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# Fluid, Electrolyte and Acid-Base Disorders

## Clinical Evaluation and Management

Second Edition

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# Preface

Like the previous edition, the second edition of *Fluid, Electrolyte and Acid–Base Disorders* provides a clear and concise understanding of the fundamentals of these clinical problems that are encountered daily in our practice. Most of the chapters have been updated and expanded. Six pertinent new chapters have been added. Also, some new study questions have been discussed.

Similar to the first edition, each chapter begins with pertinent basic physiology followed by its clinical disorders. Cases for each fluid, electrolyte, and acid–base disorder are discussed with answers. In addition, board-type questions with explanations are provided for each clinical disorder to increase the knowledge of the physician.

The revision of the book would not have been possible without the help of many students, house staff, and colleagues, who made me understand nephrology and manage patients appropriately. I am grateful to all of them. I am extremely thankful and grateful to my family for their immense support and patience. I extend my thanks to Gregory Sutorius of Springer New York for his continued support, help, and advice. Finally, I am thankful to many readers for their constructive critique of the previous edition and also expect such a positive criticism from readers of the current edition of the book.

Newark, NJ, USA Alluru S. Reddi

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# Part I

# Physiologic Basis and Management of Fluid, Electrolyte and Acid-Base Disorders

# 1 Body Fluid Compartments

Water is the most abundant component of the body. It is essential for life in all human beings and animals. Water is the only solvent of the body in which electrolytes and other nonelectrolyte solutes are dissolved. An electrolyte is a substance that dissociates in water into charged particles called *ions*. Positively charged ions are called *cations*. Negatively charged ions are called *anions*. Glucose and urea do not dissociate in water because they have no electric charge. Therefore, these substances are called *nonelectrolytes*.

## Terminology

The reader should be familar with certain terminology to understand fluids not only in this chapter but the entire text as well.

### Units of Solute Measurement

It is customary to express the concentration of electrolytes in terms of the number of ions, either milliequivalents/liter (mEq/L) or millimoles/L (mmol/L). This terminology is especially useful when describing major alterations in electrolytes that occur in response to a physiologic disturbance. It is easier to express these changes in terms of the number of ions rather than the weight of the ions (milligrams/dL or mg/dL).

Electrolytes do not react with each other milligram for milligram or gram for gram; rather, they react in proportion to their chemical equivalents. Equivalent weight of a substance is calculated by dividing its *atomic weight* by its *valence*. For example, the atomic weight of $Na^+$ is 23 and its valence is 1. Therefore, the equivalent weight of $Na^+$ is 23. Similarly, $Cl^-$ has an atomic weight of 35.5 and valence of 1. Twenty-three grams of $Na^+$ will react with 35.5 g of $Cl^-$ to yield 58.5 g of NaCl. In other words, one Eq of $Na^+$ reacts with one Eq of $Cl^-$ to form one Eq of NaCl. Because the


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electrolyte concentrations of biologic fluids are small, it is more convenient to use *milliequivalents* (mEq). One mEq is 1/1,000 of an Eq. One mEq of $Na^+$ is 23 mg.

So far, we have calculated equivalent weights of the monovalent ions (valence = 1). What about divalent ions? $Ca^{2+}$ is a divalent ion because its valence is 2. Since the atomic weight of $Ca^{2+}$ is 40, its equivalent weight is 20 (atomic weight divided by valence or 40/2 = 20). In a chemical reaction, 2 mEq of $Ca^{2+}$ (40 g) will combine with 2 mEq of monovalent $Cl^-$ (71 g) to yield one molecule of $CaCl_2$ (111 g).

Nonelectrolytes, such as urea and glucose, are expressed as mg/dL. To simplify the expression of electrolyte and nonelectrolyte solute concentrations, *Système International* (SI) units have been developed. In SI units, concentrations are expressed in terms of *moles* per liter (mol/L), where a molar solution contains 1 g molecular or atomic weight of solute in 1 L of solution. On the other hand, a *molal* solution is defined as 1 g molecular weight of solute in a kilogram of solvent. A *millimole* (mmol) is 1/1000 of a mole. For example, the molecular weight of glucose is 180. One mole of glucose is 180 g, whereas 1 mmol is 180 mg (180,000 mg/1000 = 180 mg) dissolved in 1 kg of solvent. In body fluids, as stated earlier, the solvent is water.

