PHYSIOLOGY

TISSUES AND ORGANS

An Introduction to the Study of
Systematic Physiology

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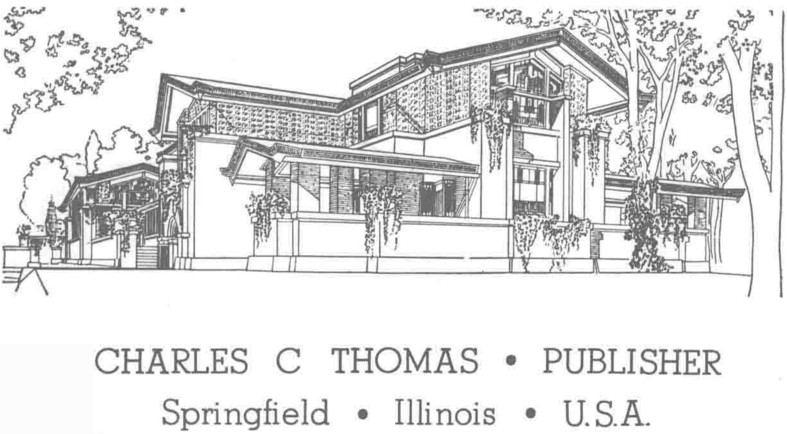

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PREFACE

THIS text was first published by the University of Queensland. Its appearance in an American edition is due to the favourable reviews received after its original appearance and the encouragement of the present publishers, Charles C Thomas • Publisher.

Obviously intended for students pursuing a particular course in a particular University, this book may still prove to have a wider application, for it is the author's belief that the customary heroic method, whereby the student is flung into the deep waters of systematic physiology and defied to swim out, is justified neither in ethics nor in the results it achieves. If the method he advocates is right, then someone more competent that he may be moved to prepare a better text along similar lines.

So numerous are the sources from which the author has drawn material facts and ideas that no attempt has been made to furnish a list. Those to whom he is indebted, and who perchance read the contents and recognize their contribution, are begged to accept this as an acknowledgment of his indebtedness.

The author's gratitude is due to his secretarial staff for their untiring patience in preparing many editions of the class notes which led to this publication, and to Mr. Tuffley for the preparation of the illustrations.

To the reviewers of the original edition, the author's thanks are due for kindly and constructive criticism, of which advantage has been taken in the preparation of this publication.

The PHYSIOLOGY *of* TISSUES AND ORGANS

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PART I.

THE PHYSIOLOGY OF TISSUES

INTRODUCTION

IN Biology you studied animals and plants. Immediately upon commencing that study you became acutely aware of the outstanding differences between living and non-living material. Contemplation and analysis of those essential differences were, to a certain extent, continued in your classes as "Principles of Biology," but the emphasis in formal courses of Biology inevitably falls upon structure. The specimens you saw were dead, the arrangements you studied were, at least over short periods of time, static.

In Physiology you take up the detailed and systematic study of living processes and the behaviour of living organisms. Life is action and change; nothing is ever exactly the same from one moment to the next. The human mind, conditioned by its non-living environment, finds great difficulty in comprehending an ever-changing universe in which nothing can be kept stable for examination, in which the very act of examination alters the behaviour or even terminates the existence of the object to be studied.

In this dilemma we can begin by attempting to apply those methods which stood us in good stead when studying non-living materials—the classical methods of physics, chemistry and mathematics. We must be prepared, however—and this condition must ever be kept in clear view—to modify those methods or to qualify the information obtained through their use in the light of experience. Particularly must we be on guard in the formulation of hypotheses, theories and laws based upon such information, and in the use of these expressions. At best they are but convenient, approximate statements of partial truths or descriptions of average behaviour.

Such qualifications are by no means unique to the field of physiology or of biological studies in general. They occur in the physical field, whether it be that of nuclear physics or blast action. It is merely that they inescapably attend every expression of biological relationship. By their very ubiquity they are in danger of being forgotten.

