



The Progress of Physiology

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ology has come of age, and has been admitted to full membership in that old world group to whom we have so long looked for guidance and inspiration.

There was one among our number, who, alas! is with us no longer, Dr. Samuel J. Meltzer, whose heart would have been greatly stirred by this occasion. Born in Russia, educated in Germany, he passed the greater part of his professional life in this country, beloved and respected by all and a strong influence for good in the development, not only of physiology, but of scientific medicine in general.

His last days were spent amid the distracting events of the great war, and the needless spread of the animosities of that conflict into the serene domain of science was a source of the deepest regret and sorrow to him. The closing years of his life were given to an earnest effort to reestablish the bonds of brotherhood among scientific workers in medicine by the formation of a *Fraternitas Medicorum* which should bind us together in a common purpose to advance the welfare of humanity. The ideals that he visualized are in process of fulfilment through the instrumentality of these international congresses. They constitute, in fact, a fraternity of scholars whose essential object is the unselfish promotion of knowledge for the benefit of the whole of mankind. This large assembly from all quarters of the globe is convincing proof of the potency of a great humanitarian ideal to rescue international amity among men of science from the evil effects of the stresses and passions engendered by political and economical differences.

If, as citizens of the United States, we feel a nat-

ural pleasure and pride in welcoming our foreign members as guests to our own country, this human emotion is in reality subordinate to the more profound sense of satisfaction that we experience in cooperating with you, our brothers and colleagues, as fellow citizens of the great republic of science, whose beneficent purposes command our common loyalty without respect to national boundaries or political separations.

The pleasure we feel in meeting again after an interval of three years is saddened by the thought that during that period some of our company who stood high in our esteem and in the record of their achievements have finished their work forever.

Starling, of England, whose ability and brilliant personality made him the natural center of these world gatherings; Magnus and Einthoven, of Holland, to whose work both physiology and medicine are so deeply indebted; and Kossel, of Germany, whose contributions to biochemistry were of such fundamental significance, were veterans in the service. They were among our greatest and most admired leaders, and they have left enduring records of their work in the history of physiology. Noel Paton, Ferrier, Anderson, Pütter, Wieland, Mandel were fruitful workers whose names have long been honored among us. Pezard, of France, and Arthur Loevenhart, of this country, were cut down in young manhood before the fine promise of their early work had reached its full accomplishment. We mourn the loss of these gifted colleagues, and as a mark of respect to their memory I ask the congress to rise and stand for a moment in silence.

THE PROGRESS OF PHYSIOLOGY¹

By Professor AUGUST KROGH

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I SUPPOSE that almost every worker in our science has given some thought to the general progress of physiology and to the problems raised by its growth, and I can not doubt that some have pondered deeply over these problems and have much more insight into them than I possess, but you must admit that on the whole the thoughts have been kept private, and nobody seems to have considered it worth while to bring the matter up for a general discussion among physiologists. When I venture to do so it is because I feel deeply the importance of the subject, and in spite of the fact that I feel even more deeply my own lack of competence in all questions involving organization. My aim is only to draw your attention to some of the

¹ Opening address before the Thirteenth International Physiological Congress, at Harvard University, August 19, 1929.

problems in the hope that means may be found to solve them.

We are all aware that physiology is a rapidly expanding science in the sense that an ever-increasing amount of work is being produced by an increasing number of workers, and the increase in attendance at the international congresses bears witness to the fact. I have tried to count from the abstracting and indexing journals the number of papers published on physiological subjects. The figures are probably not strictly comparable, but their general tendency is unmistakable. In the first year of this century, the year of the congress in Turin, titles were given in the *Physiologisches Zentralblatt* of 3,800 papers, and during the first decade only minor fluctuations took place. I find from the *Zentralblatt* and *Bibliographia* 3,900

