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THE BIOLOGICAL BASIS OF OSTEOPATHY.

Presidents's Address Fifth Annual Meeting of the A. A. A. O. at Kirksville, Mo.

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More than four years ago—on April 19th, 1897—in this hall the American Association for the Advancement of Osteopathy was organized. It represented a new idea, a new movement, in the domain of therapeutics. Those on the outer fringe of this movement were asking the question, Will it last? The record of these four years will answer. Then there were two schools; now there are a dozen. Then there were less than seventy-five practitioners; now there are sixteen hundred. Then we were recognized by legislative enactment in two states; now by one-third of the union. Then the greater portion of the public never had heard of osteopathy, and those who had heard of it considered its adherents as dupes of another fad—or fraud. Now it is recognized as a science and an art which is making for itself an enduring place in human life and human knowledge, and which is destined not only to correct much of theory, but to profoundly modify much that had passed for knowledge, on the subject of health and disease.

The germ from which this remarkable development has proceeded was the product of the brain and the life-work of one man, whom it is our delight today to honor, and whose name will be remembered among the great ones of earth—Dr. Andrew Taylor Still. We who are engaged in the practice of osteopathy before an approving public, can scarcely realize the entire severing of all relations with former theories and associations required to present and maintain a theory so revolutionary before a wholly disapproving public. Virchow, in referring to Huxley's work, says: "Freed from the formalism of the schools, thrown upon the use of his own intellect to test each single object as regards properties and history, he soon forgets the dogmas of the prevailing system, and becomes first a skeptic and then an investigator." This sentiment would apply also to Virchow himself, and we all know something of how true it is of Dr. Still. And how remarkably the work of these men is correlated. Huxley laid the foundation for the modern study of physiology or normal function. Virchow laid the foundation for the modern study of pathology or disturbed function and its results, and Dr. Still, by discovering the key to the proper correlation and sequence of these, has laid the foundation for a rational and scientific therapeutics. Some inquiry into the nature of this correlation and the elements of this basis may be profitable to us at this time.

I. THE PROBLEM.

What is that by or through which cure of disease is effected in osteopathic practice? This question has never been satisfactorily answered. Indeed, no serious attempt has ever been made to answer it. We have been content to demonstrate the method and to point to results to prove the fact, waiving its explanation. If pressed, we have shifted the question by saying that we remove obstruction to the body processes, without explaining why these processes do not need for their restoration certain chemical reactions brought about by certain drugs. With the wealth of accumulating resource ready to our hand from the labors of biologists and physiologists, constantly strengthening our position, this ought not to be so. The limits of this paper precludes any claim to an attempt to answer the question, but its purpose will have been served if it shall suggest some of the lines along which the answer is to be sought.

II. THE NEW PHYSIOLOGY.

The physiology of organs and tissues as such, the resultant of the forces of all the members of a cell-community, has been pretty well worked out. We know the laws governing circulation and respiration, the contraction of muscle, the conductivity of nerves, the processes of digestion, the action of the sense organs, and something of the physical basis of psychic phenomena. Time was when it was thought best in investigating a particular function, to select a tissue of the highest order in which the special function was most clearly differentiated; but the necessary normal environment of such a tissue involved so many complicating conditions that the results were often contradictory and always unsatisfactory. Now the vital activities of protoplasm are studied as they are exhibited, undifferentiated and uncomplicated, in low forms of life, and the most highly specialized tissue will show nothing else but difference in degree. The problems of physiology are now regarded as problems of the cell, cell action being recognized as the sole content of all vital activity. The ameba, the lowest of all living things, a little bit of homogeneous protoplasm, yet holds within its formless, organless body all the potentialities of the most complex organism, the whole secret of life.

III. THE MATERIAL PRESENTMENT OF LIFE.

We know life only as it is manifested in living substance, and change in that substance is its one constant characteristic; accumulation and dispersion are the necessary constants of life. The living form may retain its individual shape, but its component material is constantly changing; a continuous stream of material is passing through it. At one end of the process, with a few comparatively simple substances, there is initiated a long catalogue of events resulting first in building up a great number of highly complex constituents of protoplasm, with storing up of energy, and second, splitting and oxidation processes, reducing the complex to simple compounds again, with release of energy. Only in the most general way can it be said that one end of the series is represented by plant life and the other end by animal life. They overlap, and the process is the same in character wherever we may study it. The question of environment is one of condition and not of cause: even

the influence of sunlight in the synthesis of starch has been shown by Winogradsky to be not wholly indispensable, but that living substance may form starch without this supposedly necessary condition.

