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FUNCTION AND DESIGN[1]

AMONG natural sciences physiology takes a place which in one respect is different from that taken by any other. It studies the phenomena of life, but more particularly the ways in which these phenomena are related to the maintenance of life. Anatomy and morphology are concerned with the forms of living organisms and their structure; biological chemistry, as distinct from physiology, with the composition of the material in which the phenomena of life are exhibited. The province of physiology, in studying the functions of these forms and of this material, is to ascertain the contributions that they make to the organization of the living mechanism, and learn how they minister to the maintenance of its life. Function implies ministration, structure for physiology implies adaptation to function, what in a word may be termed design.

Ultimate analysis of the phenomena with which physiology deals leads to the fundamental distinction between matter in which life is manifested and matter in which it is not. Life is exhibited only in aqueous systems, containing unstable, perishable combinations of carbon with hydrogen, nitrogen, sulphur, phosphorus and oxygen, in the presence of certain inorganic ions, those which are present in the sea, the native environment originally of all forms of life; and the inalienable property that such matter exhibits when alive, and that matter which is not alive does not, is that these unstable organic combinations are forever reforming themselves out of simpler combinations that do not exhibit this property, and do so at a rate which averages at least not less than that at which they break down. This power of self-reformation, spontaneous regeneration, operates not only when living organisms, cells or communities of cells are growing or reproducing their kind; the very maintenance of living existence requires by definition that it should persist. In the absence of water the living process may sometimes apparently be suspended for a time, as it may be if the surrounding watery medium is immobilized by cold; it is a question whether this is anything more than a retardation to a rate of change that is imperceptible by the ordinary methods of observation, and a question how long such suspended animation is possible where it is possible at all. It is only where water has the kinetic activity of the liquid state that spontaneous regeneration of

[1] Address by the president of Section I—physiology—of the British Association for the Advancement of Science, Oxford, August, 1926.

living matter can in general proceed, and then it must, for when it ceases the unstable material ceases to live.

Chemical analogies for this power of spontaneous regeneration, if such exist, can only exist in part; in the present state of our comprehension of it, certainly, it is hazardous to try to trace them. The attempt so commonly made to trace one between the growth of living matter and the growth of crystals in a saturated solution, it is safe to say, is in so many respects on the wrong lines that it is merely misleading. Crystals are not alive. The molecules that constitute the crystal are set in solid formation; so long as the crystal exists they are stable and unchangeable. These molecules collect on the growing crystal, but they exist ready-made in the surrounding solution; they do not come into being by the influence of the crystal; they are themselves so constituted as to take up a set position in relation to each other and to those already ranged side by side in the crystal, as soldiers on the drilling-ground at the word "fall in"; they are available because the solution is kept saturated by the dissolving of smaller but similar crystals that for physical reasons are more soluble in the solution than the larger ones. In contradistinction to this, the molecules that enter into the composition of living matter exhibit the phenomena of life only when permeated with water molecules exercising the kinetic activity of the liquid state; they are unstable and perishable; the added molecules, some of which even during growth and all of them at other times serve but to replace those that perish, do not exist ready-made; they come into being only in conformity to the pattern and under the influence of those already in existence, a pattern that these alone can use; and they are formed out of material that is chemically different from them.

Let us for a moment consider what this spontaneous regeneration implies. Of the various chemical components of protoplasm proteins are generally considered the most important, often the only important, ones. The elucidation of the chemical principles upon which the structure of proteins rests, which took place about the beginning of this century, was, like the neurone hypothesis of the structure of the nervous system, an advance the magnitude of which only those perhaps can appreciate who began the study of physiology well back in an earlier one. For a time it seemed in each case that the problem was solved and all that was to follow was simple. Those were great days. The best-known varieties of proteins, when detached and uprooted from the place where they grew, consist of chains of about a hundred, sometimes nearly two hundred, links. Each link is an amino acid coupled by its acid group to the amino group of one neighbor and by its amino group to the acid group of its other neighbor, a molecule of water being lost at each linkage. There are not more than about twenty different amino acids, so that some of them must occur several times in the chain; in some kinds of protein one amino acid may occupy thirty or forty of the hundred places in the chain. In any such isolated protein it is probable that the order as well as the proportion in which each amino acid occurs in the molecule is fixed, and it is this specific order and proportion that accounts for the specific character and properties of the protein. What could be simpler? And only yesterday all was so obscure.

