

CHAPTER 2

Fluid, Electrolyte, and Acid-Base Imbalances

CHAPTER OUTLINE

Fluid Imbalance Review of Concepts and Processes Fluid Compartments Movement of Water Fluid Excess—Edema Causes of Edema Effects of Edema Fluid Deficit—Dehydration Causes of Dehydration Effects of Dehydration Third-Spacing: Fluid Deficit and Fluid Excess	Potassium Imbalance Review of Potassium Hypokalemia Hyperkalemia Calcium Imbalance Review of Calcium Hypocalcemia Hypercalcemia Other Electrolytes Magnesium Phosphate Chloride	Buffer System and Maintenance of Serum pH Respiratory System Renal System Acid-Base Imbalance Compensation Decompensation Acidosis Alkalosis Treatment of Imbalances Case Studies Chapter Summary Study Questions Additional Resources
Electrolyte Imbalances Sodium Imbalance Review of Sodium Hyponatremia Hypernatremia	Acid-Base Imbalance Review of Concepts and Processes Control of Serum pH Buffer Systems The Bicarbonate-Carbonic Acid	

LEARNING OBJECTIVES

After studying this chapter, the student is expected to:	
1. Explain the movement of water between body compartments that results in edema.	7. Describe the causes and effects of hypomagnesemia, hypophosphatemia, hypochloremia, and hyperchloremia.
2. Describe the causes and effects of dehydration.	8. Explain how metabolic acidosis, metabolic alkalosis, respiratory acidosis, and respiratory alkalosis develop and their effects on the body.
3. Explain the meaning of third-spacing.	9. Explain how decompensation develops and its effects on the central nervous system.
4. Discuss the causes and signs of hyponatremia and hypernatremia.	10. Explain the normal function of atrial natriuretic peptide in maintaining fluid and electrolyte balance.
5. Explain the causes and signs of hypokalemia and hyperkalemia.	
6. Describe the causes and signs of hypocalcemia and hypercalcemia.	

KEY TERMS

aldosterone	diffusion	hypervolemia	milliequivalent (mEq)
anion	diuretic	hypothalamus	nonvolatile metabolic acids
anorexia	dysrhythmia	hypotonic/hypo-osmolar	osmoreceptor
antidiuretic hormone (ADH)	electrocardiogram	hypovolemia	osmosis
ascites	extracellular	interstitial fluid	osmotic pressure
atrial natriuretic peptide	filtration	intracellular	paresthesias
capillary permeability	hydrogen ions	intravascular fluid	skin turgor
carpopedal spasm	hydrostatic pressure	isotonic/iso-osmolar	tetany
cation	hypertonic/hyper-osmolar	laryngospasm	transcellular

Fluid Imbalance

Review of Concepts and Processes

Water is a major component of the body and is found both within and outside the cells. It is essential to homeostasis, the maintenance of a relatively constant and favorable environment for the cells. Water is the medium within which metabolic reactions and other processes take place. It also comprises the transportation system for the body. For example, water carries nutrients into cells and removes wastes, transports enzymes in digestive secretions, and moves blood cells around the body. Without adequate fluid, cells cannot continue to function, and death results. Fluid also facilitates movement of body parts, for example, the joints and the lungs.

THINK ABOUT 2-1

Suggest several functions performed by water in the body and the significance of each.

Fluid Compartments

Although the body appears to be a solid object, approximately 60% of an adult's body weight consists of water, and an infant's body is about 70% water (Table 2-1). Female bodies, which contain a higher proportion of fatty tissue, have a lower percentage of water than male bodies. The elderly and the obese also have a lower proportion of water in their bodies. Individuals with less fluid reserve are more likely to be adversely affected by any fluid or electrolyte imbalance.

Fluid is distributed between the **intracellular** compartment (ICF), or fluid inside the cells, and the **extracellular** compartment (ECF). See Ready Reference 1 for a diagram showing fluid compartments of the body.

ECF includes the:

- **Intravascular fluid** (IVF) or blood
- **Interstitial fluid** (ISF) or intercellular fluid

TABLE 2-1 Fluid Compartments in the Body

	Volume Adult Male (L)	Approximate Percentage of Body Weight		
		Male (%)	Female (%)	Infant (%)
Intracellular fluid	28	40	33	40
Extracellular fluid	15	20	17	30
Plasma	(4.5)	(4)	(4)	(4)
Interstitial fluid	(10.5)	(15)	(9)	(25)
Other		(1)	(1)	(1)
Total water	43	60	50	70

Note: In elderly women, water content is reduced to approximately 45% of body weight.

- Cerebrospinal fluid (CSF)
- **Transcellular** fluids present in various secretions, such as those in the pericardial (heart) cavity or the synovial cavities of the joints

In an adult male, blood constitutes about 4% of body weight and interstitial fluid about 15%; the remaining transcellular fluids amount to about 1% of total body weight. Water constantly circulates within the body and moves between various compartments. For example, CSF forms continuously from the blood and is reabsorbed back into the general circulation. A large volume of water (up to 8 liters in 24 hours) is present in the digestive secretions entering the stomach and small intestine, and this fluid is reabsorbed in the colon, making up a very efficient *water-recycling* system.

THINK ABOUT 2-2

- a. Which body compartment contains the most water?
- b. Suggest why diarrhea may cause a fluid deficit more rapidly than coughing and sneezing with a cold.

Movement of Water

To maintain a constant level of body fluid, the amount of water entering the body should equal the amount of water leaving the body. Fluid is added to the body through the ingestion of solid food and fluids and as a product of cell metabolism (Table 2-2). Fluid is lost in the urine and feces as well as through *insensible* (unapparent) losses through the skin (perspiration) and exhaled air.

Control of fluid balance is maintained by:

- The *thirst* mechanism in the **hypothalamus**, the **osmoreceptor** cells of which sense the internal environment, both fluid volume and concentration, and then promote the intake of fluid when needed
- The hormone, **antidiuretic hormone (ADH)**, which controls the amount of fluid leaving the body in the urine (see Chapters 16 and 18); ADH promotes reabsorption of water into the blood from the kidney tubules
- The hormone **aldosterone**, which determines the reabsorption of both sodium ions and water from the kidney tubules; these hormones conserve more fluid when there is a fluid deficit in the body
- The hormone **atrial natriuretic peptide (ANP)** is a hormone synthesized and released by the myocardial cells in the atrium of the heart. Its role in homeostasis relates to reduction of workload on the heart by regulating fluid, sodium, and potassium levels. In the kidney ANP increases glomerular filtration rate (GFR) by altering pressure in the glomerular capillaries; it also reduces the reabsorption of sodium in the distal convoluted tubules through inhibition of antidiuretic hormone (ADH). Renin secretion is also reduced and thus the renin angiotensin system is inhibited. The result is fluid loss from the

TABLE 2-2 Sources and Losses of Water

Sources (mL)		Losses (mL)	
Liquids	1200	Urine	1400
Solid foods	1000	Feces	200
Cell metabolism	300	Insensible losses	
		Lungs	400
		Skin	500
Total	2500		2500

extracellular compartment and lowered blood pressure. It also reduces aldosterone secretion, leading to retention of potassium. Research has shown that ANP is elevated in patients with congestive heart failure who have increased blood volume in the atria (see Chapter 12). Research is ongoing on this peptide and its possible use in the treatment of hypertension and congestive heart failure.

THINK ABOUT 2-3

- Describe how excessive fluid is lost from the body during strenuous exercise on a very hot day. Explain how the body can respond to this fluid loss to maintain homeostasis.
- What factors may limit such responses?

Fluid constantly circulates throughout the body and moves relatively freely, depending on the permeability of the membranes between compartments, by the processes of **filtration** or **osmosis** (Fig. 2-1). Water moves between the vascular compartment or blood and the interstitial compartment through the semipermeable capillary membranes, depending on the relative **hydrostatic** and **osmotic pressures** within the compartments (see Fig. 2-1). Proteins and electrolytes contribute to the osmotic pressure of a fluid and therefore are very important in maintaining fluid volumes in various compartments. Hydrostatic pressure may be viewed as the “push” force and osmotic pressure as the “pull” or attraction force in such fluid movements. Changes in either force will alter fluid movement and volume in the compartments.

At the arteriolar end of the capillary, the blood hydrostatic pressure (or blood pressure) exceeds the opposing interstitial hydrostatic pressure and the plasma colloid osmotic pressure of the blood, and therefore fluid moves out from (or is “pushed” out of) the capillary into the interstitial compartment. At the venous end of the capillary, the blood hydrostatic pressure is greatly decreased and osmotic pressure higher, and therefore fluid tends to shift (or is “pulled”) back into the capillary. It is easier to remember the direction of movement if one thinks of the movement of nutrients and oxygen out of the arterial blood toward the cells and the flow of wastes and

carbon dioxide from the cell back into the venous blood. Excess fluid and any protein in the interstitial compartment is returned to the circulation through the lymphatic capillaries.

