Principles of
Human Physiology

TWELFTH EDITION

BY

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LOVATT EVANS
D.Sc., F.R.C.P., F.R.S., LL.D.
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the University of London

This book is intended for students of medicine and of science. It aims at presenting, necessarily in compact form, a coherent account of contemporary physiology and of cognate parts of biochemistry. Viewing the subject as a continuously unfolding branch of natural knowledge it reminds readers of its connections with the classical research of past generations.

Almost every page of this, the 12th edition, bears evidence of the author's industry and discrimination in keeping the work up to date, and it contains some 40 new figures, new formula blocks, and many new references to recent work.

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PRINCIPLES OF HUMAN PHYSIOLOGY

Originally written by E. H. STARLING, M.D., F.R.C.P., C.M.G., F.R.S.

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WITH CHAPTERS ON THE SPECIAL SENSES BY
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WITH 721 ILLUSTRATIONS, SOME IN COLOUR

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PREFACE

THIS is the eighth revision of this text-book which I have carried out since taking it over in 1928. The book on the special senses has been revised by its original author, Professor H. Hartridge, F.R.S., to whom I tender my best thanks. The rest of the book I have revised myself, and I accept responsibility for errors and omissions. The accelerating rate of expansion of all the natural sciences now makes this task of revision by one hand truly a labour of Sisyphus, for at each edition it is usually necessary to overhaul almost everything which has gone before.

More than four hundred years have passed since the name Physiology was first given to the subject. At that time it was, like other embryonic sciences, nurtured in the bosom of medicine, and clouded by magic and astrology. William Harvey, in the 17th century, was the great pioneer who showed that experiment is the only key to natural knowledge in the biological, as in other sciences. If he had been able to visit a physiological laboratory in the time of Starling I believe he would have been able, with very little help, to have understood most of the techniques then in vogue, and to appraise the conclusions drawn from contemporary experiments. In the relatively short time which has elapsed since then, so many new techniques have been introduced from other scientific disciplines that it may be doubted whether he would, without a good deal of preliminary instruction, now understand either the experiments themselves or the conclusions drawn from them. For it could safely be claimed that in the past thirty years the advances in the subject have been greater than in the preceding century, or even two centuries. The subject has been revolutionised in the last three decades, not so much by the introduction of entirely new points of view, as by exhaustive exploration, by precise methods, of what were previously in many instances mere indications of tracks in an uncharted forest.

If the task of editing by a single hand and mind is heavy, it has at least one advantage, namely that it has been done by the one hand and mind, and has therefore a singleness of outlook which should make the contents more balanced, and more acceptable to the single mind for which it has been written. This carries with it the drawback that some errors and omissions become inevitable. I am grateful to many users of the book who have been so good as to draw my attention to some of these, and among them to two readers, respectively natives of India and Japan, who drew my attention to inconsistencies.

I should perhaps say a word about the references, since these have all been introduced by me. They are not intended for the elementary reader, and may all be disregarded by such. Nor do they pretend to include by any means the most important references to any particular subject. They are of two types. The footnote references are to papers which I have myself used and found likely to be of interest to readers who may wish to follow up a particular point. The other type appears at the ends of sections or chapters, under the heading " For Reference." These are mostly of a general character, and are mainly taken from Physiological Reviews, or similar review articles ; these usually include such references as are needed to supply the key to a contemporary bibliography, and could be of use to research workers or advanced teachers.

This edition contains 41 new figures, and several new formula blocks. I am grateful to the authors who have allowed me to copy their figures, the origin of which has been duly recognised in the legends. It is unfortunate, but inevitable, that, despite the most careful pruning, which but few pages escaped, the size of the book has been increased slightly.

Once more I have to thank Dr. M. Grace Eggleton for the expert and valuable index which she has made.

Mr. A. S. Knightley, of Messrs. J. & A. Churchill Ltd., and the other members of the staff of the House of Churchill, who have been responsible for seeing the book through the press, their artists and printers, all leave me deeply in their debt for the efficiency with which they have done their work, and for their unremitting courtesy throughout.

C. LOVATT EVANS.

WINTERSLOW,
Near SALISBURY.