## Conversions and Electrolyte Composition

Table 1.1 shows important cations and anions in plasma and intracellular compartments. The table illustrates expression of electrolyte concentrations in mEq/L (conventional expression in the United States) to other expressions because ions react

**Table 1.1** Normal (mean) plasma and intracellular (skeletal muscle) electrolyte concentrations

| | | | | Concentrations | | | Intracellular concentration |
|---|---|---|---|---|---|---|---|
| Electrolyte | Mol wt | Valence | Eq wt | mg/dL | mEq/dL | mmol/L | mEq/L |
| *Cations* | | | | | | | |
| $Na^+$ | 23 | 1 | 23 | 326 | 142 | 142 | 14 |
| $K^+$ | 39 | 1 | 39 | 16 | 4 | 4 | 140 |
| $Ca^{2+a}$ | 40 | 2 | 20 | 10 | 5 | 2.5 | 4 |
| $Mg^{2+}$ | 24 | 2 | 12 | 2.5 | 2 | 1.0 | 35 |
| Total cations | – | – | – | 354.5 | 153 | 149.5 | 193 |
| *Anions* | | | | | | | |
| $Cl^-$ | 35.5 | 1 | 35.5 | 362 | 104 | 104 | 2 |
| $HCO_3^{-b}$ | 61 | – | 22 | 55 | 25 | 25 | 8 |
| $H_2PO_4^-HPO_4^{2-}$ | 31 | 1.8 | 17 | 4 | 2.3 | 1.3 | 40 |
| $SO_4^{2-}$ | 32 | 2 | 16 | 1.5 | 0.94 | 0.47 | 20 |
| Proteins | – | – | – | 7,000 | 15 | 0.9 | 55 |
| Organic acids[c] | – | – | – | 15 | 5.76 | 5.5 | 68 |
| Total anions | – | – | – | 7,437.5 | 153 | 137.17 | 193 |

[a]Includes ionized and bound $Ca^{2+}$
[b]Measured as total $CO_2$
[c]Includes lactate, citrate, etc.

**Table 1.2** Conversion between conventional and SI units for important cations and anions using a conversion factor

| Analyte | Expression of conventional units | Conventional to SI units (multiplication factor) | SI to conventional units (multiplication factor) | Expression of SI units |
|---|---|---|---|---|
| $Na^+$ | mEq/L | 1 | 1 | mmol/L |
| $K^+$ | mEq/L | 1 | 1 | mmol/L |
| $Cl^-$ | mEq/L | 1 | 1 | mmol/L |
| $HCO_3^-$ | mEq/L | 1 | 1 | mmol/L |
| Creatinine[a] | mg/dL | 88.4 | 0.01113 | μmol/L |
| Urea nitrogen | mg/dL | 0.356 | 2.81 | mmol/L |
| Glucose | mg/dL | 0.055 | 18 | mmol/L |
| $Ca^{2+}$ | mg/dL | 0.25 | 4 | mmol/L |
| $Mg^{2+}$ | mg/dL | 0.41 | 2.43 | mmol/L |
| Phosphorus | mg/dL | 0.323 | 3.1 | mmol/L |
| Albumin | g/dL | 10 | 0.1 | g/L |

[a]1 mg creatinine = 0.0884 mmol/L

mEq for mEq, and not mmol for mmol or mg for mg. Furthermore, expressing cations in mEq demonstrates that an equal number of anions in mEq are necessary to maintain electroneutrality, which is an important determinant for ion transport in the kidney. It is clear from the table that $Na^+$ is the most abundant cation, and $Cl^-$ and $HCO_3^-$ are the most abundant anions in the plasma or extracellular compartment. The intracellular composition varies from one tissue to another. Compared to the plasma, $K^+$ is the most abundant cation, and organic phosphate and proteins are the most abundant anions inside the cells or the intracellular compartment. $Na^+$ concentration is low. This asymmetric distribution of $Na^+$ and $K^+$ across the cell membrane is maintained by the enzyme, Na/K–ATPase.

Some readers are familiar with the conventional units, whereas others prefer SI units. Table 1.2 summarizes the conversion of conventional units to SI units and vice versa. One needs to multiply the reported value by the conversion factor in order to obtain the required unit.

