The breaking strain (annual oration of Medical Society of London, 1896) / by W. H. Allchin.

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THE ANNUAL ORATION—"THE BREAKING STRAIN."

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Mr. President and Gentlemen,—Among the many and varied phenomena presented to our observation by living beings, there is no one that recurs with such persistent frequency, no one that our experience leads us so inevitably to anticipate, as that such a being will in time, whether long or short, cease to exhibit those manifestations in virtue of which we speak of it as living, or, in other words, will die. It has seemed to me that I might, and I hope without too great presumption, profitably occupy the occasion which the courtesy of the Council of this Society has extended to me in putting before you some considerations which are connected with the investigation of this problem. A fundamental explanation of it I do not pretend to—that were impossible, as impossible, indeed, as it is to affirm the "why" of any other "of the sense impressions distinguished by our perceptive faculty." But it at least is as capable of scientific treatment as other phenomena, whether they be associated with living or non-living material. And the collection and classification of the facts connected therewith, as well as the recognition of the sequence and relative significance of these facts, are as much called for and as reasonably to be expected as in any other problem of natural science.

The immediate practical bearing and importance of so difficult and recondite a question in physiology may perhaps be far to seek, even for a body of medical men actively engaged in the

practice of their profession and eager to avail themselves of any new weapon that science may furnish them with in their contest with disease. But I think now and then a short time may be advantageously spent in the consideration of subjects which, though not of immediate practical use, do seem to furnish some principles of general application, and to suggest some lines of coherence among the many scattered and apparently isolated observations which we are so constantly recording. It is pleasant occasionally to dissipate in generalities, to see what bearing phenonema may have to one another, and indulge therein by way of relaxation from the laborious accumulation of individual facts. The Medical Society, no less than other societies which claim to be scientific, regards, and properly regards, with some hesitancy of approval, the time devoted to theory and speculation. But we have to-night reached the end of an active session, and the knowledge of this, as well as the recollection that my present contribution is not followed by discussion, has led me to take, not, I hope, an undue advantage of your forbearance, by offering some remarks upon a subject which, I fear, may have been already dubbed by some of you impractical and transcendental.

It will be well to obtain at the outset as complete an objective conception of the phenomena as we can—to ascertain and realise, as far as possible, the facts of the case. To begin with, it is clear that we mean by death a condition of matter when it has ceased to exhibit any of the properties which we call living. For a thing to be dead implies, properly speaking, that the thing has lived, and the term is inapplicable—or should be, were we precise in our language—to material that has not been just previously living. It will be impossible, therefore, to enter on the consideration of death without some preliminary agreement in notion of what is meant by life, which, after all, is only another aspect of the same problem.

Conformably to the principles of modern science, we seek—*pace* the new vitalism—to refer the investigation of "vital phenomena to their physical and chemical counterparts or analogies"*—to refuse, in fact, to consider vital problems as understood that cannot be measured by the standards and methods employed in the investigation of physical and chemical manifestations, fully

* "Ludwig and Modern Physiology," by Professor Burdon Sanderson, F.R.S. 'Science Progress,' March, 1895.

conscious that our results merely end in description and not in explanation, and result only in ranging our "perceptual experience" within the scope of postulated natural laws, and not pretending to assert a supersensuous causation. It is also obvious that, to form any idea of life and its correlative death, it will not suffice to confine one's attention to the higher animals and plants, still less to man only, but that to obtain a thoroughly comprehensive notion, the investigation of the simplest forms of both kingdoms must be included, and so, by excluding the highly specialised functional manifestations exhibited in the most developed, ascertain what is common to all from the simplest to the most complex, thereby reducing the phenomena to their simplest terms. So regarded, we find that the essential facts of vitality, as ascertained by observation, experiment, and experience, are:—1. The invariable presence of a certain material of very easily recognised physical properties, but of a highly complex but as yet undetermined chemical composition and molecular structure, known as protoplasm, which recent investigation has tended to show is not so homogeneous as was originally thought, though the details of its arrangement the microscope as yet has imperfectly revealed. 2. Such material occurs in isolated and distinct particles of exceeding minuteness, probably always, even in its simplest form, differentiated into cytoplasm and nucleus—the cell; or as aggregations of such particles, frequently in association with other materials less complex in composition and not possessing the properties we call life. 3. Given this substance, we call it living when it exhibits certain special forms of energy to which the collective term "irritability" may be applied, or more specifically, "contractility," "nerve power," and "secretion." They are accompanied invariably by the liberation of heat and probably always, certainly often, by electrical manifestations, both of which are identical in nature and measurable by the same means as the heat of our fires or the electricity produced by our batteries. I am not concerned now to discuss how far these living energies are mutually convertible, or whether they are or are not correlated to the associated heat and electricity; it is sufficient to say that matter which presents these characters is called living, and unless they be present life is absent. Further, it would seem that for their manifestation there must be some immediate antecedent existing agent, some stimulus, whether that be of a gross and

