An Address

ON

THE RELATION OF PHYSIOLOGY TO PHYSICS AND CHEMISTRY.

DELIVERED BEFORE THE PHYSIOLOGICAL SECTION OF THE
BRITISH ASSOCIATION FOR THE ADVANCEMENT OF
SCIENCE, DUBLIN, 1908.

By J. S. HALDANE, M.D., F.R.S.,

FELLOW OF NEW COLLEGE AND READER IN PHYSIOLOGY IN THE
UNIVERSITY OF OXFORD; PRESIDENT OF THE SECTION.

IN choosing to address you on the relation of physiology to physics and chemistry, I am aware that I have selected a subject which has already been treated from this chair by more than one distinguished predecessor. My excuse for returning to it again is that it not only possesses deep scientific interest for us all, but that a great deal remains to be said about it.

The majority of physiologists in recent times have expressed more or less clearly the opinion that physiology is the application to living organisms of the methods and modes of explanation of physics and chemistry. It is, in short, physics and chemistry applied to the activities of living organisms; so that the only explanations aimed at in physiology are, or ought to be, physical and chemical explanations. A minority, which is at present a growing one, I think, have either definitely dissented from this view, or have remained unconvinced of its truth. As one of this minority I should like to place before you as shortly as possible what seem to me to be the main reasons of our dissent. Let me add that I have carefully pondered over these reasons during many years of active physiological work.

When we look back on the history of physiology it seems perfectly evident that physiological progress has been dependent on the progress of physics and chemistry. On this point there is no room for doubt. To take only one example, where should we be in the investigation of animal metabolism but for the ideas and experimental methods furnished to us by physics and chemistry? We should know next to nothing about respiration, animal heat, nutrition, or muscular and other work. Physiology depends at every turn on physics and chemistry, and its future progress will certainly be equally dependent on advances in physical and chemical knowledge. This consideration has, I imagine, weighed very heavily in the minds of those physiologists who have concluded that physiology is nothing but applied physics and chemistry. A further fact which weighs equally heavily is that in spite of diligent search no fact contradicting the fundamental laws of conservation of matter and energy has been discovered in connexion with living organisms.

When, however, we ask what progress has been made towards the physico-chemical explanation of physiological processes, we at once enter upon controversy. We may point to advances in some directions, but they are accompanied by the appearance of unforeseen difficulties in other directions. Again, to take animal metabolism as a typical instance, the investigations of the last hundred and twenty years have enabled us to assign ultimate physical and chemical sources to the energy and material leaving the body in various forms. We can assign to such sources the energy of animal heat, muscular work, glandular, nervous, and other activity; also the carbon dioxide, urea, salts, and many other substances which leave the body or are formed within it. All of this new knowledge may be regarded as progress towards a physico-chemical explanation of life.

But there is another aspect to be considered; for side by side with what I have just referred to there has been a different kind of increase of knowledge with regard to animal metabolism. This growth of knowledge relates to the manner in which the passage of energy and material through the body is regulated in accordance with what is required for the maintenance of the normal structure and activities of the body. In Liebig's time, for instance, it was believed that the rate of respiratory exchange was regulated simply by the supply to the body of oxygen and

food material. If one breathed faster, or if the barometric pressure or percentage of oxygen in the air increased, the respiratory exchange was assumed to be also increased, just as ordinary combustion outside the body would be increased by an increased supply of oxygen. If, again, one took in more food, it was supposed that the excess went to increase the rate of combustion in the blood (luxus consumption), just as a fire is increased when more fuel is supplied. We now know that these assumptions were wholly mistaken, and that the respiratory movements, respiratory exchange, and corresponding consumption of food material in the body are regulated with astounding exactitude in accordance with bodily requirements. If, for instance, the body consumes more proteid, it economizes a quantity of fat or carbohydrate equivalent in energy value to the proteid; and from day to day the amount of energy liberated in the body is very steady. With regard to the excretion of material by the kidneys, a similar growth in knowledge can be traced. It is scarcely a century since the urine was regarded as equivalent, more or less, to the liquid part of the blood separated from the corpuscles, which were unable to pass through the very fine capillary tubules supposed to exist in the kidney substance. Gradually, however, we have learnt how extraordinarily delicate is the selective action which occurs in the kidney substance, and how efficiently this selective action maintains the normal composition of the blood. Scarcely a remnant is now left of the old filtration theories. Our ideas of tissue nutrition and growth have undergone a similar change; and it is hard to realize that only about seventy years ago Schwann could put forward the theory that cell formation and growth is a process of crystallization.

