Body Fluid Compartments 7.1

Learning Objectives

- Calculate the volume of distribution of a material based on the dilution principle
- Define the term "marker" for volumes of distribution
- List one marker for plasma, extracellular fluid, and total body water
- Calculate the ICF volume from total body water and ECF
- Calculate ISF volume from ECF and plasma volume
- Define "lean body mass"
- Give approximate values for plasma, ISF, and ICF volumes as a percent of LBM
- Describe how ISF and plasma exchange materials
- Describe how ECF and ICF equilibrate osmotic pressure
- Using Darrow—Yannet diagrams, predict the consequences of adding or subtracting water, salt, or saline from the ECF on fluid compartment size and osmolarity
- Describe how changes in plasma can alter all body fluid compartments' volume and composition

FICK'S DILUTION PRINCIPLE ALLOWS DETERMINATION OF BODY FLUID COMPARTMENTS

The physiological regulation of the amount and distribution of water in the body is critically important. We have powerful mechanisms for insuring its proper regulation including thirst and other behavioral responses and the operation of our renal systems. Before we discuss this in detail, we need to know something about how much water is there, and where it is.

The amount of water in any space can be measured by **Fick's dilution principle**. In this method, a known amount of a measurable material is injected into a person and, after the material has had time to become evenly distributed, the concentration of the material in an aliquot of the plasma is measured. The volume of distribution is calculated from the simple formula:

$$\text{Volume} = \frac{\text{amount}}{\text{concentration}} \quad [7.1.1]$$

The volume calculated by this method is the **volume of distribution** of the material that was injected. Different materials have access to different compartments. **Deuterium oxide**, for example, is a chemical nearly identical to water and it distributes itself according to the **total body water (TBW)**. **Inulin** is a polymer of fructose that readily crosses capillary walls but cannot enter cells. Thus it distributes itself through, and is a **marker** for, the **extracellular volume**. Evans' blue dye is substance that binds to plasma proteins and is restricted to the space occupied by these proteins. On the time scale of these measurements, Evans' blue dye is restricted to the plasma because the plasma proteins largely do not leave the vasculature. Thus Evans' blue dye marks the **plasma volume**.

The calculation of the volume of distribution given in Eqn (7.1.1) is valid only if the amount of marker material in the volume of distribution is known at the time at which the concentration is measured, and only if the marker is homogeneously distributed in that volume. In some cases, some of the marker may be lost to the urine, gastrointestinal tract, skin, or lungs during the time during which equilibration takes place. These losses must be accounted for in order for the volume of

EXAMPLE 7.1.1 Determine the TBW from the Distribution of D_2O

Seven grams of D_2O was injected into a healthy 70-kg adult (100 mg kg^{-1} body weight). After a 2-hour period of equilibration, the concentration of D_2O in a sample of plasma was measured by using the isotope ratio ($^2H/^1H$) determined in a mass spectrometer. Calculations showed the $[D_2O]$ in the plasma was

$$[D_2O] = 0.0166 \text{ g dL}^{-1}$$

During the 2 hours, some of the D_2O was lost in the urine, lungs, and skin. Normally these losses are not large, averaging about 0.4% over a 2-hour period. If we assume the losses are 0.4%, we can calculate the volume of distribution of D_2O at the time of measurement as

$$\begin{aligned}\text{Volume} &= 7 \text{ g } (1 - 0.004)/0.0166 \text{ g dL}^{-1} \\ &= 6.972 \text{ g}/0.0166 \text{ g dL}^{-1} = 420 \text{ dL} = \mathbf{42.0\ L}\end{aligned}$$

This is the volume of distribution of D_2O, taken as an estimate of the **TBW**.

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distribution to be accurately determined. Example 7.1.1 illustrates this for the determination of TBW.

INULIN MARKS THE EXTRACELLULAR FLUID; EVANS' BLUE DYE MARKS PLASMA

If we inject our test person with a solution of **inulin** instead of D_2O, we find that the plasma concentration of inulin rapidly falls from its initial value, losing about 64% of its initial value within 2 hours. The inulin is rapidly excreted in the urine and the plasma inulin concentration does not reach a stable value with a single injection. The calculation of the volume of distribution of inulin by Eqn (7.1.1) is valid only if the amount of inulin in the volume of distribution is known at the time the concentration is determined, and only if the distribution of inulin in that volume is homogeneous. We can get around this problem by infusing a solution of inulin at a constant rate to reach a steady-state plasma concentration at which the rate of inulin infusion exactly balances the rate of inulin excretion in the urine (see Figure 7.1.1). When this steady state is reached, the infusion is stopped and the bladder is emptied. From then on, the plasma concentration of inulin falls as inulin is excreted in the urine. We determine the total amount of inulin in the body at the time of steady-state inulin concentration by collecting all of the urine during the next 4–6 hours and measuring its volume and the urinary concentration of inulin. Eqn (7.1.1) can then be used to calculate the volume of distribution of inulin. In this case, the amount of inulin is experimentally determined as the total amount excreted after stopping the infusion, and its concentration is the steady-state concentration. When this procedure is performed, the volume of distribution of inulin is found to be about 14 L or about one-third of the TBW.

