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Editorial

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PURPOSES IN MEDICAL RESEARCH

AN INTRODUCTION TO THE JOURNAL OF CLINICAL INVESTIGATION

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Custom has varied in the history of medical journalism; certain journals were introduced to their readers without explicit statements by their editors of the purposes which the new publications were to serve. In these instances it was left to chance or to the general knowledge of the contemporary public to find within its pages a justification for the new venture. Other journals have been explicit in the avowal of their objects. Both methods have advantages; both have disadvantages. In a discipline as old as medicine, which has continuously engaged the profound interest of men for as many centuries as has any of the other subjects in which men have exercised curiosity and the desire for knowledge, it is fitting in the interests of definiteness and with the view of making an exact statement of our conceptions, as well as in attempting to anticipate the natural inquiry of our contemporaries, to define the motives which suggest this new publication.

There is a pitfall here, which should be avoided. In the attempt to explain the purposes which actuate the publication of a new journal, the impulse may be, as Naunyn¹ pointed out in the case of Wunderlich, to make too precise the limits within which the thought which underlies the undertaking is to be confined. The doors in medicine must naturally be kept open so that influences, no matter whence derived, may contribute their share to the understanding and elucidation of the problems which constitute the proper province of medicine. But that a danger lies here history has made amply apparent. For there has never been a time either in the ancient or in the modern world when medicine was far removed from the influences of neighbor-

¹ Naunyn, B., *Deut. Arch. f. klin. Med.*, 1922, cxi, 1-27. *Die deutsche Heilkunde vom Anfang des neunzehnten Jahrhundert.*

ing disciplines. It has in point of fact often benefited by importing for its own guidance the conceptions which prevailed in other domains of inquiry, whether these conceptions were borrowed from the physical or from the biological world. But it has also suffered from this habit. The latest bondage into which medicine was led and from which it was freed less than a century ago was due to the influence of romantic metaphysics at the beginning of the 19th century. The record of the history of medical progress gives us no assurance that, without constant watchfulness, we shall escape in the future enticements from the proper direction which thought and activity might pursue in the study of human disease.

Since the renaissance, men of science have indeed been continuously eager to escape from those influences which tended to focus their interests on the contemplation alone of natural phenomena and have sought, under the stimulus supplied by Francis Bacon, to enlarge knowledge by coming actually into contact with the facts and forces of nature. But they have likewise been alive to the dangers inherent in this pursuit, for side by side with the collection of facts and the making of experiments, rules were sought by the application of which science might in some measure be assured that in the management of its discoveries it was proceeding along paths which led to correct generalization. That is to say, the method of deduction in natural science as the sole method of investigation was finally abandoned and the method of induction, of experiment, was added. It was soon found that even this reform did not suffice; infinite experimentation might very well produce facts in endless variety. But facts, divorced from meaning have never for long periods of time held the attention of men. Science has constantly insisted on arranging facts in order, with the view to arriving at some statement of their significance. How soon after the time of Bacon this problem came prominently into the view of experimental scientists the following observations of Boyle² show:

. . . . if men could be perswaded to mind more the Advancement of Natural Philosophy than that of their own reputations, 'twere not me-thinks very uneasie to make them sensible, that one of the considerablest services that they

² Boyle, R., *Certain Physiological Essays*, London, 1661, 8-9.