It is not recorded that in the rush of this advance any one stopped to reflect what number of formations such a protein might still possibly have. Supposing it were a chain of only fifty links, a very simple case; if all the links were different the number of possible permutations is denoted by the innocent-looking symbol $\underline{|50}$. If, instead of all being different, one kind of link recurred ten times, the number would be reduced to $\underline{|50}/\underline{|10}$. If, in addition, there were four that recurred four times and ten that recurred twice, it would be further reduced to

$$\underline{|50}/\underline{|10} \times (\underline{|4})^4 \times (\underline{|2})^{10}.$$

It would now consist of a chain of only fifty links, of which there were only nineteen different kinds, and the number of different arrangements of its parts would be about 10^{48}. Astronomy deals with big figures. Light, it is said, takes 300,000 years to travel from one end of the Milky Way to the other; this distance expressed in Ångstrom units, 10,000,000 of which go to a millimeter, would be less than 10^{32}. So far are we from knowing the structure of protein molecules. So far are we from knowing what variations in disposition of the parts in such a molecule may not occur without our being within a measurable distance of detecting them. For if the number of possible varieties of a protein whose molecular weight is known, and known to be exceptionally small, and which contains the several amino acids in a known proportion, is as great as this, the number that is possible when that proportion may be changed is practically incalculable, each change in proportion being capable of a number of new arrangements that could be calculated, as was done for our hypothetical case.

But in the living cell where these chains are put together each link must first be fashioned and then forged into the chain; unfinished chains *in statu nascendi* must exist which our analytical methods can never detect. In such unfinished chains the order presumably in which the amino acids are linked up is observed, but the proportion must be different from that in the finished product; for in a chain of nearly a hundred links a particular amino acid, cystine, for instance, may occur only once.

Now it is possible that the analogy of crystal formation may be applied to the reproduction of the characteristic order in which the linkings occur, and that the parts out of which a new chain is to be formed may be collected and brought into position alongside of the corresponding parts of an existing chain by forces that are similar to those that determine the latticed relations of atoms in a crystal. But something more than this is required to account for the linking up of these links by the loss of water, and still more for the fashioning of the links themselves. In plants all varieties of amino acids come into being as required; in animals, it is true, some must be supplied ready-made in the medium in which the proteins grow; but even in animals some of them can be formed from material of a totally different nature.

Wherever this is the case we have to suppose that it is by selective emphasis of certain otherwise unemphasized but possible arrangements of atoms or groups of atoms, evidence for the occurrence of which under similar conditions in the absence of life is generally not obtainable. Specific catalyzed syntheses must cooperate with the forces that merely sort out and place in proper order the assembled parts, and must fashion for them the particular links that they need at each step. Specific catalytic agents playing an important part in cell chemistry are familiar in the enzymes found in digestive secretions and also locked away within the cells themselves. There is much to support the idea that such agents act by modifying the chaotic, indeterminate, kinetic agitation of certain kinds of molecules in their immediate neighborhood in such a way that the relative positions in space of groups capable of reacting with one another tend to become those in which reaction is likely to occur and to occur in conformity with a certain pattern. The peculiar thing about the chemistry of living matter is not that the reactions that are characteristic in it are novel, but that in the rough and tumble of ordinary liquid systems their occurrence is almost infinitely improbable. Where there is life circumstances exist which make them the rule. Any one conversant with work in animal metabolism can supply many illustrations; for instance, it has been shown that in a simple solution of the amino acid alanine traces of methyl glyoxal occur; in the animal body there is reason for thinking the reaction may become practically quantitative. Forces which determine the relative positions of adjacent foreign molecules and so affect their behavior are something to which there is no analogy in the growth of crystals in a saturated solution.

