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THE GROWING OPPORTUNITIES FOR MEDICAL RESEARCH[1]

IT is related of the rugged English surgeon, John Abernethy, that on entering the lecture hall at the beginning of a new medical session he once exclaimed "Good God! What will become of you all?" An attractive and persuasive lecturer, Abernethy gained no distinction in original research; indeed, his dogmatic attitude is said to have been repressive rather than stimulative of original inquiries. An attempt to answer the question Abernethy asked was, later on, made by another British surgeon of entirely different stamp, namely, Sir James Paget, an eloquent lecturer who besides was a truly great investigator of pathological and surgical problems, one who cherished the ideal of uniting scientific studies with practical activities throughout his professional life. He made some statistical studies to determine what actually did become of the students whom he taught in the medical school, and his conclusion was that, as a general rule (with but few exceptions), "such as the student had been, such was the practitioner." The validity of this rule was certainly demonstrated in the case of Paget himself, for, in his first winter session in the medical school, while working in the dissecting room, he found by means of a pocket lens that certain specks in the voluntary muscles were parasitic worms and not, as earlier observers had thought, spicules of bone; as a result of his observations a piece of the muscles containing the specks was sent to R. Owen, who confirmed the discovery and gave to the worm its scientific name, *Trichina spiralis*. Young Paget, who showed his ability to discover new things in his first year in the medical school, later on became, as you know, so great a pathologist that he rose to a place in England comparable with that occupied by Rudolph Virchow in Germany and so great a surgeon that he is always numbered among surgeons of the first rank. His name, you will recall, is attached permanently to a well-known disease of the breast and to an equally well-known disease of the bones.

This morning it was my good fortune to be present during a part of the session when students of this school, members of your Undergraduate Medical Association, were reporting some of the original observations and experiments that they had carried on.

[1] An address delivered to the Undergraduate Medical Association of the University of Pennsylvania, Friday, April 3, 1925.

during the past year. The reports of such researches augur well, I believe, for the future of those who conducted them. For, notwithstanding the contrary opinion held by some medical educators, I am convinced that those who learn how to observe and to think for themselves during their undergraduate careers are more likely to be successful, in later life, in teaching, in practice and in research, than are those who are content merely to acquaint themselves with the observations and reflections of other men. During the period when I was in charge of the teaching in the medical clinic of the Johns Hopkins Medical School I asked each fourth year student to undertake some small piece of original work. In watching the subsequent careers of those students I have been deeply gratified to find how many of those who had shown the greatest industry and enthusiasm in that work have already become distinguished as practitioners, teachers or investigators. Nothing else has seemed to me to equal in importance, during a student's undergraduate period, the cultivation of the spirit and the methods of scientific inquiry. The mere learning of facts that have been accumulated by others is of far less significance than training in the method of science, recognizing the importance of the continual expansion of knowledge, learning how to participate in such expansion and acquiring a love for and the determination to pursue original studies. In this respect, my own observations as a teacher have been entirely in accord with those of Sir James Paget.

The scientific method of solving problems is now commonly resorted to by all productive workers, no matter what their special fields of work. The principles involved are relatively simple and have been clearly defined by Professor John Dewey in a little volume entitled "How We Think"; I have, myself, attempted to illustrate their value for the solution of problems of diagnosis in an article written for *Oxford Medicine* (Vol. I) under the title The Rationale of Clinical Diagnosis. When one is confronted by a difficulty, that is to say, when one has a problem to solve, the quickest and best way of overcoming the difficulty, of solving the problem, is to make a systematic attack upon it. Such a systematic attack includes: (1) the acquisition of data that will help to locate and to define the problem, (2) the arrangement of the data in various ways and brooding over them as thus arranged in order that suggestions of solution of the problem may occur to the mind, (3) the reasoning out in detail of the implications of each suggestion of solution that arises in consciousness, and (4) the thorough testing of such suggestions thus minutely worked out as to their implications by comparison with the actual data that have been accumulated, resorting to further observation and experiment to extend these data when necessary in order to determine the validity or the non-validity of the hypothetical suggestion of solution.

All these stages of the program must be passed through; they are essential serial steps in orderly problem solving. And if the investigator will keep them definitely in mind in planning his work and during his prosecution of the work not only will he save himself much time and trouble but he will also greatly increase the likelihood of his arriving at sound conclusions. No matter what the original task that one sets for himself, be it say the discovery of the mode of regeneration of peripheral nerves, or the devising of methods for the prevention of the ill-effects of an infection or an intoxication, or the ascertainment of the significance of the content of the blood in a given variety of ions, or the experimental production in an animal of a disease in which one is interested, the only satisfactory method of accomplishment lies in the process of accurate observation, of well-conceived experimentation for the refinement of observation, and of intensive and patient reflection, which I have just now referred to as the essential features of the method of science.