could do Mankind were to set themselves diligently and industriously to make Experiments and collect Observations, without being over-forward to establish Principles and Axioms, believing it uneasy to erect such Theories as are capable to explicate all the Phaenomena of Nature, before they have been able to take notice of the tenth part of those Phaenomena that are to be explicated. Not that I at all disallow the use of Reasoning upon Experiments, or the endeavouring to discern as early as we can the Confederations, and Differences, and Tendencies of things: For such an absolute suspension of the exercise of Reasoning were exceeding troublesome, if not impossible so in Physiology it is sometimes conducive to the discovery of truth to permit the Understanding to make an Hypothesis in order to the Explication of this or that Difficulty, that by examining how farre the Phaenomena are, or are not, capable of being salv'd by that Hypothesis, the Understanding may ev'n by its own Errors be instructed. For it has been truly observed by a great Philosopher, That Truth does more easily emerge out of Error than Confusion. That then that I wish for, as to Systems, is this, That men in the first place would forbear to establish any Theory, till they have consulted with (though not a fully competent Number of Experiments, such as may afford them all the Phaenomena to be explicated by that Theory, yet) a considerable number of Experiments in proportion to the comprehensiveness of the Theory to be erected on them. And in the next place, I would have such kind of superstructures look'd upon only as temporary ones, which though they may be preferr'd before any others, as being the least imperfect, or, if you please, the best in their kind that we yet have, yet are they not entirely to be acquiesced in, as absolutely perfect, or incapable of improving Alterations.

Medicine has shared this interest in arrangement with the rest of science. The significance of Sydenham is to be found precisely in this connection. But how inadequate arrangement is in itself in the attempt to arrive at significance is to be observed in the further extension of his method by the later systematists, Sauvage and Linné.

Activity in certain other directions has likewise resulted in disappointing experience. This result is seen, for instance, in the application to medicine of methods developed in other fields of inquiry. Illustrations of the futility of this sort of activity are to be found in the work of Borelli and the iatro-mathematical school, in that of van Helmont and the iatro-chemists, and in that of Boerhaave, Cullen and others in attempts to introduce isolated methods of measuring, as for instance of temperature, into the study of disease. In the first instance, methods were used which perhaps could not lead to an understanding of morbid phenomena; in the second, the methods were in point of fact not developed sufficiently to render profitable their

application to disease processes. Methods of induction if used alone failed, when they were merely borrowed, just as had the method of deduction. Medicine was not alone in these experiences. Indeed, if we are to credit reporters of the history of other sciences, similar experiences have been encountered in them so that it is now a general conclusion that, in order to achieve development in natural science, both methods should be employed.

It is a noteworthy observation that just at the time when Borelli, van Helmont, and others were seeking to advance medicine by importing into it the developments made in other disciplines and were meeting with what proved to be indifferent success, parallel developments were taking place due to the work of men whose interest originated in speculation aroused primarily by curiosity as to the behavior of the body itself. Out of this curiosity came the genuine advances of Mayow, Harvey and Sydenham. But the employment of a method presupposes that in a proposed inquiry the use of the method selected is advantageous in the solution of the problem. It has just been pointed out that medicine has before now been urged to adopt methods believed either by others or by medical men themselves to be advantageous in medical research. Error lay at the basis of this belief. That was true of the nature philosophers in Germany, with the result that for a generation medicine became a branch of metaphysics. That was true of the mechanics and mathematics of the 17th century when applied to medicine under the influence of Borelli; it was true of chemistry "applied" to medicine by van Helmont. The same erroneous program was proposed by Johannes Müller when he and his successors urged the "application" of physiology to medicine. Mathematics, mechanics, physics, chemistry, physiology as independent disciplines has each had its proper objects of inquiry; all have been aware of their appropriate problems in the phenomenal world. Their signal achievements are the common knowledge and have been the wonder of all men. Nor can there be doubt that the interest which their pursuit has aroused has exerted profound influence on medicine itself. But the primary objects of interest in medicine cannot properly be stated in terms appropriate to them.

Medicine must, like the other sciences, be properly credited with having specific objects of interest on its own account. If it is true that

medicine has not always been clear as to what these objects are, this may be due to the fact that the definition of its objects has not always been clear. It may perhaps be for this reason that it has so often been deflected from the straight path of its proper pursuit. For it cannot be the object of medicine or of any other discipline to "apply" the methods of other sciences to itself, whether of anatomy or physiology, whether of physics or chemistry. Medicine in the light of its history might properly pause at each new stage of its development and make the attempt to define for itself its legitimate scope and objects. It might do what Sir Philip Sidney said he had done in deciding how he had best write:

Fool! said my muse to me, look in thy heart, and write.

