SCIENCE

Vol. LXVI July 22, 1927 No. 1699

CONTENTS

SCIENCE: A Weekly Journal devoted to the Advancement of Science, edited by J. McKeen Cattell and published every Friday by

THE SCIENCE PRESS

New York City: Grand Central Terminal.

Lancaster, Pa. Garrison, N. Y.

Annual Subscription, $6.00. Single Copies, 15 Cts.

SCIENCE is the official organ of the American Association for the Advancement of Science. Information regarding membership in the Association may be secured from the office of the permanent secretary, in the Smithsonian Institution Building, Washington, D. C.

Entered as second-class matter July 18, 1923, at the Post Office at Lancaster, Pa., under the Act of March 8, 1879.

MEDICAL RESEARCH AND ITS ORGANIZATION[1]

Occasions such as the one in which we are participating are peculiarly significant. They mark the advancement of knowledge—its principles and practice—through a training of both the mind and the hand in the power to comprehend and extend knowledge. All knowledge comprises one vast domain; there is to-day scarcely a line of separation between the pursuit of the knowledge called "humanistic" and that called "scientific." The object is one, since in both what is sought is the interpretation of nature, whether in the physical world about us or in the mind and spirit within. In all these fields, we are now used to exercise the privilege of free inquiry and to substitute for authority the evidences of our perceptions.

This high privilege is on the whole a recent acquisition. Although we date our intellectual freedom from the Renaissance period, it is fruitful to reflect on the diverse ways in which the revival of learning in the fourteenth, fifteenth and sixteenth centuries affected on the one hand the development of letters and art, and on the other that of science. The interest awakened in the literature of Greece and Rome was shown in the admiration not only for the works of poets, historians and orators, but also for those of physicians, anatomists and astronomers. In consequence, scientific investigation was almost wholly restricted to the study of the writings of authors like Aristotle, Hippocrates, Ptolemy and Galen, and it became the highest ambition to explain and comment upon their teachings, almost an impiety to question them. Independent inquiry and the direct appeal to nature were thus discouraged, and indeed looked upon with the utmost distrust if their results ran counter to what was found in the works of Aristotle and Galen.[2]

It is not without significance for us that it was the anatomists of the sixteenth century who broke with tradition and determined to examine the human body for themselves, and it was owing chiefly to the labors of two independent geniuses, contemporaries for a time at the University of Padua, Galileo and Harvey, working in very different spheres, that the old order was overthrown and a new era inaugurated.

For medicine as well as for the physical sciences

[1] Address made at the Convocation for the Conferring of Advanced Degrees, Brown University, June 14, 1927.

[2] Harvey, W., "Motion of the Heart and Blood in Animals," translated by Robert Willis, Everyman's Library, 1906; Introduction by E. A. Parkyn, p. vii.

these two men were of supreme importance. From Harvey's discovery of the movements of the heart and blood vessels dates not only the science of physiology, but that of medicine itself. It has been well said that this great discovery stands to medical practice much in the same relation as the discovery of the mariner's compass stands to navigation.[3]

Harvey's epochal book was published in 1628. It seems probable that he began teaching his doctrines to his classes as early as 1616—the year of Shakespeare's death. For more than ten years, Harvey delayed any formal publication of his experiments and deductions, meanwhile inviting criticism and opposition to his views from all sources, in order that the complete truth, free from any falsities and misconceptions, might be disclosed. To-day as it did then, his modest treatise stands as a landmark in human history, and a perusal of the methods of experiment employed and the mode of presentation adopted arouses feelings only of admiration and emulation. The fundamental thesis of Harvey's teaching is expressed in almost winged words by a modern physiologist:[4] that only by searching out and studying the secrets of nature by way of experiments can we hope to attain in the words of Job "to a comprehension of the wisdom of the body and the understanding of the heart," and thereby gain that mastery of disease and pain which will enable us to relieve the burden of mankind.

The announcement of the discovery produced a sensation; it was opposed, but not by the younger physicians. Among those who discerned its significance was the philosopher Descartes. The material effect was not fortunate. Harvey's medical practice fell off. Patients feared to put themselves under the care of one accused by the ignorant and envious of being crack-brained, and of putting out new-fangled and dangerous doctrines. This fate of great innovators is still not unknown. There was fortunately one man in a high place who showed lively interest in the discovery. Charles I supported Harvey and appointed him his personal physician. It is interesting to reflect that this monarch, whatever opinion may be held of his other qualities, by aiding Harvey and Van Dyke showed himself an enlightened patron of art and science.[5]

Hardly more than half a century separates the astounding figure of Harvey from the overwhelming figure of Newton—"the lawgiver of the universe" in the phrase of his contemporaries. Both men were enemies of mere speculation, and upholders of the experimental method, and both were conspicuous by reason of the extreme caution with which they promulgated their discoveries. Newton even less than Harvey was possessed of the passion, verging on fanaticism, for scientific discovery which has distinguished many men. He had almost to be cajoled into the enunciation of the discovery of the law of gravitation, and he all but failed to complete the *Principia,* because he detested controversy.