APPLY YOUR KNOWLEDGE 2-1

Predict three changes that could alter normal movement of fluid in the body.

Many cells have mechanisms to control intracellular volume. A major factor in the movement of water through cell membranes is the difference in osmotic pressure between the cell and the interstitial fluids. As the relative concentrations of electrolytes in the interstitial fluid and intracellular fluid change, the osmotic pressure also changes, causing water to move across the cell membrane by osmosis. For example, if an erythrocyte is placed in a dilute hypotonic solution (low osmotic pressure), water may enter the cell, causing it to swell and malfunction.

THINK ABOUT 2-4

- Explain how a very high hydrostatic pressure in the venule end of a capillary affects fluid shift.
- Explain how a loss of plasma protein affects fluid shift at the capillaries.
- Explain how a high concentration of sodium ions in the interstitial fluid affects intracellular fluid levels.

Fluid Excess—Edema

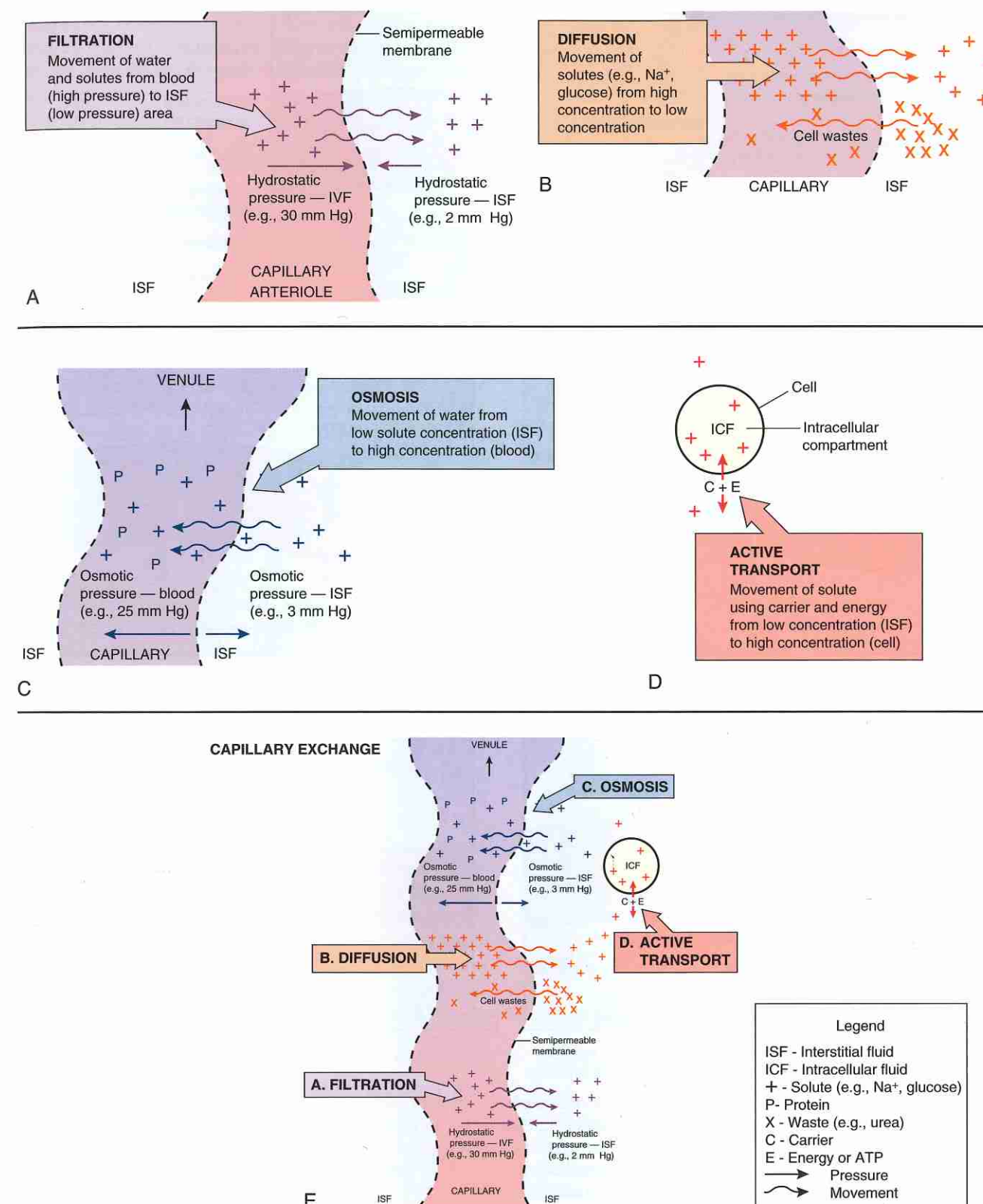
Fluid excess occurs in the extracellular compartment and may be referred to as **isotonic/iso-osmolar**, **hypotonic/hypo-osmolar**, or **hypertonic/hyper-osmolar**, depending on the cause. The osmolarity or the concentration of solute in the fluid, affects fluid shifts between compartments, including the cells.

Edema refers to an excessive amount of fluid in the interstitial compartment, which causes a swelling or enlargement of the tissues. Edema may be localized in one area or generalized throughout the body. Depending on the type of tissue and the area of the body, edema may be highly visible or relatively invisible, or not accurately reflect the amount of fluid hidden in the area; for example, facial edema is usually visible but edema of the liver or a limb may not be. Edema is usually more severe in *dependent* areas of the body, where the force of gravity is greatest, such as the buttocks, ankles, or feet of a person in a wheelchair. Prolonged edema interferes with venous return, arterial circulation, and cell function in the affected area.

Causes of Edema

Edema has four general causes (Fig. 2-2).

- The first cause is *increased capillary hydrostatic pressure* (equivalent to higher BP or blood pressure), which

