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## SOME APPLICATIONS OF PHYSICAL CHEMISTRY TO MEDICINE[1]

THE growth of knowledge, like most processes of growth, is autocatalytic. It is self stimulating. The discovery of fact, principle or idea speeds the discovery of new facts, principles and ideas. Progress is thereby self accelerating, although the acceleration is not constant, but increases for a time after each discovery only to slow up or to come to a constant velocity until some new catalyst is discovered. A remarkable feature of this growth of science, a feature which shows that knowledge is indeed an organic whole, is that an idea or fact discovered in one branch of science often serves as a catalyst to a very remote and apparently unrelated branch.

Nowhere is this illustrated better than in the repercussions between physics, chemistry, biology and medicine. The study of what is going on in an evacuated glass tube provided with electrodes, when there is a strong difference of potential between those electrodes, results in the discovery by a physicist, Crooks, of the so-called "cathode ray"; study of this ray by another physicist, Röntgen, leads to the discovery of the X-rays set up when the cathode rays impinge on glass, metal or other solid surface, and as a result the physician is provided with a means of seeing the bones, the stomach, intestines, heart, ureters, and gall-bladder of a living man; of learning whether these are normal or not; and he is in addition provided with a means of treating successfully many hitherto hopeless conditions.

But the effects of this discovery do not stop here; even more important to physiology and medicine is the resulting study of the mechanism by which the X-rays act upon the body. For it is clear that if substances are opaque to X-rays, they must absorb such rays. And when they absorb such rays the energy in the ray is passed to some substances in the tissues, or to substances which have been introduced into the cavities of the body to make their outlines visible. Now molecules of substances which have absorbed energy are in a quite different condition from molecules of the same substance which have not. Energy is that which gives the power of acting. So substances which have absorbed energy are thereby rendered far more reactive than they were before.

[1] Lecture given at the University of Buffalo, April 12, 1927, on the Harrington Foundation.

Being thus reactive they become more toxic, or more curative. Or they may be destroyed.

Hence the study of the luminosity of gases in partially evacuated electrode tubes, besides causing a revolution in physical theory, ultimately resulted in providing a method for introducing energy into the interior of the tissues of the body, which energy is useful in destroying tissues which are overgrowing, such as cancers, or various glands, or in destroying parasites.

A tremendous and rapid development of diagnosis and therapeutics, a development still in progress, has thus resulted in medicine from a discovery made in a totally different field of science. It is indeed as if in the body of knowledge an organ called physics secreted a hormone, which led to the intense development of another remote organ, called medicine. And it is almost certain that medicine or biology thus stimulated will ultimately react on physics to produce in its repercussion as great an effect on it. When this repercussion comes it will probably revolutionize the physicist's conception of matter.

It is indeed true that all of the organs of the body of knowledge are thus metabolically and nervously coordinated and they act and react on each other leading either to an acceleration of development of old organs, or to their atrophy, just as in the body of a tadpole, the thyroid hormone enormously stimulates the development of the limb buds, while it produces atrophy of the tail and the gills, organs no longer useful in the changed conditions of the life of the progressive organism.

Nowhere is this interdependence of the sciences better illustrated than in the interrelation of medicine and physical chemistry; and no better example can be found than here of the saying that a scientific man never knows what he is doing. For he, no more than others, can look into the future to see what the consequences of his work will be. The results are always concealed from him. All that he can see is the effect of ideas after they are past. He is blind; for no one can see even sixty seconds into the future. The past is illuminated by the light of memory; the future is wrapped in the impenetrable darkness of fate, or lighted only by the deceptive and ghost-like glimmer of the law of probability.

