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## THE ACTION OF REMEDIES IN DISEASE.

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GENTLEMEN,—The Section whose work we inaugurate to-day is devoted to the subjects of *Materia Medica* and Pharmacology. The occasion of our meeting is one on which we have every reason to congratulate ourselves. The International Medical Congress meets in this country for the first time, and affords an opportunity which has never before been equalled in Great Britain, for personal intercourse and exchange of ideas between men from every country in which the study of medicine and of the science of life occupies an intelligent position.

The vastness of this study, the many subjects of separate interest which it includes, and the unfortunate limitations in the power of the human intellect, have necessitated its subdivision into many departments, one group of which has been consigned to the charge of this Section.

I have purposely used the word group ; for the title of our Section shows that it embraces not one, but several subjects. The words "*Materia Medica*" no doubt imply a description of the agents used in the treatment of disease ; but this description is not restricted to the physical properties of these agents, it includes also their actions and their uses in disease. The department of *materia medica* encroaches, therefore, on the one side upon the science of physiology, and, on the other, upon the art of treating disease ; while it concerns itself, at the same time, with physics, chemistry, botany, and zoology.

This "many-sidedness" has led to the introduction of special terms applicable to the chief subdivisions, and as each subdivision deals with questions which are distinct in themselves, it has become



individualized not only by a separate designation, but also, in great measure, by forming an independent subject of study and investigation.

The introduction into the title of our Section of the word Pharmacology illustrates the necessity which has now arisen for this subdivision. To this word we no longer assign the old significance which it bore as a mere synonym of *materia medica*. It now implies the science of the action of remedies, and it accordingly deals with the modifications produced in healthy conditions by the operation of substances capable of producing modification. It constitutes the chief basis for the application of remedies in disease, it closely allies itself to therapeutics, and constitutes the most important connecting link between *materia medica* and the art of medicine.

It is clearly appreciated by all who are actively interested in the progress of pharmacology, that it is essentially an experimental science, and that its advancement can be obtained only by the application of the experimental method. This method, indeed, is as old as science itself; and, although it has been the instrument by which all true progress in medicine has been achieved, during a long period in the history of medicine it had been distorted by the importation of metaphysical phantasies, and dominated by the contending theories of the schools. From data of the most insufficient description, theories were involved of wide application; and in no department of medical knowledge was this more strikingly manifested than in pharmacology and therapeutics.

Fanciful resemblances between medicines and pathological products or normal structures were considered sufficient to explain the effects of the medicines, or to indicate the conditions of disease in which they should be applied. The resemblance between the white spots on the leaves of *Pulmonaria officinalis* and the morbid product tubercle, led to the use of this plant in diseases of the lungs: the colour of the common carrot formed an indication for the administration of the carrot in jaundice; and the heart-like shape of the fruit of *Limocarpus anacardium*, and the reniform shape of the fruit of *Anacardium occidentale*, were considered sufficient characters for the administration of the one



in diseases of the heart, and of the other in diseases of the kidneys. The doctrine of "Signatures," which prevailed for many years, and was accountable for these and many other absurdities, now mainly possesses the interest of affording an example of the ever-existing desire for guiding principles in the application of remedies—a desire which found satisfaction also in the systems of Paracelsus, Stahl, Brown, Rasori, and Hahnemann.

These and all other systems that have been propounded erred in the insufficiency of the facts on which they were constructed. The knowledge of the age in which each of them was introduced lent for a time a plausible support in their favour, but it was insufficient to disprove them. Each in turn, however, was discarded as knowledge advanced, and supplied the data required for refutation.

This knowledge was the fruit of observation. In its crudest form observation restricted itself to the noting of the symptoms of disease, and of the changes produced in those symptoms by treatment. It is exemplified in the writings of Hippocrates, Theophrastus, Celsus, and Aretæus; and, in the present day, in the records of so-called experience. The general symptoms of a disease were ascertained, the changes produced by the administration of remedies were observed, and the result was reserved as a guide for the treatment of other cases. An experiment, in fact, was performed, but the experiment was one in which the conditions were complex, and the causes of fallacy numerous.

In the early history of medicine, when the normal conditions of life were unknown, and when the conceptions of diseases were, in most cases, mere fancies of the imagination, erroneous doctrines and applications inevitably resulted from the restricted employment of this method of observation. Even at the present time, its employment is surrounded by difficulties and fallacies of a similar description. Notwithstanding the remarkable advances in biological science that have followed the application of the methods of research inaugurated by Bacon and Galileo, the normal composition and functions of the component parts of body, and much less their abnormal conditions in disease, are in very few, if in any, instances thoroughly understood. The labour



of years has resulted in proving but too distinctly their complexity, and perhaps, above all, in making it apparent that much is unknown. The mere separation of the symptoms of disease from the mental or moral reactions of the individual is, even in many instances, a matter of difficulty. It is far from being an easy task to estimate the effects produced upon the patient by the remedy that has been administered, not only on account of the nature of the problem, but also because of the tendency—too often irresistible—on the part of the observer to confound sequences with consequences. Experience has, in all ages, supplied proofs that the aphorism—*Sublatâ causâ, tollitur effectus*—is in the art of medicine little more than a disappointing mockery.