## Osmolarity Versus Osmolality

When two different solutions are separated by a membrane that is permeable to water and not to solutes, water moves through the membrane from a lower to a higher concentrated solution until the two solutions reach equal concentration. This movement is called *osmosis*. Osmosis does not continue indefinitely but stops when the solutes on both sides of the membrane exert an equal *osmotic force*. This force is called *osmotic pressure*.

The osmotic pressure is the colligative property of a solution. It depends on the number of particles dissolved in a unit volume of solvent and not on the valence, weight, or shape of the particle. For example, an atom of $Na^+$ exerts the same osmotic pressure as an atom of $Ca^{2+}$ with a valence of 2. Osmotic pressure is expressed as *osmoles* (Osm). One *milliosmole* (mOsm) is 1/1000 of an osmole, which can be calculated for each electrolyte using the following formula:

$$\text{mOsm / L} = \frac{\text{mg / dL} \times 10}{\text{Mol wt.}}$$

*Osmolarity* refers to the number of mOsm in 1 L of solution, whereas *osmolality* is the number of mOsm in 1 kg of water. However, osmolality is the preferred physiological term because the colligative property depends on the number of particles in a given weight (kg) of water.

The osmolality of plasma is largely a function of $Na^+$ concentration and its anions (mainly $Cl^-$ and $HCO_3^-$) with contributions from glucose and urea nitrogen. Since each $Na^+$ is paired with a univalent anion, the contribution from other cations such as $K^+$, $Ca^{2+}$, and $Mg^{2+}$ to the osmolality of plasma is generally not considered. Therefore, the plasma osmolality is calculated by doubling $Na^+$ and including the contribution from glucose and urea nitrogen (generally expressed as blood urea nitrogen or BUN), as follows:

$$\text{Osmolality (mOsm / kg } H_2O) = 2[Na^+] + \frac{Glucose + BUN}{18 \quad 2.8}$$

where 18 and 2.8 are derived from the molecular weights of glucose and urea, respectively. Because serum glucose and urea concentrations are expressed as mg/dL, it is necessary to convert these concentrations to mOsm/L by dividing the molecular weights of glucose (180) or urea nitrogen (28) by 10. Normal serum values are $Na^+$ = 142 mEq/L, glucose = 90 mg/dL, and urea nitrogen = 12 mg/dL. The serum osmolality, therefore, is:

$$\text{mOsm / kg } H_2O = 2[142] + \frac{90 + 12}{18 \quad 2.8} = 284 + 5 + 4 = 293$$

The normal range is between 280 and 295 mOsm/kg $H_2O$ (some use the value 285 ± 5 mOsm/kg $H_2O$). Inside the cell, the major electrolyte that contributes to the osmolality is $K^+$.

## Total Osmolality Versus Effective Osmolality

The term *total serum* or *plasma osmolality* should be distinguished from the term *effective* osmolality or *tonicity*. Tonicity is determined by the concentration of those solutes that remain outside the cell membrane and cause osmosis. $Na^+$ and glucose remain in the extracellular fluid compartment (see the following text) and cause water movement. These solutes are, therefore, called *effective osmolytes* and thus contribute to plasma tonicity. Mannitol, sorbitol, and glycerol also behave as effective osmolytes. On the other hand, substances that can enter the cell freely do not maintain an osmotic gradient for water movement. Urea can penetrate the membrane easily and therefore does not exert an osmotic force that causes water movement. For this reason, urea is referred to as an *ineffective osmolyte*. Urea, therefore, does not contribute to tonicity. Ethanol and methanol also behave like urea. The contribution of urea is thus not included in the calculation of effective osmolality. Effective osmolality is calculated using the following equation:

$$\text{Effective osmolality}\,(\text{mOsm / kg } H_2O) = 2[\text{Na}] + \frac{\text{glucose}}{18}$$

The normal range for effective osmolality is between 275 and 290 mOsm/kg $H_2O$.

### Isosmotic Versus Isotonic

The term *isosmotic* refers to identical osmolalities of various body fluids, e.g., plasma versus cerebrospinal fluid. However, when discussing osmolalities of solutions used clinically to replace body fluid losses, the terms *isotonic*, *hypotonic*, or *hypertonic* are used. A solution is considered isotonic if it has the same osmolality as body fluids. When an isotonic solution is given intravenously, it will not cause red blood cells to change in size. However, a hypotonic solution will cause red blood cells to swell, and a hypertonic solution will cause red blood cells to shrink. Isotonic solution that is commonly used to replace loss of body fluids is 0.9% NaCl (normal saline).

