An Address

ON

CHEMISTRY IN RELATION TO PHARMACOTHERAPEUTICS AND MATERIA MEDICA.

An authorised translation of "*Die Chemie in ihrem Zusammenhang mit Pharmakotherapie und Materia Medica*," delivered at the Eleventh International Medical Congress on Thursday, April 5th, 1894.

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THE TERM AND SCOPE OF PHARMACOTHERAPEUTICS.

"THERAPY" or "therapeutics," by which terms we understand the art of serving the cause of humanity by assuaging human suffering and healing human ill, avails itself of every means in its power to arrive at these ends; *elle prend son bien où elle le trouve*. And the art of therapeutics, like all of us here assembled at this Eleventh International Medical Congress, has discovered that all ways lead to Rome. To Rome therapeutics has come—now in the guise of electricity, now as a water cure, now as psychical influence; so that we here are able to review, as they defile like armies before us, electro-therapy, pneumo-therapy, hydro-therapy, hypnosis and psychic suggestion, and compare their merits as healing agents when placing themselves at our orders to combat disease and put death to flight. But most ancient of all the branches of medical art is that which makes use of drugs; and in the hands of the inexperienced drugs can cause death (*pharmakela*—the use of medicines or poisons), so that the science and art of the introduction of medicaments into the human body with the view of healing it carry with due right the appropriate title of "Pharmacotherapeutics." And at one time pharmaco-therapeutics was the most important branch of the healing art, though in our days it has declined and occupies but a second, or perhaps, I should say, third place. For operative surgery, proud of its victories, and as admired as admirable, full of vigour and sap, has distanced the ancient branch. And, again, we see hygiene, young, fresh, lovely, and assured beforehand of all suffrages, taking its place in the front of all medical science, confident in the future success of its attempts to render the arts of healing superfluous by preventing the malady. Why, then, it may be asked, do I essay to interest you in an art which seems to be growing old under our eyes; whose past, it is true, is very honourable, but whose future hardly seems to promise the triumphs that have fallen to the lot of surgery and of hygiene. My reply is simple—because we shall not be able to dispense with this essential branch of our art; because, as much in external as internal medicamentation, we must for the present make use of pharmaco-therapeutics.

THE PRIME IMPORTANCE OF CHEMISTRY.

The substances that we employ in medicine are composed of chemical bodies, or are, perchance, pure chemical bodies; and to understand their physiological action we must have recourse to biology and chemistry; while to appreciate their application in disease it is necessary to study pathology and therapeutics. Chemistry, in its wide sense, enables us to understand the composition, the structure, and what I would term the affinities of a substance, as it is chemistry that enables us to analyse by tests, and to construct and reconstruct by synthesis. The relations between chemistry, on the one hand, and pharmaco-therapeutics and materia medica, on the other, are so intimate, so indissoluble, and so obvious that it almost seems to me superfluous to trouble you with their consideration. However, you will not mind, I hope, if I take the liberty of submitting to you a few points which may not be new, but which at any rate have the merit of being *apropos*, and may by thought upon them make us better appreciate chemistry. To pile stones on the top of each other is not to construct an edifice. Without a definite plan, without a general view—that is, a com-

prehensive conception of the whole constructive scheme—there can be no scientific edifice durably reared. Therefore, it would not be sufficient to make pharmaco-therapeutics a science to say that if it has arisen without preconceived ideas it is founded upon observations extending from the most ancient date with regard to the effects produced by the administration of certain substances to the sick; nor is it sufficient to claim that pharmaco-therapeutics has availed itself of experiments on healthy man and on animals, and has taken into consideration physiological results and the fruits of clinical study. A sound basis of operation from which to inquire into the use of medical substances is required. We must know, if we would satisfy the claims of science, the mode of action of these substances, and understand how it comes about that they possess the power to produce or remove functional troubles. And it is here that chemistry comes to our aid—chemistry in general, chemistry in its largest sense. I in no way lose sight of the incomparable services of biological chemistry and physiological experiment. Who of us would overlook the assiduous and successful work of Coppola, Gracosa, Pellacano, Albertoni, and of all that young Italian school that is now marching victoriously along the route traced out for them by Fraser and Brown? The method of action of medical substances has been and will be rendered more clear and comprehensible by their researches; but this is not enough. The conscientious striver after truth will always find himself face to face with one problem, a problem in the solution of which lie concealed—an inextricable secret so far—the true phenomena of life. We recognise this, for everywhere, where we are powerless to comprehend the action of medical substances upon the living organism as being due to their own inherent properties, we do not hesitate to call to our assistance the unknown properties of living protoplasm, and attribute the phenomena to them; but it is chemistry that should tell us that we must not be discouraged by the enigma of life. Enigma there is doubtless, but let us recall that Lavoisier first named life "a chemical function," and that—once given that the creature lives—from that point it obeys neither more nor less than dead (or material) nature the general laws of chemistry.

