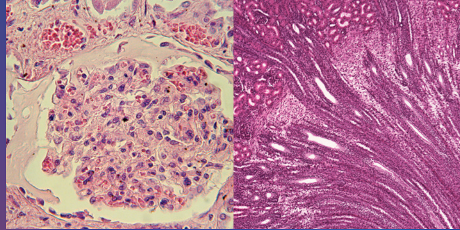

Essential Fluid, Electrolyte and pH Homeostasis

Gillian Cockerill | Stephen Reed

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In loving memory of
MW, EMS, IW and JFH

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Preface

> 'All vital mechanisms, no matter how varied they may be, have always but one end, that of preserving the constancy of the conditions of the internal environment.'

With these words, Claude Bernard in 1857 gave what was probably the first definition of the process we now know as 'homeostasis', even though the term, derived from the Greek *homoios* meaning 'the same', was not coined until the 1920s.

Those events that collectively constitute 'life' can all be described in terms of chemical and physical processes; cell biology in particular is chemistry in disguise! The purpose of this short text is to act as a primer for students meeting key topics for the first time, but sections of this book will also be useful as a quick revision guide for more advanced students. The text, supported by diagrams, aims to explain physiochemical processes related to the homeostatic maintenance of:

(i) electrochemical neutrality (anion/cation balance);
(ii) osmotic balance (regulation of the concentrations of solutes inside and outside cells, and
(iii) hydrogen ion balance.

The mechanisms of fluid, electrolyte and acid-base homeostasis are fundamental to normal cellular function and therefore have a major impact on the health of the individual, and an imbalance may lead to a life-threatening situation. Processes of fluid, electrolyte and acid-base regulation that are physiologically interrelated are the ones which students often find most difficult to understand, partly because of their complexity.

This introductory text is divided into three main Parts dealing initially with basic physicochemical concepts, then aspects of normal and abnormal physiology. Each part is presented as a number of Sections which are essentially ‘bite-sized chunks’ of key information. The book is designed such that it may be read as continuous prose, or, and because each Section more or less stands alone, the reader may dip into the text for the purposes of review or revision of particular topics. Some concepts are described in several sections to ensure that relevant sections are fairly self-contained, but will also allow the reader the opportunity to revisit and consolidate essential material. The contents covered range from basic chemistry and physiology to more advanced concepts which are applied to clinically relevant situations. Selected aspects of analysis and discussion of some of the pitfalls of interpretation of laboratory data are also to be found. There are numerous Self Assessment Exercises based on understanding of key concepts, data-handling problems and case studies for reinforcement of the learning process. We hope the text will be of value to laboratory staff and ward-based staff in endeavouring to understand what many see as a ‘very difficult’ topic area.

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PART 1

Background theory and basic concepts

Overview

The purpose of Part 1 is to review some important concepts of physical chemistry and to introduce key ideas of physiology, all of which will provide underpinning knowledge for deeper study in Parts 2 and 3. Although some understanding of solutions, acids, bases, pH and buffers may have been acquired from previous studies, these topics are included here for revision; some readers may choose to omit certain sections.

An overview is given of body fluid compartments, their volumes and their chemical compositions. Importantly, concepts relating to osmotic balance and electrical neutrality of physiological fluids are also discussed.

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SECTION 1.i

Introduction and overview

The human body is, by weight, predominantly water: the total volume[1] being distributed into two major compartments. The larger proportion is located inside cells (intracellular fluid, ICF) with a smaller volume occurring as extracellular fluid (ECF). To function effectively, cells must maintain correct fluid volume balance, ionic balance, osmotic balance and acid-base balance. Two fundamental physicochemical phenomena, namely electroneutrality and osmosis ('osmoneutrality'), have significant effects on cellular function. Homeostatic mechanisms operate to maintain physiological steady-state conditions of ionic and solute concentrations.

Body fluids are complex 'cocktails' of various chemicals such as (a) ions (electrolytes), notably sodium, potassium, calcium, chloride, phosphate and bicarbonate, (b) small molecular weight metabolites such as glucose, urea, urate (uric acid) and creatinine, and (c) larger molecular weight compounds, for example, proteins and lipoprotein complexes.

Qualitatively, the chemical composition of most body fluids is substantially the same, but quantitatively, the chemical content of the different body fluids varies considerably. *Overall*, the total volume of water in our bodies does not vary greatly, and nor does the *overall* chemical composition of the fluids, as both volume and composition are carefully regulated to maintain homeostasis. However, as is often the case in physiological systems, there is at the molecular level a

[1]One should always refer to fluids (i.e. liquids and gases) in terms of *volume* rather than amount.

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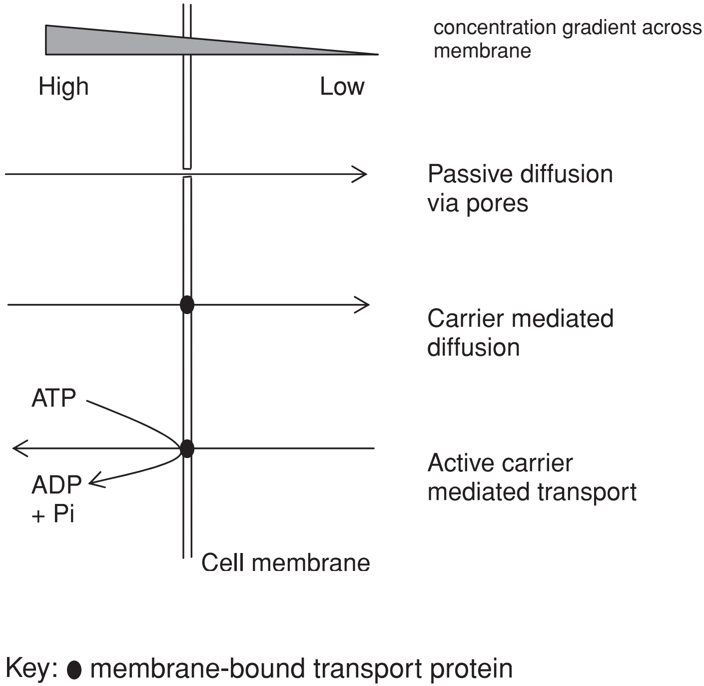


