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## Recent Advances in our Knowledge of the Bodily Functions

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THE PRESIDENT:—Gentlemen, I shall not embarrass Dr. Best by attempting to add another eulogy to the world-wide tributes which were paid to him and Dr. Banting, following their very important discovery a few years ago. Their work brought great distinction both to themselves and to the University of Toronto. Nor is it necessary to introduce Dr. Best, indeed it might be regarded as an impertinence for an ordinary annual member of the Club to introduce an Honorary life member. It is enough to say that we appreciate very much this opportunity of hearing the Professor of Physiology in the University of Toronto. The subject of his address is recent advances in our knowledge, (that is to say, in the knowledge of pathologists) of the bodily functions. Dr. Best.

DR. BEST:—Mr. President and gentlemen, there are several reasons why I am pleased to speak to the members of the Canadian Club today. I would like to take this opportunity to thank you for the honorary life membership which was conferred on me some six years ago.\* The subject which I am taking today is one in which I am deeply interested. Knowledge of bodily functions is of course knowledge of physiology. Physiology is the study of functions. In its broadest sense it includes the study of the activities of all forms of life and their adaptation to their environment. In a more restricted sense you might define it as the study of the functions of the body, the allocation of each function to the proper organ, the correlation of these activities and their control by nerves, chemical,

\*On the occasion of the *Insulin* meeting, March 5, 1923.

or other means. Some of us study physiology on the uni-cellular organisms. It is surprising perhaps that the rate of penetration of carbonic acid into the cell of uni-cellular organisms should have a practical relation to respiration in man. Distinguished scientists say that carbonic acid penetrates much more easily than other acids of the same strength, and this result enables the physiologist to explain why the carbonic acid of our blood is one of the main stimulants of respiration and penetrates to that little center in our brain from which all the respiratory movements are controlled. Most of us confess, however, that we prefer to work on the higher forms of life; but whether we work with uni-cellular organisms or on the higher forms all our experiments have as their fundamental object the alleviation of human suffering.

Physiology is enjoying a popularity today such as it has never had in the past. Indeed the science is growing so rapidly that it is threatening to break up into subdivisions. Advances in physics and chemistry are being applied with great rapidity to the knowledge of the functions of the living body. At the international Physiological Congress held in Boston last summer physiologists from more than forty countries were present. After the Congress one hundred and sixty eminent physiologists representing twenty-one different countries came to the University of Toronto and spent several days looking over the laboratories. We are very happy that the English school is maintaining its lead in the study of physiology. But other countries are pressing it very closely and wonderful contributions are being made from all parts of the world.

It was interesting to hear some years ago at Stockholm the views of an eminent English professor of Physiology as to the reasons why various nationalities were interested in physiology. He thought that the Italians were interested in the science because of their love of what is beautiful. It is difficult to imagine anything more beautiful than the movements of the delicate valves and veins which permit uninterrupted flow of the blood to the heart but resist any flow in the opposite direction. Or the movements of the valves in the heart itself, or the opening of millions of air sacs in the lungs, or the distribution of blood-vessels in the

muscles. He thought it interested the Germans because of the opportunity to arrange their facts in martial array and it is true we learn a lot by statistical methods of approach. The French interest, he said, comes of their love of excitement. It is difficult to imagine anything more exciting than waiting for the results of some properly controlled and extended experiment in physiology. And the British scientists he thought were interested because it is the greatest game in the world.

And it is a wonderful game, full of pitfalls for the unwary who seek to solve its mysteries, (a good reputation is easily ruined by making unwarranted deductions from physiological data). It is full also of wonderful satisfaction. Perhaps there is no greater satisfaction than the establishment of some new fact. It is possible that satisfaction is a little greater if one sees an immediate practical application of this fact through the preservation of health or the alleviation of disease. But one may rest assured that even though no practical application is apparent, this fact will play its rôle some day. I might take all my time in discussing any one of the scores of aspects of this subject, but I have decided to treat very lightly a number of aspects.

