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APPLIED PHYSIOLOGY

BY

SAMSON WRIGHT

M.D., F.R.C.P.

JOHN ASTOR PROFESSOR OF PHYSIOLOGY, UNIVERSITY OF LONDON, MIDDLESEX HOSPITAL MEDICAL SCHOOL. SOMETIME EXAMINER IN PHYSIOLOGY TO THE UNIVERSITIES OF OXFORD, LONDON AND LEEDS; THE ROYAL COLLEGE OF SURGEONS OF ENGLAND; THE ROYAL COLLEGE OF SURGEONS OF EDINBURGH; THE CONJOINT BOARD IN ENGLAND; THE CONJOINT BOARD IN IRELAND

WITH THE COLLABORATION OF

MONTAGUE MAIZELS, M.D., F.R.C.P.

PROFESSOR OF CLINICAL PATHOLOGY, UNIVERSITY OF LONDON, UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL

AND

JOHN B. JEPSON, M.A., B.Sc., D.Phil., A.R.I.C.

SENIOR LECTURER IN BIOCHEMISTRY, COURTAULD INSTITUTE OF BIOCHEMISTRY, MIDDLESEX HOSPITAL MEDICAL SCHOOL

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PREFACE TO THE NINTH EDITION

THIS edition of *Applied Physiology* is virtually a new book; more than half the text has been rewritten and the rest has been carefully revised to reflect the present state of knowledge. The subject matter has been radically rearranged. The opening chapter now deals with the "Regulation of the Internal Environment," a theme made classical by Claude Bernard and developed by many great physiologists like Sherrington, Haldane, and Barcroft in this country, and Cannon, Lawrence Henderson, and Van Slyke in the United States. The "constancy of the internal environment" is the outstanding generalization of physiology; the first 130 pages of this book, which illustrate the principle by many examples, have enabled me to review under one heading numerous themes which are usually treated apart because they fall into what conventional classification treats as separate systems. On the clinical side this chapter deals with many topics of practical importance, such as water and salt lack and excess; tests of renal function; renal failure; acidæmia and alkalæmia; diabetes insipidus; œdema; blood changes in obstruction of the alimentary canal; disorders of the cerebrospinal fluid. Other newly arranged chapters are those on "Metabolism," "Endocrine Control of Metabolism" and "Reproduction."

An important feature of this edition is an increase in the number of illustrations. About 200 new figures have been added, bringing the total up to 688; these figures have been carefully chosen, mainly from recent papers; most of them have been redrawn or modified to make them more suitable for teaching purposes. My experience makes me doubt whether illustrations are adequately or properly used. Many welcome them as mere padding material which leaves less text on the page and enables one consequently to cover the ground more quickly. It is curious that though diagrams are studied with care, illustrations which summarize the results of actual experiments and so represent first-hand evidence are merely glanced at. I again draw attention to the Appendix (p. 1118) in which two figures are carefully described and analysed. It might be worth the reader's while to examine many of the illustrations in the text in the same thorough way. The sources of all the figures are fully acknowledged in the text; I might add that any paper that contains a figure worth borrowing is invariably well worth reading. Professor Diamond and the Commonwealth Fund of New York kindly gave me permission to prepare the three new colour plates from the beautiful illustrations in the book by Blackfan, Diamond, and Leister, *Atlas of the Blood in Children*.

As in the past, the references have been restricted to a few key papers which I have found especially useful; they will serve to introduce the reader to the copious literature of the subject.

The terminology in the chapters on the "Nervous System" and "Autonomic Nervous System" with few exceptions follows that used by

Ranson and Clark in their *Anatomy of the Nervous System*; but mention is made in brackets of the older terms which still have a wide currency.

When this book first appeared more than twenty-five years ago it was something of a pioneer venture. The point of view which it advocated was set out in the original Preface (which has been regularly reprinted) and illustrated by the text itself. In selecting the material for discussion I have always had in mind the needs and interests of both undergraduate students and postgraduate readers, including those preparing for the higher examinations, who wish to keep abreast with current developments in both pure and applied physiology. The subject matter is presented in considerable detail because the details are needed for a proper understanding of the workings of the body in health and disease and are often of great practical importance in the care of patients; but I leave it to the good sense of the individual reader to concentrate on his needs and to ignore what he considers to be outside his field of interest. In this way he can make the book as long or as short as he wishes.

