

Key Terms

acidosis (p. 483)

alkalosis (p. 483)

buffer (p. 483)

dehydration (p. 479)

electrolyte balance (p. 481)

extracellular fluid (p. 478)

hyperkalemia (p. 482)

hyperventilation (p. 485)

hypokalemia (p. 482)

hypoventilation (p. 485)

intake (p. 479)

interstitial fluid (p. 478)

intracellular fluid (p. 478)

kaliuretic (p. 482)

Kussmaul respirations (p. 485)

metabolic acidosis (p. 485)

metabolic alkalosis (p. 486)

output (p. 479)

respiratory acidosis (p. 485)

respiratory alkalosis (p. 485)

skin turgor (p. 480)

transcellular fluid (p. 478)

Objectives

1. Describe the two main fluid compartments and the composition of body fluids.
2. Define *intake* and *output*.
3. Explain the effects of water imbalances, fluid shift, and fluid spacing.
4. List factors that affect electrolyte balance.
5. Describe the most common ions found in the intracellular and extracellular compartments.
6. List three mechanisms that regulate pH in the body.
7. Discuss acid–base imbalances: acidosis and alkalosis.

The old saying “you’re all wet” has some truth to it. Between 50% and 70% of a person’s weight is water. In the average man, water makes up 60% of the weight (about 40 L); in the average woman, water makes up about 50%. An infant is composed of even more water—up to 75%. Because adipose tissue contains less water than muscle tissue, obese persons have less water than thin persons.



BODY FLUIDS: DISTRIBUTION AND COMPOSITION

FLUID COMPARTMENTS

Water and its dissolved electrolytes are distributed into two major compartments: an intracellular compartment

and an extracellular compartment (Figure 25-1). The intracellular compartment includes the water located in all the cells of the body. Most water, about 63%, is located in the intracellular compartment.

The extracellular compartment includes the fluid located outside all the cells and represents about 37% of the total body water. The extracellular compartment includes the water located between cells, called **interstitial fluid**, water within blood vessels (plasma), and water within lymphatic vessels (lymph). **Transcellular fluid** is extracellular fluid and includes cerebrospinal fluid, the aqueous and vitreous humors in the eyes, the synovial fluids of joints, the serous fluids in body cavities, and the glandular secretions. Interstitial fluid and plasma are the largest extracellular compartments.

COMPOSITION OF BODY FLUIDS

Intracellular and extracellular fluids vary in their concentrations of various electrolytes. **Extracellular fluids** contain high concentrations of sodium (Na^+), chloride (Cl^-), and bicarbonate (HCO_3^-) ions. The plasma portion (extracellular) contains more protein than do other extracellular fluids. **Intracellular fluid** contains high concentrations of potassium (K^+), phosphate (PO_4^{3-}), and magnesium (Mg^{2+}) ions. The concentration of an ion is indicated when it appears in brackets; thus, $[\text{H}^+]$ means the concentration of the hydrogen ion.

5. Which of the following is least true of aldosterone?
 - a. It is a mineralocorticoid.
 - b. It is the "salt-retaining" hormone.
 - c. It determines the membrane permeability of the collecting duct to water.
 - d. It causes the tubular reabsorption of sodium and water.
 6. ADH
 - a. is released in response to excess blood volume and a dilute plasma.
 - b. determines the membrane permeability of the collecting duct to water.
 - c. makes the collecting duct impermeable to water.
 - d. determines the pore size of the glomeruli.
 7. A drug that blocks the renal reabsorption of Na^+ causes
 - a. defecation.
 - b. diuresis.
 - c. oliguria.
 - d. hypernatremia.
 8. Why is glucose normally not excreted in the urine?
 - a. No glucose is filtered.
 - b. All filtered glucose is reabsorbed.
 - c. Glucose is used up by the metabolizing nephron units.
 - d. Glucose is converted to ammonia in the distal tubule and excreted as urea.
 9. A drug that blocks the effects of aldosterone
 - a. increases the reabsorption of Na^+ and water.
 - b. is kaliuretic.
 - c. may cause an increase in plasma K^+ .
 - d. causes oliguria.
 10. Oliguria
 - a. refers to a lowered serum potassium.
 - b. develops in response to hypotension.
 - c. is a response to a diuretic drug.
 - d. most often accompanies a decline in serum creatinine.
- Go Figure**
1. According to Figure 24-1
 - a. The kidneys are located in the pelvic cavity.
 - b. The calyx is the opening through which the renal artery and renal vein enter and leave the kidney.
 - c. The renal column is the same as the renal pyramid.
 - d. The kidneys are connected to the urinary bladder by two ureters.
 2. According to Figure 24-2
 - a. The glomerulus sits within the renal pelvis.
 - b. The glomeruli are attached to both the afferent and efferent arterioles.
 - c. The peritubular capillaries sit within Bowman's capsule.
 - d. The collecting duct empties urine into the loop of Henle.
 3. According to Figure 24-2
 - a. Blood from the afferent arterioles drain into the collecting duct.
 - b. The loop of Henle is a hairpin-like tubular structure between the proximal and distal tubules.
 - c. The proximal convoluted tubule is closer to the collecting duct than is the distal convoluted tubule.
 - d. Blood from the peritubular capillaries drains into the renal artery and abdominal aorta.
 4. According to Table 24-2
 - a. ADH is a neurohypophyseal hormone whose target cells are in the collecting duct.
 - b. Aldosterone, like ADH, is a salt-retaining steroid.
 - c. An excess of aldosterone or ADH causes diuresis.
 - d. Both ANP and BNP are secreted by the renal cortex.
 5. According to Figure 24-3
 - a. Renin converts angiotensin I to angiotensinogen.
 - b. Converting enzyme changes angiotensin I to angiotensin II.
 - c. Aldosterone changes angiotensin II to converting enzyme.
 - d. Inhibition of converting enzyme expands blood volume and elevates blood pressure.
 6. According to Figure 24-4
 - a. Aldosterone exerts its effect primarily on the proximal convoluted tubule.
 - b. Filtration occurs across the glomerulus into Bowman's capsule.
 - c. ADH exerts its effect primarily on the descending limb of the loop of Henle.
 - d. Most tubular secretion occurs across the glomeruli.
 7. According to Figure 24-6
 - a. The detrusor muscle forms the wall of the urinary bladder.
 - b. The urinary bladder wall has rugae for expansion.
 - c. The urinary bladder is drained by a urethra.
 - d. All of the above are true.