VITAL PHENOMENA AND THEIR MEANING.

The familiar phrases "living force" or "vital phenomena" serve us to design the outward expressions of condensed energy in dead material, being borrowed from the manifestations of life. In dead material, we are all aware, force can appear as thermal energy, as electricity, as light, or as mechanical expression, and we can go back along this line of transformations and see all the changes unmake themselves. In living protoplasm—considered as the unit of the psychic and reproductive functions—the essential phenomena are the same. There is the same change of rôles, the same production of warmth, electricity, mechanical energy, and chemical energy. We know that the living cell "reacts," as we please to term it, to variations of temperature, electricity, light, and energy, chemical and mechanical; but this irritability in the cell, this aptitude of the cell to change one form of energy for another, resembles the transformations that take place in dead material, as the stimulants of the living cell, without which the vital phenomena do not appear, are just the different forms of energy which arrive to it from its environment, and which it changes into chemical energy. For life the cell must have warmth and moisture. Take away the moisture or lower the temperature to the necessary point, and life becomes latent or disappears. In dead nature the same takes place. We are all familiar with the admirable experiments of Professor Pictet,¹ bearing upon this point. He proved by them beyond dispute that chemical energy disappeared and reappeared in accordance with the temperature to which certain substances were submitted, and that water is every whit as indispensable as a proper temperature for the maintenance of the phenomena of life. Certain it is that life is a chemical function, but the point is—Is not the chemical function a sort of life? Did not the father of medicine show a wonderful insight in counting water and fire among the four elements of which the universe is composed?

Now if we examine closer the special problems which fall within the scope of pharmaco-therapeutics, if we examine the results which follow the introduction of drugs—healing

[¹ And more recently in England the researches of Professors Dewar and Fleming.—ED. L.]

or poisonous—into the organism of man and animals, it must appear that we can never learn how to solve the problems without looking for their explanation in these “vital elements,” as I may term them. The manifestations of their agency in the behaviour of the living organism have so characteristic an imprint that even Claude Bernard himself did not hesitate to place chemical and purely physical action in the comparative background. I will give examples of my meaning. How are we to understand the fact that the ingestion of infinitesimal quantities of certain substances which pass through the organism without causing in it the least change can provoke such disordered chemical actions as to occasion death? How are we to understand the fact that different parts of the organism seem to be able to distinguish these substances one from the other? We must admit special elective functions proper to the life of the cells. How are we to understand the facts that nothing but a change in the quantity of their dosage, the duration of their administration, and the method of their application suffices to make of certain toxic substances stimulants or paralyzants? How are we to understand the fact that insoluble substances like arsenic, cannabis indica, and lead can defy that well-known axiom, *Corpora non agunt nisi soluta*, and manifest therapeutic and toxic action. We must admit the presence and agency of some unknown power within the living cell. How, again, are we to understand the therapeutic power exhibited by solutions of iodine and bromine which have apparently been diluted to the deprivation of all chemical action, unless we attribute to the living cell the power of liberating the iodine and the bromine from such dilute solutions? Thanks to my compatriot and dear colleague at the University of Amsterdam, Professor van t’Hoff, thanks to the admirable work of Arrhenius and of Ostwald, thanks to congresses of physicians and chemists, light seems to me to be about to be shed upon all these dark places in pharmaco-therapeutics. And it has not been Mahomet who has gone to the mountain, but the mountain which has come to him. In other words the study of the chemical affinities of dead matter has revealed to us the secrets of the living cell.