The plan upon which the course in Physiology proceeds in this Department is that of a logical progression from the familiar to the unfamiliar, and from the academic to the applied. It commences with a study of the basic structural units, the cells. Next it deals with the organs, composed of those cells in various proportions and arrangements suitable to the functions subserved. These two sections form the subject matter of this publication. Next follows the study of the systems, which makes up the major part of most standard text-books in Physiology. This is succeeded by a consideration of the way in which the systems are integrated to give a total organism reacting as a unit, and of the way in which this total organism becomes adapted to the many and extreme variations in its general environment. Finally, the application of Physiology to the practical problems of medicine, industry and animal production is taken up in diverse manners, according to the more specific needs of the students concerned.

Biochemistry is, for academic reasons, dealt with as a separate discipline. It must be clearly realized, however, that this separation is artificial. Constant reference is made in this publication, and through the whole of the course in Physiology, to biochemical matters. The converse is equally true. The knowledge possessed by the student when he leaves the Department should be a unified knowledge. It should be difficult for him to distinguish the exact source of any particular piece of information, unless the clue is very clearly evident in the item itself. In post-graduate specialities, Biochemistry often appears as a separate discipline, but in undergraduate studies its proper place is that of a subdivision.

The number of diagrams and illustrations which can be included in a publication whose cost is to remain within the student's reach is limited. You will find in the Museum, however, a fairly representative collection from many sources, which you will be expected to use and with which considerable familiarity will be expected. The time devoted to didactic lecturing has been cut to permit your self-education by this method.

Information has been presented in this publication in as concise a form as clarity will permit. You will need to pay much closer attention to the individual statements, therefore, than is customary with the average text-book. You will also need to consult standard text-books for the expansion of the information given here, for this is not intended as anything more than an introduction to systematic study.

CHAPTER 1

THE BEHAVIOUR OF LIVING MATTER

Life—" The property which differentiates a living animal or plant, or a living portion of organic tissue, from dead or non-living matter ; the assemblage of the functional activities by which the presence of this property is manifested." (Shorter Oxford Dictionary, Second Edition.)

Life cannot be defined except in terms of activities which all have tacitly agreed to consider as characteristic of life. What are these activities ? Almost every text book in Physiology has endeavoured to enumerate or describe them. Many have sought to advance one particular activity as *the* characteristic of living matter ; but I would rather urge you to emphasize the words " assemblage of functional activities " included in the Oxford Dictionary's description.

The following characteristics are those most frequently described, but you must remember that the items may overlap, that they do not completely describe living matter and that another author may very well prefer a different list. (This illustrates the difficulty of applying the logical methods of the exact sciences to living matter.)

(i) **Irritability:** When sufficiently disturbed, living matter commonly responds in some way. It may be by contraction, as in the case of the amoeba or a muscle cell ; it may be by secretion, as in the case of a gland cell ; or it may be by the propagation of an electric disturbance, mild in the case of a nerve cell, or surprisingly great as in the electric organ of a ray. Very often the provocative disturbance is not noticed, or is so slight as to be undetectable by our relatively crude methods of observation ; the material is then said to show " spontaneous " change. How far true spontaneity can be substantiated is a debatable matter.

(ii) **Resiliency:** We know from experience that living material which has reacted in the manner just described does not remain in its new state. If the stimulating disturbance is discontinued, the material usually returns to its previous state. (But not always immediately, indicating a complex relationship between cause and observed effect.) In some cases, a return towards the original state may occur even if the stimulating disturbance is continued. This tendency to return to a " normal " condition, to adapt or accommodate itself to disturbances, to persist in spite of interference is, perhaps, hinted at in the derivation of the word " life " from an Indo-European root meaning " to continue, last, endure " (loc. cit.).

(iii) **Energy changes:** No system can undergo an alteration or rearrangement without energy changes being involved, even if the total energy content of the final form is the same as that of the original. We have already seen that a prominent characteristic of living material is irritability, or responsiveness to disturbances. It follows, therefore, that energy changes are equally characteristic.

As in all other energy changes, a proportion of the energy is dissipated as heat. Apart from this, free energy may appear in any of the forms already familiar to you—thermal, chemical, electrical, radiant, kinetic.