obvious character brought to bear from outside or more subtle and obscure arising intrinsically. For the display of these properties and essentially included in the conception of life, is the presence in the cell of an adequate supply of non-living material—food, whereby its nutrition, as we say, is maintained. Regarded more closely, the three-fold functions above enumerated are the outcome of, or the expression of, protoplasmic nutrition, and as they are the essentials of vitality, nutrition and life may be to that extent regarded as synonymous terms. So far what I have said is within the range of verification by observation. The simplest speck of living matter, call we it animal or plant (or multiply the difficulty by speaking of an intermediate group, the Protista), equally with the highest known organism, may be seen to move, not infrequently in a manner strongly suggestive of purpose, to avoid or pursue in its movements this or that object, to engulph other material upon which it feeds and upon the presence of which its continued existence as living matter is absolutely dependent. Equally is it known by observation and experiment, no less than by experience, that the manifestation of life is subject to certain conditions of the environment of the cell, conditions that are familiarly known as temperature, moisture, sunlight, and atmosphere, including a due supply of oxygen and the like, certain degrees of which are favourable, as others are fatal, to the vitality of the protoplasm. Experience provides us with no knowledge of vitality apart from these conditions, and the vital phenomena we are familiar with may be regarded as the resultant of these external influences brought to bear upon the nutritive changes taking place in protoplasm. But just as for purposes of clearness of thought and to obtain the desired objective conception of our subject we consider the intrinsic protoplasmic changes apart from the influence of the extrinsic environment, so we have further to recognise that the range of variation within which the latter is consistent with life is very considerable, and that the living protoplasm has a considerable range of adaptability by which it adjusts itself to altered conditions. This power of adaptation we are in the habit of regarding as an inherent property of living matter, a factor of its vitality, just as the power of self-nutrition and the manifestation of irritability are other factors, all inextricably involved, and perhaps but different aspects of one and the same. If to these qualities be added the tendency to

death which sooner or later asserts itself, we have a summary of the characters by which we affirm that a given object lives.

It is necessary to consider a little more in detail what was just now spoken of as nutrition, to ascertain, as far as may be, the intricate nature of the processes therein included as bearing on their relation to the particular subject of my present remarks. That the living being is dependent on food, that this food undergoes certain changes in the living tissue, and that certain waste products of such changes are thrown off, are among the commonplaces of our experience, and are questioned by none, any more than the fact that, associated with this continuous ingestion, change, and excretion, there are evolved certain energies, some of which are peculiar to living substance. Indeed, so precise is most of our knowledge on this point, that what has been called the balance-sheet of energy, in which the work done by the body (in this case the body of some one of the higher animals) is accounted for by the food-stuffs used, has been prepared with such an approach to accuracy as to justify the expectation that it will ultimately be capable of being presented in such a form as to satisfy the most critical physiological auditor. But beyond such a view—a very superficial view—of the question, there remain deeper aspects of the problem, where we are not nearly on such firm ground, and where hypothesis and conjecture do duty at present for more positive knowledge; but so long as these hypotheses are admitted as such, and are in harmony with, or at all events not flagrantly opposed to, other fundamental concepts, we may claim to be pursuing the right path, at all events for the present, and until we are brought to a stop by the proof or even strong probability that our assumptions are erroneous. It is in respect to the exact relationship which exists between the ingesta and the living elements of the tissues in the course of those changes which eventuate in the liberation of vital energy that conjecture prevails, and, as may be supposed, no single hypothesis is wholly accepted. Are we to consider that the living protoplasm, whatever may be its ultimate structure, behaves as regards the pabulum supplied to it, as does a piece of machinery, say a steam engine, where the water and fuel are so disposed as to furnish steam power, with the result of a slight wear and tear of the mechanism and a discharge of waste in ashes and smoke, and that the machine is merely a suitable arrangement for effecting