THE APPEARANCE OF VITAL PHENOMENA IN CERTAIN CHEMICAL SOLUTIONS.

We have been accustomed to regard the neutral solution of sugar or of some neutral alkaline salt in water as an inert liquid deprived of all molecular power. We know to-day that such a solution must be held to possess the same kinetic power as if the substance dissolved were present in the gaseous state. Placed in contact with other solutions it will exercise pressure according to the laws that Avogrado and Dalton have discovered for gas. It will exercise an osmotic pressure in direct proportion to its molecular weight. But this is not all. We have to remember the electrolytic phenomena of such solutions by which their kinetic power may be rendered enormous. This conception of the molecular properties of solutions is of the highest importance both in biology and in pharmaco-therapeutics. It is not by accident that life is so closely leagued, as it were, to water. It is not by accident that living organisms contain without exception more water than solid properties—that they contain much more of it in proportion than any other terrestrial object of palpable and visible formation. It is not by accident that the youngest and most energetic organisms, those in which life is the most intense, are distinguished by containing the most water, while the tissues in which life is ready to expire have the least. Life has been compared to a torch. From a chemical point of view life is not only a torch—it may also be compared to a river. It is an ocean in which the molecules of the chemical substances therein constantly dissolve, constantly develop chemical, electrical, thermal, and mechanical energy, an energy whose seat is the living cell.

From all of this it follows as an absolute necessity that the chemical actions which constitute vital phenomena become stimulated, troubled, or altogether upset from the moment that we introduce into the system some new complicated substances in solution, whose molecular forces are now added to those of the cellular system. We are only embarrassed what example to choose when we seek in organic and inorganic chemistries proof of this point. I only wish to name one to you which seems to me conclusive. By warming pure chlorate of potassium we obtain pure oxygen, but the presence of the smallest quantity of chloride of potassium is sufficient to change part of the oxygen into ozone. In giving rise to this development of ozone the chloride of potassium

remains itself completely unaltered; but, what is more remarkable yet, this chloride of potassium itself has, like peroxide of manganese—which acts in an identical manner—the property of destroying ozone.

We find, then, here, as M. Brunck, to whom belongs the honour of having discovered the reactions, has said, a most remarkable phenomenon. We see a chemical substance, without itself appearing to undergo the least appreciable molecular change, favour the formation of a new chemical body, which, on the other hand, it has the power to destroy the moment that it is formed. There is, in fact, in the domain of organic chemistry, with no question of fermentation, a catalytic force, in considering which we have to make for dead nature a complete pendant of that which we should scarcely consider characteristic for therapeutic actions—the phenomena of excitement and paralysis, manifested by the slightest possible quantities of one and the same substance, which itself remains unaltered. And speaking always with these phenomena before our eyes and looking on the cell as a colloid or membranous mass containing several substances, organic and inorganic, at the same time dissolved in water, there is no longer any reason to be astonished that slight changes in the quantity of one substance or the other, or that the presence in one of a body that is absent in the other, suffice perfectly to change the chemical affinities of the cells, as well as to differentiate them in such a manner that each of them seems to be endowed with an elective affinity peculiar to itself. As for the manifestation of therapeutic and toxic action by bodies considered to be insoluble, of which Naegeli in a posthumous work has made so profound a study, they are also capable of the simplest interpretation. The insolubility of these bodies is not absolute, but only relative. If we throw, for example, metallic copper into water and wait for some days we shall find that a certain proportion of the copper has dissolved—i.e., one part to seventy-seven million parts of water. The copper dissolves in this manner without the least intervention of any living organism. In the same way it is not the vital function of the human organism which makes arsenic, cannabis indica, and lead display active properties when introduced in a metallic state into the body. It is the mass of water which is the agent (for the human body may be regarded as a jug of water containing forty-five litres) and the temperature.

