Textbook of Physiology and Biochemistry BDS

GEORGE H. BELL
DONALD EMSLIE-SMITH
COLIN R. PATERSON

Ninth Edition

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GEORGE H. BELL

B.Sc., M.D. (Glasg.), F.R.C.P. (Glasg.), F.R.S.E.

Professor of Physiology in the University of Dundee; Honorary Fellow of the Accadenia Anatomico-Chirurgica of Perugia

by valory and Biochemistry

DONALD EMSLIE-SMITH

M.D. (Aberd.), F.R.C.P., F.R.C.P. (Edin.)

Reader in Medicine in the University of Dundee; Honorary Consultant Physician, the Royal Infirmary and Ninewells Hospital, Dundee

COLIN R. PATERSON

M.A., D.M., B.Sc. (Oxon.), M.R.C.Path.

Senior Lecturer in Biochemical Medicine in the University of Dundee; Honorary Consultant to the Tayside Area Health Board

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Contributors

- Dr R. L. P. Adams, Department of Biochemistry, University of Glasgow (Chapters 6, 17, 18).
- Dr Marjorie Allison, Department of Medicine, University of Glasgow (Chapter 29).
- Dr B. L. Andrew, Department of Physiology, University of Dundee (Chapter 37).
- Professor E. L. Blair, Department of Physiology, University of Newcastle upon Type (Chapter 9).
- Professor I. A. D. Bouchier, Department of Medicine, University of Dundee (Chapter 20).
- Miss Margaret Browning, Department of Biochemical Medicine, University of Dundee (Chapter 43).
- Dr Sheila Callender, Nuffield Department of Clinical Medicine, University of Oxford (Chapter 22).
- Dr C. Cameron, Scottish National Blood Transfusion Service (Chapter 23).
- Dr D. A. Chignell, Department of Biochemistry, University of Dundee (Chapter 3).
- Dr C. Cohen, Department of Geriatric Medicine, University of Dundee (Chapter 46).
- Dr P. Cohen, Department of Biochemistry, University of Dundee (Chapter 15).
- Dr J. W. Crawford, Department of Obstetrics and Gynaecology, University of Dundee (Chapter 44).
- Dr B. Creamer, Department of Medicine, St Thomas' Hospital Medical School, London (Chapter 8).
- Professor J. Crooks, Department of Pharmacology and Therapeutics, University of Dundee (Chapter 43).
- Dr J. S. Davison, Department of Physiology, University of Dundee (Chapter 8).
- Dr G. S. Dawes, Nuffield Institute for Medical Research, Oxford (Chapter 44).
- Professor K. C. Dixon, Department of Pathology, University of Cambridge (Chapter 4).
- Dr W. W. Downie, Rheumatism Research Unit, University of Leeds (Chapter 43).
- Dr J. V. G. A. Durnin, Department of Physiology, University of Glasgow (Chapter 7).
- Dr G. J. F. Dutton, Department of Biochemistry, University of Dundee (Chapter 4).
- Dr M. J. W. Faed, Department of Pathology, University of Dundee (Chapter 47).
- Dr Constance Forsyth, Department of Child Health, University of Dundee (Chapter 45).
- Mr A. G. Gibb, Department of Otolaryngology, University of Dundee (Chapter 41).
- Dr H. B. Goodall, Department of Pathology, University of Dundee (Chapter 22).
- Dr D. M. Green, Department of Bacteriology, University of Dundee (Chapters 6, 23).
- Professor F. F. Hellier, Department of Dermatology, University of Leeds (Chapter 31).
- Dr Olga Hudlicka, Department of Physiology, University of Birmingham (Chapter 37).
- Dr I. Hunter, Department of Biochemistry, University of St Andrews (Chapters 5, 16).

Dr T. E. Isles, Department of Biochemical Medicine, University of Dundee (Chapters 15, 43).