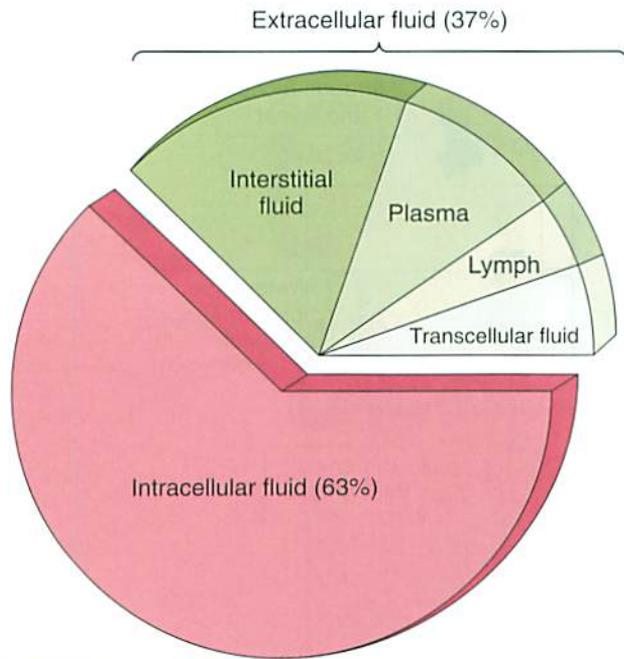


FIGURE 25-1 Fluid compartments: extracellular and intracellular.

Smaller concentrations of other ions are present in both intracellular and extracellular fluids. Although distributed across the fluid compartments, water and electrolytes can move from one compartment to another. The movement of fluid and electrolytes between compartments is well regulated.



Do You Know...

What Is So “Normal” about Normal Saline and Why It Is Normally Given?

Some patients become deficient in body fluids. These may be surgical patients who are not permitted to drink, patients who have been vomiting, or those who are unconscious and unable to eat or drink. These patients often receive intravenous infusions of solutions that resemble plasma in ionic composition. Normal saline, for example, contains 0.9% sodium chloride, a concentration equal to that of plasma. Because the concentration of “salt” in normal saline resembles that of plasma, it is considered normal.

WATER BALANCE

Normally, the quantity of water taken in, which is **intake**, equals the amount of water eliminated from the body, which is **output**. Water balance exists when intake equals output (Figure 25-2). As part of your clinical responsibilities, you will be measuring intake and output.

WATER INTAKE

Although water intake can vary considerably, the average adult takes in about 2500 mL every day. About 60% comes from drinking liquids; an additional 30% comes from water in foods, while 10% comes from the

breakdown of foods. This latter portion is called the *water of metabolism*.

Thirst is the primary regulator of water intake. The thirst center is in the hypothalamus of the brain. As the body loses water, the thirst center in the hypothalamus is stimulated, thus causing you to drink. Drinking restores the water content of the body, so both your thirst and your hypothalamus are satisfied. Older adults have a diminished thirst mechanism and are therefore prone to dehydration.

WATER OUTPUT

In a healthy person, 24-hour intake and output are approximately equal; the individual who takes in 2500 mL of water should therefore eliminate 2500 mL. Water can leave the body through several routes: kidneys, skin, lungs, and digestive tract. The kidneys eliminate about 60% of the water as urine. About 28% is lost from the skin and lungs; 6% is eliminated in the feces, and another 6% is lost as sweat. The amount lost by sweat can vary considerably, depending on the level of exercise and environmental temperatures. Water loss through the skin and lungs increases in a hot, dry environment.

The kidneys are the primary regulator of water output. Water regulation occurs mainly through the action of antidiuretic hormone (ADH) on the collecting duct. When body water content is low, the posterior pituitary gland releases ADH. It stimulates the collecting duct to reabsorb water, thereby decreasing water in the urine and increasing blood volume. When body water content is high, the secretion of ADH decreases. As a result, less water is reabsorbed from the collecting duct, and the excess water is eliminated in the urine. Water balance is also regulated by aldosterone, discussed later in the chapter.



Do You Know...

What a Prune and a Dehydrated Person Have in Common?

A prune is a dehydrated plum. As water is removed from the plum, its skin assumes a shriveled appearance. The same process occurs in a person who is dehydrated. As fluid is lost from the body, water moves from the interstitium (tissue spaces) into the blood vessels in an attempt to maintain adequate blood volume and blood pressure. As water is lost from the interstitium, the overlying skin appears shriveled, much like a prune. Both the dehydrated patient and prune are said to have poor skin turgor.

WATER IMBALANCES

DEHYDRATION

A deficiency of body water is called **dehydration**. Dehydration develops when water output exceeds water intake and commonly occurs in conditions such as excessive sweating, vomiting, diarrhea, and use of diuretics. A dehydrated person usually has poor skin