One can multiply instances like these almost indefinitely; but I have, perhaps, said enough to show that if in some ways the advance of physiology seems to have taken us nearer to a physico-chemical explanation of life, in other ways it seems to have taken us further away. On the one hand we have accumulating knowledge as to the physical and chemical sources and the ultimate destiny of the material and energy passing through the body; on the other hand an equally rapidly accumulating knowledge of an apparent teleological ordering of this material and energy; and for this teleological ordering we are at a loss for physico-chemical explanations. There was a time, about fifty years ago, when the rising generation of physiologists, in their enthusiasm for the first kind of knowledge, closed their eyes to the second. That time is past, and we must once more face the old problem of life.

Let us first look at the answer given to this problem by many of the older physiologists. Roughly speaking, they carried physical and chemical explanation of physiological processes as far as they could, and for the rest assumed that at some point or other the physical and chemical factors are interfered with and ordered in a teleological direction by something peculiar to living organisms—the "vital principle" or "vital force." This theory, if one can call it a theory, had the negative merit that it did not lead physiologists to ignore facts which they could not explain. But in practice the "vital force" became simply a convenient resting-place for these facts. It was assumed that the vital force could do anything and everything, and that it acts "from the blue" on physical and chemical processes. Yet its action was admittedly dependent on physical and chemical conditions, such as warmth, the presence of oxygen, etc. In fact, no consistent definition was given to the conception of "vital force." It consequently never could become a working hypothesis of any value. Chiefly on this account, I think, it practically disappeared from physiology last century. Yet the class of fact which led to the theory of "vital force" is now more prominent than ever; and what Du Bois Reymond called the "spectre" of vitalism meets us at every turn, thinly disguised under such names as "cell autonomy," "vital processes," etc. It is useless to shut our eyes and deny the existence of this "spectre." We must fairly face and examine it.

However difficult it may be to imagine physico-chemical explanations of such processes as respiratory exchange, secretion, muscular activity, etc., there is nothing in the known facts relating to each process, taken by itself to preclude the possibility of such explanations. Let us then follow the Euclidian method and assume provisionally that

they are nothing but physico-chemical processes. This assumption evidently implies that each of the living cells concerned has a very complex and definite structure varying according to its functions. To take an example: a secreting cell in the kidney may be assumed to have a structure which responds to the stimulus of a certain percentage of urea or sodium chloride in the blood, and reacts in such a manner that energy derived from oxidation is so directed as to perform the work of taking up urea or sodium chloride from the blood and transferring it against varying osmotic pressures from one end of the cell to the other. This mechanism must also be assumed to have the property of maintaining itself in working order, and probably also of reproducing itself under appropriate stimuli, besides also performing various other functions. Its physico-chemical structure must thus be very definite and complex—to an extent which the older physico-chemical theories took no account of. If we look to the cells in other parts of the body we are met with the same necessity for assuming complexities of structure which seem to grow in extent with every advance in physiological knowledge, every discovery of new substances present within or around the cells, every discovery of new physiological reactions.

Let us not lose courage, however, but continue to follow the direction in which our assumption leads. In assuming that the body is an enormously complex physico-chemical structure we have only begun to face the difficulties of our hypothesis; for we have still to consider how this structure can have originated in accordance with the physico-chemical theory of life. The adult organism develops from a single cell, the fertilized ovum. It is certain that this cell does not contain in a preformed condition the structure of an adult organism. The conditions of environment in which any particular ovum develops itself are doubtless indefinitely complex from the physico-chemical standpoint, as indeed is the environment of any particular portion of matter existing anywhere. But these conditions also vary almost indefinitely in the case of different ova, whereas the adult organism to which the ovum gives rise reproduces in minute detail the enormously complex characters of the parent organism. We are thus driven to the assumption that the ovum contains within itself a structure which, given certain relatively simple conditions in the environment, reacts in such a way as to build up step by step, from materials in the environment, the structure of the adult organism. To affect this the germ cell must have a structure almost infinitely more definite and complex than that of any cell in the adult organism. Difficult as it may be to form any conception of the mechanism of a secreting cell, it is infinitely more difficult to form the remotest idea of that of a germ cell.

But we are still only at the beginning of the difficulty. The assumed tremendous mechanism of the germ cell has been developed, together with the whole of the rest of the parent organism and countless other germ cells, from a previous germ cell. What must the "mechanism" of this cell have been? And that of its endless predecessors? We have reached the Euclidian *reductio ad absurdum*.