If it attempts to do so now it will not be the first time that medicine has followed the advice of Sidney. We have, as all those interested in the progress of medicine know, for some time been inquiring whether medicine is entitled to be called a science. To us the answer to this question is clear and unequivocal. It is clear because of the nature of the case. The phenomena of interest in medicine are the phenomena of disease as these are manifest in affected persons. They are phenomena which exist as concrete entities in nature, they are indivisible, and they fall within the province of no other inquiry. They constitute the proper concern of medicine. Nor are the phenomena of disease the combination or resultants merely of other forces. They are not the resultants of forces known in physics and chemistry, nor in physiology and mathematics, nor the resultants of any combination of these. Rapid and shallow breathing for instance, as an appearance familiar in disease, may depend on a derangement of the familiar Hering-Breuer reflex, or it may depend on anoxaemia, or it may depend on a high hydrogen ion concentration. But irrespective of how this type of breathing is conditioned, it remains a unique phenomenon, even though the terms in which it is characterized are anatomical or physiological or chemical. Anatomy or physiology or chemistry may supply the methodology for analyzing the occurrence, but the occurrence is something apart from and over and above the factors into which it can be resolved. Heart failure presents the opportunity of another illustration. Phenomena are the basis

of a science, not the techniques by which phenomena are elucidated. Those of disease are, as has been said, indivisible phenomena, as indivisible as are those of botany or zoology or paleontology. When we come to the question of how to investigate them we find that they are to be studied by no single methodology any more than are those of the sciences just mentioned. The methods to be employed are those which are appropriate to illuminating the specific problems in question. In paleontology, the methods may be those of geology or comparative anatomy or petrology; in biology, they may be those of physiology or chemistry or physics.

"The aim of medicine," says Laennec,³ "is the cure of disease." And he added that there were a multitude of ways by which this end might be attained. He singled out three especially for mention; that of the empiricists, who considered it sufficient to distinguish diseases by their apparent signs; second, that of those who believed it possible to disclose the causes of disease without giving themselves the trouble of learning their effects; and third, that of those who believed it was necessary to understand the diseases. We should perhaps add by way of interpreting or perhaps of supplementing Laennec's meaning, that we believe it necessary as the basis of therapeutics to understand the mechanisms, that is to say, the processes which underlie the manifestations of disease, for it is these which it is one of our functions to attempt to correct. That is our practical aim. We have learned a lesson also in another direction. It is that, as in other disciplines, learning may be pursued for its own sake. And the reason for this is two-fold. Men have learned that the direct is not always the shortest road to the attainment of their objects. It is true that results ultimately of practical value have issued from disinterested learning. But this argument still is based on utility and leaves many persons imbued with natural curiosity without enthusiasm. It is perhaps not unfair to say that these disinterested students have not been made welcome in medicine as they have been in other departments of learning. And this is a defect in our organization even if it represents no defect in our conceptions. The problems of disease offer legitimate objects of inquiry as do problems in physiology and may be pursued

³ Laennec, R. T. H., *Archives Generales de Medicine*, 1823 i, 5.

in the same spirit. The illumination which has resulted from study of this kind requires no defence. Its value in the development of science is sufficiently established.