(iv.) **Chemical changes:** A physical system undergoing transformation with the liberation of free energy must be decreasing its potential energy content, and must eventually run down. To restore the system, energy must be added from some external source. In the case of animal life, this source is food, whose complex molecules are broken down and finally oxidized, with the liberation of energy, much of which is used to recharge the physical systems previously discharged. It should be remembered, of course, that food is ultimately derived from plant life, and its energy content from the utilization of solar energy by the plant cells. Animal cells can make very little direct use of solar energy for purposes other than raising their temperature. Chemical change is, therefore, an inevitable feature of living material, though the rate of chemical change may vary from the extremely small (as in cartilage cells) to the relatively great (as in the cells of a contracting muscle).

It may be well to include here a note on the meaning and use of the word "*metabolism.*" Etymologically, it is derived from the Greek "metabole," meaning "change." The definitions given in two standard dictionaries not only restrict this meaning, but imply a theory which is not now regarded as universally or even usually applicable. Thus, "The process, in an organism or single cell, by which nutritive material is built up into living matter, or by which protoplasm is broken down into simpler substances to perform special functions." (Shorter Oxford, **1936**). Also, "The group of phenomena whereby organic beings transform foodstuffs into complex tissue-elements and convert complex substances into simple ones in the production of energy." (Gould, **1935**).

There is now a general agreement to use the term more in the broad original sense, as indicating any or all of the processes involved in those changes which characterize living material. One speaks of "energy metabolism" as well as of "chemical metabolism," if it is desired to consider them separately; but more simply of "metabolism," if they are to be considered conjointly and correctly, as different aspects of the same fundamental processes.

(v.) **Reproduction:** Perpetuation of its own kind is a behaviour almost unique to living matter, although it can be imitated to a very limited extent by certain physico-chemical systems. In its simplest form, reproduction is simply the subdivision of a cell whose cytoplasmic mass has exceeded certain limits, to give daughter-cells of smaller mass/surface area relationship. The essential features of the transition from this to or its replacement by sexual reproduction are obscure. Its biological implications are far-reaching, however, for the emphasis is transferred from perpetuation of individual to perpetuation of racial characteristics.

CHAPTER 2

CHEMICAL FACTORS IN LIVING PROCESSES

We have already seen that the one characteristic of living matter which definitely distinguishes it from non-living matter is continuance in the midst of change. You learn in Biochemistry that there is a continuous graduation from simple organic chemical reactions to the complex chemical changes going on in living matter. Certain aspects of these changes which apply to living tissues in general may appropriately be developed at this stage.

Mass Action:

The laws of mass action are exemplified by the fundamental organic reactions occurring in living tissues just as well as by the simplest inorganic reaction. The rate of reaction between substances A and B is proportional to the product of their concentrations. Again, if the products C and D of these interactions react in reverse fashion, the rate of the reverse reaction will be proportional to the product of the concentrations of C and D. Similarly, the proportions of all four components in a reversible action of this type at the equilibrium point is determined by the familiar formula :

$$\frac{[A]\ [B]}{[C]\ [D]} = k$$

Admittedly, it is often difficult to demonstrate the operation of the law of mass action in metabolic processes, but this is due to the variety of factors which determine the concentrations of each of the components and the difficulty of keeping them sufficiently constant to permit of a successful demonstration. In spite of this great complexity, however, it is important to realize that the laws of mass action are a fundamental feature and to realize that any procedure which tends, even though indirectly, to alter the concentration of one or more of the reacting substances must affect the equilibrium. On the other hand, it must be realized that the organism as a whole not infrequently fails to exhibit the principles expressed in the laws of Le Chatelier and Van't Hoff. There are many methods by which, at least over a limited range, the whole organism successfully compensates for and resists stress placed upon it, instead of being displaced in a direction tending to undo the effect of the stress.

Equilibrium:

The word " equilibrium " is used in Biology in a somewhat wider sense than is customary in the basic sciences ; in fact, it may be used in varying senses at different times. In its narrowest sense, it conforms to the simple physical conception of absence of change ; but, from what we have already said, you will realize that such a state of affairs is exceptional in living material, and the conception savours of the ideal. In a somewhat wider sense it conforms to the chemical idea of equal and opposite reactions, the net result being constant, although the components are in continuous change.

This idea may be extended from very simple chemical interactions to quite complex processes, when it is customary to speak of the equilibrium as a "*steady state*" or "*homeostasis*." These steady states are divisible into three sub-groups: successive, simultaneous, cyclic. These may be illustrated by simple diagrams in which the letters may be taken to represent simple chemical substances on the one hand or quite complex types of behaviour on the other.

