HANDBOOK OF
PHYSIOLOGY & BIOCHEMISTRY

Originally "KIRKES'" and later "HALLIBURTON'S"

By

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PREFACE TO FORTY-SECOND EDITION

THIS forty-second edition has undergone the most complete revision the volume has had for ten years, but its general outlook and object remain the same; that is, to provide the medical student with all his essential requirements in a book which he has time to read. It is ten pages shorter than its predecessor.

In order to incorporate the many new facts which have accumulated into a readable form, a very large number of the sections have been almost completely rewritten, such as the Vasomotor System, Lymph, Artificial Respiration, Chemistry, Muscle Contraction, the Nerve Impulses, Effects of Cold, Adrenal Cortex, Control of Urine Secretion, and Intermediate Metabolism; and a very large number of alterations have been made in almost all others.

So many of the old illustrations, known to generations of students, have been replaced that the book presents a very different appearance from what it had in a few editions ago. In the nature of things, this has necessitated the omission of many items of physics and chemistry, which the student now learns at an earlier stage.

Once again I have had the advice of many friends. Professors Katz of University College, London, Long of Yale, Landis of Harvard, my colleagues Drs Robson, Bell and Mendel, have been good enough to look over some of the new sections of which they have special knowledge, but they cannot in any sense be considered responsible for them. I have also been specially indebted to Dr Jones and to my daughter, Dr Summerhays, who has read the whole text and made many suggestions. The excellent index I owe to Mr George Stonard.

R. J. S. McDOWALL

KING'S COLLEGE
LONDON
1955

PUBLISHER'S NOTE

It may be not uninteresting briefly to recount something of the history of this book. The original author was William Senhouse Kirkes, of St Bartholomew's Hospital, and the first edition appeared in 1848; it consisted of 705 pages, and contained 97 illustrations. The title-page mentions that Dr Kirkes was assisted by Mr James Paget, who was then Lecturer on Physiology at St Bartholomew's Hospital. Dr Kirkes appears to have been a student under Mr (afterwards Sir) J. Paget, and to have been impressed with the need of making more permanent his spoken lectures, and in his preface he thanks Mr Paget for allowing him the free use of his manuscript lecture notes. The book was, for its time, one of great excellence, reflecting the clear and accurate method of exposition which always distinguished Sir James Paget's work, and *Kirkes' Physiology* rapidly became the students' favourite text-book, and new editions appeared rapidly: in these the book grew a little in size and in the number of illustrations, but showed otherwise but little change until the fourth edition came out in 1860, when Mr Savory's name appeared as editor upon the title-page. Mr (afterwards Sir William) Savory was another of St Bartholomew's worthies, and at that time was Lecturer on Comparative Anatomy and Physiology at that Hospital. With the appearance of the sixth edition (1867), Mr Morant Baker (then Demonstrator of Anatomy) was associate editor, and by this time the book was different in both matter and arrangement, so that little of the original "Kirkes" remained. Up to this time the publishers had been Taylor, Walton & Maberly, of Gower Street. In 1869, however, the book became the property of my grandfather (seventh edition), and this edition and the next (eighth, in 1872) were not much more than reprints of the sixth edition. The ninth edition (1876), however, was completely revised, and Dr Klein, then the Lecturer on Physiology, appears to have been largely responsible for the improvement. From the tenth to the thirteenth (1892) edition, the editorship was shared between Mr Morant Baker and Dr Vincent D. Harris, his senior Demonstrator, and as successive editions appeared, the work of keeping the publication up to date fell more and more upon the shoulders of the latter.

In 1896, when a new edition was necessary, Mr Baker had died, and Dr Harris was retiring from active teaching, so my father had to look round for a new editor. Acting upon the advice of his friend, the late Sir William Gowers, he applied to Professor Halliburton, and when the latter accepted the position, the long association between the book and St Bartholomew's Hospital was severed. During the fifty-four years of this association the book saw thirteen editions. Under Professor Halliburton's guidance, which began in 1896, the book entered upon a new era of prosperity; in twenty-nine years seventeen editions—totalling one hundred and sixteen thousand copies—were published; so, as the book had become an entirely new one, the name of Kirkes was dropped and *Halliburton's Physiology* became its recognised title.