in 1904 (congress in Brussels), 3,500 in 1907 (Heidelberg) and 4,300 in 1910 (Vienna), but then a rapid increase took place and in 1912 the figure was 6,700. I have no reliable statistics for the years from 1913-1919, but for 1920 the *Jahresbericht* gives the titles of 11,500 papers; for 1923 (Edinburgh) the figure is 14,000 and for 1926 (Stockholm) it reached 18,000, and there is no doubt that it is increasing further. I had the impression that physiological papers now were on an average shorter than 25 years ago, but a sample counting failed to substantiate this impression and showed the average length to be then as now 10 pages. The increase in publication is due to a number of causes and to some extent it may be unreal and due to more complete indexing now, but there can be no doubt that much more work is done now and by a larger number of workers than 25 years ago. It is interesting to note that in the *Zentralblatt* for 1901 only 100 papers or 2½ per cent. were published in America or by American authors while the *Berichte* for 1926 shows about 3,500 American papers, nearly 20 per cent. of the total.

Our science has grown also in the sense that our understanding of many problems of fundamental importance has been broadened and deepened. We are all more or less familiar with the enormous expansion of knowledge in the field of nutrition and in the study of hormones. Less spectacular, but I think equally important progress has been made in the physiology of muscle and nerve and in the problems of the circulation. We have become acquainted recently with the long-continued work of Pavlov and his school on the cerebral functions, and I think we can say that the investigation of the nervous system is making satisfactory progress in spite of its tremendous complication.

Physiology has been brought in much closer contact with the allied and fundamental sciences. Twenty years ago the application of statistical and mathematical analysis to our problems was very uncommon and unfamiliar to most physiologists, and there were even those who deprecated it violently. Though there is still room for much further progress the statistical weapons are wielded successfully by a large and increasing number of investigators.

In many ways the results and methods of pure chemistry and physics are utilized and successfully adapted to our problems, and I trust we can claim some reciprocity, since the use of micromethods, initiated mainly within our domain, where their services are invaluable, is spreading to other provinces of science. It is extremely gratifying from a general point of view to see how even the most advanced ideas and methods of physics and chemistry are inspiring the work of a few of our colleagues. I use

the words "from a general point of view" on purpose, because for my own part the fact shows me that development is taking place along lines where I can not follow and I believe we have to admit that with the rate at which advance is now taking place in the sciences the useful span of life in the front line of research is likely to be cut short for many of us, because our view-points and even our methods become antiquated.

While we have every reason to rejoice over the growth and progress of our science I think we must admit at the same time that there is room for much improvement and even that some aspects of the situation are unsatisfactory. Physiology is growing unwieldy. It is impossible for any single human being to be familiar with modern physiology in all its branches in the sense in which the great teachers of 20 or more years ago were familiar with the physiology of their time. We have to face the splitting up of physiology into more or less separate and independent sciences, and we are confronted with the problem of finding the right lines of cleavage. Research is bound up closely with teaching, and the lines of cleavage are determined and will be determined to a very large extent by the university chairs and departments which are brought into existence. It is the practical teaching situation which has made pharmacology an independent science, while as a branch of research it can scarcely be distinguished from pure physiology. We have seen biochemistry grow up and obtain independent chairs and laboratories in the universities of many countries, and I believe we all agree that this has been a most happy development which will be carried on into those universities and medical schools which have not yet effected the separation.

A few universities, and Copenhagen among them, have made a new departure in creating separate chairs and department for biophysics. This is justified from the point of view of teaching and for other practical reasons, but I do not think it is the thing most urgently needed from the point of view of research with which we are here concerned. Our physical problems have so far usually been rather elementary, but I must admit that the situation is rapidly changing and it is quite possible that new discoveries like that of radiations from rapidly growing tissues may in a near future make biophysical departments generally desirable or even necessary.