If we consider for a minute the muscular system, which comprises roughly half the body weight, we know the muscles are made up of thousands of little fibres, each of which has its own blood supply, its own nerve. Inside are little fibrilles which are units of the contracting mechanism. It is surprising, that such a relatively soft structure as muscle is capable of such tremendous force. If a man of two hundred pounds is able to raise his body on a horizontal bar, his muscles are working at a mechanical disadvantage of ten to one, which means the force of his muscles is something over a ton. We find their rates of movement differ greatly. The muscles which control the eyelids have very rapid contraction while the muscles which force food out of the stomach have a slow rate. But for wider contact we have only to look at the lower forms of life. The muscles which close the shells in certain forms require a minute or more to contract or release, but the muscles which activate the wings of a wasp contract and expand 18,000

times a minute. When we study the chemical change which goes on in muscles we find that during muscular contraction there is little utilization of protein or fat but there is a great utilization of a complex sugar. This sugar is broken down during the muscular action and built back again during the period of relaxation. This does not mean that the diet of an athlete should consist largely of sugar. The diet of an athlete should be balanced in much the same way as for a sedentary person. The amount may be increased depending on the amount of energy expended. Examining the muscles of an animal at the end of a long run we find there is no depletion of fat or protein but in many cases there is definite loss of sugar.

At the Olympic games at Amsterdam in 1928, ten Marathon runners presented themselves at the laboratory at the end of their twenty-six weary miles, a fair part of which was over the cobble stones of Amsterdam. These runners submitted their blood and on analysis we are able to demonstrate that in three cases at least the blood sugar concentration had fallen to a very low level and this was undoubtedly one of the factors which produced the condition in which they were. We found that those who carried sugar during the entire course, or had it given to them, were not suffering from this complication.

It has been demonstrated that the speed of a runner is the result of two things; the force he can exert which is dependent upon the strength of his muscles and their arrangement, and the friction in his muscles. This latter holds him back. A man may be a good runner because of great force or because of the small resistance in his muscles. It is possible to determine both these factors by the same method that was used in the war in determining the velocity of shells. It was hoped to carry out this investigation at Amsterdam but that was found impossible.

However when the fastest male runner and the fastest women's relay team came back to Canada, with the co-operation of the several authorities and the Connaught Laboratories it was possible to conduct experiments here. The results in a word are these. It was shown that Williams was a phenomenal performer, not because he could exert a larger portion of his body weight as force

but because the resistance in his muscles was less than that of other people. In the same way it was shown that the members of the girls' relay team were not exerting a very large proportion of their body weight as force, but for the first time it was demonstrated that the resistance in the stretch of their muscles was very very small.

Now if we turn to the nervous system, results of even greater importance have been obtained. The nerves are made up of little insulated fibres, some adapted to the carrying of impulses. The investigation of the nervous system has been greatly facilitated by the use of amplifying systems such as we use for radio reception but the system we use in the laboratory amplifies these small changes to a much greater extent than ordinary receiving sets. If a small apparatus which consists really of two wires is placed on a nerve it is found that during quiescence there is no disturbance of the amplifier; but when impulses are sent along this nerve, they can be led off to the amplifier, recorded as sound if necessary, or recorded on a phonographic plate and studied at will. There are a number of fascinating things which have arisen from this study. Suppose we put this little apparatus on the optic nerve inside the brain and shield the eyes from light. It has been done many times. Then there is no disturbance of the amplifying system. But when we remove the shield from the eyes, a tremendous volley of electrical changes passes along the optic nerve and by processes about which we know little they are changed into the sensation we call vision.

An even more interesting thing has been developed recently by an English physiologist. They have placed this little electrode consisting of two small wires on a nerve which contains fibres, coming from two end organs, one in muscle which may respond to temperature changes, the other a tactile organ, say, the skin. Then this main nerve carries stimuli from these two sources. If the muscle is stimulated a very characteristic set of waves pass up the main nerve and can be recorded and studied by the amplifying apparatus. When the other end organ in the skin is stimulated, another perfectly defined and characteristic set of waves pass up this nerve, but they are different from those that come from the muscle. The sense organs in our bodies have the power of

sending a code to the brain. This is a very phenomenal development in my opinion. It requires little imagination to think what we may learn from it. What will happen when we place these electrodes in the vicinity of the higher centres? If we place this little electrode on the nerve going to the chief muscle of respiration, we find every eighteen or twenty times a minute a series of impulses are sent down. In the same way in the nerve going to the heart we find impulses are being sent down. This amplifying system has yielded a great many very important results.

