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THE PRESENT TENDENCIES AND METHODS OF PHYSIOLOGICAL TEACHING AND RESEARCH[1]

SOME thirteen months ago, at my inaugural lecture at University College, London, an occasion which represented also the completion of the great gift which that college owes to the Rockefeller Foundation, I had the temerity to speak upon an analogous though narrower subject, "The present tendencies and the future compass of physiological science." I say narrower, since in that lecture I attempted to deal only with the side of research: to-day I am even more rash—I propose to lay down the law also on an aspect of the subject of which I am still less competent to judge, its rôle in education.

On the former occasion I was astonished to find, in spite of the nature of some of my conclusions, how little immediate opposition was aroused. None of my more conservative colleagues wrote to deplore my Bolshevistic tendencies: none of my older friends came to expostulate with me in private: the only public comment I evoked was one in the *British Medical Journal,* approving much of what I said, but somewhat reproachful because I had discussed only the science and not the teaching of physiology. I will try to remove that reproach this evening.

THE INTERNATIONALISM OF PHYSIOLOGY

On that previous occasion, as on this, I started by stressing the international nature of scientific relations. Science and medicine can progress only by being truly international, by utilizing the discoveries and experience of all workers in all lands, by creating that good feeling and understanding between men in every country, which is the basis of cooperation in study and research. Science is not a purely intellectual thing: the history of learning throughout the ages, up to the present time, is a sufficient witness of that truth. Like any human enterprise it depends upon the human factors of courage and persistence, of good will, fellowship, trust and comprehension. These human factors were the basis of the Rockefeller gift to University College, of which I spoke a year ago. No less are they the basis of the invitation with which you to-day have honored me, a stranger, in asking me to give this annual address.

You may reflect: "Why, surely such sentiments are not controversial, they will arouse no bitterness or

[1] Annual Gross Lecture to the Pathological Society of Philadelphia.

contradiction!" In the abstract—no. Yet let us consider the concrete case. In 1923 an International Congress of Chemists met in Cambridge; the Germans—among them the most distinguished of living chemists—were forbidden to attend. In 1924 an International Congress of Mathematicians met in Toronto, with a similar restriction. In 1923 an International Congress of Physiologists met in Edinburgh: Germans, Austrians and Hungarians came, under the chairmanship of an Englishman who had lost two sons, killed in the war: the French and the Belgians stayed away in protest. In defence of the prohibition at Toronto it was urged (privately to me) that it was a lesser evil to hinder the advance of science than to run the risk of associating with men who signed the German professors' manifesto of 1914. Of the prohibition at Cambridge no defence was deemed necessary. And yet in 1796 a distinguished French scientific sailor, a prisoner of war in England, Chevalier de Rossel, dined in London as a guest of the Royal Society Club: while in 1802, within six months of the end of the long and bitter struggle which closed with the Treaty of Amiens, a number of eminent French officials, and at least one scientist, had done the same. In such a degree have we gone back instead of forward in our civilization. It is not unnecessary to protest the international status of learning.

Physiology as a Science

Mankind makes all kinds of excuses for its beliefs; the excuses are often not the real reasons; the real reason doubtless for what I am now going to say is that I have no medical qualifications myself, and naturally try to find excuses why physiologists should have no medical qualifications. You may discount what I say as far as you find necessary, bearing that in mind. These, however, are the excuses which I offer.

Physiology in Britain, but not always or usually in other countries, is in the faculty of science, as well as in the faculty of medicine. Our recruits are not drawn mainly from medical students or from qualified medical men. To that, I believe, the present high standard of physiology in Britain is largely due. With us physiology is no more "the handmaiden of medicine" than physics is the handmaiden of chemistry. Physiology may be necessary to medicine, medicine to physiology; but physiology has its own needs, its own problems, its own methods and habits of thought. In the solution of its problems physiology should no more be led by apparent utility than should physics. If a problem be unsolved, it is worth solving; if a phenomenon appear mysterious, it must be investigated; if two facts seem to be related, the relation must be explored; quite independently of the supposed utility or uselessness of the inquiry. The nervous impulse, muscular contraction, ciliary movement, the physical chemistry of hemoglobin require no more excuse for their study than does the structure of the atom. Whenever and wherever we see an opening for research, there the attack must be delivered, quite regardless of whether the results to be achieved are to benefit mankind, to enrich the medical profession or merely to satisfy our intellectual curiosity. For we can not judge whither our researches are to lead. This again may seem obvious; but it is not. Yes, one will be told, all very well in theory, but the department of physiology was built and endowed so handsomely because of its relation to medicine: were it not for the needs of medicine, physiology would be housed and treated with much less honor and indulgence. I am aware of that; it is primarily in order to secure the greatest possible return that one demands freedom. The gift of freedom, however, requires faith on the part of the giver; discipline, organization, servitude would obviously produce the greater immediate return. The improvement of knowledge demands faith as well as dollars.