It is natural and useful that laboratories specialize in certain directions, and such specialization is sometimes accentuated by their official status, so that they may be laboratories for the study of definite problems or groups of problems as endocrinology, muscular work, etc. I do not think, however, that cleavage of

physiology along such lines will become permanent or general, and I feel sure that harmful results would be inevitable if it did become general and effective. The activities of the organisms which we are studying are too intimately correlated to allow much specialization of this kind. A serious attack on any definite problem may lead into a different province of physiology, and fortunately the workers are usually free to carry on the attack regardless of artificial boundaries.

Physiology as a science has taken its origin from the necessities of practical medicine, and even now the large majority of workers in physiology have had the benefit of a medical education and hold their appointments in medical schools. Nevertheless we all hold physiology to be an independent science, and most of the work done in physiological laboratories has no direct relation to medicine. The line of development which I think should be followed is to establish in one direction a branch of physiology which is much more intimately in contact with practical medicine and in the other direction a branch which is much more independent.

I think that work done on this side of the Atlantic has contributed more than anything else to the growing understanding of the fact that the problems of disease are mainly physiological and can not be solved by the methods of clinical observation, morbid anatomy, bacteriology or serology alone, even in cases where these sciences are absolutely essential. It is the functional reaction of the organism to the attack of disease and to the therapeutic measures which is after all the central problem. A large and increasing proportion of physiological research is carried on in hospital laboratories by men and women who are at the same time practicing the art of healing. Much of this work is very valuable, but sometimes the outlook is rather narrow, and I believe that a great deal could be gained by expert physiological direction and coordination. I think the time has come when special chairs and laboratories should be established for the physiology of disease, morbid physiology or experimental medicine, if you prefer that name. The main point is that the leaders of such laboratories should have no regular duties connected with the treatment of patients, but they must have a small number of beds at their disposal for the temporary study of selected cases, and they must of course be in close and constant contact with the clinical wards. It goes without saying that they must have facilities for studying disease experimentally on animals. Within the field of blood circulation and innervation of blood vessels with which I am personally acquainted, I have had the desirability and even necessity of cooperation with the practical medicine brought home to me again

and again. I have learned also that the theoretical problems regarding kidney function require for their solution a close study of clinical cases, and I can not doubt for a moment that great benefit to patients will ultimately result from such a study. Much can be done in this direction by means of existing facilities, but I anticipate an acceleration of progress from the creation of special chairs as outlined, and I feel sure that the resulting contributions to practical medicine would amply and within a short space of time repay the communities for the initial outlay on such departments and for their maintenance.

The other line of development which I would suggest is not perhaps such a pressing need, but ultimately I believe it to be of scarcely less importance. It is the creation in the science schools and in close cooperation with the departments of zoology of chairs and laboratories for comparative physiology, animal physiology or zoophysiology. The name does not matter much, though I confess that there is one name with which I have no sympathy—that of “general” physiology. I suspect that it is often used to denote just those aspects of a problem which are considered most important from an individual point of view. In my opinion a general physiology which can describe the essential characteristics of matter in the living state is an ideal to which we may hope that our successors may attain after many generations, and I want to emphasize that the route by which we can strive toward the ideal is by a study of the vital functions in all their aspects throughout the myriads of organisms. We may find out, nay, we will find out before very long the essential mechanisms of mammalian kidney function, but the general problem of excretion can be solved only when excretory organs are studied wherever we find them and in all their essential modifications. Such studies will be sure, moreover, to expand and deepen our insight into the problems of the human kidney and will prove of value also from the narrowest utilitarian point of view.

For a large number of problems there will be some animal of choice or a few such animals on which it can be most conveniently studied. Many years ago when my teacher, Christian Bohr, was interested in the respiratory mechanism of the lung and devised the method of studying the exchange through each lung separately, he found that a certain kind of tortoise possessed a trachea dividing into the main bronchi high up in the neck, and we used to say as a laboratory joke that this animal had been created expressly for the purposes of respiration physiology. I have no doubt that there is quite a number of animals which are similarly “created” for special physiological purposes, but I am afraid that most of them

are unknown to the men for whom they were "created," and we must apply to the zoologists to find them and lay our hands on them.