"I see I have made myself a slave to philosophy; I will resolutely bid adieu to it eternally, except what I do for my private satisfaction, or leave to come out after me; for I see a man must either resolve to put out nothing new, or become a slave to defend it."

Newton's objectivity was extraordinary; in spite of the wonderful success of his theory he did not think that the law of gravitation was the final expression of gravitational phenomena—a piece of scientific caution which we have seen justified in our day.

To those of us charged with the responsibility of searching out scientific aptitude, it is wholesome to learn that the reflective youth, unlike most great mathematicians, gave no evidence of mathematical precocity. Even when at nineteen he entered Cambridge he had no definite intention of studying mathematics; it was the chance picking up of a book on astrology at a country fair which turned his mind in this direction, and yet when he took his B.A. degree four years later he had discovered the binomial theorem and invented the differential calculus.

The past one hundred years have seen the triumph of the experimental method; the deepest problems of which we are aware have been explored with confidence because of the perfection of method and of instruments of extreme precision. In the physical world we stand in awe of the marvels being accomplished as, to take two or three spectacular examples, in the field of atomic structure, of radiology and of aviation. The medical biological field is also being cultivated, with results no less significant perhaps for science as a whole.

Since the greater speed of discovery has come with the last half century, it may be of interest to inquire briefly into some of the advances in medical science, with which subject I am myself more familiar. That this science should have lagged somewhat and indeed still grows more slowly than the mechanical and physical sciences need scarcely evoke comment. As was remarked by Claude Bernard,[6] "the object of science is

[3] Simon, Sir John, "Motion of the Heart and Blood in Animals," Everyman's Library, 1906; p. ix, Editor's Introduction.

[4] Starling, E., *Lancet,* 1923, ii, 869.

[5] Harvey, W., "Motion of the Heart and Blood in Animals," Everyman's Library, 1906; p. xviii, Editor's Introduction.

[6] Bernard, Claude, "An Introduction to the Study of Experimental Medicine," English Translation, 1927, p. 67.

everywhere the same: to learn the material conditions of phenomena. But though this goal is the same in the physico-chemical and in the biological sciences, it is much harder to reach in the latter, because of the mobility and complexity of the phenomena which we meet." Under these circumstances it is no wonder that at a period when the physical sciences were being enriched by experiment, medicine still remained a subject of philosophical systemization—a condition called by the philosopher Locke the Romance-way of physic, because it is more easy for men to build castles in the air of their own than to survey well those that are on the ground.[7]

It is usual to date the beginning of what we are pleased to call the present or modern era of medical research from the establishment of the germ origin of disease. In truth, no such sharp distinction as this is to be drawn; the germ theory of disease is a logical outgrowth of the state of development of chemistry and physiology in the middle period of the nineteenth century, and those two sciences had contributed then, as they continue to contribute in ever-increasing volume, to the store of biological knowledge.

And yet there is truth in the view that new impetus and new hope were suddenly brought into medicine through the pregnant discoveries of Pasteur, Lister and Koch, which did so much to aid the growth of preventive and curative medicine. The pursuit of microbiology, the science of the infinitely little, is still under full swing. The quest has broadened greatly within the past few years. The mere study of the elusive parasite has given way to a much more searching investigation of its intimate properties, its precise chemical constitution, on which depends its power for inflicting injury, and on a real understanding of which rests man's power of defense against harmful action; and the knowledge already gained in this difficult field is of very great significance. The quest is also taking into account a remarkable capacity for variation among these minute parasites, affecting their propensity for inducing disease and raising far-reaching questions as to the origin of the parasitic forms and their relation to the far greater number of non-disease producing microbes with which man in common with all living things lives in intimate daily communion.

The newer studies have brought the knowledge of parasite and host, the animal and plant, into closer and more equitable relationships, and have thus shown a way by which epidemics on an experimental scale may be profitably investigated among laboratory animals and made to yield information valuable in itself and even informing in respect to epidemics in man.

[7] Brown, John, Horae Subcivae, 1st Series, p. 19.