1. *Composition of Living Substance.*

Substances which enter into the nutrition of the human body are classed as proteids, carbohydrates and fats. The former comprise the chief mass of the tissues and are by far their most important constituent. They present a very great variety of forms. Hammersten names three general divisions, ten sub-divisions and thirty-two specific forms, and in his table the words "and others" occur four times. But we must remember that practically nothing is yet known of the composition of proteid, that it must vary not only for each specific tissue in the body, but that an indefinite number of changes is involved in reaching these tissue forms. An indication of these changes is seen in the digestion of proteid, in which a succession of albumoses ends in peptone, which in its turn disappears by transformation as soon as it is absorbed by the intestinal epithelium, never being found in the blood; and there are probably other changes while it is yet food, before it has become any part of living substance. The multiplicity of tissues depends on differences in their proteid constituent. Indeed, all biological differentiation probably has its physical basis in differentiation of the proteid molecule.

The carbohydrates are comparatively simple combinations of the three elements, carbon, hydrogen and oxygen. In contrast with the proteids, nitrogen is absent. They are widespread, but in some forms of living substance cannot be demonstrated. The sugars and glycogen are their important representatives in the human body.

The fats, while widespread principally in animal cells, are not an essential constituent of living substance. They are composed of glycerine and various fatty acids, the varying proportions of these determining the characteristic fat of the several animal tissues.

It has been shown that carbohydrates and fats may be derived by chemical transformation from proteids, and that, conversely, they are consumed in the building up of proteid. Pflüger has called them the satellites of the proteid. Verworn says: "The proteids stand at the center of all organic life * * * that which constitutes the life of an organism, wherein the living differs from the dead organism, is the metabolism of the proteid. * * * Vital motion, metabolism, is a complex motion very sharply characterizing the living organism; it consists in the continual self-decomposition of living substance, the giving off to the outside of the decomposition products, and in return, the taking in from the outside of certain substances, which give to the organism the material with which to regenerate itself and grow by the formation of similar groups of atoms, i. e., by polymerization. This is characteristic of all living substance."

2. *Difficulties of Physiological Chemistry.*

Mosso has said that "the living human body is like a laboratory where one meets 'no admittance' at every door and corner."

The determination of the chemical composition of living substance, if not impossible, is at least not accomplished, and not possible by any methods of chemical research now known. The beginning of the process of analysis kills

it and it is dead substance which is analyzed. Dead protoplasm is composed of comparatively stable molecules whose constitution may be expressed by a definite chemical formula. Even of these only a few are known. At one end of the series they are food elements, at the other, excretion products, both being outside the arcana of life. The stream of matter passing through an organism reaches a point at which it passes from the condition of dead matter to living substance. At another point it passes again from the condition of living substance to dead matter. We are not able to locate these points. We do not know where digestion ends and life begins. Nature makes no leaps, but passes by imperceptible gradations from one condition to another. If our knowledge of dead organic matter is limited, of organized matter under the direct influence of life we know even less. It is known that living substance has a very complex structure; that there are a large number of compounds, varying in different kinds of cells and in different conditions, which are constantly being formed, transformed and decomposed, by syntheses, rearrangements, cleavages and oxidations. The most of these compounds are used again in the organism, the product of each change furnishing the material for the succeeding change.

In living substance, the matter exists in the form of a large number of very complex labile compounds—complexes of molecules. Verworn objects to the term "living molecule" as applied to these complexes, as the word molecule signifies a definite chemical compound of some stability, while instability and change are the essential characteristics of living substance. He therefore suggests the term "biogen" to designate those exceedingly complex compounds that are at the focus of life and by means of which vital phenomena are manifested. They are constantly being formed in the process of assimilation, which through an ascending series of changes occurring along many different lines closely related and interwoven, culminates in living substance, and decomposed in the process of dissimilation, through a descending series of changes in which the biogens are broken down into simple, stable compounds with release of energy in the form of heat or work done.

