pede the flow of adrenoxidase-plasma throughout the whole length of the nerve, and by thus increasing the pressure of this substance in the axis-cylinder, cause an excess of it to flow into the networks of the internodal segments or true nerve-cells. A sudden influx of oxygen-laden adrenoxidase into the phosphorus-laden myelin from end to end of the nerve cannot but as suddenly incite a reaction entailing, as in all cells, the liberation of energy.

This conception meets the various biological and experimental facts that have stood the test of time. Nervous energy has been identified with electricity since Galvani's discoveries; and the galvanometer, the current generated by the electric organs of the sheath-fish, the torpedo, the electric eel and various vegetable and animal tissues have all served to show that this view is sound. Thus, the row of internodal segments around the axis-cylinder, or what I regard as the only true nerve-cells, correspond in their general structure and composition with the "electric cells"—also long and slender—in the spinal cord of the electric eel. Again, as stated by Verworn,[225] "these electric organs have the same embryonic origin as cross-striated muscles, to which also in their adult state, they possess great similarity." I have submitted evidence showing[226] that muscular contraction is also produced by a sudden influx of adrenoxidase (oxidizing substance)—MacMunn's myohæmatin—into the muscular elements where they also combine with a substance containing nucleo-proteid—myosinogen and a carbohydrate, glycogen. The same correspondence asserts itself in other directions: Sensory nerves are structurally similar to motor nerves, the sensitive "end-organs" affording *prima facie* evidence that irritablity is the initial factor when nerve impulses are to be incited. This same irritability accounts for the fact that electric stimulation in the course of a nerve will evoke impulses, since the nerve-cells themselves are stimulated. Heat increases and cold decreases the velocity of an impulse: this is readily accounted for by the fact that myelin is liquefied by heat and hardened by cold. Alcohol impairs conductivity: this is because it becomes oxidized at the expense of the adren-

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[225] Verworn: *Loc. cit.*, p. 269, 1899.
[226] *Cf.* vol. I, p. 261, in the first three editions.

oxidase. Indeed, it is an established fact that deprivation of oxygen and asphyxia by anæsthetics likewise impair the conductivity of nerves.

The fact that my interpretation explains these various features of the question seems to me to indicate that, in its general lines at least, it is poised on a solid foundation. Although the nerve-impulse has been identified with electricity, the process through which it is produced and its nature as a physiological entity have not been found. Indeed, in the last edition of his work, Landois[227] states that "the nature of the physiological nerve-stimulus in the normal body is not known,"—a fact readily accounted for when we realize that the two original sources of energy, the granulations of leucocytes and adrenoxidase, were themselves unknown.

And this applies to all the living structures of the organism, since, in the light of my views, all cells of whatever kind are perpetuated as living entities through the intermediary of these two sources of energy. One salient feature asserts itself, however, in this connection, viz., the masterful rôle of adrenoxidase. The proteid is, in truth, the living substance, but it is as dead substance that it enters the body. It is through the presence of adrenoxidase that it is endowed with life in the leucocyte, and that its identity as living tissue is sustained in the cell. Its active principle, acting as catalytic, is the true vitalizing agent in this process, since it is able, as such, to raise the oxidizing activity of the oxygen it carries to a very high potency, and thus to provide the proteid with a correspondingly great amount of heat-energy, by combining continuously with the phosphorus of the nuclein to which the proteid is anchored. As the proteid contains all the chemical constituents that render it *viable*, the heat-energy thus supplied to it increases the vibratory amplitude of its atoms to that compatible with the living state, and it becomes *living* tissue. In other words, heat-energy becomes transformed into vital energy. Adrenoxidase, as catalytic and oxidizing agent, is thus the life-giving and life-preserving constituent of all cells.