Perhaps no subject of wide investigation has yielded more startling and valuable information than that relating to the physiological effects of the so-called internal secretions. If indeed we wish to correlate present-day outlook in medical practice with earlier happenings, we could choose no more fecund example than the master work of Claude Bernard on the sugar-liberating functions of the liver, to which he first applied the phrase. Contemporary investigation by physiological and chemical means of this class of substances, the chemical messengers, or so-called hormones of the body, through which many of its functions are integrated, has been rich in surprising rewards. Almost everyone is familiar with the relationship of the "stunted, pot-bellied, slavering cretin,"[8] with defect of the internal secretion of the thyroid gland, and we stand awed before the now common fact of the transformation of the cretin into a normal, comely, intelligent child merely by the administration of the substance of the thyroid gland of animals. And we are growing familiar with the instances of gigantism and of excessive obesity, resulting from pathological conditions of the complex pituitary gland, the small body which sits on the fantastic Turkish saddle at the base of the brain. The physiological effects as well as the practical uses of epinephrine, the peculiar secretion of the adrenal glands, would seem to bear daily testimony to that regulatory mechanism, through which fear is expressed and courage reinforced; while the saving graces of insulin, the hormone regulating the sugar consumption of the body, have rendered the lives of many thousands of victims of diabetes tolerable and happy. This is a very incomplete list of even our present knowledge of these subtle, integrative, chemical messengers of health and disease. Others regulate at the proper moment the order of the digestive secretions, determine secondary sexual characteristics, and even stand watch and ward over the generation of human life itself.

There is no sharp line between health and disease, and no sharp distinction between the functions called physiological and pathological. A knowledge of the body will include all the biological processes with which we can deal. The animal body has often been compared to a watch, and the physician with the expert watchmaker, and it has been hoped that in due time doctors will be as good at their craft as watchmakers are at theirs. It is true, of course, as John Brown, the gifted author of "Rab and his Friends," has pointed out, that the watchmaker is not called on to mend the watch while it is going, and that this makes all the difference. But the simile is far more

[8] Starling, E., *Lancet*, 1923, ii, 869.

imperfect than this, since the most cunning of Swiss watches which tolls the precise minute of the day or night, shows the day of the month, the quarters of the moon, and even other successive events, is so far simpler than the beautifully constructed and ingeniously integrated animal body, that it is almost an offense to compare one with the other.

The vocation of medicine is multiple; hence the need for specialization. In recent times, the scientific medical investigator has also become a specialist. Since medicine is one of the biological sciences, it is natural to ally it with biology as an educational discipline. But this definition has become too narrow. The growth of medical science, as a biological science, has brought it into more and more intimate relationship, first with classical chemistry and now with classical physics, to the great benefit of both medicine and biology. A generation ago we saw the rise of biochemistry as an independent subject of research and knowledge; to-day we are witnessing the beginnings of biophysics as a similar independent subject. There is hardly a direction in which classical chemistry and classical physics are moving forward, in which biology and medicine do not promise presently to follow.

These circumstances call for specially trained men possessing the temper and aptitudes of the investigator to pursue medical research. Indeed, so formidable has become the demand for the investigation of medical problems that particular provision is being made in universities and special institutions founded to fulfill this demand. On all sides the persons with these qualities are being scrupulously sought in increasing numbers. In order to provide for them the most favorable opportunities for work, a kind of organization of research is being undertaken. This is a new thing as a purely scientific experiment, and hence it may be well to inquire just what is embraced under the term of "organized medical research."

There are known conditions under which scientific discoveries have been made in the past. The strong individuality of the gifted investigator is well illustrated by the two extreme examples dealt with at the beginning of this address. It were futile to attempt any organization which purposes to promote discovery by such persons as these. Indeed, it is not intended at all, and probably would prove impossible ever to organize the subject-matter of research and the extraordinary minds which are the chief means of making discovery. It is now recognized that the progress of science, while strictly logical, is not uniform. The whole body of scientific knowledge does not move and can not be moved forward on a wide front. As a matter of fact, the reverse process occurs; progression takes place now at one, and now at another part of the front—after which, and perhaps slowly and with great effort, the rest of the column moves on. In the meantime, still another thrust occurs, and now perhaps at a new part of the line, necessitating a still further general readjustment.

And so with an infinity of pushes and pauses, owing to the efforts first of one and then of another group of investigators, and at different periods, one observes a larger problem to be cleared, but perhaps never completely solved. As Newton has said, physical laws deal with relations between phenomena, not with causes; and causes need not be mathematical at all. Moreover, the physical laws we enunciate must be regarded as provisional and approximate. Hence the progress of science means the closer and closer approximation to the objective—perfect, immutable laws.

The first indications of an experimental advance may occur many years ahead of the explanation of the phenomena involved, and until the latter appears, the real significance of the discovery may be missed. Thus, Hopkins observed that small animals failed to develop normally on a carefully balanced, adequately caloric diet, not imagining the fault to lie with the want of almost imponderable quantities of necessary vitamines, substances still of elusive chemical composition, the existence of which at the time was unknown. Now we designate with almost a half dozen letters of the alphabet as many supposedly vitamine entities which control as many physiological and pathological functions of the animal body.