I might strengthen my argument by referring to the further difficulty over any physico-chemical conception of what occurs in the sexual fusion of the male and female cell, or in the process of partial reproduction after injury, or in the facts established by Driesch and others with regard to the extraordinary reproductive powers of each cell in developing embryos. But I have purposely confined my references to more simple and well-known facts; for the more simply the argument can be put, the better. I confess that as a physiologist I am struck with amazement at the manner in which heredity is often discussed by contemporary writers who endeavour to treat the subject from a mechanistic standpoint. Sometimes, indeed, the germ cell is acknowledged to be a complicated structure, but at other times it is treated as a "plasma," which can be mixed with other "plasma," divided, or added to, as if for all the world it were so much treacle! I have tried to place clearly before you the assumptions in connexion with heredity which to my mind make the physico-chemical theory of life unthinkable, even if it be tenaciously clung to in connexion with those ordinary physiological phenomena where, as already explained, it has proved so disappointing.

Our aim as physiologists is to render physiological

phenomena intelligible—in other words, to obtain general conceptions as to their nature. The point now reached is that the conceptions of physics and chemistry are insufficient to enable us to understand physiological phenomena. But if so, we need not sit down in despair, for we can look for other working conceptions. Are we justified in doing this? I think we are.

There is a prevalent popular idea that the world as presented to us under the conceptions of physics and chemistry is more than our own imperfect conception of reality, and corresponds completely with reality itself. Philosophy has shown us, however, that this idea must be erroneous; for if it were correct, knowledge of such a world would be impossible. This was first clearly pointed out almost two hundred years ago in this city by one of the greatest of Irishmen, George Berkeley, at that time a Fellow of Trinity College.¹ The lesson taught by Berkeley, Hume, and their successors is not that physical science is of less value than it appears to be, but that its fundamental hypotheses are only working hypotheses, applicable only so far as they successfully fulfil their purpose. Each different science is thus free to employ whatever working hypotheses may prove most useful in interpreting the order of phenomena with which it deals. We are thus perfectly justified in seeking to find a conception of life which will serve as a better working hypothesis than that of life as a physico-chemical process.

I venture to think that the conception we are in search of lies very near to hand and is indeed in common use, though in a form which has hitherto been too ill-defined for deliberate scientific employment. It is simply the conception of the living organism, which stands, or ought to stand, in the same relation to biology as the conceptions of matter and energy to physics, or of the atom to chemistry. Let me try to give more definition to this conception. A living organism is distinguished by the fact that in it what we recognize as specific structure is inseparably associated with what we recognize as specific activity. Its activity expresses itself in the development and maintenance of its structure, which is nothing but the expression of this activity. Its identity as an organism is not physical identity, since from the physical standpoint the material and energy passing through it may be rapidly changing. In recognizing it as an organism we are applying an elementary conception which goes deeper than the conceptions of matter and energy, since the apparent matter and energy contained in, or passing through, or reacting with, the organism are treated as only the sensuous expression of its existence. Even the environment is regarded as in organic relation with the organism, and not as a mere physico-chemical environment. It follows that for biology we must clearly and boldly claim a higher place than the purely physical sciences can claim in the hierarchy of the sciences—higher because biology is dealing with a deeper aspect of reality. It must also be the aim of biology gradually to penetrate behind the sensuous veil of matter and energy which at present seems to permeate the organic world at all points.

Let us now see how the conception just defined can be used as a scientific working hypothesis. In accordance with it any form of physiological activity is presumably related essentially, and not accidentally, to the other details of activity and structure in the same organism. Stated generally, therefore, the problem of physiology is not to obtain piecemeal physico-chemical explanations of physiological processes, but to discover by observation and experiment the relatedness to one another of all the details of structure and activity in each organism as expressions of its nature as an organism.

The first step in physiological or morphological discovery is to observe the bare sensuous fact of some detail of physical or chemical change, or of composition or structure, in connexion with an organism. It is only, however, when we find that this detail is not accidental that it becomes of biological interest. We can observe its constancy or otherwise in the same organism or similar organisms—that is to say, the constancy of its relations to other details of structure and activity. Or we can by experiment search for the element of constancy when it is at first sight hidden from our view. In so far as we find this, it seems to me that we reach physiological or biological explanation; but evidently the process of reaching it is at any stage in knowledge only imperfectly

realized, since new details of activity and structure are constantly being revealed.