The view that regards the solutions of salts as mediums in which the chemical molecules are perpetually striving to assert their individuality has contributed, on the other hand, in the most efficacious manner to elucidate the action of some of the drugs that are most in use. I have particularly in my eye now the purgative and diuretic salts, the chlorates, iodides, and bromides, whose therapeutic effects are obtained upon doses that may be called massive when comparing them with the infinitesimal doses of which we have just spoken. Since my dear and honoured colleague of the University of Amsterdam, Professor Hugo de Vries, discovered the law of isotonic solutions, and since the admirable work of Professor Hofmeister of Prague and of his pupils, the effects of purgative and diuretic salts have been recognised to depend uniquely upon their pure chemico-physical properties. On the other hand, we owe to the zeal and perseverance of Professor Hofmeister of Prague again a series of very beautiful researches on the imbibition of salt solutions by tablets of pure agar-agar gelatine, which demonstrate to proof that all that we have hitherto considered the elective affinity of the living cell can be explained in the most natural manner in the world by its colloid condition and chemical constitution. Add to this that the quickness of chemical action, according to the interesting chemical researches of Vladinarsky, is in no way impaired by the colloid state of the medium in which the substances are placed, and you will easily arrive at a conception of the immense progress that pharmo-therapeutics has made by the agency of physical chemistry. Among the salts that I have named the iodides and bromides are also to be found. Their therapeutic effects are, I need not say, altogether specific. What is more natural than the belief that we ought to attribute the results to the iodine and bromine themselves; and we all know that some long time ago my colleague at the University of Bonn, Professor Binz, was able to demonstrate that it is the living cell which frees the iodine and bromine from solution. The fact is not, however, proved to universal satisfaction.

I should never finish my task if I tried to place before you all the points of the new view on the actions of drugs, poisonous and otherwise, whose pharmaco-therapeutics are traceable to the theories of modern chemistry. Let us glance

only at the catalytic fermentative actions which take place everywhere in living protoplasm, and which without doubt play a preponderating rôle in the therapeutic effects of drugs. These can no longer be considered the appanage of the living cell. They also take place in dead matter.

CHEMISTRY IN RELATION TO MATERIA MEDICA.

If I now stop theorising it is not from fear lest anyone in this Areopagus of science should say: To what practical good does all this tend? Evidently it is not to-day or to-morrow that the art of medicine will profit by chemistry. But all these new ideas have rendered necessary new methods of experimentation, and new methods of investigation; and a new track is now being traced by human genius, along which there is much to discover; and from the moment that the new physical methods shall have been applied to the study of drugs (all honour to M. Dreser, who has here taken the initiative in his investigation into diuresis) medical art will profit and will find in chemistry a sure and trusty guide in its efforts to serve humanity.

In speaking of chemistry in its relation to *materia medica* I do not employ the words *materia medica* in the sense in which Dioscorides used them. I employ them in their strictest and primitive sense to mean the collection of drugs and medicaments in use in our days—our *thesaurus medicaminum*. *Materia medica* recruits from botany, zoology, and above all from chemistry; but its immense progress of late is due to chemistry. The active principles of almost all our drugs are now known to us. They have been isolated, prepared and elaborated; the chemical constitution of their active principles is no longer a secret. We know that sugar and glucosides and aromatic oils belong to chemical groups, and are as well defined as the alkaloids derived from pyridine or chinoline. Every day the number of contumelious substances—substances which do not wish to reveal to us their secrets—grows less. Chemistry has revealed to us the presence of more than twenty alkaloids in opium, and of more than six in quinine; and it will soon be extremely difficult to name the drug, of animal or vegetable origin, in which there have not been found one or several active principles. And, going from victory to victory, chemistry has also succeeded in producing a great number of alkaloids by the synthetic manner. These have not been the exceptionally lucky strokes (*coups de maître exceptionnels*). No, the constitution and composition of other bodies that chemistry has not yet reproduced for us are already familiar to the chemist, who can transform morphine into codeine and *vice versa*, and worthless cupreine into effective quinine. We may predict with every confidence that the manufacture by synthesis of all the known alkaloids is only a question of time for chemistry. But the triumphal march of chemistry does not stop here: it has constructed for us new alkaloids endowed with therapeutic effects of great value; it has furnished us, *inter alia*, with apomorphine and apocodeine.