SOME COMMON ABBREVIATIONS

A.C.H. = Adrenal cortical hormone.
A.C.T.H. = Adrenocorticotropic hormone.
A.D.H. = Anti-diuretic hormone.
A.D.P. = Adenosine diphosphate.
A.N.T.U. = Alpha-naphthylthiourea.
A.P.E. = Anterior pituitary extract.
A.T.P. = Adenosine triphosphate.
B.A.L. = British Anti-Lewisite (= 2 : 3 dimercaptopropanol).
B.M.R. = Basal metabolic rate.
B.P. = Blood pressure.
C.10 = Bistrimethylammonium decane diiodide, or decamethonium iodide.
C.R.O. = Cathode ray oscillograph.
D. = Diodrast.
D.B.T. = Dry bulb temperature.
D.C.A. or
D.O.C.A. = Desoxycorticosterone acetate.
D.N.A. = Deoxyribose nucleic acid
D.O.P.A. = Dihydroxyphenylalanine.
D.P.N. = Dipyridino nucleotide.
D.T*m*. = Diodrast transport maximum.
E.C.G. = Electrocardiogram.
E.E.G. = Electroencephalogram.
E.P.P. = End plate potential.
E.T. = Effective temperature.
F.F. = Filtration fraction.
F.S.H. = Follicle-stimulating hormone.
G.F. = Glomerular filtrate.
I.U. = International unit.
I.C.S.H. = Interstitial cell-stimulating hormone.
L.H. = Luteinizing hormone.
M.Eq. = Milli-equivalent.
M.E.V. = Million electron volts.
M.L.D. = Minimal lethal dose.
mM = Millimole.
M.T. = Methyl testosterone.
N.T.P. = Normal temperature and pressure.
P.A.H. = Para-amino hippuric acid.
P.G.A. = Pteroylglutamic acid.
P.F. = Plasma flow.
P.M.S. = Pregnant mare's serum (similar to F.S.H.)
P.U. = Pregnancy urine or chorionic gonadotropin.
P.R. = Pulse rate.
R.H. = Relative humidity.
R.N.A. = Ribonucleic acid
R.Q. = Respiratory quotient.
S.D.A. = Specific dynamic action.
S.T.P. = Standard temperature and pressure.
T.Ac. = Testosterone acetate.
T.E.A. = Tetraethylammonium chloride.
T*m*. = Transport maximum.
T.P.R. = Total peripheral resistance.
U.S. = Unconditional stimulus.
V.D.M. = Vaso depressor substance.
W.B.T. = Wet bulb temperature.

SOME UNITS AND CONSTANTS

Prefixes used in nomenclature, in addition to usual ones :—

Pica = 10^{-12} *i.e.*, one-million-millionth (p.)
Micro = 10^{-6} *i.e.*, one-millionth (μ).
Milli = 10^{-3} *i.e.*, one-thousandth, etc. (m.)
Centi = one-hundredth (c.)
Kilo = 10^{3} *i.e.*, one thousand (k.)
Mega = 10^{6} *i.e.*, one million, etc.
E.g., 1 Kilo calorie = 1 Calorie = 10^{3} calories.
1 Micro calorie= 10^{-6} calories.

The following abbreviations and signs are employed for units :

mile	mi.	milligram	mg.
kilometre	km.	microgram (= 0·001 mg.)	μg. (or γ).
metre	m.	kilogram-metre	kg.m.
centimetre	cm.	gram-centimetre	g.cm.
millimetre	mm.	cubic metre (1,000 l.)	cu.m. (or m^3).
micron (10^{-3} mm.)	μ	litre	l.
millimicron (10^{-6} mm.)	mμ.	millilitre (= 1·000027 c.c.).	ml.
Angstrom unit (10^{-7} mm. or 10^{-4} μ.)	A.U. or Å.	cubic centimetre	c.c.
		cubic millimetre	c.mm.
millionth micron (10^{-9} mm.)	$\mu\mu$.	hour	hr.
square metre	sq.m. or m^2.	minute	min.
kilogram	kg.	second	sec.
gram	g.	millisecond (0·001 sec.)	msec. (or σ).
centigram	cg.	microsecond (0·001 msec.)	μsec.

1 farad (F) = an electrical capacity which holds 1 coulomb when charged to 1 volt.
microfarad = μF.

1 Microcurie (μC) = radioactivity of $3{\cdot}7 \times 10^{4}$ disintegrations per second.

1 Roentgen (*r*) = radiation producing 1 electrostatic unit of ions of both signs in 1 ml. air at 0° C. and 760 mm. Hg.

$$1\text{ cal.}\begin{cases} = \text{heat to raise 1 gram of water through } 1^\circ\text{ C., } e.g.\text{, from } 14{\cdot}5^\circ\text{ C. to} \\ \quad 15{\cdot}5^\circ\text{ C. One cal. } (15^\circ\text{ C.}) = 4{\cdot}1855\text{ joules.} \\ = 4{\cdot}2 \times 10^{7}\text{ ergs} = 42{\cdot}7 \times 10^{3}\text{ g.cm.} \end{cases}$$

1 micro cal. = 42 ergs = $42{\cdot}7 \times 10^{-3}$ g.cm.
1 Cal (or 1 kilo cal.) = 1,000 cal. (= 4 B.Th.U. or 0·00004 Therms.)