Dr R. V. Thomasa, Laparteen of Biochemater, University

- Dr B. E. Johnson, Department of Dermatology, University of Dundee (Chapter 31).
- Dr J. C. Kernohan, Department of Biochemistry, University of Dundee (Chapters 21, 28).
- Professor R. D. Keynes, Physiological Laboratory, University of Cambridge (Chapter 34).
- Professor G. H. Lathe, Department of Chemical Pathology, University of Leeds (Chapter 21).
- Dr J. A. R. Lenman, Department of Medicine, University of Dundee (Chapters 33 to 42).
- Dr P. R. Lewis, Physiological Laboratory, University of Cambridge (Chapter 34).
- Dr N. E. Loveless, Department of Psychology, University of Dundee (Chapter 42).
- Mr L. A. Mackenzie, Department of Medical Physics, Tayside Area Health Board (Appendix).
- Dr D. Maclean, Department of Medicine, University of Dundee (Chapters 27, 40).
- Dr P. B. Marshall, Department of Pharmacology and Therapeutics, University of Dundee (Chapter 40, 43).
- Dr P. E. G. Mitchell, Department of Biochemical Medicine, University of Dundee (Chapter 3).
- Mr H. R. Noltie, Department of Physiology, University of Dundee (Chapters 37, 40).
- Dr Maureen Palmer, Department of Physiology, Queen Elizabeth College, London (Chapters 8, 10).
- Professor W. W. Park, Department of Pathology, University of Dundee (Chapter 23).
- Dr N. Patel, Department of Obstetrics and Gynaecology, University of Dundee (Chapter 44).
- Dr J. M. Patrick, Department of Physiology, University of Nottingham (Chapters 27, 28).
- Dr M. J. Purves, Department of Physiology, University of Bristol (Chapter 33).
- Dr P. M. H. Rack, Department of Physiology, University of Birmingham (Chapter 37).
- Dr T. D. M. Roberts, Department of Physiology, University of Glasgow (Chapter 38).
- Dr J. G. Robson, Physiological Laboratory, University of Cambridge (Chapter 41).
- Professor I. C. Roddie, Department of Physiology, The Queen's University of Belfast (Chapters 25, 26).
- Professor P. Sleight, Department of Cardiology, University of Oxford (Chapter 25).
- Professor J. W. Smith, Department of Anatomy, University of St Andrews (Chapter 31).
- Dr D. A. S. Stansfield, Department of Biochemistry, University of Dundee (Chapters 33, 43).
- Dr M. J. Stewart, Department of Clinical Chemistry, University of Edinburgh (Chapters 2, 30).
- Dr D. Thirkell, Department of Biochemistry, University of St Andrews (Chapters 5, 16).
- Professor D. B. Thomas, Department of Anatomy, University of St Andrews (Chapter 22).

- Dr R. Y. Thomson, Department of Biochemistry, University of Glasgow (Chapters 11, 12, 13, 14).
- Dr A. S. Todd, Department of Pathology, University of Dundee (Chapter 22).
- Dr G. R. Tudhope, Department of Pharmacology and Therapeutics, University of Dundee (Chapter 7).
- Dr M. Turnbull, Department of Pharmacology and Therapeutics, University of Dundee (Chapter 43).
- Dandes (Chapters 24 22), of each E. D. Keping, Physical Liberary et Lavaring
- of Cambridge (Campor 14), rotalism G. H. Luby, Department of Chemical Extrology,
- Dr. J. R. Lenman, Department of Nederline University of
- Durace (Caspers Star 43).
 P. R. Levis, Physiological Labors vs., Linivasius of Cana-
- V. F. Loreless, Department of Pre-training, University of
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- In it. Nobe. Department of Products University of Dooder Convers V 40).
- b Maurice Palmer, Department Physiology, Queen
- Personal W. W. Park, Democratic of Equiphology, University
- it N. Parel, Department of Observe and Georgeology,
- [39] M. Pennik, Department of Physiology, University of Southerham & Eugene 22, 38;
- M. M. J. Parres, Department of President, University of
- M. M. Kark, Detainment of a chings, Operators of the maghein (Clapper 37).
- T. (= M. Roberts, Department (("symology, University of Chapter, 16).
- 34 C. Robson, Physiological Courterty, University of Carchitelge (Chapter 41)
- Forest T. C. Roddie, Decartmen Promotogy, The Green's University of Belfur, Ghapter - 20.
- Youtstock P. Sleight, Department of miletings, University of Oxford (Chapter 25)
- Trace or J. W. Seiner, Dipartment Latomy, Classessip of St. Andrews (Chapter 31)
- Dr.D. A. Stantifield, Disposition of Archimistry, Laiversity of Dander (Chapter 12, 43).
- Da.M. J. Stewart, Department of County of University of Edinburgh Character 4, 30
- Oc D. Thrifeell Department of Storic visity, Colvertity of St. Anthrews Chapters 5, 10.
- Protess r.D. B. Thomas, Department of Areasants, University of St. Andrews (Engine 22)

- Dr I. C. Whitfield, Neurocommunications Research Unit, University of Birmingham (Chapter 41).
- Dr S. P. Williamson, Liver Unit, King's College Hospital, London (Chapter 20).
- Dr K. G. Wormsley, Department of Pharmacology and Therapeutics, University of Dundee (Chapters 10, 20).
- Dr J. Wray, Department of Biochemistry, University of St Andrews (Chapter 19).
- Lucase (surpress)
 Professor E. J. Blein Department of Physiology, thirteentry of
- Newstelle upper Tyde (Chapter V)