More than ever before I am indebted to friends and colleagues for their help, especially to my collaborators Professor Montague Maizels and Dr. John B. Jepson. Professor Maizels has advised and assisted me in the preparation of the chapters on the "Internal Environment" and the "Blood," and on matters relating to Clinical Pathology. Dr. Jepson has rewritten the chapter on "Metabolism" and has advised and assisted me on matters relating to biochemistry and physical chemistry throughout the book; his contribution has been specially notable in the chapters dealing with the "Endocrines" and "Nutrition." Dr. Cyril Keele has helped with the "Endocrines" and "Reproduction." Mr. W. F. Floyd has contributed the section on "Clinical Electroencephalography" and has advised on electrophysiological matters. I gratefully acknowledge help from: Dr. Moran Campbell, Miss Mary Chennells, Dr. C. E. Dent, Dr. P. W. Nathan, Dr. Eric Neil, and Professor David Slome. Special thanks are due to Dr. I. Calma, who has been good enough to prepare the Index.

The publishers, and especially Mr. G. T. Hollis, M.A., have been unfailing in their kindness and consideration. They have agreed readily to all my suggestions for improving the book. They have permitted without impatience or hint of complaint most extensive and repeated alterations in the proofs; by their indulgence I have been able to incorporate in the text references to the major advances in knowledge which took place while the book was passing through the press and to make the consequential alterations needed to maintain self-consistency. My daughter Sandra Wright devoted much skill and patience to transmuting a long and difficult manuscript into a clear and intelligible typescript. My secretary Miss R. Bambridge has given me devoted service in the long and complex task of seeing the book through the press. My warmest thanks are extended to them all.

S. W.

MIDDLESEX HOSPITAL MEDICAL SCHOOL,
January, 1952.

FROM THE PREFACE TO THE FIRST EDITION

THIS book is based on the various courses of lectures I have given both in the department of Physiology in the Middlesex Hospital Medical School and to men working in the wards and the various departments of the Hospital. My aim has been to present clearly and concisely how the various functions of the body are performed. To economize space, no account is given, however, of the peripheral mechanism of vision or of hearing; otherwise, the ground is covered fairly completely. As the book is intended for medical readers, I have throughout laid emphasis on and devoted particular attention to those functions which are commonly deranged in disease. I have kept in view Dr. Haldane's dictum, that the aim of physiology is to consider how the internal environment of the body is kept constant in spite of continual alterations in the external environment. Throughout the text numerous cross references have been inserted which may help to clear up doubtful points, and are especially intended to impress on the reader that the subject must be considered as a coordinated and integrated whole, and that it does not deal with a series of isolated and independent organs and systems.

I have not attempted, in the more strictly applied sections of the book, to cover the ground completely, but I have selected from the mass of material available the problems of the greatest practical importance, and particularly those which are, perhaps, not so fully discussed in text-books of pathology or medicine.

I must confess to have paid some attention to the requirements of the various examining bodies. The physiological sections may prove useful to men reading for the second M.B. examination of the various Universities, and in particular I hope it will be helpful to men preparing for the Primary Fellowship examination of the Royal College of Surgeons. The applied sections may be found helpful by men reading for their final examinations, and perhaps even for the higher examinations of M.D. or M.R.C.P.

It seems to me unfortunate that in the teaching of physiology greater use is not made of the wealth of clinical material present in the wards of the Hospitals, which could readily be made available. The main facts of the physiology of the nervous system and the ductless glands, at any rate, could thus be clearly demonstrated; and the interest of the student would be aroused when he finds that he is considering in his physiological studies the same patients that he will have to deal with when doing his clinical work. This is the method I have adopted whenever possible in this book. In considering the cerebellum, for example, a full account is given of the symptoms and signs of lesions to this structure in the *human* subject. This enables the student of physiology to draw his conclusions concerning the functions of the organ, and at the same time familiarizes him with the clinical

aspects of disorders of the cerebellum. If a course of demonstrations such as I have suggested became an integral part of all courses in physiology, the medical student would enter on his clinical studies with a much sounder knowledge of the practically important parts of the subject, and with at least an elementary knowledge of medicine.

S. W.

MIDDLESEX HOSPITAL MEDICAL SCHOOL,
September, 1926.

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NOTE

As was explained in the Preface, some passages in this book are wholly or mainly of *clinical or specialist interest*. In order to guide the pre-clinical student in his reading, a list of such passages, with page references, is given below. These may either be wholly *omitted* by him, or studied with discretion. Particulars are also given of topics which are treated in considerably greater detail than he needs; in these cases, he might be wise to try to grasp only the main outlines of the discussion.

