A Course in Clinical Disorders of the Body Fluids and Electrolytes

Geoffrey M Berlyne

A Course in Clinical Disorders of the Body Fluids and Electrolytes

GEOFFREY M. BERLYNE

MD, FRCP, FACP

Professor of Medicine

Downstate Medical Center

State University of New York;

Co-Director,

Division of Renal Diseases

Downstate Medical Center,

Brooklyn,

Chief, Section of Nephrology,

Brooklyn V A Medical Center,

Brooklyn, New York

BLACKWELL SCIENTIFIC PUBLICATIONS

OXFORD LONDON EDINBURGH BOSTON MELBOURNE

Editorial offices:
Osney Mead, Oxford, OX2 OEL
8 John Street, London, WC1N 2ES
9 Forrest Road, Edinburgh, EH1 2QH
52 Beacon Street, Boston, Mass., USA
214 Berkeley Street, Carlton
Victoria 3053, Australia

First published 1980

DISTRIBUTORS

USA
Blackwell Mosby Book Distributors
11830 Westline Industrial Drive
St Louis, Missouri 63141

Canada
Blackwell Mosby Book Distributors
86 Northline Road, Toronto
Ontario, M4B 3E5

Australia
Blackwell Scientific Book Distributors
214 Berkeley Street, Carlton
Victoria 3053

British Library
Cataloguing in Publication Data
Berlyne, Geoffrey Merton
A course in clinical disorders of the body fluids and electrolytes.
1. Water-electrolyte imbalances — Programmed instructions
I. Title
616.3'9 RC630
ISBN 0-632-00356-1

Photoset, printed and bound in Malta by Interprint Limited

Introduction

This book is aimed at the senior medical student, the MRCP candidate and hospital resident who frequently has difficulty in understanding the principles of management of fluid and electrolyte problems. Having spent many years in correcting fluid and electrolyte imbalances with resident hospital staff in various countries, I thought that a semi-programmed course on disorders of the body fluids and electrolytes was necessary. I have put it in a semi-programmed form like its companion volume, *A Course in Renal Diseases*, so that the reader cannot day-dream while reading the book. I believe that the intelligent reader will grasp the essentials of fluid and electrolyte problems from this book more readily than from standard form texts and so will be better able to appreciate the more detailed review articles on the subjects should he wish to have a deeper knowledge.

This book is printed in a small, soft-back format to enable the reader to keep it in his coat pocket, and read it whenever he has a chance. The times for each chapter are but a rough guide. Most chapters are too long to be completed at one sitting; and no one should read for more than 30 minutes at one time.

The programming instructions must be followed. This means that the paragraphs are deliberately scrambled to prevent anyone from browsing through the book. I hope the reader enjoys using the book as a pocket teaching machine.

For those readers living in countries where SI units are used, I have printed the SI values in italics, but have kept the standard (mass) units in regular print.

I would like to thank my colleagues, and the residents, fellows, and students of our renal programme at Downstate Medical Center, State University of New York, for reading the chapters as they were prepared and making appropriate and valuable suggestions to improve the text. Dr. E. Goldberger gave kind permission to reproduce several of the figures from his book, *A Primer of Electrolyte and Acid–Base Disorders*, 5th Edition. Lea & Febiger.

New York, March 1979 **G. M. Berlyne**

How to Use This Book

In each chapter:

1 Follow the programme instructions.
2 Stop for at least 15 minutes after every 30 minutes' learning. This makes your learning more efficient and your life more bearable.
3 Never use the index until you have read the entire book.
4 Follow the printed order of the chapters.

Contents

Time for this chapter: $1\frac{1}{2}$ hours

Chapter 1
Body fluids

1.1 Water is the principal constituent by weight of the mammalian body. The various tissues have different water contents, thus the water content of the brain is 82 per cent by weight, whereas the water content of bone is 20 per cent by weight. The lowest water content is found in adipose tissue which has a water content of 10 per cent. Look at Table 1.1 in which the water content of the various tissues is compared.

Table 1.1

Tissue	Water content as %
Brain	82
Skeletal muscle	76
Liver	68
Kidney	83
Blood	83
Skin	72
Bone	22
Adipose tissue	10

In the average man there is less fat than in the average woman, so that the percentage of water in the average male body will be higher than in the female body. This is shown below:

Sex	Water content as % of total body weight
Male	60.6
Female	50.2

Now answer the question:

Question What tissue has the lowest water content?

