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Chapter 1:

Basic Physiology

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1 Basic Physiology

Water is the most abundant component of the body. Body fluid is essential for the life as it helps in transport of nutrients, electrolytes, gases, and wastes and also helps to maintain body temperature and cell shape. An understanding of the physiology of body fluids is essential to plan appropriate management of patients' fluid and electrolyte disorders. In this chapter, we will discuss the body's fluid compartments (i.e., their location, size, and composition), normal water balance, electrolytes, and their distribution, and finally, the units of measurement.

TOTAL BODY WATER

The total body water (TBW) content of a person varies mainly with body weight, but it also varies with age, sex, and fat content [1]. Total body water content is about 60% of body weight in a young adult male and about 50% in a young adult female [2]. Because the water content of adipose tissue is relatively low, an obese person will have proportionately less body water as compared to a lean person. The highest percentage of TBW is found in newborns (as high as 80%), which declines with age. The average total body water in different groups is shown in Table 1.1. The measurement of TBW can be performed via indicator dilution techniques using Deuterium oxide ($2H_2O$), tritium oxide ($3H_2O$), oxygen-18 labelled water, or more recently via bioelectrical impedance analysis [3].

Distribution of body fluid

Total body water is commonly divided into two volumes: the intracellular fluid (ICF) volume and the extracellular fluid (ECF) volume (Figure 1.1) [4].

Table 1.1 Average total body water as a percentage of body weight

Age	Adult male	Adult female	Elderly	Adult obese	Infant	Neonate
Total body water (% of body weight)	60%	50%	50%	50%	70%	80%

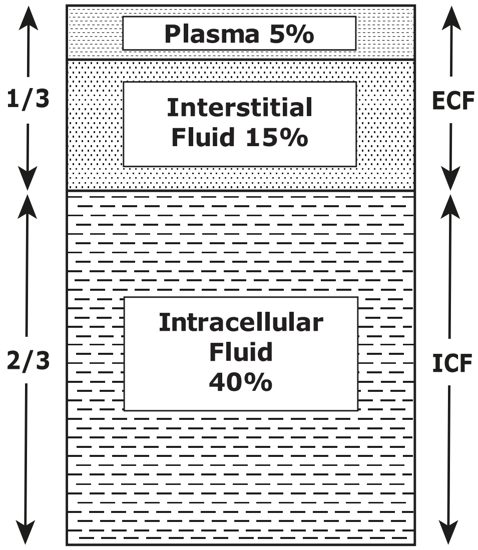

Figure 1.1 Body fluid compartments.

Intracellular fluid

ICF is defined as all the body water within cells. The ICF is normally two third of total body water and 40% of total body weight. Water balance regulates the ICF volume.

Extracellular fluid

ECF is defined as all body water outside the cells - within the tissue spaces (interstitial fluid), the blood vessels (intravascular fluid or plasma), and the lymphatic vessels (lymph). The ECF is normally one third of total body water and 20% of total body weight. As shown in Figure 1.1, ECF is subdivided into extravascular (interstitial) fluid ($3/4^{th}$ of ECF or 15% of total body weight) and plasma or intravascular volume ($1/4^{th}$ of ECF, 1/12 total body water or 5% of total body weight). There is another small compartment of ECF that is referred to as transcellular fluid. This compartment includes cerebrospinal fluid and fluid in the synovial, peritoneal, pericardial, and intraocular spaces. Sodium balance regulates the ECF volume.

For better understanding, the distribution of fluid volume in a 70 kg man is summarized in Table 1.2.

BODY FLUID AND ELECTROLYTES MOVEMENT

The movement of water and electrolytes between ICF and ECF compartments is regulated to stabilize their distribution and the composition of body fluids. The cell membranes that separate fluid compartments are selectively permeable. Water passes freely and readily through cell membranes in response to changes in solute concentration; therefore, the osmolalities in all compartments are equal. Two major determinants of water and electrolyte movements from one compartment to another are hydrostatic pressure and oncotic pressure [5]. Major water retaining solutes in ECF, ICF, and intravascular compartments are sodium, potassium, and plasma protein, respectively.