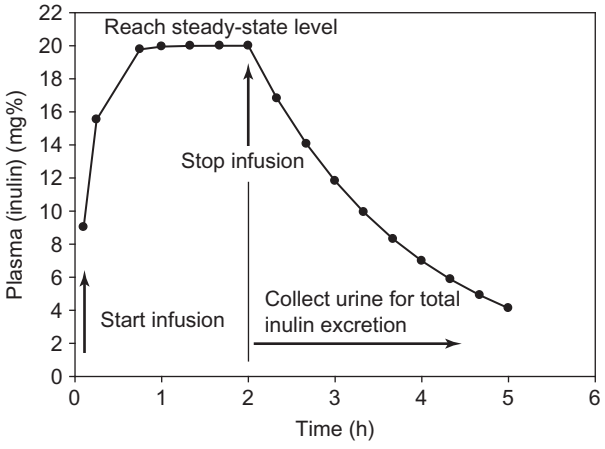

FIGURE 7.1.1 Determination of the volume of distribution of inulin by infusing an inulin solution continuously until a steady-state plasma concentration is reached. At this point, the bladder is emptied and the infusion is stopped. All urine is then collected for 4–6 hours. During this time all of the inulin in the body is excreted. This can be determined by measuring the volume of the urine and its concentration of inulin. Then Eqn (7.1.1) can be used to determine the volume of distribution.

Now suppose that we inject a solution of Evans' blue dye. In this case, the clearance of Evans' blue dye from the plasma is much slower than that of inulin, and some 4–6% of the material is lost from the plasma each hour. If we measure the plasma concentration of the dye 10 minutes after injection (using spectrophotometry and the absorbance of plasma at 627 nm, subtracting the absorbancy at 627 nm of a plasma sample taken before injection of dye), there will be sufficient time for equilibration of the dye within its volume of distribution without large losses of material. When we calculate the volume of distribution under these circumstances, we find that Evans' blue dye distributes in a volume of about 3.5 L or about 5% of the body weight.

THE MAIN FLUID COMPARTMENTS ARE THE *INTRACELLULAR* COMPARTMENT, THE *INTERSTITIAL* COMPARTMENT, AND THE *PLASMA*

Table 7.1.1 shows the three markers we have discussed here and their volume of distribution. The volumes of distribution for D_2O, inulin, and Evans' blue are different because only certain fluid compartments are accessible to these materials. D_2O distributes itself like water and it is a *marker* for the total body water or TBW. Inulin is a polymer of fructose that can cross the capillary wall but cannot penetrate cells. Thus the intracellular volume is inaccessible to inulin, but inulin can get just about everywhere else. Inulin is a *marker* for the extracellular fluid compartment or ECF. Evans' blue is a dye that binds to plasma proteins that are confined to the intravascular volume, the volume contained in the closed circulatory system. Thus Evans' blue dye is a *marker* for the volume of the plasma, the fluid contained within the circulatory system that is not within the cells of the blood. These relationships are shown in Figure 7.1.2. One of the main fluid compartments is not directly measured using these markers. This is the **interstitial fluid (ISF)** that lies between the cells and the vasculature.

Clearly, the volume of fluid that is part of the TBW but that is not extracellular is the intracellular fluid (ICF). From Figure 7.1.2, it is clear that we can calculate the ICF volume as

TABLE 7.1.1 Volumes of Distribution of D_2O, Inulin, and Evans' Blue Dye

Marker	Volume of Distribution (L)	Percent of Body Weight	Fluid Compartment
D_2O	42	60	Total body water
Inulin	14	20	Extracellular fluid
Evans' blue dye	3.5	5	Plasma

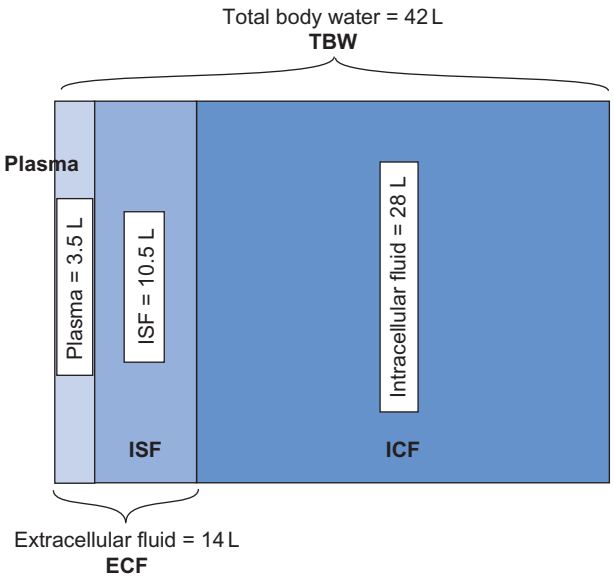

FIGURE 7.1.2 The relative volumes of distribution of D_2O, which marks the total body water, inulin, which marks the extracellular fluid, and Evans' blue, which marks the plasma.

[7.1.2] $$ICF = TBW - ECF$$

where ICF is the intracellular fluid volume, TBW is the total body water, and ECF is the extracellular fluid volume. In this case, the ICF is 42 − 14 L = 28 L. Most of the body's water is inside the cells that make up the body. Figure 7.1.2 also makes it clear that there is some fluid that is outside the cells but is not contained within the vasculature. This fluid is called the **interstitial fluid**. From Figure 7.1.2, we can see that we can calculate the ISF volume as

[7.1.3] $$ISF = ECF - plasma$$

In the case that we consider here, the ISF is 14 − 3.5 L = 10.5 L.

The three fluid compartments shown in Figure 7.1.2, the **plasma**, the **ISF**, and the **ICF**, comprise the three major fluid compartments of the body. There are a variety of smaller compartments such as the **intraocular fluid**, **cerebrospinal fluid**, **synovial fluid**, and **gastrointestinal secretions**. These smaller compartments are sometimes called **transcellular fluid compartments** because they are separated from the plasma by a cellular layer other than the capillaries. Although these compartments usually are smaller than the major fluid compartments, sometimes their volume can become much larger, and there are pathological conditions that can be associated with each of them. Examples of these include **glaucoma**, **hydrocephaly**, and **diarrhea**. Despite their importance, we will not discuss them further.