## Body Fluid Compartments

As stated, the major body fluid is water. In a lean individual, it comprises about 60% of the total body weight. Fat contains less water. Therefore, in obese individuals the water content is 55% of the total body weight. For example, a 70 kg lean person contains 42 L of water ($70 \times 0.6 = 42$ L). This total body water is distributed between two major compartments: the *extracellular fluid* (ECF) and *intracellular fluid* (ICF) compartments. About one-third (20%) of the total amount of water is confined to the ECF and two-thirds (40%) to the ICF compartment (Fig. 1.1). The ECF compartment, in turn, is divided into the following subdivisions:

1. Plasma
2. Interstitial fluid and lymph
3. Bone and dense connective tissue water
4. Transcellular (cerebrospinal, pleural, peritoneal, synovial, and digestive secretions)

Of these subdivisions, the plasma and interstitial fluids are the two most important because of constant exchange of fluid and electrolytes between them. Plasma and interstitial fluid are separated by the capillary endothelium. Plasma circulates in the blood vessels, whereas the interstitial fluid bathes all tissue cells except for the formed elements of blood. For this reason, Claude Bernard, the French physiologist, called

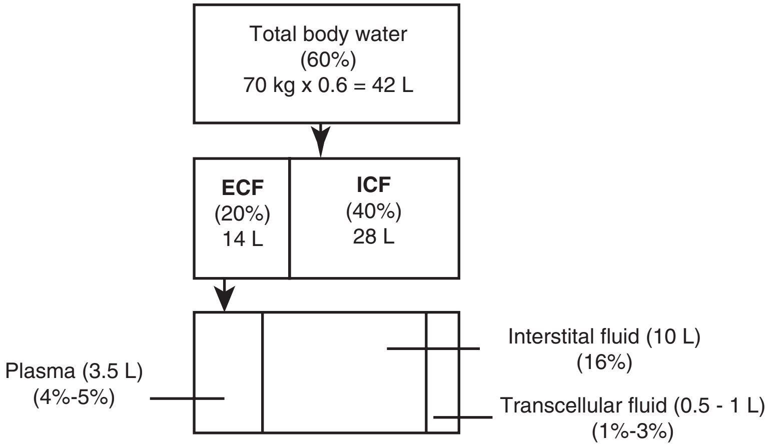


**Fig. 1.1** Approximate distribution of water in various body fluid compartments: *ECF* extracellular fluid, *ICF* intracellular fluid. A 70 kg lean man has 42 L of water, assuming the total body water content is 60% of the body weight (70 × 0.6 = 42 L)

the interstitium "the true environment of the body" (*milieu interieur*). Figure 1.1 summarizes the distribution of water in various body fluid compartments.

## Water Movement Between ECF and ICF Compartments

In a healthy individual, the ECF and ICF fluids are in osmotic equilibrium. If this equilibrium is disturbed, water moves from the area of lower solute concentration to the area of greater solute concentration in order to reestablish the osmotic equilibrium. The following *Darrow–Yannet* diagram illustrates this point (Fig. 1.2). Let us assume that a lean male weighs 70 kg and the osmolality in both ECF and ICF compartments is 280 mOsm/kg $H_2O$. His total body water is 60% of the body weight; therefore, the total body water is 42 L. Of this amount, 28 L are in the ICF and 14 L are in the ECF compartment. What happens to osmolality and water distribution in each compartment if we add 1 L of water to the ECF? Initially, this additional 1 L of $H_2O$ would not only increase the ECF volume but it would also decrease its osmolality from 280 to 261 mOsm/kg $H_2O$ (total ECF mOsm (280 × 14 = 3,920 mOsm)/new ECF water content (15 L) = 3,920/15 = 261 mOsm). Since the ICF osmolality is higher than this new ECF osmolality, water will move into the ICF until a new osmotic equilibrium is reached. As a result, the ICF volume also increases. The net result is an increase in volume and a decrease in osmolality in both compartments. These changes are shown in Fig. 1.2.