It would be unequalled ingratitude to fail to recognise the imperishable services that chemistry has rendered to *materia medica* in endowing it with the alkaloids and the pure active principles because there are a few black clouds on the horizon. That there are such I do not deny, but they are not wholly the fault of chemistry. Is the gunsmith responsible for the accidents that a new firearm may cause in the hands of a client who does not know how to use the weapon properly? Surely not. Why did not the purchaser take the trouble to understand the structure of the gun. Why was he not more careful? Why did he pay no attention to warnings? Why did he behave like a happy child, with nothing more important to do than to display his new acquisition to all the world and to put it to the test with the *insouciance* of youth? On the other hand, should not the gunsmith help to avoid such disasters by explaining matters to the purchaser? And if he is not himself sufficiently informed and does not thoroughly understand the mechanism of the weapon, should he have offered it for sale? Either party may be to blame. What I would convey by my parable is this: by a very pardonable illusion, to which the many physicians and some chemists have given way, it has become generally believed that the active principles of drugs, when chemistry can furnish them for us in a crystallised state, are pure chemical bodies, and that identity of name guarantees identity of chemical composition. This illusion is rapidly being dispelled, but, alas, not without having done harm to physicians and their patients. As far as the chemical purity of crystalline products is concerned, it is to-day a secret of Polichinello that crystallised quinine contains cin-

chonidine, that atropine contains hyoscyamine and atropamine, and that pilocarpine contains jaborandi. As much in organic as in inorganic chemistry we come across this phenomenon of mixed crystallisation. The crystallisation of substances is no guarantee of their chemical purity. These facts are sufficient to condemn entirely the new therapeutic system that M. Burggraeve has wished to inaugurate under the name of "dosimetric medicine." Dosimetric medicine is doubly on the wrong track—first, in assuming the chemical purity of active crystallised principles of which it exclusively makes use, and secondly, in enunciating the therapeutic heresy that the administration of a single active principle is worth much more than the administration of the drug from which the active principle has been derived. I do not hesitate to describe this dosimetric profession of faith as a heresy. The drugs that are most used are admirably made compositions in which different principles, working for or against each other, are found together. Their therapeutic effect on the system is altogether different from the effect that would be obtained by adding and subtracting the therapeutic effects of each ingredient. Recent pharmaceutical researches have conclusively demonstrated this fact. I do not wish to say too much against domestic medicine. I think it has been, on the whole, inoffensive. Alas! I cannot say as much of the unreasonable faith which leads persons to believe that similarity of name and of active principle in crystalline form will produce chemical and pharmaceutical identity. *Ingentem, regina, jubes renovare dolorem!* We all know the grievous results that may be caused by giving aconitine or digitalin derived from different sources. Here again the progress of chemistry promises improvement. The animal organism is most sensitive to stimulus, and modern chemistry has so many methods of stimulus at its disposal that the task will not be too arduous. It is a question which interests all civilised countries, which is brought forward at all medical and pharmaceutical international congresses, and which is in most urgent need of a satisfactory solution.

THE VAGARIES OF MODERN PHARMACY.