Kinetic C.G.S. unit of force = 1 dyne = force which, acting on mass of 1 gram, causes it to move with an acceleration of 1 cm. per second, per second.

Gravitational unit of force = 1 gram weight = 981·5 dynes.

Kinetic unit of work = 1 erg = 1 dyne-cm. = $23{\cdot}84 \times 10^{-9}$ calories = $10{\cdot}16 \times 10^{-4}$ g.cm. 1 joule = 10^{7} ergs.

Gravitational unit of work = 1 g.cm. = 981·5 ergs = 23·4 micro cals. 1 kg.m. = 2·34 cal. (= 0·468 c.c. O_2 at 5 Cal/l.).

Kinetic Unit of Power = 1 erg. per second.
1 kilowatt = 10^{3} watts = 10^{10} ergs per second.

Gravitational Unit of Power = 1 g.cm. per second.
1 horse-power = 0·746 kw = 457 kg-m. per minute.

Mole (M) = 1 g. molecule = 6×10^{23} molecules. Molar = 1 g. molecule per l.
Millimole (mM) = M $\times 10^{-3}$: Millimolar = 1 mg. molecule per l.
Micromole (μM) = M $\times 10^{-6}$.

Osmotic pressure of molar solution (undissociated) = 22·4 atmospheres.

Osmotic pressure of binary electrolyte (whose degree of dissociation = δ) in molar solution = $(1 + \delta) \times 22{\cdot}4$ atm. = $(1 + \delta) \times 22{\cdot}4 \times 760$ mm. Hg.

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CHAPTER I

INTRODUCTION

THE name "physiology," derived from a Greek root with the Latin equivalent *Physiologia*,* and originally connoting "natural knowledge," was first used in 1542 by Fernel,† but was not generally adopted until the 19th century. It now signifies the study of the phenomena presented by living organisms, the classification of these phenomena, and the recognition of their sequence and relative significance, the allocation of every function to its appropriate organ, and the study of the conditions which determine each function.

Life is the indefinable of biological science, as time and space are indefinables for the physical sciences. By this is meant that we cannot even approximately define life without the idea itself being implicit in our definition. Our business is, given living things, to study their phenomena.

The fundamental phenomena of life are essentially identical in all living organisms. The interest of mankind was, however, naturally awakened in connection with his own body, and the science, growing up as ancillary to medical studies, has always taken man as its chief type of study. Further, the choice of the higher animals in general receives justification from the fact that, whereas morphology must proceed from the lowest to the highest organisation, the science of function presents its problems in their clearest form in the most highly differentiated organisms. In the unicellular animal all the essential functions of living beings are carried out, often simultaneously, in one little speck of protoplasm. It is only when, as in the higher animals, the chief parts of the body have highly specialised functions that it becomes possible to peer into the details of these functions with some chance of understanding them.

Organisation. What are the fundamental phenomena which distinguish living things? Their distinctive feature is perhaps *organisation*, and in the higher members this organisation becomes more and more distinct. This greater complexity of organisation runs parallel with increasing range and power of adaptation, attained by the setting apart of special structures (organs) for the performance of definite functions. The parallelism between the development of function and structure justifies us in the assumption generally, though often only tacitly, made by physiologists, that the structure is the determining factor for the function. Further, as living animals show progressively increasing differentiation of structure in all their parts, and with this an increased power of adaptation of each part, so by increasingly delicate co-operation between their various parts, they display a progressive advance in *integration* which further augments the powers of the individual to adapt itself to its surroundings.

Energy Expenditure. When dealing with the higher animals, we are inclined to lay stress on the phenomena involving a discharge of energy. The life of a man in the ordinary sense of the term is made up of those movements which place him in relationship with his environment. For these movements, as for the maintenance of a constant body-temperature, a continual expenditure of energy is necessary. Experience teaches us that these movements come to an end in the absence of food or of oxygen, and that an increased call on the energies of the body must always be met by an increased demand for air and food. Two further processes must therefore be included among those making up our conception of life, viz. the function of assimilation (the taking in and digestion of food), and the function of respiration, by which oxygen is absorbed and carbon dioxide is excreted into the surrounding atmosphere.

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* FULTON. *Yale J. Biol. Med.*, 1930, **3**, 59; *Science*, 1933, **78**, 109.