**FIGURE 2-1** Movement of water and electrolytes between compartments.

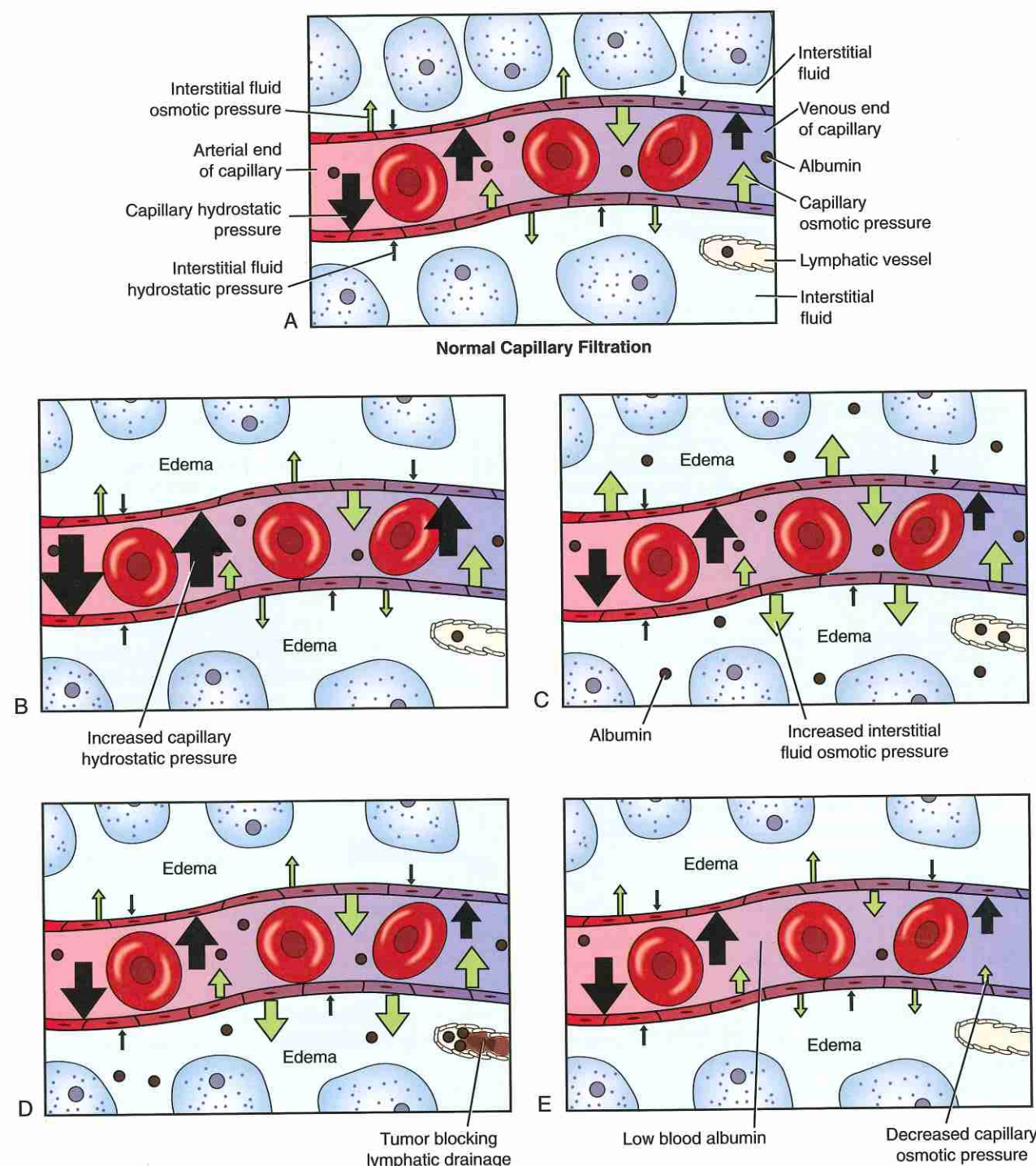


FIGURE 2-2 Causes of edema. **A**, Normal capillary filtration without edema. **B**, Edema due to increased capillary hydrostatic pressure. **C**, Edema due to increased interstitial fluid osmotic pressure from increased capillary permeability. **D**, Edema due to blocked lymphatic drainage. **E**, Edema due to decreased capillary osmotic pressure from hypoalbuminemia. (From Copstead-Kirkhorn LC: Pathophysiology, ed 4, St. Louis, 2009, Mosby.)

prevents return of fluid from the interstitial compartment to the venous end of the capillary, or forces excessive amounts of fluid out of the capillaries into the tissues. The latter is a cause of pulmonary edema, in which excessive pressure, often due to increased

blood volume, can force fluid into the alveoli, interfering with respiratory function.

Specific causes of edema related to increased hydrostatic pressure include increased blood volume (**hypervolemia**) associated with kidney failure,

pregnancy, congestive heart failure, or administration of excessive fluids. In pregnancy, the enlarged uterus compresses the pelvic veins in the seated position and when a pregnant woman must stand still for long periods of time, the pressure in the leg veins can become quite elevated, causing edema in the feet and legs. In some people with congestive heart failure, the blood cannot return easily through the veins to the heart, raising the hydrostatic pressure in the legs and abdominal organs and causing **ascites**, or fluid in the abdominal cavity.

2. Second, edema may be related to the *loss of plasma proteins*, particularly albumin, which results in a decrease in plasma osmotic pressure. Plasma proteins usually remain inside the capillary and seldom move through the semipermeable capillary membrane. The presence of fewer plasma proteins in the capillary allows more fluid to leave the capillary and less fluid to return to the venous end of the capillary.

Protein may be lost in the urine through kidney disease, or synthesis of protein may be impaired in patients with malnutrition and malabsorption diseases or with liver disease. Protein levels may drop acutely in burn patients who have large areas of burned skin; the subsequent inflammation and loss of the skin barrier allow protein to easily leak out of the body.

Frequently *excessive sodium levels* in the extracellular fluid accompany the two causes just mentioned. When sodium ions are retained, they promote accumulation of fluid in the interstitial compartment by increasing the ISF osmotic pressure and decreasing the return of fluid to the blood. Blood volume and blood pressure are usually elevated as well. High sodium levels are common in patients with heart failure, high blood pressure, kidney disease, and increased aldosterone secretion.

3. Edema may result from *obstruction of the lymphatic circulation*. Such an obstruction usually causes a localized edema because excessive fluid and protein are not returned to the general circulation. This situation may develop if a tumor or infection damages a lymph node or if lymph nodes are removed, as they may be in cancer surgery.

4. The fourth cause of edema is *increased capillary permeability*. This usually causes localized edema and may result from an inflammatory response or infection (see Chapter 5). In this case, histamine and other chemical mediators released from cells following tissue injury cause increased capillary permeability and increased fluid movement into the interstitial area. Protein also leaks into the interstitial compartment, increasing the osmotic pressure in ISF and thus holding more fluid in the interstitial area. A general increase in capillary permeability can result from some bacterial toxins or large burn wounds, leading to both hypovolemia and shock.

THINK ABOUT 2-5

- a. In some cases of breast cancer, many of the axillary lymph nodes are removed. Why are injections not usually done on the affected arm?
- b. Explain why severe kidney disease may cause generalized edema.
- c. Explain why the feet may become swollen when one sits for long periods of time, but the swelling decreases when one lies recumbent in bed.
- d. Explain how protein-calorie malnutrition results in ascites.

Effects of Edema

- A local area of swelling may be visible and may be very pale or red in color, depending on the cause (Table 2-3).
- *Pitting* edema occurs in the presence of excess interstitial fluid, which moves aside when firm pressure is applied by the fingers. A depression or “pit” remains after the finger is removed.
- In people with generalized edema there is a significant increase in *body weight*, which may indicate a problem before there are other visible signs (see Fig. 2-3).
- *Functional impairment* due to edema may occur, for example, when it restricts range of movement of joints. Edema of the intestinal wall may interfere with digestion and absorption. Edema or accumulated fluid around the heart or lungs impairs the movement and function of these organs.
- *Pain* may occur if edema exerts pressure on the nerves locally, as with the headache that develops in patients

TABLE 2-3 Comparison of Signs and Symptoms of Fluid Excess (Edema) and Fluid Deficit (Dehydration)

Fluid Excess (Edema)	Fluid Deficit (Dehydration)
Localized swelling (feet, hands, periorbital area, ascites)	Sunken, soft eyes
Pale, gray, or red skin color	Decreased skin turgor, dry mucous membranes
Weight gain	Thirst, weight loss
Slow, bounding pulse; high blood pressure	Rapid, weak, thready pulse, low blood pressure, and orthostatic hypotension
Lethargy, possible seizures	Fatigue, weakness, dizziness, possible stupor
Pulmonary congestion, cough, rales	Increased body temperature
Laboratory values:	Laboratory values:
Decreased hematocrit	Increased hematocrit
Decreased serum sodium	Increased electrolytes (or variable)
Urine: low specific gravity, high volume	Urine: high specific gravity, low volume

Note: Signs may vary depending on the cause of the imbalance.



FIGURE 2-3 Pitting edema. Note the finger-shaped depressions that do not rapidly refill after an examiner has exerted pressure. (From Bloom A, Ireland J: *Color Atlas of Diabetes*, ed 2, St. Louis, Mosby, 1992.)

with cerebral edema. If cerebral edema becomes severe, the pressure can impair brain function because of ischemia and can cause death. When viscera such as the kidney or liver are edematous, the capsule is stretched, causing pain.

- With sustained edema the *arterial circulation* may be impaired. The increased interstitial pressure may restrict arterial blood flow into the area, preventing the fluid shift that carries nutrients into the cells. This can prevent normal cell function and reproduction and eventually results in tissue necrosis or the development of ulcers. This situation is evident in individuals with severe varicose veins in the legs—large, dilated veins that have a high hydrostatic pressure. Varicose veins can lead to fatigue, skin breakdown, and varicose ulcers (see Chapter 12). These ulcers do not heal easily because of the continued insufficient blood supply.
- In dental practice, it is difficult to take accurate impressions when the tissues are swollen; dentures do not fit well, and sores may develop that often are slow to heal and become infected because the blood flow is impaired to the gingival tissues.
- Edematous tissue in the skin is very susceptible to tissue breakdown from pressure, abrasion, and external chemicals. Proper skin care is essential to prevent ulceration, particularly in an immobilized patient (see Chapter 25).

THINK ABOUT 2-6

- List three signs of local edema in the knee.
- Explain why persistent edema in a leg could cause weakness and skin breakdown.

Fluid Deficit—Dehydration

Dehydration refers to insufficient body fluid resulting from inadequate intake or excessive loss of fluids or a combination of the two. Losses are more common and affect the extracellular compartment first. Water can shift within the extracellular compartments. For example, if fluid is lost from the digestive tract because of vomiting, water shifts from the vascular compartment into the digestive tract to replace the lost secretions. If the deficit continues, eventually fluid is lost from the cells, impairing cell function.

Fluid loss is often measured by a change in body weight; knowing the usual body weight of a person is very helpful in assessment of the extent of loss. As a general guide to extracellular fluid loss, a *mild* deficit is defined as a decrease of 2% in body weight, a *moderate* deficit as a 5% weight loss, and *severe* dehydration is a decrease of 8%. This figure should be adjusted for the individual's age, body size, and condition.

