structure, almost all proteins can serve as functional buffers. Taken together, the proteins serve as the largest buffering system in the body. The amino and carboxyl groups found on amino acids enable proteins to absorb or donate H^+ ions as needed to maintain physiologic pH. One of the primary proteins that carries out this function is hemoglobin.

Phosphate Buffering System

Phosphates play a key role in regulating pH in the intracellular environment. Phosphates (PO_{4-}) can take on an acidic form, dihydrogen phosphate, or a basic form, hydrogen phosphate, to buffer pH changes.

Carbonic Acid–Bicarbonate System

The buffering system most commonly discussed is the **carbonic acid–bicarbonate system**. Carbon dioxide, carbonic acid, hydrogen ions, and bicarbonate ions (HCO_3^-) all play a role in this buffering system. When CO_2 combines with water, H_2CO_3 (carbonic acid) is formed. The H_2CO_3 then dissociates, yielding H^+ (a strong acid) and HCO_3^- (a weak base). The chemical reaction of H_2CO_3 formation and dissociation is the following:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

The equation moves in both directions. When CO_2 levels are elevated, the equation *moves toward the right*, forming more H^+ and HCO_3^- ions. Likewise, when H^+ ion levels are elevated, the equation *moves toward the left*, as H^+ ions are converted to CO_2 and the CO_2 is exhaled. The carbonic acid–bicarbonate buffering system plays a significant role in the body, as two organs, the lungs and kidneys, use this buffering system to compensate for alterations in physiologic pH. Because of this system, arterial blood gases (ABGs) values include arterial carbon dioxide and bicarbonate levels, along with other factors (see Box 8-1).

Renal and Respiratory Compensations for Acid-Base Disturbances

As mentioned, the lungs and kidneys utilize the carbonic acid–bicarbonate buffering system to adjust any pH disturbances. Both organs relate to the environment in such a way that excretion or retention of acidic and basic compounds occurs in order to regulate blood pH. When the lungs and kidneys attempt to adjust pH disturbances, the process is called **compensation** (see Fig. 8-2). The lungs respond to acid–base disturbances within minutes, with the response reaching maximal levels by 24 hours. The response, though, cannot be maintained indefinitely. The kidneys require hours to a day to compensate; however, the response can be maintained for much longer.

Respiratory Compensation for Acid-Base Disturbances

Under normal conditions, the lungs correct pH imbalances by increasing or decreasing ventilation as needed. An increase in ventilation decreases CO_2. As CO_2, is exhaled, H^+ ion concentration falls (raising pH) by *moving the buffer equation toward the left*:

$$CO_2 + H_2O \Leftarrow H_2CO_3 \Leftarrow H^+ \text{ and } HCO_3^-$$

Decreased ventilation retains CO_2. The retention of CO_2 *moves the buffer equation toward the right*, resulting in an elevation of H^+ ion level and a decrease in pH (see Fig. 8-3).

$$CO_2 + H_2O \Rightarrow H_2CO_3 \Rightarrow H^+ \text{ and } HCO_3^-$$

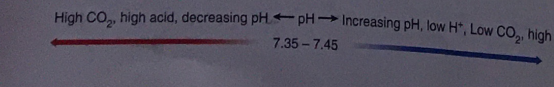

FIGURE 8-1. pH and relationship to H^+ and CO_2.

BOX 8-1. The Carbonic Acid–Bicarbonate Chemical Reaction

This chemical reaction within the bloodstream can go back and forth according to the amount of acids or bases or CO_2 in the bloodstream.

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ \text{ and } HCO_3^-$$

Example 1: If there is excess CO_2 in the bloodstream, the equation moves toward the right, which shows that more acid (H+), which is a very strong acid, is created. The bloodstream becomes high in acid in a condition called acidemia (also called acidosis). *[HCO_3^- is a weak base and cannot neutralize H^+]*

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ \text{ and } HCO_3^-$$

Example 2: If there is an excess of H^+ in the bloodstream, the equation moves toward the left, which shows that more CO_2 is created and CO_2 is exhaled vigorously by the lungs. This reduction of H^+ then makes the blood alkalemic (also called alkalotic).

$$CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow H^+ \text{ and } HCO_3^-$$

Because of the link between ventilation, CO_2, and pH, carbon dioxide levels in the bloodstream are kept in a narrow range. The normal range for **partial pressure of carbon dioxide (P_{CO_2})** is **35 to 45 mm Hg.** Sometimes the P_{CO_2}, specifically within the arterial blood, is written as $PaCO_2$. Chemoreceptors in the brain closely monitor H^+ ion levels and send signals to the respiratory center in the medulla to adjust ventilation, and subsequently carbon dioxide levels, as needed. When the blood pH is too low (acidic), the ventilation rate increases, causing exhalation of CO_2, which in turn reduces acid in the blood and raises pH. The opposite occurs when blood pH is too high (alkaline). Ventilation is suppressed, increasing CO_2 levels in the bloodstream, which creates H^+ and lowers the pH (see Table 8-1).

CLINICAL CONCEPT

The two important premises to understand are:

1. **Hyperventilation reduces CO_2**, diminishing H^+ and raising pH.
2. **Hypoventilation causes retention of CO_2**, which increases H^+ ion levels and decreases pH.

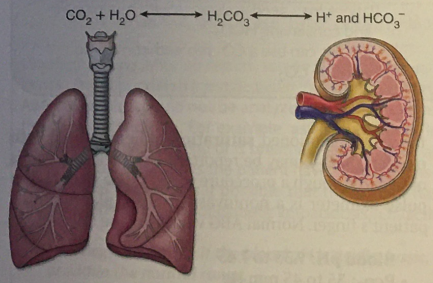

FIGURE 8-2. Acid–base balance via the lungs and kidneys.

Renal Compensation for Acid-Base Disturbances

The kidneys compensate for acid–base disturbances by regulating the excretion or reabsorption of two factors of the carbonic acid–bicarbonate system: H^+ and HCO_3^-. In conditions in which pH is too low, or acidic, the kidneys excrete more acid (H^+) and reabsorb more base (HCO_3^-). These actions lessen the amount of acid in the blood while adding more base (HCO_3^-), thereby raising blood pH and compensating for acidosis. Likewise, in conditions in which pH is too high, the kidneys reabsorb more H^+ and excrete more HCO_3, thereby lowering the pH, compensating for alkalosis. The kidneys' compensation is slow and may take days to reach maximal effectiveness. Therefore medical interventions are commonly necessary to facilitate balancing the bloodstream's pH (see Table 8-2).

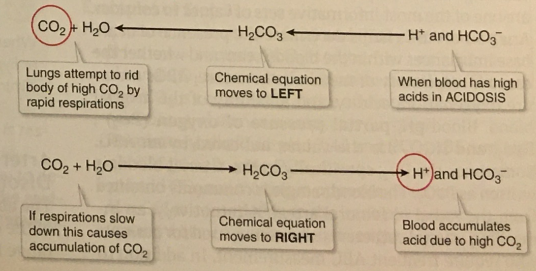

FIGURE 8-3. Respiratory compensation for acid–base disturbances.

TABLE 8-1. Respiratory Compensation for Acid-Base Imbalances and Medical Intervention

The lungs attempt to correct metabolic acid-base disturbances when they occur but are often insufficient to complete compensation. This is when medical intervention is necessary.

Condition	Blood pH	Respiratory Compensation	Medical Intervention
Metabolic acidosis *Excess H+ or lack of base is in the bloodstream due to toxicity or illness*	<7.35	Respirations increase in depth and rate to blow off CO_2	Treatment to resolve the origin of the acid-base disturbance (e.g., insulin in DKA). Sodium bicarbonate administration may be necessary.
Metabolic alkalosis *Excess base or lack of acids in blood due to toxicity or illness*	>7.45	Respirations slow down to increase CO_2 retention	Treatment to resolve the origin of the acid-base disturbance (e.g., in vomiting, administer antiemetic medication). Acetazolamide administration increases HCO_3^- excretion.