THE TBW VARIES WITH BODY COMPOSITION

Most of the soft tissues are 70−80% water, but bone and fat contain little water (see Table 7.1.2). Many different tissues contribute to overall body composition and the mixture of these tissues leads to the normal body composition of 60% water by weight. This number is a generalization and clearly does not pertain to all people because people differ considerably in their bodily composition.

TABLE 7.1.2 Percent Water Composition by Weight of Different Tissues

Tissue	Percent Water by Weight
Muscle	76
Blood	83
Brain	75
Liver	68
Bone	22
Fat	10

In the early 1940s, motivated in part by standards used for admission to the US armed forces, Albert Behnke proposed that the body could be partitioned into two parts: (1) **lean body mass**, **LBM**, and (2) excess fat. The LBM included "essential fat" that was necessary for health and included the fat in the brain, spinal cord, bone marrow, and internal organs. Originally the essential fat was set at 10% of body weight, but it has since been revised to about 3%. The LBM is typically 73% water by weight. This percentage is a consequence of the definition of LBM. Thus the LBM of any individual can be calculated from the TBW as

[7.1.4] $$\text{Lean body mass} = \frac{TBW}{0.73}$$

The "excess body fat" is defined as the body weight in excess of the LBM. We calculate it as

[7.1.5] $$\text{Excess body weight} = \text{body weight} - LBM$$

The criterion for obesity is somewhat arbitrary. Where does one draw the line between obese and "overfat" in a continuous distribution? A common **definition of obesity is body fat in excess of 20% of total body weight**.

WATER COMPOSITION OF THE LBM VARIES WITH AGE AND SEX

Aging is a gradual process of desiccation. This begins soon after birth. The LBM of the neonate is 81% water; that of the adult is 73% water, as described above. There appears to be little change in the composition of the LBM from early adulthood to middle age. The change in relative water content is additive to the gradual increase in body fat seen in many people with age, so that the TBW gradually decreases with age when expressed as a percentage of body weight.

Generally speaking, females have less TBW when expressed as a percentage of body weight. This is generally attributed to the greater contribution of body fat to

	Cell	Interstitial fluid	Plasma
Na^+	10	142	142
K^+	145	4	4
Ca^{2+}	0.0002	2.8	5
Mg^{2+}	1	1.4	1.5
Total cations	156	150.2	152.5
HCO_3^-	10	27	24
Proteins	60	4	18.5
Phosphates	50	1.2	2
Cl^-	5	111	100.5
Other anions	31	7.0	7.5
Total anions	156	150.2	152.5

FIGURE 7.1.3 Composition of the plasma, interstitial fluid, and typical cell fluid. All values are in milliequivalents per liter. The equivalent is a chemical unit meaning the amount of something required to remove or supply 1 mol of H^+ ions, or supply or remove 1 mol of electrons in a redox reaction. The concentration unit of mEq L^{-1} is related to mmol L^{-1} by the charge on an ion: mEq $L^{-1} = |z| \times$ mM, where z is the valence (+/− integer) for the ion. Here $z =$ mEq mmol^{-1}. Thus 1 mM $Ca^{2+} = 2$ mEq L^{-1}.

the total body weight rather than any difference in the composition of the LBM.

THE FLUID COMPARTMENTS CORRESPOND TO ANATOMIC COMPARTMENTS

The three major fluid compartments exist in well-defined anatomical regions that have barriers to the direct transfer of material. The plasma is separated from the ISF by the layer of cells that forms the capillary walls. The ISF is separated from the cells by the aggregate of the membranes of the cells of the body. These barriers are not impervious, however, and exchange of both solutes and water across these barriers is required for the continued health of the cells. As an example, the capillary wall effectively restricts transfer of plasma proteins from the plasma to the interstitial space, whereas most small molecular weight solutes and water can cross the capillary wall fairly easily. The result is that the ISF is low in protein compared to the plasma, but otherwise it is nearly identical to plasma. However, not all capillary beds are identical (see Chapter 5.10) and the interstitial fluid composition varies among the tissues. The approximate composition of the fluid compartments is shown in Figure 7.1.3.

BODY FLUIDS OBEY THE PRINCIPLE OF *MACROSCOPIC ELECTRONEUTRALITY*

Because electrical forces are so large, separation of charges within an electrolytic solution is not possible because the ions would quickly move to neutralize charge separation. The practical consequence of this is that the sum of all positive charges in a solution must be equal to the sum of all the negative charges:

$$\sum_i C_i^+ = \sum_i C_i^- \qquad [7.1.6]$$

where i indicates each of the chemical species in the solution. This principle is called **macroscopic electroneutrality**. Its application is evident in Figure 7.1.3 in which the total cation concentration is the same as the total anion concentration. It is possible for there to be local separation of charge, but the fraction of charge separated in this way is very small and not noticeable on the macroscopic scale. Separation of charge across a membrane produces the membrane potential, and this is extremely important, but the imbalance in charge on the macroscopic scale is tiny.

THE GIBBS–DONNAN EQUILIBRIUM ARISES FROM UNEQUAL DISTRIBUTION OF IMPERMEANT IONS

The major difference in composition between plasma and ISF (see Figure 7.1.3) is that the plasma contains much higher concentrations of large, negatively charged proteins. This difference also produces differences in the concentration of small diffusible ions. To analyze this situation, we begin with a hypothetical example shown in Figure 7.1.4.