Concrete examples will make the matter clearer, and I shall first take as an example, the progress of knowledge in relation to animal heat. It was of course common knowledge from early times that in the higher animals a certain amount of warmth in the body is present during life. With the invention of the thermometer the body temperature could be measured and its extraordinary constancy observed. When Lavoisier measured the heat production of an animal, and compared the output of heat with the output of carbon dioxide and disappearance of oxygen in respiration, an immense step forward was taken. This step was in two distinct respects a very great one. In the first place it revealed an element of identity between organic and inorganic phenomena, since heat production in an animal was shown to be accompanied by chemical changes quantitatively identical with those accompanying heat production by oxidation outside the body. In the second place, and from the distinctively physiological point of view, it revealed a fundamental relation between heat production, respiratory exchange, and the consumption of food.

As regards the first of these points, I should like to say definitely that I, for one, firmly believe that could we only understand them fully we could bring organic and inorganic phenomena under the same general conceptions. Lavoisier's discovery, like that of Mayer in relation to the sources of muscular energy, was a great advance in this direction. But this is a very different thing from an advance in the direction of rendering life intelligible in terms of physico-chemical conceptions as we commonly understand them. Lavoisier's discoveries did nothing in the direction of reducing to physico-chemical terms the apparent teleological or, as I should prefer to say, "physiological" element in the phenomena of animal heat.

It is to the second point that I wish to direct special attention at present. Lavoisier's discovery rapidly brought the phenomena of animal heat into direct relation, not only with respiration, but with nutrition, circulation of blood, excretion, and other processes; and it was gradually discovered that the maintenance of a constant body temperature renders physiologically intelligible a large number of phenomena in connexion with different bodily activities—for instance, increased metabolism with fall of external temperature, sweating or increased circulation through the skin with muscular work, the relative constancy of metabolism during starvation, and the physiological equivalence of proteid, carbohydrate, and fat in proportion to their energy values. These phenomena are intelligible on the assumption that warm-blooded animals actively maintain a certain body temperature, just as they maintain a certain bodily structure and composition. This mode of explanation is not a physico-chemical one, but I venture very confidently to assert that it is a physiological one, and in fact the only kind of explanation which really interests and appeals to a true physiologist. The thread of identity which has been traced through the phenomena just referred to seems to me to have proved a real scientific clue.

As another example I may perhaps be allowed to refer shortly to the regulation of breathing, as this is a subject on which I have recently been working. Current accounts of the clock-like action of the respiratory centre during normal breathing, with the expansion and contraction of the lungs acting as a sort of governor through the vagus nerves always filled me with suspicion, as it seemed to me that such a regulation was altogether unlike a physiological one. This led me to investigate the matter further, along with Mr. Priestley; and we had the satisfaction of being able to prove that the ventilation of the lungs is actually regulated with exquisite exactness, in such a way as to keep the partial pressure of carbon dioxide in the alveolar air and presumably, therefore, in the arterial blood, constant. In reality, therefore, the lung ventilation is regulated in accordance with the requirements of respiratory exchange; and what seems to be true physiological explanation has been advanced a short stage.

The advance of knowledge with regard to the circulation might be made the text of a similar discourse. By a process of abstraction the circulation of the blood may be regarded as a mere mechanical process, connected only by the accidents of physical structure with other physiological

processes. Under the influence of mechanistic theories the blood pressure and rate of blood-flow through different organs were indeed for long supposed to be the primary determining cause of the physiological activities of these organs, just as the rate and depth of breathing were supposed to determine the consumption of oxygen by the body. Evidence is, however, accumulating on all hands that the blood supply to various parts, like the air supply to the lungs, is in reality determined by physiological requirements. In other words, it is a direct expression of the nature of the organism, just as the common-sense idea of life would lead us to expect.

I may pass next to a branch of physiological knowledge which is still in its early infancy. Under the influence of mechanistic ideas physiology has for long left completely out of account investigation into the formation and maintenance of organic structure. For mechanistic explanations structure had to be assumed, and as a consequence anatomy was left high and dry in a position of helpless isolation. If, however, the real aims of physiology are those which I have tried to indicate, the separation between physiology and anatomy must tend to disappear, for the structure, no less than the activity, of each part must be determined by its relations to the structure and activities of other parts in the organic whole of the living organism. We can investigate these relations, just as we investigate the connexion of secretion with respiratory exchange, circulation, or the composition of the blood; and they must evidently be physiological relations. Our aim is not the hopeless one of giving a physico-chemical explanation of the development and maintenance of organic structure, but simply to discover the physiological relations which determine the structure of each part and its maintenance. Many facts bearing on this subject have recently been brought to light by the application of experimental methods to embryology, and by the study of reproduction of lost or injured parts, and of grafting; also by the study of so-called "internal secretion" in connexion with various organs. It seems clear, however, that we are only at the beginning of a vast development of knowledge in this direction, and that for this development far more refined methods of dealing with the chemistry of the body will be required.