Medicine has not always given so frank an answer as to its function as the answer of Laennec, on occasion being over modest; on occasion being overwhelmed by the meagreness of its own success in comparison with that of other sciences; on other occasions still, being imperfectly aware of its purpose. If we adopt the aim of medicine as Laennec stated it we may still fail to agree, as he intimates, on how this object is to be attained. On certain preliminary matters, however, we cannot fail to agree. First, we must continue to classify diseases. Second, we must pursue our studies by the methods common to the natural sciences. For having drawn our attention afresh to the underlying importance to be attached to the procedure of classification proposed by Sydenham we are indebted to Professor Faber of Copenhagen. No one now interested in disease, would willingly dispense with the aid which has been gained by the identification and grouping of diseases. It is necessary only to refer to the fevers to see how by their grouping, knowledge or perhaps better understanding of them has been gained. The need for continuing this activity is still present. Facts and relations are continuously being discovered; new categories are still being suggested. The arrangement and classification of these often precedes the development of adequate knowledge for their comprehension. The significance of nosology for hygiene is immediately apparent. Hygiene has quickly learned its lesson. It has learned, where it has been successful, that the control of disease depends on preventing the entrance into the body of disease producing agents by ingestion or by controlling the habits of intermediate hosts. Further than this the classification of fevers occasioned the first great success of nosology in the domain of therapeutics. Certain directions in which effort may be expended have now been clearly indicated. But the success of nosology in other groups of disease has not yet been clearly displayed. Other categories have indeed been separated, depending on disturbances either of the organs or of systems and relations within the body. And, finally, we have come to recognize still others which depend on heredity or on constitutional organization. It is necessary only to mention psychic disturbances and in-

sanity to appreciate the fact that these, since the time when they were admitted to be diseases, have been treated as constituting a separate group.

Viewed from a different angle it has been customary to regard diseases as falling into groups depending on their duration; on their being either acute or chronic. A relation to the possibility of recovery has usually been implied, but is not yet clearly defined. The acute diseases, it is scarcely necessary to say, include the fevers, the communicable diseases, and although usually not brief in duration, tuberculosis, syphilis and rheumatic fever may be grouped here. In this group the etiological agents are either already known or the belief is entertained that their discovery is possible and awaits the use of suitable methods for the purpose. Indeed the success in treatment which has already attended the discovery of the etiological agents in this group has been the basis for the belief that the discovery of their etiology is the key to the solution of the therapeutics of disease in general. In this expectation it is possible even now to see an error unless the consequences of an injury can be prevented either at the time of onset or in an early stage after the injury is received. So happy an outcome may, however, not always be possible in states which involve constitutional manifestation, or faulty "anlage" and the infirmities of old age. For some of these, medicine must still be under the necessity of providing relief; for others, such as exophthalmic goitre, of the means of providing correction; and of others still, such as diabetes, of preventing its occurrence. In the case of the so-called chronic diseases, in Bright's disease, heart disease, and chronic degenerative diseases of other organs we may perhaps look forward to the time when, should they prove to be preventable, a technique for accomplishing this result becomes available. But that time is not yet. Therapeutics must perforce concern itself therefore with the later states in the abnormal conditions which succeed those attending the infliction of injury and the early stages when the arrest of its operation may still be possible. It is unnecessary to recall the fact that a difficulty arises in the circumstance that the early stage is often not to be detected. An instance of this difficulty is seen in the establishment of mitral stenosis, the detection of which may be delayed for several years after an infection so slight as scarcely to have aroused anxiety; or of Bright's

disease, many years after the patient has passed through an attack of scarlet fever so mild as to have been detected only by the occurrence of a contact infection. In the later stages, when they can be detected, the therapeutics of diseases of this nature, that is to say of the heart and the kidneys, are no longer to be managed on the basis of etiology. These diseases constitute new states, the management of which must be undertaken with the new set of circumstances in view. So far etiological classification has been an approach to therapeutics in the group of communicable diseases only, where control is associated with prevention, or with the destruction of the causative agent in the host; the problem is that of the control of a foreign substance introduced into the body, the damage from which is combatted either with or without stimulation of the physiological reserves which the body can provide. The problem is the problem of invasion; it differs from the problem of continuous adjustment and control which derangements of the functions of organs and of bodily systems necessitate.