† SHERRINGTON, The Endeavour of Jean Fernel, 1946. (Cambridge Univ. Press.) *Arch. néerl. de Physiol.*, 1947, **28**, 369.

The substances which make up our foodstuffs are all capable of oxidation. In this process of oxidation there is liberation of heat. In the body a similar oxidation occurs, and energy is thus set free which is available for the activities of the living organism.

Before we can make any accurate investigations of the conditions which determine these activities, we must know whether the laws of the conservation of mass and the conservation of energy hold good for the processes within the living body. Thousands of experiments have been made, in which the total income of the body, viz. food and oxygen, has been weighed, and compared with the total output, viz. carbon dioxide, water, and urea, etc. In every case complete equality has been obtained, *i.e.* no matter is created or destroyed by living things.

With regard to the energy balance we can only speculate at present, though it is commonly assumed that the laws of thermodynamics hold good for the living, as for the inanimate, world. Living things undoubtedly manufacture materials of high energy content, but it is believed that this can only be done by using free energy from other sources—in plants from sunlight, in animals by using the energy thus stored by plants. A complete account of the free energy exchanges is not at present possible, but as a first approximation the heat energies can be measured. For this we have, in the first place, to measure the material income and output of the body, and to determine the total heat which would be evolved by the oxidation of the foodstuffs ingested to the carbon dioxide, water, etc., that are given out. We must then compare the figure so obtained with the *actual* output of heat by placing the animal in a specially constructed calorimeter, described in Chapter XLI. Rubner * thus measured in dogs the energy income and output of the body, and more elaborate experiments were made on men by Atwater and Benedict, a summary of whose results are given below :

INCOME AND OUTGO IN MAN DURING 143 DAYS

(Atwater and Benedict) †

Number of subjects used.	Condition.	Total number of days of experiment.	Average daily net income (calculated potential energy of material oxidized). Calories.	Average daily net outgo (energy given off by body). Calories.	Percentage difference.
4	Rest	41	2,246	2,246	0·0
3	Work	66	4,682	4,676	− 0·1
3	Special diet	26	2,290	2,305	+ 0·7
2	Special diet and work	10	3,719	3,702	− 0·5

The important deduction to be drawn from these observations is that the foodstuffs which are oxidised in the body develop in this process exactly the same amount of energy as when they are burnt outside the body.

From one aspect, therefore, the animal body may be looked upon as a machine for the transformation of the potential energy of the foodstuffs into kinetic energy, represented by the warmth and movements of the body as well as by other physical changes. In the living organism, however, it is not easy to distinguish between the source of energy and the machinery. When we endeavour to trace the foodstuffs after their entry into the body, we lose sight of them at the point where they apparently form an integral part of the living tissues. During activity there is a discharge of the products of oxidation of this

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* RUBNER. *Ztschr. f. Biol.*, 1894, **30**, 73. Gesetze des Energieverbrauchs bei der Ernährung. (Deuticke, 1902).

† ATWATER and BENEDICT. *U.S. Dept. Agricult. Bull., No.* **136**, **1903**, **p. 194.**

living matter, which therefore becomes reduced in mass. This disintegration of the living matter, associated with activity, is always followed by a period of increased integration by the assimilation of more food. Our conception of life must therefore involve the idea of a constantly recurring cycle of processes, one of *anabolism*, repair, or assimilation, and the other, associated with activity, of *katabolism* or dissimilation. Together they are called *metabolism.*

In the process of assimilation substances of high potential energy are formed, and this energy is obtained either from that imparted to the system at the moment of assimilation, as *e.g.* in the assimilation of carbon from carbon dioxide under the influence of the sun's rays, or from that contained in the foodstuffs themselves. In animal cells it is the latter method which is adopted and a foodstuff therefore connotes some substance which can be taken in by the cell and can serve it as a source of chemical energy. In assimilation there may also be a synthesis of more complex from less complex compounds, without their necessary entry into the structure of the living molecule. Assimilation requires the ingestion of food into the organism, and then its digestion, *i.e.* its solution in the juices of the cells. These two processes are often succeeded by an actual growth in the living material. Digestion is effected in most cases by the production of solutions containing *enzymes* which have the power of hydrolysing the different foodstuffs.

In the process of dissimilation in most organisms the energy for their activities is derived from oxidation, and this also yields heat. A necessary condition therefore is the presence of oxygen. As a result of this oxidation, products are formed which are of no further value and are therefore *excreted, i.e.* turned out of the cell. The chief of these are carbon dioxide and water. There are also many substances resulting from the oxidation of nitrogenous substances which have to be excreted.