It was in connexion with the facts of reproduction and heredity that the difficulties of the mechanistic theory of life were found finally to culminate. For the distinctively biological theory of life, to which I have endeavoured to give some definition, these difficulties do not exist. They are, it is true, not solved; but they are set aside as being due to wrong initial assumptions, and therefore purely artificial. The difficulty remains of reconciling the fundamental conceptions of biology with those of physics and chemistry. This is, however, a matter of which the discussion must be handed over to philosophy, which has many similar matters to deal with. If it is a fundamental axiom that an organism actively asserts or maintains a specific structure and specific activities, it is clear that nutrition itself is only a constant process of reproduction; for the material of the organism is constantly changing. Not only is there constant molecular change, but the living cells are constantly being cast off and reproduced. It is only a step from this to the reproduction of lost parts which occurs so readily among lower organisms; and a not much greater step to the development of a complete organism from a single one of the constituent cells of an embryo in its early stages. In all these facts we have simply manifestations of the fundamental characters of the living organism. The reproduction of the parent organism from a single one of its constituent cells separated from the body seems to me only another such manifestation. Heredity, or as it is sometimes metaphorically expressed, organic memory, is for biology an axiom and not a problem. The problem is why death occurs, what it really is, and why only certain parts of the body are capable of reproducing the whole. These questions carry us, at least in part, beyond the present boundary lines of biology. They involve those ultimate questions which, as has just been pointed out, it is the province of philosophy to deal with.

To turn to another set of questions, the distinctively biological standpoint in biology involves a change in what has in recent times become the ordinary attitude towards organic evolution. Since our conception of an organism is

different in kind, and not merely in degree, from our conception of a material aggregate, it is clear that in tracing back life to primitive forms we are getting no nearer to what is called abiogenesis. The result of investigation in this direction can only be to extend further the domain of biology and widen biological ideas. Our aim must be, in short, not to reduce organic to inorganic phenomena, but to bring inorganic phenomena into the domain of biology.

I am well aware that it will be strongly maintained that the change of front which I have urged as necessary involves the giving up of all real attempt at scientific explanation in biology. As already explained, this is a philosophical question, and I shall not attempt to deal further with it here. What immediately concerns us as biologists is whether the change of front will further or hinder biological advance, particularly in physiology. Now the first requisite of a working hypothesis is that it should work, and I have tried to point out that as a matter of fact the physico-chemical theory of life has not worked in the past and can never work. As soon as we pass beyond the most superficial details of physiological activity it becomes unsatisfactory; and it breaks down completely when applied to fundamental physiological problems, such as that of reproduction. Those who aim at physico-chemical explanations of life are simply running their heads at a stone wall, and can only expect sore heads as a consequence. It seems to me that the proposed change of front is only the conscious adoption of a common-sense idea which is somewhat vaguely, perhaps, present in the minds of all men, and which has in reality guided biological advance in the past. This idea, as I have tried to show, is a working hypothesis which actually works, and affords clear guidance for future advance.

I would fain add a few words as to the relation of physiology to psychology and ethics, for this is a subject of deep human interest. We know that at any rate the higher organisms are conscious and intelligent. This fact brings physiology into touch with a new element in the behaviour of organisms. The subject is far too great a one for me to attempt to discuss here, but I should like to say that it appears to me very clear that just as biology is something more than physics and chemistry, so psychology is something more than physiology, with the added assumption that consciousness is tacked on to certain physiological processes, if such a crude conception has any definite meaning. We can, it is true, by a process of abstraction treat sensation from the purely physiological side, as in investigating the physiology of the sense organs; but this is physiology and nothing else, for we are leaving out of account the distinctive elements of consciousness. At our present stage of knowledge life is not intelligence, and men or animals as intelligent individuals involve a deeper aspect of reality than biology deals with. Our fundamental physiological working hypothesis cannot be successfully applied to the phenomena of intelligence, and the sooner and more definitely this is realized the better for physiology.