The Royal Society of London, in an eloquent preamble to its year book, points out to would-be benefactors that, in its considered opinion, more good is done, a greater end is served by endowments available for the general purpose of improving knowledge, than by funds devoted, or restricted, to specific objects. To take a few of the special needs of medicine at the present time, a knowledge of the meaning and nature of growth underlies all our attempts to deal with cancer; yet the study of growth as such is not the function of medicine, or of any handmaiden of medicine, but rather of the free sciences of zoology, physiology, biochemistry and biology in its widest sense. Again the effects of specific chemical substances, the relation between pharmacological action and chemical structure, require not an acquaintance with medicine or a pleasant bedside manner, not even a desire to benefit suffering humanity, but the highest form of chemical and biological skill. So long as medical students are the chief attendants on our courses, we are not really likely to forget the needs of medicine; but we should aspire rather to lead medicine along the paths of science than to push science along the paths of medicine.

The war was decided largely by the Grand Fleet. Yet how often was that fleet in action, what "good did it do," reckoning it crudely, how many Germans did it kill? Its functions were negative; it denied the sea to the enemy; it allowed the life of the nation and of its armies to operate behind a silent and invisible shield. Such, I often think, is one rôle of physiology in medicine. Medicine has a difficult and urgent task, a task which brooks no delay. One function of physiology is to keep the seas clear and free for that task. There are quackeries enough. To-day in London there are qualified medical practitioners earning a large income, exploiting the credulity of sick people, by using the childish box of tricks associated with the name of Abrams. There are many other such types of fraud. You know them just as well as we do. Without a scientific education how can a medical practitioner deduce that a potency of 50 in a homeopathic medicine represents a concentration of one molecule in about 100,000 visible universes! Common sense may be a safeguard from the cruder frauds and quackeries, but clothe them in a flowery garb of science and without science your medical practitioner will be deceived. I like to tell my students, at the beginning of their course, that by learning to think physiologically in terms of what is known, rather than of what might be the case in another world, they are avoiding the pitfalls, both of belief and unbelief which would otherwise beset them. This is one rôle of physiology, a rôle possible only if physiology remains, not a handmaiden to medicine, but an independent interpreter of science, an intellectual discipline of free man in touch with science, equipped with all the tools of science, ready always to attack scientific fraud or to approve scientific discovery in any of the medical subjects. Your medical profession, no less than ours, needs a police force to guard it from quasi-scientific hypocrisy and fraud.

There is a further reason, in your country especially, why physiology should have its roots in science rather than in medicine, and that lies in the great facilities offered, in your full time medical units, for laboratory research. The applied physiology, the medical physiology, can be done in the medical units: all the more reason for encouraging your university laboratories to pursue their scientific problems.

If then, physiology is to be primarily an independent science and not a servitor of medicine, certain necessary consequences must follow. Its professors and teachers must be scientists, trained and qualified in science, not necessarily in medicine. At present many of them are qualified rather in medicine than in science. In many countries the only pathway to physiology is the long and troublesome one which leads a student to a medical degree: little wonder that the ablest intellects are often sidetracked in the sciences, physics, chemistry and biology, which make no such demand on their disciples. Pasteur was a chemist, Bayliss was catholic in his science, but had no medical degree. Barcroft, Langley, Hardy, Mines and Lucas (to name a few from the school of physiology at Cambridge) came to physiology through gates other than those of medicine. Most of these would have refused to enter had there been no other gate. Physiology can ill afford to lose such recruits.

Physiology then must have its roots in science, must attract students who have no intention of pursuing medicine as a profession. In this respect our science labors under one fundamental difficulty; it is an intermediate science, physics, chemistry and biology must precede it, and quite naturally the ablest students are filtered off and retained by the teachers in those other sciences. At Cambridge the schools of physics and applied mathematics, by their old established fame, attract the cream of the scientific ability of the country. That ability is often enough not specialized in one subject, but general. It happens to be devoted to physical science—it might equally have been devoted to physiological. I often think, with envy, of what would be done in physiology could we have a selection, for ten years, of the best brains which enter the Cavendish Laboratory at Cambridge!

This difficulty is not insuperable. At present there is a tendency to specialize too young. Students come from our schools with little general education, perhaps with a smattering of chemistry and physics, and proceed to specialize at once. It should be impossible for students of science absolutely to neglect the study of physics, chemistry and applied mathematics, as at present sometimes they do; it should be equally impossible for them to neglect the study of at least one biological subject, as they usually do. If only that principle could be conceded, we physiologists would get a fairer share of the good brains available. At present they tend to be monopolized by the simpler and more elementary sciences of chemistry and physics.

There is one institution in Britain which you do not possess here, which might perhaps be a great help to you in peopling your great and growing departments; that is the instruction of a certain number of "honor students" in the medical sciences. In England no department of physiology feels that it is "doing its job" unless it has a certain small proportion of its ablest students spending an extra year, or more, in studying advanced physiology, biochemistry or pathology after the completion of their ordinary course. These students may be medical students, who are spending a year or two by the roadside, during their medical training, in order to appreciate their science more fully and to learn how research is done; or they may (as is often the case at Cambridge) be students of science only, who are studying physiology or biochemistry purely as a science. These students are the most valuable element in our laboratories; they are the people from whom our research workers are made. For their work we give them an "honors degree" in science (B.A. or B.Sc.), which is an asset to them in their later career. There may arise certain administrative difficulties in the formation of such groups of science students in your schools; difficulties, however, can be overcome, and with the great and growing need of scientific workers for the great departments which are being organized all over your country, you might be well advised to consider the adoption of some such system.