TABLE 8-2. Renal Compensation in Acid-Base Disturbances and Medical Intervention

The kidneys attempt to correct acid-base disturbances when they occur but are often too slow to reach complete compensation. This is when medical intervention is necessary.

Condition	Blood pH	Renal Compensation	Necessary Medical Intervention
Respiratory acidosis *Excess CO_2 has accumulated, which is generating H^+*	<7.35	Kidneys attempt to excrete H^+ and conserve HCO_3^-	Patient may need assistance with ridding body of CO_2 • Requires intubation and mechanical ventilation • Can also administer sodium bicarbonate ($NaHCO_3$)
Respiratory alkalosis *Lungs blow off too much CO_2, creating less H^+ in blood*	>7.45	Kidneys attempt to retain H^+ and excrete HCO_3^-	Patient may need assistance with retaining H^+ and conserving HCO_3^- • Patient can use a CO_2 rebreather mask to increase CO_2

CLINICAL CONCEPT

The lungs and kidneys are two organs that to work to maintain acid-base balance. Therefore if ventilation is suboptimal or if renal dysfunction occurs, acid-base imbalance can occur.

Arterial Blood Gases

In studying acid-base disturbances and compensation by the lungs and kidneys, **arterial blood gas (ABG)** levels are one of the most informative sets of values to consider. Analysis of ABGs helps determine the presence of acid-base imbalances within the bloodstream and whether the cause is respiratory or metabolic in nature. ABGs measure oxygenation, acidity, and alkalinity of the arterial blood. Blood pH, **partial pressure of oxygen (Po_2)**, Pco_2, and HCO_3 are the values indicated by an ABG. Sometimes the Po_2, specifically in the arterial blood, is written as PaO_2. The blood sample is commonly obtained from the radial or femoral artery. Alternatively, an indwelling arterial catheter is sometimes used for patients who require frequent ABG measurement. In addition to the values mentioned, **saturation of hemoglobin with oxygen (SaO_2)** may be reported. This measurement is obtained through a procedure called **pulse oximetry**. A pulse oximeter is a noninvasive sensor placed on the patient's finger. Normal ABG values are the following:

- **Blood pH:** 7.35 to 7.45
- **Pco_2:** 35 to 45 mm Hg
- **Po_2:** 90 to 100 mm Hg
- **HCO_3^-:** 22 to 26 mEq/L
- **SaO_2:** 95% to 100%.

CLINICAL CONCEPT

When measuring ABGs, low Po_2 is classified as *hypoxia* or *hypoxemia*, elevated Pco_2 is termed *hypercapnia*, and diminished Pco_2 is termed *hypocapnia*.

Arterial Blood Gases and Acid-Base Disorders

The ability to interpret ABGs affords an understanding of the etiology behind acid-base disorders. The normal range for blood pH is 7.35 to 7.45. If blood pH is lower than 7.35, the bloodstream is acidic and the condition is termed **acidemia** (also called **acidosis**). If the blood pH is greater than 7.45, the bloodstream is basic and the condition is termed **alkalemia** (also called **alkalosis**). In addition to these classifications of acidosis and alkalosis, acid-base disturbances are categorized as respiratory or metabolic, based on the origin of the disturbance.

Respiratory Acid-Base Disturbances

Respiratory acidosis and alkalosis are marked by abnormalities in carbon dioxide levels, leading to the acid-base disturbance. For example, in **respiratory acidosis**, retention of CO_2 causes a reduction in pH. Often, respiratory acidosis arises with compromised gas exchange in the lungs, as may occur with chronic obstructive pulmonary disease (COPD), infection, foreign body obstruction, and asthma. In **respiratory alkalosis**, lower-than-normal CO_2 levels reduce H^+ ion levels and increase pH. Respiratory alkalosis occurs with hyperventilation.

Metabolic Acid-Base Disturbances

Metabolic acid-base disturbances involve an origin other than the pulmonary system and abnormal CO_2 levels. Metabolic acid-base disturbances may manifest for a variety of reasons, including toxicity, diabetes, renal failure, and excessive gastrointestinal (GI) losses. **Metabolic acidosis** may result from increased production of acids other than CO_2, as occurs in diabetic ketoacidosis (DKA), or from the excessive loss of a base, such as bicarbonate through, for example, prolonged diarrhea. **Metabolic alkalosis** develops from excess base, such as retention of sodium bicarbonate or from loss of H^+ ions, as may result from prolonged vomiting.

When interpreting ABGs, a clinician needs to determine if the patient is enduring an acid-base imbalance and, if so, the source of the imbalance, whether respiratory or metabolic.

ABG values are not the whole story, however. They must be interpreted in relation to the patient's vital signs, history, and physical examination. When analyzing ABG results in conjunction with all other indicators, use questions in a step-by-step process (see Box 8-2). Remember to evaluate the whole clinical picture, including Po_2 and SaO_2.

Anion Gap

In addition to ABGs, another piece of information useful in determining the cause of an acid-base imbalance is the anion gap. The term **anion gap (AG)** represents the concentration of the *unmeasured* anions (negatively charged ions) in the bloodstream when comparing the

BOX 8-2. Steps for Interpreting Basic Arterial Blood Gas Disturbances

When analyzing ABG lab results, remember that the patient's clinical condition must be taken into consideration. ABG lab results should not be analyzed alone apart from the patient condition. For example, ask if the patient is having difficulty breathing or is breathing rapidly. Look at the respiratory rate. Does the patient have a renal or gastrointestinal disorder? Is it possible that the patient has drug or chemical toxicity or diabetic ketoacidosis? Or lactic acidosis?

Step 1. Begin by asking if the blood pH is acidic, basic, or within the normal range.
- pH <7.35 indicates acidosis
- pH >7.45 indicates alkalosis
- pH 7.35–7.45
  - Normal if PCO_2 and HCO_3^- are normal
  - Normal but compensations are occurring if PCO_2 and HCO_3^- are abnormal

Step 2. Identify the PCO_2 level. Is it high, low, or normal?
- Normal = 35–45 mm Hg
- High >45 mm Hg
- Low <35 mm Hg

Step 3. Determine if the acid-base disturbance is respiratory or metabolic.

Comparing the pH and PCO_2 levels enables you to determine if the respiratory system is the origin of the acid-base imbalance or if the acid-base imbalance is metabolic in origin. Examine both the pH and the PCO_2 levels and use these rules:

- If ***pH and PCO_2 are moving in opposite directions***, meaning if the PCO_2 is high and the pH is low, then the PCO_2 levels are contributing to the acid-base disturbance and thus it is ***respiratory in nature***. If the PCO_2 is low and the pH is high, the PCO_2 levels are contributing to the acid-base disturbance and thus it is ***respiratory in nature***.
- If ***PCO_2 is normal or is moving in the same direction as pH, meaning if the PCO_2 is normal or high and the pH is high***, the condition is ***metabolic in nature*** (i.e., not due to respiratory involvement). If the PCO_2 is normal or low and pH is low, the condition is ***metabolic in nature*** and is not due to respiratory involvement.

Examples of Step 3:

Respiratory acidosis: pH <7.35 and PCO_2 >45 mm Hg
- pH is low = acidosis, PCO_2 is high
- pH and CO_2 are moving in opposite directions. The high CO_2 is contributing to the acidic pH; thus the acid-base imbalance is respiratory in origin.

Respiratory alkalosis: pH >7.45 and PCO_2 <35 mm Hg
- pH is high = alkalosis, PCO_2 is low
- pH and CO_2 are moving in opposite directions. The low CO_2 is contributing to the basic pH; thus the acid-base imbalance is respiratory in origin.

Continued

BOX 8-2. Steps for Interpreting Basic Arterial Blood Gas Disturbances—cont'd

Metabolic acidosis: pH <7.35 and PCO_2 <35 mm Hg or normal

- pH is low = acidosis, PCO_2 is low
- pH and CO_2 are moving in the same direction. The pH is low (acidic) and CO_2 is low; thus CO_2 is not causing the acidic pH so the disturbance is metabolic in origin.