We can write the free energy change for Na^+ transfer across the membrane

$$\begin{aligned}\Delta\mu_{Na_o \Rightarrow Na_i} &= \mu_{Na_i} - \mu_{Na_o} \\ &= \mu^0 + RT\ln[Na^+]_i + z\Im\psi_i \\ &\quad - \mu^0 - RT\ln[Na^+]_o - z\Im\psi_o \\ &= RT\ln\frac{[Na^+]_i}{[Na^+]_o} + z\Im(\psi_i - \psi_o)\end{aligned} \qquad [7.1.7]$$

and we can write the free energy for Cl^- transfer similarly as

$$\begin{aligned}\Delta\mu_{Cl_o \Rightarrow Cl_i} &= \mu_{Cl_i} - \mu_{Cl_o} \\ &= \mu^0 + RT\ln[Cl^+]_i + z\Im\psi_i - \mu^0 \\ &\quad - RT\ln[Cl^+]_o - z\Im\psi_o \\ &= RT\ln\frac{[Cl^+]_i}{[Cl^+]_o} + z\Im(\psi_i - \psi_o)\end{aligned} \qquad [7.1.8]$$

At equilibrium, $\Delta\mu = 0$ for any process. Setting both Eqns (7.1.7) and (7.1.8) to zero, we get

$$\begin{aligned}-\frac{RT}{z\Im}\ln\frac{[Na^+]_i}{[Na^+]_o} &= (\psi_i - \psi_o) \\ -\frac{RT}{z\Im}\ln\frac{[Cl^+]_i}{[Cl^+]_o} &= (\psi_i - \psi_o)\end{aligned} \qquad [7.1.9]$$

Recalling that $z = 1$ for Na^+ and $z = -1$ for Cl^{-1} and that $-\ln a = \ln 1/a$, we rewrite Eqn (7.1.9) as

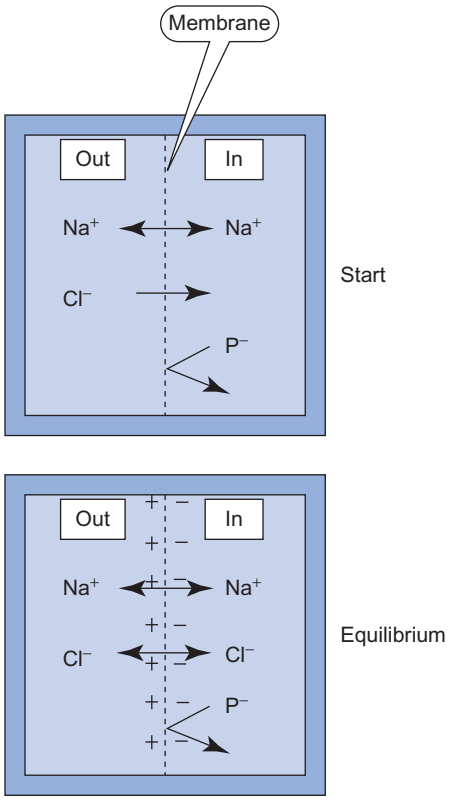

FIGURE 7.1.4 Establishment of the Gibbs–Donnan equilibrium. Initially, a membrane separates a solution of NaCl from NaP, where P is an impermeant anion. Initially, $[Cl^-]$ is higher on the left than on the right, so it diffuses to the right. Movement of Cl^- carries a charge so that a negative charge builds up on the right. This negative charge attracts the Na^+ ions, which follow the Cl^-. Eventually a concentration difference in both Cl^- and Na^+ is established across the membrane and their gradients are in equilibrium with the membrane potential so that the net flux of both ions goes to zero. The ratio of the ions at equilibrium is the Gibbs–Donnan ratio.

$$[7.1.10] \qquad \frac{RT}{\mathfrak{I}}\ln\frac{[Na^+]_o}{[Na^+]_i} = (\psi_i - \psi_o)$$
$$\frac{RT}{\mathfrak{I}}\ln\frac{[Cl^-]_i}{[Cl^-]_o} = (\psi_i - \psi_o)$$

These equations are variants of the Nernst equation. The right-hand side of both of these is just the membrane potential. Thus we can equate the two left-hand sides of the equations in Eqn (7.1.10) and we have

$$[7.1.11] \qquad \frac{RT}{\mathfrak{I}}\ln\frac{[Na^+]_o}{[Na^+]_i} = \frac{RT}{\mathfrak{I}}\ln\frac{[Cl^-]_i}{[Cl^-]_o}$$

which gives

$$[7.1.12] \qquad \frac{[Na^+]_o}{[Na^+]_i} = \frac{[Cl^-]_i}{[Cl^-]_o} = r$$

The ratio of the ions in the two compartments is a constant, r, called the **Gibbs–Donnan ratio**. **The Gibbs–Donnan ratio between plasma and the ISF in most capillary beds is 0.95**, when "in" refers to the plasma compartment and "out" refers to the ISF compartment.

CHANGES OF PLASMA VOLUME AND COMPOSITION TRANSFER TO ALL FLUID COMPARTMENTS

As discussed in Chapter 5.10, fluid in the plasma exchanges rapidly with fluid in the interstitial space. In addition, many of the solutes of plasma also readily exchange with solutes in the interstitial space. Although the ISF generally is not identical to the plasma, it is very similar and differs mainly in the lower protein concentration in the ISF. The capillary wall keeps the fluids separate,

EXAMPLE 7.1.2 Calculate the Gibbs–Donnan Potential Across the Capillaries

The potential is given by the Nernst equation (see Eqn 7.1.9):

$$E_m = \psi_i - \psi_o = RT/\mathfrak{I}\ \ln[Na^+]_o/[Na^+]_i = 8.314\ \text{J mol}^{-1}\ \text{K}^{-1} \times 310\ \text{K}/96,500\ \text{C mol}^{-1} \times \ln 0.95$$
$$= 0.0267\ \text{V} \times (-0.05) = \mathbf{-1.37\ mV}$$

The concentrations of ions listed in Figure 7.1.3 do not conform to the Gibbs–Donnan ratio of 0.95. The reason for this is that the values in Figure 7.1.3 are expressed as mEq per liter of solution and not per liter of solvent water. Plasma proteins, at about 7 g%, occupy a significant fraction of the volume of plasma, and only about 93% of the plasma volume is water. Using a figure of 98% for ISF, we can calculate the concentration per liter of water for plasma and ISF and get the values in Table 7.1.3.