Physical chemistry itself was in a large measure a result of a discovery by botanists. Plants, as you know, are among the most interesting of animals. They differ from other animals in that they are sessile —they do not move from place to place; and they possess chlorophyll, a wonderful apparatus for catching and utilizing the ethereal vibrations of light. From this captured light they derive their own vitality; and they imprison part of it, which they do not need themselves, in oxygen which turned loose in the air constitutes a great reservoir of vitality from which we and all animals get our life. Now plants have a circulation not so unlike the circulation of the blood of animals. It is a circulation of sap; a sap containing food—mineral and organic—which streams up to the leaves and buds and growing parts and nourishes them. The pressure of this sap was first measured by Stephen Hales, who also measured the pressure of blood, two centuries ago.

It has always been a puzzle to botanists how the movement of this sap is produced, and many of the great botanists have worked upon this problem. Among them were Dutrochet in France, and many years later De Vries in Holland and Pfeffer in Germany. These earlier workers had the idea that the rise of the sap might be due to a process which was similar to that which occurred when a pig's bladder full of sugar solution was placed in water. Water then entered the bladder and a very high pressure was thus generated leading to the distention of the bladder. This process was called osmosis. The passage in of the water was called endosmosis; that of the sugar out, exosmosis. It might be that in the roots, water was thus imbibed and the sap expanded in volume was forced upward and into all the twigs of the plant. Modern work makes it doubtful whether this is the mechanism, but one begins with a simple theory. To make this a scientific theory it was necessary to measure the pressure of sap on the one hand and the pressure which solutions of substances in water were capable of exerting when they expanded, on the other. It was necessary to see whether such an osmotic pressure could account for the rise of the sap.

The botanists De Vries and Pfeffer measured the osmotic pressures of salt and sugar solutions, and largely because of these measurements a new science was born, the science of physical chemistry. The botanists did not know they were creating this new science. They themselves did not solve the problem of the movement of sap. That is a vital problem and according to Professor Bose's recent work, involves the vital pumping activity of certain cells of the plant, analogous in their rhythmicity to the beating of an animal's heart. But while De Vries and Pfeffer did not solve their problem, out of their work two fundamental concepts came; the first was contributed by the great Dutch chemist, van't Hoff. From the observations of Pfeffer he showed that the osmotic pressure measured by the botanist was exactly that pressure which a number of molecules of hydrogen gas equal to the number of sugar molecules in the sugar solution would exert if the molecules of gas were confined in a volume as large as that of the solution; and furthermore the variation of the osmotic pressure with temperature was the same as that of hydrogen gas with temperature.

This idea of van't Hoff when united with the facts of Pfeffer made a catalyst which stimulated a great volume of work throwing light on the nature of solutions; and it caused that development of physical chemistry, of the application of the methods of physics to the study of chemistry, which resulted in the splendid growth of knowledge in this branch of science which occurred from 1880–1920.

The other great contribution, developing from the facts discovered by these botanists, was that made by Arrhenius. De Vries found that most salt solutions had a higher osmotic pressure than van't Hoff's law of correspondence between osmotic and gas pressure indicated. The Swedish physical chemist, Arrhenius, pointed out that this was probably due to the dissociation of molecules of salt into two or more fragments, a dissociation analogous to that which occurred in some gases, such as nitrogen pentoxide, and that the extra pressure observed was due to these dissociated parts of molecules. Furthermore, he identified the dissociated parts with the ions described by Faraday and Clausius. These ions were electrically charged bodies which carried the current resulting when electrodes were put into a salt solution. This fruitful idea was established as a fact by experiment.

Thus was founded the theory of ionic dissociation which revolutionized chemistry, and of which the application to medicine have been extremely important.

Something further was required, however, to make these two simple and illuminative conceptions of value to medicine. This something was the discovery that such colloids as existed in living matter were electrically charged. This discovery was made by Sir William Hardy in Cambridge, England, about 1898. He found that the protein particles in solution when subjected to the action of electrodes—that is of the electric field—often migrated in the field, sometimes going in the direction of the current to one electrode, sometimes to the other, and sometimes not moving. Since all particles which migrate in an electric field must be electrically charged, this proves that protein colloidal particles were often electrically charged.