Thus, addition of 1 L of water to ECF decreases the final osmolality to 273 mOsm/kg $H_2O$ (total body mOsm (280 × 42 = 11,760)/new total body water (43 L) = 11,760/43 = 273 mOsm) and increases water content in the ICF by 0.72 L and ECF by 0.28 L (ICF mOsm (280 × 28 = 7,840)/new osmolality (273) = 7,840/273 = 28.72 L). It should be noted that these changes are minimal in

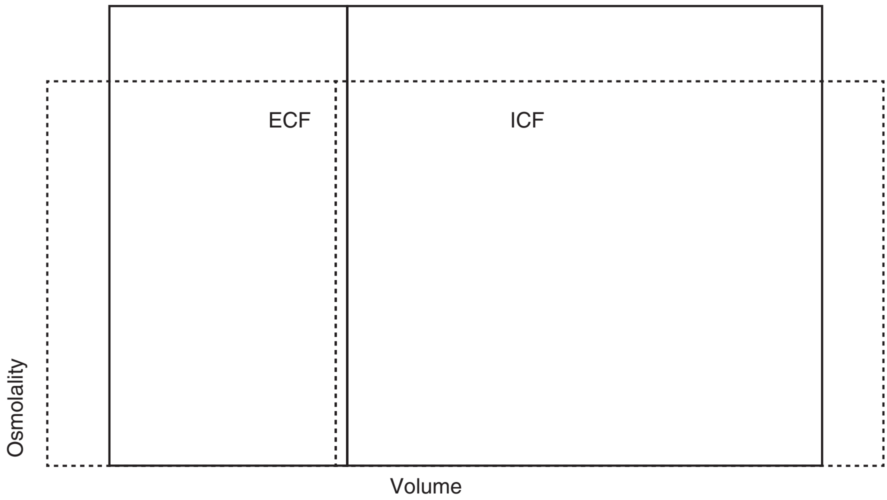


**Fig. 1.2** Darrow–Yannet diagram showing fluid and osmolality changes in the ECF and ICF compartments following addition of 1 L of water to the ECF. Initial state is shown by a *solid line* and final state by a *dashed line*. Width represents the volume of the compartments, and height represents osmolality

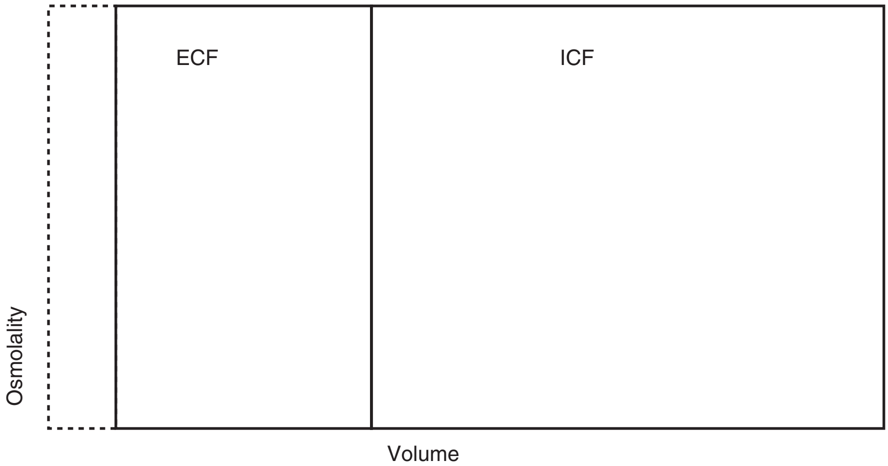


**Fig. 1.3** Darrow–Yannet diagram showing volume change following addition of 1 L of isotonic NaCl

an individual with normal renal function, since the kidneys compensate for these changes by excreting excess water in order to maintain fluid balance.

Let us use another example. What would happen if 1 L of isotonic (0.9%) saline is added instead of pure water to ECF? Since 0.9% saline is isotonic, it does not cause water movement. Therefore, body osmolality does not change. However, this isotonic saline will remain in the ECF compartment and cause its expansion, as shown in Fig. 1.3. Healthy individuals excrete saline to maintain normal ECF volume.

## Study Questions

**Case 1** A 28-year-old type 1 diabetic male patient is admitted to the hospital for nausea, vomiting, and abdominal pain. His weight is 60 kg and the initial laboratory values are:

$Na^+$ = 146 mEq/L
$K^+$ = 5 mEq/L
$HCO_3^-$ = 10 mEq/L
BUN = 70 mg/dL
Glucose = 540 mg/dL

*Question 1* Calculate this patient's plasma osmolality and explain his fluid shift.