In conclusion, let me endeavour to state shortly the main contention which I have endeavoured to place before you. It is that in physiology, and biology generally, we are dealing with phenomena which, so far as our present knowledge goes, not only differ in complexity but differ in kind from physical and chemical phenomena; and that the fundamental working hypothesis of physiology must differ correspondingly from those of physics and chemistry.

That a meeting-point between biology and physical science may at some time be found, there is no reason for doubting. But we may confidently predict that if that meeting point is found, and one of the two sciences is swallowed up, that one will not be biology.

REFERENCE.

1 *Treatise concerning the Principles of Human Knowledge*, 1710.

THE Department of State Medicine and Public Health of Western Australia has commenced the publication of a monthly bulletin. It is intended for the information of local health authorities and others interested in public health work, and to keep them in touch with what is going on at head quarters, and in Western Australia as a whole. The body immediately responsible for its publication is the Central Board of Health; it meets weekly, and consists of five members. Its president is Dr. T. D. Lovegrove.

A Clinical Lecture

ON

CHOREA.

DELIVERED AT THE LONDON SCHOOL OF CLINICAL
MEDICINE.

By GUTHRIE RANKIN, M.D., F.R.C.P.,

PHYSICIAN TO THE DREADNOUGHT AND ROYAL WATERLOO HOSPITALS.

CHOREA was first described by Sydenham in 1686. It is a prevalent affection among children, especially girls. It also occurs occasionally in adults, and in them is almost invariably met with in women during pregnancy. Irregular muscular movements, closely resembling but totally distinct from true chorea, sometimes result from emotional causes, and the popular name of St. Vitus's dance is properly applied to this hysterical and often epidemic disorder, which generally occurs under the influence of religious excitement, and which in the Middle Ages was cured by a pilgrimage to the shrine of St. Vitus at Zabern. This form of dancing mania was for long confused, and regarded as identical, with Sydenham's chorea; and one reason for this confusion existed in the belief—which is still entertained by some observers—that imitation may act as an existing factor of Sydenham's disease even among children. And the possibility of a mimetic variety of chorea must not be too lightly set aside, as the following experience will show. Many years ago, when driving one summer afternoon through a small outlying village in Scotland, my progress was arrested in the main street by a crowd of children surrounding a girl of about 12 years of age, who was obviously the victim of an acute attack of chorea. The movements of the unfortunate child were extravagant, and were evidently a source of intense interest and merriment to her youthful onlookers, and of cruel imitation by some of the more precocious of them. Within a week or ten days the local doctor had no fewer than fourteen cases of chorea on his attendance list. It may be presumed that probably the worst cases only came under his observation, and that many others of a milder type also resulted from the street exhibition of which I had been an accidental observer. Hysteria could hardly be accepted as an explanation applicable to a number of children in a country village, and such epidemicity seemed more readily to be explained by a theory of mimicry than by any other. The village doctor himself had no doubt on the matter, especially as, in his previous experience, chorea was not an ailment which figured largely in his daily work.

In true chorea the muscular movements are involuntary, purposeless, and liable to intensification under the influence of mental perturbation or emotional excitement. They cease during sleep. The demands made by education upon the nervous reserve of quickly-growing children, particularly such as are of an anxious temperament and ambitious of attaining a high degree of excellence in their school-work, are responsible, in no small measure, for the onset of the disease. The peculiar and intimate association which exists between chorea, cardiac disease, and rheumatic affections is well recognized, but the nature of the relationship has not, so far, been ascertained. Morley Fletcher concludes, from a careful examination of 580 cases, that "chorea is a manifestation of rheumatic fever, but that many other causes may co-operate in the production of the disease." Legay, of Paris, published statistics in 1897 which went to show that the disease occurs, for the most part, in children with a neurotic heredity who have recently suffered from an infectious disorder. In the majority of instances the infection was rheumatic, but he quoted many cases in which chorea was apparently directly due to the poison of measles, scarlet fever, varicella, influenza, and tuberculosis. Sturges has pointed out that it is a not uncommon sequela of whooping-cough. When rheumatism attacks children, it tends to exert its influence more on the heart and pericardium than on the joints, so that, if care be not taken to seek for evidences of endocarditis or pericarditis, the true association of chorea with the rheumatic poison may be overlooked. In most fatal cases one or more of the cardiac valves are found diseased, and the interdependence of chorea with rheumatism, in the