In 1928 revision became again necessary; and as Professor Halliburton found that he needed help in preparing it, the assistance of his successor at King's College, Professor McDowall, was secured and his name added to the title.

In the thirty-fifth edition (1937) " Biochemistry " appeared on the title-page for the first time and in 1939 the thirty-sixth edition was considerably enlarged.

Since 1930 Professor McDowall has had sole responsibility for the volume, which in its present form is almost entirely his work. It is only fair, therefore, that his name should now stand alone in the place of honour on the title-page, while Halliburton can be added to Kirkes as a tribute to the past editorial succession.

JOHN MURRAY

November 1944

In 1948 the Centenary of the HANDBOOK was celebrated by the commencement of a complete revision, the whole book being reset and issued in 1950; since then two further editions have been called for.

Professor McDowall is still, I am glad to say, editor, and with his skill and guidance the book, now more than a hundred years old, has retained its vitality and up-to-dateness unimpaired and indeed even increased. Such a long and successful life for any book is surely a fine tribute to the energy and distinction of its successive editors.

J. M.

1955

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CHAPTER I

PHYSIOLOGY

THE subject of Physiology treats of the study of the phenomena occurring in all living things, but for the present purposes it is limited to the study of the activities of the animal body, especially that of man. It is part of the greater subject of Biology or the study of living things.

In making such a study we can approach the subject in a number of ways.

From Anatomy we learn the gross structure of the body, and from Histology, that is the study of its microscopic structure, we get a firmer basis from which to infer a possible function. We learn, for example, that the bodies of animals are composed of cells of great variety and that each organ has its own peculiar specialised cells arranged in a definite pattern. The appearance of the cells is often distinctive and may tell us whether they are protective, secretory, nervous, or connective.

By a chemical study of the tissues and of the various substances found in living things and of those taken into them, we are able to relate to each other the various chemical processes which take place as they might be carried out in a chemical laboratory. This constitutes Biochemistry. From it we learn how the body breaks down the various substances found in nature, makes use of them, and returns to its environment those it does not need or has used.

By a study of the movements and other physical processes which take place in the body (Biophysics), we understand the mechanics and dynamics of the body. From this we understand, for example, how the blood circulates and how air is sucked into the lungs.

Physical Chemistry, too, adds its quota and indicates such things as the principles by which substances may pass through the various membranes of the body, especially those of the cells themselves.

In Biology we trace the structural functions of organs of lower animals and how they have been evolved, and we see how, as we go down the animal scale, the processes become simpler and simpler until all the more essential ones are performed by a single cell, a cell which is alive and capable of reproducing itself. There we find ourselves up against the problem of life itself which so far has defied complete analysis, but by the study of Physiology from its various angles we find out many of the factors on which it depends and how we can do much to assist in its prolongation and to add to its happiness, which is the function of Medicine.

CHAPTER 2

THE STRUCTURE AND CHARACTERISTICS OF LIVING THINGS

The Structure of Living Things.—All living things are composed of minute cells the form of which can be seen with the aid of a microscope. They are at first unicellular and the simplest, such as the amœba, remain so, but all the larger animals rapidly become multicellular and amongst the various cells there is a division of labour (so to speak), different cells having different functions but all being co-ordinated for the benefit of the animal as a whole.

The essential and peculiar constituent of cell structure is the jelly-like substance *protoplasm* which is largely protein in nature, but does not remain alive unless it is associated with at least the chlorides of sodium, calcium, and potassium in solution in water. If a cell is placed in a solution in which any one is absent, or not in its proper proportion, it rapidly dies, but if properly kept it will not only live but multiply. For more prolonged activity a great variety of other substances are probably necessary in minute amounts. There is some argument as to the nature of protoplasmic structure. Certainly when treated so as to stain or preserve it a fibrillar network is seen, and this has been seen in untreated specimens of white blood corpuscles which are singularly like amœbæ in their appearance and activities.

Controlling the activities of every living cell is a *nucleus* which stains more deeply than the rest of the cell, and the nucleus may show a nucleolus. The function of the various parts is unknown, but the chemical composition of nuclei has been shown to be quite different from the rest (cytoplasm) of the cell. Some cells have more than one nucleus.