This brings me to a short consideration of some facts on physiology in the circulation. This nerve that goes to the heart lies in the neck just under the large artery, if it carries stimulants to the heart the heart is stopped. Now it is possible, as many know, to stimulate that nerve in the neck of a man, and this is said to become the procedure in certain Oriental treatment, in jiu jitsu methods. If this nerve is stimulated we have reason to believe it liberates a chemical substance in the heart muscle. Nerve stimulation liberates a chemical substance which acts on the heart muscle. This is fascinating. It brings the whole thing a little nearer to us. It was difficult to understand how nerve muscles could cause contraction of the muscle of the heart but when it is shown that this impulse may liberate an active chemical substance it makes the whole situation a little clearer. What a wonderful little pump the heart is! It weighs less than a pound, yet during severe exercise it is capable of pumping fifteen or sixteen gallons of blood a minute. Those of us who reach the age of sixty or sixty-five have hearts which have pumped well over fifty million gallons of blood. Not a bad performance for a small pump.

I should just like to say a few words about the other end of the circulation, capillary circulation. If we look at a muscle when it is quiet it may have seven or eight little capillaries open, and there are many records of the passage of the red blood cells through these little capillaries. A good deal has been learned about the circulation by making moving pictures of this phenomenon. We find if this muscle is excited it begins to contract vigorously and the same area may have hundreds and hundreds of blood vessels open in the same time, thus permitting the blood cell to get rid of its load of oxygen.

Now just a word about respiration. I mentioned that carbonic acid is a very efficient regulator of our breathing. If even a slight change occurs with the concentration of this gas in our lungs, the respiration may be doubled or tripled. Even though we breathe fresh air in and out, there is a very large volume in our lungs it prevents any rapid change in the air which comes in contact with the lung surface. In spite of this wonderful mechanism for control, if we wish to send impulses to our lungs from the brain, we can upset the thing very easily. If you merely breathe vigorously for a short time, you can breathe out this acid to such an extent, that your heart begins to fail, your blood pressure falls, and in four or five minutes you become unconscious. This has often been demonstrated to medical students. The moment they become unconscious the reflex is broken, and they are saved. The lungs are composed of millions of little air cells which if spread out would occupy from ninety to one hundred square yards of surface. This must be so, because of the volume of the blood, during exertion, circling four and five times a minute through these lungs and each of the twenty-five billion little red blood cells must be exposed to the air.

Now I am going to speak for a few minutes about the glands. If we take for instance first the little pituitary gland, a puny thing which nestles deep in our brains, we know this can produce chemical substances which control bodily functions. We can make an extract of the interior portion of this gland and feed it to animals and produce healthy animals nearly double the size of the ordinary type. The posterior part of this gland, we have been accustomed to think, contains one chemical substance; but quite recently in a series of brilliant investigations it has been shown these different functions are produced through the agency of quite different substances, one of which is able to produce contraction of the muscle of the stomach or bladder, another regulates the flow of water from the tissue through the kidneys, while another has another function not very well understood as yet.

Now as to the thyroid gland. In certain cases where there is failure of growth, failure of mental development, these can be corrected in a most wonderful way by giving

these substances derived from the thyroid in the diet. There is probably no more wonderful transformation than that produced by feeding a little of this thyroid gland to a child born with a deficient amount. A well-known English chemist has produced the chemical substance responsible for this in crystalline form, and a small amount of this substance produced the same effect as the administration of the extract from the gland. We also know in many cases there is an excess of this substance produced in the thyroid, and this results in loss of weight. These conditions can be produced and studied in laboratories. The parathyroid glands have important effects and were long confused with the thyroid.