The capillaries in different vascular beds differ in their permeabilities, so that the interstitial fluid protein content also differs, which subsequently slightly alters the interstitial fluid ionic composition as a consequence of the Gibbs–Donnan equilibrium (see Chapter 5.10).

TABLE 7.1.3 Concentration of Na^+ and Cl^- in Plasma and ISF

Ion	ISF (mEq L^{-1})	Plasma (mEq L^{-1})	ISF (mEq L^{-1} water)	Plasma (mEq L^{-1} water)	Gibbs–Donnan Ratio
Na^+	142	142	144.9	152.7	0.95
Cl^-	111	100.5	113.3	108.0	0.95

so that vascular flow can be maintained, while allowing this exchange.

The aggregate plasma membranes of the body cells separate the ICF from the ISF. These membranes prevent the free movement of solutes, as must be the case in order for the ICF to maintain a composition vastly different from the ISF. Maintenance of the composition of the ICF is the job of the plasma membrane, and this requires the input of energy and the operation of both passive and active transport mechanisms—the ion pumps and secondary active transporters. Despite this, alterations of the composition of the ISF have consequences for the composition of the ICF. In almost all cells, **aquaporins allow water transport that equilibrates the osmotic pressure across the plasma membrane**. Altering the osmolarity of the ISF nearly immediately alters the osmolarity of the ICF. Thus changes in the plasma are reflected in changes in the ISF, which in turn are reflected in changes in the ICF.

DARROW–YANNET DIAGRAMS DEPICT FLUID COMPARTMENT COMPOSITION AND VOLUME

Darrow–Yannet diagrams divide the body fluids into the ICF and the extracellular fluid (ECF), represented by rectangles. The height of the rectangles represents the concentration of osmotically active particles or the osmolarity; the width represents the volume of the compartment. The area of the rectangles is the osmolarity times the volume which is the amount of osmotically active particles, in osmoles, in the compartment.

The principles used in thinking about the volume and composition of the body fluids are simple:

- First, water equilibrates the osmotic pressure throughout all body fluids.
- Second, Na^+ stays extracellular.
- Third, intracellular materials stay intracellular.

Although these generalizations are not strictly true, they are close enough so that we can see what happens when various alterations in body fluid composition or volume occur. We consider here three changes in the overall composition of body volume and composition.

INGESTING OF WATER EXPANDS BOTH ECF AND ICF VOLUMES

What would happen if a "typical" individual were to drink 1 L of water? Before drinking the water, the individual has an ICF compartment of 28 L and an ECF compartment of 14 L, and both have an osmotic pressure of about 300 mOsM. This situation is depicted in Figure 7.1.5. After 1 L of water is consumed, water is

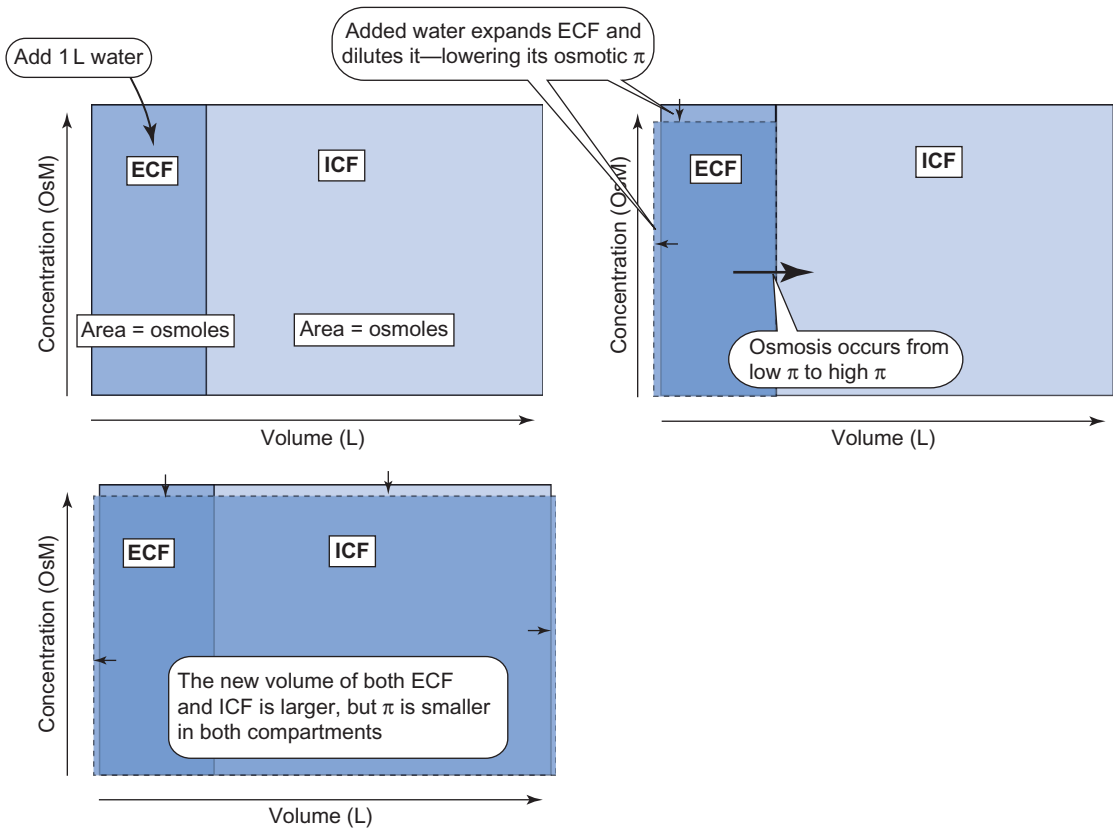

FIGURE 7.1.5 Darrow–Yannet diagram of the normal volume and total osmolarity of body fluids (left top). The height of the rectangles indicates the osmolarity and the width of the rectangles indicates the volume of the body fluid. After ingestion and absorption of 1 L of water, the extracellular fluid is diluted and expanded. This causes osmotic flow of water into the intracellular compartment, diluting and expanding it (top right). At steady state, both the ECF and ICF are diluted to about 293 mOsM. Both the extracellular and intracellular fluid compartments are expanded by a total of 1 L; 0.33 L of this is in the extracellular fluid compartment and 0.67 L in the intracellular fluid compartment (bottom).