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APPLIED PHYSIOLOGY

I

REGULATION OF CONSTANCY OF INTERNAL ENVIRONMENT [MILIEU INTÉRIEUR]

THE INTERNAL ENVIRONMENT (MILIEU INTÉRIEUR)[1]

Internal Environment (Milieu Intérieur.)—Claude Bernard pointed out that the external environment of the organism as a whole, *e.g.* atmospheric air in our own case, is not the external environment of the individual cells of the body. The cells are carefully insulated from the general external environment and are bathed by the fluid in the minute spaces between the cells—the so-called *tissue* or *interstitial fluid*. Interstitial fluid can normally be collected only with great difficulty; fortunately, however, its crystalloid composition is almost identical with that of plasma which is easily obtained for analysis. It is customary in fact to use plasma analyses as a guide to variations in the composition of the interstitial fluid. Claude Bernard called the interstitial fluid and the plasma the *internal environment* (*milieu intérieur*).[2] He emphasized that in spite of the very wide range of variation that occurs in the composition of the external environment, the internal environment by contrast is kept remarkably constant as a result of the intervention of many compensatory mechanisms. The way in which the constancy of the internal environment is maintained with respect (for example) to acid-base equilibrium, osmotic pressure, concentration of individual solutes or of ions (sugar, Na^+, K^+, Ca^{++}), and temperature is one of the most important problems of physiology. The constancy of the internal environment is not absolute; under normal conditions slight variations occur as with all so-called physiological "constants." If the stresses imposed on the system become too great the composition of the internal environment may alter significantly, often with disastrous effects. Claude Bernard pointed out that the constancy of the composition of the *milieu intérieur* is "the condition of a free life." If by a "free life" is meant vigorous and effective activity of the organism as a whole, the aphorism is extremely apt. Thus a deviation of H^+ ion concentration from the normal *p*H of 7·4 to 7·0 or 7·8, a change of serum calcium from 10 mg. to 5 or 15 mg-%, a change of blood sugar from 100 to 30 mg-% may cause loss of consciousness and the danger of imminent death.

Living cells are always undergoing change, but to survive and function

[1] Claude Bernard, *Introduction to the Study of Experimental Medicine* (English translation), N.Y., 1949. Olmsted, *Claude Bernard, physiologist*, N.Y., 1938. Barcroft, *Architecture of Physiological Function*, Cambridge, 1934. Cannon, *Wisdom of Body*, N.Y., 1932. Sherrington, *Man on his Nature*, Cambridge, 1951. Sunderman and Boerner, *Normal Values in Clinical Medicine*, Philadelphia, 1949.

[2] "Qu'est-ce que ce milieu intérieur? C'est le sang, non pas à la vérité le sang tout entier, mais la partie fluide du sang, le plasma sanguin, ensemble de tous liquides interstitiels, source et confluent de tous les échanges élémentaires." (Claude Bernard.)

normally their integrity in all respects, *i.e.* their form, chemical composition and chemical organization must be constantly and fully restored and preserved. Cells maintain the composition of their organic constituents not by inactivity but by ceaseless activity. Innumerable enzymes are constantly breaking down all the organic cell constituents, both large and small; on the other hand synthetic enzymes are constantly making good this "chemical erosion" by rebuilding the cell structure from the components of the diet and from cellular débris. The stability of the living cell is a *dynamic* one, resulting from the establishment of a balance between the breakdown and repair reactions. The most comprehensive generalization of physiology is that the organism reacts to environmental changes (internal or external) in such a manner as to preserve the integrity of the whole organism and of its constituent parts.

The fluid inside the tissue cells is called the *intracellular fluid*; when its composition is compared with that of the surrounding medium (the *interstitial* or *extracellular fluid*) marked differences are revealed (p. 5). To maintain the characteristic pattern of its electrolyte content the cell must use energy which is derived from catabolic processes (p. 8). In order that a cell may function normally it must maintain the constancy of its own internal "private" composition and also be bathed in a surrounding fluid of utterly different composition which also must be kept approximately constant. Thus, if the Na^+ ion concentration in the interstitial fluid is decreased, the excitability of nerve fibre and skeletal and heart muscle diminishes; in the absence of interstitial Na^+ ions, excitability disappears.

The body then is a highly sensitive, highly efficient self-regulating and thus self-preserving mechanism; it automatically preserves the constancy of its own private internal world in the face of the widest variations in the character of the outside world. But with the development of *intelligence*, man need no longer depend exclusively on his inborn unconscious reactions; he can devise new supplementary protective methods. Thus he helps to maintain the constancy of body temperature at the North Pole and Equator by attending to such matters as clothes and shelter; in "conditioned" houses he can even provide for himself the external environment most congenial and convenient to his body and mind. At high altitudes he can overcome the effects of oxygen lack (*anoxia*) not only by automatic physiological reactions but also by deliberately providing himself with a supply of pure oxygen or by encasing himself in a pressurized chamber in which the atmospheric conditions present at sea level are maintained.

BODY WATER AND BODY FLUID. GENERAL SURVEY OF WATER AND FLUID EXCHANGES[1]

Body Water.—Water is the largest constituent of the body; about 65–70% of the total body weight consists of water. The body of a man weighing 70 kg. thus contains about 50 L of water. The water content of most tissues is 70–80%, the skeleton being the principal exception with a water content of about 20%. It is a little surprising that bones should

[1] Gamble, *Extracellular Fluid*, Harvard University Press, 1949. Peters, *Body Water*, Springfield, Illinois, 1935. *Physiol. Rev.*, 1944, *24*, 49.

contain even so much water, but it must be remembered that one-third of the weight of a fresh bone consists of organic material dissolved in water (the inorganic salts constitute the other two-thirds).