 [Yorkestor I. I. D. Brachten Department of Medicine
- University of Damine (Chapter 20)
- (2) Sheelg Callender, Nuffield Department of Clinical Medicine, 131 (see page of Oxford (Chapter 22).
- Dr.C. Capturon, Scouler National Bland Transfersion bereiter
- Dr. D. A. Cldgrell, Department of fluctum at a University of Overlac (Chinese 3).
- Dr.C. Coner, Degenment of General Medicine, Francisco, or Dander Chapter 44
- De P. Coffen. Depletrages, of Biochemory, University of Director (Copier 15).
- Dr. W. Freedon Department of Obsteriound Consecutors.
- 3); B. S., very Department of Michellers, Sc Thomas Hospital Mental School, Landon (Cospier 8).
- Professor J. Consect Department of Phintment along young Thempearing Lee 18thy of Danadee (Chapter 43)
- Dr. L. S. Cerrson, Department of Previology, University of Design Chings 81
- (i) G. S. Larges, Nullylid Torustate for Medical Referency, (Artificial O'Dorner & C.).
- Protester E. C. Dreen, Department & Path Jogy, Dobertin, of Control of Congress.
- ir W. V. Downie, Blimmert en Remarch Unit, University of
- 24.1 V. G. 5. Parella, Deparation of Physiology, University
- (is to 1 to Dayton, Department of Stationary, University
- Dr M. J. W. Fard Department of Periodogra, Conversor of
- Detaillable Possyn, Department of Child Houlds University
- W. A. G. Albb. Department of On lar agalogy. University
- or Darves Caspinia. De Dischalle, University of
- Double (Cream Depart 22).
 Dr D. M. Cream Department of Instructions of
- Parkers L. Hell et Department at Dermatology, Cnivers in
- Dr. Orga, Haillades, Deiminssent of Physiology, University of
- Or I. Hance, Department of Broth mastry, University of St. Andrews (Chapters S. 16.

Preface to the ninth edition

Texts inevitably change as each year adds to knowledge, but sometimes changes are sometimes are sometimes of a different kind. We still mourn Norman Davidson's untimely death only a few days sometimes and before the publication of the last edition. Over twenty-five years his knowledge and make the days of the success of this combined textbook of physiology and before the success of this combined textbook of physiology and before the success of this new edition. Therefore, despite the change of editors, we are again using the abbreviation 'BDS' by which the book has been known for so many years.

We now welcome Colin Paterson of the Department of Biochemical Medicine in the University of Dundee. His continuing practical experience of both biochemistry of Dundee. His continuing practical experience of both biochemistry of Dundee, and to back and and clinical medicine is increasingly rare today and makes him an especially appropriate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate and postgraduate of the task of producing a textbook used by undergraduate of the task of the task of the task of task

The changes begun in the eighth edition have been widely extended in this one. The chapters have been re-arranged, and two new chapters, on immune mechanisms and on hepatic and biliary function, have been introduced. Eleven chapters have been rewritten and all the others have been extensively revised. The transition to S.I. units is now almost complete and we have provided information on the new units and on the conversion factors in the Appendix.

Dundee, 1976

G.H.B.

D.E-S.

Acknowledgements

We owe a great debt to an increasing number of contributors, whose names are given on the next page. Some are responsible for virtually whole chapters, some have made much smaller, but still valuable, contributions to the chapters whose numbers are linked to their names. They all took a great deal of care in revising the text for this edition and in many cases in rewriting large sections. We are grateful, too, for their remarkable tolerance of our editorial activities. We also thank many colleagues who have gone to considerable trouble to provide new illustrations.

We should like to express our gratitude to Mrs Margaret Glenday and Mrs Sheena and mile of another won 5W Moreland for their skilled and painstaking secretarial work, to Miss Mary Benstead more in a paper of the who has prepared more than 180 new illustrations for this edition, to Mrs Sheryl Spedding and Mr A. R. Whytock for their help with the illustrations and to the staff of the paper of their assistance. Dundee University Library for their assistance.

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1 Introduction

In the subjects of physiology and biochemistry we are concerned with living matter at two levels. The biochemist is concerned mainly with molecular events in the cell while the physiologist is more concerned with the intact organ or the whole organism. There is no need to justify the treatment of the two subjects in one book; nearly every chapter in this book contains both chemical and physiological information.

Physiologists and biochemists are concerned essentially with changes in the organism or its parts as it reacts to changes in the internal or external environment. They try to take a cinematographic view of living material; however, they frequently find it necessary to stop the cine-film from time to time to make a detailed examination of a single frame. For example, the chemical analysis of a tissue is a statement referring to one particular instant and a series of such analyses may indicate a progressive change from which the biochemist is able to build up a dynamic picture of the chemical activities of the tissue. Similarly the microscopic examination of a single section of a tissue is of value in showing its minute anatomy, but it may give little information as to its function. Such a section indeed represents only a momentary glimpse of what may be a continuously changing process.