the required changes in the material consumed, itself undergoing no—or practically little—alteration in the process? The relationship of the living structure (mechanism) to its fuel seems scarcely so simple as this; some at least of the food-stuffs duly elaborated in the processes of digestion, in the lymph and blood channels, and, possibly also in the liver through which they pass before reaching the tissue elements, would seem to be incorporated in the very tissue itself, to form an integral part of it, to be raised up to that height of molecular complexity and corresponding instability which pertains to the living particle, which is no sooner reached than it over-topples, so to speak, to be as continuously replaced, falling from the zenith of complexity to some more stable construction, disengaging energy in the change, and so passing from the pinnacle at which it may be pronounced living, which is no sooner reached than it breaks down into the condition again of non-living matter from which it had just been built up. In such a fashion it may be conceived that this living material is maintained, that the progressive stages of construction (anabolism or assimilation) passing over at a certain point, as yet not grasped, into a re-arrangement of molecules of the destructive or catabolic order, constituting thereby a perpetual succession of interchanges, a "cyclosis in which the organism returns after every cycle to the same point of departure, ever changing yet ever the same"*—in fact, life itself.

It would seem that but a small proportion of the nutritive ingesta is destined to actual living tissue construction, and that proportionately only a little of the total resulting vital energy is associated with the interchanges here postulated; but no hypothesis, as far as I am aware, has yet ventured to suggest exactly which of the specific energies are thus liberated, or, indeed, how far, if at all, they are independent of the probably less complex interchanges which take place in that major portion of the ingesta which are regarded as never becoming actual constituents of tissue, but which consist mainly of an oxidation process carried out within the range of influence of the protoplasmic metabolism. The terms "fixed" and "circulating"—the former singularly inapt—have been used to denominate these

* Address in the Section of Biology at the meeting of the British Association for the Advancement of Science, 1889, by Professor J. Burdon Sanderson, M.D., F.R.S.

two varieties of food as it finally reaches the tissues. Such, then, in summary, is what we mean by life, the processes of which are the subject matter of the physiologist's inquiry, to become the province of the pathologist when they overstep the ill-defined line which separates health from disease. By experiment and observation, constantly aided by the progressive advance of chemistry and physics, is our knowledge becoming more accurate and precise. But at the beginning and end of the subject, so to speak, are questions to which as yet but the most uncertain answer can be offered. Given the living protoplasm, given this material with its vitality, how has it come into being, how does it come to an end? With the "why" as an explanation true science has no concern, but the "how" is its legitimate scope of inquiry. Different as these questions may be at first sight, they are not, I venture to think, as different as they may appear to be, and I suspect any knowledge of the one will materially assist to a comprehension of the other.

Before proceeding to consider the nature of death, what is implied by it, and how it comes about, it is worth while to inquire whether death is an invariable termination to life, whether, in short, every being that lives does sooner or later die. If we confine ourselves to the higher forms of life the reply would undoubtedly be "Yes," but this cannot be so readily affirmed if we regard the simplest forms of existence. Here we note a close connexion between the mode of origin of life and the conditions of its termination. Universal experience shows that such beings as propagate sexually, whether animals or plants—or, in other words, beings which originate from the union of distinct sexual elements, and themselves consist of aggregations of cells and cell derivatives resulting from this union—will sooner or later die, even though, so far as can be recognised, their surroundings and conditions of existence remain the same as when their vitality was at its prime. On the other hand, those organisms which reproduce by a process of fission cannot, with a possible partial exception to be presently noted, be said to die, but to continue their existence in their progeny, which primarily consists of the constituent material of their parents, the whole of the parent body being used up in the formation of the descendants. If we regard, as I think we are entitled to do, fissuring of a protoplasmic unit (cell) as the exhibition of an extreme and peculiar form of