3. Chemistry of Living Substance is "Chemistry of Motion."

Enough is known of these changes to enable us to form a picture in outline of the process as a whole, and osteopathy claims that this picture is now clear enough to require the study of disease from a new viewpoint, and to provide a new basis of therapeutics. The genesis of living substance may be expressed in this statement: *The chain of events in metabolism is a closed chain and into this metabolic cycle no substances but those that serve as food can ever enter.* Material not suitable for its upbuilding cannot be imposed upon living substance. It will take in only food elements, and only such quantity of those as its needs determine, without regard to the supply which may be available. The only way in which other substances, *e. g.* drugs, can become incorporated with living substance is by destroying it. Acids and poisons unite with it in that way. The constituent events of the metabolic cycle do not follow each other in a single line, but in many lines. Pfluger has emphasized the importance of the polymerization of the proteid molecule in growth—assimilation, in living substance, in which the simple molecule takes in from the materials of the environment atoms of food elements, attaching them to itself until it becomes a polymeric molecule. It then breaks down into simple molecules,

each of which repeats the process for itself, again and again, forming in that way numbers of chains of many similar links. Dissimilation is the reverse of this process, the end products being principally water, carbon dioxide, and urea. The successive chemical reactions in each chain or line have been compared to explosions, on account of the great lability of the compounds.

It will readily be seen that this metabolic cycle, including as it does such an immense number of constituent elements, is capable of almost infinite variation. The number and arrangement of the atoms concerned in each event, of the events in each chain, and of the chains in the cycle will account for all the variety in organic nature. Differentiation is but an expression of the variation of this cycle. All the various tissues in any organism, the differences in the same tissue or substance in different organisms, and even individual peculiarities all are due to variations of this cycle, so that the familiar expression, "one man's meat is another man's poison," has its foundation in the fundamental facts of organic structure. The continuance of life requires that this cycle shall remain intact. Its elements may be modified. One line of changes may take place more rapidly than others, thereby storing material. Another line may be retarded. But if any link drops out, the whole chain comes to a standstill in death. This order of events may vary widely in different organisms and under different conditions. The one essential factor of its existence is that its material content shall be in ceaseless change. It is, therefore, a physiologic concept. It is the fundamental physiologic concept.

Life, therefore, does not represent a static condition of the matter in which it is manifested. A static condition means death. Life represents a mode of motion of its material presentment.

4. *Chemical Composition not the Sole Factor in Organization.*

Protoplasm, the basis of all organisms, is something more than a chemical compound. Even Verworn's complex hypothetical biogens do not stand for organized protoplasm. It is a complex of biogens. Wilson says: "Brucke long ago drew a clear distinction between the chemical and molecular composition of organic substances on the one hand, and on the other hand, their definite grouping in the cell by which arises organization in a morphological sense. Claude Bernard in like manner distinguished between *chemical synthesis* through which organic matters are formed, and *morphological synthesis* by which they are built into a specifically organized fabric." And again he says of the cell that it has "a morphological organization, which though resting upon, is not to be confounded with the chemical and molecular structure that underlies it."

The bridge between chemistry and morphology is not yet built. Of its subtler features we are wholly ignorant. Stereo-chemistry, by revealing to us the space-relations among the elements of protoplasm, may, by reason of the great number and variety of those elements, suggest the almost infinite possibility of variation, and thus explain the evident diversity of protoplasmic structure as seen in plants and animals, in individuals, and in the same individual at different times. The biogen compounds of different cells differ from each other. "Each cell possesses its own specific composition, and its own characteristic metabolism." The morphological end of the bridge is expressed in the cell by the division into cytoplasm and nucleus, which, broadly speak-

ing, is coincident with the beginning of physiological division of labor, the nucleus being more generally concerned with synthetic processes and the cytoplasm with destructive metabolism. The cell then is the lowest form of independent organization capable of maintaining the essential processes of life. This is true in unicellular organisms and is also true of the constituent cells of multicellular organisms in which each cell must in a measure lead its independent life. Even the most highly developed tissue cells possess a morphological organization similar to the egg-cell or the protozoon. Physiologically, however, the association of cells in the higher organism requires a compromise, and the autonomy of the individual cell is in some degree, and unequally as to its various activities, made subservient to the life of the organism as a whole. Thus in the lowest organisms the properties of irritability, contractility, secretion are equally developed—or undeveloped. In the highest organism each group of cells, while retaining all the "native" properties of protoplasm, are highly differentiated for the exhibition of some one property, muscle cells for contractility, nerve cells for irritability, gland cells for secretion, and so on, in order that their particular function may be performed in times and amounts to meet the requirements of the cell community.