This discovery completed the fundamental work on the electrical state of the protoplasmic constituents. Protoplasm was seen to consist of colloids which often at least were electrically charged; and the salts present were also in the form of electrically charged particles.

It is impossible to give those who were not at the time engaged in studying these problems a conception of the wonderfully clarifying effect on biology and medicine of these few simple facts and theories. But a basis was at once given for the explanation of many until then wholly obscure things. The speaker was so fortunate as to have a part in this great clarification. It provided a scientific basis for the many important contributions of electro therapeutics, including the recent development of diathermy; it gave an explanation, incomplete to be sure, of the electrical phenomena of living things and of electrical stimulation and depression. The reason why the acidity or alkalinity of the tissues was so important for their normal function was seen to be a natural result of this dissociation, since any change in hydroxyl or hydrogen ion concentration at once changes the state of aggregation and the physiological activity of these proteins. The discovery of the importance of hydrogen and hydroxyl ions led to the recognition of the diseased state of acidosis; of the importance of the maintenance of the neutrality of the tissues and organs. And recently it has led also to the recognition of the evil results of deviation in the other direction toward alkalosis. The pathological states of acidosis and alkalosis appeared from this discovery first as a probability, and then by experimentation as established facts. And the results of upsetting the acid-base equilibrium, or the balance of the salt solution, in the blood and tissues, could be forecast in theory and were established in practice.

For the first time, also, we had an explanation of why mercury, silver, gold and copper salts should be so vastly more toxic than salts of sodium, potassium, magnesium, calcium and iron. This followed from the discovery that the amount of energy liberated when the ions lost their charges was a measure of their toxicity. Sodium, in the metallic form, was so extremely toxic and caustic because it contained a vast store of energy which it liberated when it changed to the ionic form; and mercury and silver in the ionic or salt form were so toxic and caustic because they contained a large amount of energy which is liberated in changing toward the state of metallic mercury or silver or when united with any substance.

There was still another of its concepts which was destined to throw great light on physiological and pathological processes. This was the concept of oxidation developed by physical chemistry. It may be called, indeed, the electric theory of oxidation. It was the next step necessary to take if we were to be able to give an electrical description of life; for oxidation—that is respiration—is the means by which all living things get their energy.

Before the era of physical chemistry there was no good conception of oxidation other than the ordinary one of union with oxygen. This is of course the original meaning of the word oxidation, which signifies literally *a souring,* for the reason that acids are produced when oxidation occurs of most although not of all materials. The word oxygen itself means literally the "maker of acids." But there was no general explanation of the nature of all oxidations such as that of metals by acid, of the iodine in iodides by ferric salts and so on, where oxygen was not involved. The physical chemist discovered what was really at the bottom of all oxidation whether they were due to oxygen or not. In all cases of oxidation he found that there is an increase in the number of positive valences in the substance oxidized, or, what is equivalent to this, a decrease in the negative valences. And, finally, when the electrical and electronic nature of valence was finally understood a few years ago, it was seen that in every case of oxidation, the oxidized substance lost a negative electron, and thus gained a positive charge. In other words, in every oxidation there is always a flow of electricity—of positive electricity—since the current is always supposed to be in the direction of movement of the positive, from the oxidizing to the oxidized body. Oxidation, then, was seen to be in reality also an electrical affair; and every electrical current to be endowed with the potentialities of oxidizing. The great value of this conception of physical chemistry to medicine consisted in that it gave for the first time a rational explanation of the electrical currents which are found everywhere in the body. As every physician knows, whenever the heart beats there is an electrical disturbance which is propagated from the heart throughout the body. By leading off from the hands or from one of them and the feet, or from tongue to foot, or in other ways, these currents may be made to traverse circuits outside the body, and are then readily perceived and registered by a galvanometer. These extra corporeal currents have now become a valuable means of investigating the physiology of the heart beat and of aid in diagnosis of heart disease of various kinds. The exact way in which these currents are generated in the heart is still not certainly known, but enough is known to permit the statement that they are correlated with the process of oxidation which occurs in the heart muscle and which supplies the energy for its muscular contraction.