Metabolic alkalosis: pH >7.45 and PCO_2 >45 mm Hg

- pH is high = alkalosis, PCO_2 is high
- pH and CO_2 are moving in the same direction. The pH is high (basic) and CO_2 is high; thus CO_2 is not causing the alkaline pH, so the disturbance is metabolic in origin.

Step 4. Determine if the condition is a compensated or uncompensated condition.

Uncompensated: pH will be abnormal

- Use the previous steps to determine if the condition is respiratory or metabolic in nature.

Compensated: pH is normal or nearing normal

- Use the previous steps to determine if PCO_2 is contributing to the original acid–base disturbance. If so, a compensated respiratory condition is present. If not, the disorder is metabolic in nature, and PCO_2 is compensating.

COMPENSATED RESPIRATORY ACIDOSIS

pH = initially low, elevating to normal, PCO_2 >45 mm Hg, HCO_3^- (>26 mEq/L)

- pH = initially low, PCO_2 = high
- pH and PCO_2 are initially in opposite direction, so it is respiratory in nature
- High bicarbonate compensating for high CO_2 and acidic pH

COMPENSATED RESPIRATORY ALKALOSIS

pH = initially high, lowering to normal, PCO_2 <35 mm Hg, HCO_3^- (<22 mEq/L)

- pH = initially high, PCO_2 = low
- pH and PCO_2 are initially in opposite direction, so it is respiratory in nature
- Low HCO_3^- compensating for low CO_2 and basic pH

COMPENSATED METABOLIC ACIDOSIS

pH = initially low, elevating to normal, PCO_2 <35 mm Hg, HCO_3^- (<22 mEq/L)

- pH = initially low, PCO_2 = low
- pH and PCO_2 are initially in same direction, so it is metabolic in nature
- Original acidity of blood not due to CO_2, low CO_2 is compensating for low base (i.e., acidic pH)

COMPENSATED METABOLIC ALKALOSIS

pH = initially high or lowering to normal, PCO_2 >45 mm Hg, HCO_3^- (>26mEq/L)

- pH = initially high, PCO_2 = high
- pH and PCO_2 are initially in same direction, so it is metabolic in nature
- Original alkalinity of blood not due to high CO_2, high CO_2 is compensating for alkalinity of the blood

CASE STUDY 1

Patient A is enduring an asthma attack and is brought into the emergency department. The patient's vital signs are: Temp: 98.4°F, Pulse: 110 beats/min, Resp rate: 24 shallow breaths/min, BP: 136/86 mm Hg.

ABGs are:

- Blood pH: 7.30
- P_{CO_2}: 58 mm Hg
- P_{O_2}: 88 mm Hg
- HCO_3^-: 28 mEq/L
- SaO_2: 88%.

Step 1. Does the blood pH show an acidotic, alkalotic, or normal bloodstream?

In this problem, the blood is acidic at pH 7.30, which is less than 7.35; therefore the condition is acidosis.

Step 2. What is the Pco_2?

A P_{CO_2} of 58 mm Hg is elevated beyond the normal range of 35–45 mm Hg.

Step 3. Is the acid–base imbalance caused by a respiratory or metabolic source?

pH (low) and PCO_2 (high) are moving in opposite directions. The high PCO_2 is causing the low pH, indicating it is a respiratory disturbance and therefore respiratory acidosis.

The high P_{CO_2} indicates a ventilation problem, and the P_{O_2} and SaO_2 are also low, further confirming a lung problem.

Step 4. Is this a compensated or uncompensated problem?

The pH is abnormal; therefore the condition is uncompensated. The body is attempting to compensate by reabsorption of HCO_3^- at the kidney. $HCO3^-$ is slightly elevated at 28 mEq/L vs. the normal range of 22–26 mEq/L.

Result

Because of the low blood pH and high P_{CO_2}, this is **uncompensated respiratory acidosis.** The kidney is attempting to compensate through the reabsorption of HCO_3^-.

CASE STUDY 2

Patient B is unconscious and brought into the emergency department because of suspected drug toxicity. Vital signs include: Temp: 97.8°F, Pulse: 90 beats/min, Resp rate: 12 breaths/ min, BP: 100/70 mm Hg.

The patient's ABGs are:

- Blood pH: 7.29
- P_{CO_2}: 32 mm Hg
- P_{O_2}: 95 mm Hg
- HCO_3^-: 13 mEq/L
- SaO_2: 98%.

Using the previous step-by-step process:

Step 1. Does the blood pH show an acidotic, alkalotic, or normal bloodstream?

In this problem, the pH is less than 7.35; therefore the condition is acidosis.

Step 2. What is the Pco_2?

The P_{CO_2} is 32 mm Hg, which is low. This indicates the lungs are eliminating CO_2 excessively.

BOX 8-2. Steps for Interpreting Basic Arterial Blood Gas Disturbances—cont'd

Step 3. Is the acid–base imbalance caused by a respiratory or metabolic source?

As pH (low) and PCO_2 (low) are moving in the same direction, PCO_2 is not contributing to the acid–base imbalance. The acid–base disturbance is metabolic in nature. Also, because the P_{O_2} and SaO_2 are normal, the lungs are functioning well.

Step 4. Is this a compensated or uncompensated problem?

The pH is abnormal, so the condition is uncompensated. The lungs in this case are trying to compensate for the low pH in the bloodstream by exhaling CO_2, but the compensation is inadequate.

Result

Because of the low blood pH and low P_{CO_2}, the condition is uncompensated metabolic acidosis. The lungs attempt to compensate for the acidosis by increasing ventilation to decrease CO_2. In cases of metabolic acidosis, a further step would be to calculate the anion gap to help narrow the list of possible causes.

CASE STUDY 3

Patient C is having an anxiety attack and comes to the emergency department. Vital signs are as follows: Temp: 98.1°F, Pulse: 121 beats/min, Resp rate: 28 breaths/min, and BP: 138/88 mm Hg.

The patient's ABGs are:

- Blood pH: 7.58 mm Hg
- P_{CO_2}: 28 mm Hg
- P_{O_2}: 93 mm Hg
- HCO_3^-: 22 mEq/L
- SaO_2: 92%.

Step 1. Does the blood pH show an acidotic, alkalotic, or normal bloodstream?

The pH is greater than 7.45; therefore the condition is alkalosis.

Step 2. What is the Pco_2?

The P_{CO_2} is 28 mm Hg, which is low. The lungs are hyperventilating, exhaling CO_2.

Step 3. Is the acid–base imbalance caused by a respiratory or metabolic source?

As pH (high) and PCO_2 (low) are moving in opposite directions, a respiratory condition is occurring. The P_{O_2} and SaO_2 are on the low side, additionally indicating a pulmonary problem.

Step 4. Is this a compensated or uncompensated problem?

The pH is abnormal; therefore this is uncompensated. The hyperventilation is causing a reduction in CO_2, elevating pH. The kidneys are attempting to compensate by excreting HCO_3^-.

Result

Because of the high blood pH, low P_{CO_2}, and low HCO_3^-, this is uncompensated respiratory alkalosis.

CASE STUDY 4

Patient D has endured 3 days of nausea and vomiting caused by a virus. Vital signs are as follows: Temp: 101.1°F, Pulse: 98 beats/min, Resp rate: 12 breaths/min, BP: 90/60 mm Hg.

The patient's ABGs are:

- Blood pH: 7.61 mm Hg
- P_{CO_2}: 49 mm Hg
- P_{O_2}: 99 mm Hg
- HCO_3^-: 49 mEq/L
- SaO_2: 99%.

Step 1. Does the blood pH show an acidotic, alkalotic, or normal bloodstream?

A pH of 7.61 indicates alkalosis.

Step 2. What is the Pco_2?

The P_{CO_2} is high.

Step 3. Is the acid–base imbalance caused by a respiratory or metabolic source?