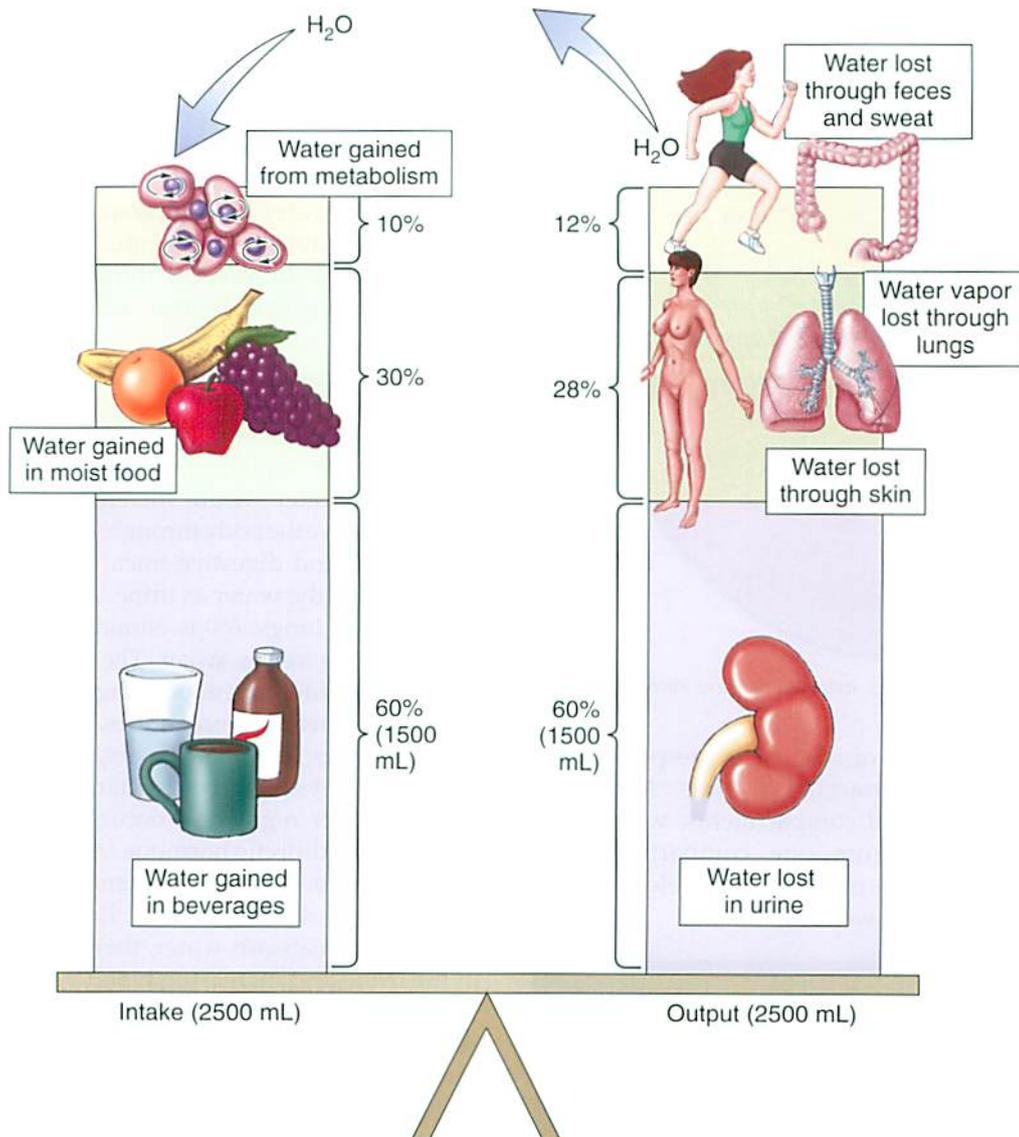


FIGURE 25-2 Water balance: intake equals output.

turgor. **Skin turgor** is assessed by pinching the skin and then observing how quickly the skin flattens, or returns to its normal position. If a person is well hydrated, the pinched skin quickly flattens out. The skin of a dehydrated person, however, flattens out more slowly, giving the skin the appearance of a tent—hence the term *tenting*. Tenting is caused by the depletion of fluid in the interstitial space. If untreated blood volume and blood pressure continue to decline, the person develops a low-volume (hypovolemic) shock.

EDEMA

The body can retain excess water and deposit it in various compartments, especially the interstitial space. Fluid retention is called *edema*. Edema can be intracellular or extracellular. Generally, we are concerned with interstitial edema. Excess body water can accumulate in various parts of the body. For example, water accumulation in the lungs is called *pulmonary edema*; it causes hypoxemia and cyanosis. Cerebral edema is the

accumulation of water in the brain; it causes a life-threatening increase in intracranial pressure and evidence of neurological dysfunction. Water accumulation in the ankle region is called *pedal edema*. As you can see, the consequences can be mild (pedal edema) or life threatening (pulmonary edema and cerebral edema). The goal of therapy is to remove excess fluid, relieve the symptoms, and treat the underlying cause of the edema.

? Re-Think

1. List four extracellular compartments.
2. Compare the volume of the interstitial space during dehydration and edema.

WHY DOES FLUID SHIFT?

The fluid shifts because of a change in the “pushing and pulling” forces affecting the capillaries. (See Chapter 19 for a discussion of capillary exchange and

the mechanisms of edema formation.) The forces include the capillary filtration pressure, plasma oncotic pressure, effect of lymphatic drainage, and effects of plasma protein that becomes trapped in the tissue space. Alteration of any of these factors affects water movement.

DAILY WEIGHTS AND FLUID BALANCE

The daily measurement of body weight provides a reliable estimate of fluid balance. For example, if a person with heart failure suddenly gains 4.4 lb, you should suspect fluid retention. How is the amount estimated? One liter of water weighs 2.2 lb (1 kg). If a person has a sudden weight gain of 4.4 lb, you can assume that that person has retained 2 L of fluid. Another example is when a patient is given a diuretic and loses 2.2 lb overnight. You can assume that the patient excreted 1 L of fluid.

? Re-Think

A 210-lb edematous man was given a powerful diuretic; he lost 2 kg in 12 hours. How much does he weigh after losing that water weight?

FLUID SPACING—IN OTHER WORDS

Fluid spacing is a clinical term that refers to the distribution of body water. First spacing refers to the normal distribution of water as described previously. Second spacing refers to the accumulation of water in the interstitial spaces (interstitial edema). Generally, with adequate treatment, this water can be reabsorbed and excreted. Third spacing refers to the accumulation of water in spaces from which it is not easily absorbed. For example, the water that accumulates in the abdominal cavity as ascites is not easily reabsorbed. Similarly, the excess water that accumulates within the digestive tract as a result of a paralytic ileus is unavailable for easy reabsorption. The amount of water in “third spaces” can be large and life threatening. Monitoring of water distribution is a common clinical concern.

ELECTROLYTE BALANCE

Electrolyte balance exists when the amounts of the various electrolytes gained by the body equal the amounts lost. *Electrolyte imbalances* are common, serious clinical challenges. Electrolytes are important components of the body fluids. The kidneys control the composition of body fluids by regulating the renal excretion of electrolytes. Table 25-1 includes the major electrolytes and their normal levels and functions.

QUICK REFERENCE: ELECTROLYTES

Chapter 2 describes the chemical characteristics of electrolytes. You will want to review several of the terms listed here for quick reference:

- **Ion:** An element or compound that carries an electrical charge. Common ions are Na^+ , Cl^- , K^+ , Ca^{2+} , and Mg^{2+} .
- **Cation:** A positively charged ion, such as Na^+ , K^+ , and Ca^{2+} .
- **Anion:** A negatively charged ion, such as Cl^- and HCO_3^- (bicarbonate). Most proteins (such as albumin) carry a negative charge.
- **Electrolyte:** Substances that form ions when they dissolve in water, such as NaCl (salt):



- **Ionization:** The chemical reaction caused when an electrolyte splits into two ions

MOST IMPORTANT IONS

SODIUM (Na^+)

Sodium is the chief extracellular cation, accounting for almost 90% of the positively charged ions in the extracellular fluid. Sodium plays a key role in the regulation of water balance. The primary mechanism regulating sodium concentration is aldosterone. Aldosterone stimulates the distal tubule and upper collecting duct of the nephron unit to reabsorb sodium. Usually, “when sodium moves, water moves”; this

Table 25-1 Major Ions and Their Functions

ELECTROLYTE	PLASMA LEVEL (mEq/L)	FUNCTIONS
Sodium (Na^+)	136–145	Chief extracellular cation Regulates extracellular volume Participates in nerve-muscle function
Potassium (K^+)	3.5–5.0	Chief intracellular cation Participates in nerve-muscle function
Calcium (Ca^{2+})	4.5–5.8	Strengthens bone and teeth Participates in muscle contraction Helps in blood clotting
Magnesium (Mg^{2+})	1.5–2.5	Strengthens bone Participates in nerve-muscle function
Chloride (Cl^-)	95–108	Chief extracellular anion Involved in extracellular volume control
Bicarbonate (HCO_3^-)	22–26	Part of bicarbonate buffer system Participates in acid-base balance
Phosphate (PO_4^{3-})	2.5–4.5	Strengthens bone Participates in acid-base balance

means that aldosterone causes the reabsorption of both Na^+ and water.