the power of contractility, which is possessed in some degree by all matter that is living (induced by some stimulus, the nature of which is quite unknown), but only manifested on certain occasions, then we bring the reproductive act of these asexual organisms into line with the common properties of living matter, and facilitate its consideration and description. If each resulting portion of a fissured cell continues to exhibit, after its separate existence, the characteristics of all living material as possessed by its parent, its power of self-nutrition with all therein implied, and its powers of adaptability, within limits, to varying conditions, and in due time to subdivide into two portions, each again continuing the *rôle*, then, indeed, such beings cannot be said to die, except by accident, and are essentially immortal. No greater difference in identity exists between parent cell and progeny than exists in the parent cell itself at successive periods of its own existence, consisting, as that existence does, of ceaseless changing with continuity of character. All unicellular organisms, however, do not appear to be capable of unlimited propagation by fission. It has been long known that the infusoria, which are among the highest developed of the protozoa, do, after a series of such multiplications, gradually exhibit a slackness in their fissuring, until at length the act is no longer repeated, and the individual dies. But should the infusorian meet with another of its kind in a like state of enfeeblement, and a temporary conjugation between the two occur, they will then separate, reinvigorated with a new lease of vitality, and continue their propagation by fission until again exhausted. Such a condition is one of less complete immortality than obtains in other protozoa and protophyta, but it falls considerably short of the inherent mortality that pertains to all forms of multicellular life. Among the metazoa and metaphyta by no means can senescence and death be averted, however favourable may be the conditions for their continued existence. But even then some multicellular organisms do not wholly die. The body of the individual undoubtedly perishes, but the sexual elements contained therein, and for the production and care of which the individual soma finds its chief *raison d'être*, whereby the species may be maintained, continue to live, given only suitable conditions, and the fertilised ovum resulting from these elements, consisting as it does of integral parts of the parents, develops and grows, thus main-

taining generation to generation in structural continuity. Death, therefore, which is a condition only known in the higher divisions of living beings, comes to mean a cessation of some only of the activities possessed by these beings—the greater proportion of their activities it must be admitted, and those which concern the maintenance and well-being of the individual as opposed to those by which the race is continued. It is the mass of the body that dies, that which lives or can live, conditions being favourable, constituting but a minute fragment compared thereto, in the highest forms of all a mere particle, and this participates in its partner's death unless removed to suitable surroundings. I need scarcely say that I make no reference to organisms being killed, that is to say, being subjected to unfavourable conditions cf the environment. Countless myriads of immortal protozoa die, but that is due to the nature of their surroundings; they do not contain within themselves the inevitable destiny of death which they cannot avoid. Similarly, myriads of the equally immortal sperm and germ elements of the higher and highest developed forms perish from like causes. My remarks obviously apply to death as a natural phenomenon, and as such it has a somewhat more restricted scope than at first appears.

The relationship of the sexual element to the enveloping and protecting soma is worth a moment's thought. Possessing as it does when suitably blended a potentiality of growth and development to the parent form, and dependent on the soma for such nourishment as it may require, it nevertheless maintains a passive existence in the midst of its surroundings, waiting, so to speak, its chances, which accident may prevent from ever coming to it. Meanwhile, the body continues to exhibit the functional activities of its vitality, however simple, however complex, until these processes of themselves gradually fail and finally cease. We are accustomed to recognise in the course of existence of a living being three stages: one of growth and development, one of maintained maturity, and a third of decline and senility terminating in death. For the most part, if not absolutely, these stages are characterised by very considerable differences, both in respect to the origin of life and to the cessation of it. During the first period the multiplication of the tissue elements and their individual increase in size, and more remarkably their differentiation of structure and specialisation of function, are all at the maximum,

fresh living tissue elements are formed by the division of pre-existing ones, and the generation and development of material prevail everywhere, notably, however, in one situation in a laggard fashion and sometimes scarcely at all, viz., among the portions which will ultimately give rise to the reproductive elements. Their inactivity is in marked contrast to the often rapid development of surrounding structures, they multiply but little, and differentiate scarcely at all, retaining throughout this period an embryonic character, such as they have possessed since they underwent the first stages that followed their separation from their parents. At this stage, when all efforts are put forth on behalf of the individual, its reproductive power is but slight or entirely wanting, and in the natural sequence of events, and accidents apart, death is unknown. When, however, full development is attained and the individual is complete, then a difference in the relative properties of these phases is seen. The efforts of the soma are directed to the maintenance of its structural integrity. The fully differentiated tissues exhibit their own functions and harmoniously work to the same end, viz., the life of the individual. Now the reproductive elements are mature, and the individual is capable of taking part in reproducing its kind. In a vast number of living beings the sexual elements are produced in the same individual, when self-fertilisation may or may not occur: in the highest forms they are borne in different bodies; but, be that as it may, the stage of maturity is that in which the sexual power of the individual is at its maximum, the formative functions of the tissue have largely diminished or even ceased, and death again except from mischance does not occur. Finally, after this stage has lasted a certain time more or less peculiar to each species, and not, perhaps, wholly unconnected as regards duration with the length of the preceding period, the organism begins to fail in its activities, to live less perfectly, and, as we say, to grow old, the tissue elements are no longer or but imperfectly renewed, those that remain atrophy and degenerate, the power of reproduction has departed, the individual has fulfilled its destiny, it has lived and reproduced, it now remains but to die. But death now is not an accident, it is an inevitable, inexorable event. Such a course is altogether in harmony with the principles which we recognise as natural selection and the survival of the fittest. The being that has filled its mission only

cumbers the ground, consumes nourishment required for those still in the fulness of their powers, and occupies valuable space; death for such is the fittest that can happen.