Successive: $A + B \rightleftharpoons C + D \rightleftharpoons E + F$

Simultaneous: $A + B \begin{array}{l} \rightleftharpoons C + D \\ \rightleftharpoons E + F \end{array}$

Cyclic: $\begin{array}{c} A + B \\ \downarrow\uparrow \\ A + B \end{array} \rightleftharpoons C + D$

Still further latitude is taken by biologists when they speak of a "*moving equilibrium*." Here the term equilibrium is justified if the conditions are examined over a relatively short period of time in which there is no observable shift in the equilibrium point; but if, on the other hand, the processes are examined over a long time interval, definite changes will be observed. A cell, for instance, may justifiably be regarded as in equilibrium with its environment, or at least to enjoy a steady state, when examined in normal surroundings; but the cell is inevitably ageing and will certainly be in a somewhat different equilibrium position if examined again at a much later date. The very molecules of which a cell is composed in two months' time will be very different from those which make up its structure to-day. (This latitude is taken not only by the rebellious biologist, but also by the conservative physicist when he regards the galaxies.)

When some stress is brought to bear upon a system in equilibrium, the point of equilibrium is shifted. Its *displacement* may be continuous, in the moving equilibrium just described, or discontinuous. In either case, the stability of the equilibrium may be affected by the shift. In general, the further the equilibrium point is shifted from the position it normally occupies in living material, the less stable will it become. Eventually, if the displacement is sufficiently great, a *breakdown* may occur. In general, once a system starts to break down, its disintegration will pursue a course which is the reverse of growth, i.e., breakdown will occur more and more rapidly until a certain speed is assumed, which will only slacken off again as the disintegration approaches finality. The functional result of evolution has been to extend the range of conditions under which the delicate equilibrium of living tissue can be preserved from disintegration in the face of environmental stresses.

Assistants of Equilibrium:

The idea of catalysis is quite familiar to you, and the catalytic nature of enzymes has been explained to you in your chemical and biological studies. It should be quite apparent that the complex, unstable, organic substances which make up living tissue could not achieve the characteristics of life unless some mechanism were present to regulate the myriads of possible interactions, particularly to speed up those which are essential to living processes. It should be apparent also that such regulators would, in general, require to be highly specific. This regulating mechanism is provided by the large number of substances given, rather arbitrarily and often inconsistently, the various labels of enzymes, vitamins, activators and carriers. While these names have certain advantages and have become established by usage, it must be recognised that these sub-divisions are artificial and that the substances so classified play very similar fundamental roles. It seems, further, that the production and activity of some of these regulators (e.g., enzymes, activators) are under the control of the genes.

Typically, *enzymes* are substances which speed up the establishment of an equilibrium between reacting substances in living material. It frequently happens that the equilibrium point is markedly eccentric; i.e., there are far greater concentrations at the equilibrium point of one set of reactants than of the other. The action of the enzyme, as of any catalyst, is to speed up arrival at that point and not to affect the proportions of the reactants characteristic of the point. The enzyme will facilitate the reverse reaction just as well as it facilitates the forward reaction, if the components are removed as fast as they are formed.

The word "*vitamin*" was originally given to a substance which was found to be necessary in a diet to preserve health, although required only in traces. A special name was justified as long as the nature and mode of action of the substance were not known. In many cases this position is not now true, and substances still known as vitamins would be better classified as regulants and their action in tissues described under one of the other headings. Thus the main principles of the vitamin B complex are known to be essential constituents of enzymes, co-enzymes or carriers, in the complex processes of tissue oxidation. The heterogeneous chemical nature of vitamins is a further argument against the use of this vague term.

The nature and action of *activators* will be taken up in connection with tissue differentiation. It is only necessary to say here that there is no hard and fast distinction, chemically or functionally, between these activators and hormones. A *carrier* is a substance which picks up a reactant from one source and conveys it to another point for use. The conveyance may be over an appreciable distance, e.g., the carriage of oxygen by haemoglobin, or merely through molecular dimensions, as in the conveyance of oxygen from solution in the tissue fluid to oxidizable substrate in the course of tissue oxidation.