Hyponatremia (hye-per-nah-TREE-mee-ah) refers to excess Na^+ in the blood and is the result of excess water loss or increased Na^+ intake. Note the types of patients who develop hyponatremia:

- Older persons following surgery or fever. They are apt to have a low blood volume and diminished thirst mechanism.
- Patients who have been on prolonged diuretic therapy because of the loss of excessive water as urine.
- Uncontrolled diabetic patients with hyperglycemia. The glucosuria requires the excretion of large amounts of water (polyuria) leading to dehydration and hyponatremia.

Hyponatremia refers to a decrease in the concentration of plasma Na^+ . Normal plasma Na^+ levels are essential for normal brain function. Often, a patient becomes hyponatremic because of excess water in the blood. The blood literally is diluted out with water, causing a dilutional hyponatremia, a condition that is serious because it can result in delirium and seizures. For example, a person with heart failure often has an expanded blood volume and a dilutional hyponatremia. Sometimes, runners drink too much water during a marathon, causing a dilutional hyponatremia. Psychiatric patients sometimes “water binge”; they too are at risk for dilutional hyponatremia.

POTASSIUM (K^+)

Potassium (K^+) is the chief intracellular cation. The primary hormone regulating K^+ concentration is aldosterone. Aldosterone stimulates the distal tubule and upper collecting duct of the nephron unit to excrete K^+ into the urine. The kidney is the primary organ responsible for the excretion of excess K^+ . The monitoring of serum K^+ levels is an important clinical responsibility. Whereas only 2% of the K^+ is located in the extracellular space, plasma K^+ is important for normal muscle function, especially cardiac function. Changes in plasma levels of K^+ cause serious cardiac dysrhythmias.

Hyperkalemia (hye-per-kah-LEE-mee-ah) refers to excess K^+ (>5.5 mEq/L) in the blood. The primary cause of hyperkalemia is kidney disease, because the kidneys play a major role in the elimination of K^+ . Hyperkalemia is an emergency situation and is treated in several ways, including dialysis or the IV administration of an insulin-glucose solution. Dialysis removes K^+ from the blood. The IV insulin drives the glucose and K^+ into the cells, lowering plasma levels of K^+ .

Hypokalemia refers to a lower than normal amount of K^+ (<3.5 mEq/L) in the blood. Hypokalemia usually presents as muscle fatigue, leg cramps, abdominal distention, and cardiac rhythm disturbances. The most common cause of hypokalemia is the prolonged use of K^+ -losing diuretics, known as **kaliuretics**

(cal-ee-yoo-RET-iks). Some diuretics, such as spironolactone, are not kaliuretic and cause the kidney to reabsorb potassium. These diuretics are called “potassium spargers”; they can cause hyperkalemia. Maintaining normal K^+ levels in a patient who requires diuretic therapy is a major clinical concern. You must know which diuretics excrete K^+ and which diuretics reabsorb or “spare” potassium. Large amounts of K^+ can also be lost through vomiting (or nasogastric tubes) and diarrhea. Hypokalemia is a serious condition and is treated by the administration of K^+ .



Do You Know...

Why Acidosis Can Cause Hypokalemia?

As acidosis develops, the body attempts to decrease the plasma $[\text{H}^+]$ by moving it from the blood into the cells. As H^+ enters the cells, it kicks K^+ out of the cells into the blood, where it is filtered by the kidneys and excreted in the urine. When the acidosis is corrected, the H^+ leaves the cells and goes back into the blood. The K^+ then re-enters the cells, thereby making the person hypokalemic.

CALCIUM (Ca^{2+})

Calcium is necessary for bone and teeth formation, muscle contraction, nerve impulse transmission, and blood clotting. Of the body's calcium, 99% is in the bones and teeth. Parathyroid hormone is the primary regulator of plasma levels of calcium. Hypercalcemia and hypocalcemia are described in Chapter 14. (Do not confuse the terms *hypercalcemia* and *hyperkalemia*.)

MAGNESIUM (Mg^{2+})

Next to K^+ , magnesium is the most abundant cation in the intracellular fluid. Magnesium is important in the function of the heart, muscles, and nerves. Kidney disease is the major cause of hypermagnesemia. Other causes include overuse of magnesium-containing antacids. (Did you think that over-the-counter drugs couldn't kill you?) Hypomagnesemia is often seen in critically ill persons. It can be caused by aggressive diuretic therapy and is also seen in patients with chronic alcoholism, as well as in pregnant women with preeclampsia (high blood pressure of pregnancy).

CHLORIDE (Cl^-)

Chloride is the chief extracellular anion, and it usually follows sodium. That is, when sodium is actively pumped from the tubules into the peritubular capillaries, chloride follows the sodium passively. Changes in the plasma levels of chloride affect acid-base balance through its effect on bicarbonate. For example, when the plasma chloride level decreases (hypochloremia), the plasma bicarbonate level increases and causes alkalosis. Hyperchloremia, on the other hand, causes a decrease in the plasma bicarbonate level and a state of acidosis. Like sodium, chloride is greatly affected by diuretic therapy.

BICARBONATE (HCO_3^-)

Bicarbonate is an important anion in acid–base balance. Bicarbonate is an alkaline (basic) substance that helps remove excess acid (H^+) from the body. It is also the form in which carbon dioxide (CO_2) is transported in the blood. Bicarbonate excretion is controlled by the kidneys. Bicarbonate can be either reabsorbed or excreted, depending on the body's needs.

OTHER IONS

The plasma contains other ions, such as sulfate (SO_4^{2-}) and phosphate (PO_4^{3-}). The normal laboratory values for the major ions are summarized in Table 25-1.

2+2 Sum It Up!

The volume and composition of body fluids are closely regulated. Body fluids are found in two main compartments; most body fluid (63%) is in the intracellular compartment, and the remaining 37% is in the extracellular compartment. The extracellular compartment contains interstitial fluid, plasma, lymph, and transcellular fluid. The electrolyte composition of the body fluids is important. The chief extracellular cation is sodium; the chief intracellular cation is potassium. Excesses and deficiencies of water and electrolytes cause serious clinical problems.