IV. STIMULI THE OCCASION OF ALL VITAL PHENOMENA.

The activities of living organisms consist of responses to stimuli. A stimulus may be anything which produces a change in spontaneous vital phenomena. The character and degree of response depends upon the chemical and physical forces involved in the constitution of the organism and its relations to its environment.

Typical living substance existing in an ideal environment, in which the conditions of vital phenomena—the character of the surrounding medium, the food supply, moisture, heat and light—were exactly suited to its needs would by reason of what Hering terms "the internal self-regulation of metabolism" present a condition of chemico-physical metabolic equilibrium. The spontaneous vital phenomena would present a uniform succession of events. But any change in the environment would be followed by a change in the metabolism of the living substance, an adaptive adjustment of internal conditions to external conditions. Life being manifested only by a constant change of matter, the first response would be to the presence of waste products of metabolism, which as soon as separated from the living substance are foreign matter, inimical to the welfare of the organism. It, therefore, responds to their presence by excretory action. We may imagine that the matter next to that eliminated is now moved up to take its place and that a succession of such responses occurs throughout the series involved in the integrity of the living substance. At the beginning of the series there will be a demand for new material, which will be shown by the response of the organism to the presence of food. Thus the maintenance of the equilibrium of the matter and energy of living substance itself may be conceived as a series of responses to stimuli. But these we cannot segregate and study separately, as they are inseparably bound up with life, and remain or disappear with it.

1. Forms of Stimuli.

Observation of changes in the activities of the organism in response to

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changes in the environing conditions, has already yielded to investigation much of value, and is pregnant with promise of much more. Davenport recognizes eight agents that act as stimuli on living organisms, viz: Chemical substances, water, density of the environing medium, molar agents, gravity, electricity, light, heat. The effect of these, separate or combined, in modifying the course of spontaneous vital phenomena, constitute the field of cellular physiology, and pathology. It will be seen that this includes all physiological processes, when we recall that the individual cell of the body may be conceived as existing in an environment consisting of neighboring cells (including the nerve filament that may supply it), water, chemical substances (in the blood and lymph), nutrient substances, waste products, heat, and, in some cases, light; and the resultant of the variously combined effect of these upon the differentiated and specialized forms of cell substance is seen in the different physiologic functions. The action of these cells will be influenced by variations of the heat of the body, as in fevers and inflammation; by the presence of nutrient substances as in digestion and assimilation; by the presence of waste matters, as in excretion; by various manifold stimuli conveyed to them by the nerves; and in a thousand complex forms many of which we cannot yet analyze.

2. Response Property of Organism, not of Stimulating Agent.

The mechanism of the metabolic cycle precludes any effect of stimuli except in two directions, viz., excitation or depression. The successive changes have a specific order of sequence. Qualitative change in the cycle would mean death. Only quantitative change is possible. The multitude of cycles which we may imagine in progress at the same time in living substance, may be changed in their relations to each other. Some may be excited, some depressed and some stopped altogether. The infinite variety thus made possible justifies the supposition that the protoplasm in any individual may never twice be the same in structure. Protoplasm, therefore, is not to be regarded as a chemical, but as a morphological concept.

An important factor in the functioning of cells in a multicellular organism, is that the component cells, no matter how widely differentiated, morphologically and physiologically, have their limits of capacity for response approximately in the same plane; otherwise there would be no such thing as co-ordination of function. This plane varies as between different individuals and in the same individual at different times. These considerations explain the varying effect of drugs upon different persons, or upon the same person at different times, and it also explains why drug medication can never be reduced to an exact science.

V. DISEASE FROM THIS VIEWPOINT.

We have seen that protoplasm is "a highly irritable automatically adjustable substance," and that the cells in a human body respond to the stimuli of varying external conditions in an adaptive way, not only with reference to the cell itself, but also to that of the whole body, and we are now prepared to inquire into the abnormal conditions constituting disease.

1. Is Disturbance of Metabolic Cycle.

It is coming to be recognized that disease is only a disturbance of natural processes; that pathology is only abnormal physiology. The conception of

pathological conditions until recently obtaining, based on macroscopical and microscopical findings, is found to be too narrow. Morphology gives us only the products of variation. We must go back of tissue changes and alterations in body fluids for the causes and beginnings of pathology. In so doing it will be found that changes and perversions of nutrition precede changes in structure.