The proteid lives as long as its physical properties are such as to enable it to subserve adequately its function in the cell;

[227] Landois: "T. B. of Human Physiol.," Amer. edition, p. 631, 1905.

there comes a time, however, when worn, it must be removed. Here new factors are introduced, viz., the various hydrolytic triads, proteolytic, lipolytic and amylolytic (also brought to the cell by leucocytes, we have seen), to break down the proteids and what carbohydrates may be adjoined to them—fats in the nerve-cell, glycogen in the muscle-cell, etc. Again does adrenoxidase assume control: Itself a part of the triads, it carries on its rôle as "ferment of ferments" in each triad, and submits to hydrolytic cleavage the worn-out constituents of the cell, thus converting them into benign and eliminable waste-products.

The two phases of the living process, the building up of living tissue, *anabolism*, and the breaking down of worn-out tissue, *catabolism*, are thus incited and governed by the oxygen-laden secretion of the adrenals.

On the whole, the evidence submitted in this and other sections appears to me to warrant the following conclusions:

As to the conversion of proteid into living substance and its maintenance as such in the cell: (1) *the proteid constituent of the nucleo-proteid granules is the focus of the vital process, the true living substance;* (2) *although it enters the body lifeless, it contains all the constituents of living substance and acquires life in the leucocytes through the agency of the adrenoxidase these cells contain;* (3) *adrenoxidase being both a catalytic and an oxidizing agent it causes, when combining with the phosphorus-laden nuclein of the leucocyte's nucleus, the liberation of sufficient heat-energy to amplify the atomic vibrations of the proteid to a point compatible with life, and thus transforms it into living substance;* (4) *when the proteid enters the cell and is drawn to the network along with its nuclein moiety, its living state is also sustained by adrenoxidase, but by that constituting the network, while the nuclein with which this adrenoxidase combines is that linked to the proteid;* (5) *life is perpetuated in the cell by the incessant arrival of particles of living substance which continue their existence therein, linger for a time, then leave the cell as waste.*

As to the functional mechanism within the cell: (1) *The physico-chemical processes that sustain life occur in, or around, the networks of the nucleus and cytoplasm, the affinity of the*

adrenoxidase granules composing these networks for phosphorus causing them to attract the nucleo-proteid granules and to combine with them; (2) *in the nucleus the two bodies are replaced, gradually as they are being used, by the absorption of granules of both kinds from the exterior;* (3) *the network of the cytoplasm is also rebuilt as its granules are being used, but by the nucleus, which projects fresh granules of adrenoxidase into its threads;* (4) *the nucleo-proteid granules are continuously being taken up by the network from the accumulations of these granules stored in the cytoplasm between its meshes;* (5) *the ground-substance between the meshes of the network is passive in the vital process, being a depository for the stored nucleo-proteid granules, waste products, salts, etc.;* (6) *when the nucleo-proteid granules, and what carbohydrates may be present, are worn out, they are broken down by the various hydrolytic triads (ferments) also brought to the cell by the leucocytes, and converted into benign wastes which are cast out through the vacuoles into the lymph spaces and ultimately eliminated.*

In the nervous system, the biochemical processes involved correspond, on the whole, with those of cells in general. Yet the neuron, as previously stated, is not a cell-unit as now generally taught, but an organ; it presents, moreover, structural peculiarities as to the manner in which its blood is distributed to its cells. As to this feature of the problem: (1) *nerve-cells differ from ordinary cells in that they are supplied with adrenoxidase by capillaries (fibrils) that empty directly into their networks;* (2) *in the chief cell of the neuron, the "cell body," these capillaries, or "neuro-fibrils," reach the network or cytoreticulum, which is, as in other cells, composed of adrenoxidase (oxychromatin) granules, and immersed in a plasmatic cytoplasm containing groups of nucleo-proteid (basichromatin) granules;* (3) *in the neuraxon or nerve, the axis-cylinder fibrils allow the adrenoxidase to traverse their walls (as it does through those of ordinary capillaries) and to enter the slits of Lantermann in the myelin, which slits in turn open into the networks in this substance.*