? Re-Think

Explain the following statement. Aggressive diuresis with a loop diuretic, such as furosemide (Lasix), may cause a person to become hypokalemic, dehydrated, and hypotensive.

ACID–BASE BALANCE

A normally functioning body requires a balance between acids and bases. Acid–base balance is described according to its regulation of pH. Why is the regulation of pH so important? All chemical reactions in the body occur at a particular pH; any alteration in pH interferes with these reactions.

QUICK REFERENCE: ACIDS AND BASES

Chapter 2 describes acids, bases, and pH. You will want to review several terms for quick reference:

- **Acid:** A substance that dissociates (splits) into H^+ and an anion such as Cl^- (e.g., $\text{HCl} \rightarrow \text{H}^+ + \text{Cl}^-$). An acid donates a hydrogen ion (H^+) during a chemical reaction.
- **Base:** A substance that combines with H^+ during a chemical reaction and removes H^+ from solution (e.g., $\text{OH}^- + \text{H}^+ \rightarrow \text{H}_2\text{O}$). A base is an H^+ acceptor. The hydroxyl ion (OH^-), for example, combines with H^+ to form water (H_2O).

- **pH:** A unit of measurement that indicates the number of H^+ in solution. Remember that as the number of H^+ increases, the pH decreases. As the number of H^+ decreases, the pH increases. The normal plasma pH ranges from 7.35 to 7.45. A plasma pH of less than 7.35 is called **acidosis**, and a plasma pH greater than 7.45 is called **alkalosis** (Figure 25-3, A).

WHERE THE ACID (H^+) COMES FROM

Remember that H^+ is acid. Most H^+ comes from the body's chemical reactions during metabolism. For example, when glucose is metabolized in the presence of oxygen, it produces carbon dioxide (CO_2), water, and energy. The CO_2 combines with water and forms an acid (carbonic acid). When glucose is metabolized in the absence of oxygen, it forms lactic acid (H^+). When fatty acids are metabolized very quickly, they yield ketoacids (H^+). Finally, when proteins are metabolized, some of them yield sulfuric acid (H^+). All these acids are produced by metabolizing cells. To maintain acid–base balance, the body must neutralize and excrete the excess acids.

HOW THE BODY REGULATES pH

Three mechanisms work together to regulate pH: buffers, respirations, and kidney function (see Figure 25-3, B).

BUFFERS

The buffer system is the first line of defense in the regulation of pH. A **buffer** is a chemical substance that prevents large changes in pH. There are two parts to a buffer, called a *buffer pair*, which consists of a “taker” and a “giver.” A buffer pair works like this: If $[\text{H}^+]$ in the blood increases, the taker part of the buffer removes H^+ from the blood. If the $[\text{H}^+]$ decreases, the giver part of the buffer donates H^+ to the blood. By removing or adding H^+ , the buffer pair can maintain a normal blood pH. The body has numerous buffer pairs; the most important are the bicarbonate buffers, phosphate buffers, hemoglobin, and plasma proteins.

LUNGS

The respiratory system is the second line of defense in the regulation of pH. What does breathing have to do with pH? CO_2 can combine with water to form an acid (H^+). Because breathing controls CO_2 levels, it also affects $[\text{H}^+]$ or blood pH (Figure 25-4, A).

How Decreasing the Respiratory Rate Decreases pH

By decreasing the respiratory rate, the body retains or accumulates CO_2 . The CO_2 combines with H_2O to form H^+ . The increase in $[\text{H}^+]$ causes the pH to decrease. This is the basis for the development of respiratory acidosis (see Figure 25-4, B).

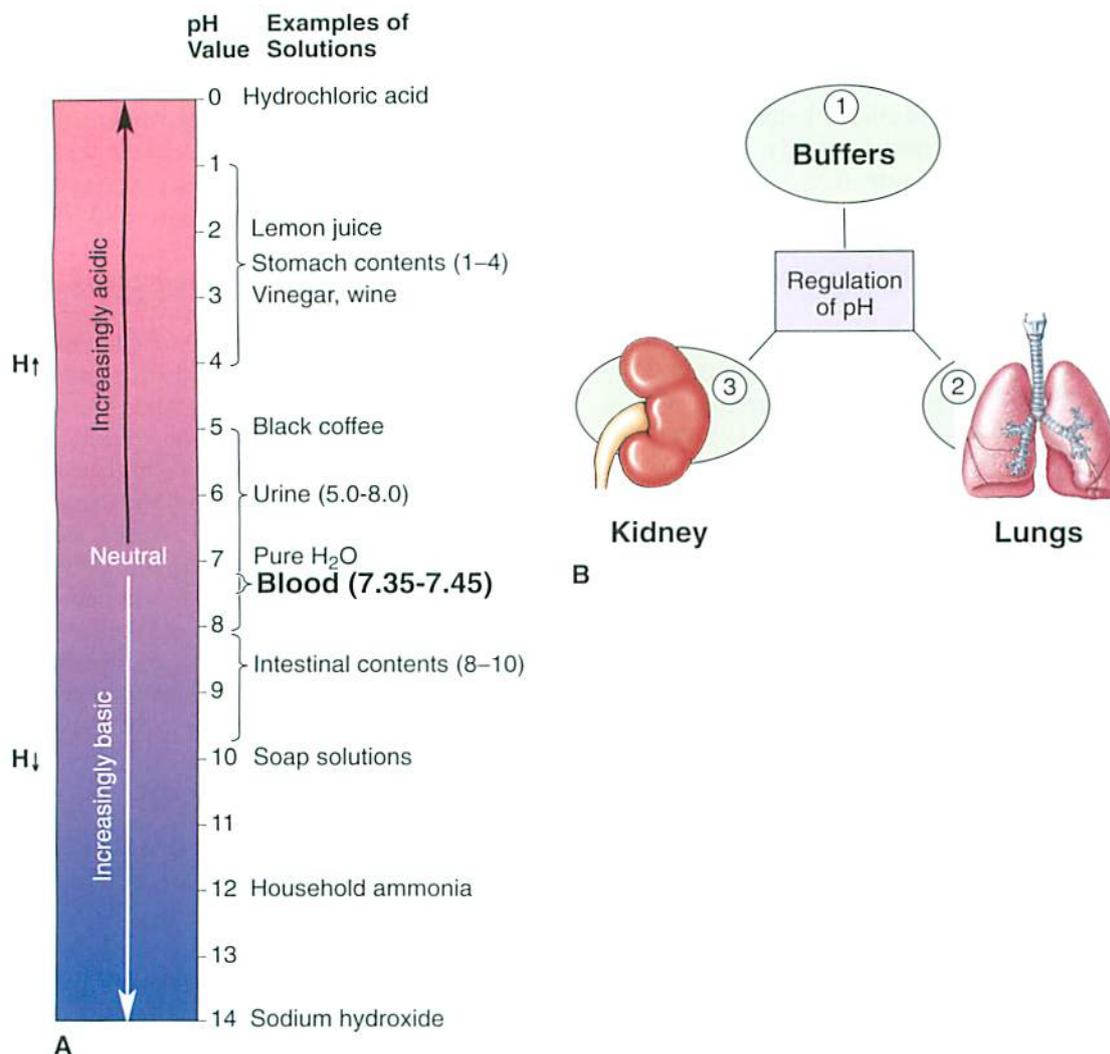


FIGURE 25-3 A, pH scale. B, Regulation of pH by buffers, lungs, and kidneys.