Body water is found :

(i) *inside* the cells—*intracellular* water ;

(ii) *outside* the cells—*extracellular* water. The extracellular water is further subdivided into : (*a*) water in the *plasma* ; (*b*) *interstitial water*, present in the cracks and crevices (*tissue spaces*) which lie between the tissue cells. Additional minor divisions of the extracellular water are : *lymph* (in the lymphatic vessels), *cerebrospinal fluid*, and *aqueous humour* (in the anterior chamber of the eye).

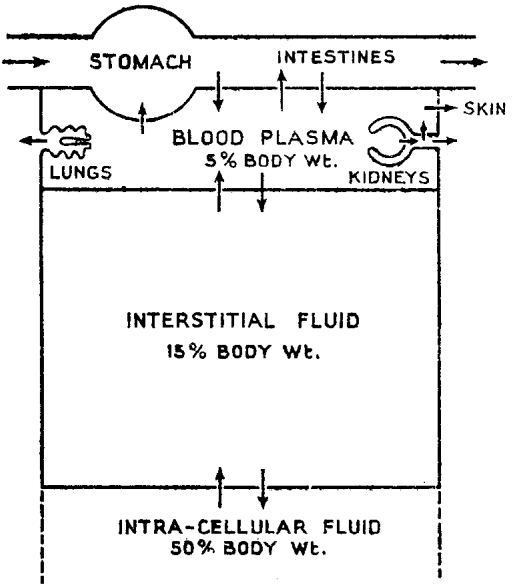

FIG. 1.—Diagram showing Principal Compartments of Body Fluid and Main Fluid Exchanges that take place in the Body. (After Gamble, *Extracellular Fluid*, Harvard University Press, 1949.)

Approximate quantitative data for a man weighing 70 kg. and for one weighing 60 kg. are summarized below (see also Fig. 1) :

Total body weight	100%	70 kg.	60 kg.
Total body water	70%	50 L	42 L
(i) Intracellular water . . .	50%	35 L	30 L
(ii) **Extracellular water**. . .	20%	15 L	12 L
(*a*) **plasma**	5%	3·5 L	3 L
(*b*) interstitial water . .	15%	11·5 L	9 L

Water Intake and Water Loss.—Body water is constantly carrying out exchanges with the external environment (Fig. 1).

(1) Water is normally *absorbed* into the body from the *bowel*; it can also be introduced artificially, *e.g.* by subcutaneous or intravenous injection.

(2) Water is *eliminated* from the body:

(i) via the *kidney* in the urine;
(ii) via the *skin* (*a*) in so-called insensible perspiration and (*b*) in sweat;
(iii) via the *lungs* in the expired air;
(iv) to a minor degree via the *large intestine* in the fæces, in lactating women in the *milk* (and from time to time in the *tears*).

(3) It must also be remembered that water is constantly being *formed* in all tissues as an end-product of the oxidation of the foodstuffs.

Approximate quantitative data (both average and range) for these exchanges per day are as follows:

Water intake: as water, 1500 c.c. [range: 0 to several litres per hour];
in food, 1000 c.c. [depending on composition of diet];
from oxidation in tissues, 300 c.c.

Water loss: in urine, 1500 c.c. [range: under 20 c.c. to over 1200 c.c. per hour];
via skin { insensible perspiration [constant at 600–800 c.c.]
sweat [range: 0 to nearly 2 litres per hour];
via lungs, 400 c.c.;
in fæces, 100 c.c. [increased in diarrhœa].

Over a reasonable period of time water intake and water loss must be equal if the normal water balance is to be maintained. Water intake can be reduced to nothing, the only source of water then being the small volume formed during the oxidation of foodstuffs. Water loss, however, cannot normally be reduced to the same degree; thus

(i) insensible perspiration from the skin and water loss by evaporation from the lungs never fall below about 1000 c.c. per day; and
(ii) a minimal flow of urine of about 400 or 500 c.c. per day is needed for the excretion of waste products.

Excessive water loss produces dehydration, and excessive water retention produces hydration; lowered water content of the blood is called *anhydræmia* and excessive water content *hydræmia*.

Body Fluid.—Body water plus its dissolved solutes is called body fluid. Body fluid can be regarded as lying in three *compartments* (Fig. 1):

(i) the *intracellular* fluid which is bounded by the membranes of the individual cells;
(ii) the *plasma* which is bounded by the walls of the blood vessels, and specifically in the capillaries by a thin-walled endothelium;
(iii) the *interstitial* fluid (*tissue* fluid) which is separated from the intracellular water by the cell membranes and from plasma by the capillary endothelium.