Moreover, if the forces that determine the reproduction of a certain order in the arrangement of the parts of a protein are similar to those that determine the lattice pattern of a crystal, the crystals with which the comparison is made are solid, and life is manifested only in liquid aqueous systems. The analogy should rather be with the formation of liquid crystals, a phenomenon that is itself as yet too unfamiliar to shed common light on the obscurity of spontaneous regeneration. The ordered disposition of the ultimate components of protoplasmic systems is such as to leave play, generally but little checked, for the fluid properties of water, and in some modified degree too of molecules and ions dissolved in water. Even a solid jelly may include within its protein framework a hundred times its weight of water in which diffusion is free to take place almost as if the framework were not there, and protoplasm, with commonly twenty times as much protein in it as this, more often resembles a fluid of varying viscosity than a solid gel, which means that the great protein chains float and drift in the whirlpool of kinetic agitation, observing, it may be, so far as is possible, certain unstable relations to their kind, but with no rigid fixity. It is commonly felt that the behavior of unicellular organisms makes the hypothesis necessary that there is an insoluble surface layer that keeps the watery contents of the cell from dispersing in the water that surrounds it. Much experimentation, and no lack of speculation, has not made clear what the nature and structure of this limiting layer is. It may be that the flexible cohesion at many alternative points between clinging floating chains of amino acids, the innermost of which are made fast to the nucleus, may go some way to maintain the identity of the cell and prevent its contents from scattering.

But in the chemical make-up of protoplasm, proteins, the most abundant component, are not the only ones that are necessary. Preeminent among the others are the nucleic acids. When we consider what has been learned of the behavior and of the chemical composition of the nuclear chromosomes, and that according to Steudel's reckoning the nucleic acids form 40 per cent. of the solid components of these chromosomes, into which are packed from the beginning all that preordains, if not our fate and fortunes, at least our bodily characteristics down to the color of our eyelashes, it becomes a question whether the virtues of nucleic acids may not rival those of amino acid chains in their vital importance. From Steudel's figures it can be reckoned that there are about half a million molecules of nucleic acid in a single sperm cell of the species with which he was working.

But in addition to nucleic acids there are also strange compounds of higher fatty acids containing suspiciously significant groups, identical in their general character with those found also in nucleic acid, namely, phosphoric acid, organic bases and sugar; and besides these there are the mysterious sterols. All of these are frankly insoluble in water, and yet have in some part of their composition features that make them not indifferent to water or even to the molecules and ions that exist in true solution, in the liquid state, within the cell. The physical condition of these insoluble substances in the aqueous system of the cell is still little understood. All that can be said with certainty is that they must modify its homogeneity even more than the long floating chains of amino acids, however much these may be linked together one with another. If the characteristic behavior of living matter is rightly regarded as due to the order that it introduces into the movements and spatial relationships of foreign molecules in its vicinity, then these insoluble components may well be expected to play a leading rôle by forming films and surfaces that permeate its texture and delimit its parts.

Such an analysis of the chemical meaning of material life viewed in the light of scientific facts has to be largely an exercise of the imagination, but it may present itself as an intellectual necessity. If it is right to regard the power of spontaneous self-regeneration as the distinctive property of living matter, it is not intellectually possible to be content with a phrase and dismiss it. A phrase is itself an image, and an image, however shadowy, has parts and dimensions. Those who feel it an intellectual necessity to explore unexplored lands can not procure maps, but that does not justify their setting out with no forethought or reasoned plans.

The beginning of life, if it is an intellectual necessity to trace this, would thus appear to have been in the coming together of atoms of certain elements in such a pattern that this power in its simplest form resulted from its design. Some might call this event fortuitous, others the predictable outcome of the inherent properties of those elements, the inevitable operation in the course of time of the laws of chance. Those who call it fortuitous may go so far as to regard the whole history of life as fortuitous, and give priority to the concurrence of the atoms over the properties and functions that are revealed by the concurrence. The others may look on life as the fulfilment of the destiny of these elements, and give priority to the potential properties of matter over the concurrence which was no more than their epiphany.

If this analysis is approved and the distinctive property of living matter, the power of self-regeneration, depends upon the power of limiting the movements and directing and controlling the spatial relations of surrounding molecules so as to modify their chemical behavior, it is the exercise of this same power that leads to the formation of substances such as starch, glycogen and fats; and in so far as such substances contribute to the regeneration of the living matter, the power of forming them contributes to its survival. Where energy is necessary for such synthetic rearrangements of adjacent matter—where, that is, the rearrangement involves coercion of atoms into positions of strain in which they have the potential energy of position which we call chemical energy—this energy may be derived from the radiant energy of the sun or from the combination of oxygen with adjacent organic matter. In the latter case the combination is again a manifestation of the power of ordering the disposition of surrounding molecules and directing their movements so that they behave as in other circumstances they would be but little prone to do. The energy so liberated, besides contributing to the formation of new living matter or of the material to be used in its formation, may serve in other ways to promote the processes by which life is maintained. It may accelerate them by imparting increased kinetic activity or rise of temperature, or may bring about movements that are resisted by external forces, and so enable the living system to do work.