All animal cells also have an " attraction sphere " which is prominent in actively dividing cells, a fact which suggests its importance in the process of cell division.

The Functional Characteristics of Living Things.—Life has been described as resting on a tripod of security, nourishment, and reproduction. On the first two depends the life of the individual, on the third the continuance of the species. Living things, therefore, show signs of activity. Of these the one most universally demonstrable is that of *assimilation*. It takes food with which to build its body and to be transformed into mechanical energy, and it takes in oxygen. This latter activity is usually the most easily shown sign of life. By studying oxygen-intake we can discover whether a man or an amœba is alive.

Living things also have the power of *excretion*, that is, of getting rid of the waste products of their bodily activities. They have the power of growth and of reproduction. Growth is really the characteristic of living things, for machines such as engines do, in a sense, assimilate and excrete. The *growth* of a living thing is not, however, like that of crystals by addition but by the multiplication of its existing elements and intake into its substance. Even when a tissue has ceased to grow in the ordinary sense it still has to repair itself, for there is a considerable amount of wear and tear associated with living. Actually the individual cells of the body are constantly dying and being replaced. Living material is, therefore, never in a static condition, but is also undergoing intramolecular rearrangement, the total sum of which is called metabolism.

Many cells show the power of *irritability*, that is, the power of responding to an external agent or stimulus.

The Relation of the Cell to its Environment

The simplest animal organism, consisting of a single cell, is in immediate contact with its environment water, from which it receives its nutrient material and oxygen, and to which it returns its waste materials. Even in the most complex animal each cell leads a similar life in immediate contact with the tissue fluid in which it is bathed. Only certain cells come into immediate contact with the external environment, the other cells of the body all benefiting indirectly through this contact, but this local cellular environment is brought into contact with the external environment in which the animal lives by means of the blood supply. For example, some of the cells of the respiratory tract are adapted for the passage of oxygen, while certain cells of the digestive tract permit the intake of nutrient materials. The oxygen and nourishment from the environment are transported by way of the specialised cells to every other cell in the body. This transport is accomplished by the circulation of the blood.

At the same time, however, the individual cells of the complex animal body are not subjected to the vagaries of supply from the outside world, but are bathed in tissue fluid of constant composition. The constancy of the internal environment was first described by Claude Bernard, the famous French physiologist of the nineteenth century. The body possesses mechanisms by which it maintains in the tissue fluid such essential substances as water, sodium, potassium, calcium, glucose, and many others at an almost fixed concentration. It possesses stores of such substances which it can draw on if the supply fails temporarily, and delicate mechanism which adjusts its intake from the alimentary canal and lungs, and its excretion, especially by the kidney, so that if the supply of any particular substance is in excess it is not held in the body. The subject is dealt with later in more detail (see " The Constancy of the Internal Environment").

The Interrelationship of Structure and Function of Individual Tissues

The microscopic appearances of organs and tissues concern the subject of Histology, but here it may be indicated how individual tissues play their part. It should, however, be pointed out that although heredity and evolution are important in the development of the structure of an organ, its activity is equally so, as the individual tissues grow or degenerate according to the use to which they are put. We are familiar with the increase of muscle of the arms and thickening of the skin of the hands which occurs as the result of hard manual labour, and also with the effects of training generally. If we consider animals generally we see an evolution of both structure and function ; a convenient example of this is seen in the evolution of the nervous system, which is considered later.

The Functions of the Epithelial Tissues

All free surfaces are covered by one or more layers of simple cells which are adapted to the needs of the part.

Stratified epithelium, which covers the exposed part of the body and constitutes the outer layer of the skin, is many cells thick. The outer layers become squamous, flattened, and may be horny, and eventually are shed as scales. Where there is any special irritation the outer layers are much thickened, as on the palms of the hands or the soles of the feet. This may occur also after more obvious injury to the skin, which is essentially the protective epithelium of the body.