If you would enjoy reading a fuller account of these processes written by a master of the experimental method as applied in physiology and pathology, let me recommend to you most heartily the perusal of Claude Bernard's "Introduction à l'étude de la médecine expérimentale," which is fully as interesting to-day as it was when it was first published in 1865. Hitherto this valuable treatise has been available only in the French language, but I am glad to learn through Mr. Abraham Flexner that an English translation is shortly to be issued by the Macmillan Company. Do not overlook it!

The problems that present themselves for solution to those of us who work in medicine are infinite in number and in variety, but, in the last analysis, they all have a bearing upon (1) the nature and preservation of health and (2) the cure, the amelioration or the prevention of disease, in living organisms. A healthy organism is one that makes adequate responses to the environmental influences that impinge upon it; a diseased or an anomalous organism is one that exhibits inadequate responsivity to environmental influences. Obviously, therefore, our medical tasks include studies of the substances and forces within the organisms that react, studies of the various influences in their environment that stimulate to reaction, and studies of the reactions themselves as they occur.

What a developed living organism (or phenotype) is at any given time that it is studied would seem to depend (1) upon the substances and energies that

lay within it at the moment of its start and (2) all the changes that have occurred within it as a result of influences in the surroundings in which it has been immersed from the time of its start up to the moment of study. For human beings, this would appear to be true of the foetus, of the child, of the adolescent, of the mature individual and of the senescent. If we desire clearly to understand how men, women or children will respond to physical changes, to chemical changes, to psychological changes and to sociological changes in their environment, we can scarcely hope to do so without knowing much about how they have begun, much about how they have developed, and much about the influences to which they have been exposed and how they have reacted to those influences.

Without much knowledge of the inherited (genotypic) and environmental (paratypic) elements of a given constitution we are likely to be unable satisfactorily to understand the disposition or the nondisposition of the person possessing that constitution to the development of various disease processes, or to the exhibition of inadequate somatic or psychic responsivity to external stimulation. That is why in medicine investigators are no longer content to study the anatomy, the physiology and the pathology of developed organisms only, extremely important as such studies are, but feel that they must inquire also into the problems of inheritance on the one hand and of growth and development on the other. For in order to understand how living organisms have come to be what they are and why there are such variations in different organisms in their modes of response to apparently identical environmental stimuli genetic and comparative studies are indispensable. It is no accident that one person develops influenza and another does not, that of two persons suffering from typhoid fever one dies and another recovers, that one woman weighs two hundred and fifty pounds and her neighbor of the same age only eighty, that of two boys exposed to the same temptation one yields while the other resists, that of two members of a class one is a gold medallist and the other is "plucked," or that of three young women surrounded by similar emotional stimuli one shows elation, one depression and the third apathy. Medical men, however, are far, as you know, from being able, in every case, as yet to explain these diversities of response. I believe, however, that such divergent modes of reaction will prove to be susceptible of explanation and that as medical science progresses we shall gradually acquire the knowledge that will enable us to predict when, where and how disease will develop, and why some people think, feel and behave adequately and others inadequately. Gradually, too, with the increase in our powers of prediction we shall also see an augmentation of our power to control. During the past century the ability of medical men to predict and to control in the domain in which they work, has, it is true, grown enormously, but all will admit that this growth, gratifying as it is, must be regarded as infinitesimal compared with that to which our profession aspires.

The idea is at present very widespread that scientific work in medicine is and can be done only in laboratories and, particularly, in the laboratories devoted to the study of the preclinical sciences. That is, of course, a very grave error. Though the establishment of such scientific laboratories has tremendously extended and favored opportunities for original research bearing upon medical problems, nevertheless the work in our better medical and surgical clinics, not only in the laboratories attached to them but also at the bedside should be, can be, and, indeed, I believe is, just as truly scientific as that which is carried on in the laboratories of the preclinical branches.