In this case, pH (high) and PCO_2 (high) are moving in the same direction, thus indicating a metabolic acid–base disturbance. The high CO_2 is not causing the alkaline pH. Also, the P_{O_2} and SaO_2 are normal, indicating normal lung function. Therefore the lungs are not causing the alkalosis.

Step 4. Is this a compensated or uncompensated problem?

The pH is abnormal, so this is uncompensated. The body is attempting to retain acids in the bloodstream by slow respirations (which increases CO_2) and neutralize the elevated bicarbonate levels.

Result

Because of a high blood pH and high P_{CO_2}, this is an uncompensated metabolic alkalosis. The lungs are attempting to compensate by breathing slowly but cannot accomplish full compensation.

CASE STUDY 5

Patient E presents to the emergency department in a coma with no history. The ABGs are:

- Blood pH: 7.37
- P_{CO_2}: 47 mm Hg
- P_{O_2}: 85 mm Hg
- HCO_3^-: 28 mEq/L
- SaO_2: 87%.

Step 1. Does the blood pH show an acidotic, alkalotic, or normal bloodstream?

In this problem, the blood pH is between 7.35 and 7.45, which is within the normal range. However, both PCO_2 and HCO_3^- values are abnormal, indicating some type of compensation.

Step 2. What is the Pco_2?

The P_{CO_2} is 47 mm Hg. This is a high P_{CO_2}, which means the lungs are hypoventilating and retaining CO_2.

Continued

BOX 8-2. Steps for Interpreting Basic Arterial Blood Gas Disturbances—cont'd

Step 3. Is the acid-base imbalance caused by a respiratory or metabolic source?

pH is normal, but PCO_2 is high, as is HCO_3^-, so further analysis is required. Compensation for an acid-base disturbance is likely occurring. The low Po_2 and SaO_2, coupled with the high PCO_2, indicate a pulmonary problem is likely. The elevated bicarbonate levels are indicative of a compensation to address the higher-than-normal PCO_2 due to respiratory problems.

Step 4. Is this a compensated or uncompensated problem?

The blood pH is normal, whereas PCO_2 and HCO_3^- are abnormal, indicating a compensated condition. The kidneys are trying to reabsorb enough HCO_3^- to neutralize the H^+ caused by high Pco_2.

Result

Because of the normal pH, high Pco_2, and high HCO_3^-, this is compensated respiratory acidosis.

measured cations (positively charged ions), $[Na^+]$ and $[K^+]$, and *measured* anions, $[Cl^-]$ and $[HCO_3^-]$, of the blood. The AG is calculated by summing the measured cations, $[Na^+]$ and $[K^+]$, and subtracting the measured anions, $[Cl^-]$ and $[HCO_3^-]$. To maintain electrochemical balance, the body's total number of cations should equal the total number of anions. Normally, though, a small number of unmeasured free anions exist in the bloodstream. These unmeasured anions comprise the normal AG between measured cations and anions (see Fig. 8-4). The major unmeasured anions include negatively charged plasma proteins (albumin), sulfates, and phosphates. The calculation of anion gap only applies to cases of metabolic acidosis.

Anion Gap Range

The normal range for the AG is 8 to 16 mEq/L, although laboratories may slightly differ in their reference range. The AG can be high, normal, or low. A normal AG has a small number of unmeasured anions in the bloodstream (see Fig. 8-4). A low AG is uncommon but can be caused by decreased unmeasured anions (usually low protein, especially hypoalbuminemia), increased unmeasured cations, or laboratory error. A high AG has a value between 16 and 20 mEq/L and may occur in specific instances of metabolic acidosis, such as DKA.

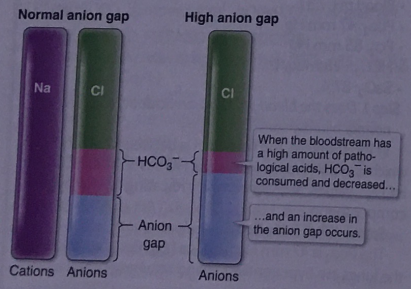

FIGURE 8-4. The normal anion gap versus high anion gap within the bloodstream. The bloodstream normally has a certain level of unbound anions, called the normal anion gap. When the bloodstream has an increased amount of acids, as in diabetic ketoacidosis, the anion gap is increased.

CLINICAL CONCEPT

The AG equation given by $[Na^+ + K^+] - [Cl^- + HCO_3^-]$ works on the assumption that a patient has a normal albumin level. Low serum albumin reduces the accuracy of the AG calculation.

Increased Anion Gap in Metabolic Acidosis

In certain instances of metabolic acidosis, the AG increases. The increase occurs when large amounts of unmeasured acids, such as ketones in DKA, are added to the blood. Ketones dissociate into H^+ ions and keto-anions. Bicarbonate, a measured anion, buffers the H^+ ions. As this buffering occurs, the amount of measured anions (bicarbonate) in the blood decreases, whereas the unmeasured anions (keto-anions) increases. The AG, indicative of unmeasured anion, thus increases. The AG becomes important to clinicians in differentiating underlying causes of metabolic acidosis, as some causes of metabolic acidosis, such as GI loss of bicarbonate, do not present with an elevated AG.

CLINICAL CONCEPT

Calculating the AG is clinically useful, as it helps differentiate types of metabolic acidosis disease states.

Metabolic acidosis with an elevated AG is found in the following conditions:

- Lactic acidosis
- Ketoacidosis
- Renal failure
- Overdose of acetylsalicylic acid (ASA), also known as aspirin
- Ingestion of methanol or ethylene glycol

Metabolic acidosis with a normal AG is found in the following conditions:

- GI loss of HCO_3^-
- Increased renal HCO_3^- loss
- Hypoaldosteronism
- Ingestion of ammonium chloride
- Hyperalimentation

CLINICAL CONCEPT

Intravenous (IV) fluid replacement with K^+ may be needed in some states of acidosis due to the shift of K^+ from the intracellular to the extracellular space and potential K^+ ion loss in the urine.

Acid-Base Disturbances and Electrolytes

Changes in pH can influence the movement of ions between the intracellular fluid (ICF) and extracellular fluid (ECF), and vice versa, and changes in electrolyte levels can influence the pH state. Ion movement is driven by the electrochemical gradient. Changes in this gradient, due to changes in one or more ions, can profoundly affect the movement of other ions. Two of the ions most affected by alterations in pH levels are K^+ and Ca^{++}. Many of the systemic signs and symptoms of acid–base disturbances are not simply due to pH changes, but rather the impact of H^+ ion concentration on electrolyte movement.

Relationship Between H+ and K+

Both K^+ and H^+ ions are positively charged, and both ions move freely between the ICF and ECF. As such, these ions are often exchanged for one another, and changes in H^+ concentration can affect the movement of K^+ ions and vice versa. In the case of acid–base disturbances, shifts in potassium are more pronounced in acidosis than alkalosis and are also greater in metabolic acidosis than respiratory acidosis

Acidosis and Hyperkalemia. In the intracellular and extracellular electrolyte environment, excess H^+ in the bloodstream causes ion movements. H^+ ions move into the cells, and K^+ ions move out of the cells into the bloodstream. The bloodstream thus becomes high in K^+, causing *hyperkalemia*. However, the total body level of K^+ is unchanged. The bloodstream appears as though it is hyperkalemic. As soon as the state of acidosis resolves, the K^+ levels re-equilibrate between the intracellular and extracellular environment.

Also, in acidosis, the kidney, which usually excretes K^+, is inundated with H^+ and selectively excretes H^+ in lieu of K^+. This causes K^+ to accumulate in the bloodstream because the kidney is not excreting it. Therefore although the blood may seem to have high potassium levels, the body content of K^+ is not changed. However, high levels of K^+ retained in the blood (hyperkalemia) are a serious complication of acidosis because this has effects on cardiac tissue. Hyperkalemia can cause dysrhythmias, or in severe cases, cardiac arrest. As soon as the acidosis condition is resolved, K^+ is once again excreted by the kidney and blood levels equilibrate back to normal.