The services rendered by chemistry to therapeutics is not an exhausted subject. Certainly our predecessors already possessed a goodly medicinal treasury, but it seems very insignificant when compared with what we now utilise. Chemistry has loaded *materia medica* and pharmacology with wealth; it is the mother of new remedies, and we are proud of its aid; it has given us our anæsthetics, antiseptics, hypnotics, and antipyretics. These groups of remedies enable us to give relief in many cases where our forefathers were quite helpless. To them chloroform, ether, carbolic acid, iodoform, creosote, chloral, the salicylates, and antipyrin were all alike unknown. But here, again, and more so than with respect to the alkaloids, there are shadows in the picture. Chemists and chemical manufacturers add more and more to our store of remedies day by day without stint or truce, without heeding the despairing cries of physicians already overstocked with drugs. We are tempted to cry out for mercy. This is no exaggeration, for these new chemical products are all forced upon the same therapeutic market under the most attractive names, and all proclaimed aloud with the noise of most perfect advertising machinery. This is now done to an extent that, in my opinion, is detrimental to the interests of therapeutics. I am not speaking of quack remedies, the orvietana of our day, of those secret specifics which the medical man views with wholesome horror, to which, and to whose use, the old adage, *Trompeurs, Trompés, Trompettes*, can be so well applied. I am speaking of genuine well-known products; for, unfortunately, modern industrial chemistry, in manufacturing and in placing at the disposal of medical men these drugs, does not at all object to their being purchased by the general public. If this be not so, why do their proprietors select for their names the fascinating names that act as veritable flags to attract the public—for instance, anti-nervine, anti-phthisine, anti-rheumatine, anti-dysenterine, and, most expressive of all, migrainine. I fully appreciate the difficulty of finding new names for these new products, and can understand that the manufacturer would shrink from giving them the names derived from their chemical composition, for these, generally speaking, could only be pronounced with linguistic gymnastics and intolerable strain upon our memory. I must, with great regret, note that we have departed from the ancient method, which taught us to denominate new products according to their origin, and have followed freely a course of seeking for euphonious, sonorous names, proclaiming the therapeutic use and effect of the drugs designated by

them. It is not sufficient nowadays to have a good remedy—say agathine; we must be assured of its superlative excellence, hence aristol. Do you want to prescribe for a patient who is “out of sorts,” you have euphorine; for a lack of appetite, you have orexine. You desire to procure sleep for him: you have hypnal, hypnon, somnal, or somniferine. You wish to lower a febrile temperature: do not let the emergency trouble you, for you have antipyrin, antifebrine, antithermine, thermomine, thermofugine, pyrodine, and thermidine. You want to assuage pain? *Eh bien*, you have awaiting your orders analgesine, analgeine, exalgeine, exodyne, and neurodyne. Or you have to deal with a case of heart disease: you have cardine. Or you desire to stimulate urinary secretion: you have diuretine, pheduretine, and uropheine. To check the formation of pus there is a remedy termed pyoktanine; and to combat spasms antispasmine. I do not wish to exhaust your patience, and I will spare you the enumeration of the antiseptics, the disinfectants, the microbicides *e tutti quanto*. Ten years exactly have elapsed since my honoured colleague Professor Rossbach of Jena published an article full of wit and sound sense on these tendencies of modern therapeutics, and in those days we had not the long lists of antiseptic and antipyretic remedies. Nor was it then imagined that the essential extracts of the organs of animals, of which the late Professor Brown-Séquard and M. C. Paul were the earliest to explain the therapeutic value, would find a place in *materia medica*, nor cultures of microbes. It was not foreseen that we should have to chronicle in 1894 the sale not only of séquardine, but also of veritable bacterial products such as tuberculine, tuberculocidine, antituberculine, antitoxine, κ. τ λ. How shall we check the fury of this flood? There seems no reason why it should come to an end.

Technical chemistry will continue, by analogical arguments from the structure of well-known bodies, to construct by synthesis new substances. These will be submitted to our judgment in the hope that they will prove more useful than our preparations in present employ. Bacteriology and all the experimental sciences will continue to search for toxins and antitoxins corresponding with each infectious disease and all characteristic lesions of each organ. This is the duty of the chemist and bacteriologist; but we, on whom fall the responsibilities involved in our art, must not be content to modestly lower our eyelids and say with Tartuffe—

“*Par de pareils objets les âmes sont alléchées,
Et cela fait venir des coupables pensées.*”

We must adopt a frank attitude and openly oppose such of these novelties as we do not approve of or understand.

THE OVER-HASTY PROFESSOR.