Unlike water, solutes cannot pass freely through cell membranes even though there is a significant difference in solute concentration between ICF and ECF. The movement of solutes occurs through active and passive transport mechanisms. Active transport by sodium-potassium pumps (Na^+-K^+-ATPase) is the major force maintaining the difference in

Table 1.2 Distribution of fluid volume in body compartments

Fluid type	Total	ICF	ECF	Interstitial	Plasma
% of body weight	60%	40%	20%	15%	5%
Volume for 70 kg weight	42.0 L	28.0 L	14.0 L	10.5 L	3.5 L

cation concentration between the ICF and ECF [2]. Sodium and potassium are compartmentalized into extracellular and intracellular spaces, respectively, by sodium-potassium pumps present in all cell membranes.

NORMAL WATER BALANCE

A healthy adult person consumes an average of 2000 ml of water per day. Fluid intake and output are balanced during steady-state conditions as summarized in Figure 1.2.

Daily water intake

Major sources of water intake are oral intake in the form of liquids (drinking water or beverages), water in food, and water synthesized in the body by oxidation. Thirst primarily regulates water intake. The loss of water increases osmotic pressure in the extracellular fluid, stimulating osmoreceptors in the brain's hypothalamus thirst center, which, in turn, triggers a sensation of thirst, prompting individuals to drink. Conversely, drinking and the resulting stomach distension inhibit the thirst mechanism.

Daily water loss

Routes of water loss are kidneys, feces, sweat (sensible perspiration), evaporation of water from the skin (insensible perspiration), and lungs during breathing. The kidney plays a major role in water balance. By regulating volume of urine, kidneys adjust water output from the body.

Oral or intravenous (IV) fluid intake and urine output are important measurable parameters of body fluid balance. While calculating the daily fluid requirement of the body, it is important to know and consider insensible fluid input and loss.

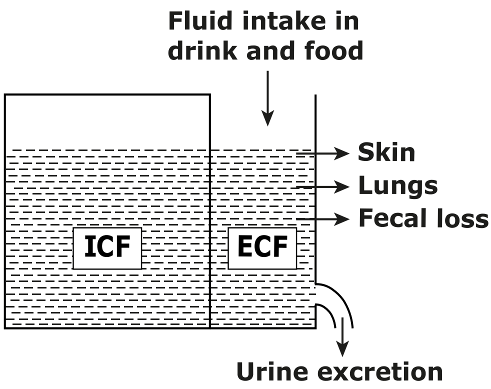

Figure 1.2 Daily water intake and loss in the body.

Insensible fluid input = 300 ml water due to oxidation.

Insensible fluid loss = 1000 ml (500 ml through the skin, 400 ml through the lung, and 100 ml through stool)

Normal Daily Insensible Fluid Loss =

Fluid Loss - Fluid Input = 1000 - 300 ml = 700 ml

Water loss is increased during exercise, excessive sweating, fever, burns, and surgery. This basic information is necessary to determine daily fluid requirements for patients receiving IV fluids. The daily fluid requirement for a normal person is calculated by adding together the amount of fluid lost in urine and insensible losses. In a normal person, the insensible daily loss is about 700 ml. So, daily fluid requirement = urine output + 700 ml.

DISTRIBUTION OF ELECTROLYTES

The normal electrolyte compositions of each fluid compartment differ markedly, as summarized in Tables 1.3 and 1.4. For example, the ECF compartment contains a high concentration of sodium, chloride, and bicarbonate but only a small quantity of potassium. In contrast,

Table 1.3 The electrolyte concentration of body fluids		
Electrolytes	**ECF (mEq/L)**	**ICF (mEq/L)**
Sodium	142.00	10.00
Potassium	4.30	150.00
Chloride	104.00	2.00
Bicarbonate	24.00	6.00
Calcium	5.00	0.01
Magnesium	3.00	40.00
Phosphate and sulfate	8.00	15.00

Table 1.4 Major ions in ECF and ICF		
	ECF	**ICF**
Major cation	Sodium	Potassium and magnesium
Major anion	Chloride and bicarbonate	Phosphate, sulfate and protein

the ICF compartment contains a high concentration of potassium, magnesium, phosphate, sulfate, and proteins. Furthermore, as sodium is confined chiefly to the ECF compartment, sodium-containing fluids are distributed throughout the ECF. As a result, sodium-containing fluids expand the volume of both the interstitial and intravascular spaces (the interstitial space expansion is approximately three times as much as the plasma).