Pavement epithelium (endothelium) covers less exposed parts. In general, it lines many of the body cavities, including the blood- and lymph-vascular system, the alveoli of the lungs, the serous cavities (pleuræ, pericardium, and peritoneum), and also the synovial cavities of the joints. The cells are flat and permit free passage to gases and fluids, in the case of the lung alveoli, interchange of gases occurs and in the serous cavities free movement of the lungs, heart, and abdominal viscera is obtained through the lubricating action of the fluid (lymph). It is only a single layer thick.

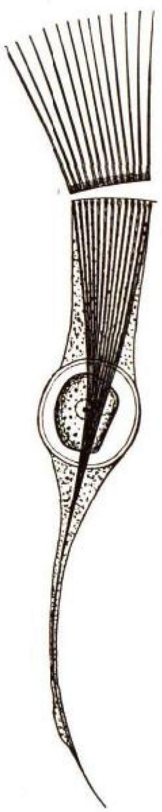

FIG. 1.—Ciliated cell from the intestine of a mollusc. (Engelmann.)

Transitional epithelium is an intermediate variety which is only a few layers thick and only becomes flattened on its surface. It is found only in the urinary tract, where it protects against the chemical substances of the urine and probably prevents reabsorption.

Columnar epithelium is a more active type of epithelium. It manufactures special substances from the blood which we know as secretions and it has selective powers controlling absorption into the blood. It does both as it covers the mucous membrane or lining of the alimentary canal and some of the tubules of the kidney. Most glands are infoldings from such columnar epithelial surfaces, and wherever such tissue is seen it can be assumed that it has these functions.

Ciliated Epithelium

The ciliated cell is usually columnar in shape and surmounted by a bunch of fine tapering filaments which were originally called cilia because of their resemblance to eyelashes.

In the larger ciliated cells, the border on which the cilia are set is bright and composed of little knobs, to each of which a cilium is attached ; in some cases the knobs are prolonged into the cell protoplasm as filaments or rootlets (fig. 1). The bunch of cilia is homologous with the striated border of columnar cells.

The function of the cilia is to cause a movement of substances or objects along the surfaces they line. For example, cilia line the air passages (but not the alveoli) and they cause a current of mucus and entangled dust to move towards the throat (fig. 2). In the Fallopian tubes and upper part of the uterus they assist the movements of ova, and in the ducts of the testes those of the spermatozoa. The tail of a spermatozoon may itself be regarded as a cilium ; some protozoa also move by means of cilia. Cilia are found also in the ventricles of the brain and in the central canal of the spinal cord ; in the gills of marine animals and in the gullet of the frog.

Ciliary motion may conveniently be studied in the latter, or in the gill of a mussel kept moist by a 0·6 per cent. saline. It may be observed under the microscope and, in the case of the frog, the movements of minute pieces of carbon may be studied.

The cilia are seen to be in constant rapid motion, each cilium being fixed at one end, and swinging or lashing to and fro. The general impression given to the eye of the observer is very similar to that produced by waves in a field of corn, and the result of their movement is to produce a continuous current in a definite direction, and this direction is always the same on the same surface, being usually in the case of a cavity towards the external orifice.

The exact explanation of ciliary movement is not known ; whatever may be the precise cause, the movement must depend on some changes going on in the cell to which the cilia are attached, for, when the latter are cut off from the cell, the movement ceases, and when severed so that portions of the cilia are left attached to the cell, the attached and not the severed portions continue the movement.

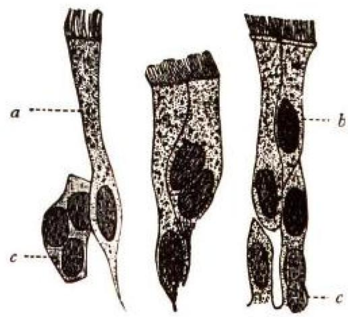

FIG. 2.—Ciliated epithelium from the human trachea. *a*, Large fully-formed cell ; *b*, shorter cell ; *c*, developing cells with more than one nucleus. (Cadiat.)

It would seem most likely that the movement is essentially similar to that which takes place in amœbæ or white blood corpuscles which throw out processes, and that changes in the tension of the fluid in the cilia cause them to straighten and bend.

The Effect of some External Agents on Amœboid and Ciliary Movement

Although the movements of amœboid and ciliated cells may be loosely described as spontaneous, yet they are produced and increased under the action of external agencies which excite or stimulate them.