Thus the experimental method which deals with problems of so great complexity as those with which crude observation is concerned, has failed to produce results which satisfied the generous aspirations that have, at all times, formed the incentive to medical investigation. But a new development was fortunately given to the study of the effects of remedies, by the introduction of an experimental method in which the conditions are more simple and controllable than in those forming the basis of so-called experience. The introduction of this method is due to Bichat, and by its subsequent applications by Magendie, pharmacology was originated as the science we now recognize. Bichat represents a transition state, in which metaphysical conceptions were mingled with the results of experiment. Magendie more clearly recognized the danger of adopting theories in the existing imperfections of knowledge, and devoted himself to the supplementing of these imperfections by experiments on living animals. The advantages of such experiments he early illustrated by his investigation on the upas poison, and, afterwards, by a research on the then newly-discovered alkaloid, strychnia. The results of these researches enabled him to lay the foundation for the doctrine that remedies exert their actions upon special structures; a doctrine which was afterwards further developed and illustrated in the classic researches of his pupil, Claude Bernard.

Magendie's epoch-making investigations inaugurated the present century. The value of this method was quickly appreciated, and



adopted in Germany, Italy, and Britain. It, however, necessitated experiments on living animals, and it is curious to observe that, even in his day, the embarrassments which sentimental opposition has succeeded in raising to the progress of pharmacology in this country, were not unknown in France. To this subject, Claude Bernard makes some reference in the biographical notice of Magendie, which forms the introductory chapter of his work on the "Effects of Poisonous and Medicinal Substances." He there furnishes us with an argument against the views of those who oppose experiments on living animals, which has the special interest of having been written, apparently, chiefly in defence of experimenters in this country, where, as he rightly supposes, prejudices are most strongly developed and stated. As all science must be founded on experiment, so the science of life, he remarks, necessitates vivisection, because the phenomena of life occur only in living beings; but experiments on living beings, governed and inspired by a true scientific spirit, do not deserve the reproach of cruelty, any more than the vivisections of the surgeon prompted by the idea of saving the life of his patient.

On this subject, however, I propose afterwards to make some further remarks; but, before doing so, I would briefly refer to the results that have already been obtained by the experimental study of pharmacology during the present century.

By the experimental method, I do not refer to that which is associated with the name of Hippocrates, which searches for truth by means of experiments of a complicated description, in which the data are in great measure unknown, and almost entirely beyond the control of the experimenter. It would, at the same time, be impossible to deny that by observation of the effects of remedies upon patients, much advantage and many valuable results have been gained. A large number of remedies have been introduced, even though their physiological action was entirely unknown, and several of these yet retain their position as valuable means of treating disease. On the other hand, the greatest number of them have certainly been discarded as knowledge advanced, and not a few retain their position simply because other and more trustworthy reasons for their employment have been brought to light.



This light has been derived from the experimental method, which, while it does not neglect crude observations, endeavours as far as possible to simplify the conditions of the experiment, by using as the subjects of experiment animals in whom the conditions admit of being controlled. A certainty is thus given to the results which could not otherwise be obtained, and applications to disease acquire a prominence which is in striking contrast to the ephemeral and fleeting opinions which are derived from the empirical method. Magendie's research on strychnia may be cited as an illustration of this. He demonstrated the action of this substance upon the spinal cord, by experiments upon the lower animals, so thoroughly, that subsequent investigations have added but little to his results. He also recognised the advantage that might be expected from its administration in disease, and proposed its application in cases of paralysis. This application was first effected by Fouquier, and since that time strychnia has retained its position as a remedy in paralysis.

Since that time also, the method has been applied to the investigation of a large number of active substances, with results of the highest importance to humanity. Rational explanations have been discovered for previously observed therapeutic facts, and it has become possible to apply many known remedies with judgment and confidence. Previously unknown therapeutical actions have been brought to light; and symptoms of disease, which before were beyond control, can now be alleviated by the production of definite remedial actions.

To the members of this Section it must seem almost a superfluous task to recall examples in support of these statements. Let me content myself by instancing merely the action of ergot on the blood-vessels; of aconite, digitalis, and a host of other substances upon the heart; of nitrite of amyl upon the blood tension; and of the large groups of substances which act as emetics, diaphoretics, cathartics, diuretics, and cholagogues. Many of the examples I have cited will be considered with detail in the discussions and papers which are to engage the attention of the Section, and I now do no more than refer to them in illustration of the great benefit which pharmacology, and, therefore, therapeutics, has derived from the adoption of the experimental method.