I could say a great deal about the internal secretion of the pancreas. Since original publication in February, 1922, between four and five thousand articles have been written from all parts of the world on the subject of insulin. Publications are appearing at about the rate of a thousand a year; and it requires secretarial assistance to card-index and tabulate this literature on this one subject. In 1922 it was very difficult to make more than twenty or thirty units of insulin a day and the cost of production in the Connaught Laboratories was about one dollar per unit. The other day in looking over the production of insulin in the Connaught laboratories, the director of which, as you know, is Dr. Fitzgerald, I was investigating a lot of from twenty to thirty million units of insulin, which represented the production of the laboratories for a period of several weeks. The active principle responsible for the antidiabetic activity of insulin has been obtained in crystalline form. It is probably a very distinct chemical substance, the exact nature of which we don't know as yet. This work was done originally by a Professor Abel, a chemist of Johns Hopkins University, and more recently was confirmed by an English chemist working in collaboration with one of the chemists at the Connaught Laboratories.

The little gland above the kidneys contains a substance of great physiological interest. If you prepare this substance and inject it into an animal all the reactions which the animal would have for defence or flight are manifested. If you inject it into a cat the animal at once bares its claws and shows

its teeth and ruffles its fur. All the features of fright or rage can be produced by the injection of the active principle of this little gland above the kidneys. Perhaps this is not the only mechanism, but it is interesting and of great importance that an extract of this gland can raise blood pressure, accelerate the heart, and increase the blood supply to the muscles.

I am going to take the few minutes left to consider very briefly some of the recent advantages we enjoy from study of the central nervous system, the higher cells of the brain. A great deal of evidence is obtained by psychologists on this aspect of the subject. They depend upon subjective sensations. The physiologist is not satisfied with this type of approach and depends upon the objective. Both the biologist and psychologist will say that ultimately it will be possible to explain many of these psychic phenomena on definite physiological bases. The physiologist who has contributed most in this subject is Ivan Pavloff, who has worked for many years at Leningrad. Pavloff is now eighty years old. He continued his work through the Russian revolution. He has been a very severe critic of the Soviet Government but in spite of that they have encouraged his work, but have made it impossible for him to leave the country for more than a very limited period of time. Pavloff's method of approaching this very intricate subject has been by the study of what we call "conditioned" reflexes. In order to establish conditioned reflexes it is necessary to have present the higher cells of the brain. We have all kinds of the other type of reflexes over which we have no control but during the course of months certain new reflexes which depend on the higher senses may be built up. Suppose we present food to a laboratory animal, a dog. There is an immediate secretion of saliva. If this little duct which runs from the gland to the mouth is exposed, we can record and tabulate the flow. If, at the same time the meat is given to the animal, a light of a certain color is shown in the room, for instance, a blue light, then, after a number of experiments, the animal not only reacts when the meat is presented, but, if the blue light is flashed, there is an immediate secretion of saliva. It will not react to another colored light, but has formed a definite reflex to this light. The same

thing can be done with all types of other animals. If a certain part of its body is stimulated, it develops this reflex. If a tuning fork is sounded it develops the reflex and will not respond to a sound of any other pitch. If that type of cell in the human being or animal which is responsible for interpreting the impulses which go along the optic nerve to the brain is destroyed, if these higher centres are interfered with in any way, the animal can still see, but it is impossible for it to distinguish between objects. It still can tell the difference between darkness and light and avoid objects, but can no longer recognize people with whom it was familiar. The psychologist would say the animal sees but does not understand. The physiologist, as a result of definite experimental efforts, states the lower centres in these subjects' brains are still functioning, it can still see, but because the higher centres are gone, it has lost the power of analyzing stimuli. That is only an illustration. There are all kinds of types, and the different areas in the brain are associated with these different types of phenomena. A great deal of the brain has already been mapped out and we know what parts are responsible for the association of certain ideas. There still remains, however, a great uncharted area in the frontal hemisphere which is as yet unexplored.

I am afraid I have used a great number of technical terms. If, however, I have been able to show you that well-planned, adequately controlled, series of experiments in this field are leading to interesting results, I am satisfied. The physiologist believes as some one has said that the advance of our science is limited not by nature's unwillingness to reveal but only by man's inability to comprehend.