This is all merely a restatement of the commonplaces of biology, necessary only as part of the attempt to correlate them physiologically with the fundamental property of that which is alive to regenerate itself at the expense of material that is not alive. This faculty implies the power of introducing order into the chaotic movements of adjacent matter in conformity with patterns that it possesses. It is a faculty resident in material that is capable of incalculable variation. The number of permutations of its parts that are possible without affecting the results of such analysis as is practicable defies calculation. Their calculation, were it possible, would lead to figures that are so large as to mean no more than the dimensions of the universe. Some of these permutations confer synthetic powers which others do not. When they appear, are they not what biologists call for short mutations? But when they appear, if they retain the power of self-regeneration, and if they minister to its maintenance, they will *ipso facto* survive. For whatever promotes persistence of this power must itself survive.

A disposition of matter in molecules or aggregates, unstable and incalculably variable, that has and retains the power of determining the disposition of matter not yet so disposed in such a way as to conform to its own disposition or to patterns which help it to exercise this power, is all that must be premised for the whole of evolution to follow. Variations that do not or cease to contribute to the retention of this power do not survive. The condition of survival is ministration to self-regeneration, that is to the maintenance of life.

Before the days of vertebrates, in pre-Silurian time, an unstable variation in the disposition of atoms and organic combinations of atoms occurred in certain types that was mainly protein in character, a protein to the making of which little short of 200 amino acid links must contribute. Coupled to this protein, which probably is not the same in all species of animals in which it is found, is another group containing iron that is probably always the same. This group is of remarkable nature, and is closely related to one that occurs in the far older substance chlorophyll. This complex substance hemoglobin had the power of attaching to itself two atoms of oxygen for each atom of iron that it contained in such a way that it could be readily detached and made available for effecting oxidations. Such was the service that this variation rendered that it is safe to say that without it there could be no vertebrate creation. It is this service that has made it possible for it to survive to this day, when in the human species alone it is being produced at the rate of about 10,000 tons a day. The story of the service of chlorophyll would, of course, be more remarkable than this.

Natural selection applies to the survival of the chemical forms of living matter as it does to complex living organisms. These forms, infinitely protean in their variety, survive and persist in so far and so long as they minister to its self-regeneration. It is the principle of survival by service. Function alone gives permanence to structure. Structure without design is a pathological excrescence that has in itself the seeds of its own destruction. What does not minister to self-regeneration has no enduring share in life, for self-regeneration is the key to life.

Why is it that what may be termed official physiology takes so little cognizance of the doctrine of evolution? These branches of biological study appear to follow courses so exactly parallel that they never meet.

The doctrine of evolution digs down into the foundations of scientific philosophy. If a physiologist addressing physiologists ventures to say anything on this subject of supreme appeal to all biologists it must be in exaltation of the work of those who have approached it from the morphological side, and it may be in hopeful anticipation of the ultimate share in the elucidation of some of its problems to be borne by physiology.