In this book the terms 'physiology' and 'biochemistry' are used in a relatively narrow sense. We are concerned primarily with human aspects of the two subjects but where necessary we shall refer to events in other animals, although one cannot assume that what is true of another animal also applies to man. In biochemistry much of our understanding of metabolic processes was derived originally from studies on bacteria. While much of this information is now known to be relevant also in animals and man, major differences have also been found.

Structure and Function

The single cell is the functional unit of the body and each tissue is made up of vast numbers of cells. It must not be imagined, however, that a single cell is a simple uncomplicated structure. Although the ordinary light microscope may reveal little difference between one part of its cytoplasm and another, the electron-microscope and modern biochemical techniques have revealed an amazing complexity. It is, however, not yet possible to define the subtle difference between a living cell and a mere aggregation of molecules.

In the case of the more complex animals such as birds and mammals, the first characteristics of life that come to mind are warmth and movement. If a non-hibernating animal is still and cold it is assumed to be dead. By taking in food and oxidizing it an animal obtains energy which is used to produce heat or movement. The energy is obtained by the breakdown of body constituents by a process known as catabolism. The energy obtained by these catabolic processes may also be used for anabolic or synthetic processes such as those necessary for growth. Since both processes occur side by side it is convenient to use the word metabolism when referring to the total chemical changes occurring in the cell or in the body. So long as

metabolic processes continue, however slowly, the cell is alive; their arrest is death. Since these chemical processes are under the control of enzymes the cells can move or grow only within certain limits of temperature. If the temperature is too high the enzymes are destroyed, while at low temperatures enzymic reactions are retarded and finally cease.

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Living material is organized, that is, it has a definite structure. Moreover, particular functions, such as movement or secretion or conduction, are carried out by cells or organs whose structure is peculiarly fitted to these purposes. For a cell to survive there must be integration of function within it. In multicellular organisms there must be co-ordination of the activities of various cells, either by chemical messengers (bormones) or by a system of nerves.

Growth is a characteristic feature of living material. Growth of a single cell, however, cannot go on indefinitely because, as the cell increases in volume, its surface through which oxygen and food materials are admitted becomes so far removed from its centre that the supply of essential material to the latter is endangered. Before this stage is reached the cell divides into two daughter cells, a process known as reproduction.

Because a cell does not live in isolation, and is dependent on obtaining its food from outside, it must be capable of reacting to changes in, its environment. Such changes are called stimuli. If a stimulus increases the rate of chemical changes in the cell it is said to excite; if it decreases the metabolic rate it is said to depress, or to be an imbibitory stimulus.

Living organisms possess two properties which at first sight seem to conflict. These are best described under the headings of adaptation and homeostasis. Simple forms of life can survive over a wide range of temperature and can adapt themselves to changes in their environment and to the foodstuffs available. Indeed, if they could not do so they would soon die. The study of adaptation forms a large part of the subject of physiology, for the cells of the body can adjust themselves to a wide variety of changes. On the other hand, many physiological reactions are directed towards preserving a constant physical and chemical internal environment. All the cells in the body except those on the surface are provided with a fluid environment of relatively constant temperature, hydrogen ion concentration and osmotic pressure. This permits many bodily activities, the functioning of nerve cells and the working of enzymes for example, to be carried out under optimum conditions. Small changes in the composition of the extracellular fluid produce reactions which quickly restore the internal environment to its original state. This maintenance of a constant environment for the cells is known as homeostasis.

It is generally appreciated that the body regulates its internal environment with some accuracy. For example we know that it keeps its hydrogen-ion concentration remarkably constant. But to leave it at that is simply to admire it from a distance without making enquiries about the working of the regulatory mechanisms. The first requirement of such a mechanism is a detector of deviation from the standard conditions; the appropriate regulator must then be 'instructed' to reduce the devia-

tion. The new state of affairs is continuously assessed by the detector and the regulator is given fresh instructions. In other words the activity of the regulating device is constantly modified on the basis of information fed to it from the detector: such systems are termed 'feed-back' or 'control' mechanisms. Sensory receptors in muscles and joints send information to the central nervous system about length of muscles and angle of joints and movement and posture are regulated; cells sensitive to osmotic changes in the blood regulate the loss of water from the body; receptors in blood vessels detect changes in blood pressure and allow appropriate adjustments in the output of the heart and the calibre of the blood vessels. In many cases, however, the detecting mechanism is still to be discovered-for example we do not yet know how the blood volume, or the concentration of glucose in the blood, is detected. Both, however, are regulated within quite narrow limits.