Dehydration is a more serious problem for infants and elderly people, who lack significant fluid reserves as well as the ability to conserve fluid quickly. Infants also experience not only greater insensible water losses through their proportionately larger body surface area but also an increased need for water owing to their higher metabolic rate. The vascular compartment is rapidly depleted in an infant (*hypovolemia*), affecting the heart, brain, and kidneys. This is indicated by decreased urine output (number of wet diapers), increased lethargy, and dry mucosal membranes.

Water loss is often accompanied by a loss of electrolytes and sometimes of proteins, depending on the specific cause of the loss. For example, sweating results in a loss of water and sodium chloride. Electrolyte losses can influence water balance significantly because electrolyte changes lead to osmotic pressure change between compartments. To restore balance, electrolytes as well as fluid must be replaced. Isotonic dehydration refers to a proportionate loss of fluid and electrolytes, hypotonic dehydration to a loss of more electrolytes than water, and hypertonic dehydration to a loss of more fluid than electrolytes. The latter two types of dehydration cause signs of electrolyte imbalance and influence the movement of water between the intracellular and extracellular compartments (see Electrolyte Imbalances).

THINK ABOUT 2-7

- Explain why an infant is more vulnerable than a young adult to fluid loss.
- If more sodium is lost from the extracellular fluid compartment than water, how will fluid move between the cell and the interstitial fluid compartment? Explain the result.



FIGURE 2-4 Testing for dehydration. Loss of skin elasticity or turgor is a sign of dehydration. Skin that does not return quickly to its normal shape after being pinched indicates interstitial water loss. (From Patton KT, Thibodeau GA: *Anatomy & Physiology*, ed 8, St. Louis, 2013, Mosby.)

Causes of Dehydration

Common causes of dehydration include:

1. Vomiting and diarrhea, both of which result in loss of numerous electrolytes and nutrients such as glucose, as well as water; drainage or suction of any portion of the digestive system can also result in deficits
2. Excessive sweating with loss of sodium and water
3. Diabetic ketoacidosis with loss of fluid, electrolytes, and glucose in the urine
4. Insufficient water intake in an elderly or unconscious person
5. Use of a concentrated formula in an attempt to provide more nutrition to an infant

Effects of Dehydration

Initially, dehydration involves a decrease in interstitial and intravascular fluids. These losses may produce *direct* effects such as:

- Dry mucous membranes in the mouth (see Table 2-3)
- Decreased *skin turgor* or elasticity (Fig. 2-4)
- Lower blood pressure, weak pulse, and a feeling of fatigue
- Increased hematocrit, indicating a higher proportion of red blood cells compared with water in the blood
- Decreasing mental function, confusion, and loss of consciousness, which develop as brain cells lose water and reduce function

The body attempts to *compensate* for the fluid loss by:

- Increasing thirst
- Increasing the heart rate
- Constricting the cutaneous blood vessels, leading to pale and cool skin

- Producing less urine and concentrating the urine, increasing the specific gravity, as a result of renal vasoconstriction and increased secretion of ADH and aldosterone

THINK ABOUT 2-8

Describe three signs or symptoms of dehydration that are direct effects, and three signs that indicate the compensation that is occurring in response to dehydration.

Third-Spacing: Fluid Deficit and Fluid Excess

Third-spacing refers to a situation in which fluid shifts out of the blood into a body cavity or tissue where it is no longer available as *circulating fluid*. Examples include peritonitis, the inflammation and infection of the peritoneal membranes, and burns. The result of this shift is a fluid deficit in the vascular compartment (*hypovolemia*) and a fluid excess in the interstitial space. Until the basic cause is removed, fluid remains in the “third space”—in the body, but is not a functional part of the circulating fluids. Simply weighing the patient will not reflect this shift in fluid distribution. Laboratory tests such as hematocrit and electrolyte concentrations will indicate third-spacing. In the case of burns, the third spacing is evident as edema in the area of the wounds.

THINK ABOUT 2-9

Based on the information given previously on fluid excess and fluid deficit, describe three signs and symptoms of third-spacing related to a large burn area.

Electrolyte Imbalances

Sodium Imbalance

Review of Sodium

Sodium (Na^+) is the primary *cation* (positively charged ion) in the extracellular fluid (Table 2-4). *Diffusion* of sodium occurs between the vascular and interstitial fluids. Sodium transport across the cell membrane is controlled by the sodium-potassium pump or active transport, resulting in sodium levels that are high in extracellular fluids and low inside the cell. Sodium is actively secreted into mucus and other body secretions. It exists in the body primarily in the form of the salts sodium chloride and sodium bicarbonate. It is ingested in food and beverages, usually in more than adequate amounts, and is lost from the body in perspiration, urine, and feces. Sodium levels in the body are primarily controlled by the kidneys through the action of aldosterone.

Sodium is important for the maintenance of extracellular fluid volume through its effect on osmotic pressure because it makes up approximately 90% of the solute in extracellular fluid. Sodium also is essential in the

TABLE 2-4 Distribution of Major Electrolytes

Ions	Intracellular (mEq/L)	Blood (mEq/L)
Cations		
Sodium (Na)	10	142
Potassium (K)	160	4
Calcium (Ca)	Variable	5
Magnesium (Mg)	35	3
Anions		
Bicarbonate (HCO_3^-)	8	27
Chloride (Cl^-)	2	103
Phosphate (HPO_4^-)	140	2

Note: There are variations in "normal" values among individuals. The concentration of electrolytes in plasma varies slightly from that in the interstitial fluid or other types of extracellular fluids.

The number of anions, including those present in small quantities, is equivalent to the concentration of cations in the intracellular compartment (or the plasma) so as to maintain electrical neutrality (equal negative and positive charges) in any compartment.

conduction of nerve impulses (Fig. 2-5) and in muscle contraction.

It is important to note the relative changes of electrolytes and fluids associated with the individual's specific problem to put the actual serum value in perspective. For example, excessive sweating may result in a low serum sodium level if proportionately more sodium is lost than water or if only water is used to replace the loss. If an individual loses more water than sodium in perspiration, the serum sodium level may be high.

Hyponatremia

Normal blood sodium levels are presented inside the front cover. Hyponatremia refers to a serum sodium concentration below 3.8 to 5 mmol per liter or 135 **mil-liequivalent (mEq)** per liter.

Causes of Hyponatremia

A sodium deficit can result from direct loss of sodium from the body or from an excess of water in the extracellular compartment, resulting in dilution of sodium. Common causes of low serum sodium levels include:

1. Losses from excessive sweating, vomiting, and diarrhea
2. Use of certain **diuretic** drugs combined with low-salt diets
3. Hormonal imbalances such as insufficient aldosterone, adrenal insufficiency, and excess ADH secretion
4. Early chronic renal failure
5. Excessive water intake

THINK ABOUT 2-10

- a. A high fever is likely to cause deep, rapid respirations, excessive perspiration, and higher metabolic rate. How would this affect the fluid and electrolyte balance in the body?
- b. List several reasons why drinking a fluid containing water, glucose, and electrolytes would be better than drinking tap water after vomiting.

Effects of Hyponatremia

- Low sodium levels impair nerve conduction and result in fluid imbalances in the compartments. Manifestations include fatigue, muscle cramps, and abdominal discomfort or cramps with nausea and vomiting (Table 2-5).
- Decreased osmotic pressure in the extracellular compartment may cause a fluid shift into cells,

resulting in hypovolemia and decreased blood pressure (Fig. 2-6).

- The brain cells may swell, causing confusion, headache, weakness, or seizures.

Hypernatremia

Hypernatremia is an excessive sodium level in the blood and extracellular fluids (more than 145 mEq per liter).