Ciliary and amœboid movements are increased by small rises in temperature and by dilute alkalies. Additional movement increases the demand for oxygen (Gray). Lack of oxygen causes cessation of ciliary movement. So also does cold, a fact which may be important in the inception of the common cold. Temperatures above 45° C., acids, strong alkalies, and anæsthetics have a similar effect.

More detailed information on the subject is to be found in the writings of Gray and of Negus.

The Functions of the Connective Tissues

In these tissues, in addition to the cells, there exist fibres which act mechanically for the support and protection of tissue, and in many cases the fibres so predominate that the cells are scarcely seen. It is a matter of debate whether the fibres are altered cells or are deposited in the intercellular substance.

Fibrous tissue is a typical holding or connective tissue and its characteristic is that it does not stretch. It consists of bundles of white fibres. It forms, therefore, the tendons of muscles, the sacs of joints, part of the pericardial sac of the heart, and innumerable sheets of fibrous tissue or fascia to which muscles are attached or bones held together. Fibrous tissue is formed in wounds after injury, and since it tends to shrink often causes unsightly contractions in scars. If, however, it is subjected to sustained tension it will stretch. The fibres are composed of the protein material collagen which is converted into gelatin by boiling. For this reason we boil or stew the meat of an old animal which tends to be fibrous or tough. The activity of the fibroblasts or cells which form the tissue appears to require the presence of vitamin C in the diet.

Elastic tissue has fewer fibres which are yellow in colour, and which, as their name suggests, give elasticity to the part. Elastic fibres are found in blood vessels where they appear to be joined together as membranes. They are frequent in the lungs and they assist in holding together and in giving elasticity to the cartilages of the trachea and bronchi. They are well seen in the ligamentum nuchæ connecting the skull to the vertebral column.

Areolar tissue is the name given to the loose connective tissue which contains not only fibres of both kinds but cells. The cells are of several varieties. The *fibroblasts* in connection with which the fibres of the tissue are developed. The *histiocytes* which are characterised by their taking up vital dyes, that is, dyes injected in a living animal ; they are probably part of the reticulo-endothelial, macrophage or scavenging, system of the body. There are also cells which may be granular, the *mast cells*, or non-granular, the *plasma cells*, which are very like the basophil white cells and the lymphocytes of the blood. They probably have the function of dealing with bacteria which may gain access to the tissue. *Pigment cells* are also sometimes seen.

In addition, areolar tissue stores fat in large vesicular fat cells which, when excessive, cause it to be known as **adipose tissue.** It is also in the areolar tissue that water is extensively stored. This may be stored not only as free fluid but apparently also within the fibroblastic cells which may become quite swollen.

The other tissues are dealt with more appropriately in relation to the systems of which they form a predominant part.

The General Functional Design of the Higher Animal Body

As we have said, all living things have activities, but by far their most important is that of keeping themselves alive by feeding and protecting themselves. This all the more elaborate animals do by means of their voluntary muscles which are under the control of the brain.

The voluntary muscles, which we shall discuss in detail later, are structures which, by contracting, perform mechanical work, and in doing so transform chemical into mechanical energy with the evolution of heat. They act like engines and use what is essentially the same fuel as the internal-combustion engine of a motor-car, namely, carbon and hydrogen, which are transformed into carbon dioxide and water. Carbon and hydrogen are the essential constituents of the hydrocarbon, petrol, and also of the carbohydrate, glucose, which is used by the body.

These substances are supplied to the muscle by an artery which carries the carbon, hydrogen, and oxygen, a combustion mixture analogous to that supplied by the carburettor to the engine of a motor-car. The exhaust, which is chiefly carbon dioxide and water, is taken away by the veins.

Now the substances necessary for the engine, *i.e.* the fuel and the oxygen, have to be supplied from the outside world. The blood in the artery has been previously pumped to the lungs which, we have already noted, are specialised organs in contact with the outside world, via the windpipe, while the nourishment is picked up by that portion of the blood which passes to the digestive tract which is in continuity with the external environment at the mouth. As we shall see later, the detailed structure of the lungs and the alimentary canal are such that the blood is spread out very thinly on an enormous surface, much larger than the total skin surface of the body and so it takes up what it needs very rapidly.