Although the regulation of the internal environment reaches its highest development in man, he has gone still further by attempting to control his external environment. At first this involved the wearing of clothing, the building of shelters and houses, and the use of artificial heating, lighting and ventilation. These have not all proved to be unmixed blessings. Artificial lighting, for example, while it makes life more pleasant in the darkness of winter, introduces new problems of fatigue and extended hours of work. With the advent of the industrial era, unfavourable environments were created in which men had to work; although many of these dangers have been mitigated, we are now, because of so-called advances in technology, struggling against the evils of pollution. Man now climbs high in the air and descends to great depths in the sea; a few have even ventured into space and experienced the low gravitational forces of the moon. A great many new biological problems have appeared, some of which may be regarded as 'applied physiology'.

Our knowledge of the properties and functions of living cells is incomplete, but we know that the laws of conservation of matter and energy apply to the animal body just as certainly as they apply to non-living material. Investigation of living matter is largely a matter of observation supplemented by the methods of physics and chemistry. Thus we may measure pressures and potentials, make chemical analyses, or trace the pathways of radioactive substances through the body. The results of these observations are correlated, interpreted in the light of previous knowledge, and used as evidence for or against a particular hypothesis. While physiology and biochemistry are unlikely to become exact sciences comparable with physics or mathematics, their study may be of great practical importance in leading to methods for the diagnosis and treatment of disease.

At one time the organic basis for a patient's symptoms could be established only at post-mortem examination. The trend in modern medicine and surgery, however, is to study the living patient in order to understand the way in which normal physiological and biochemical processes have broken down, for disease is increasingly regarded as disordered physiological or biochemical processes which the homeostatic mechanisms have been unable to correct. For example chemical methods have been used for many years for the examination of the body fluids, to provide important diagnostic information and to control treatment; the treatment of diabetes mellitus depends almost entirely on material and methods originally

developed in the laboratory. Similarly much of our recent knowledge of cardiac diseases, cardiac failure and the surgical treatment of cardiac abnormalities is based upon physiological studies made in the laboratory or in the clinic.

The bodily activities depend so closely on one another that the workings of one part of the system cannot be comprehended without an understanding of the functioning of the whole. For example, in thinking of the activities of the heart we have to bear in mind the influence of the peripheral blood vessels, of the central nervous system, of respiration and of the chemical changes occurring in cardiac muscle. Our subject may, therefore, be likened to a circle: it is difficult to know where to enter it to begin our study, for it is only when we have completed the circle that we can fully understand our subject. For this reason we need to consider briefly the subject as a whole before beginning a more detailed description of its various parts.

The source of all the energy required by the body for carrying out muscular activity, for respiration, for the beating of the heart and the working of the nervous system, is the food. This consists mainly of proteins, fats and carbohydrates which are oxidized (burned) in the tissues. In addition to sources of energy the food must contain inorganic substances which are necessary to make good the loss of salts in the excreta and to provide material for the formation of blood and bone. The food must also supply certain substances which the body cannot synthesize, such as vitamins and essential amino acids. Since fluid is lost continuously by way of the kidneys as well as by the skin and lungs, water must be drunk to make good this loss. When food is swallowed it reaches the stomach and small intestine, where it is broken down by enzymes into substances of simpler chemical constitution which are absorbed through the lining of the small intestine into the blood stream and distributed throughout the body.

The oxygen required for combustion of the foodstuffs reaches the blood through the lungs. During breathing the chest expands and air flows into the lungs which are spongy organs richly supplied with blood vessels. Oxygen diffuses readily through the very thin walls of the capillary vessels of the lung tissue, becoming attached to the haemoglobin contained in the red cells in which it is distributed throughout the body by the circulation. The carbon dioxide produced in combustion in the tissues is taken up by the blood and carried to the lungs where it escapes from the blood and is exhaled. By-products of oxidation not needed by the body reach the kidneys in the blood and are excreted into the urine.

The heart is a two-sided muscular pump which drives the blood along the blood vessels. The left side pumps blood to the heart muscle itself, to the skeletal muscles, the brain and other organs. The blood from these parts returns to the right heart which sends the blood to the lungs where oxygen is taken up and carbon dioxide is eliminated. The oxygenated blood then returns to the left side of the heart and is pumped out to the tissues. The blood is conveyed away from the heart at a fairly high pressure in thick-walled tubes, the arteries. These vessels branch repeatedly and become smaller in diameter, with thinner and thinner walls. In the tissues the smallest blood vessels, the capillaries, are bounded by a single layer of cells through which gases, fluid, or chemical substances of small molecular size move easily. The blood is drained away from

the tissues at low pressure in wide vessels (the veins) with relatively thin walls.