Alkalosis and Hypokalemia. As acidosis may lead to hyperkalemia, alkalosis is linked to hypokalemia, as K^+ ions shift into the cells from the plasma. This movement of potassium from the ECF to the ICF lowers serum potassium, resulting in *hypokalemia*. Also, in alkalosis, transport mechanisms in the kidneys result in additional K^+ loss in the urine.

The Effect of Potassium Levels on pH. Because of the interrelatedness of H^+ and K^+ ion movements, changes in K^+ ion levels can lead to acid–base disturbances. Hypokalemia may cause alkalosis, as H^+ shifts into cells to compensate for lower-than-normal K^+ levels, whereas hyperkalemia may cause acidosis as H^+ ions enter the bloodstream.

The Effect of pH on Calcium Levels. Calcium ion levels are also affected by pH disturbances. Calcium is transported in the blood in a free, ionized form or attached to the plasma protein albumin. The binding and transport of calcium by albumin is a reversible process influenced by H^+ ion concentration. In acidosis, H^+ ions compete with Ca^{++} ions for binding sites on albumin. Thus in acidosis, free, ionized forms of calcium increase, leading to hypercalcemia. In alkalosis, with fewer H^+ ions to compete for binding sites on albumin, free, ionized calcium levels decrease as more calcium binds to albumin. Alkalosis is thus associated with hypocalcemia.

pH, Electrolyte Levels, and Cellular Functioning. Electrolyte disturbances due to changes in pH can have a profound impact on several cellular processes, particularly in excitable cells such as neurons and muscle cells, including the cells of the heart. Potassium, in particular, affects the resting membrane potential of myocardial cells.

In acidosis, which may result in hyperkalemia, the increased K^+ ion levels cause the resting membrane potential of cells to become more positive, making them hyperexcitable. In hypokalemia associated with alkalosis, reduced K^+ ion levels cause the resting membrane potential to become less positive and the cells less excitable. Changes in the resting membrane potential affect the functioning of the heart, neurons, and muscles. The heart's functionality can be compromised to the point that severe arrhythmias, and even cardiac arrest, develop.

pH-induced changes in albumin binding affinity for calcium and the subsequent changes in free, ionized calcium also negatively affect cells. Hypercalcemia,

which can develop in acidosis, increases the threshold for depolarization, making cells less excitable. In hypocalcemia due to alkalosis, lower-than-normal Ca^{++} levels increase the excitability of cells. The link between pH, K^+, and Ca^+ levels and cell excitability provides yet another example of the critical importance of maintaining these factors within a narrow range.

Pathophysiologic Concepts Regarding Acid–Base Imbalances

There are four states of acid–base imbalance in the bloodstream:

1. Respiratory acidosis
2. Respiratory alkalosis
3. Metabolic acidosis
4. Metabolic alkalosis

Each has a different etiology, clinical presentation, compensatory mechanism, and treatment.

Respiratory Acidosis

Respiratory acidosis occurs when the body accumulates too much CO_2 and cannot exhale it sufficiently. The development of respiratory acidosis indicates inadequate exchange of carbon dioxide within the lungs, leading to an elevation in CO_2 known as *hypercapnia*. Hypercapnia pushes the carbonic acid–bicarbonate buffer equation to the right, producing more H^+ and HCO_3^-:

$$\mathbf{CO_2 + H_2O \Rightarrow H_2CO_3^- \Rightarrow H^+ \text{ and } HCO_3^-}$$

As CO_2 converts into H^+ ions, pH levels fall. The shift in pH due to elevated CO_2 can occur rapidly or over an extended period. The hallmark of respiratory acidosis is a pH below 7.35 and a P_{CO_2} above 45 mm Hg.

Epidemiology

The incidence of respiratory acidosis is different for its varied etiologies.

Etiology

Box 8-3 lists common causes of respiratory acidosis.

Pathophysiology

Respiratory acidosis develops when the lungs are unable to remove sufficient CO_2, causing it to accumulate in the bloodstream. When CO_2 is high, the $\mathbf{CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ \text{ and } HCO_3^-}$ shifts to the right, creating increased acid (H^+). Higher H^+ ion levels reduce the pH. In respiratory acidosis, insufficient CO_2 elimination leads to CO_2 levels rising above 45 mm Hg.

Chemoreceptors in Chronic Respiratory Acidosis

In chronic respiratory acidosis, as may occur with COPD, the respiratory center in the medulla becomes insensitive to high CO_2 levels. Normally when CO_2 rises in the bloodstream, the chemoreceptors in the medulla stimulate increased ventilation to rid the body of CO_2. However, in long-term COPD, high CO_2 levels do not stimulate the medulla and respirations as expected. Patients with long-term COPD live with hypercapnia and precariously balanced blood pH values because of this adaptation.

BOX 8-3. Causes of Respiratory Acidosis

PULMONARY
- Chronic obstructive lung disease, such as asthma, emphysema, and bronchiectasis
- Pulmonary edema
- Pneumonia
- Airway obstruction, such as laryngospasm, bronchospasm, and aspiration
- Underventilation by mechanical ventilation
- Hypoventilation secondary to obesity, postoperative pain, abdominal distention, or use of abdominal binders
- Excessive fatigue or weakness of rib cage muscles
- Cystic fibrosis

NONPULMONARY
- Overdosage of anesthetic, sedatives, and narcotics
- Neuromuscular disorders, such as Guillain–Barré, myasthenia gravis, and advanced multiple sclerosis
- Severe spinal deformities
- Central nervous system depression related to cerebral infarct, meningitis, or trauma
- Cardiopulmonary arrest

CLINICAL CONCEPT

Patients with long-term COPD retain CO_2, which increases susceptibility to respiratory acidosis.

Clinical Presentation

Patients in respiratory acidosis complain of anxiety, restlessness, headache, lethargy, fatigue, shortness of breath, rapid breathing, and cough. Advanced respiratory acidosis leads to confusion, somnolence, and possible coma. The effects of excess CO_2 are commonly referred to as "carbon dioxide narcosis."

Physical Examination Findings

The thoracic examination of patients with respiratory acidosis usually reveals obstructive lung disease with compromised air exchange. The signs include diffuse wheezing, hyperinflation of the lungs, barrel-shaped chest in emphysema, decreased breath sounds, hyperresonance on percussion, and prolonged expiration. Rhonchi may also be heard. Cyanosis and clubbing may indicate the presence of chronic hypoxia. Confusion, disorientation, somnolence, or stupor can be present with high levels of P_{CO_2}.

ALERT! Respiratory acidosis can occur with severe asthma despite the patient having tachypnea. The breathing rate is increased, but the breaths are very shallow and do not eliminate CO_2. CO_2 accumulates, causing increased production of acids in the bloodstream.

Compensatory Mechanisms and Values

As discussed, the kidneys are the primary means of compensation when an acid–base imbalance is respiratory in nature. In respiratory acidosis, respiratory compensation is incapable of totally counteracting the pH disturbance. In acute respiratory acidosis, the kidneys attempt to compensate by reabsorbing HCO_3^- and excreting H^+. ABG values for *uncompensated respiratory acidosis* reveal a pH less than 7.35 and a CO_2 level greater than 45 mm Hg. If the kidneys can successfully compensate for the pH abnormality by reabsorbing additional bicarbonate (HCO_3^-), then pH value normalizes. ABG values for *compensated respiratory acidosis* reveal a pH that is normal, CO_2 level greater than 45 mm Hg.

Treatment

Treatment of respiratory acidosis centers on improving gas exchange. Oxygenation of blood may be maintained by administering oxygen. Bronchodilation is attempted via oral and parenteral adrenergic agents. If the compromised lung function is due to a pulmonary infection, treatment of the infection is required. If gas exchange does not improve, endotracheal intubation with mechanical ventilation is necessary.