Answer 1. Bone. Go on to **1.3**.
2. Fat. Go on to **1.4**.
3. Muscle. Go on to **1.6**.

1.2 You should not be reading this. Read **1.1** again and follow the instructions, otherwise you are wasting your time

1.3 Your answer— bone.

You are not correct. Bone has 22 per cent water content whereas fat has only 10 per cent. Look again at Table 1.1 and answer the question correctly.

1.4 Your answer—fat has the lowest water content.

You are correct.

Obviously a fat man will have a lower percentage of water in his body than will be found in a thin woman. If an average man weighs 70 kg and of this 60 per cent is water, then the absolute amount of water in his body will be $70 \times 60/100 = 42$ litres. This quantity of water is referred to as Total Body Water or TBW. Total Body Water can be measured by several methods:

1. Desiccation. This method is suitable for small animals and consists of weighing the animal before and after drying the carcass to constant weight in an oven for a few days at 95°C. This is not suitable for large animals or man for obvious reasons, but is a method which is free of major error for small laboratory animals

2. Dilution methods. The principle of these methods is the administration of a known quantity of a substance which readily diffuses throughout the water in the entire body. After equilibrium has been attained (which may take several hours), the concentration of the administered substance is determined in the plasma and from this observed dilution of the substance, the volume of its distribution determined, with an appropriate correction for the loss of the substance excreted from the body. If a marker is used which distributes throughout body water then this volume of distribution is Total Body Water.

$$\text{TBW} = \text{Volume of distribution.}$$

$$= \frac{\text{Quantity administered} - \text{Quantity excreted.}}{\text{Concentration of marker in plasma water.}}$$

Question If you have to determine Total Body Water repeatedly in the same man, what type of method would you use?

Answer 1. Desiccation. Go on to **1.5**.
2. Dilution. Go on to **1.7**.
3. Don't know. Go on to **1.8**.

1.5 Your answer—desiccation.

You are wrong. Can you place a man in an oven at 95°C and dry him out and then expect him to live and repeat the experiment? You are not thinking, try and concentrate. Read **1.4** again.

1.6 Your answer—muscle.

You are guessing. You must concentrate on what you are reading. Go back and re-read **1.1** and pay particular attention to the Table.

1.7 Your answer—dilution methods should be used to measure Total Body Water in man.

You are correct. The substances which can be used for the measurements of total body water should have the following properties—

1. Diffuse throughout the body water.
2. Should not be specifically bound to any cellular or extracellular component.
3. Metabolized either not at all or very slowly.
4. Readily measured accurately.
5. Non-toxic.

Commonly used substances are:

(1) Antipyrene, a chemical compound introduced initially in the treatment of pyrexia, and easily measured chemically. It is slowly excreted and slowly metabolized.

(2) Isotopes of water,—deuterium hydroxide (D_2O) and tritiated water (^3H_2O) are treated by the body as if they were ordinary water, and are particularly suitable for the determination of total body water. Deuterium oxide is expensive and for its accurate measurement a mass spectrograph is required which is costly and not available in every hospital. Tritiated water, on the other hand, is not expensive and is readily measured in a liquid scintillation counter usually to be found in nuclear medicine laboratories of all major hospitals. These measurements using isotopes of water give Total Body Water results which are identical.

They are however, about 2 litres greater than the result of the antipyrene determined total body water volume, presumably due to deuterium and tritium exchanging with isotopic hydrogen in proteins and carbohydrates.

(3) In experimental animals, urea, alcohol, and thiosulphate are substances used to measure total body water, but urea and alcohol are both metabolized and about 10 g or more of urea is also concomitantly produced in the body during the time of equilibration. This makes them less ideal than tritiated water for measuring Total Body Water.

Question If you do repeated total body water measurements on the same subject would you expect the results from antipyrene or thiosulphate to be identical with those obtained by using tritiated water?

Answer 1. Yes. Go on to **1.9**.
2. No. Go on to **1.10**.

1.8 Your answer—I don't know.

How could you choose this? You should have read **1.4** again if you were unable to choose the correct answer. An answer such as 'I don't know' is an admission of ignorance of the contents of **1.4**. Go back and re-read it. Then choose the correct answer without guesswork. Don't waste your time.