The reason of the present situation—or imbroglio—is obvious. By the side of the chemist stands the busy practitioner, or the over-wrought professor. Both are oppressed by the sense of the insufficiency of their art; neither has the time to observe, reason, and conclude. It is the professor who publishes with railroad haste his observations and impressions, for he is ever haunted by the fear lest another should precede him in the new discovery. He it is who makes others follow, sheep-like, in the wake. He constitutes himself a bustling *impresario*, always on the look-out for a new sensation, agitating himself and the public, and, finding that he has before him a fickle, unquiet, impatient audience, he hastens to deal with new subjects, if not every day, at least every week. During the year 1893 sixty-eight new chemical products have been recommended to me, this figure not being inclusive of entirely new drugs or their active principles. In each case we are told that the new product is of the very first importance, of exceptional therapeutic value, and perfectly harmless. *Fistula dulces canit volucres dum decipit auceps*. The wise man will not be taken in. He will be guided by therapeutic teaching such as that of the immortal Baglivi, the author of the pregnant phrase, “*Ars tota in observatione*,” or by the teaching of my honoured friend Professor Semmola, delivered with all his *maestria Italianni* from his chair in the University of Naples, a university which has lately set a glorious example to Europe by proclaiming that a drug that is efficacious cannot be harmless. Nearly all new remedies have their period of success, be it but for an hour, and this is due to “suggestions” either by medical men or patients; but, with few exceptions, these panaceas are doomed to be laid aside as forgotten and antique curiosities.

THE USES OF FEDERATION.

The century in which we live is an epoch of national and international leagues. Is it not time that the physicians and chemists and, for that matter, public functionaries of the world form an international association against the abuse of new remedies? Yet as leagues are apt to do more talking than practical work, let us decide to act. Medicine, the healing art, is an applied science, and we are anthropotechnicians. It is our duty to apply all accomplished progress in natural sciences to the profit of suffering humanity, and to seek in such progress a better basis of operation or a new supply of weapons. But it is also our imperative duty to be severe towards ourselves, and never to abandon the true path, traced for us by observations and experience extending over centuries of trial. Let us, my colleagues, never forget that our master, the master of us all, the great Hippocrates, while warning us that the opportunity quickly slips by, and that life is short, taught us first of all that ART IS LONG. Do not let us be too hasty. Let us follow with respect to new therapeutic methods and new remedies the example of one of the greatest benefactors of humanity—the immortal Jenner—who patiently waited ten years before he published his discovery, deeming that it was impossible to scrutinise too carefully or control and test too fully his results, and seeing that it was only by repeating his observations and experiments that he would be able to discern the false from the possible, the possible from the probable, and the probable from the TRUTH. But all old advice is not good. Do not heed old Celsus when he says: *In ancipite morbo plus valet anceps remedium quam nullum*, for we can never foretell the intensity and extent of the reparatory forces of the diseased organisms, and we can never be too chary in introducing remedies in doubtful cases, lest we check the activity of the organs in the exercise of the defensive powers with which they have been so liberally endowed by nature; and if we do employ remedies, let us employ those that are well known; those that have been tested in every way, on the purity of which we can rely; those whose action and special characteristics have been rendered brightly manifest by the experience of many years. We must not be bigoted advocates of ancient remedies or stubborn opponents of new remedies. We must continue to study, to examine, to observe, and to strive in every way to render firmer the foundation of therapeutic science.

Arris and Gale Lectures

ON

THE PHYSIOLOGY OF LYMPH FORMATION.

*Delivered before the Royal College of Surgeons on
Feb. 9th, 1894,*

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LECTURE III.

Influence of the Nervous System on Lymph Formation.

MR. PRESIDENT AND GENTLEMEN,—Several attempts have been made to show that the nervous system may influence the formation of lymph apart from its action on the blood-vessels. Thus, many years ago, Ostroumoff drew attention to the fact that, after stimulating the lingual nerve on the side for some time with gradually increasing stimulus, a marked cedema of the tongue was produced on the side on which the nerve was stimulated. The increased flow of lymph in the tongue on stimulating the lingual nerve was demonstrated by Rogowicz in other ways. Heidenhain, investigating the phenomena known as pseudo-motor, ascribes the motor effects of stimulating the lingual nerve to the secretion of lymph that is thereby produced, and does not regard it as an insuperable objection to this explanation that the pseudo-motor effects can be obtained even after the death of the animal, when there is no longer any circulation. The well-known phenomenon denoted as Ranvier's cedema has also been cited in favour of the nervous origin of dropsy, and we have many clinical cases which are supposed to put the nervous origin of cedema under certain conditions beyond doubt. I have investigated the influence of the nervous system on the flow from the thoracic duct, and compared the