The name "*hormone*" was originally given to substances regarded as chemical messengers which were formed by certain tissues and dispatched to other sites for the control of various chemical reactions. The more closely these substances are studied, the more tenuous becomes any essential distinction between their mode of action and that of enzymes or vitamins.

Conditions of Equilibrium:

Many conditions other than the mere supply of reactant substances affect the equilibrium point. Some of these conditions, such as temperature, are physical and will be considered in the next chapter. Others are chemical and should be noted here. The very term "concentration of reactant substances" defines the importance of water. The amount of water available to living tissue, as distinct from the amount obtainable, depends amongst other things upon the osmotic pressure within and without cells. While electrolytes normally have a marked effect upon osmotic pressure, non-electrolytes and even colloids are of importance in living tissues, since many membranes (see Chapter 4) are permeable to electrolytes but not to colloids. In many cases, ions such as Na^+, K^+ and Ca^{++} have further specific effects upon chemical processes, which are at present ill-understood, the relative proportions being almost as important as the absolute concentrations. The H-ion concentration of the solution is also a matter of great importance to the chemical behaviour of living tissues, partially through an effect upon the reacting substances, but also very largely through its physico-chemical effect upon the dispersion and nature of the protein molecule. These factors will be considered in more detail in Biochemistry.

Action of Poisons:

The very delicate equilibria characteristic of living material may be completely and permanently upset by a variety of conditions. Chemical substances which destroy life are known as poisons, and are divisible roughly into five classes :—

(1) Enzymatic—Destroying or preventing the action of the enzymes determining the interactions characteristic of life; e.g., fluorides.

(2) Protoplasmic—So altering the structure of the protoplasmic colloids that the medium for proper interaction is destroyed; e.g., heavy metals.

(3) Osmotic—So altering the distribution of water that the appropriate reactions cannot proceed; e.g., strong salt solutions.

(4) Ionic—Altering the specific effect of ions upon tissue reactions; e.g., removal of Ca^{++} by citrate.

(5) Depletive—Removing or preventing the supply of any necessary reactant substances; e.g., CO combining with haemoglobin and preventing the carriage of oxygen.

CHAPTER 3

PHYSICAL FACTORS IN LIVING PROCESSES

Just as the comprehension of the chemical behaviour of living tissues must be developed from a knowledge of simple non-living chemical reactions, so an understanding of their physical behaviour must be developed from a knowledge of simple physical principles. Just as Biochemistry has come to occupy a position in its own right as a field of biological study, so Biophysics has been recognised as a major sub-division. Unfortunately, Biophysics has come into being rather independently along three lines between which there is still insufficient co-ordination. These lines are : (a) the effect of physical forces applied from without to living tissues ; (b) physical phenomena produced by living tissues ; and (c) the use of physical concepts in the study of body mechanics. Special aspects of all three fields are considered at appropriate points in both undergraduate and post-graduate training, but the student must enter upon his physiological studies with a full realization that physical factors are just as important in the study of living tissues as chemical factors, and that the knowledge that he has gained in the study of Physics must be in large measure carried forward and applied as occasion arises. At this point certain broad aspects only will be considered.

Mechanical Factors:

Mechanical restraint exercises a most important effect upon cell behaviour, particularly in relation to multiplication. Restraint of moderate degree applied equally on all sides of a cell will prevent any tendency the cell may have to multiply. Hence the development of tissues is self-limited. Should any part of this restraint be removed, any cells which have the inherent power to do so will multiply, and this process will continue until the restraints are re-applied. As long as the mechanical restraint is moderate and evenly applied, cell functions can continue ; but should undue pressure be applied at one part of the cell circumference, then the cell will be deformed and the physical processes of diffusion between the cell environment and certain parts of the cell will be disturbed. In multicellular animals further interference will be effected upon transport systems within the organism. If this undue pressure is maintained upon a tissue some cells will die, multiplication will be restricted, and the size of daughter cells will be diminished. The result will be atrophy of the tissue. If the pressure be applied intermittently, however, the tissue is likely to show compensatory reaction with increased multiplication. This differential effect between continuous and intermittent pressure has important pathological implications.

If an uneven pressure be excessive, disintegration of the cell is likely to occur. Even a moderate pressure, if very rapidly built up, will do the same. The peak pressure reached by the blast-wave from an explosion, for instance, may not be very great, but the