Moreover, it is now becoming clear that these currents, thus traversing the body, are in some cases at least of very great importance to it. Many years ago the speaker discovered that the well-known polarity which all organisms show, both plant and animal, was at least in some instances accompanied by, if it was not the expression of, an electrical polarity. By organic polarity I mean the difference between the root and the apical end of willow and other stems; the tendency of the apical bud to hold back the development of buds below it; the tendency of the piece of a hydroid, a sessile animal, to form a polyp at one end and stolons or roots at the other. I found that that part of the animal which would most rapidly regenerate a part cut off was always electrically negative (to the current outside the body) to the part which regenerated more slowly, and I suggested that these differences of electrical potential between different parts of an organism, small though they were, might be of very great value particularly in the differentiation of organs and tissues in the course of embryonic development.

This suggestion has now been put on a very much firmer basis by the discovery by Child that there is a gradient of metabolism, which is accompanied by a gradient of an electrical kind, in all developing organisms; the nervous system, or its fundament, is the point of maximum growth and chemical change, and this point is electro-negative to the rest of the body; and that this gradient in some way or other controls development along the axis. It is an important factor in inheritance and in the attainment of the form of any animal. Furthermore, Lund has succeeded in showing that by altering the electrical polarity it is possible by minute currents to alter the character of the development; thus showing that my guess as to the importance of these currents in embryology was correct.

The physical chemical conception of the electrical nature of oxidation has, therefore, been of importance in interpreting the cause of the electrical phenomena of living things and has helped in the unraveling of the complicated mechanism of inheritance. It explains at once the dependence of these electrical currents upon respiration and vitality, and accounts for their origin.

In another way too this electrical theory of oxidation is of value although not many applications of the facts to medicine have yet been made. It furnishes a basis for understanding why some things can be oxidized and others can not be. Clark, in Washington, has particularly shown the relation between the ease of oxidation of any substance and what is known as the potential of an oxidizing electrode immersed in a solution in which the substance is undergoing oxidation. Among the results obtained by the use of this method has been the proof that when methemoglobin is formed in the blood there has been an oxidation of the iron in the hemoglobin molecule so that it has become ferric iron; whereas in the ordinary oxyhemoglobin the iron is not oxidized but is in the ferrous state. This discovery will probably eventually throw light on the mechanism of hemoglobin respiration and will perhaps enable us to understand the nature of the union between oxygen and hemoglobin.

These are simply a few of the applications in medicine and cognate sciences of the fundamental conception of physical chemistry that all oxidation is a process of an electrical nature.

But there is a more important aspect even of this work than those presented. The great problem of biology is the source and nature of our vitality. It is known that as long as we live we continue to breathe and that variations in our vitality are accompanied by variations in tissue respiration and by electrical phenomena of the highest interest. I will mention only one of these curious phenomena which has to do with the alteration of the electrical resistance of the body under stress of the emotions. This phase of animal electricity was being particularly studied five or six years ago by Professor A. D. Waller, the able English physiologist, just before his death. The effect of emotion was demonstrated to me by his son, Mr. J. C. Waller. An electrode moistened with salt water was put on the palm and another on the middle of the back of my hand and these electrodes were connected with a galvanometer. It was then found that there was a current running through the tissues of my hand, from back to front or *vice versa.* I do not for the moment recall which way it went, but that is of no consequence for our purpose. When this current was balanced through the galvanometer by another current just equal to it and running in the opposite direction, the galvanometer mirror came to rest and the spot of light reflected from this mirror remained steady. A horn of a motor was then suddenly sounded behind me. The instant this noise was made the galvanometer mirror was deflected. There was an instantaneous increase in the current through the palm of my hand, due either to an increased electromotive force or decreased resistance of some or all of the tissues of the hand under the influence of the emotion caused by the noise. The current through the galvanometer was thus increased and the spot of light swung off the scale of the galvanometer. After it returned to normal the following experiment was tried. Mr. Waller picked up a pin where I could see him and started toward me saying: "I am going to prick you with this pin." The instant he said this and approached me, the current of my hand changed again and just in the same direction as before and the spot of light swung off the scale, so violent was the electrical disturbance set up by this remark and action.