How Increasing the Respiratory Rate Increases pH

By increasing respiratory rate, the body exhales, or blows off, CO₂. The decrease in CO₂ causes a decrease in [H⁺] and an increase in pH; this is the basis of respiratory alkalosis (see Figure 25-4, C).

How the Respiratory System Knows

How does the respiratory system know that it should increase or decrease the respiratory rate? The medulla oblongata, the respiratory center in the brain, senses changes in [H⁺]. As plasma pCO₂ increases, the [H⁺] in both the plasma and cerebrospinal fluid also increases, thereby stimulating respiratory activity. The respiratory center then increases the rate and depth of breathing, thereby increasing the excretion of CO₂ by the lungs. As plasma [H⁺] decreases, the medullary respiratory center sends a slow-down signal, thereby decreasing the rate of breathing and the excretion of CO₂ by the lungs. The ability of the respiratory rate to respond to changing pCO₂ forms the basis for the

respiratory compensatory mechanisms in metabolic acidosis and alkalosis.

KIDNEYS

The kidneys are the third line of defense in the regulation of pH. The kidneys help regulate pH by reabsorbing or excreting H⁺ as needed. The kidneys also help regulate pH by reabsorbing and excreting bicarbonate (HCO₃⁻), a major buffer. Because the kidneys are major H⁺ eliminators, patients in kidney failure are generally acidotic.

ACID-BASE IMBALANCES

When the body is unable to regulate pH, acid–base imbalances develop. The acid–base imbalances in the blood are called *acidosis* and *alkalosis*. These imbalances are common, exert generalized effects, and are often life threatening. The acid–base imbalances, their causes, and compensatory mechanisms are summarized in Table 25-2.

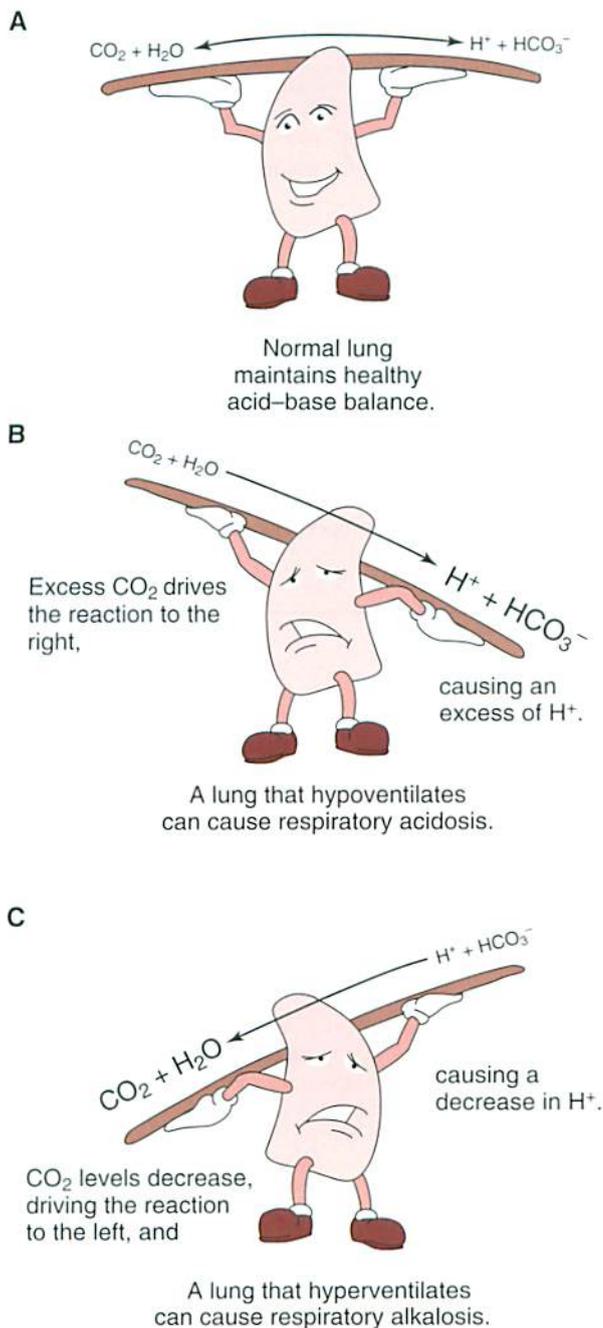


FIGURE 25-4 Respiratory control of acid–base balance. **A**, Normal respiratory rate. **B**, Hypoventilation causes respiratory acidosis. **C**, Hyperventilation causes respiratory alkalosis.

ACIDOSIS

A decrease in plasma pH below 7.35 is acidosis. (Remember that an increase in the plasma $[\text{H}^+]$ results in a decrease in pH.) The two types of acidosis are respiratory acidosis and metabolic acidosis. **Respiratory acidosis** is caused by any condition that decreases the effectiveness of the respiratory system or causes prolonged **hypoventilation**. For example, chronic lung disease (emphysema), high doses of narcotics, splinting of the chest, and injury to the medulla oblongata may all cause a decrease in respiratory activity. The

hypoventilation, in turn, increases the plasma levels of CO_2 . The excess CO_2 forms H^+ , decreases pH, and causes acidosis (see Figure 25-4, B). Because the acidosis is caused by a respiratory dysfunction (hypoventilation), it is classified as a respiratory acidosis.

How does the body try to correct respiratory acidosis? First, the buffer systems remove some of the excess H^+ . Then the kidneys excrete the excess H^+ and increase plasma bicarbonate (HCO_3^-). The ability of the kidneys to correct respiratory acidosis is called the *renal compensation for respiratory acidosis*. The respiratory system, however, cannot correct this pH imbalance because it is the dysfunctional respiratory system that is causing the acidosis.

Metabolic acidosis is a decrease in pH caused by nonrespiratory conditions. For example, kidney disease, uncontrolled diabetes mellitus, prolonged vomiting of intestinal contents (with loss of bicarbonate), and severe diarrhea (with loss of bicarbonate) are common causes of metabolic acidosis. A patient with poor kidney function is unable to excrete H^+ and becomes acidotic. A patient with uncontrolled diabetes mellitus produces excess ketoacids that overwhelm the buffer systems, accumulate in the plasma, and cause ketoacidosis.