The skeletal muscles are the main effector tissues. By their contractions the position of the bones is altered and respiration and speech are made possible. The highly complex movements of the limbs in walking, and of the tongue in speech, are co-ordinated by the central nervous system, consisting of the brain and spinal cord. Nerves called efferent or motor nerves leave this system and pass to all the structures of the body and control muscular movement as well as the secretion of some of the glands, the heart beat and the calibre of the blood vessels. Central control is, however, of no value unless the centre has full information about events in the body and around it. This information is conveyed to the central nervous system by the sensory or afferent nerves which carry impulses from the eye, the ear, the skin, the muscles and joints, and the heart, the lungs and the intestines. The sensory nerves are actually much more numerous than the motor nerves. Although many of the activities occurring in the central nervous system are exceedingly complex, relatively few rise to consciousness. We are quite unaware, for example, of the muscular adjustments needed to maintain balance or to move our eyes so that images of the external world are kept fixed on the retinae. These adjustments are called reflex and the pathways involved, namely sensory nerves, central nervous system and motor nerves, are called reflex arcs. The lowest part of the brain, the medulla oblongata, is responsible for the muscular movements of respiration, for the control of the heart rate and the regulation of the blood vessels, and is concerned in the maintenance of posture. The cerebellum, which lies above the medulla, is concerned with co-ordination of muscular movements. The fore-part of the brain, the cerebrum, has a layer of grey matter (nerve cells) on its surface and also masses of grey matter within. The grey matter is interconnected by innumerable nerve fibres which together make up the white matter. The cerebrum is concerned in all the higher mental activities and with reading, writing and speaking, as well as in so-called voluntary movements, the perception of touch and in the special senses of vision and hearing.

In addition to the rapidly acting co-ordinating mechanism of the nervous system there is a chemical (humoral) system which operates more slowly. For example, during the digestion of food in the duodenum a chemical substance (hormone) called secretin is produced in the mucous membrane, absorbed into the blood and carried to the pancreas which responds by pouring out its digestive juices. The thyroid gland in the neck produces a hormone which is absorbed directly from the gland into the blood stream and influences the metabolic activity of the cells of the body.

Under the heading of reproduction, we consider the processes necessary for the maintenance of the species. The male cells, the *spermatozoa*, are produced in the testis and when deposited in the female genital tract one of them may fertilize an *ovum* produced in the ovary. This sets off a series of complicated changes, mainly under hormonal control, to provide for the growth of the fertilized cell in the uterus. By repeated division the fertilized ovum develops into the embryo whose nutrition in the uterus is carried out by transfer of materials across the placenta. At the end of pregnancy the muscular wall of the uterus contracts, the fetus is delivered and then acquires oxygen directly, by breathing air into its lungs, instead of

indirectly through the placenta. In the meantime the mother's mammary glands have enlarged in preparation for lactation and soon after parturition they produce milk for the nourishment of the infant.

Many of the organs of the infant, especially the central nervous system, the kidneys and the liver, are incompletely developed at birth and only achieve full functional capacity after some years. An important landmark in development is puberty. At this time the gonads complete their development and in so doing produce the physical and mental changes characteristic of the adult. The ovaries continue to produce ova till the menopause in the fifth decade, but the production of spermatozoa by the male persists much longer.

The Composition of Living Tissues

The living body contains, in addition to a large amount of water, protein which is the main nitrogenous constituent of all living material, a variable amount of fatty material known collectively as lipid, a small amount of carbohydrate, and mineral salts. In man the relative proportions of these constituents, especially fat and carbohydrate, vary greatly from one person to another, and in the one individual at different times in his life, according to his nutrition. Nevertheless, the composition of the human body may be represented roughly as shown in Table 1.1.

Table 1.1 Approximate composition of a man weighing 70 kg (154 lb)

guage briggature	Percentage	kg
Water		-
Fat	15	10-5
Protein	12	8-4
Carbohydrate	0.5	0.35
Minerals	2.5	1.75
	100	70

The chief constituent of living matter is water. Its importance in both the structure and functioning of the tissues is discussed in many chapters in this book, especially Chapters 2 and 30, but some preliminary considerations are given here.

The body of a healthy adult male consists of some 65 to 70 per cent of water and about 15 per cent of fat; the remainder is accounted for by the solid parts of cells and supporting structures. The considerable variations in total body water between one person and another are the result of differences in fat content since the amount of water in the fat-free parts of the body is remarkably constant. This accounts for the fact that the water content of the body of the female (50 to 55 per cent) is rather less than that of the male. In very fat people the body water may be no more than 40 per cent of the total body weight. In the fetus the relative proportion of water in the body is much higher, for example 94 per cent at the third month of fetal life. The reasons for these differences are not known.