Whatever explanation may be given of this curious alteration in the electrical resistance or e.m.f. of the body under the influence of emotion, in both these cases probably the emotion of fear, they are certainly sufficiently remarkable. They merit a careful study and, as you all know, Dr. Crile, with his great genius for seeing far into things, has at once attacked this very problem and brought it into relation with many diseased states. According to his view there is some kind of a reciprocal variation in resistance between the liver and brain.

No one can predict the future, but I have a feeling that the investigation and elucidation of these curious electrical disturbances, which are usually correlated with oxidative changes and with the emotions, will ultimately throw great light on the nature of vitality, and also perhaps on the causes of disturbed personality, states of mind, which have at present no tangible clue as to their origin.

Among the most important developments in physical chemistry of recent days has been the development of photochemistry. This seems to be the great field of the immediate future. Here there have been two very fruitful ideas or conceptions introduced which are playing havoc with old theories of chemistry and letting in a flood of light upon regions which have been obscure. These two fundamental conceptions are (1), the idea that molecules and atoms may exist in several different forms, these forms differing in the amount of energy they contain; and (2), what is known as the quantum theory. The quantum theory is the theory that energy is radiated through space in definite units which are called quanta. A quantum of energy is numerically equal to the product of a constant, the quantum constant, of which the value is $6.547 \times 10^{-27}$ ergs seconds, multiplied by the frequency of the vibration of the energy radiated.

The first of these conceptions, that atoms and molecules which are alike in other respects may differ in the amount of energy they contain and so behave differently, is due in large measure, in its later development at least, to the work of Baly, of Liverpool, but is an essential part of the conception of the atom developed by Niels Bohr. Bohr showed that the atom of hydrogen might exist in several different forms, the single electron which it contains revolving about the positive center in several different possible orbits. When the electron was farthest out the electron orbit had the largest amount of potential energy in it; and as it was easily displaced from this position to one of the orbits nearer the nucleus, it radiated the difference of energy of the two orbits when it was displaced. This conception is of very great importance to physiology and medicine. It means that a substance which is in its stable and energy poor form, where it is very unreactive, may be raised by the absorption of energy to another form in which it is very reactive and unstable. Thus chlorophyll when it absorbs energy from the sunlight passes the energy thus absorbed, or a part of it, into the oxygen of carbonic dioxide. The oxygen thus enriched with energy dissociates from the carbon atom, leaving the latter to unite with water to make the carbohydrates. The oxygen contains more energy and is larger than it was when in the form of carbon dioxide as some of the electrons are out in larger orbits. When this oxygen is drawn into our lungs and sent by the blood to the tissues it unites with the cells of the body and passes this imprisoned sunlight over to them; and it is in this way that we get energy. The oxygen atom when it has lost its energy returns again to the form of the oxygen in carbon dioxide. If there is mentality, as well as energy, in sunlight, it is quite possible that we secure our mentality also from oxygen; and that in this way our vitality is derived from the sun. The energy passed to the living matter by the oxygen is in turn passed by it to the foodstuffs, which as they come into the body are in their most stable and unreactive form. The carbohydrates, fats and proteins, thus enriched by this energy which came from the oxygen, are rendered highly reactive and are enabled thus to change into the myriad of things they change into in the course of metabolism. Thus this conception of atoms having available energy in them and existing in different states, of which the most reactive may be called the living state, enables us to form a pretty clear idea of the fundamental metabolism of the body. Above all, it makes clear for the first time why oxygen is necessary for the metabolism of the body, and why growth stops as soon as anesthesia is produced and respiration stops.