On the part that function plays in the determination of structure it is to be supposed that physiology will ultimately, at any rate, have something more to say. May I submit to the consideration of physiologists certain points in the physiological development of the machinery of the body where, unless I am mistaken, it is possible to detect the operation of function in determining the design of the machine? The properties and behavior of cells result from the properties and behavior of the material composing them. When a muscle cell contracts this is, in general terms, a reversible rearrangement of its parts in response to some alteration in the distribution of forces within or about it due to a disturbance from without. Such reversible reaction to adequate disturbance is a property common in the material of which living cells are composed. In addition to this reversible type of reaction there are irreversible reactions which are characteristic of other kinds of cells, and it is what we call connective-tissue cells that I would ask you to consider. There are several kinds of connective-tissue cells, but they are alike in that they produce and discharge into their vicinity material of a characteristic composition; in some of the commonest this material is chemically collagen, the substance out of which gelatine can be obtained. In course of time these cells come to be embedded in the material which they deposit about themselves and so form one kind of connective tissue. Cells capable of behaving in this way are found, however, which have not yet exercised their faculty; these fibroblasts are then undifferentiated wandering cells that have found no abiding place in the community in which they have their birth. What it is that makes them settle down and start producing the material in which they come to be imbedded has never yet been determined. But the most striking structures to which they give rise are the tendons and aponeuroses that make the muscles fast to the bones, and the ligaments that bind the bones to one another. The material that they deposit is composed of inextensible fibers that lie in the case of tendons, at any rate so exactly and exclusively in the line of the resultant of the tension set up in the muscle to which they attach themselves, that it is difficult to believe that the disturbance which starts them producing their characteristic secretion is anything else than the pull exerted on them by the muscle fibers to which they are attached; the recurring external disturbances that produce reversible states of tension in the muscle, indirectly producing in them an irreversible reaction, which consists in the discharge of material that by its inextensibility can transmit the tension along the line of the force that provokes its deposition. In their simplest form cells of this kind deposit the wavy fibers in areolar tissue which, when straightened out under the action of a displacing force, set a limit by their inextensibility to the dislocation of the part first affected, and so distribute the action of the displacing force over surrounding areas. It is interesting to note that the origin of cells of this kind has been traced to the mesothelium cells that line tissue spaces and serous cavities, the clefts that make the gliding displacements of parts over one another possible. The deposition of fibrous material seems here, as in the tendons and ligaments, to be the result of reaction to the recurring disturbances set up by displacements, such, for instance, as those of the lungs, the alimentary tract, the heart and pulsating vessels, and the deposition occurs in the line of strains set up by the displacing forces. The service rendered by this behavior of the cells is that the fibers which they deposit, in virtue of their inextensibility, limit the extent of displacement at any one point by distributing it to surrounding parts.

The other component of areolar tissue, the elastic fibers, is similarly produced by other cells. These fibers take a straight course between their attachments; displacements in the line of their deposition are rendered possible by their stretching, and are recovered from by their elasticity.

The contribution made by such cells to the fabric of the body appears to result from the recurring operation of disturbances, to which they react by depositing fibers along the lines of disturbance.

More striking are the properties of cells upon which the formation of the skeleton depends. The cells that make bone not only secrete fibrous collagen, they also encrust the fibers with insoluble lime salts, and it has long been subject of comment that the rigid bone that results always comes to lie in the line of prevailing strains and stresses. The analysis of the structure, for instance, of the head and neck of the human femur, by Wolff and others who have followed him, shows how strictly this is true. Calculations prove that no particle of bone lies anywhere but where the strains dictate. We can predict with certainty, it seems, that it will be found that bone cells are composed of material that in reacting to physical forces directs, in constant relation to the line of action of those forces, the deposition of the substances which make up this connective tissue. Bone can only arise where strains and stresses set up this reaction, and the greater the strain or stress the denser the deposit. When a bone is fractured many bone cells are dislodged, and in the abundance of nutriment that ruptured vessels supply, these cells, released from their imprisonment, multiply. At first the force of gravity and the twitching of muscles acting on the soft semifluid tissues between the broken ends of the bone supply stimuli that are indeterminate in direction, and such reaction as occurs results only in the formation of loosely ordered calcareous fibers; but even this soft callus gives some degree of rigidity, sufficient to restrict the strains gradually to more and more clearly defined lines along which in proportion a stronger reaction can take place. Once it is established that bone corpuscles react to strain and stress by discharging collagen, the intimate spatial disposition of which, as well as of the lime salts with which it comes to be encrusted, is determined by the directing forces to which it is exposed; and once it is recognized that the law of spontaneous regeneration requires that this reaction will persist in proportion to the prevalence of these forces, not only must the gradual replacement of callus by appropriate permanent bone necessarily follow, bone in which no particle persists except it be in the line of constantly recurring stress and strain, but it will also necessarily follow that the position of every spicule of bone in the skeleton, cancellous or compact, is the expression of a physiological reaction to the forces of gravity and muscular tension. The evolution of the machinery of the connective tissues seems to be not entirely the result of natural selection and the survival of individuals in which this machinery chanced to be of appropriate design. The appearance in early vertebrates of the material that is characteristic of the bone corpuscle seems to have ensured that skeletons would take a shape determined by the direction of the forces to which these corpuscles were exposed, and that the formation of this skeleton is as much a reaction to recurring stimuli as are the reflexes, composite movements and postures characteristic for the species.