1.9 Your answer—yes.

TBW is the same by both methods. No. You have not read **1.7** carefully enough. Tritiated water gives a larger TBW space than is found with antipyrene or thiosulphate methods read **1.7** again to find out why.

1.10 Your answer—different results of Total Body Water are obtained depending on the method used.

You are correct. From Paragraph **1.7** there is a simple lesson to be learned:
That using the usual chemical or physical methods of measurement of Total Body Water gives results which may vary due to the method used, and *it is, therefore, extremely important to define the method used when describing Total Body Water.* Changes in Total Body Water (TBW) are not meaningful if, for example, before the experimental stress TBW is measured say by tritiated water, and after the stress by antipyrene. The methods usually employed are sufficiently reproducible to be dependable and sensitive enough to show small changes if the same test is repeated. In clinical practice, however, the easiest and most accurate

test of a change in total body water over a period of a few hours or days is by measuring the *change in body weight* determined by weighing the patient. Apart from actual removal of tissue or fluid in surgical operations and childbirth, a rapid change in body weight is a good indication of a change in total body water.

In the pregnant woman there is an increase in total body water as measured by deuterium of about 7 litres after the end of the first trimester, not accompanied by clinical oedema. About half of this is attributable to the water content of the pregnant uterus, fetus and amniotic fluid.

In the neonate, infant and child the total body water as expressed as a percentage of body weight differs from that in the adults. Look at Table 1.10.

The relatively high body water content of the infant and child, compared to adult man is due to the higher percentage of extracellular fluid in the infant and child compared to the intracellular fluid.

Question There is an increased amount of TBW per kg of body weight in the infant compared with the adult. What is the reason for this?:

Answer
1. Increase in percentage of ECF. Go on to **1.12**.
2. Increase in relative amounts of both ECF and ICF. Go on to **1.14**.
3. Increase in relative amount of internal organs compared to whole body weight. Go on to **1.16**.

Table 1.10

Age	Total body water (%)	Ratio of extracellular fluid to intracellular fluid
0–1 days	79	1.25
1–10 days	74	1.14
1–3 months	72.3	0.80
3–6 months	70.1	0.75
6–12 months	60.4	0.83
2–3 years	63.5	0.73
5–10 years	61.5	0.56
10–16 years	58	0.48

1.11 Your answer—The ECF provides the milieu interieur.

You are correct.

ECF is divided into 4 compartments:

1. Intravascular fluid compartment.
2. Extravascular fluid compartment.
3. Inaccessible bone water.
4. Transcellular fluids.

Let us consider each of them in turn—

First of all, the intravascular compartment. This is the plasma inside the vascular tree i.e. inside the heart chambers, the arteries and veins of all sizes, and the capillaries. It excludes the cellular components of the blood— the red cells, white cells and platelets, which are part of the intracellular compartment. The plasma is in equilibrium with the extravascular part of the ECF. The plasma is unique in its high protein concentration of 6 to 7 g/100 ml, which is important in maintaining an adequate oncotic pressure in the capillaries and attracting interstitial fluid back into the intravascular compartment. Oncotic pressure is the osmotic pressure exerted by colloids i.e. large molecules. In healthy man, the plasma proteins are the main factor contributing to oncotic pressure. The capillaries are permeable to small molecules, but not to large molecules, thus the osmotic pressure exerted by small molecules such as electrolytes is unimportant in the capillaries where larger molecules, such as colloids, exert oncotic pressure which attracts fluid back into the capillaries.

Read this last paragraph again after you have looked at the diagram. Draw the diagram yourself. See how the plasma proteins exert oncotic pressure and pull the fluid *back* into the capillary: hydrostatic pressure does the opposite. The result is an equilibrium.

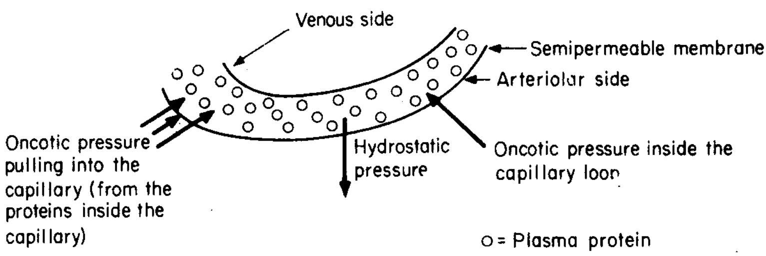


Fig. 1.11

Now answer the question.