Probably the most remarkable work along these lines of photochemistry is at present being done by Professor Baly, of the University of Liverpool, in England. He has succeeded in making several typical vital syntheses by means of ultra-violet light. He has thus made possible a concrete theory of the origin of living matter on the earth's surface by the action of light.

This same conception makes clear also why light is necessary for the proper development of the bones and teeth. Vitamine D, the antirachitic one, is indeed nothing else apparently than ergosterol which has been enriched in energy by the absorption of light. It is either the enriched ergosterol itself, or a derivative of the enriched form.

The second conception, that of the radiation of energy in quanta, is at present upsetting the old idea of light and matter. It is having also an effect in biology. Certain frequencies, or only certain quanta, are absorbed by the blood pigment, hemoglobin. It is a very important and wholly unsolved problem what becomes of this energy which is absorbed. Is it reradiated at a different wave-length or is it passed on to cholesterol or some other constituent of the wall of the red blood cell so as to make the antirachitic vitamine or some other vitamine? Why is the blood red? It must be that the particular light absorbed is of use to the body in some way or other. I leave this problem with you to reflect upon. It may be that the healing power of light on wounds may be an indirect effect of the absorption of light by the blood pigment rather than a direct effect upon the wound tissue itself. Perhaps its action in tuberculosis is also correlated with this red color. What we need is the study of the particular wave-lengths of quanta of energy which are made use of in tuberculosis and in the healing of wounds, in the prevention of rickets and so on. Perhaps each tissue may have a favorable reaction to some specific frequency of the light, absorbing certain quanta but not others.

In the University of Cincinnati some very interesting experiments are being carried out along these lines. It has been found for example that bacteria are not killed by all ultra-violet light rays, but only by certain specific wave-lengths. And the enzymes are killed by other frequencies, so that it has been possible to sterilize various enzymes without in any way injuring them by exposing them to certain specific wave-lengths. This work of Professor Schneider and his associates may have very important results for the sterilization of vaccines, serums and so on. In other words, the lethal effect of light, and particularly of ultra-violet light, does not increase gradually as the wave-lengths of light used are shortened and the frequency and energy is increased, but no effect is produced until a certain frequency, a certain definite amount of energy, is reached when a very fatal action is found to occur. There is no doubt that the application of the newer conceptions of radiant energy will greatly enlarge the usefulness of ultra-violet light, X-rays and ordinary light, in their therapeutic applications. Photochemistry is the newest of the branches of physical chemistry but it promises to be one of the most valuable in its medical applications.

Still another development of physical chemistry and physics of recent years promises to be of great value in biology. I refer to the cathode rays and radio-activity. The effects of negative electrons when shot out of atoms or poured upon living tissue from a cathode ray tube are remarkable. I will first consider the latter way of applying them. The wonderful tube, recently perfected by Dr. Coolidge, of the General Electric Company, enables us to apply electrons to tissues in far greater dose and traveling with far greater speed than has been possible hitherto. What the ultimate effects of this electrical bombardment of tissues are it is too soon to say. Certainly, however, their effects are striking in the extreme. When the cathode particles traveling at high speed strike any object they do several things. They cause many things to fluoresce. They generate also very short X-rays which penetrate the tissues much deeper than the cathode particles themselves can do. Even a second of exposure of the belly of a rat to a sufficient dose will kill the animal not immediately, but after a certain time. The rays are extremely destructive, as the amount of energy thrown upon the spot by these particles moving almost with the speed of light is very great. Whatever the ultimate usefulness in medicine of this tube may prove to be, it has placed in the hands of the investigator a new instrument; and we may look forward with confidence to useful knowledge derived from its employment.