Accurate classification and a knowledge of the processes of disease and their relief and cure are then the proper objects of inquiry in medicine. No other discipline is, as has been said, primarily concerned with disease, nor has it contact with patients who exhibit the manifestations of disease. On account perhaps of the social importance of epidemic diseases, bacteriologists as apart from physicians have it is true busied themselves with the communicable affections. But the diseases due to microbic agents have after all a curious external relation not common to other disease groups; their prevention, their management, as hygiene prevents and manages them, requires no necessary contact with infected individuals. Management so far as cure is concerned naturally involves an equipment different from that of the bacteriologist. It is, however, remarkable that development in this direction, perhaps with the exception of lobar pneumonia, has not been due to the efforts of those concerned with the care of patients. It has been especially true of the identification of bacterial agents of disease, that medicine is indebted for this advance to bacteriologists, not to its own practitioners or professors. A dependence on the outside world for the solution of its problems is in part a reproach to medicine. Probably no injury has yet been suffered by society as a result of this dependence. But those advances

that depend on knowledge of disease in patients and on actual direct contact with diseased persons, have been made by the practitioners of medicine themselves. In this way is to be explained the significance Sydenham, Jenner and Laennec have for us; they have taught us the use of the classification of diseases, the fact that fevers are preventable, an approach to the diagnosis of visceral disease by means not immediately obvious. These have after all constituted the primary advances in medicine. It is this experience which encourages us in the belief that the development of medicine is in all probability the work of physicians properly trained and supplied with adequate equipment.

If this is the teaching of history, and these the problems of medicine, the future pathway becomes clear. We are concerned with the therapeutics both of acute and of chronic diseases as well as with the health of the body and the relief from its disabilities during the years of its decline. The development of the therapeutics of infectious diseases dependent on the discovery of bacteria has for two generations been so absorbing as to dwarf the interest medicine has always displayed in conditions associated with derangement of the organs and with the ailments of advancing age. But the latter rather than the former group counts the greater number of victims—a number which is the greater, the greater is the success which is achieved in the solution of problems connected with immunity and hygiene. The diseases of the later years occasion what one might name the therapeutics of physiological disharmony. They present conditions which give rise to extreme difficulty in therapeutics. Their nature is still obscure, in large measure because the mechanisms on which they depend have scarcely been analysed. Success in treating them can scarcely be expected until more knowledge has been accumulated of the normal mechanisms on a deviation from which they depend.

Medicine has, therefore, significant tasks, tasks of great complexity. That we are aware of them is evident when the efforts are reviewed which are being made in the contemporary study of Bright's disease, in the study of heart failure, in the study of hormonal derangements. We have begun to study these diseases which involve abnormal physiological processes as scientists always study, by whatever means natural science has to offer which promise success. We are engaged

now in the struggle to fit ourselves for the work of overcoming the difficulties involved in mastering the methodology we must use—be it physics, physiology, nosology or chemistry. These are, it need scarcely be pointed out, the methods employed likewise in biology; that the methods are the same is not surprising, in view of the fact that the living system which is studied in medicine does not differ from that which is the concern of biology in general, except that one has in medicine not always the advantage of adopting simple material to serve the purposes of one's experiments.

This, then, is the task which academic medicine in the United States, now become self-conscious, has set itself; it is the task of Clinical Investigation. Its business involves a legitimate interest in learning as well as a means for furthering the methods which lead to the cure of disease. It is vitally concerned in the success of both these projects. It ought, as it has been, to be concerned with the arrangements, both in education and in organization for accomplishing its ends. We must appreciate the fact that there is perhaps no single road of salvation open; the search for the single road has often led hunters far afield.

To give substance to ideas like these is the purpose which lies behind the work of the new university clinics which are being founded in many parts of our country. They mean to take on new functions. Those on which they lay emphasis, indicate the adoption of a wider interest in the problems of concern to medicine. In addition to the traditional responsibility for teaching they avow the desire to contribute to an increase of knowledge. They are drawing to themselves new men, trained in a new way; they are being supplied with new hospitals properly equipped with laboratories in which to pursue what Bernard called the *observation provoquée*. These activities testify to the development of a new spirit. This is the spirit which has called the American Society for Clinical Investigation into being. It is the spirit to which the Journal for Clinical Investigation desires to give expression. It is a spirit which the Journal wishes to foster and of which it hopes to be worthy.