certain, however, that the revolt of the biochemist against the idea of a restriction to human curiosity will continue. Biochemistry will continue to function as if all knowledge, even that of life, were accessible to human understanding. The past has taught that the solution of one problem always opens up a new one. New discoveries in physics, in mathematics, in theoretical chemistry furnish new tools to biochemistry, new tools for the solution of old problems and for the creation of new ones. So long as Life continues, the human mind will create mysteries and biochemistry will play a part in their solution.

CLINICAL INVESTIGATION[1]

By Dr. FRANCIS G. BLAKE
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THE second article of the constitution of this society begins with the sentence, "The objects of this society shall be the cultivation of clinical research by the methods of the natural sciences; the unification of science and the practice of medicine; the encouragement of scientific investigation by the practitioner, and the diffusion of a scientific spirit among its members."

One need not stop to ask, perhaps, to what extent these objects have been advanced in a material sense since the inception of this society twenty-three years ago. The expansion of the clinics during this period particularly with respect to the provision of more adequate hospital wards, laboratories and equipment for clinical investigation has been phenomenal and is familiar to you all. The funds for carrying on clinical research in these laboratories, though undoubtedly not keeping pace with those that have been provided for bricks and mortar, have nevertheless increased surprisingly and perhaps as fast as is wholesome in a period of rapid expansion, when the finding of men suited for research, by reason of a primary interest in the search for new knowledge and the simultaneous possession of those rare, but essential qualities of initiative and originality, is usually more difficult than the finding of material resources. In spite of this difficulty, the number of those engaged in clinical research has likewise multiplied many times during this period, to such an extent, indeed, that the published products of their labors have resulted in a deluge which at times bids fair to engulf us, whether by volume or by depth, I will leave to you to decide.

While these matters need not detain us, it is, perhaps, pertinent to inquire to what extent the character and direction of clinical research and the nature of the methods it employs have been advanced, or perhaps it would be better to say, have been changed during this period of expansion in material facilities and in human activity; whether in fact these more important aspects of clinical research have kept pace with the evident material progress. To do so, it is obviously necessary to have a clear conception of what clinical research is or purports to be, and also just what is meant by the phrase quoted from the constitution—"by the methods of the natural sciences."

Clinical investigation, if "the unification of science and the practice of medicine" be the worthy goal that the writers of our constitution conceived it to be, should not concern itself primarily with physiology or chemistry, with physics, mathematics, or biology, nor even with the application of these subjects by the physiologist, or chemist, or physicist or biologist to the problems of clinical medicine, but primarily with the study of the phenomena of disease by clinicians thoroughly familiar with disease in all its varied aspects through intimate and constant contact with disease in the field—whether this be in the home, the office, the out-patient clinic, or the wards of the hospital should matter little, provided the contact be comprehensive enough to give a reasonably complete picture of the disease in question.

Furthermore, I believe it should be kept in mind that the purpose of this study of disease should be primarily to find out about disease, largely for the fun of doing it, to discover the circumstances or conditions under which disease develops, the nature and mechanism of the disturbances of function and structure which take place during the course of disease, and the circumstances or conditions under which recovery or death occur. Secondarily, this may lead, and fortunately sometimes will, to the discovery of methods of prevention, amelioration or cure, but these practical and humane purposes should, I believe, be kept in the background, if clinical investigation is not to be too soon diverted and frequently misled in following its main purpose, the elucidation of the phenomena of disease.

In this connection I should like to quote a paragraph by Slesinger[2] in a recent article entitled "The Drift of the Social Sciences."

> Social science shares with medical science the necessity of having to free itself of the desire to do good and of

[1] Presidential address, American Society for Clinical Investigation, Atlantic City, May 4, 1931.

[2] *Survey Graphic*, 19: 24, 1931.

measuring its success by the amount of good accomplished. The medical sciences are only recently beginning to abandon the therapeutic aim in research. It is not to be wondered at, therefore, that the younger social scientists find themselves still slightly hampered by an attitude growing not out of this subject matter, but out of the personnel attracted to the field during a stage in the development of research when welfare was more important than truth.