Recalling our conception of the process of metabolism in living substance, of a closed chain of a very large number of successive events, the completion of each event, marking the formation of a substance differing from any of the others, each of which in turn is instantly transformed, and therefore, never appearing normally as a separated product, we are prepared to understand how the interruption of a metabolic process at any point would, by causing an accumulation of the normal substance produced at that point, result in a pathological condition.

a. Variation in time or site.—Minot says, "Analysis of normal necrobiosis and degeneration forces us to recognize that all, or nearly all, the modes of indirect cell-death which the pathologist encounters in morbid tissue, recur under healthy normal conditions. To put the conclusion in its correct form we need only to reverse it, saying: Most and probably all pathological necrobiosis and degeneration of cells are essentially identical with normal processes, and are pathological owing to the arbnormality of their occurrence in time or site."

b. A metabolic link dropped out.—Verworn says, "Thus it can be imagined that in metamorphic processes the appearance of foreign substances in the cell depends upon the fact that, as a result of chronic stimulation, one or more processes in the normal metabolism are gradually decreased or have entirely dropped out, so that compounds that normally are formed, but on account of immediate further transformation do not accumulate, are now stored in quantity, because the processes in the metabolism that are necessary to their transformation no longer exist."

c. Stoppage at the wrong point.—Bunker says, "In fatty degeneration for instance, the cells seem to have lost the power of completing the proteid anabolism from carbohydrate and the process stops at the fat stage. The cell then loses its protoplasm through ordinary vital waste, and deposits the fat, instead of new protoplasm. This deposited fat, not having reached the stage of organic combination where it can be oxidized with physiological rapidity, gradually accumulates to the final destruction of the cell as such. In myxedema and in the amyloid, hyalin and colloid types of degeneration, it would seem that the stops occur at the different stages of normal cell activity, with the result that in each case, otherwise normal material fails of complete metamorphosis, and is deposited in the tissues. In glycosuria, however, the excess of glucose on account of its solubility, is carried off in the body fluids and is eliminated as such. However this may be, the products of cytoplasmic degeneration seem always to be normal physiological substances, their excess, location and environment making them pathological, proving Huxley's definition of dirt as 'matter out of place' to be true physiologically as well as physically."

2. Is Due to Failure of Normal Response.

It would transgress the limits of this paper to further discuss the analogies

justifying the conclusion, but the statement may be ventured that all disease may be ascribed to a failure of protoplasm to respond; first to the stimulus of its own internal vital phenomena, resulting in an interruption of the metabolic cycle—disturbed nutrition; and second, to the stimulus of abnormality in its environment—pathological products and bacteria—resulting in neoplasms, autointoxications and infections; and such failure to respond when continued can eventuate only in death.

a. Extraneous stimulation not necessary.—But if the capacity for response still remains, we will have this condition: Pathologic substances, by their presence in the organism act as stimuli at two points; first, at the point of initiation of the abnormal process there may be such reaction to their presence as will tend to restore normal metabolic conditions by overcoming the cause of stoppage or irritation, as in "self-limited" diseases; second, the mechanism of elimination will react to their presence by increased excretory processes to get rid of the products of stoppage or irritation. *If the conditions are right these reactions will take place if need be to the full limit of the reacting power of the cells exhibiting them.* In other words, *the cure of disease requires the presence of no other stimulus than that of its own products.* The application of any extraneous stimulus in the form of drugs, electricity, heat, water, what not—with the idea of revitalizing or reforming in any direct way, the metabolic cycle, is not only futile, but wholly superfluous, and "adding insult to injury." Nature neither needs nor can use any assistance in her work. What nature does need and what we may do is to maintain suitable external conditions. Therapeutics then has only to do with the elements of the environment in which nature works. In this sense antidotes to poisons are necessary; heat may be applied to chilled tissues, and water may serve as a food element, or for cleansing, externally and internally.

b. Effect of environing conditions on degree of response.—If living substance responds to abnormalities in such a way as to bring about their correction, disease ought always to be cured spontaneously; indeed, it ought to be wholly prevented. That it does so respond is seen in the constant elimination of waste products of metabolism; and that there is sometimes a failure in spontaneous removal of abnormalities may be due to one or both of two conditions; to exhaustion of the power of response, or to interference with its manifestation. The first is illustrated systemically in the effects of starvation, overwork, excessive use of drugs, alcohol, etc. The second is the basis of the peculiar therapeutics of osteopathic practice and requires some examination of the mechanics of vital processes.