Question What is plasma oncotic pressure?

Answer 1. Osmotic pressure of electrolytes. Go on to **1.17**.
2. Osmotic pressure of large molecules such as proteins. Go on to **1.19**.

1.12 Your answer—There is an increase in the percentage of ECF in infancy.

You are correct. Total Body Water can be divided into 2 major compartments as you can see in the Fig. 1.12. Look at it carefully, and draw it on a piece of paper. Memorize the figures given for an adult man.

(1) Extracellular fluid compartment (ECF).
(2) Intracellular fluid compartment (ICF).

The concept of compartments is perhaps not really adequate. A better description is that of Robinson and McCance (1952) who likened the ECF to the continuous phase of an emulsion and the ICF to the disperse phase. A more appropriate description would be to liken the body fluid to a solution in which micelles were suspended. The ECF is then the continuous phase and the ICF analogous to the fluid contents of the micelles themselves.

The ECF is an all-pervading fluid surrounding the cells. It is kept constant in composition within fairly narrow limits, so that it is, in truth, the constant 'milieu interieur' or internal milieu of Claude Bernard, in which osmolality, chemical and ionic composition and pH are rigidly controlled. Thus extremes of diet i.e. (from starvation to gluttony) over- and under-hydration, and activity have minimal effects on the composition of the EFC and the cells are thereby protected from changes in their external environment.

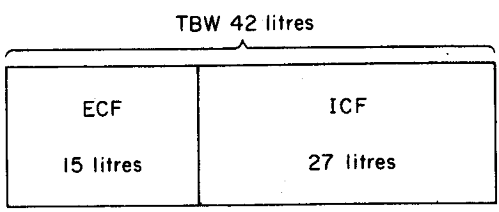


Fig. 1.12 Relative sizes of extracellular and intracellular compartments.

Question What provides the constant milieu interieur?

Answer 1. The ECF. Go on to **1.11**.
2. The ICF. Go on to **1.13**.
3. Total Body Water. Go on to **1.15**.

1.13 Your answer— the ICF provides the milieu interieur.

No. The continuous phase of the body fluids is the ECF, which provides the milieu interieur. The ICF composition varies from cell to cell, there being differences in, for instance, the pH in the muscle cell when compared to pH in the leucocyte, as well as differences *inside* the cell in the various subcellular compartments i.e. mitochondria, lysosomes, cytosol, endoplasmic reticulum, and nuclei. Constancy of the milieu interieur is a function of the ECF, not the ICF. Read **1.12** again. It is best to consider the cystol as the ICF and the subcellular particles as each having their own pH, ionic composition and metabolic functions i.e. islands in the cytosol.

1.14 Your answer— There is an increase in the relative amounts of both ECF and ICF.

You are partially correct, but you have not based your answer on **1.10**. Go back and read it, paying particular attention to the Table. Then answer the question correctly.

1.15 Your answer— Total body water provides the milieu interieur.

No. You have not read **1.12** properly. Re-read it. There is no point in guessing. If you cannot concentrate stop reading now and begin again when you can devote your attention to the writing without distraction.

1.16 Your answer— There is an increase in the relative amount of internal organs.

You are correct, but this is not the reason stated in **1.10**. Read **1.10** again and you will find that there is an increase in the amount of ECF kg body weight in childhood when compared with that in adults.

1.17 Your answer— Oncotic pressure is the osmotic pressure of electrolytes.

No. This is not so. It is the osmotic pressure of the large molecules such as proteins. Read **1.11** again more carefully.