*Answer* Plasma osmolality is calculated by using the following formula:

$$\text{Plasma osmolality} = 2[\text{Plasma Na}^+] + \frac{\text{Glucose}}{18} + \frac{\text{BUN}}{2.8}$$
$$= 2[146] + \frac{540}{18} + \frac{70}{2.8} = 347\ \text{mOsm / kg H}_2\text{O}$$

Because plasma osmolality is elevated, water initially moves out of cells, i.e., from the ICF to the ECF compartment, and causes expansion of the latter until a new steady state is reached. The patient receives insulin and normal saline. Repeat blood chemistry shows:

$Na^+$ = 140 mEq/L
$K^+$ = 4.2 mEq/L
$HCO_3^-$ = 20 mEq/L
BUN = 40 mg/dL
Glucose = 180 mg/dL

*Question 2* Does increase in BUN contribute to fluid shift?

*Answer* No. Although BUN contributes 14 mOsm to plasma osmolality, no fluid shift will occur on its account. The lack of fluid shift is due to its ineffectiveness as an osmole, i.e., urea crosses the cell membrane easily and does not establish a concentration gradient.

*Question 3* Calculate this patient's plasma tonicity (effective plasma osmolality).

*Answer* Tonicity is a measure of the osmotically active particles from $Na^+$ and glucose. Therefore, the serum concentration of BUN is not included in the calculation. The plasma tonicity is:

$$2[140]+\frac{180}{18} = 290 \text{ mOsm / kg } H_2O$$

**Case 2** A 30-year-old patient with AIDS (acquired immunodeficiency syndrome) is admitted for weakness, weight loss, fever, nausea, vomiting, and mental irritability. His blood pressure is low. The diagnosis of Addison's disease (a disease caused by deficiency of glucocorticoid and mineralocorticoid hormones produced by the adrenal cortex) is made. Admitting laboratory values are as follows:

$Na^+$ = 120 mEq/L
$K^+$ = 6.2 mEq/L
$Cl^-$ = 112 mEq/L
$HCO_3^-$ = 14 mEq/L
BUN = 70 mg/dL
Glucose = 60 mg/dL

*Question 1* Explain the fluid shift in this patient.

*Answer* This patient lost $Na^+$ than water from the ECF compartment due to mineralocorticoid (aldosterone) deficiency. As a result of low serum $Na^+$, his plasma osmolality is low. Decreased plasma osmolality causes water to move from the ECF to the ICF compartment. The net result is the contraction of ECF volume and a transient increase in ICF volume and reduction in osmolality in both compartments, as shown in Fig. 1.4.

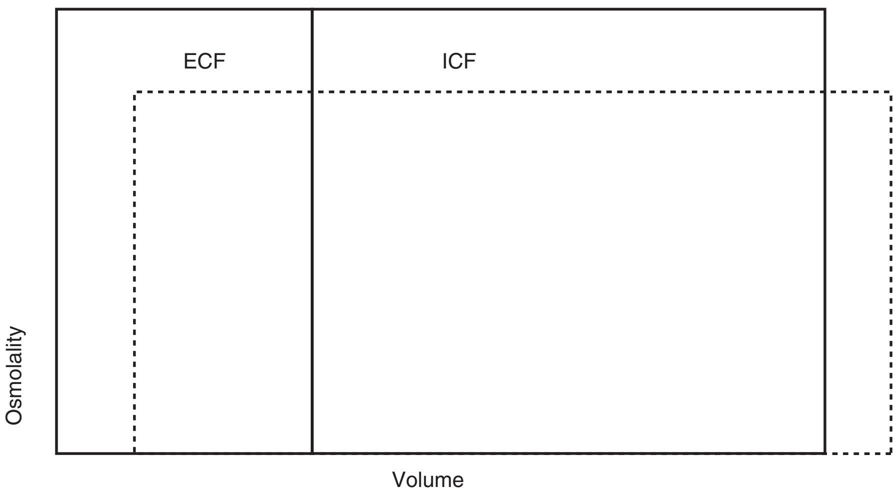


**Fig. 1.4** The net result in this patient is the contraction of ECF volume and a transient increase in ICF volume and reduction in osmolality in both compartments. Initial state is represented by *solid line* and final state by *dashed line*