THE PRESENT TENDENCIES OF PHYSIOLOGY: BIOCHEMISTRY

Physiology has two chief aspects, the biological and the physical. On the one side the fundamental problem is reproduction, growth, repair; on the other side mechanism, manner of working. Those two aspects require at present different methods of approach, different tools, though ultimately their tools and methods will be recognized as common. There has, of recent years, been perhaps an overemphasis of the physical aspects of the science; that, you may think, sounds strange from me, but J. S. Haldane, who knows me better, abuses me sometimes for being a "vitalist." The physiology of reproduction, of tissue growth, has been largely neglected, both in teaching and research, in many laboratories. That must change, and we must insist on the physiology of growth as being no less essential than the physiology of mechanism. This will depend upon a fuller cooperation with biologists and upon a recognition by botanists and zoologists of the wider scope of a physiological technique.

The first and most striking tendency of physiology to-day is the adoption of chemical methods of analysis. Indeed, some of the most progressive and enlightened chemists see the future developments of organic chemistry, partly in the realm of physical, but largely in that of biochemistry. In the past biochemistry has dealt with comparatively simple problems, mainly with the analysis of the material of which the cell is composed after it has been killed—chemical anatomy, so to speak. It has analyzed and tabulated the in-goings and the out-goings of the body. A living creature, however, is an event, or a series of events, in time as well as space, and the sequence and interplay of those events provide a far more complex problem than that of the nature of the background against which they happen to be played. Just as anatomy is seeking new methods, is beginning to pursue its studies by experiments on the living, rather than by observation of the dead, so biochemistry is passing on, beyond the simple organic chemistry of the structure of the matter which was once alive and is studying the events which occur in the actual living cell. Modern physics is getting inside the structure of the atom, chemistry inside the structure of the molecule; so anatomy—in some places—is attempting to find principles inside the visible structure of the tissue, and biochemistry inside the visible structure of the cell.

Biochemistry differs from physiology proper in using chemical methods of analysis. The older type of organic chemistry is not sufficient. Biochemistry is concerned, not principally with the bodies taken in or given out, not mainly with the structure of the background of the play, but rather with the sequence of events which actually occur in front of it. The chemist in his test-tube works with countless millions of molecules, all acting in the same way; the biochemist, on the other hand, deals with a mechanism in which molecules may pass, one at a time, through a living machine. He needs a finer means of analysis than classical organic chemistry can provide. It is necessary for him to get inside the mechanism and to dissect it by an ultrachemical technique. In so doing he must try to develop a special kind of chemistry, something finer and more subtle than the statistical methods of the chemical laboratory. He needs, moreover, to study the effects of factors such as diffusion, surface tension, interfacial forces, which on the large scale exert only a relatively small effect, but in bodies of the minute dimensions of the mechanism of the living cell assume a preponderant importance. To take an analogy, the velocity of movement of a big wave is little influenced by surface tension, while in the velocity of propagation of a ripple, surface tension is the determining factor. Similarly in a test-tube diffusion is relatively slow; in a blood corpuscle, owing to its dimensions, very rapid. Chemists have studied the kinetics of reactions in order to arrive at the laws of chemical dynamics. Biochemists, however, need to study them because of their actual incidence and importance in the events of life; and often biochemists, for this reason, find themselves compelled to develop a technique of their own, and in so doing may make advances of considerable interest in general chemistry and science. The recent and brilliant work of Hartridge and Roughton has brought the study of the time-course of the reactions of hemoglobin with gases—reactions which occupy only a few hundredths of a second—under direct experimental observations. Their methods can be applied to the investigation of other rapid chemical reactions. Warburg, studying the synthesis of carbohydrate by green cells, has found the simple relation that, in all parts of the spectrum, four quanta of energy are absorbed in the storage of one molecule of CO_2; and the same investigator has brought cell oxidation into a new relation with surface forces and catalytic agents. Hopkins, and also Meyerhof, have gone some way in the description of the chemical mechanism by which, if not ferments themselves, something very like them, works. The isolation of insulin, to be followed some day, one hopes, by its description as a chemical body and finally perhaps by its synthesis, opens up many new and mysterious problems regarding the chemical structure of carbohydrates and their synthesis and breakdown in the body. The specific and amazingly powerful action of the most minute quantities of the accessory food factors—the so-called "vitamins"—has impressed upon us the necessity for the finest experimental chemical and physical skill if we are to isolate them and possibly finally to synthesize them. The mechanism of immunity and its fantastic dependence on organized chemical structure emphasize the same fact. Biochemistry is becoming, and will probably remain, our chief highroad in the analysis of the behavior of the living mechanism.

There is one disastrous tendency at the present time, the separation of physiology from biochemistry. I am glad to agree that biochemistry is just as important as—more important than—classical physiology; a separate department, a separate professor, a separate staff may be desirable. But just as one may regret the ridiculous and dangerous nationalisms by which the political world is torn, so we may regret the divisions of space and contact which occur between physiologists and biochemists in many universities. Are A B C and D physiologists or biochemists? Is it necessary to make A go half a mile to use a chemical technique; B to go 100 yards to use a kymograph? or is it desired simply to duplicate departments of physiology?