It is sometimes well to see ourselves as others see us. Let us be sure of our own position in medicine before casting the first stone, as we are perhaps too prone to do, at our younger brothers struggling for a place in the field of science.

Without further delay, let us now turn to a brief consideration of the meaning, for clinical investigation, of the phrase, already quoted, "by the methods of the natural sciences." At the risk of stressing the obvious, let me make it clear at once that I conceive this phrase to refer, not to the techniques or tools used, but to the methods of approach employed in the natural sciences. There are, of course, two methods—on the one hand, observation, analysis and deduction, the so-called descriptive method, still held honorable by some because of its antiquity if for no other reason; on the other hand, the inductive, experimental method, held, it would appear, in higher esteem by most, perhaps because of its relative youth and vigor. To show that this is so, at least among many of those who are devotees of the biological sciences, one need only quote the following from a recent paper on "The Rise of the Experimental Method." Referring to Vesalius on the structure of the human body, and Copernicus on the arrangement of the universe, works which appeared in 1543, the author[3] says, "Intellectual activity of this order had not been witnessed since the days of Aristotle, and one might add that these two books represent the last of the really great achievements of the Aristotelian method in science."

To argue concerning the relative superiority of one method over the other would appear to me to be a somewhat fruitless pastime so far as clinical research is concerned; to hold that the experimental method is necessarily superior to the observational and descriptive method is to hold a narrow and partial view. Both methods are merely complementary halves of the whole, a view so well expressed by Francis Bacon in the "Advancement of Learning," when he says, "All true and fruitful natural philosophy hath a double scale or ladder, ascendent and descendent, ascending from experiments to the invention of causes, and descending from causes to the invention of new experiments; therefore I judge it most requisite that these two parts be severally considered and handled."

[3] Fulton, *Yale Jour. Biol. and Med.*, 3: 299, 1931.

Whether one begins by ascent of the ladder and then descends or reverses the process and begins by descent and then ascends seems to me immaterial, and should depend in each particular case upon the nature of the subject under investigation. What really matters is that he goes both ways and particularly that he stops to think when he reaches the ends of the ladder, whether top or bottom. Are we too busily engaged at present in scrambling up and down the ladder, too little engaged in pausing to think at the top or at the bottom? Again, I merely ask the question and leave you to ponder over the answer.

I do not propose, then, to ask to what extent experimentation is replacing observation, the inductive method, the deductive method in the field of clinical research, but rather, what is the place of each in clinical investigation. To my mind at least, disease is the inductive experiment of Nature, random though it may be, which the investigator in the field of clinical medicine must observe and describe in all its particulars, if he is to develop rational hypotheses to test by experiment. Furthermore, whether he uses merely his natural senses in making observations or turns to the microscope, the test-tube or the balance, appears to me to make little difference, provided he selects the tools most appropriate for the particular problem he is studying. Are the labor and tools of the cabinet maker, because of their precision, superior to those of the artist? I doubt if you will think so. Observation of natural phenomena, analysis and deduction, the descent of the ladder, appears to me to be the first step in clinical investigation and will, I believe, continue and rightly, to engage our time and attention, and perhaps a considerable part of it, certainly for many years to come.

What, then, is the place of the inductive experiment, the ascent of the ladder in clinical investigation? Its value as a method of approach needs no argument to support it. Its application, however, is infinitely more difficult because the subject of experiment is man. On occasion it is possible, when the procedures employed are harmless or when willing and often courageous volunteers offer themselves as subjects for experimentation. Otherwise, the clinical investigator must have recourse to animals to test his hypotheses, must go to the laboratory and become temporarily a pathologist or bacteriologist, a chemist or physiologist. That he is increasingly able to do so is all to his credit, but when he does so let him remember that he has temporarily abdicated his position as a clinical investigator, and that if clinical investigation is to profit he must return to the more difficult problems of the clinic to test out there the hypotheses that he has in turn developed during his sojourn in the laboratory.