absorbed from the intestines into the plasma, diluting it. This dilution sets up osmosis of water from the region of low to high osmotic pressure: from the plasma to the ISF. This movement occurs rapidly and the ISF is diluted. Thus all of the ECF is diluted. This in turn sets up an osmosis of water from the ECF to the ICF: the ICF becomes diluted. At the end, the osmotic pressures in all three compartments are equilibrated and both are diluted to the same degree. This can happen only when both extracellular and intracellular compartments are expanded by the same degree.

INGESTING NACL EXPANDS THE ECF BUT SHRINKS THE ICF VOLUME

What happens after eating and absorbing 10 g of NaCl? In this case, we assume that no water is ingested at the same time. The absorbed NaCl will be placed into plasma, causing an increase in the concentration of osmotically active solutes. We assume here that the NaCl remains entirely extracellular. The increased osmolarity of the ECF will draw fluid out of the intracellular compartment, shrinking it and increasing its osmolarity. These events are shown diagrammatically in Figure 7.1.6.

EXAMPLE 7.1.3 Osmolarity and Volume of Fluid Compartments After Drinking Water

The TBW in a person is 42 L and the extracellular volume is 14 L. Assuming the initial osmolarity of the fluids is 300 mOsM, what would be the volume and osmolarity of the body fluids after drinking 1 L of water?

The ICF volume is given by ICF = TBW − ECF = 42 − 14 L = 28 L.

The total osmotically active solute is $42\ \text{L} \times 300\ \text{mOsM L}^{-1} = 12{,}600$ mOsM.

The final osmolarity will be the total osmoles divided by the total volume:

$$12.6\ \text{Osmol}/43\ \text{L} = 293\ \text{mOsM}$$

The volume of the ECF will be given by V = amount/concentration = 14 L × 300 mOsM/293 mOsM = **14.33 L**.

The volume of the ICF will be given by the similar relation: 28 × 300 mOsM/293 mOsM = **28.67 L**.

Thus drinking water expands both ECF and ICF and dilutes both compartments.

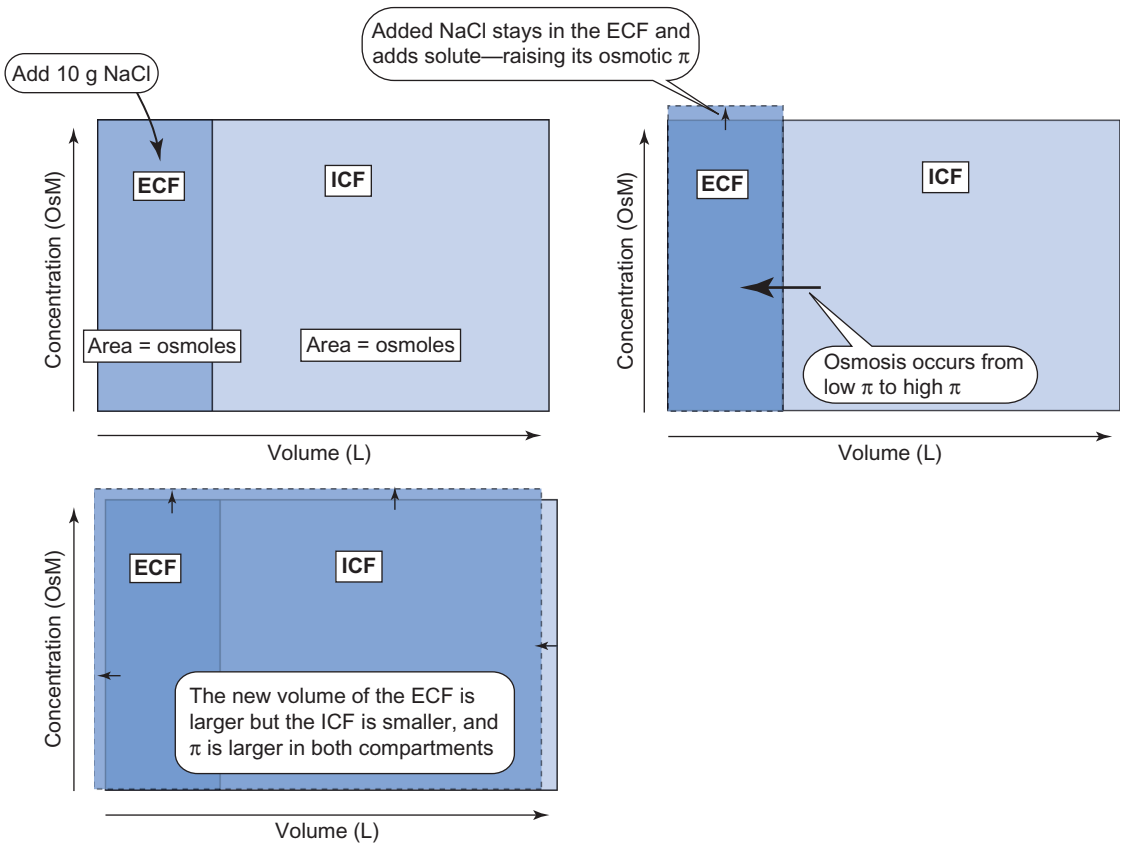

FIGURE 7.1.6 Darrow–Yannet diagram of the normal volume and total osmolarity of body fluids (top left). The height of the rectangles indicates the osmolarity and the width of the rectangles indicates the volume of the body fluid. After ingestion and absorption of 10 g NaCl, the extracellular fluid becomes more concentrated because there are more osmotically active solutes in it. Water moves from the intracellular fluid into the extracellular fluid because the osmotic pressure is higher in the ECF. Because Na remains extracellular, the extracellular body fluid compartment expands.