If biochemistry is to remain our chief highroad our students must be given a rather special training in chemical methods. In the second examination for medical degrees in the University of London, there is a wise provision; a special examination in organic chemistry for all medical students. This chemistry is taught by biochemists. In these days, however, of hydrogen ions, of Donnan equilibria and colloid chemistry, a knowledge of organic chemistry is not enough; the elements of physical chemistry are equally important; and if ever we succeed, at University College, in attaining control of what we teach while groaning under that strange incubus the University of London, we shall have a special course in physical and organic chemistry, taught in the departments of physiology and biochemistry.

BIOPHYSICS

Differing from biochemistry only in technique, but not in purpose, as a means of analysis of the ultimate events, is the application of more purely physical methods. Physiology in the past has been very much influenced by and dependent upon the development of instruments, and owing to the special nature of their difficulties physiologists have often been responsible for considerable advances in the design of instruments. The string galvanometer of Einthoven, especially in its latest form, capable of registering electric oscillations of wireless frequency directly, and his recent methods of recording sounds (up to the high frequencies of a Galton whistle) simply by their direct action on a quartz fiber about four millionths of an inch in diameter, are examples of such advance. There are many other recent instances—the reversion spectroscope of Hartridge, the use of the cathode ray oscillograph by Gasser and Erlanger for recording the action current of nerve, the development of calorimetric and electric means of studying the energy exchanges of animals, the use of electrometric methods of measuring ionic concentrations, the investigation of membrane equilibria and surface forces—all these require a skilful adaptation of physical technique to our special biological problems. It is obvious that in the utilization of the methods, mental and material, of the physicist and the skilled designer of instruments, we are again on one of the mainroads to the future. Many problems of a physical nature remain to be solved; for example, the effect of X-rays on living cells remains at present a mystery; so do the electric change accompanying the excitation wave and the mechanism by which work is produced with the expenditure of chemical energy in the muscle. The actions of specific physical factors, *e.g.*, light, heat and touch, on the sense organs have scarcely begun to yield to investigation. In these respects we are only at the beginning of knowledge and we await further and finer physical methods of analysis.

If such physical methods are to be taught in a reasonable time, to our unfortunate and overburdened students, a certain preliminary education is necessary. Botany, as usually taught in a girl-school, according to the opinion of two very distinguished English botanists, is not a help but a hindrance to a future scientific career. There are few intellectual difficulties about girl-school botany. The most striking defect which the majority of students show is their complete incapacity to face and overcome for themselves an intellectual difficulty of any kind. They may be able to read and absorb like blotting paper; they may be able to reproduce results as accurately as a penny-in-the-slot machine; but give them a problem and they gaze at it blankly. It is unfortunate, for medicine will provide them later with problems enough. One cure for it, simple as it may seem and unpopular as it will be, is (I believe) to insist on the teaching of theoretical mechanics and mathematics in the schools.

Theoretical mechanics is the foundation of all experimental and natural philosophy. Without a theoretical knowledge of the elementary properties of matter, all natural philosophy is moonshine. Moreover, theoretical mechanics, in an elementary way, is a philosophy in itself; it has a kind of formal precision of proof and statement, it provides certain fundamental intellectual difficulties, and it is the basis of all the physics which our students must learn later. If a knowledge of theoretical mechanics were required before entry to a medical school, as it was made recently at Manchester, not only should we be spared the presence of a certain small proportion of students who are constitutionally incapable of exact thought, but the remainder of the students would be spared the difficulty of understanding physics without a proper intellectual basis. We should have taken the first step towards making our doctors scientists; of protecting them from Abrams and a horde of other quasi-scientific imposters.

"EXPERIMENTAL" PHYSIOLOGY

Side by side with these new direct paths toward the physical and chemical solution of our problems, there remains the old mainroad, a road which one can see no chance of physiologists wishing to discard, the road provided by the so-called experimental method. The word "experimental" is used in a special sense in physiology, as implying observations made upon live animals, or upon organs removed from live animals. It implies rather the analysis of the animal than the analysis of the cell; it is sometimes more akin to modern anatomy than to biochemistry. Many experiments which we wish to make in physiology can not unfortunately, at any rate at first, be made on man, and it is necessary to employ animals to attain a degree of analysis which is possible in no other way. There can be no doubt that a careful and cautious application of experimental technique must lead, and must continue to lead, to progress in our conception of the working of the body of the more complex organisms. Moreover, even from the point of view of studying the cell, there are certain advantages in working with highly differentiated cells, such as those of muscle, nerve or kidney, and so investigating cell-function in a purer form than in the Jack-of-all-trades provided by the unorganized, undifferentiated animal. This great mainroad will certainly remain an essential means to progress in physiology, though it has a not unimportant side-road leading to anatomy. The analysis of the living nervous system, of reflexes and reactions, can not be attained merely by a study of the isolated nerve; nor can it be reached only by experiment and observation on man; it requires experiments on live animals. So also the study of digestion requires such experiments —operative interference with animals, the means of isolating actual digestive juices, and the study of their production under various circumstances. So also kidney function, pancreatic function, endocrine function, cardiac function, all require experiments on animals. One can only hope that the criminal folly of anti-vivisection will not render such progress impossible in the future. You in this country have been wise; you have not yielded an inch to the false sentiment, the childish credulity, the wicked cruelty of anti-vivisection. We have yielded an inch and they want to make it an ell. Anti-vivisection in England has seriously hindered the merciful work of medical progress and education. Take my advice, the only advice I dare give you, and use the whole of your resources to prevent any such interference with your liberties.