Although the need for oxygen is so general a quality of living protoplasm, its presence does not seem to be necessary for all kinds of life. Indeed, most cells can survive for a short time in its absence, and can even carry out oxidative processes by indirect reactions. Further, many bacteria are known which are anaerobic, *i.e.* exist only in the absence of oxygen. Examples of such are bacillus tetanus and the bacillus of malignant œdema.

The activities of a living cell or organism can be regarded in every case as dependent originally on environmental change, and are of such a nature that they tend to preserve the organism intact. The property of reacting in such a manner to changes in the environment is fundamental to all protoplasm and is spoken of as *excitability*, and any change which will influence an organism and cause a response in it is known as a *stimulus.* Stimuli may be of various kinds. Thus mechanical, thermal, chemical, electrical changes, light and so on may act as stimuli. The reactions which they evoke in every case involve changes in the metabolism of the cell. Sometimes this change may be assimilatory in character, or at any rate a reduction of dissimilation. In such a case the stimulus is spoken of as inhibitory, because it diminishes or prevents the output of energy by the organism. The frequent result of a stimulus is an increased output of energy, which may appear in the form of movement, heat, or chemical change.

A common feature of all dissimilatory changes evoked by the application of a stimulus is that the energy of the response is many times greater than the energy represented by the stimulus, the excess, of course, being supplied at the expense of the potential energy of the material of the living protoplasm.

Growth, Reproduction. If the anabolic process predominates, we obtain growth. Closely associated with growth is the power possessed by all living organisms of repair, *i.e.* the replacement by newly formed healthy material of parts which have been damaged.

The process of growth does not, in the individual, proceed indefinitely. At a certain stage in its life every organism divides, and part of its substance is thrown off to form one or more new individuals, each of them endowed with the same properties as the parent organism. In all the higher forms the parent organism begins to undergo decay, until finally death takes place.

Adaptation. All these phenomena, viz. organisation, assimilation, respiration, the discharge of energy, growth, reproduction, and death itself, are bound up in our conception of life. All living organisms have one feature in common, viz. they are endowed with the power of *adaptation.* Adaptation is " the continuous adjustment of internal relations to external relations." A living organism is a highly unstable system which tends to undergo disintegration if its average environment is changed beyond certain narrow limits. The real environment of the living cells is the tissue fluid in which they live; this *internal environment* tends to be altered by changes in the general environment in which the animal is placed. It is evident that the condition for survival of the organism must be that changes in the environment are counteracted so that, whatever the general environment may be, the internal environment stays within viable limits. This is what is meant by adaptation.

We have no knowledge of how living things first came into existence, but having once arisen in a primitive form, the " adaptation," *i.e.* the reactions of the primitive living material to changes in its environment, must become ever more and more complex, since only by means of increasing variety of reaction is it possible to provide for the stability of the system within greater and greater range of external conditions. The difference between higher and lower forms is therefore one of complexity of reaction, or of range of adaptation.

Organism and Environment. Though it is a philosophical point on which there is no need to dwell, it should be emphasised that organism and environment must be viewed as a whole. But so far as possible the organism adjusts itself to any changes in its environment or " adjusts its internal to its external relations."

This " adjustment of internal to external relations " is possible only within strictly defined limits, limits which increase in extent with rise in the type of organism, and in the complexity of its powers of reaction. Among the chief of them are temperature, and the presence of food material, water and oxygen. Many organisms are killed by the alteration of only a few degrees in the temperature of their environment. In the higher animals a greater stability in face of such changes has been accomplished by the development of a heat-regulating mechanism, so that, provided sufficient food is available, the temperature of the body is maintained at a constant level. In the primitive condition, the food material must be of a given character and form a constant constituent of the surrounding medium. In the higher forms, the development of a complex digestive system has enabled the organism to utilise many different kinds of food, while the storage of excess as reserve material provides for a constant supply of food to the cells of the body, even when it is temporarily wanting in the environment. Moreover, but few cells of the higher organisms are called upon to face the vicissitudes of light, temperature, chemical composition, etc., of the general environment: instead, most of the cells of the body live in darkness and in contact only with that inner environment, the blood and tissue fluid, the composition and temperature of which are kept constant by wonderfully adapted arrangements. The name *homeostasis* (homoiostasis) was given by Cannon to the condition of uniformity which results from the adjustments of living things to changes in their environment.

Many man-made devices exhibit adaptative properties, *e.g.* thermo-regulators and servo-mechanisms in general. The subject of *cybernetics** studies such goal-directed activity, in which there is stabilised directing on to a definite course, and recognises two types of machine, those which, like servo-mechanisms or automatic controls, are body-like, and those which, like computing machines, are mind-like in operation. The application of such studies to biological phenomena is, of course, analogical and not explanatory.