I want to say a word for the study of comparative physiology also for its own sake. You will find in the lower animals mechanisms and adaptations of exquisite beauty and the most surprising character, and I think nothing can be more fascinating than the senses and instincts of insects as revealed by the modern investigations.

Just as in the case of pathological physiology, a good beginning has been made in the study of this group of problems and an increasing number of papers are published which can be justly classed as comparative or zoophysiological. There are a few chairs and departments in this branch of our science, but I suggest that it is time to increase their number, to coordinate efforts, to offer and to invite cooperation with zoology departments, with field biology and zoological investigation also along the morphological lines. I venture to believe that such cooperation will be fruitful not only to the physiologists seeking it, but also to our elder brethren in the departments of zoology.

The establishment of new chairs and departments requires the sympathetic interest and active cooperation of faculties and university authorities, but there are many points on which we ourselves individually and by our united efforts can improve unsatisfactory conditions in physiology and increase the efficiency of physiological publication.

When I try to picture the evolution of physiological truth I am struck by the similarity with the evolution of life itself upon our planet. Ideas are conceived, facts are elaborated with immense joy and with infinite labor. A large number die without ever coming to the light of publication, and of those which are published an appalling proportion sink to the bottom and can only be dug out as fossils from dusty library shelves. Many succumb in controversies with other ideas and facts and a minority only survive in the sense that they beget new ideas and give rise to the discovery of new facts. I believe that this enormous waste is on the whole inevitable and bound up inseparably with the difficulties which physiological investigation has to overcome. I look upon controversy especially as one of the chief ways in which truth is approached. We may fondly imagine that we are impartial seekers after truth, but with a few exceptions, to which I know that I do not belong, we are influenced and sometimes strongly by our personal bias and we give our best thoughts to those ideas which we have to defend. Nevertheless we should of course all do our best to avoid controversy, in the sense that we should take every possible care

to verify our facts and substantiate our conclusions before publishing our results.

When I attempt to pass in review the physiological literature of to-day I notice certain defects which are too common and which could no doubt be remedied to a certain extent. In a recent small book of instructions for medical writers I find the statement that what is needed in scientific papers is facts and again facts and still more facts. I venture to disagree emphatically with this statement. Facts are necessary, of course, but unless fertilized by ideas, correlated with other facts, illuminated by thought, I consider them as material only for science. I am prepared to submit the thesis, revolting though it may seem, that too many experiments and observations are being made and published and too little thought is bestowed upon them. It is a statement not too infrequently met with in physiological papers that a certain experiment has been repeated on, say, 47 animals. Very often, though by no means always, such a routine procedure is sheer waste of time and animals, and at the root of the apparent diligence lies a mental inertia which carries the experimenter along the accustomed groove with a minimum of exertion of the mind. But physiological experimentation which shall lead to reliable results and carry us forward requires constant exertion, constant attention to details which may be trivial or may turn out to be of vital importance.

When experimental results are found to be in conflict with those of an earlier investigator the matter is often taken too easily and disposed of for instance by pointing out a possible source of error in the experiments of the predecessor, but without inquiring whether the error, if present, would be quantitatively sufficient to explain the discrepancy. I think that disagreement with former results should never be taken easily, but every effort should be made to find the true explanation. This can be done in many more cases than it is actually done; and as a rule it can be done more easily than by anybody else by the man "on the spot" who is already familiar with essential details, but it may require a great deal of imagination and very often it will require supplementary experiments.

It is an almost invariable custom of editors of journals to reject papers which do not contain new "facts." It is natural to be skeptical toward reasoning not supported by facts, but it must happen in many cases and to many physiologists that their thoughts are illumined by facts which were incompletely understood by those who brought them forward, and I remember more than one occasion where published experiments could be given a much more consistent explanation than that adopted by

their authors. In such cases a more liberal interpretation of the rules of the journals would serve the interest of our science, and I venture to think that the publication of papers discussing facts already known should be encouraged.