Finally, let us turn for a brief moment to a consideration of what changes, if any, are taking place in the direction and scope of clinical research. The historical background has been presented in so masterful a way by Faber[4] that I would not have the temerity to discuss it, even if time permitted. Furthermore, I shall have to limit myself to one field—etiology. Only let me recall that shortly before the founding of this society, under the influence of the rapid advances in bacteriology in the latter part of the nineteenth century, the search for the specific causes of disease was perhaps the most dominant and fruitful activity of the time. In the intervening period it has become more and more apparent to the clinical investigator, a fact of course long recognized in physiology through the influence of Claude Bernard, that the search for specific causes, whether they be living organisms, chemical substances, deficiencies or what not, is but one aspect of a many-sided picture and that a real comprehension of the etiology of disease resides in an understanding of all the conditions or circumstances under which it develops. Here we are concerned with pathogenesis, not etiology in the conventional usage of the word; the study of the interplay of specific agents, environmental factors, and human susceptibilities. Examples are superfluous. To have discovered the tubercle bacillus, its biological characteristics and chemical constitution, does not explain tuberculosis; to have learned the environmental factors which favor its occurrence, still leaves something wanting. The characteristics, susceptibilities and reactions of the host must also be known. The interrelationships of these three factors, and perhaps others, must be studied before one can arrive at an adequate understanding of the pathogenesis of the disease, a point of view so ably illustrated by the studies of Opie[5] in this field. I have cited but one example. Numerous others will occur to you, not only in the field of infectious diseases, but also in the trend of current investigations in diseases of the heart, the blood, the endocrine glands and so on.

Not only is this principle, this attempt to understand all the factors involved and their interrelationships, found in the work of those who are interested primarily in the pathogenesis of disease, but obviously also in the studies of those who are concerned with the phenomena of already existing disease. Consequently, I will not stop to bother you with further illustrations, but will venture to close with the doubtless rash prophecy that in this change in the direction and this enlargement in the scope of clinical investigations lies the evidence that clinical medicine is rapidly approaching a maturity of thought which has characterized the other biological sciences for a longer period of time.

OBITUARY

PROFESSOR SOLON I. BAILEY

DR. SOLON IRVING BAILEY, Phillips professor, emeritus, in Harvard University, died at his summer home in Norwell, Massachusetts, on June 5. His "History and Work of the Harvard Observatory," on which he had been engaged since his retirement in 1925, was published during the week of his death. The final instalment of his "Peruvian Meteorology" is now in press. He had indeed satisfactorily rounded off an industrious and useful scientific life; but although in his seventy-seventh year, he had not yet resigned his interest in the subject of variable stars in globular clusters—a field in which his most notable scientific contributions lie. Within the past two months, with the "History" and the "Meteorology" completed, he resumed his study of the periods of variable stars in the southern globular clusters, planning to devote a year to measurement and computation.

Professor Bailey was born at Lisbon, New Hampshire, December 29, 1854. He received the degree of A.B. from Boston University in 1881, M.A. from Harvard in 1888, and Sc.D. (honorary) from San Augustin University in Arequipa, Peru, in 1923. He became a member of the staff of the Harvard Observatory in 1887, being appointed assistant professor in 1898 and Phillips professor of astronomy in 1912. He was acting director of the Harvard Observatory from 1919 to 1921. His academic distinctions include membership in the National Academy of Sciences, the American Academy of Arts and Sciences, the Astronomische Gesellschaft and the Royal Astronomical Society. He is survived by a widow, Mrs. Ruth E. Bailey, and a son, Professor Irving W. Bailey, of Harvard University.

It is difficult in a short notice to give a fair account of the important services rendered by Professor Bailey to the Harvard Observatory and to astronomy. For three decades he was E. C. Pickering's closest associate in the development of the Harvard Observatory. In two particular instances Bailey guided the work of the present director: he pointed out in 1914 the importance of using the Mount Wilson reflectors for the problems of globular star clusters, and in 1921 he assisted, in a remarkably sympathetic, self-

[4] "Nosography in Modern Internal Medicine," New York, 1923.

[5] "The Harvey Lectures," 197, 1928–29.