How does the body try to correct metabolic acidosis? First, the buffer system removes some of the excess H^+ . Second, the respiratory system helps remove excess H^+ through **hyperventilation** or **Kussmaul (KOOS-mall) respirations**. Hyperventilation decreases plasma CO_2 and therefore decreases $[\text{H}^+]$ and increases pH. The increased respiratory activity is called the *respiratory compensation for metabolic acidosis*.



Do You Know...

Why You Can Hyperventilate Yourself into a Hypocalcemic Tetany?

An anxious person often hyperventilates, causing a respiratory alkalosis. Calcium is less soluble in alkalotic blood. Consequently, the plasma levels of calcium decrease. Because calcium is necessary for normal nerve conduction, nerve function is impaired, and the person experiences numbness and tingling. If the person continues to hyperventilate, the plasma levels of calcium may decline so much that an episode of hypocalcemic tetany could occur.

ALKALOSIS

An increase in plasma pH above 7.45 is alkalosis. The two types of alkalosis are respiratory alkalosis and metabolic alkalosis. Respiratory alkalosis develops from hyperventilation and the resulting decrease in plasma CO_2 and $[\text{H}^+]$. Common causes of respiratory alkalosis include anxiety and aspirin (salicylate) poisoning. Any condition that causes hyperventilation causes **respiratory alkalosis** (see Figure 25-4, C).

The body tries to correct respiratory alkalosis by the buffers and the kidneys. The buffers donate H^+ to the

Table 25-2 pH Imbalances

IMBALANCE	CAUSES	COMPENSATIONS
Acidosis (pH <7.35)		
Respiratory acidosis	Any condition that causes hypoventilation (chronic lung disease such as emphysema, asthma, splinting of the chest, high doses of narcotic drugs, myasthenia gravis)	Kidneys excrete H^+ and reabsorb HCO_3^- (renal compensation for respiratory acidosis)
Metabolic acidosis	Kidney disease, diarrhea, diabetic ketoacidosis, lactic acidosis, vomiting of intestinal contents	Increased respiratory rate to blow off CO_2 ; Kussmaul respirations (respiratory compensation for metabolic acidosis)
Alkalosis (pH >7.45)		
Respiratory alkalosis	Any condition that causes hyperventilation (anxiety)	Kidneys retain H^+ and excrete HCO_3^- (renal compensation for respiratory alkalosis)
Metabolic alkalosis	Persistent vomiting of stomach contents (loss of HCl), gastric suctioning, overingestion of antacids and bicarbonate-containing drugs	Decreased respiratory activity to retain CO_2 (respiratory compensation for metabolic alkalosis)

plasma, thereby decreasing pH. The kidneys decrease the excretion of H^+ ; H^+ retention decreases pH. The kidneys also increase the excretion of bicarbonate. The ability of the kidneys to correct respiratory alkalosis is called the *renal compensation for respiratory alkalosis*. The respiratory system cannot correct this pH disturbance because it is the overactivity, or hyperventilation, of the respiratory system that is causing the alkalosis.

Metabolic alkalosis is an increase in pH caused by nonrespiratory disorders. Metabolic alkalosis can be caused by overuse of antacid and bicarbonate-containing drugs; persistent vomiting of stomach contents (loss of HCl); and frequent nasogastric suctioning (loss of HCl). The body tries to correct metabolic alkalosis through buffers, the kidneys, and the respiratory system. The buffers donate H^+ , thereby decreasing pH. The kidneys decrease their excretion of H^+ . Finally, the respiratory system corrects the pH by hypoventilation. Hypoventilation increases plasma CO_2 and H^+ and decreases pH.

Note that the respiratory system can both cause a pH imbalance and help correct a nonrespiratory pH imbalance. Similarly, the kidneys can both cause and correct pH imbalances. The ability of the lungs and the kidneys to correct a pH imbalance is called a *compensatory function*.

? Re-Think

1. Define acidosis and alkalosis.
2. Explain how the lungs can both cause acidosis (respiratory acidosis) and help correct metabolic acidosis.
3. Explain how the kidneys correct respiratory acidosis as in ketoacidosis.

2+2 Sum It Up!

Plasma $[H^+]$ is expressed as pH. The normal plasma pH range is 7.35 to 7.45. It is regulated by three mechanisms: buffers, respirations, and kidney function. Acid–base balance is essential for the proper functioning of millions of chemical reactions in the body. Thus, acid–base imbalances pose a serious threat to health. The imbalances are classified as acidosis, a plasma pH less than 7.35 (respiratory and metabolic), or alkalosis, a plasma pH higher than 7.45 (respiratory and metabolic). There are respiratory and renal compensatory mechanisms.

As You Age

1. As the kidneys age, the tubules become less responsive to antidiuretic hormone (ADH) and tend to lose too much water. The excess water loss is accompanied by a decrease in the thirst mechanism. As a result, the older person is prone to dehydration.
2. The ability to reabsorb glucose and sodium is also diminished. The presence of excess solute (sodium and glucose) in the urine contributes to excess urination and water loss. In addition, impaired reabsorption of glucose interferes with blood glucose monitoring in diabetes.
3. The kidney tubules are less efficient in the secretion of ions, including the hydrogen ion (H^+). As a result, the older person experiences difficulty in correcting acid–base imbalances.
4. With immobility and diminished exercise, calcium moves from the bones into the renal tubules. There the calcium precipitates, causing kidney stones.