In like manner when the remarkable power of cod liver oil to prevent rickets in the young had been clearly shown, no one could have suspected that a like effect was produced by certain rays of the sun, and even less that in both instances the beneficial action is determined by a reciprocal, quantitative relation in the phosphorus-calcium content of the blood. Just now that the study of radiation effects—of X-ray and of radium emanations—is claiming so much attention, we wish to ascertain what it is that takes place, which on the one hand leads to that kind of injury of animal cells that sometimes produces cancerous conditions, and on the other the beneficial changes that result in the actual cure of pre-existing cancerous growths. That the radiations alter in some way the physiology of cells—normal or cancerous—may be assumed; it is the how that is being sought, and the nature of the alterations induced. The ability to grow animal cells indefinitely outside the body has provided an almost perfect material for the biological testing of the effects of physical and chemical agents, from which in due time a new cell physiology will doubtless emerge.

Among investigators the rarest are those men with a presentiment of new truths; the far greater number merely develop and follow the ideas of others. In a few instances the presentiment is extraordinary, but it is always likely to be a brilliant example of the scientific use of the imagination. Of the first order of magnitude was Harvey's assumption of the existence of minute vessels uniting the arteries and veins and completing the circuit of the circulation. In his day the microscope was too primitive to reveal them; in fact, Malpighi's discovery of the capillaries occurred four years after Harvey's death and thirty years after the publication of the "Motion of the Heart and Blood in Animals."

At all periods, voices have occasionally been raised to decry the domination of medicine by science. These timid souls would return to the less aided senses in order to provide the so-called intuitive faculty of the physician with greater latitude. Just now this thesis has been put forward by an eminent German surgeon—Sauerbruch—and an active controversy has been started. The weight of opinion, fortunately, is more modern and logical, for while it is properly admitted that superficial science can never compensate for slipshod observation, and while it is allowed that one doctor's wits are sharper and quicker than another's, yet it is urged with easy conviction that without true knowledge even the supremely intuitive can reach no real goal nor pass beyond the limits of the "inspired ignoramus."

If, therefore, we may not seek to organize the subject-matter of research, we may nevertheless undertake to organize the facilities which make the prosecution of research more consistent and less a matter of chance. In carrying out this purpose, we must ever keep in mind that the outstanding discoveries in science are the accomplishments of real men and usually of great men. Now, as it has been well said, great men are just those who bring with them new ideas and destroy errors. They do not, therefore, respect the authority of their predecessors and they do not move in an ordered way. While it is of course true that the discoveries of the great men preceding them stand at the base of their own discoveries, yet neither is ever the promoter of absolute and immutable truths. "Each great man belongs to his time and can come only at the proper moment, in the sense that there is a necessary and ordered sequence in the appearance of scientific discoveries. Great men may be compared to torches shining at long intervals to guide the advance of science. They light up their time, either by discovering unexpected fertile phenomena which open new paths and reveal unknown horizons, or by generalizing acquired scientific facts and disclosing truths which their predecessors had not perceived. If each great man makes the science which he vitalizes take a long step forward, he never presumes to fix its final boundaries and he is destined to be outdistanced and left behind by the progress of successive generations. Great men have been compared to giants upon whose shoulders pygmies have climbed, who nevertheless see further than they. This simply means that science makes progress subsequently to the appearance of great men, and precisely because of their influence. The result is that their successors know many more scientific facts than the great men themselves knew in their day. But a great man is, none the less, still a great man, that is to say—a giant."[9] And who would presume to confine, that is to restrict by organization, a band of giants? It is enough to provide them, as they may now hope to be provided, with suitable material resources with which to perform their gigantic, wonder-working tasks, of which they are often the unconscious agents. This, and as it seems to me, this alone is the purpose and the justification for the organization of science: to afford opportunity commensurate with the objects to be attained, for both the giants and their associates of smaller stature, for him who blazes the trail and him who clears the path, since both operations are needed in order that knowledge may be increased and the light be made to enter the still dark places, and the spirit of man be thereby enlarged and made to shine with ever greater brilliance.

SIMON FLEXNER

THE ROCKEFELLER INSTITUTE
FOR MEDICAL RESEARCH,
NEW YORK, N. Y.

SCIENTIFIC EVENTS

THE CONVERSAZIONES OF THE ROYAL SOCIETY

THE first of the two conversaziones given annually by the Royal Society has taken place at Burlington House, when, as usual, an array of exhibits was provided for the instruction and entertainment of the visitors.

According to an article in the London *Times* one of the most striking demonstrations was that of Mr. A. A. King, who showed the application of ultraviolet radiation from a mercury vapor lamp to the detection and estimation of minute quantities of arsenic. When a mercury-arsenic stain on a piece of filter-paper sensitized with mercuric chloride is examined in ultra-violet light the unchanged mercuric chloride fluoresces blue, while the mercury-arsenic stains stand out as a black disc. Arsenic stains,

[9] Bernard, Claude, "An Introduction to the Study of Experimental Medicine," English Translation, 1927, p. 41.