HUMAN PHYSIOLOGY

In spite of their necessity in the analysis, there are certain fundamental objections to and difficulties about experiments on animals, difficulties due to the fact that the animal is not a willing and conscious agent in the experiment, objections which can be avoided only by observations made on man. It is strange how often a physiological truth discovered on an animal may be developed and amplified, and its bearing more truly found, by attempting to work it out on man. Man has proved, for example, far the best subject for experiments on respiration and on the carriage of gases by the blood, and an excellent subject for the study of kidney, muscular, cardiac and metabolic function. Apart from observation of the behavior of man experimented upon by disease, it is often possible to subject a healthy man even to quite extreme conditions without lasting injury. Moreover, experiment on man has the great advantage that it often leads directly to the kind of application which is required in medicine. Experiment on man is a special craft requiring a special understanding and skill, and "human physiology," as it may be called, deserves an equal place in the list of those mainroads which are leading to the physiology of the future. The methods, of course, are those of biochemistry, of biophysics, of experimental physiology; but there is a special kind of art and knowledge required of those who wish to make experiments on themselves and their friends, the kind of skill that the athlete and the mountaineer must possess in realizing the limits to which it is wise and expedient to go. Experiments on animals have generally, for the sake of safety, to precede experiments on man; but until a truth which has been discovered, or hinted at, by other methods has been applied to man, it has not really, so to speak, attained its majority. This is the branch of physiology specially applicable to medicine and there is need in our schools of a special place for human physiology.

This experiment on the teaching of human physiology is being made in England, and it is a delight and encouragement to find how extensively it is being made here too. At Manchester some four years ago, during the reorganization of the medical school, histology was transferred to the department of anatomy and physiology was subdivided into three subdepartments of chemical, experimental and human physiology. The last named subdepartment, under my colleague, Dr. F. W. Lamb, provided a most interesting experiment in the teaching of physiology. From the day when the students arrived in the department they were instructed in the art of making experiments on themselves and others. I shall long remember the pathetic sight, on the first afternoon of the session, when thirty or forty students would be struggling with a needle to extract blood from their own, or preferably from someone else's finger!

The number of experiments that can be performed is very large—the ordinary circulatory and respiratory phenomena of course can be exhibited, the properties of blood, the characteristics of muscular exercise, the facts of vision, hearing, touch and balance and the reflex mechanisms of the body. Sometimes indeed an unrehearsed incident may add to the instruction, as when an injection of adrenalin was given to a subject who proved to be suffering from hyperthyroidism.

A further object of the scheme was to induce the students to study the range of normality in presumably healthy people, by a collection of ordinary data from a large number of their fellows. There is nothing necessarily abnormal in a pulse rate of 40 or in a pulse rate of 90, in a resting man. It is so often assumed, because the average pulse rate is 78, that any wide divergence from 78 is "abnormal." The students were persuaded also to collect the data of observations made on themselves, in the hope that thereby they might be induced to see that, in their own bodies, they possess—immediately available—some of the finest experimental material. By such means they could be induced to "think physiologically" in terms of a healthy working organism, to acquire confidence in making experiments on themselves and others, a necessary preliminary to successful experiment (for all treatment should be regarded as experiment) on the sick.

It is not necessary—I should be ashamed—to excuse this human physiology on the grounds of expediency. Perhaps a generation ago such excuses would have been necessary. To-day the physiology which can be done on man is just as good and just as scientific physiology as can be done on a lower animal or upon an isolated organ. It is just as notable for the precision and beauty of its results.

The experiment made at Manchester was more than justified—it was a palpable success. It is an encouragement to find the success attending similar experiments in your schools. One had only to examine the note-books kept by the students (not by one or two, but by nearly all) of their course in human physiology —note books sometimes almost like text-books in their completeness—to realize that the course certainly had achieved its object of making the students think of physiology in terms of man, and of man in terms of physiology. One had only to talk to the students themselves about it. It is early yet to see its result on the younger generation of medical men in Manchester; but I may be forgiven for hoping that this course will prove one of the important factors which may make the medical education in that school second to none in Britain.

Some day we hope to adopt a similar course at University College; at present we are prevented from making this change (among others) by the examination system pertaining in the University of London. Medical students are overburdened people and if they can not be examined in a subject nothing short of a miracle will induce them to study it. At present, under an antiquated system, our students are examined in enormous numbers in another laboratory, often inadequately equipped, where little but the ancient rites pertaining to frog's muscles can be performed. Until we are able, under some more rational system, to examine our own students and to take account of their work throughout their course, it will not be possible to try this excellent experiment fully in London. I commend it, however, to those of you who are free agents.

Quite apart from direct physiological research on man, the study of instruments and methods applicable to man, their standardization, their description, their reduction to a routine, together with the setting up of standards of normality in man, are bound to prove of great advantage to medicine; and not only to medicine but to all those activities and arts where normal man is the object of study. Athletics, physical training, flying, working in submarines or coal-mines, all require a knowledge of the physiology of man, as does also the study of conditions in factories. The observation of sick men in hospitals is not the best training for the study of normal man at work. It is necessary to build up a sound body of trained scientific opinion versed in the study of normal man, for such trained opinion is likely to prove of the greatest service, not merely to medicine, but in our ordinary social and industrial life. Haldane's unsurpassed knowledge of the human physiology of respiration has often rendered immeasurable service to the nation in such activities as coal-mining or diving; and what is true of the human physiology of respiration is likely also to be true of many other normal human functions.