UNITS OF MEASUREMENTS

It is important to understand the basic terminology used to measure the concentration and composition of body fluids and their interrelationship.

Ions: An ion is an atom or group of atoms with an electric charge. Ions are divided into anions and cations as shown in Figure 1.3.

Anion: When an ion has a negative electric charge, it is called an anion (i.e., Cl^-, HCO_3^-, phosphate).

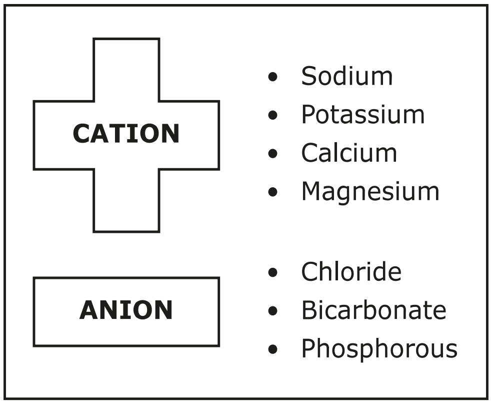

Figure 1.3 Major Cations and Anions.

Cation: When an ion has a positive electric charge, it is called a cation (i.e., Na^+, K^+, Mg^{2+}).

If cation and anion are confusing, here is a simple method to remember.

A**n**ion: **"n"** - negative charge

Ca**t**ion: **"t"** - + positive charge

Different ways by which solute concentrations can be measured are milligram per decilitre (mg/dL), milliequivalent per liter (mEq/L), or milliosmoles per liter or kg (mOsmol/L or mOsmol/kg).

Moles and millimoles

The unit millimole (mmol) is used in practice instead of mole (mol) for convenience as it is smaller and more practical to handle in medical and scientific settings.

$$6.022 \times 10^{23}$$

A mole represents a specific number of particles. One mole of any non-dissociable substance contains approximately 6.022×10^{23} particles. To clarify with an example, consider salt (NaCl). It contains an equal number of atoms: one sodium (Na^+) atom for every chloride (Cl^-) atom, even though they have different atomic weights, with 23 mg for Na^+ and 35.5 mg for Cl^-. If we compare one dozen mangoes to one dozen bananas, they represent the

Table 1.5 Atomic and molecular weights of important substances

Substances	Symbol or formula	Atomic or molecular weight
Calcium	Ca^{2+}	40.1
Carbon	C	12.0
Chloride ion	Cl^{-}	35.5
Hydrogen ion	H^{+}	1.0
Magnesium ion	Mg^{2+}	24.3
Oxygen	O	16.0
Phosphorus	P	31.0
Potassium ion	K^{+}	39.1
Sodium ion	Na^{+}	23.0
Ammonium	NH_4^{+}	18.0
Bicarbonate ion	HCO_3^{-}	61.0
Phosphate ion	PO_4^{3-}	95.0
Water	H_2O	18.0

same quantity of fruit, but their weights differ.

Mole: One mole (mol) of any substance is defined as the atomic or molecular weight of that substance in gm.

Similarly, one millimole (mmol) is equals to one-thousandth of a mole or the molecular (or atomic) weight in milligrams.

So to determine the amount of any substance in one mole, we need to know the atomic (molecular) weight of that substance (Table 1.5).

The atomic weight of Na^{+} is 23. Thus, 23 mg of Na^{+} represents 1 mmol. Therefore, 23 mg of Na^{+} in 1 liter of water results in a Na^{+} concentration of one mmol/L.

Equivalent and milliequivalent

The equivalent is a relative term; it refers to a mole of ionic charges.

Equivalent: The equivalent weight of an element is its atomic weight in gm multiplied by its valence.

For ions that carry a single charged mole equals an equivalent (i.e., Na^{+}, K^{+}, Cl^{-}, H^{+}). But if the ion carries a charge that is greater than one, numbers are no longer equal. So, for example, one mole of calcium ion (Ca^{2+}) equals two equivalents.

So, Equivalents = Moles × Valence

A comparison of the normal value of serum electrolytes concentration in mmol/L and mEq/L is shown in Table 1.6.

Molecules must be quantified in moles (e.g., a mole of glucose) because they carry no charge. However, in practice, they are usually measured in mg or gm because of their simplicity and convenience. The following formula can be used to convert mg/dL to mmol/L.

$$\text{mmol/L} = \frac{\text{mg/dL} \times 10}{\text{Atomic Weight}}$$

Ions can be quantified as either moles or equivalents.