I may further illustrate the value of the results obtained by this method, and, I may even say, the necessity for pursuing it, by considering for one moment the action of digitalis and of anæsthetics.

The former substance was introduced into practice by Drs. Cullen and W. Thormic. Towards the end of the last century, and therefore, answering to the inauguration of the experimental method, and to the foundation of pharmacology as a science, it was introduced as a remedy for dropsy ; and on the applications which were made of it for the treatment of that disease, a slowing action upon the cardiac movements was observed, which led to its acquiring the reputation of a cardiac sedative. Numerous observations were made on man by the originators of its application, by Dr. Sanders and many other physicians, in which special attention was paid to its effects upon the circulation, but no further light was thrown upon its remarkable properties, with the unimportant exception that in some cases it was found to excite the circulation. It was not until the experimental method was applied in its investigation, in the first instance by Claude Bernard, and subsequently by Dr. Dybkowsky, Pelikan, Meyer, Boehm and Schmiedeberg, that the true action of digitalis upon the circulation was discovered. It was shown that the effects upon the circulation were not in any exact sense sedative, but, on the contrary, stimulant and tonic, rendering the action of the heart more powerful, and increasing the tension in the blood-vessels. The indications for its use in disease were thereby revolutionized, and at the same time rendered more exact, and the striking benefits which are now afforded by the use of this substance in most diseases were made available to humanity.

The introduction of anæsthetics into medical practice has certainly produced more benefit than that of any class of substances. The insensibility which they produce is a condition which can be readily established by the most crude method of experiment, as it requires merely the exhibition of the substance and the observation of the effect ; and this simple process of investigation is that by which their introduction was effected. Following upon this introduction and the wide extension of their employment, however, it was soon found that insensibility was not



their only effect. They produced insensibility, but they also produced other actions, which assumed a grave importance, as they were occasionally sufficient to destroy life. The nature of these additional actions became, therefore, a matter of interest, for upon them apparently depended many questions governing the indications for the use of anæsthetics and the treatment which should be adopted in order to avert or counteract their dangerous effects. No sufficient light, however, could be thrown upon them by the simple experiments which were sufficient to prove that these substances produce insensibility. By observing the phenomena presented by a patient in the anæsthetic condition, the mechanism by which the dangerous effects were caused could not be revealed. It could not even be determined whether death were produced by an action upon the brain, or upon the heart, or upon the respiration. The necessity for extending the investigation of their action to lower animals, in whom the experimental conditions could be controlled and varied, became obvious; and the researches which have already been undertaken by Hermann, Paul Bert, Ferguson, Coates, and McKendrick, have furnished much information with regard to those difficulties that could not be solved by mere observations of effects in human beings. They have provided indications for forming an opinion of the relative dangerousness of many anæsthetics, of the class of cases in which each should be specially avoided, and of the means by which their dangerous actions may be best counteracted; and it is needless to remark that, if results of such importance can be obtained by no other means than by experiments upon the lower animals, the performance of such experiments is an imperative duty.

I have already defined pharmacology as the science of the action of remedies, and pointed out that, like every other science, it must be founded upon experiment; while, from the nature of its problems, the experiments must be performed upon living beings. These propositions are generally recognized by those who are engaged in the study of the means of treating disease; and upon their application the present condition of medical art and science is dependent. Embarrassment and difficulties have, however, been encountered in the application of the last proposition, which, for-



unately, have not assumed an equal importance in every country. In Britain, however, they have assumed an importance which constitutes a crisis in the history of pharmacology. Exaggerated and erroneous statements of the horrors of experiments on the lower animals, and ignorant assertions regarding the history of medical progress, have raised a sentimental clamour before which a representative Government has found itself powerless. An Act has been passed, imposing restrictions of the most harassing description upon those who are engaged in pharmacological and physiological research, and relegating to officials, who are utterly ignorant of the subject, the duty of deciding what investigations shall be undertaken. Under this Act, no one is permitted to perform an experiment upon a living vertebrate animal who is not furnished with a licence from the Home Secretary, who is all-powerful to grant or refuse licences at his pleasure. I need not say that the imposition of the degrading restrictions contained in this Act was opposed by the indignant remonstrances of the profession. It was characterized as unjust to the profession, detrimental to the interests of society, and an obstruction to the progress of knowledge. The Act was, however, passed, and now, according to the law of this country, "any person may inflict any pain, short of torture, on any domestic animal, and any torture he pleases on any non-domestic animal;" but he cannot inflict the most trifling injury upon any animal, whether domestic or wild, so long as his object is a scientific one, unless he is first furnished with a licence.