This conception of the way in which the vertebrate connective tissues take their shape transfers a large share of the development of the bodily form back into the nervous system, in which the machinery is stored that directs and determines the habitual movements and postures that in reaction to external disturbances are specific. A physiological account of the evolution of the nervous system, one certainly that is based on the chemical constitution and chemical behavior of its component parts, must seem almost infinitely remote from practical investigation. But the work of Pavlov has made one thing clear, that by a physiological reaction in it machinery may come into existence which did not exist before. The repeated occurrence of a disturbance at times that are uniformly related to the normal operation of existing machinery results in the acquirement of a new reaction which must require machinery that is new. It is rendered probable, if not proved, that this new machinery is situated in what may be called the growing point of the central nervous system, the cortex of the cerebral hemispheres, the part where all is not cut and dry, where cells retain more of the properties of the developing neuroblasts, the properties that enable them to grow out through the embryonic tissues along courses that make it certain that the maturing organism will behave in a manner true to type. In the formation of a conditioned reflex two events are made to occur in the cerebral cortex at times which are uniformly related to one another; one of these events, from the constitution of the nervous system, necessarily results in a certain activity of some muscle or gland, the other has been hitherto in no way related to such a result; after many repetitions of the association of these events it is found that that one which previously had never resulted in this particular activity comes to have this result as certainly as the other.

The sight and smell of food in any hungry animal results in the secretion of saliva because the cells to which the effect of these visual and olfactory stimuli is referred are anatomically connected with cells that set the salivary gland in action; the cells on which some particular sound takes effect are not anatomically connected with them, and this particular sound has therefore no effect upon them. But with the establishment of the conditioned reflex the anatomical connection comes into existence. As a result of a functional reaction of nerve cells to disturbances in other nerve cells with which they were not previously anatomically connected, a structure appears which is indistinguishable so long as it lasts from the structures that constitute any other reflex arc. The conditions that determine its persistence or effacement have been, and are being, studied as thoroughly as were those which allow it to appear. The outcome of these studies must be of incalculable importance in evolutional physiology. They are being watched with the keenest interest doubtless by all biologists, but more especially by those who believe that physiology has to take a much bigger part in the solution of some of the fundamental difficulties of biological science than it has been able to take in the past.

But if and when it is possible to trace the origin of structures to functional reactions of cells, and to reactions that depend upon the chemical properties of the cell substance; and if and when this is possible not only in the connective tissues, but also in the nervous system, the functions of which have so controlling an influence on the operation of every part of the body; until it becomes clear that the results of changes in such influence reappear in succeeding generations, the study of functions can have no bearing upon the ultimate problem of biology, the evolutional history of life upon the earth. Pavlov communicated to the last International Congress of Physiology in 1923 some results of experiments that he had done upon this subject which, when confirmed, would electrify the atmosphere. Conditioned reflexes that are established only after many—eighty or a hundred—repetitions of the associated stimulus, in each succeeding generation require fewer and fewer repetitions, and in the fourth may be established after only four. In April of this year he wrote to say that owing to other work he had not been able to give the necessary time to confirmation of these results. We are content to wait.

In the great question whether characteristics developed in the life of an individual have any influence on descendants, experimental evidence must come slowly. In what is called parallel induction a step has been taken which is probably of greater importance than is generally conceded. External influences that affect the bodily characteristics of an organism affect also the germplasm in such a way that these characteristics appear in the first, and even, in a less degree, in the second generation, born after the external influences have ceased to operate. While such experiments furnish evidence only of a temporary change in the properties of the germplasm, one that may be put down to the lodgment in it of unassimilated foreign matter that is gradually eliminated, the fact that the eternal germplasm has been shown to be subjected to temporal influences must not be belittled. A true mutation is not eternal. Our descendants may be able to dispense with hæmoglobin. Whether the hereditary melanism that in certain moths, it is said, can be induced by food infected with manganese, is something more than such parallel induction, I hope there may be some present who can say.