Experimental Biology

We have spoken hitherto of four well-defined tendencies. There is another, a fifth tendency, not so obvious in England, but more obvious in this country, which is just as certain, I think, to make itself felt. To me it seems obvious that in the future zoology must inevitably look to experimental methods to amplify its fields. Call it experimental biology, or general physiology, or what you like, it may not have its home in an institute of medical sciences, but it will be physiology none the less. Just as biochemistry is, or should be, good and scientific chemistry, even though it be not studied in an ordinary chemical laboratory, so zoologists may find themselves adopting a special type of physiology, applicable to their special problems; and this will be, or should be, good physiology. Hitherto zoology has been largely concerned with following out the implications of the theory of evolution mainly, if not exclusively, by observational and morphological methods. Botany, on the other hand, has long recognized a special branch of physiological botany. In this respect botanists perhaps have been fortunate, since we so-called physiologists have not stolen the most interesting side of their subject from them! Physiologists deal with the physiology of animals, but only occasionally with that of plants. We are often, however, very ignorant of zoology, and the study of animals and of animal cells from the comparative physiological and functional standpoint has been largely neglected. Simply from the point of view of expediency, that of finding more suitable animals and cells and functions for our study, it is urgently desirable that physiology should be in close touch with zoology. Quite apart from that, however, physiology has to offer, in its greater elasticity of technique, a whole new armory of weapons to the zoologist by which to pursue his own proper studies. It is obvious that the evolution and synthesis of function are of far greater interest and value than those merely of structure. One can look forward to the day when a closer and growing cooperation will exist between physiology and zoology, by which advance on such lines may be assured.

The Synthesis of Function

I have just spoken of the synthesis of function. Up to comparatively recently the tendency of physiology has been rather towards analysis, and some physiologists have tended to forget the existence of the animal as a complete organized whole. If analysis be necessary, so resynthesis is also necessary. Perhaps the study of zoology by physiological methods, or of human physiology, may help to correct this tendency. The physical and chemical analyses of a painting reveal nothing but paint and canvas; yet it is obvious that something besides paint and canvas go to make a picture. The pure chemist and the pure physicist are often singularly ignorant of biology. They can not fit the living creature into their scheme of things and they tend sometimes to hypnotize themselves into the belief that scientifically speaking no account need be taken of it. It is perhaps worth emphasizing, therefore, that until a physicist or a chemist has learned something about the way in which animals or cells evolve and grow and behave, he has missed a large part of the natural universe. It is true that biologists should have passed through the fire, should have been hardened by the exact sciences. A physiologist without such training is only half-educated, apt to be "woolly headed" and diffuse, unacquainted with the background against which the events of life are played. A physicist or chemist, however, who is totally ignorant of biological truth, unacquainted with the biological standpoint, is equally only half educated. If and when a student of the exact sciences comes to physiology, he can produce results of service only if he be ready to adopt for awhile another standpoint and to regard life from the biological aspect. For that reason, just as one should welcome any tendency for future students of biology to study rigorous theoretical mechanics at school, and physics and chemistry at their university, so one would welcome—if one met it—the converse tendency for all students of the so-called exact sciences to study for awhile at least one biological subject. The principles of biology are as certain as those of physics, the hypotheses are no more strained, the generalizations are just as great landmarks of human achievement; and as the study of the exact sciences may make a biologist less "woolly-headed," so a study of biology may make a physicist or a chemist less inclined to be too certain of the complete objective existence of all he sees, or thinks he sees, perhaps more humble and more liberal in face of the great mysteries of the universe.

Examinations

You will see that I make no small claims for physiology: unfortunate, however, the student who has to face an examination in all these aspects of the subject. He will have but little leisure—which will be a pity since medicine requires sane and healthy men, hardened indeed by work, but tempered by play. In many professions or services one finds promotion by merit. In the faculty of arts, where there is no laboratory work, such promotion may be difficult. In a subject taught practically in a laboratory, by several teachers, with proper records kept in note-books and attendance-sheets, the difficulty may be discounted. The abolition of the present preposterous and inhuman system of continual preparation, for artificial and often external examinations, in favor of some better arrangement, would seem to be the only way of avoiding an overburdening of our unfortunate students. You are free in this country to develop your own institutions, to make what experiments you like. Progress in education, like progress in science, demands experiments; broad and courageous experiments unhampered by the objections of those who hate to make an extra effort.