INFUSION OF ISOTONIC SALINE EXPANDS THE ECF VOLUME BUT DOES NOT CHANGE THE ICF VOLUME

Isotonic saline is *defined* as a solution of NaCl that does not cause movement of fluid when placed in contact with body cells. Thus we would expect no movement of solutes and presumably negligible movement of body cell solutes, when isotonic saline is infused. If we were to infuse 1 L of a solution of NaCl, we would expect all of it to expand only the ECF compartment. Thus the final volume of the ECF would be 15 L with an osmolarity of 300 mOsM, and the ICF volume and osmolarity would remain unchanged. This situation is shown in Darrow–Yannet diagrams in Figure 7.1.7.

THE KIDNEYS REGULATE BODY FLUID VOLUME AND COMPOSITION BY ACTING ON THE PLASMA

From the above discussion, we see that alterations in the plasma volume or concentration become transferred to the ISF and from there to the ICF. This establishes a fundamental concept of the regulation of body fluid volume and composition: it is accomplished by acting directly on only the plasma. Thus the kidneys and, indeed, other organ systems participate in the regulation of the body fluid volume and composition by acting solely on the plasma. Figure 7.1.8 illustrates this concept schematically.

EXAMPLE 7.1.4 Osmolarity and Fluid Compartment Volumes After Ingesting Salt

After ingesting and absorbing 10 g of NaCl, without water, what would the volume and osmolarity be of the ECF and ICF?

The total osmotically active solute before ingesting the NaCl was 42 L × 300 mOsM = 12.6 Osmol.

10 grams of NaCl adds 2 Osmol mol^{-1} × 10 g NaCl/58.4 g NaCl mol^{-1} = 342 mOsmol.

The total osmolarity after ingesting 10 g NaCl = total osmoles/total volume = 12.942 Osmol/42 L = **308.1 mOsM**.

The volume of the ECF is given by volume = total osmotic solutes/osmolarity. The total osmotic solute is what was present before the salt, plus the salt:

ECF = [14 L × 300 mOsM + 342 mOsM]/308.1 mOsM = **14.74 L**

The volume of the ICF is calculated similarly as: ICF = 28 L × 300 mOsM/308.1 mOsM = **27.26 L**.

Thus ingesting salt alone concentrates both fluid compartments, expands the ECF, and shrinks the ICF.

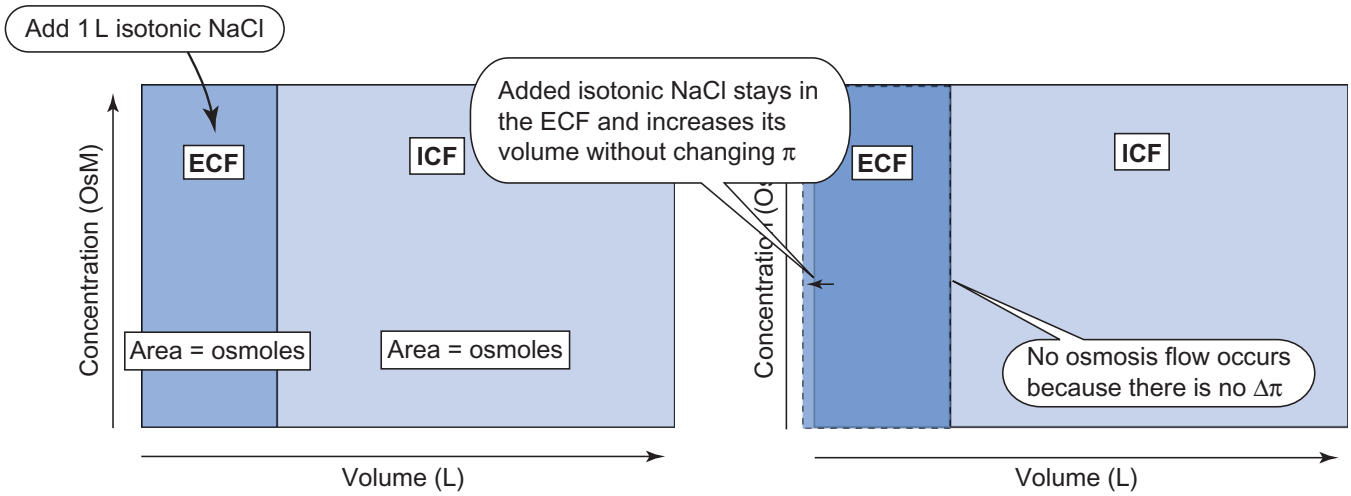

FIGURE 7.1.7 Darrow–Yannet diagrams of the normal volume and composition of body fluids before (left) and after (right) infusion of 1 L of isotonic saline (0.9% NaCl). In this case, all of the volume expands the extracellular fluid compartment with no change in the intracellular fluid compartment volume or osmolarity.