c. Protoplasmic mechanics.—The relations of the metabolic cycle to the conditions of its expression are very aptly illustrated by Davenport, who compares the protoplasmic mass to a factory, with many boilers and engines, much shafting and belting, and countless machines doing the most varied work. The amount of energy developed in the boilers and the efficiency of the engines and machines varies with certain conditions, such as the amount of heat applied to the former, and the friction and waste in the latter. The limiting mechanical conditions are reached when the boiler is rent by the steam pressure, a breakdown is caused by friction or a part rusts through and crumbles away. The limiting dynamical conditions are reached when the heat no longer suffices to form steam in the boiler, or the power is insufficient to run the machine. In either case at the structural or the dynamical limit,

work ceases. In protoplasm the *structural* limiting conditions are of two main sorts—mechanical, in which the gross structure becomes broken down, as in drying or freezing; and chemical, in which the composition becomes changed as in the effect of poisons, high temperature, strong electric current, etc. The *dynamical* limiting conditions are the absence of oxygen or other food stuffs, the absence of water necessary to the solution and circulation of the food, light, and too low a temperature. "Thus the conditions essential to metabolism are the absence of causes mechanically rupturing the machine, the absence of agents of such intense activity as to change profoundly its molecular constitution, and the presence of those agents—food, heat, light, and water—which supply or distribute the energy of metabolism. Given protoplasm under these conditions, and normal metabolism must occur; without them there is no metabolism." Surely if such a figure correctly illustrates the conditions in a bit of apparently homogeneous jelly-like protoplasm, it is not inappropriate when applied to so complex a structure as the human body!

3. Physical Conditions our only Field of Intervention.

We have seen that equilibrium in the ingestion and output of substances—normal continuity of the metabolic cycle—by the cell is the essential internal condition of the integrity of the vital processes. This equilibrium will be maintained by reaction of the cell to changes in its environment to the full limit of its reacting power. In order that this power of reaction shall be normally expressed, it is necessary that the physical conditions of the cell substance shall be normal. We are barred from any direct participation in the vital processes so far considered. We cannot impose upon the organism an exercise or a condition not required by the laws of its economy. Our field of intervention must then lie in the *physical relations* existing in the organism. Let us examine these conditions.

a. Size of cell.—The size of the cell is one of these conditions. By the operation of certain mathematical laws of growth governing the relation of surface to mass, the single cell is kept very small, so that a close relation between the cell and surrounding medium is possible. In plants where air is the medium, exposure is secured by extensive external branching. In animals where the medium is liquid, exposure is secured by extensive circulatory channels. Its bearing on the mechanics of nutrition is the only reason for referring to this here.

b. Movement of cell substance.—Another condition is the movement of protoplasm within the cell, a characteristic clearly shown in low forms of life, in which constant currents in the cell substance are found. In the hair-like pseudopodia, which many of these organisms throw out, outflowing and return currents are to be seen. Even when these pseudopodia themselves are so slender as to be almost to the limit of visibility under the microscope, these currents have still been demonstrated. Similar movements in cell substance either *en masse* or of a fluid portion through the interstices of a recticulum occur in the human body in the cells of glands, epithelium, muscles, nerves, in the blood, and possibly others. These movements aside from their relation to the special function of the cell, are necessary to the ingestion of nutrient material, the exchange of material between different parts of the cell, and the egestion of waste products.

c. Contractility.—Perhaps the most important physical property of the

cell is that of contractility, a property that is characteristic of protoplasm, and although the complex requirements of such an organism as the human body have resulted in highly specialized cells for certain properties, yet these cells have lost none of the fundamental properties of protoplasm. For instance, muscle cells, differentiated for contraction, still exhibit irritability and secretion. Gland cells differentiated for secretion are still irritable and contractile. Nerve cells differentiated for irritability still secrete as required by their own metabolism, and retain contractility as shown in the contraction and ameboid movements of ganglion cells in the lengthening and shortening of their dendrites. In the ameba, stimulation producing contraction causes a drawing in of the pseudopodia and the coming to rest finally in the shape of a sphere, the expression of extreme contraction. This causes a reduction of the metabolism, possibly directly, certainly by restricting movements of cell substance, below the point necessary for its continuance, and if the stimulation is maintained, death results. This phenomenon has been the subject of research by many investigators and in a great variety of organisms. Verworn very concisely states the results when he says that "it is found to be a common law that all elements, the contractility of which can be clearly expressed * * * without exception die in the phase of contraction. * * * Overstimulation, in its most general significance is nothing but that which has been termed elsewhere, external causes of death." On the other hand, the effect of stimuli is sometimes to cause inhibition of contraction. In unicellular organisms this is evidenced by cessation of the rhythm of the contractile vacuole, swelling of the protoplasm from the imbibition of water, the formation of other vacuoles, and death in the phase of expansion. Thus the two extremes, maximum contraction and total inhibition of contraction, when persistent, result in death. Between these two points the vital condition of the organism will vary from time to time, as one or the other limit is approached, but because this is something which is not amenable to manipulation on the dissecting table, under the microscope, or in the test tube, it has received scant attention. Nevertheless the conclusion is forced upon us that the conditions of mechanical stress in the cell structure and in the tissues, varying in degree and in time, the result of chemical, thermal or other stimuli, acting either directly or as mediated by disturbed nerve mechanisms, are important factors in the problem of the causation of disease.