Most tissues contain more than 70 per cent water. Exceptions are adipose tissue (50 per cent), bone (30 per cent) and teeth (5 per cent). Table 1.2 shows that by far the greatest amount of water is to be found in muscle which accounts for the largest part of the body mass.

Table 1.2 Percentage of the total body water which is found in the various tissues and organs

Muscle	50-8	Brain	2-7
Skeleton	12-5	Lungs	2-4
Skin	6-6	Fatty tissue	2.3
Blood	4.7	Kidneys	0-6
Intestine	3-2	Spleen	0-4
Liver	2.8	Rest of body	11.0
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In its capacity as a solvent (Chap. 2) water plays a fundamental role in cellular reactions. A very large number of substances are soluble in water; other substances such as fats can be carried in fine emulsions or be rendered water-soluble in other ways. Certain other properties of water are also of importance. The high heat capacity of water and its high latent heat of evaporation both contribute to the control of body temperature (p. 5).

In the normal course of events a large amount of water is lost from the body daily and a corresponding amount is taken in, so that water balance is maintained. As shown in Figure 1.3, the amount of water gained and lost by an adult man engaged in a sedentary occupation in a temperate climate is about 2½ litres per day.

Water is gained by the body from two main sources. Most of it is taken in by the mouth in the form of food and drink, but a small amount of water is normally formed in the tissues as the result of the oxidation of the hydrogen of foodstuffs. The amount of water ingested in the diet varies, of course, over very wide limits according to habit, climate and occupation.

The amount of metabolic water formed in the tissues as the result of the oxidation processes described in Chapter 14 is about 300 ml in man, that is about 14 per cent of his total daily fluid intake. This water is formed in the cells and is of great value to the organism, since its formation is not accompanied by the great osmotic changes associated with the intake of large amounts of fluid. It is of great importance to the hibernating animal which lives for long periods on metabolic water.

Figure 1.3 gives no idea of the great turnover of fluid which takes place in the body in the course of a day. In 24 hours a man secretes 1 to 1.5 litres of saliva; 1 to 2 litres of gastric juice; 0.5 to 1 litre of bile; 0.6 to 0.8 litre of pancreatic juice and 3 litres of intestinal juice. All this fluid, with the exception of about 100 ml which escapes in the faeces, is reabsorbed.

The composition of the human body in terms of elements is shown in Table 1.4. The most abundant elements are carbon, oxygen and hydrogen, but minerals such as calcium and phosphorus are also plentiful. Other minerals such as iodine and iron are present only in small quantities. Nevertheless their presence in the diet is of great nutritional importance (Chap. 7).

Table 1.4 Composition of the human body (per cent by weight)

Oxygen	65	Chlorine	0-15
Carbon	18	Magnesium	0.05
Hydrogen	10	Iron	0-004
Nitrogen	3	Iodine	0-00004
Calcium	1.5	Copper)	
Phosphorus	1-0	Manganese	
Potassium	0-35	Zinc	
Sulphur	0-25	Fluorine (traces
Sodium	0-15	Molybdenum,	
		etc.	

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Fig. 1.3 Daily gains and losses of water by an adult man with a sedentary occupation in a temperate climate. In hotter climates the amounts of water drunk and lost in the sweat are greatly increased.

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2 The Properties of Water

Water is so familiar as a major constituent of the body that its importance, both as a structural molecule and as a participant in reactions, is easily overlooked.

Approximately 70 per cent of the body is water, and its importance is such that the loss of only 10 to 20 per cent can lead to death. In contrast almost all of the body fat and 50 per cent of the tissue protein must be lost before death by starvation occurs. The tissues contain different proportions of water depending on their function. Thus adipose tissue and bone only contain about 30 per cent water by weight, whereas muscle, which accounts for about one-third of the body mass in a lean person, contains almost one-half of the body water.

The body water may be divided into three or four functional compartments which are discussed further in Chapter 30. The water molecules are free to pass between these compartments and all water molecules in the body can be regarded as equivalent and interchangeable.

In this chapter we examine the role of water in the body as well as the way in which the unique properties of water allow it to play its essential role in biochemical reactions.

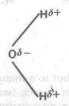
The Role of Water in Temperature Control

Water has a high heat capacity. This means that compared with other liquids relatively large amounts of heat are required to raise its temperature. Since water makes up a large proportion of the body, the body temperature is little affected by large changes in heat production, and since the latent heat of evaporation of water is high, the evaporation of small amounts of water in sweat from the skin leads to the loss of a relatively large amount of heat. Similarly, the high latent heat of solidification is a protection against freezing of the tissues when the environmental temperature drops below zero, while the likelihood of freezing of the tissue water is further reduced because the dissolved solutes depress its freezing point.