In this sketch of the successive periods of existence, and for the moment confining our attention to human existence, there may be noted with advantage the relation they bear to the incidence of disease. Disease, which is but a departure from normal living, such departure being detrimental or even fatal to the well-being of the individual, associated with some changes from the normal structure, ill defined in its limits because normal structure and function are ill defined and not accurately known, induced by some unsuitability in the conditions of the environment or imperfection in the original germ plasm whence the individual developed—disease, I say, has, like death, no natural connection with the stages of growth and maturity. All maladies occurring at this time are non-natural and are, or should be, preventable, and, apart from hereditary or congenital affections, the causes of which should have been averted in the parents or should have been prevented from perpetuation, are wholly due to external influences. On the other hand, during the decline of life disease as signifying a functional shortcoming from the normal standard of the prime is a natural incident. We may be able to show that a healthy old age is free from many of the ills commonly ascribed to it, and even that some not inconsiderable reparative power may be retained by the tissues, but nevertheless it is in the natural course of things for the tissues generally, some more than others, to degenerate, to become, that is to say, less complex in chemical composition and therefore more fixed and less capable functionally. One may be surprised now and then with exceptional cases in which the nervous or even the muscular energies have been unusually prolonged, just as the procreative power is occasionally sustained until an advanced age, but however long beyond the usual they may survive there is a limit to their manifestations. Did time allow it would be interesting to compare the clinical features of the diseases as they occur at these age periods, but I content myself with pointing out the normal incidence of disease, which in all cases approximates towards dissolution, as occurring simultaneously with the natural tendency to death.

If now we pass from the soma as a whole to consider the various constituent tissues as they exist in the highest forms of

life we are struck by several notable circumstances. Among the varied component parts of the mature soma, all derived from the fertilised ovum and in their earliest beginnings identical in appearance, the widest range of ultimate differentiation is attained. Whilst some, such as nerve cells and muscle fibres, represent the maximum of departure from the primary embryonic elements and with that the highest specialisation of function, others, like the white blood corpuscles and the simpler cell elements of the connective tissues or of the deeper layers of some epithelial surfaces, are but slightly removed in appearance from their embryonic ancestors, have differentiated but little, and are possessed of far inferior range of vital capability. But a further and striking contrast exists between these two groups—viz., in respect to their ability to reproduce their kind. A fully developed nerve cell or muscle fibre is not known to divide and multiply either in health or under the conditions of disease, but when once its full structure is attained by a process of continued fission and progressive differentiation the tissue element undergoes only such changes as are involved in its nutritive activity until overtaken by disease and death. Not so the simpler forms; they are constantly multiplying, much indeed as free unicellular organisms, and for the most part their successive progenies resemble almost or quite exactly the parents. With this one cannot but remember that the simpler tissue elements here mentioned appear to be equally and perhaps mutually active in effecting those reparative changes which are necessitated by accident or disease, reverting in so doing nearer and nearer to the embryonic form, and so giving rise to the healing tissue. Here, then, from this point of view, it will be seen that the highly differentiated tissue elements, like the more complex individual, invariably die, whilst the simpler forms, in proportion as they approximate to the germinal elements and as such to unicellular organisms, retain the power of multiplication and so escape from death the longest, though they have not the potentiality of development into an entire individual such as is possessed by the germ.

From the foregoing considerations we are now in the position to make these general statements:—1. That death as an incident in the evolutionary cycle is not inevitable to all living beings. 2. That whilst unicellular organisms are immortal, those of any higher grade of structure of inherent necessity die. 3. That

these latter are, given favourable conditions, continuously propagated by specialised portions of their own substance, the individual itself, apart from these portions, perishing. 4. That the power of self-division and hence of perpetuation with avoidance of death, is lost by cells which have advanced beyond the most rudimentary stage of differentiation, such power being restricted to those elements which retain their embryonic character, and most completely by those which form the sexual elements.