Physiological inquiry is a stream that has many sources; its waters gather from quarters far removed from one another. A marvelous meeting took place in the early years of this century when the forgotten experiments of Mendel came to the surface again, and found corroboration in the cytological studies that from about the same time had pursued their slow obstructed way above ground in the endeavor to elucidate the changes in the nucleus of maturing germ cells. In a resting germ cell the chromosomes form an even number, characteristic for the species; they consist of half that number of pairs of homologues, one of each pair descended from the paternal element in the last zygosis, the other from the maternal. At one of the cell divisions by which the germ cell gives rise to the mature gamete, with half the characteristic number of chromosomes, there occurs a segregation of the two members of each pair so that they pass into different gametes; the exact cytological equivalent of Mendelian segregation of allemorphic pairs of characters. To-day the study of genetics and of the "topographical anatomy of the chromosomes," with its "groupings" and "crossings over," seems to call out for chemical assistance. It may be that in the lifetime of some of us those confluent streams of thought and experiment are to be joined by yet another that rises in the vast, remote and, as it must appear to some, muddy swamps of physiological chemistry; and it then, forgetting its "foiled, circuitous wanderings," will form with them a "majestic river, brimming and bright and large."

J. B. LEATHES

THE RELATION OF EVOLUTION TO MEDICINE[1]

NOT so very long ago the phrase "art of healing" covered quite satisfactorily nearly every activity of the medical profession. To-day the term "scientific medicine" seems to have displaced the older phrase—but not actually, for while recent advances in medicine can definitely be laid to the development of scientific methods of investigation and to our increasing familiarity with fundamental facts concerning organic life, the *art* of medicine still relates to the skill with which our newly acquired knowledge is applied in the fields of medicine and surgery. Medical science, therefore, pertains more specifically to our efforts toward acquiring a better understanding of biological laws which may serve as a basis for originating newer and improved methods of curing and of preventing human ailments and diseases. In other words, it constitutes the foundation upon which the practice of medicine is being remodelled along more substantial and scientific lines.

This recent development has brought within the range of medical research certain branches of biological science whose relevant value has heretofore been rather obscure, if recognized at all.

While the practice of medicine is primarily concerned with that which lies beyond the range of normal variation, our ability to analyze any abnormality is directly proportional with our knowledge of what constitutes normal conditions and the normal range of variation. In the past, the treatment of an abnormality has consisted, figuratively, of an attempt to directly force it back within the normal; modern medicine, however, tries rather to preserve normal conditions, or, in the presence of abnormalities, to eliminate them by reinforcing those factors which ordinarily safeguard the body against them. Hence the very basis of our future progress may be said to depend upon our knowledge of what constitutes normal conditions and of the biological factors which ordinarily maintain them, quite as much as upon our familiarity with those factors which are capable of disturbing that state of normalcy.

[1] From the Department of Surgery, Yale University, New Haven, Conn.

Health, and disease or abnormality of any sort, are merely interactions between the human organism and its environment; health constitutes the normal phase, the others result from the introduction of some element of disturbance.

In the study of human ailments and disorders, we must realize that man is *not* a specially created being placed here to dominate over all the previous inhabitants of this globe; physically, he is merely one of a countless number of similarly constructed, highly complex organisms. So completely does he duplicate in his physical being the vital organs, the various distinctive tissues and an almost uniform homology of the skeletal segments of other creatures that the physical modifications by which he is distinguished from them seem very superficial. All his physiological processes and specific structures carry so far back into the remote past that, in comparison, man's stature and body-form would seem to be a very superficial source of differentiation and a very modern acquisition, while his mental superiority would seem to be an endowment of only yesterday.

What is the relationship of evolution to medicine? The problem of evolution permeates every fundamental branch of medical education in such a manner as to signify that it represents a most important and unexplored source of biological knowledge which should prove of inestimable value to future medicine.

After the anatomist has familiarized himself with the structures of the modern human body, he immediately finds himself plunged into the problem of evolution. Why? Because in his search for advanced knowledge he must naturally turn his attention toward their original source and attempt to learn the history of their development.

The various branches of biology consider the phenomena of life as displayed by all types of living organisms, ranging from the tiniest single-celled protozoa to the largest and most highly organized forms, including man. In those studies a classification of these forms of life according to their grades of organization and according to phylogenetic strains disclose their evolutionary relationships in a striking manner.

Embryology explains to us the modern development of the highly complex individual from a single-cell stage. It has bared to us many secrets regarding the evolution of mankind. But the present embryological process is, of itself, a product of evolution, having become more intricate as each higher level of organization was attained by the matured creature. Thus while the prenatal process serves primarily for the creation of a new individual, it still retains phenomena which bind man inseparably with the lower forms of life—a fact which is more clearly demonstrated in comparative embryological studies.