Respiratory Alkalosis

Respiratory alkalosis occurs when CO_2 levels in the blood are low, often due to hyperventilation. Causes of hyperventilation include stress and anxiety, drug toxicity, and head injuries. The reduction in CO_2 resulting from hyperventilation lowers H^+ ion levels and elevates pH, shifting the carbonic acid–bicarbonate buffer equation toward the left:

$$\mathbf{CO_2 + H_2O \Leftarrow H_2CO_3^- \Leftarrow H^+ \text{ and } HCO_3^-}.$$

Etiology

Respiratory alkalosis is a common acid–base abnormality observed in critically ill patients. It is also common in patients with hyperventilation due to anxiety. Box 8-4 lists common causes of respiratory alkalosis.

Pathophysiology

Hyperventilation, with a subsequent reduction in CO_2 and H^+ ion levels, causes respiratory alkalosis. Many of the signs and symptoms present in persons with respiratory alkalosis relate to the ion disturbances that may develop with hypocapnia, such as hypocalcemia and hypokalemia.

BOX 8-4. Causes of Respiratory Alkalosis

PULMONARY
- Pneumonia
- Pulmonary edema
- Pulmonary embolus
- Asthma
- Lung disease with shortness of breath (asthma, pneumonia, acute respiratory distress syndrome [ARDS], fibrosis, pulmonary embolism)
- Hypoxia with hyperventilation
- Overventilation by mechanical ventilation

NONPULMONARY
- Anxiety
- Pain
- Liver disease
- Fever/infection/sepsis
- Central nervous system disorders (tumors, cerebrovascular accidents)
- Salicylate intoxication
- Alcohol intoxication

Clinical Presentation

In respiratory alkalosis, tingling of extremities (paresthesia), muscle cramps, tetany, dizziness and/or syncope, confusion, anxiety, seizures, and coma may occur. Cardiac symptoms include palpitations, dysrhythmias, and hypotension. Many patients with hyperventilation due to anxiety feel as though they are enduring a cardiac problem.

Physical Assessment Findings

Many patients enduring hyperventilation appear anxious and are frequently tachycardic. With acute hyperventilation, obvious chest wall movements and use of intercostal muscles to breathe are visible. Hypocalcemia may elicit muscle spasms, as well as Chvostek's and Trousseau's signs. Underlying pulmonary disease may be present with signs such as crackles and rhonchi. If the patient is hypoxic, cyanosis may be apparent. The patient may have focal neurological signs or a depressed level of consciousness. Cardiac rhythm disturbances often occur.

Compensatory Mechanisms and Values

Because the lungs cannot adequately compensate for the acid–base disturbance, as indicated by the low CO_2, the kidneys carry out the majority of compensation by reabsorbing H^+ into the bloodstream and excreting HCO_3^-. The compensation can take hours to days to accomplish, so medical intervention is needed. In *uncompensated respiratory alkalosis*, blood pH is above

7.45 with a CO_2 level lower than 35 mm Hg. If the kidneys compensate successfully through absorption of H^+ and excretion of HCO_3^- ions, ABG values reveal a pH that is normalizing or decreasing toward normal and CO_2 less than 35 mm Hg.

Treatment

Treatment of respiratory alkalosis lies in identifying the underlying trigger that has produced hyperventilation. Pain management or sedation may be required to slow and control the respiratory rate. One common treatment for respiratory alkalosis involves patients breathing into a paper bag. This allows for rebreathing of exhaled CO_2 to bring CO_2 levels back up to a normal range. A CO_2 rebreather, available in the clinical setting, is a type of breathing apparatus that recycles the exhaled CO_2 and adds O_2 to compensate for the oxygen consumed by the user.

CLINICAL CONCEPT

Hyperventilation is the most common cause of respiratory alkalosis. Simply rebreathing into a paper bag can replace lost CO_2.

Metabolic Acidosis

Metabolic acidosis is due to an excess of acid not related to CO_2. The primary findings are a pH below 7.35 but with normal or lower-than-normal CO_2 levels, indicating that CO_2 is not driving the reduction in pH. One of the primary causes of metabolic acidosis is a metabolic condition that leads to acidic end products, such as ketones or lactic acid. Alternatively, excessive bicarbonate loss due to kidney or GI tract disorders can reduce pH levels.

Metabolic acidosis is mainly divided into processes associated with a normal (8 to 16 mEq/L) or an elevated AG (greater than 16 mEq/L) (see the section on the AG). Addition of acids, such as ketones, increases the anion gap, whereas loss of a base, such as bicarbonate, does not alter it.

Epidemiology

Morbidity and mortality in metabolic acidosis are dependent on the underlying condition. If severe forms of metabolic acidosis go untreated, death may result.

Etiology

Box 8-5 contains a list of common causes of metabolic acidosis.

Pathophysiology

Metabolic acidosis is a condition characterized by an arterial pH lower than 7.35 in the absence of an elevated PCO_2. Three primary mechanisms may lead to the condition of metabolic acidosis:

1. Increased level of acids in the bloodstream
2. Decreased excretion of acids
3. Loss of base from the bloodstream

Increased production of acids that occurs under certain metabolic conditions may lead to metabolic acidosis. Diabetic ketoacidosis (DKA) is one of the most common causes of metabolic acidosis. In DKA an accumulation of keto-acids leads to widespread metabolic acidosis. In another example, when widespread ischemia is present, cells with the capacity to rely on anaerobic metabolism produce lactic acid. The accumulation of lactic acid leads to the development of lactic acidosis, which is a type of metabolic acidosis. Alternatively, toxic ingestion or medication overdoses with acidic substances can cause metabolic acidosis. An example is aspirin toxicity, which causes ASA accumulation in the bloodstream. Metabolic acidosis may also develop when there is a reduction in the ability of the kidneys to excrete H^+ or to reabsorb HCO_3^-. For example, prolonged diarrhea, in which intestinal contents, including bicarbonate, are lost, can also result in metabolic acidosis.

As previously discussed, acid–base imbalances alter electrolyte levels. In metabolic acidosis, the kidneys excrete H^+ in lieu of K^+. Thus K^+ accumulates in the bloodstream. Hyperkalemia develops and potentially disrupts the functioning of the heart. Arrhythmias, peaked T waves, QRS widening, and ventricular fibrillation may manifest. Tachycardia is the most common cardiovascular effect seen with mild metabolic acidosis, as hypotension from decreased contractility of the heart may develop. Serum calcium levels elevate in metabolic acidosis due to reduced binding of Ca^{++} to albumin. Hypercalcemia causes muscle weakness, confusion, and lethargy.

Clinical Presentation

The signs and symptoms of metabolic acidosis are widespread and are often due to abnormal serum potassium and calcium levels. The patient complains of respiratory distress as the lungs attempt to compensate for the acidosis. Neurological symptoms include headache, drowsiness, confusion, seizures, neuromuscular fatigue, twitching, and coma. GI symptoms such as nausea, vomiting, and anorexia are common. Cardiovascular symptoms present as hypotension, dysrhythmias, and decreased cardiac contractility.

BOX 8-5. Causes of Metabolic Acidosis

INCREASED NONCARBONIC ACIDS
- Diabetic ketoacidosis
- Lactic acidosis
- Alcoholic ketoacidosis
- Uremic acidosis
- Ingestion of toxic substances (antifreeze, aspirin)
- Intestinal, biliary, or pancreatic fistulas
- Hypocalcemia, hypokalemia, or hypomagnesemia

BICARBONATE LOSS
- Prolonged diarrhea
- Renal tubular acidosis
- Interstitial renal disease
- Ureterosigmoid loop
- Ingestion of acetazolamide or ammonium chloride

Physical Assessment Findings

The patient is tachypneic and in respiratory distress. Cardiovascular signs may include weak pulses, tachycardia, hypotension, and arrhythmia. The patient may have GI pain and vomiting. Excessive vomiting can lead to dehydration. Signs of dehydration may include tachycardia, dry mucous membranes, and delayed capillary refill. Patients with DKA may present with fruity odor to their breath due to ketone production. Metabolic acidosis can also cause confusion, lethargy, and possibly coma or seizures.