Causes of Hypernatremia

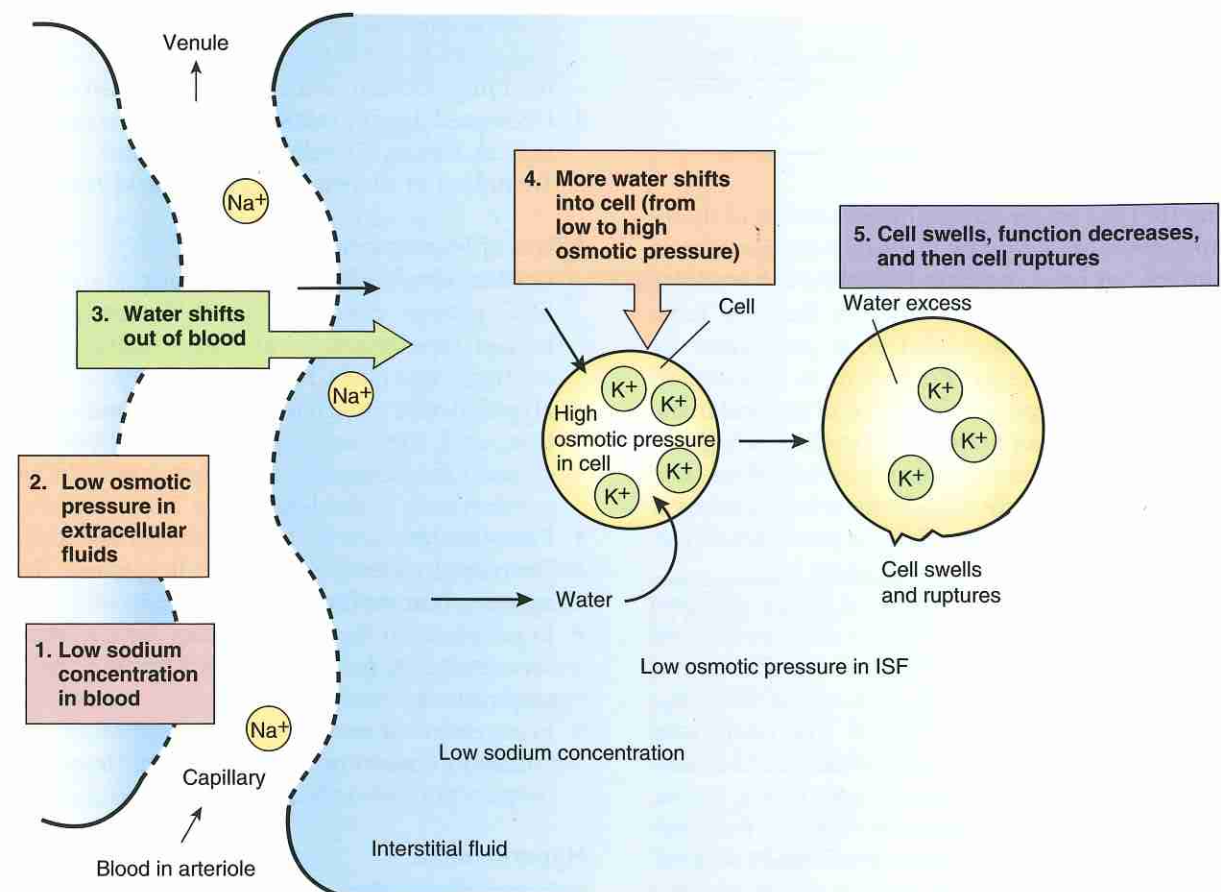
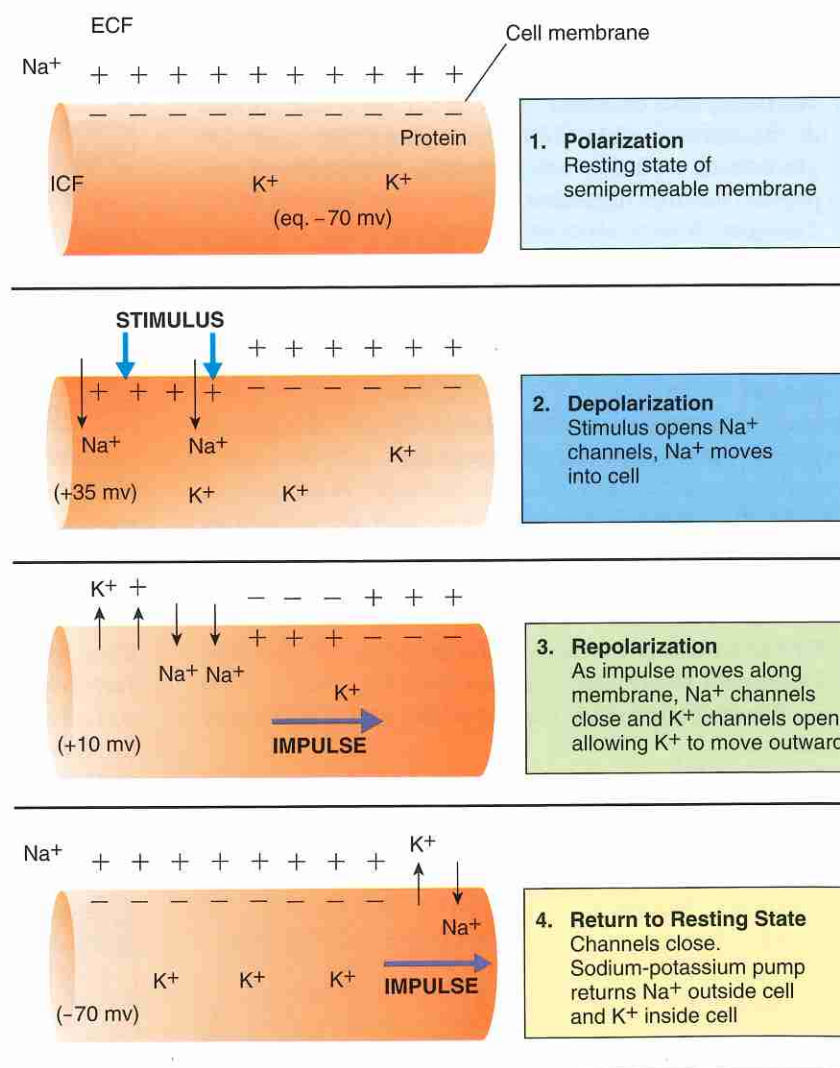
Excess sodium results from ingestion of large amounts of sodium without proportionate water intake or a loss of water from the body that is faster than the loss of sodium.

Specific causes include:

1. Insufficient ADH, which results in a large volume of dilute urine (diabetes insipidus)

TABLE 2-5 Signs of Sodium Imbalance

Hyponatremia	Hypernatremia
Anorexia, nausea, cramps	Thirst; tongue and mucosa are dry and sticky
Fatigue, lethargy, muscle weakness	Weakness, lethargy, agitation
Headache, confusion, seizures	Edema
Decreased blood pressure	Elevated blood pressure

FIGURE 2-5 Role of sodium and potassium ions in the conduction of an impulse.**FIGURE 2-6** Hyponatremia and fluid shift into cells.

2. Loss of the thirst mechanism
3. Watery diarrhea
4. Prolonged periods of rapid respiration

THINK ABOUT 2-11

Hypertatremia accompanied by an elevated hematocrit value indicates what fact about body fluids?

Effects of Hypertatremia

The major effect of hypertatremia is a fluid shift out of the cells owing to the increased osmotic pressure of interstitial or extracellular fluid; this effect is manifested by:

- Weakness, agitation
- Firm subcutaneous tissues (see Table 2-5)
- Increased thirst, with dry, rough mucous membranes
- Decreased urine output because ADH is secreted

Note that the manifestations can change depending on the cause of the problem: If the cause of hypertatremia is fluid loss caused by lack of ADH, urine output is high.

THINK ABOUT 2-12

- a. Compare the effects of aldosterone with those of ADH on serum sodium levels.
- b. List the signs and symptoms common to both hyponatremia and hypertatremia and also any signs that differentiate the two states.
- c. Explain how sodium imbalances affect cardiac function.

Potassium Imbalance**Review of Potassium**

Potassium (K^+) is a major intracellular cation, and therefore serum levels are very low (3.5 to 5 mEq per liter or 3.5 to 5 mmol per liter) compared with the intracellular concentration that is about 160 mEq per liter (see Table 2-4). It is difficult to assess total body potassium by measuring the serum level. Potassium is ingested in foods and is excreted primarily in the urine under the influence of the hormone aldosterone. Foods high in potassium include bananas, citrus fruits, tomatoes, and lentils; potassium chloride tablets may be taken as a supplement. The hormone insulin also promotes movement of potassium into cells (see Chapter 16).

Potassium levels are also influenced by the *acid-base balance* in the body; acidosis tends to shift potassium ions out of the cells into the extracellular fluids, and alkalosis tends to move more potassium into the cells (Fig. 2-7). With acidosis, many **hydrogen ions** diffuse from the blood into the interstitial fluid because of the high hydrogen ion concentration in the blood. When these hydrogen ions move into the cell, they displace potassium out of the cell to maintain electrochemical neutrality. Then the excess potassium ions in the interstitial fluid diffuse into the blood, leading to

hyperkalemia. The reverse process occurs with alkalosis. Acidosis also promotes hydrogen ion excretion by the kidneys and retention of potassium in the body. Potassium assists in the regulation of intracellular fluid volume and has a role in many metabolic processes in the cell. It is also important in nerve conduction and contraction of all muscle types, determining the membrane potential (see Fig. 2-5). Most important, abnormal potassium levels, both high and low, have a significant and serious effect on the contractions of cardiac muscle causing changes in the **electrocardiogram** (ECG) and ultimately cardiac arrest or standstill.