To sum up. Our objects in the study of physiology include the description of the chief reactions of the body to changes in its environment, the analysis of

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* FN. v. WAGNER. Probleme u. Beispiele Biologischer Regelung. 1954 (*Stuttgart: Thieme*).

these reactions into the simpler reactions of which they are made up, and the assignment to each differentiated structure of the organism its part in every reaction. We must determine the conditions under which each response takes place, so that we may learn to evoke it by application of the appropriate change of environment.

In attacking this problem our methods cannot differ fundamentally from those of the physicist and chemist. In every case our experiments will consist in the observation and measurement of processes of one kind or another which we shall hope to interpret in terms of mass or energy. Physiology, if it could be completed, would therefore describe, in the language of physics and chemistry, the *how* of every process in the body. It would state the sequence of events and would summarise these as so-called " laws." These laws would, however, no more explain the phenomena of life than does the " law of gravitation " explain the fact that two masses attract each other with forces directly proportional to the product of their masses. Nor can we hope to explain physiological phenomena by reference to the laws of physics and chemistry, since these themselves are only expressions of sequences, and not explanations. With every growth in science, however, its generalisations become wider and its laws summarise ever more extensive groups of phenomena. The principle of adaptation is the only formula which will include all the phenomena of living beings. This principle must provisionally be accepted as fundamental by the biologist, as the physicist accepts the first law of thermodynamics.

The consciousness of the inadequacy of our explanations, which must be experienced with great force the more deeply the physiologist endeavours to peer into the processes within the living cells, at one time led some to the assumption of a special quality in living organisms which was designated as " vital activity." Such views are classified together under the term " *vitalism.*" As a working hypothesis it must be sterile because there is no evidence that the introduction of vitality enables the known laws of nature to be overruled in any way: whatever the living thing accomplishes, it may do so with the aid of quite orthodox phenomena. That the presence of life does, however, result in an orderly marshalling of these orthodox phenomena, and that in a quite peculiar way, could hardly be questioned. This again, is a philosophical point and need not detain us further than to note the apt remark of Claude Bernard, that " vital force directs phenomena which it does not produce; physical agencies produce (in living things) phenomena which they do not direct." In many cases, however, the terms " *vitalism* " and its antithesis " *mechanism* " are used unjustifiably. The phenomena of living matter are not arbitrary, and since the conditions are infinitely complicated, they are incapable of arbitrary simplification when compared with those concerned with the study of non-living matter, and are hence more difficult to analyse or to control. The physiologist, basing his belief in the principle of adaptation must reject vitalistic " explanations " and seek to discover by experiment the conditions which determine the appearance of phenomena in living things. But he must equally reject an arrogant and superficial doctrine of " mechanism " which would suppose that life can be the outcome of any chance encounter of physical and chemical phenomena, and here again the principle of adaptation must be his guide in refusing to accept the suggestion that physiology is nothing more than applied chemistry and physics. Holding these aims always before him, he must abide by the answer he receives from his experiments as to the ways and means of adaptation, and can hope for little more.

Throughout this chapter we have admitted no necessary dividing line between the different classes of phenomena in the conceptual universe, although in the present state of our knowledge we are far from being able to include the whole of them under the same general laws. It might be objected that in taking up this attitude we have left out of account one supreme fact, viz. the existence of *consciousness* in ourselves. As a comparative and objective study, however, physiology is concerned, not with the study of consciousness, but with the conceptions in consciousness of the *phenomena* presented by living beings.

THE METHOD OF PHYSIOLOGY. Physiology derives most of its inspiration from observations incidental to the phenomena of our daily life and from those made in the course of medical practice. In the prosecution of his enquiries the physiologist often must make appeal to other sciences, but especially to chemistry and physics. In the first place the chemistry and physics of the various separate organs of the animal body must be investigated. This involves first an accurate knowledge of the gross and minute structures, and hence requires the aid of anatomy and histology. Here very frequently, too, comparative anatomy and histology furnish valuable clues to function.

Then the chemical, physical and physico-chemical build must be taken into consideration with a view to the determination of the changes which these exhibit under altered conditions of environment, chemical or physical in nature.