Compensatory Mechanisms and Values

Unlike respiratory acidosis, in which the kidneys attempt to excrete excess acids, in metabolic acidosis, the lungs, along with the kidneys, attempt to compensate. In metabolic acidosis, the high H^+ ion levels stimulate chemoreceptors, which in turn stimulate the respiratory center to increase the respiratory rate. Elimination of CO_2 pulls H^+ ions out of the bloodstream, increasing the blood pH. This is evident in the carbonic-bicarbonate equation as it moves to the left:

$$CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow H + \text{and } HCO_3^-$$

Deep, rapid breathing due to metabolic acidosis is referred to as Kussmaul's breathing. Kussmaul's breathing is particularly common in DKA. The lungs ventilate rapidly to attempt to rid the body of CO_2 and, consequently, decrease H^+ levels. In addition, to compensate for metabolic acidosis, the kidneys, if healthy, reabsorb HCO_3^- and excrete H^+. Compensatory mechanisms require hours to days to remedy the condition, often necessitating medical intervention. The hallmark of *uncompensated metabolic acidosis* is pH less than 7.35 with normal to low CO_2 levels, indicating CO_2 is not the reason for the acidic pH. HCO_3^- values will also be lower than normal (<22 mEq/L).

A higher-than-normal AG is due to excess acids, as may occur in DKA or ingestion of acidic compounds. A normal AG indicates the reduced pH is due to loss of basic compounds, such as bicarbonate.

In *compensated metabolic acidosis,* pH is normal or rising toward normal. PCO_2 is lower than normal (<35 mm Hg) as CO_2 is exhaled to compensate for the acidic pH. The kidneys reabsorb more HCO_3^- and excrete H^+ ions to compensate.

Treatment

All types of metabolic acidosis require treating the underlying cause. For example, if the cause is DKA, insulin is needed. If the metabolic acidosis is caused by kidney failure, in which the kidneys cannot effectively remove H^+ ions from the blood, hemodialysis is required. Correcting the underlying disorders and restoring electrolyte and fluid balance are critical. IV sodium bicarbonate may be utilized in severe cases of metabolic acidosis when pH is lower than 7.20. Caution is needed, as excessive use of sodium bicarbonate may produce a rebound metabolic alkalosis.

Metabolic Alkalosis

Metabolic alkalosis is a blood pH greater than 7.45 with a normal or higher-than-normal CO_2 level. It is caused by excessive loss of acids unrelated to CO_2 or an increase in bicarbonate levels, such as with retention of sodium bicarbonate. Loss of acids can take many forms, including intracellular shift of H^+ ions from the plasma, as occurs with hypokalemia, or loss of H^+ through the GI tract, as occurs with severe vomiting. The use of certain diuretics can result in the loss of H^+ ions by the kidneys, resulting in alkalosis. Administration of excess sodium bicarbonate and volume depletion are the primary reasons for bicarbonate excess, which also results in metabolic acidosis.

Epidemiology

Metabolic alkalosis is an acid–base disturbance that commonly occurs in hospitalized patients. The more elevated the pH beyond the normal range, the higher the morality rate.

Etiology

Box 8-6 lists common causes of metabolic alkalosis.

Pathophysiology

The most common cause of metabolic alkalosis is depletion of H^+ ions. Loss of H^+ ions occurs primarily through the kidneys and GI tract. Gastric secretions contain large amounts of hydrochloric acid (HCl). Any process that depletes gastric fluid, such as severe vomiting or GI tract suctioning, can result in metabolic alkalosis. Development of metabolic alkalosis due to gastric loss of H^+ ions is a concern for individuals suffering from bulimia, who frequently induce vomiting.

BOX 8-6. Causes of Metabolic Alkalosis

- Bicarbonate ingestion
- Excess IV sodium bicarbonate
- Potassium-wasting diuretics
- Loss of gastric fluids from vomiting, gastric suctioning, diarrhea, or binge–purge syndrome
- Cushing's syndrome
- Primary hyperaldosteronism
- Secondary hyperaldosteronism

potassium and calcium levels. The patient complains of respiratory distress as the lungs attempt to compensate for the acidosis. Neurological symptoms include headache, drowsiness, confusion, seizures, neuromuscular fatigue, twitching, and coma. GI symptoms such as nausea, vomiting, and anorexia are common. Cardiovascular symptoms present as hypotension, dysrhythmias, and decreased cardiac contractility.

Physical Assessment Findings

The patient is tachypneic and in respiratory distress. Cardiovascular signs may include weak pulses, tachycardia, hypotension, and arrhythmia. The patient may have GI pain and vomiting. Excessive vomiting can lead to dehydration. Signs of dehydration may include tachycardia, dry mucous membranes, and delayed capillary refill. Patients with DKA may present with fruity odor to their breath due to ketone production. Metabolic acidosis can also cause confusion, lethargy, and possibly coma or seizures.

Compensatory Mechanisms and Values

Unlike respiratory acidosis, in which the kidneys attempt to excrete excess acids, in metabolic acidosis, the lungs, along with the kidneys, attempt to compensate. In metabolic acidosis, the high H^+ ion levels stimulate chemoreceptors, which in turn stimulate the respiratory center to increase the respiratory rate. Elimination of CO_2 pulls H^+ ions out of the bloodstream, increasing the blood pH. This is evident in the carbonic-bicarbonate equation as it moves to the left:

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Deep, rapid breathing due to metabolic acidosis is referred to as Kussmaul's breathing. Kussmaul's breathing is particularly common in DKA. The lungs ventilate rapidly to attempt to rid the body of CO_2 and, consequently, decrease H^+ levels. In addition, to compensate for metabolic acidosis, the kidneys, if healthy, reabsorb HCO_3^- and excrete H^+. Compensatory mechanism is needed. If the metabolic acidosis is caused by kidney failure, in which the kidneys cannot effectively remove H^+ ions from the blood, hemodialysis is required. Correcting the underlying disorders and restoring electrolyte and fluid balance are critical. IV sodium bicarbonate may be utilized in severe cases of metabolic acidosis when pH is lower than 7.20. Caution is needed, as excessive use of sodium bicarbonate may produce a rebound metabolic alkalosis.

Metabolic Alkalosis

Metabolic alkalosis is a blood pH greater than 7.45 with a normal or higher-than-normal CO_2 level. It is caused by excessive loss of acids unrelated to CO_2 or an increase in bicarbonate levels, such as with retention of sodium bicarbonate. Loss of acids can take many forms, including intracellular shift of H^+ ions from the plasma, as occurs with hypokalemia, or loss of H^+ through the GI tract, as occurs with severe vomiting. The use of certain diuretics can result in the loss of H^+ ions by the kidneys, resulting in alkalosis. Administration of excess sodium bicarbonate and volume depletion are the primary reasons for bicarbonate excess, which also results in metabolic acidosis.

Epidemiology

Metabolic alkalosis is an acid–base disturbance that commonly occurs in hospitalized patients. The more elevated the pH beyond the normal range, the higher the morality rate.

Etiology

Box 8-6 lists common causes of metabolic alkalosis.

Pathophysiology

The most common cause of metabolic alkalosis is depletion of H^+ ions. Loss of H^+ ions occurs primarily

The kidneys may contribute to metabolic alkalosis if they are unable to retain adequate H^+ or excrete HCO_3^- at the necessary level.

As observed with the other acid–base disturbances, electrolyte imbalances may play a role in pH abnormalities and vice versa. Metabolic alkalosis may develop in response to hypokalemia. Hypokalemia may develop with the use of certain diuretics or in Cushing's syndrome, in which elevated amounts of aldosterone increase K^+ ion excretion by the kidneys. With the loss of potassium ions, H^+ ions shift into the intracellular space, depleting H^+ ion levels in the bloodstream. Metabolic alkalosis also commonly occurs in cardiac resuscitation. Administration of large amounts of sodium bicarbonate are needed to neutralize the lactic acidosis that forms in cardiac arrest. Excessive amounts of sodium bicarbonate in the bloodstream can exceed the capacity of the kidneys to excrete the bicarbonate. Finally, metabolic alkalosis can lead to hypokalemia and hypocalcemia. These electrolyte disturbances account for some of the signs and symptoms associated with metabolic alkalosis.