Why are the terms "mmol" or "mEq" used instead of "moles" or "equivalents"?

In routine practice, we prefer using "mmol" (millimoles) or "mEq" (milliequivalents) to express concentrations rather

Table 1.6 Normal plasma electrolyte concentrations

Electrolyte	mEq/L	mmol/L
Cations		
Sodium	136 to 145	136 to 145
Potassium	3.5 to 5.0	3.5 to 5.0
Calcium total*	4.5 to 5.6	2.2 to 2.6
Ionized*	2.2 to 2.6	1.05 to 1.3
Magnesium*	1.4 to 1.7	0.70 to 0.85
Anions		
Chloride	96 to 106	96 to 106
Bicarbonate	22 to 26	22 to 26

*Value in mg/dL: The normal values for total calcium and ionized calcium are 8.5-10.5 mg/dL and 4.3-5.3 mg/dL, respectively. The normal value of magnesium is 1.7–2.1 mg/dL.

than "moles" or "equivalents" This preference arises from the extremely low concentrations of most molecules and ions in serum.

In day-to-day practice, we use a millimeter, which is 1/1000 of the meter. Similarly, "mmol" or "mEq" represents 1/1000 of a mole or equivalent. For example, consider the serum potassium value, which might be expressed as 0.004 moles or equivalents per liter. However, converting it to 4 mmol/L or mEq/L provides a more practical, straightforward, and convenient value for everyday use in clinical practice.

The relationship between mEq and mg

Formula to convert mg/dL to mEq/L: To convert from milligrams per deciliter (mg/dL) to milliequivalents per liter (mEq/L), you can use the following formula:

$$\text{mEq/L} = \frac{\text{mg/dL} \times 10 \times \text{Valence}}{\text{Mol. Weight}}$$

Example: If 1 gm of salt (NaCl) is added to 1 liter of water, what will be its concentration in mEq/L?

NaCl 1 gm/L = 1,000 mg/L = 100 mg/dL

Valence of NaCl = 1

Molecular weight = 58.5 (Na^+ mol. wt. 23 and Cl^- mol. wt. 35.5).

$$\text{mEq / L} = \frac{100 \times 10 \times 1}{58.5} = 17.1$$

1 gm NaCl/L = 17.1 mEq/L

So, 1 gm of NaCl contains 17.1 mEq sodium and 17.1 mEq chloride, or the Na^+ concentration of NaCl = 17.1 mEq/gm.

Formula to convert mEq/L to mg/dL: To convert mEq/L to mg/dL, you can use the following formula:

$$\text{mg/dL} = \frac{\text{mEq/L} \times \text{Mol. Weight}}{10 \times \text{Valence}}$$

Example: If 1 liter of NaCl solution contains 154 mEq of NaCl, what is the amount of NaCl in mg/dL?

NaCl mEq/L = 154

Molecular Weight = 58.5 (Na^+ mol. wt. 23 and Cl^- mol. wt. 35.5)

Valence = 1

$$\text{So, mg/dL} = \frac{154 \times 58.5}{10 \times 1} = 900.9$$

So, in a 1-liter solution of NaCl with 154 mEq of NaCl, there is 9009 mg/L of NaCl salt.

When 9009 is divided by 154, the result is 58.5.

Therefore, 100 ml of NaCl solution containing 1 mEq of NaCl has 58.5 mg of salt.

These values, derived from both equations (Na^+ concentration is 17.1 mEq/gm of NaCl, and 1 mEq contains 58.5 mg NaCl), are useful for the calculation and interchangeability of routinely used substances.

Conversion factors helpful in day-to-day practice are summarized in Table 1.7.

Examples of conversion

Find out K^+ concentration in mEq in 10 ml ampoule of 15% potassium chloride (KCl)

10 ml of 15% KCl = 1.5 gm KCl/ampoule

1 gm of KCl contains 13 mEq of K^+ (as per Table 1.7).

So, 1.5 gm KCl = 1.5 × 13 = 19.5 mEq of K^+.

Answer: 10 ml amp. of 15% KCl contains 19.5 mEq of potassium.