As to the functional relationship between the cell-body of the neuron and its neuraxon or nerve, the manner in which nerve impulses are produced, and the nature of these impulses: (1) *the "cell-body" of a neuron is not a nerve-cell but a co-ordinating center endowed with marked irritability; as such it can react to nervous impulses and cause its own neuraxon or nerve to generate such impulses;* (2) *it performs this function by contracting around the upper end of the axis-cylinder fibrils that project into it; the (centripetal) current of adrenoxidase-laden plasma being thus impeded (proportionally as to degree and time, with the vigor and duration of the impulse), the pressure of this fluid in the fibrils is increased throughout the whole length of the nerve, and an excess of adrenoxidase is driven into the networks of the myelin;* (3) *the phosphorus- and fat-laden myelin being the cytoplasm of the true nerve-cell (the internodal segments around the axis-cylinder), the network of adrenoxidase immersed in it is the focus of chemical activity as in other cells, and the source therefore of the nerve impulse;* (4) *the true nerve-cells are the biochemical homologues of the cells constituting the electric organs of various animals, and the nerve impulse corresponds (as to its nature) with the impulses derived from such organs;* (5) *the waste products, which include lecithin, cerebrin, purin bases and phosphoric acid, are eliminated from nerve-cells, as elsewhere, into lymph channels, viz., into the peri-cellular lymph spaces around the cell-bodies; into the spaces between the nerves in nerve-bundles, and into the space between these bundles and their outer covering, Henle's sheath.*

Adrenoxidase is thus shown to be the dominating principle in nerve-cells as well as in all other cells. It is able not only to endow non-living though viable proteids with vitality by bringing into play and governing the activity of various other physico-chemical bodies, but it can also sustain the vital process it has initiated, in all the cells of an organism. Again, while we may define Life, with Herbert Spencer, as "the continuous adjustment of internal relations to external relations," or with de Blainville as "the two-fold internal movement of composition and decomposition, at once general and continuous," the need of a governing and vitalizing physical principle has asserted itself by the introduction into the problem at various times of an exogenous "vital principle," or a separate and distinct "vital force," etc. But such agencies do not bear close scrutiny. Spencer[228] closes his chapter on the "Dynamic

[228] Spencer: "Principles of Biology," vol. i, p. 122, 1898.

Element of Life" with the statement: "We find it impossible to think of Life as imported into the unit of protoplasm from without; and yet we find it impossible to conceive it as emerging from the co-operation of the components." The active principle of adrenoxidase was unknown at the time these lines were written; its rôle, we have now seen, is precisely to endow the protoplasm with life without introducing a problematic factor into the process.

General Remarks.—Notwithstanding the considerable and painstaking labor that physiologists have bestowed upon the questions of absorption, assimilation and metabolism—which labors have furnished much of the evidence I have submitted in these pages—none have remained shrouded in greater obscurity. As to absorption of food products from the intestine, Howell, for instance, says:[229] "The energy that controls absorption is furnished.....by the wall of the intestine, presumably in the epithelial cells. It constitutes a special form of imbibition which is not yet understood." According to prevailing views, the products of gastro-intestinal digestion should be found in the blood after their passage through the walls of the intestine: Mendel writes:[230] "Beyond the intestinal wall, in the blood and lymph stream, the cleavage products seem, for the most part, to be missing." The fluid proteids should also penetrate freely to the tissue-cells: Howell states: "The proteids of the blood, which are supposed to be so important for the nutrition of the tissues, are practically indiffusible, so far as we know. It is difficult to explain their passage from the blood through the capillary walls into the lymph." The prevailing knowledge of the intracellular exchanges is even less satisfactory: Sir Michael Foster[231] closes a study of metabolism in his text-book with the statement that, after all, it "consists mostly of guesses and gaps."

The reason for this deplorable lack of knowledge upon questions which represent the very foundation of all that we, physicians, should thoroughly understand before pretending at all to study diseased states intelligently, is not difficult to find.

[229] Howell: "T. B. of Physiology," p. 772, 1910.
[230] Mendel: Med. News, May 20, 1905.
[231] Foster: cited by W. G. Little, Liverpool Med.-Chir. Jour., Jan., 1905.

Without the functions the data submitted have led me to attribute to the adrenal secretion and the granulations of leucocytes, the problems of respiration, absorption, and metabolism are absolutely unfathomable.