The extent to which the muscles need oxygen determines the rate at which it is supplied, for the carbon dioxide produced increases the respiratory movements while when more blood reaches the heart it increases automatically its output.

The substances of the exhaust from the engine, carbon dioxide and water, are likewise transported to the lungs, skin, and kidney by which they are returned to the outside world.

A cycle is completed by the plants which under the influence of sunlight transform the carbon dioxide and water back into carbohydrate, the chief nourishment of animals.

In this description of the body the heart and lungs appear as the servants of the muscles, and it is an important fact in curative medicine that physical and mental rest put the whole body at rest.

So far many substances which we need for nourishment have not been mentioned. They correspond to the materials of which the engine is made and need only be supplied in very minute amounts. In the case of the body the most important substance concerned is protein, which is the essential chemical component of all living things. Its detailed composition is discussed later, but here it may be said that amongst its essential constituents are nitrogen and sulphur. The chemical changes which take place in the various substances in the body are known as Metabolism.

The muscles are also in contact with the external environment by means of the nervous system, and here we may contemplate how many of our movements are the result of stimuli from the outside world. Such stimuli usually determine at least the exact time at which the movements are made, through, of course, the intervention of the brain.

The study of muscular movement may be considered to be a suitable point at which to commence the study of Human Physiology, for what has been said of the muscle applies to every cell and tissue of the body, but, with the exception of the heart, none are more active than the voluntary muscles and none make such demands on the organism as a whole.

The term **organ** is a loose anatomical one and is applied to structures which can be conveniently separated by dissection. Commonly, however, they have a well recognisable characteristic microscopical structure and function.

In performing the bodily functions the organs themselves are arranged in groups which are, by convention, known as **systems.** Thus the respiratory system includes all structures and processes which are concerned with the uptake of oxygen and elimination of carbon dioxide, but there are really no hard-and-fast boundaries to any system, as they all work together for the benefit of the whole body.

CHAPTER 3

EXCITABILITY AND STIMULATION

Excitability or **Irritability** is the power which certain tissues possess of responding by some change (transformation of energy) to the action of an external agent which, whatever its nature, we call the **stimulus.**

The nature of the response depends on the nature of the tissue. Some tissues move, some secrete, some discharge electricity, *e.g.* the electric organs of some fishes.

Excitable tissues may be stimulated by mechanical or chemical agencies. They may also be stimulated by suitable electrical stimuli, and in the study of excitability the latter stimuli are generally used as they do not damage the tissue and are easily controlled. The tissues in the body are stimulated by nervous impulses. We can see the response to such stimulation in the nerve to a muscle of a frog. It may be stimulated by a tap or pinch, by a chemical agent (acid or salt), by a direct or an induced current, and normally by the nervous impulses which reach it from the nerve centres. When we make a voluntary movement, we cause a nervous impulse to pass down an excitable nerve to an excitable muscle. Some tissues are specially excitable to certain kinds of stimuli rather than to others. For example, unstriated muscle is most easily stimulated by stretching. Glycerol stimulates nerve but not muscle directly; while ammonia stimulates muscle but not nerve.

We may regard stimuli as liberators of energy ; muscle and nerve and other irritable structures undergo disturbances in consequence of a stimulus. A stimulus may be compared to the blow or spark that causes dynamite to explode, or the match applied to a train of gunpowder. So in muscle or nerve the effect is often out of all proportion to the strength of the stimulus ; a light touch on the surface of the body may elicit very forcible nervous and muscular disturbances ; and, moreover, the effect of the stimulus is propagated along the nerve or muscle without loss. (See "The Nature of the Nerve Impulse").

Electrical Stimulation

Stimulation of an excitable tissue may, as we have seen above, be brought about chemically or mechanically, but most conveniently by an electric current from a cell or a battery supplying 1–2 volts. This method has the great advantage that within limits it does not damage the tissue and may be repeated many times. It is not necessary to describe in detail the electrical apparatus.

Wires from the positive and negative poles of the cell form the electrodes, the former being known as the anode and the latter as the cathode. With a direct current stimulation occurs only at the "make" and the "break," but not when the current is "flowing" (see next page).