From such conclusions, then, naturally follows the question which is at the root of the subject, How is it that the vital processes decline and cease after a manifestation over a tolerably definite period more or less peculiar to each species of animal and plant, peculiar to them in the same sense as a specific size or shape is peculiar? What is the immediate antecedent to the cessation of vital activity as invariably seen in sexually propagating organisms? Whence comes, and what is the nature of the breaking strain which disrupts the ceaseless interchanges which constitute life? It may be at once admitted that no satisfactory answer can be given, and any attempt thereat, however reasonable, only pushes the question a step further back; but even that, if sure and certain, is a gain—it would be one more stage in the ascertainment of the sequence of phenomena which is the function of science, though leaving the "first cause" still unknown as being beyond the range of our perceptive faculty. To begin with, it has been shown that all protoplasm, all living matter, is not of necessity mortal. It is only certain specialised forms of protoplasm that are so distinguished, only certain individual living beings which inevitably die. If these two groups of individuals be contrasted, some clearer definition of the problem may be forthcoming. In the one case the individuals consist of but single isolated and independent particles of living matter (cytoplasm and nucleus), each possessing and manifesting all the phenomena which make up life; each particle is irritable, responsive to a stimulus, and exhibiting contractility (usually so disposed as to effect its locomotion) and some solvent (secretory) action on the foreign matter which constitute its necessary food and in virtue of which its nutrition is maintained. Each particle is endowed with a certain degree of the power of adaptation to its surroundings, which in turn exerts a modifying influence upon it; and, lastly, it can and does possess the capability of self-division,

splitting its entire self into two similar parts which differ from the parent individual only in bulk—a difference that is rapidly lost by simple growth from suitable ingesta.* Such individual beings, then, are all capable, all living, each one is complete in its vitality, and never, except by accident, dies.

The individual of the other group consists not of one but of many cells aggregated into colonies and masses of countless sizes and shapes; such cells, incapable for the most part of independent existence and mutually dependent for their well-being, collectively constitute the living individual. The organism thus constructed, so far as living goes, does no more than the simpler unicellular being, but it lives more perfectly, more elaborately, its vital processes of movement, of nervous manifestation, of secretion—in short, of its entire nutrition—are developed and exhibited at a higher pitch of perfection; its range of adaptability to the environment, of resistance or yielding to surrounding influences, may be greater, but in the long run it attains no further object than that accomplished by its simpler neighbour, viz., the propagation of its species, whilst the price it pays for its greater elaborateness of living is its inevitable death. Thus stated it would seem that the differences between these groups are of degree rather than of kind. The more complex vitality of the one is associated with a greater complexity and differentiation of structure, a subdivision of labour, that is, special functions being associated for their more perfect performance with more highly specialised structures, though these same structures, in proportion as they are differentiated, lose the power of self-division which is possessed in common with the other vital powers by the simplest form of protoplasm. These are but grades, and all intervening degrees are to be found between the highest and lowest beings. Nor is the difference as regards the incidence of death fundamental; whilst the one individual lives wholly in his immediate descendants, the other lives but in part, his own identity being lost in his death. But however much this mode of stating the case may conduce to a clearer understanding of the problem at

* It cannot reasonably be argued that this division into two is a virtual death of the parent individual in anything like the same sense as we speak of the death of a higher animal or plant, or that the progeny of the latter perpetuate their parents in the same sense that the resulting halves of a fissured cell do so.

issue, there still remains the unsatisfied question, How is it (or in common phrase, what is the cause of?) the organism, once that it has reached its maturity, in the full plentitude of its powers both for its own existence and for its own perpetuation, gradually comes to fail, grow old, and die? Why should it not, when once fully established, so continue for all time and remain immortal itself as well as perpetuated in its descendants? Wherein is the explanation to be sought? Is it in the continued effect of surrounding circumstances and conditions, the adverse influence of which gradually prevails, or is it from some inherent defect in the vital processes which becomes intensified by time and constant repetition? In whatever direction the source and nature of the disturbing influence are to be looked for, it would assuredly seem to be in that same region where are to be found the conditions which determine the chemical and molecular changes that constitute nutrition and vitality itself; and inasmuch as cell division, which is the essential of propagation, is but a phase of that aspect of nutrition known as contractility, it would appear that what knowledge we may come to acquire of the intimate nature of life will equally provide us with the explanation of the conditions of its origin and of its termination, inextricably linked as these phenomena are. Conceiving as we do that the energies of vitality are the sensible expression of continuous interchange in a highly complicated material, one phase of which is a building up, or assimilation, to be succeeded at some higher degree of complexity and instability by a breaking down and dissimilation, is it in the anabolic stages that the inherent antecedent that finally arrests the metabolism, and with it life, is to be found? or is it that in the catabolic descent, materials may be formed which exert a slowly increasing pernicious influence on the entire process, autogenitic poisons, in fact, that are invariable accompaniments of protoplasmic change? Or, lastly, may it be some failure in the stimulus, the existence of which is involved in our conception of this same protoplasmic activity? Conformably with our fundamental hypothesis of the nature of nutrition, it is difficult to see any other direction in which to look for our desired antecedent. Expressed in terms more in accordance with our grosser conceptions of physiology, does death result from some imperfection in the nutritive material (ingesta), or in some toxic product of waste (egesta), or for want