But one of the most interesting of the recent works in this direction is that of the Dutch physiologist, Zwaardemaker. We have atoms within us which are generating these cathode rays. So far as we know at present the element potassium is the only element in the body which is radioactive. It is the only element which generates cathode rays at any other than very rare intervals. The whole of the very weak radioactivity of our tissues is due to the presence of this element. Some atoms of potassium are going to pieces every second in our bodies. When they do so disintegrate they discharge a negative electron which is moving at about two thirds of the velocity of light and the rest of the atom changes into something else. What that something else is, is not known, I believe. A negative electron moving almost with the velocity of light may cause very remarkable things to happen in any molecule it passes through. Potassium is for some reason necessary for all forms of life. Howell found that it was necessary in the heart for the impulse from the vagus nerve to reach and stop the heart. Zwaardemaker has suggested that it is necessary perhaps for the sensitivity of every synapse in the body.

Zwaardemaker has made the following calculations:

There are in the body about 40 grams of potassium. This is an enormous number of atoms. It is approximately $6 \times 10^{23}$. The radioactivity of potassium is small when compared with radium. It is only about four one millionths as active as radium. The total number of atoms decomposing per second is not large, but in the body it is 80,000. Eighty thousand atoms of potassium then are decomposed in our tissues every second and discharging this number of electrons at a very high velocity. These electrons have 0.022 ergs of kinetic energy, or they furnish 1,900 ergs per day. This is 45 microgram-calories. The amount of energy thus liberated is hence very small, almost inconceivably small. It is in the ratio of 1: 35.5 billions when compared with the whole basal metabolism. But small though it is it may be of very great importance. Zwaardemaker states that it is possible to replace the potassium in the perfusion fluid of the heart with an equal dose of other radioactive material such as radium emanation or uranium. He computes that in one eighth of a cc. of our bodies there are eight trillion potassium atoms, of which each second one arrives at the end of its life as potassium and changes into something else, at the same time shooting out of its nucleus a single negative electron with one third microerg of energy. Of this energy one half is lost in 1 mm.; and in 2 mm. only one fourth remains. This charge traveling at high speed will effect the molecules it passes through. Every part of the one eighth of a cc. is every second subjected to this influence. In muscle and nerve especially this is happening, as they contain the most potassium; in bone and lungs it is almost absent. Therefore, says Zwaardemaker, every second there is a stimulus of one third microerg applied in every one eighth cc. of the body. "In the presence of the proper receptors noticeable results from a stimulus of this size might be expected." "For example, the minimum energy perceived by the eye is about $0.7 \times 10^{-10}$ ergs. The energy of a beta particle from potassium is 4,000 times this. A star of the first magnitude twinkles at night with 30 to 40 times less energy than that of a potassium atom when it explodes. The amount of energy necessary for the ear to hear is $0.3 \times 10^{-8}$ ergs per second on the drum. In 17 thousandths of a second, the minimum time necessary for the perception of sound, this would give $1.1 \times 10^{-10}$ ergs, which is the one twenty-five hundredth part of that of a potassium atom on exploding. The energy of an ordinary conversational voice at two meters distance is figured to be on the ear drum $1 \times 10^{-9}$ ergs. The potassium atom has 275 times this amount. Zwaardemaker suggested in this way that the energy thus set free in the proper place and with the proper receptors to catch it may be a very important factor in the automaticity and activity of the nervous and muscular and other systems of the body.

There are still other even more fundamental conceptions than any yet quoted from the field of physical chemistry, which will probably in the course of time be applied to biology and medicine. These are the new conceptions of the nature of time and mass and energy which have already upset all the foundations of mechanics and physics. Their effects on biology are already beginning. No one can say what they will do to and for this science; they seem, however, to have the effect of putting mentality of some kind into the inorganic as well as the organic and thus to open entirely new vistas in biology. They suggest a method by which matter can be made; and they offer, or seem to offer, an escape from the purely mechanistic theories of conduct and life. It would take much longer, however, to consider these revolutionary conceptions than we have time for to-night; and I will only call your attention to them in passing. Those of us who are alive twenty years from now will probably in that time have passed through a revolution of biological thought as great as any the world has ever seen. And this revolution will unquestionably have important consequences for the physician and his patient.