Figure 1.1 Membrane transport. Passive osmotic, passive mediated and active mediated mechanisms

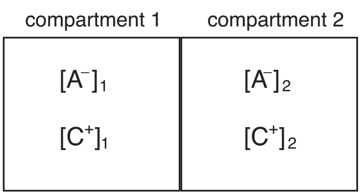
dynamic state of flux and continual change occurring, with fluid and solutes moving between compartments. These movements are driven by physicochemical gradients which arise due to osmotic, electrochemical and concentration[2] differences across cell membranes. Fluid movement between the intracellular and extracellular compartments is directed by osmosis (a particular form of passive diffusion), but because the outer plasma membrane of cells is relatively impermeable to most solutes, especially ions, active or passive carrier mechanisms are required to transport such components between compartments.

[2] Strictly speaking, it is thermodynamic 'activity' rather than concentration gradients which determine the dynamic flux of molecules across a membrane.

Electrochemical gradients *across* cell membranes arise due to the number and nature (principally their size and charge) of the solutes distributed on either side of the membrane. An imbalance in electrical charge across certain membranes is physiologically essential for example to allow nerve impulse conduction and for the initiation of muscle contraction, for example. However, for most cells, an equal distribution of total number of anions and cations is the norm. In addition to the necessity for electrical neutrality *across* a membrane, i.e. between compartments, the numbers of negative and positive charges *within* a particular compartment or body fluid must also be equivalent.

Normal hydrogen ion concentration in most body fluids is very low, in the nanomolar range, compared with concentrations of other ions such as sodium and potassium which are present at millimolar concentrations. Homeostatic mechanisms that regulate hydrogen ion balance are of necessity very sensitive to avoid the wide fluctuations in pH which might seriously impair enzyme function, leading to consequent cell dysfunction.

Physiological control of body fluid volumes and their chemical composition is fundamental to the health and wellbeing of cells, tissues and whole organisms, and as such represents a major purpose of homeostasis. Several physiological systems are involved with normal fluid and electrolyte homeostasis, and thus disorders of the kidneys, liver, endocrine system and gut can all lead to fluid, electrolyte or pH imbalance.



Electrical Neutrality.

The numerical product of the cations and ions in compartment 1 = the product of cations and anions in compartment 2; $[C^+]_1 \times [A^-]_1 = [C^+]_2 \times [A^-]_2$

Total cation concentration in compartment 1 = Total anion concentration in compartment 1, $([C^+]_1) = ([A^-]_1)$. Similarly for compartment 2.

The specific nature of anions and cations in the two compartments may differ.

Figure 1.2 Ionic balance within and between compartments

The organs that play the most significant role in fluid and electrolyte homeostasis are the kidneys, which process approximately 140 litres of fluid containing a significant quantity of solutes, including electrolytes, each day. Thus, it is not surprising that renal disease is often associated with serious fluid and electrolyte imbalances. Mechanisms for the normal renal handling of water, sodium and potassium, and calcium, in particular, are controlled by the endocrine system via the actions of anti-diuretic hormone (also called vasopressin), aldosterone and parathyroid hormone respectively. Endocrinopathy of the pituitary, adrenal cortex or parathyroid glands will therefore result in fluid and electrolyte imbalance. Renal regulation of proton excretion and bicarbonate reabsorption is a crucial aspect of pH homeostasis but, in contrast to water and electrolyte balance, is not under hormonal control.

The gastrointestinal tract secretes and subsequently reabsorbs a large volume of electrolyte-rich fluid on a daily basis, hence conditions leading to severe vomiting or diarrhoea can also result in significant losses of water, electrolytes or acid-base disturbances. Indeed, fatalities due to cholera infection are invariably due to dehydration as a result of the action of a microbial toxin interfering with normal water and electrolyte reabsorption in the colon. Additionally, the liver, one of the gastrointestinal-associated organs, contributes to acid-base balance through its role in ammonia metabolism and urea synthesis.

Changes in fluid balance, within an individual, can also occur frequently even in times of good health. Many of us suffer the side-effects, notably headache, of periods of especially underhydration, causing tissue cells to shrink, due simply to deficient fluid intake even though we are in all other respects ‘well’. Cellular overhydration resulting in cellular swelling is much more likely to be due to a homeostatic abnormality, but headache is also an early sign of fluid overload. Severe changes in hydration may occur after physical trauma resulting in injury to the body; this includes major surgery, so during the ‘post-op’ recovery period, surgeons and intensive-care physicians monitor fluid and electrolyte balance very carefully in their patients.

It is not only volume changes across cell membranes that are associated with pathology. If the volume of blood in the veins and arteries increases, the individual will suffer from high blood pressure (hypertension), a state which can have serious effects on, for example, the cardiovascular system, leading possibly to a stroke. Kidney damage can be either the cause or effect of hypertension. Conversely, if blood