Clinical Presentation

The symptoms of metabolic alkalosis are widespread, affecting the neurological, cardiovascular, GI, and musculoskeletal systems primarily through alteration in ion levels. Patients may present with confusion, dizziness, agitation, weakness, vomiting, diarrhea, and possibly seizures.

Physical Assessment Findings

The physical signs of metabolic alkalosis are nonspecific and multisystemic. Hypokalemia due to metabolic alkalosis can cause muscular weakness, myalgia, muscle spasms, and cardiac arrhythmias. Hypocalcemia may also develop and present as tetany, Chvostek's sign, and Trousseau's sign. Fluid volume status can also change. Evaluation of this status includes assessment of orthostatic changes in blood pressure and heart rate, mucous membranes, presence or absence of edema, skin turgor, weight change, and urine output. In patients with metabolic alkalosis who are suffering from bulimia, erosion of the teeth enamel and dental caries may be present.

Compensatory Mechanisms and Values

Similar to metabolic acidosis, both the lungs and kidneys attempt to compensate in states of metabolic alkalosis. Chemoreceptors detect the higher-than-normal pH of the blood and induce a reduction in ventilation. By slowing the breathing rate, the lungs retain CO_2, thereby raising H^+ content of the blood and lowering pH. The kidneys compensate by reabsorbing H^+ into the bloodstream and excreting HCO_3^-. This can take days to reach the point of adequate compensation; therefore medical intervention is necessary. In *uncompensated metabolic alkalosis* pH is greater than 7.45 with normal-to-high CO_2 levels, indicating CO_2 is not causing the elevation in pH. Elevated HCO_3^- values are present (>26 mEq/L). pH will be normal or reducing toward normal in *compensated metabolic alkalosis*, with an elevated PCO_2 (>45 mm Hg). CO_2 retention by slow ventilation of the lungs helps reduce pH levels.

Treatment

Treatment of metabolic alkalosis includes electrolyte and fluid replacement. Potassium-sparing diuretics may be administered if the cause of alkalosis is diuretic use. Acetazolamide, which reduces HCO_3^- reabsorption in the kidneys, may also be used to treat conditions of moderate to severe metabolic or respiratory alkalosis.

Mixed Disorders

Clinicians must also be aware that more than one type of acid–base disturbance can be present at any given time. These mixed acid–base disorders manifest when more than one underlying condition disrupts pH. Analysis of ABG values, AG, and patient presentation are critical in determining the course of the acid–base disturbance and the underlying causes of the coexisting disturbances.

Chapter Summary

- An acid is defined as any compound that donates hydrogen ions (H^+) in solution.
- A base is a compound that accepts H^+ ions in solution.
- When H^+ ions predominate in a solution, the solution is acidic. When basic ions predominate in a solution, the solution is alkaline.
- Buffers resist changes in pH by donating or accepting H^+ ions as needed.
- Three main buffer systems that exist in the body are protein, phosphate, and carbonic acid–bicarbonate system.
- The lungs and the kidneys regulate the body's acid-base balance through use of the carbonic acid–bicarbonate buffer system.
- Blood pH, partial pressure of oxygen (Po_2), partial pressure of carbon dioxide (Pco_2), and bicarbonate ion concentration (HCO_3^-) are the values indicated by an ABG.

- The normal pH of blood is 7.35 to 7.45. A pH level lower than 7.35 is acidemia (also called acidosis); a level greater than 7.45 is alkalemia (also called alkalosis).
- A chemical buffering system used by the body is the carbonic acid–bicarbonate system: $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+$ and HCO_3^-. Both the lungs and kidneys utilize this system to compensate for acid–base disturbances.
- During hypoventilation the lungs retain CO_2; during hyperventilation, the lungs blow off CO_2.
- The greater the amount of CO_2 in the body, the greater the formation of H^+ ions.
- Four possible acid–base disturbances occur in the body: respiratory acidosis, respiratory alkalosis, metabolic acidosis, and metabolic alkalosis.
- Hypoventilation, which causes Pco_2 greater than 45 mm Hg, results in respiratory acidosis; hyperventilation, which causes Pco_2 less than 35 mm Hg, results in respiratory alkalosis.
- An excess of acid or a loss of HCO_3^- in the blood causes metabolic acidosis. In uncompensated metabolic acidosis, HCO_3^- will be lower than 22 mEq/L and the pH will be lower than 7.35.
- Metabolic alkalosis is caused by excessive loss of acids, shift of H^+ ions into the intracellular space, or increase in bicarbonate in the bloodstream. In uncompensated forms, the blood pH will be greater than 7.45 and the bicarbonate concentration greater than 26 mEq/L.
- Acid–base imbalances affect serum electrolyte levels. Acidosis is generally associated with hyperkalemia, and alkalosis with hypokalemia. Due to altered albumin binding affinity for Ca^{++} with pH changes, acidosis may cause hypercalcemia and alkalosis may cause hypocalcemia.

Making the Connections

Disorder and Pathophysiology

Signs and Symptoms	Physical Assessment Findings	Diagnostic Testing	Treatment
Respiratory Acidosis | Lungs are not ventilating; retaining too much CO_2, creating too much H^+. Commonly due to COPD, severe asthma, or any cause of reduced ventilation.			
Dyspnea. Respiratory distress. Patient may be lethargic, stuporous, or comatose.	Diminished respiratory rate. Cyanosis. Clubbing if chronic hypoxia.	Uncompensated: blood pH less than 7.35. Pco_2 greater than 45 mm Hg. Po_2: low. Urine: acidic.	Treat the lung disorder for better ventilation. Bronchodilation. Antibiotics if pneumonia. Intubation and mechanical ventilation if needed.
Respiratory Alkalosis | Lungs are hyperventilating; losing too much CO_2 creates too little H^+ in the blood. Commonly due to hyperventilation secondary to anxiety or shallow respirations in asthma.			
Hyperventilation. Anxiety. Palpitations. Paresthesia. Patient may have pain.	High respiratory rate. Tachycardia.	Uncompensated: blood pH greater than 7.45. Pco_2 less than 35 mm Hg. Urine: basic.	Slow the breathing rate; CO_2 rebreather. Patient may need sedative.
Metabolic Acidosis | Excessive acid in the bloodstream (e.g., ketoacids or lactic acid) or excessive loss of HCO_3^- (e.g., GI tract loss). Commonly due to DKA, lactic acidosis, drug toxicity, or GI loss of excessive HCO_3^- as in diarrheal illness.			
Symptoms according to etiology of disorder: respiratory distress, headache, drowsiness, confusion, seizures, fatigue. GI symptoms of nausea, vomiting, and anorexia are common.	Tachycardia. Hypotension, weak pulses. Dehydration signs may be present: dry mucous membranes, poor skin turgor, and delayed capillary refill. Patients with DKA may present with fruity odor to their breath. Metabolic acidosis can also cause confusion, lethargy, and possibly coma or seizures.	Uncompensated: blood pH less than 7.35. Pco_2 normal or slightly low. Serum K^+: high. Urine: acidic. Electrocardiogram (ECG) changes caused by hyperkalemia: arrhythmias, peaked T waves, QRS widening, and ventricular fibrillation possible.	Sodium bicarbonate IV. Treat etiologic disorder (for example, if DKA, treat diabetes).

Continued

- The normal pH of blood is 7.35 to 7.45. A pH level lower than 7.35 is acidemia (also called acidosis); a level greater than 7.45 is alkalemia (also called alkalosis).
- A chemical buffering system used by the body is the carbonic acid–bicarbonate system: $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+$ and HCO_3^-. Both the lungs and kidneys utilize this system to compensate for acid–base disturbances.
- During hypoventilation the lungs retain CO_2; during hyperventilation, the lungs blow off CO_2.
- The greater the amount of CO_2 in the body, the greater the formation of H^+ ions.
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Respiratory Alkalosis			