Hypokalemia

In hypokalemia the serum level of potassium is less than 2 mmol per liter or 3.5 mEq per liter.

Causes of Hypokalemia

Low serum potassium levels may result from:

1. Excessive losses from the body due to diarrhea
2. Diuresis associated with certain diuretic drugs; patients with heart disease who are being treated with certain diuretic drugs such as furosemide may have to increase their intake of potassium in food or take a potassium supplement because hypokalemia may increase the toxicity of heart medications such as digitalis
3. The presence of excessive aldosterone or glucocorticoids in the body (in Cushing's syndrome, in which glucocorticoids have some mineralocorticoid activity, retaining sodium and excreting potassium)
4. Decreased dietary intake, which may occur with alcoholism, eating disorders, or starvation
5. Treatment of diabetic ketoacidosis with insulin

Effects of Hypokalemia

- Cardiac **dysrhythmias** are serious, showing typical ECG pattern changes (Fig. 2-8) that indicate prolonged repolarization, and eventually may lead to cardiac arrest (see Chapter 12).
- Hypokalemia interferes with neuromuscular function, and the muscles become less responsive to stimuli, as shown by fatigue and muscle weakness commencing in the legs (Table 2-6).
- **Paresthesias** such as "pins and needles" develop.
- Decreased digestive tract motility causes decreased appetite (**anorexia**) and nausea.
- In people with severe potassium deficits, the respiratory muscles become weak, leading to shallow respirations.
- In severe cases, renal function is impaired, leading to failure to concentrate the urine, and increased urine output (polyuria) results.

Hyperkalemia

In hyperkalemia the serum level of potassium is greater than 2.6 mmol per liter or 5 mEq per liter.

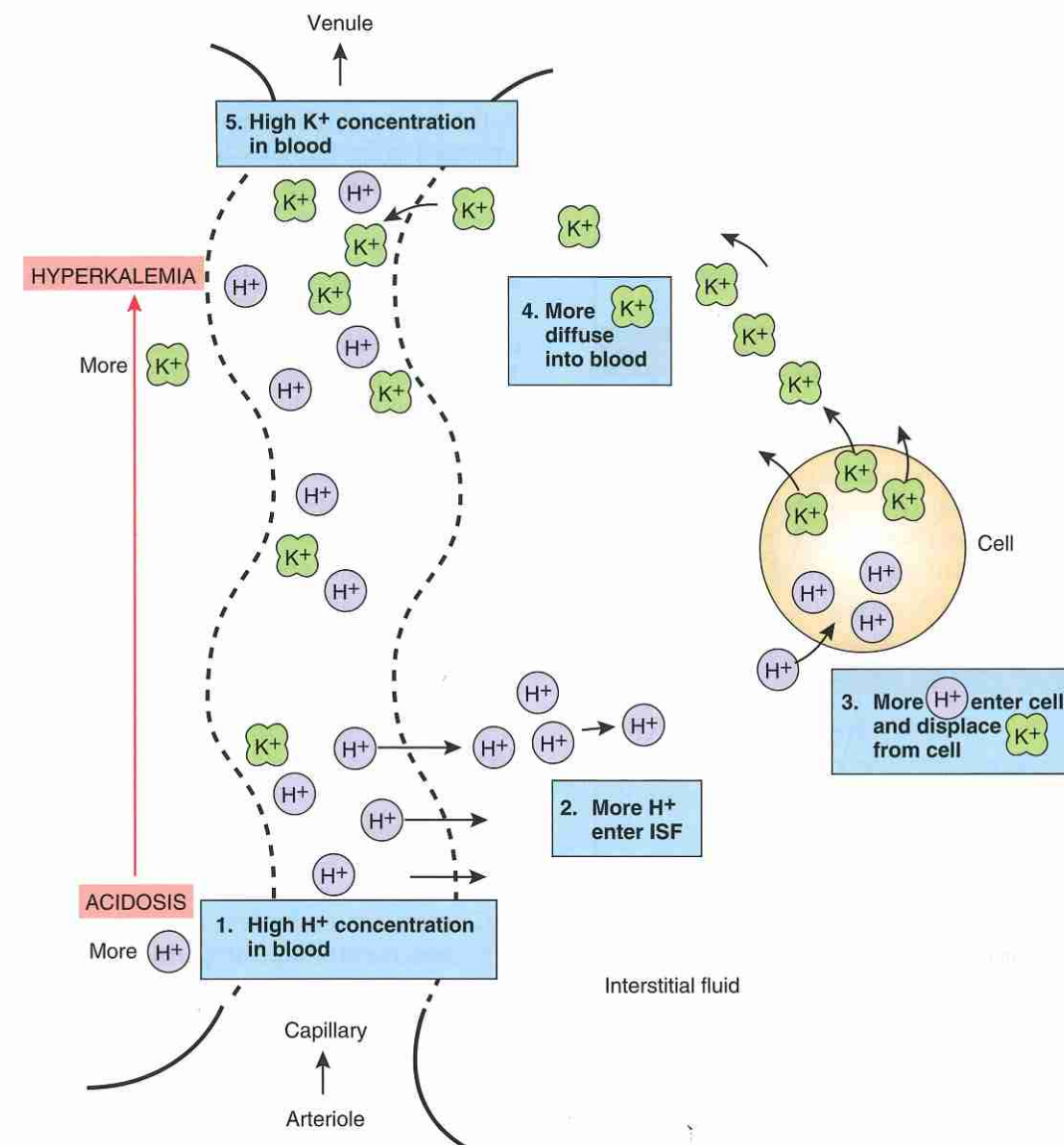


FIGURE 2-7 Relationship of hydrogen and potassium ions.

Causes of Hyperkalemia

Causes of high serum potassium levels include:

1. Renal failure
2. Deficit of aldosterone
3. Use of "potassium-sparing" diuretic drugs, which prevent potassium from being excreted in adequate amounts
4. Leakage of intracellular potassium into the extracellular fluids in patients with extensive tissue damage such as traumatic crush injuries or burns
5. Displacement of potassium from cells by prolonged or severe acidosis (see Fig. 2-7)

Effects of Hyperkalemia

- The ECG shows typical cardiac dysrhythmias (see Fig. 2-8), which may progress to cardiac arrest.

- Muscle weakness is common, progressing to paralysis as hyperkalemia advances and impairs neuromuscular activity (see Table 2-6).
- Fatigue, nausea, and paresthesias are also common.

THINK ABOUT 2-13

- a. Compare the manifestations of hyponatremia and hypokalemia.
- b. Why is any small change in potassium level considered a serious problem?

Calcium Imbalance**Review of Calcium**

Calcium (Ca^{++}) is a very important extracellular cation. Calcium is ingested in food, especially milk products,

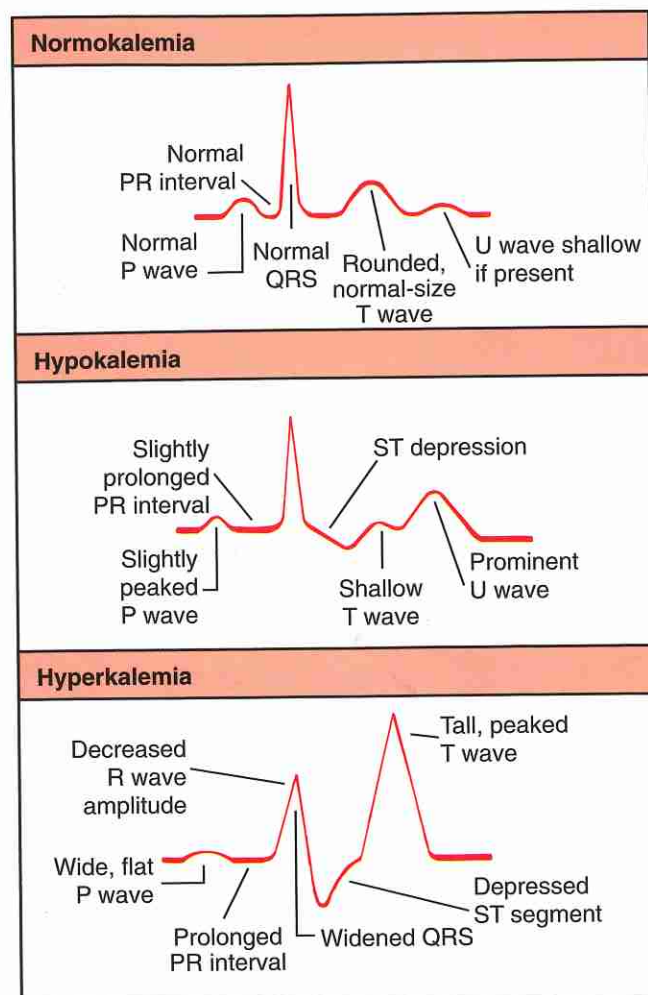


FIGURE 2-8 Electrocardiogram changes with potassium imbalance. From McCance KL, et al: *Pathophysiology: The Biologic Basis for Disease in Adults and Children*, ed 6, St. Louis, 2010, Elsevier.