I have by no means exhausted the applications of physical chemistry to medicine. In fact, I have mentioned only a very few which have particularly interested me. But I shall have compassion on you and stop with these.

I believe and hope that the development in our knowledge of energy and matter and vitality, developments which are impending, will stimulate above all the science of therapeutics, that step-child Cinderella, at present hardly tolerated, and boxed about most unkindly, to our great disgrace, in every American medical school. I believe physical chemistry, or physics with chemistry, is spinning for her a new dress, a dress shining and splendid. Once bedight in it she will dazzle the eye and warm the heart of even the oldest, most experienced and most cynical among us, and be seen for what she is, the fairest daughter among the medical sciences. And I venture to say that in no way can the science of physical chemistry serve medicine better, playing the rôle of Prince Charming, than by leading this Cinderella from her position of drudge to the throne of medicine.

For it is the neglect of therapeutics, which is, I believe, one of the most serious shortcomings of present-day medicine. And it is in this field that physical chemistry can contribute most.

ALBERT P. MATHEWS

UNIVERSITY OF CINCINNATI

## THE ABUSE OF WATER[1]

IT would appear obvious that the fundamental principles of science must not be dependent upon any casual feature, such as environment. Thus the laws of gravitation should be just as rigid on the sun or the moon as on the earth. In a science which is mainly experimental, also, such as chemistry, it would seem to be a simple matter to insure that the results of experiments were not being misinterpreted due to their environment. This might be done either by changing the conditions under which the experiments were being conducted, or by a rigorous study of the existent conditions and of their possible influence. Nevertheless, the history of chemistry affords numerous instances where whole schools of investigators have gone astray through neglect of such precautions.

A noteworthy example is given by the famous phlogiston theory, which predicated that substances which were changed by heat did so through loss of phlogiston. We now know that such substances are actually changed through combination with the oxygen of the air in which they are heated, but this explanation did not secure acceptance until the nature and properties of oxygen had been thoroughly investigated and until the effect of heating substances in the absence of oxygen had been noted. At the present time, we still allow our oxygen environment to influence our definitions to some extent. We call a body "combustible" if it burns in the air, and "non-combustible" if it does not. That such terms have no strict scientific meaning is evident if we imagine ourselves to be translated, for a moment, to a world in which the atmosphere contained hydrogen as an active component instead of oxygen. In such a world fires would be extinguished by sprinkling gasoline on them, and non-inflammable buildings would consist of solid paraffin.

The modern science of physical chemistry has been almost wholly developed through the study of very dilute aqueous solutions, and a scrutiny of this water environment suffices to show us that our present viewpoint is considerably distorted and incomplete in many respects. Water itself is almost as much a mystery to the chemist of to-day as oxygen was to Priestley. We call it $H_2O$ in the text-books, but liquid water certainly does not consist of simple molecules of $H_2O$. What the actual complexes are, and how they are changed on addition of a solute, are points on which we are entirely ignorant. The theory of dilute solutions founded by van't Hoff avoids the difficulty by assuming that we may regard the solute as existent in the gaseous state, neglecting the water absolutely as so much "dead space." This idea, though still popular in the classroom, has been shown by the more modern theory of ideal solutions to be quite erroneous. There is no direct analogy between solutions and gases; a substance such as sugar, when dissolved in liquid water, is not in the gaseous state but in the liquid. In a liquid solvent, solution and fusion are identical terms; sugar melts in hot tea just as ice melts in iced tea. The two components of a solution, solvent and solute, must be considered as equally important, but at present our procedure is to let familiarity breed contempt and to

[1] Abstract of an address delivered before the Institute of Chemistry of the American Chemical Society, State College, Pa., July 28, 1927.