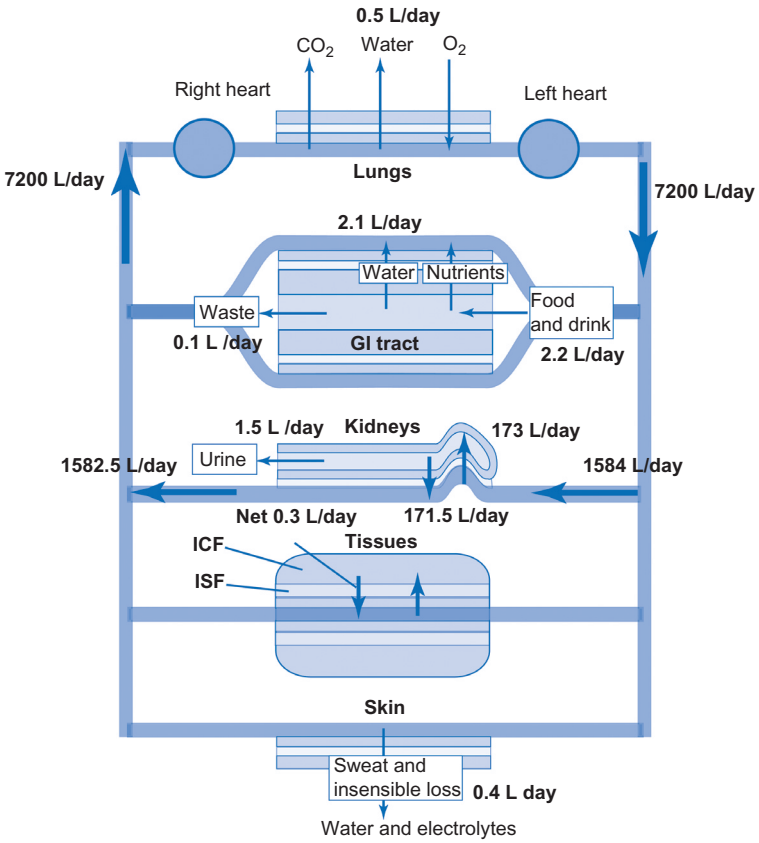

FIGURE 7.1.8 Regulation of the body fluid compartments by the kidneys, lungs, and gastrointestinal systems. The common connection between all organ systems regulating fluid volume and composition is their operation on the plasma. The kidneys have the primary function of homeostatic regulation of the body fluids by processing a large fraction of the cardiac output. The average cardiac output is 7200 L day^{-1} of which about 20%—about 1584 L day^{-1}—flows through the kidneys. Of this, about 173 L day^{-1} is filtered by the kidneys and mostly reabsorbed back into the circulation (171.5 L day^{-1}). The numbers given are approximate and average values that vary widely depending on conditions. Most variable is water loss through sweat and compensatory intake through the gastrointestinal system. Overall body balance of water and electrolytes is determined mainly by the gastrointestinal system and the kidneys, with loss through the lungs and the skin. Typical intake is 2.5 L day^{-1} = 2.2 L day^{-1} via food and drink and 0.3 L day^{-1} from metabolism; losses also total 2.5 L day^{-1} = 0.1 L day^{-1} from feces + 0.5 L day^{-1} from lungs + 1.5 L day^{-1} from urine, and 0.4 L day^{-1} from sweat and insensible loss from the skin. Changes in composition of the plasma are relayed to the tissues through the interstitial fluid.

SUMMARY

The overall function of the renal system is to regulate the volume and composition of body fluids. The body fluids consist of three major compartments: the ICF, the ISF, and the plasma. In a normal young adult male, these comprise about 40%, 15%, and 5% of body weight, respectively. These volumes can be calculated from the volume of distribution of marker substances that distribute themselves according to the TBW, ECF, or the plasma. The intracellular volume is the TBW minus the ECF; the ISF volume is calculated as the ECF minus the plasma. The volumes of the various fluid compartments vary with age, gender, and body composition. Fat tissue has little water, so excess body fat contributes excess body weight without much added water. Therefore, using the idea of an LBM containing 73% water, it is possible to estimate excess body fat from body weight and TBW.

The presence of anionic proteins in the plasma which cannot equilibrate across the capillary wall sets up a slightly unequal concentration of diffusible ions across the capillary. This is due to the Gibbs–Donnan effect, which produces a negative potential on the side of the impermeant anion. The potential can be calculated from the Nernst equation.

The body fluids reside in well-defined anatomic compartments, and there are barriers and forces that determine exchange between the compartments. The distribution of electrolytes and water can be visualized using Darrow–Yannet diagrams. In these calculations, we assume that water equilibrates its osmotic pressure across all boundaries, Na^+ remains extracellular, and K^+ remains intracellular. From this analysis, we can see that ingestion of water expands ICF and ECF compartments while diluting their osmolarity; ingesting NaCl alone expands the ECF and concentrates both ECF and ICF solutes; ingestion or infusion of isotonic saline expands only the ECF with no changes in ICF.

The renal system accomplishes its task of regulating body fluid compartment size and composition by operating solely on the plasma. Changes in plasma fluid volume and composition are then transferred to the ISF and ICF. Other organ systems also participate in this regulation.

REVIEW QUESTIONS

1. Describe the dilution principle method for determining volumes of fluid compartments.
2. What characteristics make for good "markers" for any fluid compartment?
3. What three main principles are the basis for approximate calculations of fluid compartment changes with changes in water or electrolytes?
4. Why is Na^+ present mostly in the ECF?
5. Why does water equilibrate osmolarity between intracellular fluid and extracellular fluid?
6. Why does the area of a Darrow–Yannet diagram indicate total osmotically active solutes?
7. What quantities are conserved in calculations involving volume and osmolarity of fluid compartments?
8. Based on your knowledge of Darrow–Yannet diagrams, what do you suppose would be the renal response to decreased ECF volume?