ANATOMY

I have spoken so far only of positive tendencies. There are certain negative ones which are emphasized in the organization of University College and depend upon the future of anatomy in England. These tendencies are even more obvious in this country. By an accident in British science, histology—the microscopic study of the web structure of the living tissue—has been associated with physiology. Just as a physiologist needs to know at least a modicum of physics and chemistry, so he must (or should) have an equal knowledge of anatomy and histology. These sciences, however, are not his proper job, and it is no more disgraceful for a physiologist to be ignorant of the distribution of the cutaneous nerves to the hand than to know nothing about the physical chemistry of interfaces. Histology, logically and naturally, belongs to anatomy and outside Britain it has usually been taught and administered by anatomy. Manchester, University College and to some extent Guy's Hospital, are at present the only places in England where this is recognized, and although many still shake their heads over these dangerous doctrines, I feel convinced that the time is not far distant when their example will be followed, more or less universally, so far as administrative conditions allow. There are several advantages in the surrender of histology to anatomy, though there is little need to argue them here. First, the new type of physiologist is apt to be so busy about other things that he tends to give inadequate care and interest to histology. Secondly, the new type of anatomist, the type which physiologists are singularly fortunate to have as colleagues, is one who is more interested in the structure of the living body than in the dissection of the dead one. The anatomy of to-day and of the future, in its scope and its technique, will be much the same as classical experimental physiology. Anatomy, in its problem of the structural synthesis and analysis of the living body, is bound to use a physiological technique, and one form of that technique namely, histology, which logically seems to belong to anatomy in any case, it would appear wise and just to link formally with anatomy in our schools. In the past, owing to the fact that an experimental or operational technique has been employed in elucidating the structure of such organs as the central nervous system, these also have been subjects dealt with by physiologists. The object of their studies was often of an anatomical nature, and now that some anatomists are ready to employ experimental methods, it would seem natural to relegate this portion of anatomy also to their care and to retain in physiology only such parts as relate to the actual working functions of the nervous system. It is no more disgraceful for a physiologist not to be an adept at remembering the contortions of the tracts in the nervous system than to be unacquainted with the laws of chemical dynamics. This redistribution of duties and objectives is likely to react favorably on both sciences and especially in the common ground of neurology. The working out of a real and wholesome cooperation between anatomy and physiology is, I think, likely to prove another—and not the least significant—of the great mainroads towards the future state of our common subject.

ORGANIZATION

Such then are the tendencies of physiology; whither will they lead? It is not altogether easy to predict. Biochemistry will undoubtedly expand to embrace large branches of chemistry; human physiology will stretch out its tentacles into hygiene, physical training and the study of industrial conditions. Anatomy and zoology will embrace large branches of the older classical physiology. Neurology will join hands with anatomy on the one side, and with experimental and observational psychology on the other, in the study of animal behavior and reaction. Zoology, biochemistry and physical chemistry will cooperate in studying the factors underlying reproduction and growth. One trembles rather to think of it all. There would seem little chance of the pretensions of physiology being too small, the difficulty will be rather to keep them within a reasonable compass. As soon as the business of a department becomes too large, it tends to cramp individuality and initiative and to adopt the methods of bureaucracy.

You in this country with your enormous and growing departments of medical science can never feel the freedom which we used to enjoy in the great days at Cambridge (not indeed so long ago) when Barcroft worked behind a green baize curtain in the passage and Hopkins, Lucas, Adrian and I lived together in a coal cellar; those days however have gone, for us as well as you: the war, and very necessary organization, have made them a thing of the past.

These groups of sciences are becoming in a small way like government departments, great and ugly and unwieldy things, but still necessary if the scientific community is to be served. The pleasant old days when a single man, a man like Michael Foster, could teach and lecture, write and be an authority on the whole subject, are going, if indeed they be not gone. The death of Bayliss, whom we mourn in London, has removed one of the last landmarks in that personal, individual aspect of our science. In our laboratory arrangements, in our teaching and research, in our literature, in our connections with workers in other laboratories and lands, we are becoming socialized, organized, administered. There would seem to be no alternative—it is better at any rate to be organized than to be disorganized. The chief objection, however, to organization and authority is the moral and intellectual effect which they may have upon those who use them. In a mass of detailed work a man may forget the more distant, but the real objects of his existence. It was very hard for the staff officer in the war to realize that he, in his administrative capacity, was the servant and not the master of the regimental officer. Authority, the habit of making arrangements and giving orders, lends a false impression of moral and intellectual superiority. The regimental officer in science is the man who is teaching, researching, advancing his subject. The professor, the head of the department, is useful as such only so far as he can be of service to him, can study his needs, and by the special sources of information and the special powers at his disposal, advise and help and coordinate his assistant's labors. This organization is inevitable, in larger or smaller units; we must recognize it frankly and submit to it; and one of the great questions of the future, especially perhaps for you with your faith in organization, is whether organization shall dry up the fountains of originality, or whether, with proper and reasonable precautions, originality and vitality can survive. Team work must be planned and made, but at the same time the opportunity must remain for that free and unfettered originality which our older and less business-like methods evoked. The good and business-like people, those whose childhood and youth were respectable and law-abiding and above reproach, fit so nicely into an organized scheme; yet the wicked and unbusiness-like—those whose childhood was a revolt against discipline and authority, whose manhood may be a fight against preconceived ideas and traditional errors or shortsight—are so often the ones whose gifts produce the real and material advance. In our arrangement of team work and of administrative control, in our centralization we must leave a place for the heedless person, who embarks on science as an adventure of the spirit. How can we do this? By demanding for physiology its proper place—a place as a science, a place in a philosophy of life. It is the vaguer things which claim the more adventurous minds. It is the adventurer who brings new facts and methods and hope to his more reasonable brothers. He may be wrong—he very often is—but he catalyzes the reactions of the rest, he produces reactions, where otherwise the energy may be large but the velocity is certainly small.