TABLE 2-6 Signs of Potassium Imbalance

Hypokalemia	Hyperkalemia
Cardiac arrhythmias, cardiac arrest	Arrhythmias, cardiac arrest
Anorexia, nausea, constipation	Nausea, diarrhea
Fatigue, muscle twitch, weakness, leg cramps	Muscle weakness, paralysis beginning in legs
Shallow respirations, paresthesias	Paresthesias—fingers, toes, face, tongue
Postural hypotension, polyuria, and nocturia	Oliguria
Serum pH elevated—7.45 (alkalosis)	Serum pH decreased—7.35 (acidosis)

stored in bone, and excreted from the body in the urine and feces. Calcium balance is controlled by parathyroid hormone (PTH) and calcitonin (see Chapter 16), but is also influenced by vitamin D and phosphate ion levels. For example, low blood calcium levels stimulate the secretion of PTH, which increases calcium absorption

from the digestive tract and kidneys and promotes resorption from bone.

Vitamin D may be ingested or synthesized in the skin in the presence of ultraviolet rays, but then it must be activated in the kidneys. It promotes calcium movement from bone and intestines into blood. Most people living in northern climates have reduced vitamin D because of lack of exposure of the skin to the sun; dietary supplements are recommended to ensure adequate levels during cold weather. Sun blocking agents with an SPF greater than 15 appear to reduce vitamin D synthesis. There is also increasing evidence that vitamin D deficits may contribute to the development of multiple sclerosis and certain cancers.

Calcium and phosphate ions in the extracellular fluid have a reciprocal relationship. For example, if calcium levels are high, phosphate is low. The product of calcium and phosphate concentrations should be a constant value. If levels of both calcium and phosphate rise, crystals of calcium phosphate precipitate in soft tissue. The measured or biologically active form of calcium is the ionized form, which is not attached to plasma protein or bonded to other ions such as citrate. Alkalosis can decrease the number of free calcium ions, causing hypocalcemia.

Calcium has many important functions:

- It provides the structural strength essential for bones and teeth.
- Calcium ions maintain the stability of nerve membranes, controlling the permeability and excitability needed for nerve conduction.
- Calcium ions are required for muscle contractions.
- Calcium ions are necessary for many metabolic processes and enzyme reactions such as those involved in blood clotting.

THINK ABOUT 2-14

When nerve membranes become more permeable, is the nerve more or less easily stimulated?

Hypocalcemia

In hypocalcemia, the serum calcium level is less than 2.2 mmol per liter or below 4 mEq per liter.

Causes of Hypocalcemia

Causes of hypocalcemia include:

1. Hypoparathyroidism—decreased parathyroid hormone results in decreased intestinal calcium absorption
2. Malabsorption syndrome—resulting in decreased intestinal absorption of vitamin D or calcium
3. Deficient serum albumin
4. Increased serum pH—resulting in alkalosis

In renal failure, hypocalcemia results from retention of phosphate ion, which causes loss of calcium; also, vitamin D is not activated, thereby decreasing the intestinal absorption of calcium.

TABLE 2-7 Signs of Calcium Imbalance

Hypocalcemia	Hypercalcemia
Tetany—involuntary skeletal muscle spasm, carpopedal spasm, laryngospasm	Apathy, lethargy
Tingling fingers	Anorexia, nausea, constipation
Mental confusion, irritability	Polyuria, thirst
Arrhythmias, weak heart contractions	Kidney stones
	Arrhythmias, prolonged strong cardiac contractions, increased blood pressure

Note: Effects on bone depend on the cause of the calcium imbalance.

Effects of Hypocalcemia

- Low serum calcium levels increase the permeability and excitability of nerve membranes, leading to spontaneous stimulation of *skeletal muscle*. This leads to muscle twitching, **carpopedal spasm** (atypical contraction of the fingers), and hyperactive reflexes (Table 2-7). Chvostek's sign, spasm of the lip or face when the face is tapped in front of the ear, and Trousseau's sign, carpopedal spasm when a blood pressure cuff blocks circulation to the hand, both indicate low serum calcium and **tetany**, or skeletal muscle spasm. Severe calcium deficits may cause **laryngospasm**, which obstructs the airway. Paresthesias are common, as are abdominal cramps.
- Heart contractions become *weak* owing to insufficient calcium for muscle action, conduction is delayed, *arrhythmias* develop, and blood pressure drops.

Note that the effects of hypocalcemia on *skeletal muscle* and *cardiac muscle* differ. Skeletal muscle spasms result from the increased irritability of the nerves associated with the muscle fibers, whereas the weaker contraction of cardiac muscle (which lacks nerves) is directly related to the calcium deficit. Also, adequate calcium is stored in the skeletal muscle cells to provide for contractions, whereas contraction of cardiac muscle relies on available extracellular calcium ions passing through the calcium channels. This is the basis for action of one group of cardiac drugs.

THINK ABOUT 2-15

Explain the different effects of low serum calcium on skeletal muscle and cardiac muscle.

Hypercalcemia

In hypercalcemia the serum calcium is greater than 5 mEq per liter or greater than 2.5 mmol per liter.

Causes of Hypercalcemia

Excessive serum levels of calcium frequently result from:

1. Uncontrolled release of calcium ions from the bones due to neoplasms; malignant bone tumors may directly destroy the bone, and some tumors, such as

bronchogenic carcinoma, may secrete PTH in excess of body needs

2. Hyperparathyroidism
3. Immobility, which may decrease stress on the bone, leading to demineralization
4. Increased intake of calcium due either to excessive vitamin D or to excess dietary calcium
5. Milk-alkali syndrome, associated with increased milk and antacid intake, which may also elevate serum calcium levels

Effects of Hypercalcemia

- High serum calcium levels depress neuromuscular activity, leading to muscle weakness, loss of muscle tone, lethargy, and stupor, often with personality changes, anorexia, and nausea (see Table 2-7).
- High calcium levels interfere with the function of ADH in the kidneys, resulting in less absorption of water and in polyuria. If hypercalcemia is severe, blood volume drops, renal function decreases, nitrogen wastes accumulate, and cardiac arrest may ensue.
- Cardiac contractions increase in strength, and dysrhythmias may develop.
- Effects on bone vary with the cause of hypercalcemia. If excess PTH is the cause, bone density will be decreased, and spontaneous (pathologic) fractures may occur, particularly in the weight-bearing areas, causing bone pain. If intake of calcium is high, PTH levels will be low, and more calcium will be stored in the bone, maintaining bone strength.

THINK ABOUT 2-16

Describe the effect of each of the following conditions on serum calcium levels and on bone density: (1) hyperparathyroidism, (2) renal failure, and (3) very large intake of vitamin D.

Other Electrolytes

Magnesium

Magnesium (Mg^{++}) is an intracellular ion that has a normal serum level of 0.7 to 1.1 mmol per liter. About 50% of total body magnesium is stored in bone. Serum levels are linked to both potassium and calcium levels. Magnesium is found in green vegetables and is important in many enzyme reactions as well as in protein and DNA synthesis. Magnesium imbalances are rare.

Hypomagnesemia results from malabsorption or malnutrition, often associated with chronic alcoholism. Low serum levels may also occur with the use of diuretics, diabetic ketoacidosis, hyperparathyroidism, and hyperaldosteronism.

Low serum magnesium leads to neuromuscular hyperirritability, with tremors or chorea (involuntary repetitive movements), insomnia, personality changes, and an increased heart rate with arrhythmias.

Hypermagnesemia usually occurs with renal failure. Excess magnesium depresses neuromuscular function,

leading to decreased reflexes, lethargy, and cardiac arrhythmias.

Phosphate

Phosphate ions (HPO_4^{--} and H_2PO_4^-), are located primarily in the bone but circulate in both the intracellular and extracellular fluids. The serum level is normally 0.85 to 1.45 mmol per liter.

Phosphate is important:

- In bone and tooth mineralization
- In many metabolic processes, particularly those involving the cellular energy source, adenosine triphosphate (ATP)
- As the phosphate buffer system for acid-base balance, and it has a role in the removal of hydrogen ions from the body through the kidneys
- As an integral part of the cell membrane
- In its reciprocal relationship with serum calcium

Hypophosphatemia

Low serum phosphate levels may result from malabsorption syndromes, diarrhea, or excessive use of antacids. Alkalosis and hyperparathyroidism are other causes.