The problems of the clinics and those of private practice differ from those of the preclinical institutes only in their greater diversity and complexity, and knowledge is now being advanced in the clinics and in the clinical subjects by means of precisely the same scientific methods of inquiry as are used in the more elementary branches of science. When there are problems to be solved the same principles of study apply anywhere and everywhere. Even in the busy life of a medical practitioner the condition of each patient met with ought to be looked upon as a special problem for solution and the work of solution of that problem will be the more effective the closer the principles of the method of science are adhered to. But, aside from this daily application of the scientific method it should not be forgotten that a number of most important discoveries in medicine have been made by general practitioners, busy men with fine brains, who, despite the pressure upon them of multitudinous activities, still found the time to engage intensively in the prosecution of original inquiries. As Sir James Paget once said, "none find so much time to spare as they that have too much to do and do it with all their might." Jenner's discovery of vaccination, Koch's early studies upon wound infection, Lister's work on antiseptics, Mackenzie's observations of cardiac irregularities and Banting's work on insulin, are shining examples of profitable research conducted by men in practice. And though our great institutes for experimental research and our laboratories and organized clinics in the medical schools offer extraordinary facilities for the conduct of original investigations, the time will never come when practitioners of medicine and surgery can afford to

neglect the opportunities that practice yields for accurate, original investigation or for the deliberate, logical reflection that helps to expand the confines of knowledge. Moreover, minute accretions to the store of knowledge are not to be despised; indeed, were it not for the continuous collection of such small increments fewer of the so-called great discoveries would be made, since for the most part great discoveries are nothing but the summits of structures composed of a mass of minor investigative results.

Men who continuously insist upon the cross-examination of the evidences of their senses, men who, when they observe an object or an event, try to consider also all the conditions in which that object or event is situated, men who examine into the variations, the concurrences, the sequences and the mutual relations of phenomena, men who are cautious not to insert their own beliefs and expectations and wishes into their observations, men who are so distrustful of their memories that they record accurately what they observe at the time and place of observation, men who are not satisfied merely with thinking of explanations but insist upon testing them in order to see whether or not they are true, are the men who discover new things, who detect errors in conceptions that are supposed to be well founded, and who, in general, do most to contribute to the advance of our knowledge of health and disease.

The growth of knowledge has often been compared to that of an avalanche; its magnitude and its velocity must steadily increase. Every single advance prepares the way for a whole series of other advances. Every new method devised makes it easier to invent still other modes of extending observation. The physician who died in 1900, could he come to life again, would be astonished and perhaps confused by the medicine of 1925; if any one of us were to stop his medical work to-day and were to try to resume it ten years from now he would doubtless find himself almost as disoriented in special medical fields as is a patient in his general surroundings when he suffers from Korsakoff's psychosis!

You who are members of this Undergraduate Medical Association enter upon your medical activities at the most favorable period the world has ever known for the enlargement of medical knowledge and for the advancement of human welfare. Just what part each of you who will graduate here (from an institution made famous by Cope, Leidy and a long series of original investigators) will play in this enlargement and this advancement remains to be seen. There will be many difficulties in the way; for an exaggerated account of them consult the recent clever novel "Arrowsmith" by Sinclair Lewis. But difficulties are only additional spurs to determined men. Some of you will have better brains than others but each of us has to do the best he can with the brain that he possesses. Some of you will be able to command more leisure for scientific studies than will others, but again every one can secure some leisure for scientific work if he will make his life orderly. Some of you may be privileged to work in institutes devoted entirely to original research; some of you will find it advantageous to combine research with teaching; the majority, perhaps, will engage in medical practice of one sort or another and will there find the special opportunities for certain kinds of scientific work that can not be found apart from such practice. No matter where your lot may be cast the main thing is that you utilize every opportunity that comes to you to observe accurately, to record carefully, to imagine vividly, to reason logically, to experiment cautiously and to test rigidly the validity of the explanatory ideas that occur to you. For these are not only pleasures that you may enjoy; they are also obligations and responsibilities that fall upon you as medical men. May I extend to each and every one of you my very best wishes for happiness, success and duty fulfilment in your work during the coming years.

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THE TREND OF THOUGHT IN PHYSICS. II

STATIONARY STATES AND THE LAWS DESCRIBING ELECTRONIC MOTION

APART from the nature of emission of quanta during the transitions between the stationary states, there yet remains the problem of accounting for the stationary states themselves. Now the mind is content that the electron should not be allowed to move in any manner it pleases. It is content to have an equation of motion of the Newtonian form, for example, a simplification of the force equation of electrodynamics, for this case; but, having become accustomed to this, it resents any further conditions of constraint upon the motion, such as are involved in the Wilson-Sommerfeld conditions that the quantities $\int pdq$ shall be integral multiples of h, where the p's and q's are suitably chosen momenta and coordinates.

Now the question arises as to what attitude of mind it is necessary for us to get into in order that the existence of stationary states shall seem reasonable to us in terms of the criteria for reasonableness to which we adapt ourselves. This may well be considered as part of the whole question of the description of motion.

Suppose we return for a moment to the circuital