MEDICAL TERMINOLOGY AND DISORDERS
Water, Electrolyte, and Acid–Base Imbalances

Medical Term	Word Parts	Word Part Meaning or Derivation	Description
Words			
dehydration	de- -hydr/o- -ation	from or down water process	Dehydration is the loss of water that is necessary for normal body function; it occurs when the body loses more water than it takes in.
edema		From a Greek word meaning “a swelling tumor”	Edema is the accumulation of excess fluid causing swelling.
Disorders			
pH Imbalances			
acidosis	acid- -osis	From a Latin word meaning “sour” or “sharp,” as in vinegar condition of or increase	A condition in which there is excess H^+ (acid) in body fluids. The blood pH is <7.35 . Acidosis is classified as either respiratory or metabolic acidosis (described in text).
alkalosis	alkali- -osis	From a Greek word meaning “soda ash,” a basic or alkaline substance that is slippery and caustic condition of or increase	A condition in which there is insufficient H^+ in body fluids. The blood pH is >7.45 . Alkalosis is classified as either respiratory or metabolic (described in text).
Electrolyte Imbalances			
hypernatremia	hyper- -natr- -emia	above or excessive From the Latin word <i>natrium</i> , meaning “sodium” in the blood	Hypernatremia is an elevation in plasma sodium (>145 mmol/L) and can occur in response to a loss of water (most common) or a gain of sodium. Hyponatremia is a decrease in plasma sodium (<135 mmol/L); it occurs in response to a loss of sodium-containing fluids or excess intake of water (called dilutional hyponatremia).
hyperkalemia	hyper- -kal/i- -emia	above or excessive From the Latin word <i>kalium</i> , meaning “potassium” blood condition	An elevation of potassium (>5.5 mEq/L) in the blood. Three causes include: (1) failure to eliminate K^+ , as in impaired kidney function and the use of drugs such as ACE inhibitors, (2) shift of K^+ out of the cells, as occurs in tissue injury or catabolism, and (3) excess intake of K^+ , as in K^+ -rich drugs or salt substitutes. Because hyperkalemia affects the depolarization of excitable cells (nerve and muscle), hyperkalemia causes muscle weakness and cramping, nerve paresthesias, and cardiac conduction irregularities.
hypokalemia	hypo- -kal/i- -emia	below or deficient From the Latin word <i>kalium</i> , meaning “potassium” blood condition	A decrease of potassium (<3.5 mEq/L) in the blood. Three causes include: (1) excess K^+ loss as occurs in kidney and GI losses (especially diarrhea, vomiting, and GI suctioning), (2) shift of K^+ into the cells, and (3) decreased intake of K^+ .
extracellular water imbalances			Refers to an extracellular volume excess (hypervolemia) or deficit (hypovolemia). Hypervolemia is also called volume overload . It refers to excess extracellular volume and is caused by heart failure, excess steroids, liver failure, impaired kidney function, and excess intravenous fluid infusion. The excess fluid causes weight gain and can accumulate in the extremities (peripheral edema), in the abdominal cavity (ascites), and in the lungs, thereby reducing oxygenation and causing dyspnea and orthopnea. Hypovolemia refers to a diminished volume of blood and is commonly caused by excessive loss of water or reduced intake. If untreated, the condition progresses to hypovolemic shock and death.

Get Ready for Exams!

Summary Outline

Water, electrolytes, acids, and bases are tightly regulated. Fluids and electrolytes must be distributed in the body compartments in the correct volumes and concentrations.

I. Body Fluids: Distribution and Composition

- A. Major fluid compartments
- Two major fluid compartments: intracellular and extracellular compartments
 - Extracellular compartment: interstitial fluid, intravascular fluid (plasma), lymph, and transcellular fluid
- B. Composition of body fluids
- Intracellular fluid: potassium (K^+), phosphate (PO_4^{3-}), and magnesium (Mg^{2+})
 - Extracellular fluid: sodium (Na^+), chloride (Cl^-), and bicarbonate (HCO_3^-)

II. Water Balance: Intake Equals Output

- A. Intake
- The average intake of water is 2500 mL/24 hr.
 - The primary regulator of fluid intake is thirst.
- B. Output
- The average output of water is 2500 mL/24 hr.
 - Water is excreted by the kidneys, skin, lungs, digestive tract, and sweat.
- C. Water, deficiency, and excess
- Deficiency of body water: dehydration
 - Excess of body water: expanded blood volume and edema

III. Electrolyte Balance

- A. Sodium (Na^+)
- Chief extracellular cation
 - Necessary for water balance and nerve–muscle conduction
 - Primarily regulated by aldosterone
- B. Potassium (K^+)
- Chief intracellular cation
 - Necessary for nerve–muscle conduction
 - Primarily regulated by aldosterone
- C. Calcium (Ca^{2+})
- Strengthens bones and teeth; necessary for muscle contraction, nerve–muscle conduction, and blood clotting
 - Primarily regulated by parathyroid hormone
- D. Magnesium (Mg^{2+}) and Chloride (Cl^-)
- Magnesium performs important functions in heart, muscles, and nerves.
 - Chloride: chief extracellular anion; follows Na^+
- E. Bicarbonate (HCO_3^-)
- A major extracellular anion
 - Transports CO_2
 - Regulates acid–base balance

IV. Acid–Base Balance

- A. pH
- The pH refers to the concentration of H^+ .
 - The normal blood pH is 7.35 to 7.45. Acidosis occurs if blood pH is less than 7.35; alkalosis occurs if blood pH is more than 7.45.

- B. Regulation of blood pH
- Blood pH is regulated by buffers, the respiratory system, and the kidneys.
 - Buffers (the buffer pair) can donate or remove H^+ .
 - The respiratory system affects pH by regulating CO_2 .
 - The kidneys can vary their excretion of H^+ and reabsorption of bicarbonate.

V. Acid–Base Imbalances

- A. Acidosis (blood pH <7.35)
- Respiratory acidosis is caused by hypoventilation.
 - Metabolic acidosis has nonrespiratory causes, including kidney disease, uncontrolled diabetes mellitus, diarrhea, and lactic acid production.
- B. Alkalosis (blood pH >7.45)
- Respiratory alkalosis is caused by hyperventilation.
 - Metabolic alkalosis is caused by nonrespiratory conditions, including overingestion of antacids and loss of gastric contents.

Review Your Knowledge

Matching: Water Compartments

Directions: Match the following words with their description below. Some words may be used more than once.

- | | |
|------------------|---|
| a. interstitial | 1. ___ Most body water is located within this compartment. |
| b. intracellular | 2. ___ Water located within the vascular compartment (blood vessels) |
| c. plasma | 3. ___ Water located between the cells |
| d. transcellular | 4. ___ Includes water within the eye, glandular secretions, and cerebrospinal fluid |
| | 5. ___ Also called <i>tissue fluid</i> |

Matching: Ions

Directions: Match the following words with their description below. Some terms may be used more than once.

- | | |
|--------------|--|
| a. Na^+ | 1. ___ Plasma concentration of this ion determines pH. |
| b. K^+ | 2. ___ The chief extracellular cation |
| c. H^+ | 3. ___ The chief intracellular cation |
| d. Ca^{2+} | 4. ___ The ion that is elevated in hyperkalemia |
| | 5. ___ Aldosterone stimulates the distal tubule and upper collecting duct to reabsorb this cation. |
| | 6. ___ Hypoventilation causes the accumulation of CO_2 and this cation. |
| | 7. ___ Many diuretics are kaliuretic and therefore cause a loss of this cation. |
| | 8. ___ Most diuretics work by blocking the renal reabsorption of this cation. |
| | 9. ___ An increase in this ion causes acidosis. |
| | 10. ___ This ion is regulated primarily by parathyroid hormone. |