Discovery and Adventure

Scientists in the past have often been too ready to indulge in cheap philosophy. Life is not simply the motions of molecules, or even of atoms and electrons, governed merely by the laws of chance. No monist theology, such as that of Haeckel and Ostwald, in which God is replaced by Energy, gives us any new clue to the mysteries that pervade the universe. In science progress comes, as in everything, only by hard work, tempered by courageous imaginative thought. There are many difficult and fundamental problems to which physiology demands an answer. These are the problems which draw the finest intellects; to these problems we must continue to insist that physiology has a right. The age-long dispute between "vitalism" and "mechanism" may seem to serve no purpose. The unsolved problem of the complete applicability of mechanics and thermodynamics to all the processes of life may remain unsolved. The ultimate dependence of mind on nervous system, of specific biological character on specific chemical structure, may remain unproved. The paradox of apparently purposeful evolution, and the anomaly of useful adaptation, in an otherwise physical universe, may remain outside the scope of exact science. Yet all these things continue within the range of physiology and it is our duty to investigate them and our privilege to ponder over them. They add the rosy tint of adventure to the cold light of organized research. They may seem useless—many of the best things in life are "useless," in the sense that they produce no immediate return—but only so far as physiology insists on investigating, when it desires, apparently "useless" things, and so of entrapping those rarer intellects, which can catalyze the energies of the rest, only so far can physiology attain to new and unexpected truth and survive the weight which its necessary organization inevitably imposes.

The future compass of our subject, therefore, is the study of the mechanism of life in any form and by every means and device which science offers. We shall need organization, we shall need team work, we shall need the resources of business-like methods and of competent leadership; we shall require the help of every art and science; and to some of them, especially to medicine, we shall count ourselves happy if in God's good time we can bring something in return. But more than all things we shall need, indeed we must insist on retaining, freedom; liberty to research on things because they are of interest, because their study and investigation are an adventure of the human spirit, because they would seem to lead towards a solution of those fundamental problems which man, in his intellectual impudence, believes to be soluble.

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ON THE CONTROL OF THE RAT POPULATION

ASSUMING that one pair of wild Norway rats begins to breed at four months of age and produces four litters at intervals of four months between litters, and that each litter consists of six young—three males and three females—and further assuming that all the pairs of young breed in a like manner through successive generations, Professor George Gailey Chambers, of the University of Pennsylvania, has computed that at the end of ten years from the birth of the original pair, the progeny would be represented, approximately, by the number 2.3×10^{18}. This is 2.3 times one million to the third power—a number itself well-nigh incomprehensible, though amusing to play with.

If, under the same conditions computation is again made—but this time only for three years—it appears that at the end of three years there would be some 516,000 individuals. Thus, while there were two rats at the beginning of the period, there would be at the end, over 500,000, and this in three years. Such results serve to show how rapid the increase might be.[1] For obvious reasons these computations, which purposely exclude all consideration of postnatal mortality, can not be controlled by direct observations.

Bearing on these computed results, there are, however, some laboratory records which are illuminating. In 1919 Miss Duhring, who is in charge of the albino rat colony at the Wistar Institute, obtained, in 16 months from the birth of the original pair, 3,800 individuals, all the descendants of one pair of albino rats. Moreover, this result was obtained, although after the first litter of the original pair—the pairs were not mated until they were four months of age and in the later months of the period—several hundred rats were not allowed to breed at all owing to lack of cage room.

Under the conditions given for our first instance only 512 Norway descendants were to be expected at the end of the first 16 months. These observations on the albino variety show, therefore, that the conditions set for the computation in the case of the Norway are conservative, since direct observation here gives a number of albinos more than seven times that computed for the Norway.

The high numbers for the albino rat were the result of large numbers of litters from a single pair: a shortening of the time between litters, frequently to 30 days or less—and large litters—many containing 15 or more individuals. The mortality was, of course, very low. The causes for these conditions leading to rapid increase were good food, the absence of external parasites; careful handling and some exercise in the revolving wheel. Among these influences the absence of parasites and the good food are of special importance.

We may estimate the rat population of the United States at present as 120 millions. This estimate is admittedly liberal.

Under the conditions given for our first instance this number, 120 millions, would be somewhat surpassed by the progeny of one pair in four years and four months.

The Norway rat has been in the United States for at least 150 years and since, after this long lapse of time, it is estimated to number only 120 millions, it has clearly failed to live up to its reproductive potentiality as computed, for to obtain 120 millions from one pair in 150 years would require doubling the population only every 5.8 years.

To explain this slow rate of increase as compared with that to be expected from the foregoing computations we must choose between a very high postnatal mortality and a greatly restricted reproduction. Without presenting a detailed argument we can, I think, fairly conclude that the difference depends mainly on the restricted reproduction. Under the conditions in which the wild Norway usually lives, the enormous numbers, as computed, are never born.

As recent laboratory studies show, it is by food that the rate of reproduction is largely controlled. Where suitable food is plentiful reproduction is active—a relation illustrated by the abundance of rats about granaries, slaughter houses, on the water front of

[1] Previous calculations of the reproductive powers of the rat—some of which give enormous numbers—are presented by James Silver, on page 66 of the *Journal of Mammalogy*, Vol. 5, No. 1, February, 1924.