Table 1.18

	Electrolytes	ECF Interstitial plasma fluid	Interstitial fluid	ICF
Cations mEq/l	Na^+	142	145	10
	K^+	4	4	155
	$Ca_2{}^+$	5	—	3
	$Mg_2{}^+$	2	—	26
Total		153		194
Anions mEq/l	Cl^-	104	114	2
	HCO_3^-	27	31	8
	HPO_4^{2-}	2	—	95
	SO_4^{2-}	1	—	20
	Organic acids	6	—	
	Protein	13		15
Total		153		180

1.18 Your answer— The deeper layers of bone.

You are correct. The composition of extracellular fluid is shown in Table 1.18. Plasma differs from extravascular or interstitial fluid in that the latter has a lower protein content, and there are minor differences in electrolyte composition caused by the Gibbs–Donnan distribution factor. This is discussed later. Meanwhile remember that the **principal cation in ECF is sodium** i.e. it has the highest concentration and sodium is **therefore osmotically the most important of the cations,** with chloride and bicarbonate being the major anions in ECF. All other ions are in lower concentration. This is in striking contrast to the composition of intracellular fluid (ICF) which has high concentrations of potassium, magnesium, phosphate, sulphate and protein. ICF is discussed in detail later.

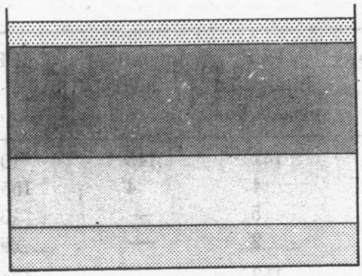
Now answer the question:

Question What is the osmotically most important cation of the ECF?

Answer 1. Potassium. Go on to **1.21**.
2. Sodium. Go on to **1.23**.

1.19 Your answer—oncotic pressure is osmotic pressure exerted by large molecules such as proteins.

You are correct. The extravascular or interstitial fluid is the fluid



Subdivisions of ECF

Fig. 1.19

surrounding the cells, and is in equilibrium with the intravascular plasma and with the fluid inside the cells (ICF). The interstitial fluid includes lymph, and mostly achieves rapid equilibrium with the plasma. However, in contrast to this the interstitial fluid of cartilage and dense connective tissue is in slow equilibrium with plasma, due to the physical gel-like structure of the intercellular tissue.

Transcellular fluids are the secretions of glandular tissues such as saliva, gastro-intestinal fluids, renal tract, respiratory tract, gonads, aqueous humour, and the cerebrospinal fluid. Inaccessible Bone Water is the water which is trapped in the deep layers of bone and is not readily exchangeable with the remainder of the ECF.

Now answer the question.

Question Where is the inaccessible bone water?

Answer 1. In the superficial layers of bone. Go on to **1.20**.
2. In the deeper layers of bone. Go on to **1.18**.

1.20 Your answer— inaccessible bone water is in the superficial layers of bone.

You are wrong. Inaccessible bone water is in the deeper layers of bone. Being surrounded by bone makes it not readily exchangeable and out of contact with the remaining ECF. Read **1.19**.

1.21 Your answer— potassium is the most osmotically active cation in the ECF.

You are not correct. Potassium is found in low concentrations in ECF (around 4 mM/1) whereas plasma sodium concentration, you will remember, is of the order of 140 mM/1. Now read **1.18** again and answer the question correctly.

1.22 Your answer— blood volume is 40 ml/kg. You are correct.

Total ECF volume can be measured by substances which diffuse through the ECF but do not penetrate the cells. At the outset it should be realized that no such ideal substance exists. Measurements of ECF volume by large molecule polysaccharides (such as in inulin) are far from satisfactory because they fail to penetrate all the ECF, as shown by the fact that the inulin space of guinea pig muscle increases after administration of hyaluronidase, suggesting an extracellular mucopolysaccharide barrier to the diffusion of inulin. On the other hand, bromide and chloride apparently penetrate into some cells, and so give values of ECF much higher than inulin space. Look at Table 1.22.

Sulphate labelled with ^{35}S gives a modest ECF space estimate suggesting failure to penetrate readily into cells. When $^{35}SO_4^{2}$ and inulin spaces are compared for the various tissues, $^{35}SO_4^{2-}$ penetrates transcellular spaces which inulin does not penetrate. It is important to realize that there is no substance which measures ECF space absolutely; each method measures a different space. The changes in that particular space in a variety of circumstances can be accurately measured by repeating the test with the **same** tracer (or the same chemical).

Now answer the question.

Question Which gives the lowest value for ECF space?

Answer
1. Bromide. Go on to **1.29**.
2. Inulin. Go on to **1.27**.
3. Sulphate. Go on to **1.30**.

Table 1.22

Method	ECF space (expressed as % body weight)
Inulin	16
Thiosulphate	16
$^{35}SO_4^{2-}$	18
$^{86}Br^-$	28
$^{36}Cl^-$	27