Find out Na^+ concentration in mEq in a 25 ml ampoule of 7.5% sodium bicarbonate ($NaHCO_3$)

25 ml of 7.5% $NaHCO_3$ = 1.86 gm of $NaHCO_3$ per ampoule

1 gm of $NaHCO_3$ contains 12 mEq of Na^+ (as per Table 1.7).

Table 1.7 Conversion between mEq and mg		
Salt	**mEq cation or anion/ gm of salt**	**mg of salt/ mEq**
Sodium chloride	17	58
Potassium chloride	13	75
Sodium bicarbonate	12	84
Calcium gluconate	4	224
Calcium chloride	14	73
Magnesium sulfate	8	123

So, 1.86 gm of $NaHCO_3$ = 1.86 × 12 = 22.3 mEq of Na^+.

Answer: A 25 ml ampoule of 7.5% $NaHCO_3$ contains 22.3 mEq of Na^+.

Osmotic pressure and osmolality

Osmotic pressure

Osmotic pressure determines the distribution of water among the different fluid compartments, particularly between the ECF and ICF.

The osmotic pressure generated by a solution is proportional to the number of particles per unit volume of solvent, not to the type, valence, or weight of the particles. To generate osmotic pressure, the solute must be unable to cross the cell membrane.

Osmole (Osm)

It is the unit of measurement of osmotic pressure. One osmole is defined as 1 gm molecular weight (1 mol) of any nondissociable substance (such as glucose) and contains 6.022×10^{23} particles.

Milliosmoles (mOsm)

mOsm is 1/1000 of an osmole. So in relatively diluted fluids in the body, the osmotic pressure is measured in milliosmole per kg of water (mOsm/kg).

An osmole (or mOsm) of a substance, such as glucose which does not dissociate into ions, is the same as a mole (or mmol). However, a mole of salts such as sodium chloride, which dissociates almost completely into sodium and chloride ions, equals 2 osmoles.

Osmolality and osmolarity

These laboratory values reflect the relationship between solute and solvent.

Osmolality

The osmolality of a solution is determined by the amount of solute dissolved in a solvent (i.e., water) measured in weight (kg).

If a solute is dissolved in 1 kg of water (solvent), the concentration of the solution is called osmolality and is expressed as mOsm/kg of the water solvent.

When osmolality is high, the solution is more concentrated, and when osmolality is low solution is diluted.

Osmolarity

The osmolarity of a solution is determined by the amount of solute dissolved in a solvent (i.e., water) measured in volume (liter).

If a solute is dissolved in 1 litre of water (solvent), the concentration of solution is called osmolarity and is expressed as mOsm/L.

Remember

When the solvent is measured in lite**r** - **"r"** - Osmolarity

and when the solvent is measured in Ki**l**ogram - **"l"** - Osmolality

As the temperature can affect the volume of solvent and solute in the solution, it can affect the value of the solution's osmolarity.

So osmolality (mOsm/kg), determined by the solvent's weight, is more accurate than osmolarity. However, the difference between these two values is negligible, and osmolarity is easier to measure, so it is used more commonly.

The osmolality of any solution is measured by measurement of its freezing point.

Plasma osmolality

Plasma osmolality is primarily determined largely by sodium salts, with a lesser contribution from ions, glucose, and urea. Normal plasma osmolality is 285 (275–295) mOsm/kg.

$$\text{Plasma Osmolality} = 2 \times Na^+ + \frac{\text{Glucose (mg/dL)}}{18} + \frac{\text{BUN (mg/dL)}}{2.8}$$

Effective osmolality

Those solutes determine the effective osmolality of the extracellular fluid (ECF), which does not freely permeate the cell membrane and act to hold water within the ECF.

Lipid-soluble solutes like urea, which can pass through cell membranes, do not affect the difference in osmotic pressure between the ECF and ICF. So, urea which contributes to the calculation of plasma osmolality does not contribute to effective osmolality. Therefore, total osmolality and effective osmolality are different.

$$\text{Effective Osmolality (mOsm / kg)} = 2 \times Na^+ \text{ (mEq/L)} + \frac{\text{Glucose (mg/dL)}}{18}$$

Under normal circumstances, glucose accounts for only 5 mOsm/kg in effective osmolality. So normally, plasma sodium concentration is the determinant and reflector of the plasma osmolality.

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