of the needful stimulus to the very changes which involve the material and determine the products? That it is the soma that dies, and that the life of the soma or individual is identical with its nutrition would, consistently with our present hypothesis, make it probable that somewhere within these concepts what we are seeking is to be found.

As may be supposed, many suggestions have been offered which find their place in one or other of these categories. Some, with Mr. Herbert Spencer, have sought to explain the phenomena by assuming a failure in the nutritive supply or in the ability to appropriate the ingesta on the part of the organism, the same conditions, in fact, as those which determine the limits of size peculiar to each living being. However true this may be, it gives no explanation for the inability displayed by the tissues. Among the theories which are based upon the determining cause of death being produced in the course of the changes which constitute life, may be mentioned that of Lendl. According to him the protoplasm in the course of its living forms waste products from which the germ plasm at first starting is free; as the cell divides these materials—termed by him "ballast"—are restricted to one of the resulting pair, and in the course of the subsequent growth and development of the organism those morphological units which form the perishable soma are loaded with ballast, whilst those which are destined to the perpetuation of the species, whether they be limited to the sexual elements, as is usually the case, or form a part of the general structure, as seen in some leaves—*e.g.*, begonia—are free from the noxious material and in consequence escape death. It need scarcely be said that no proof of this hypothesis exists any more than there does of the suggestion that it is the presence of an aldehyde in living protoplasms, which serves as the stimulus to its activities and that death is caused by a want of this substance. Others have assumed that the stimulus to vitality emanates from the nucleus which in the process of living becomes gradually exhausted and is finally extinguished.* There is one circumstance which seems to bear a very constant relation to the onset of death—viz., the reproductive effort. In very many beings this effort is made but once, and

* For the discussion of various theories on the intimate nature of death, *see* 'La Structure du Protoplasme et les Théories sur l'Hérédité par Professor Delage,' 1895.

then as a rule death soon follows. In others the effort is capable of being repeated over a period (maturity) of varying length, but when it fails senescence sets in. A review of all the circumstances would seem to show that failing vitality follows the cessation of reproductive capability rather than that this latter fails because of approaching death, and, if we may speculate with others, it appears to be among the possibilities that the lacking stimulus is to be found in connection with the sexual elements themselves—some ferment, may be, such as we assume to exist in those lately recognised internal secretions the potency and influence of which in respect to nutritive processes we are but just gaining a glimpse of. An analogue for my suggestion is perhaps to be found in the case of the thyroid and thymus glands which exercise a profound control over tissue nutrition and even over growth itself. So may it be with the reproductive organs and their products. Exhausted by their efforts to perpetuate the individual, they no longer liberate that stimulus (call it provisionally ferment, internal secretion, or what you will till more precise knowledge defines it) which is needful for the maintenance of the nutritive processes of maturity, and for lack of which the individual deteriorates and dies. May it be that there is a real truth embodied in the experiments of Brown-Séquard, however incomplete they have hitherto been in results?

Based on some such considerations as these I have put forward must be, I take it, the full comprehension of the nature of death as we are in the habit of witnessing it at the bedside. We speak of cardiac failure, of fatal intoxication, whether from within or without, of arrested nerve influence and the like, but the real meaning of such phrases, imperfect as they are and often quite inadequate to explain why death should have happened, must be somewhere in the region I have now been groping in. Moreover, the very foundations of prognosis, if not of treatment, so far as this may attempt to modify nutritive processes by drugs or other reagents, must be built upon an understanding of the intimate nature of life and the inherent causes of its failure and cessation.

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