The Role of Water as a Solvent

In order to understand the behaviour of solutes in water we must review the structure of water itself.

Structure of water. The water molecule is commonly represented as



The O—H bond is a covalent bond formed by shared electrons. However the electrons are attracted more strongly towards the heavier oxygen nucleus and this leads to the slight

negative charge $(\delta -)$ in this region, and a alight positive charge $(\delta +)$ in the region of the hydrogen nuclei. This imbalance in charge gives the molecule an electrical polarity and water is thus a polar molecule. When water molecules are in close proximity to one another, the charge attraction leads to their alignment thus:



The dashed line, representing the charge attraction, is a hydrogen bond. This is a stronger bond than the van der Waals forces which exist between uncharged molecules. A simple illustration of these differences in bond strength is provided by a comparison of the boiling points of substances, a measure of the amount of energy required to break the bonds. Ammonia, with only van der Waals forces, boils at -33° C. Methane, a molecule of similar size, boils at -161° C. However, water, with the hydrogen bonding, requires a temperature of 100° C to separate the molecules.

Mechanism of solution. For a solid to dissolve in a liquid, three things must happen: (1) the bonds between the molecules or ions of the solid must be broken, (2) the bonds between the molecules of the liquid must be broken and (3) a form of bonding must occur between the molecules of the solvent and the molecules or ions of the solute. These bonds must balance the attractions between solvent molecules and between solute molecules.

It follows that a solid consisting of strong intermolecular or interionic bonds can dissolve in a liquid with similar bonds, and the opposite is also true. Water, for example, can dissolve sodium chloride, a solid whose intra-ionic bonds are formed

Fig. 2.1 Arrangement of sodium and chloride ions in a crystal of sodium chloride.

by charge attraction and are so strong that it is fused or volatilized only with difficulty. The bonds in sodium chloride are electrostatic bonds between full positive and negative charges (Fig. 2.1). When sodium chloride dissolves in water the ions become arranged so that sodium ion is adjacent to the negatively charged oxygen atoms while the chloride ion is surrounded by positively charged hydrogen atoms (Fig. 2.2).

Fig. 2.2 Arrangement of water molecules around sodium and chloride ions in an aqueous solution.

The van der Waals forces which exist in non-polar substances are relatively non-specific and therefore compounds such as benzene and ether, in which most of the bonds are of this type, are completely miscible with one another, but not with water. Many solvents have properties intermediate between those of water and benzene. For example, ethanol, like other alcohols, can be regarded as a derivative of water in which one hydrogen atom has been replaced by an alkyl group.

In summary, water, a highly polar liquid, is a good solvent for polar molecules and ions. It does not readily dissolve non-polar or unionized molecules.

Methods of rendering substances soluble in water. While many of the molecules in animal tissues are polar there are certain classes of compounds, notably lipids, which are non-polar, and yet must be carried in solution throughout the body and take part in biochemical reactions. Such non-polar molecules are rendered soluble in water by attaching them to polar molecules which are themselves soluble in water. One example of this mechanism is provided by the plasma proteins, notably albumin, which are capable of transporting insoluble substances like bilirubin and many drugs. The albumin molecule has many charged side chains and is water soluble. It also has relatively non-polar areas which can provide the binding sites for the non-polar molecules.

Another example of the way in which non-polar substances can be made water soluble is provided by the emulsification of fats to form *micelles*. Fatty acid molecules have long non-polar hydrocarbon chains but have polar carboxyl groups at one end.

In the presence of molecules of bile salts (Chap. 10) these fatty acids arrange themselves with their carboxy groups outermost adjacent to the aqueous environment and their hydrocarbon tails in the interior (Fig. 2.3).

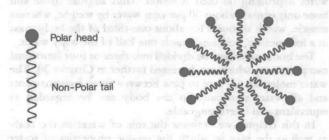


Fig. 2.3 Arrangement of fatty acid chains in a micelle.

Properties of Ions in Aqueous Solution

As we have seen, the extent to which the ions of a solute dissociate from each other in aqueous solution depends on their attraction to each other relative to their attraction to the water molecules. The dissociation of a substance in water can be represented as shown here for acetic acid:

This is a simplification of the actual process, as the free protons are attracted to adjacent water molecules to form H_3O^+ which in turn acquires a shell of further water molecules to give the structure $H_9O_4^{-+}$:

Water itself is ionized, but to a minute extent, for there are 550×10^6 water molecules to each free pair of H⁺ and OH⁻ ions. Although small, the dissociation of water is of great physiological importance in that a small change in the amount of free H⁺ ions and thus the acidity of the solution has a large effect on the behaviour of other ions in the solution.