Neurologic function is impaired with low serum phosphate, causing tremors, weak reflexes (hyporeflexia), paresthesias, confusion and stupor, anorexia, and difficulty in swallowing (dysphagia).

The blood cells function less effectively—oxygen transport decreases, and clotting and phagocytosis decrease.

THINK ABOUT 2-17

Explain how serum calcium levels are affected by low phosphate levels.

Hyperphosphatemia

High serum phosphate often results from renal failure. Dialysis patients often take phosphate binders with meals to control their serum phosphate levels. Tissue damage or cancer chemotherapy may cause the release of intracellular phosphate. The manifestations of hyperphosphatemia are the same as those of hypocalcemia.

Chloride

Chloride ion (Cl^-) is the major extracellular anion with a normal serum level of 98 to 106 mmol per liter. Chloride ions tend to follow sodium because of the attraction between the electrical charge on the ions; therefore high sodium levels usually lead to high chloride levels.

Chloride and bicarbonate ions, both negatively charged, can exchange places as the blood circulates through the body to assist in maintaining acid-base balance (see Acid-Base Imbalance). As bicarbonate ions are used up in binding with metabolic acids, chloride ions diffuse out of the red blood cells into the serum to maintain the same number of negative ions in the blood (Fig. 2-9). The reverse situation can also occur

when serum chloride levels decrease, and bicarbonate ions leave the erythrocytes to maintain electrical neutrality. Thus, low serum chloride leads to high serum bicarbonate, or alkalosis. This situation is referred to as a *chloride shift*.

Hypochloremia

Low serum chloride is usually associated with alkalosis in the early stages of vomiting when hydrochloric acid is lost from the stomach.

Excessive perspiration associated with fever or strenuous labor on a hot day can lead to loss of sodium chloride, resulting in hyponatremia and hypochloremia, and ultimately, dehydration.

Hyperchloremia

Excess chloride ion may develop with the excessive intake of sodium chloride, orally or intravenously, or hypernatremia due to other causes, leading to edema and weight gain.

THINK ABOUT 2-18

- State one cause of hypomagnesemia.
- State one cause of hyperphosphatemia.
- List and describe two signs of hypophosphatemia.

Acid-Base Imbalance

Review of Concepts and Processes

Acid-base balance is essential to homeostasis because cell enzymes can function only within a very narrow pH range. The normal serum pH range is 7.35 to 7.45. Death usually results if serum pH is below 6.8 or above 7.8 (Fig. 2-10). For example, a pH of less than 7.35 depresses central nervous system function and decreases all cell enzyme activity.

When serum pH is less than 7.4, more hydrogen ions (H^+) are present, and acidosis results. A serum pH of greater than 7.4 is more basic, indicating alkalosis or the presence of fewer **hydrogen ions**. The body normally has a tendency toward acidosis, or a lower pH, because cell metabolism is constantly producing carbon dioxide (CO_2) or carbonic acid (H_2CO_3) and **nonvolatile metabolic acids** such as lactic acid, ketoacids, sulfates, or phosphates. Lactic acid results from the *anaerobic* (without oxygen) metabolism of glucose, ketoacids result from incomplete oxidation of fatty acids, and protein metabolism may produce sulfates or phosphates.

THINK ABOUT 2-19

- When hydrogen ions are decreased, is the pH higher or lower?
- State the optimal range of serum pH and effects on normal cell function if serum pH is not in the optimal range.

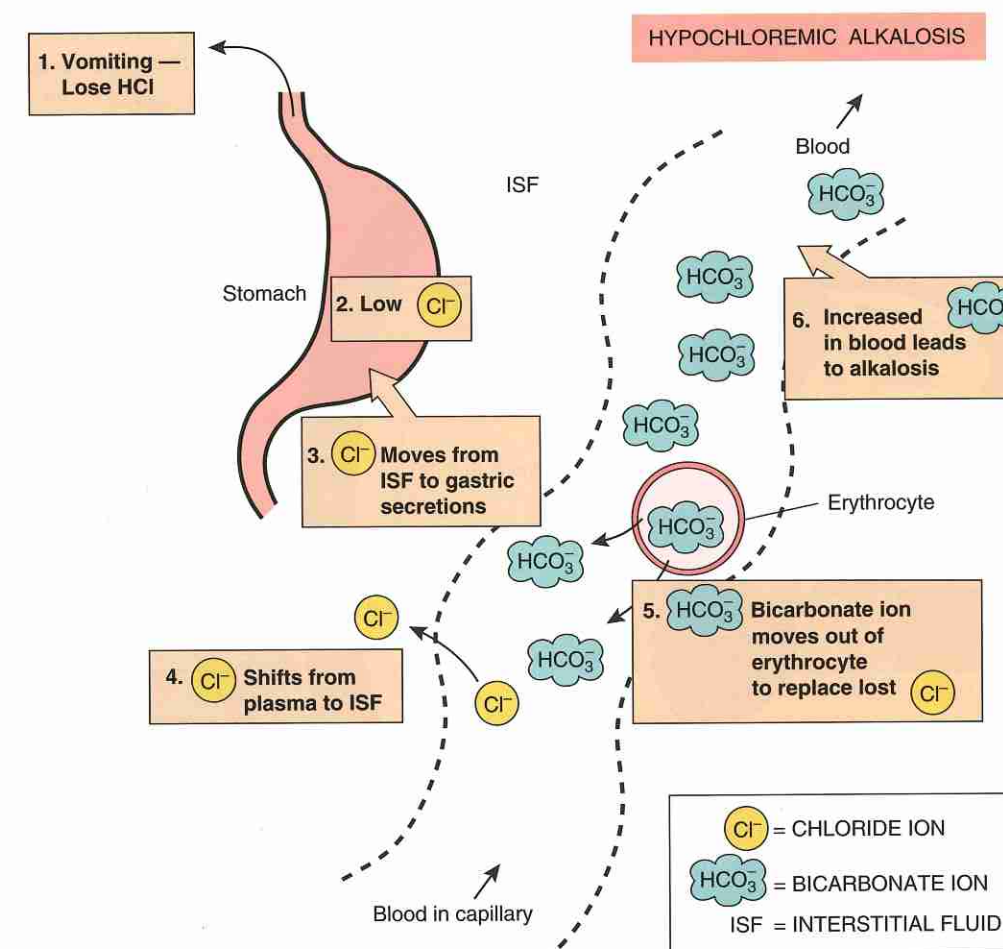


FIGURE 2-9 Schematic representation of chloride-bicarbonate shift with vomiting.

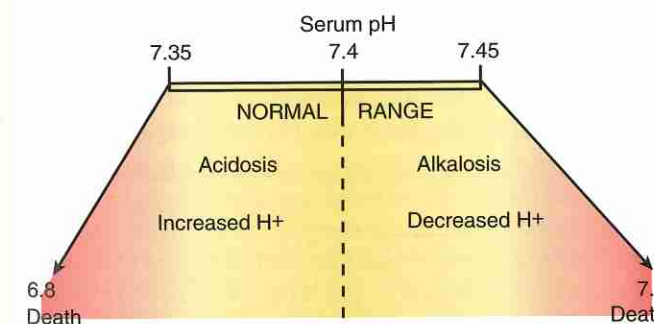


FIGURE 2-10 The hydrogen ion and pH scale.

Control of Serum pH

As the blood circulates through the body, nutrients diffuse from the blood into the cells, various metabolic processes take place in the cells using these nutrients, and metabolic wastes, including acids, diffuse from the cells into the blood (Fig. 2-11).

Three mechanisms control or compensate for pH:

- The buffer pairs circulating in the blood respond to pH changes immediately.
- The respiratory system can alter carbon dioxide levels (carbonic acid) in the body by changing the respiratory rate (see Chapter 13).

- The kidneys can modify the excretion rate of acids and the production and absorption of bicarbonate ion (see Chapter 18).

Note that the lungs can change only the amount of carbon dioxide (equivalent to the amount of carbonic acid) in the body. The kidneys are slow to compensate for a change in pH but are the most effective mechanism because they can excrete all types of acids (volatile or gaseous and nonvolatile) and can also adjust serum bicarbonate levels.

THINK ABOUT 2-20

How does the respiratory rate change when more hydrogen ions enter the blood, and how does this change affect acid levels in the body?

Buffer Systems

To control serum pH, several buffer systems are present in the blood. A buffer is a combination of a weak acid and its alkaline salt. The components react with any acids or alkali added to the blood, neutralizing them and thereby maintaining a relatively constant pH.

The body has four major buffer pairs:

- The sodium bicarbonate-carbonic acid system
- The phosphate system