d. Nerve stimuli.—Somewhat different in character and scope, but yet intimately related to cell-activities is the effect of nerve stimuli. In all the higher vertebrates and especially in man the predominating influence of the nerve is almost absolute. So dependent are the other tissue cells upon this form of stimulus that in its absence spontaneous action is lost or sinks to the lowest point. A skeletal muscle never contracts except it is stimulated, and if its nerve supply is wholly lost, its metabolism sinks to so low an ebb that it degenerates by atrophy. Gland cells are another example of this dependence, and even in the nervous system itself there is often an interdependence between ganglion cells. Much confusion still exists among physiologists as to the nature and mechanism of nerve stimuli. The older physiologists held to the conception of a complete control of all functions by a nerve force, originating in and proceeding from autocratic centers. A few materialistic physiologists of the present day deny the existence even of any "centers" in the older sense; that nerves are simply paths for more quickly transmitting

stimuli between widely separated structures and that the ganglion in the reflex arc is nothing more than a part of the conducting path over which the stimulus passes, *e. g.* from the skin to the muscle, that it is no part of the function of the ganglion to reorganize or modify the stimulus in any way. These are the extremes. The truth probably lies between them. The direct effect of nerve stimuli upon processes of metabolism; upon the processes of secretion and excretion, as in gland cells, and in the regulation of the conditions of stress—tone—in all contractile tissue, both intra- and extra-cellular, show the importance of the part they play in co-ordinating the innumerable activities in so complex an organism as the human body. The contractility of dendrites is an important point, considered in connection with the statement that the relation between the dendrites of one nerve and the axone of another is that of contiguity but not continuity, there being indeed a little piece intercalated between them, as it explains how nerve currents may be "switched."

c. Movements of medium.—Movements in the medium, by which transportation of substances is effected has been referred to above, so far as the contents of the cell are concerned. The problem of systemic circulation, important in itself, is beyond the intent of this paper, but clearly involves questions of mechanics.

At this point our discussion takes us over into the activities and relations of tissues and organs and the cause and correction of their disturbance, where in practice, the art of osteopathy demonstrates the correctness of the interpretation of nature and her laws on which it is based.

SUMMARY AND CONCLUSIONS.

Life is manifested through matter. Physicians have to do, not with the nature of life itself, but with its material medium, a continuous stream of matter entering and becoming alive, at one point, then functioning as living substance, and lastly dying and passing out at another point. This metabolic cycle is the physiologic unit. Nothing can enter it but food material. It may be hastened or retarded, but cannot be changed qualitatively. Its interruption means death.

In living substance, as in the cell, the unit of organized life, this cycle may be conceived as being in progress at every point. Every change in environing conditions is responded to by adaptive change in the cell by change in the rate of the metabolic cycle, retarding here, accelerating there. This response will be manifested to the full limit of the responding power of the cell.

When the limit of response is reached, death ensues. Below this limit we may have all degrees of response. When unimpeded it expresses normal vital activity, varied according to changing conditions of environment. When disturbed so as to impair the equilibrium of the vital activities, we call it disease.

This response is always such as tends to restore normal conditions. Disease is then the stimulus to its own cure. That cure shall result it is not necessary that stimuli shall be increased or multiplied. It is only necessary that physical conditions shall be made right, in order that existing stimuli may be effective.

These conditions are the elements of the environment, heat, light, moisture,

circulation of fluids in and to the cell, condition of contractility in the cell substance, and free intercellular intercommunication.

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