On the passing of the Act, I believe an assurance was given, by the then Secretary of State, that it was not the intention of the legislature to prevent altogether scientific research by means of experiments upon animals; and this, as well as other assurances, and modifications of the Act, as it was first introduced, had some effect in calming indignation and in lessening opposition. I cannot help thinking that this opposition was too easily lessened, and that the bribe of a few unimportant compromises induced the profession to submit but too readily to the imposition of an unjust Act, which their knowledge assured them could only be followed by injury to medical science, instead of continuing the uncompromising opposition, which was so ably advocated by Mr. Lowe.



Pharmacologists and physiologists have now had some experience of the Act, and I do not think any other opinion will be expressed than that it has impeded the development of their sciences, and rendered the prosecution of these sciences so difficult and harassing, that original investigation is now almost impossible in the country of Harvey, Bell, Reid, and Christison. It is true that, during the first few years immediately succeeding the passing of the Act, some consideration was shown to the interests of science and the aspirations of investigators, for permission was generally given for the conducting of experiments. Legislation, however, originating in hysterical clamour, is not likely to remain uninfluenced by subsequent manifestations of the same disease. There is, indeed, no malady in which firm opposition is more likely to be beneficial, and in which even the slightest exhibition of indulgent compromise is more likely to produce more frequent or more uncontrollable manifestations. The passing of the Act was largely due to compromise; the subsequent history of the operations of the Act proves that, in place of appeasing clamour, this compromise has served as a strong incentive to its continuance. Investigators, to whom the Home Office has afforded the necessary licences for performing experiments, have been assailed with unbridled invective, and influence is brought to bear upon the Secretary of State to cause him to interpret the Act as one for the entire suppression of experiments on animals. How effectively this influence has operated, or how hazardous it is to place the progress of a science entirely at the mercy of a State official, utterly ignorant of its aims and triumphs, is now being exemplified. In several instances in which the objects were of the highest interest, and in which the importance of the results could not be predicted, the Government has constituted itself the supreme arbiter of science, and has ventured to decide that certain experiments were not required, and should not be performed. I do not make this statement unadvisedly. The instances are within my own knowledge; and in one of them I have the best reasons for knowing the facts, as only the other day I experienced the mortification of being refused a licence. In this case, permission was requested for performing a few experiments on rabbits and frogs with a reputed poison used by the



natives of Borneo to anoint their arrows. If this be an active substance, it is impossible to predict what advantages might be gained from its use in the treatment of disease. But, apart from this, it is surely important to discover, in the interest of travellers, whether it really possesses toxic properties, and, if it do possess such properties, what are their characteristics, and what is the best method of counteracting its effects. I am obliged to conclude, however, that those who are now authorized to decide such questions for us entertain a different opinion, and consider that these objects, and the interests of science are insufficient to justify the most trivial infliction of pain upon rabbits and frogs. That the infliction of pain would be only trivial will, I think, be apparent, when I state that the only operation for which permission was requested was the subcutaneous injection of the poison ; for the question of the possible infliction of pain by the action of the supposed poison does not arise, as the substance might, without any infringement of the Act, be placed in the stomach, or in contact with any absorbent surface, provided no wound was inflicted. The absurd position has now been assumed by the State that an operation, implying merely such a wound as can be produced by a needle-point, is not justifiable, so long as it is performed for the purpose of acquiring knowledge, and in the hope of benefiting the human race.

To us the matter bears a most serious aspect. To us it is as clear as the light of day that the action of remedies cannot be ascertained otherwise than by experiments on the lower animals. If this method of research be denied to us, what means are we to adopt for increasing the resources of our art? How are the rich treasures, which the enterprise of travellers, and the never-ceasing discoveries of chemists, place at our disposal, to be applied, as hitherto they have in so many instances been most beneficially applied, to the treatment of disease? How are we to discover antidotes to the poisonous action of toxic agents? Experiments on man with substances regarding whose properties no knowledge exists, will ever be repugnant to medical science ; and on that account, as well as because of their entire insufficiency, they cannot be adopted as substitutes for experiments on the lower animals.



Is, then, the progress of pharmacology to be brought to an end, and the treatment of disease to lapse into the former irrationalism, so distasteful to present aspirations, which are anxiously striving to attain exactitude in the art of medicine?

So far as this country is concerned, this result must inevitably occur unless we obtain our knowledge entirely from other countries, or unless the freedom of research is again asserted among us.

I believe the latter alternative is not impossible to be attained. Much of the clamour that has been raised against experiments on animals is the outcome of erroneous information and sentimental prejudice, and many who are now taking part in this clamour, would cease to do so were their erroneous impressions removed. Let them endeavour to appreciate the problems we have to solve; let them realize the incentives that urge us to increase our knowledge; let them consider that each advancement is a gain for humanity; and in place of lending themselves to obstruction and obloquy, they will repay our exertions with praise.