I have said enough and perhaps too much on the things we can do individually. What can we do as a body? The catchword of our post-war times is organization. Can physiology be organized? When I was very much younger I had visions of leaders of physiology who could see clearly the problems to be studied and the ways of approaching them, and who might distribute them and their separate parts among the laboratories and the individual workers. At a somewhat later stage I imagined a central laboratory to which all new methods could be submitted for testing and from which only the most reliable and quickest methods would emanate. I see clearly now that all such schemes are dreams. They can never be realized and should never be realized if it could be done. The individual freedom is our chief asset, the mainspring of the really new ideas, the guarantee of progress. Physiology does not go forward as an ordered line of battle on a continuous front, but must be carried on, as some one has aptly said, as a guerilla warfare against the unknown, conducted singlehanded or by quite small units. There is no need for an extensive organization of research, but there is much need for voluntary cooperation on a limited scale between individuals and laboratories. There are many problems which can only be successfully attacked when experimental physiologists cooperate with histologists, with chemists or physicists or with clinicians, and some problems will require the combined efforts of several of these groups, but the affair is always one of local and voluntary cooperation and does not concern us here.

While I have no faith in organization on a large scale of research I think there is a wide and fruitful field for organization of what we might term the services behind the front. We all feel the difficulties of keeping abreast of the literature, and I can not doubt that the methods of indexing, abstracting and reviewing that literature could be improved and organized so as to give better service at less cost. It may be desirable to adopt a system of indexing papers according to the subjects dealt with and, if it is desirable, *one* system ought to be agreed upon and used by all the leading physiological journals and by department libraries throughout the world. It is quite conceivable that even an inferior system universally adopted would be much better than many excellent systems in use locally or a general lack of system.

We have I think a very good abstracting service. I am best acquainted personally with the German

abstracts in *Berichte*, and a high tribute should be paid to their general excellence and completeness. Very few papers in the leading languages escape their vigilance, but when I look over the numbers one by one as they come to hand to keep myself informed about the subjects in which I am interested I always feel that the distribution and arrangement could be considerably improved.

It is I think a wasteful procedure that the same papers are independently recorded and abstracted in several different languages and an even greater number of different abstracting journals. It ought to be possible to obtain some arrangement for exchange of abstracts and other mutual help and thereby effect also a saving in cost. Then there is the difficult question of getting abstracts of papers in less known languages like the Scandinavian or Russian.

I can not but feel that a large number of separate copies go to waste because they are distributed to people who can not utilize them, and that on the other hand separate copies of certain papers may be badly wanted by people who can not get them. I have been considering for years the possibility of an organization which could prevent some of this waste, but I have to confess that so far I have been unable to discover any workable scheme.

After all, it is not my business to point out to you specific remedies for this or that, but to suggest if possible broad measures which may lead to the solution of some of our difficulties. I believe that the machinery for dealing with problems affecting us all can be created without serious difficulty. The International Congress of Physiology is without any doubt the highest authority in matters pertaining to the organization of physiology and its necessary services. Why should not the congress exercise this authority?

We have met together for friendly intercourse, to be taught and to teach by demonstration of experiments and discussion of papers. The benefit to our science from a meeting like this is very great, although very difficult to estimate by visible results. Why should we not make this, our congress, which meets together regularly, into an instrument also for the organization of our necessary services, for the elaboration of rules of nomenclature and for the protection of our scientific freedom. I believe that it can be done and ought to be done.

Perhaps I am still a dreamer of dreams. I know for certain that I have not that administrative capacity which is necessary to transform my dreams into living realities, but if they contain any idea of any value I venture to hope that our administrators will take up that idea and carry it out to the benefit of our science and the greater glory of our congress.