In this way analytical physiology is built up, by experiments, carried out on living animals, or on separated parts of them surviving for a time under suitable conditions ; knowledge of the properties and functions of the various structural parts is obtained. Then, in synthetic physiology, we attempt to find how, by integrative processes, the functions of the body as a whole are synthesised from the co-operative activity of the various parts, and how the organism as a whole reacts, by appropriate adjustment of its individual organs, to changes in its external environment.*

"*Mechanisms*" *in Physiology.* In his physiological studies the student will often meet with the word "mechanism," *e.g.* "the mechanism of gastric secretion" ; ". . . of walking" ; ". . . of reflex action," etc. This rather overworked word need not be taken too seriously, because as a rule it has no more significance than the equally busy and now notorious adjective "marked." "Mechanism of" really means, as a rule, "the phenomena concerned in . . ." as *e.g.* "the mechanism of bone formation," though in other instances, which the reader can readily find as *e.g.* "The mechanism of speech," the word is more literally employed.

The Normal. Individuals of the same species resemble one another more or less closely in structure and in their physiological properties, and this tendency of biological characters towards a standard type is an expression of the approximate harmony between the organism and its environment. The resemblance is greatest between animals born of the same parents at the same time. As species further apart are considered the differences become greater, and, between the extremes of the animal kingdom, are so great that comparisons become vague.

Yet, even when the relationships between individual animals are of the closest kind, *e.g.* in the human race, these do show differences from one another. It is a duty of human physiology to study the normal human individual, since this provides an important baseline for the study of disease ; yet it is far from easy to state what is the normal of any given character. Further, in all physiological experiments the results must show a good deal of apparently arbitrary variation depending on the individual animals used. Hence the importance of proper controls, and the decision of what constitutes a significant result, cannot be overestimated. Often, in order to be certain that representative results are being considered, it is necessary to repeat experiments many times. The error of observation which is usually slight in the exact sciences, is often great in the biological ones, on account of the variability introduced by the use of varying individuals. The results are, however, capable of being treated by the application of the same laws of probability as are employed in other sciences, *i.e.* they can be treated statistically. Caution is especially necessary in drawing conclusions from a limited number of experiments, as to whether the results obtained differ from those of a control series or not. Thus if a given result happens 4 times out of 8 in one series and 7 times out of 16 in another, we are not justified in concluding that it happens more often under the conditions of the first, because chance could easily account for the difference. But 4 out of 8 in one series and 3 out of 16 in the second would be a significant difference.

It is a common practice to speak of averages, that is, of arithmetic means, as one way of overcoming the difficulty, *e.g.* we can say that the average number of red cells per cubic millimetre of blood in a given community of men is 5·2 millions. Such a method, though the simplest and the one most commonly used, is often unsatisfactory, because it does not tell us how great or how relatively frequent are the departures from the mean, so that we should have no means of knowing in the example quoted whether 4·5 millions was within the normal range or not. There is consequently a growing practice of using more accurate means for the expression of statistical results.

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* As an example of essays in synthetic physiology may be quoted J. BARCROFT'S "Features in the Architecture of Physiological Function," Cambridge, 1934.

One of the methods employed is the use of the *frequency diagram*, an example of which is given in Fig. 1, which illustrates data regarding the stature of a large number of individuals. These have been divided into frequency groups differing in stature by 1 inch. The height of each rectangle is proportional to the number of individuals having the height shown at the abscissa, the grouped figure being called a histogram. A smoothed curve, or frequency curve, drawn from this, shows the frequency with which any stature between the given limits occurs.

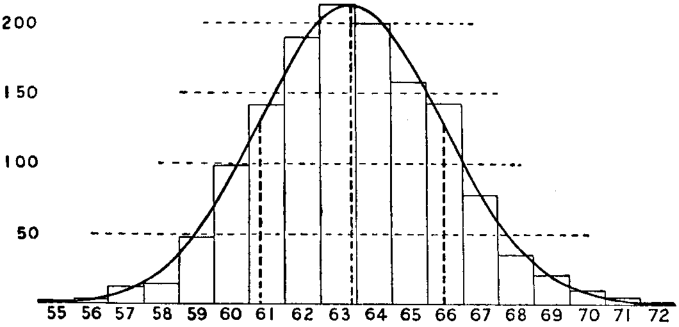

FIG. 1. Frequency diagram of distribution of stature of 1,375 women, in groups differing by one inch. (Pearson and Lee.) (From Fisher's "Statistical Methods for Research Workers." London. Oliver & Boyd.)

(Other examples are given in Chapter XXIX showing distributions for blood counts, and in Chapter XXXIII showing blood pressures.)

The *standard deviation* or mean error, is one of the means of improving the value of results; it measures the amount of variation in the individual figures from which the average was obtained. The accuracy of an average result depends on the square root of the number of observations made, so that, in a series of n determinations with individual differences summed up as Σd, it can be shown that the standard deviation of a single observation is $\pm\sqrt{\frac{\Sigma d^2}{n-1}}$, while the standard deviation of the average is given by the formula $\pm\sqrt{\frac{\Sigma d^2}{n(n-1)}}$.

To take an illustration given by Burn, we may consider the investigation of the lethal dose of a drug, as determined on a series of five cats, which gave the result as 17·44 ± 1·67 ml. The figure 1·67 is the standard deviation of the average, and means that, "if a number of determinations of the average lethal dose be made, each time on five cats, then twice out of three times the difference between the value obtained and the true value will be less than 1·67, and once out of three times this difference will be greater than 1·67." If we take twice the standard deviation, and call the result 17·44 ± 3·34 ml. the report will probably be wrong only once in twenty-two times; or if three times the S.D. or 17·44 ± 5·01 ml., then it will probably only be wrong once in 370 times.

A difference between two series of similar experiments with standard deviation $= \sigma$ may be considered to be significant if, the two series having given results of $x_1 \pm \sigma_1$, and $x_2 \pm \sigma_2$, the ratio $\frac{x_1 - x_2}{\sqrt{\sigma_1^2 + \sigma_2^2}}$ is greater than 3.

The *probable error* of a mean is given by the formula $\pm\, 0{\cdot}6745\, \frac{\sqrt{\Sigma d^2}}{n\,(n-1)}$ or, by the more convenient approximation of Peters, the probable error of the arithmetic means of a series of observations $= \pm\, \frac{0{\cdot}8455\, \Sigma(+\,d)}{n\sqrt{(n-1)}}$ where $\Sigma\,(+\,d)$ is the sum of the deviations of every observation from the mean, their sign being disregarded. The probable error determines the degree of confidence we may have in using the mean as the best representative value of a series.*

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* For further information see the book by FISHER and the articles by BURN and DUNN. A useful account is given in a chapter on Statistical Analysis, by D. J. FINNEY in BURN's "Biological Standardization," Oxford. Med. Publ., 1950.

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HISTORY OF PHYSIOLOGY

As it is impossible to realise the present position of any science without some knowledge of the history of its development, the serious student of physiology should acquaint himself with the outlines of its history. By way of introduction, some very brief historical notes, dealing with the development of various branches of physiology, are given here and there in this volume. As regards the growth of the subject as a whole, it must be remembered that no part of scientific knowledge can develop alone, but that all parts depend on each other. For instance, until a reasonable body of anatomical knowledge had been established, no physiology, as we understand it, was possible; and until physics and chemistry had reached a certain state of development, much of the early physiology could be but tales of mystery and imagination.

Starting, then, with the foundation of modern anatomy by the publication, in 1543, of the *Fabrica Humani Corporis* of Andreas Vesalius, we may put down the following names of key men whose work enabled expansion of our subject to take place in one direction or another. They form important landmarks.

Name.	Life.	Important publication.	
		Date.	Significance.
Vesalius .	1514–64	1543	Start of modern anatomy.
Galileo .	1564–1642	c. 1600	Start of modern physics.
Harvey .	1578–1667	1628	Experimental method in biology.
Boyle .	1627–91	1660	Experimental method in chemistry.
Malpighi .	1628–94	1661	Microscope used in biology.
Mayow .	1645–79	1668	Application of chemistry.
Newton .	1642–1727	1687	Development of modern physics.
Boerhaave	1668–1738	1708	Application of chemistry and physics.
Haller .	1708–77	c. 1760	Important text-book on physiology.
Lavoisier .	1743–94	1775	Combustion and respiration related.
Joh. Müller	1801–58	c. 1834	Important text-book.
Schwann .	1810–82	1839	Cell theory established.
Bernard .	1813–78	1840–70	Great experimentalist.
Ludwig .	1816–95	1850–90	Great experimentalist. Introduced graphic method.
Helmholtz	1821–94	1850–90	Applications of physics.

The first journal devoted to physiology, first appeared in 1795; the English *Journal of Physiology* in 1878, and the *American Journal of Physiology* in 1898. The first English chair of physiology, as distinct from anatomy, was founded at University College, London, in 1874, and the first in the United States of America, at Harvard, in 1876.

It is thus seen that the subject of Physiology, in anything like the form we now know it, began to take shape little more than a century ago, and so is a young subject. Biochemistry is still younger, and has mainly developed in the lifetime of many not yet old, as an outgrowth of physiology.

For more details of the history of physiology, the student may consult the following works:—

Foster (1901). Lectures on the History of Physiology. (Cambr. Univ. Press.)
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