CHAPTER 2

BIOLOGICAL ENTITIES

WITH THE CONCEPT of hierarchic organization, it becomes possible to gain a new insight into, and understanding of, the biological realm.

In the classical view, just as simple substances in nature are conceived of as being formed by molecules and atoms, biologically complex organisms are considered to be composed of cells as fundamental entities. In arriving at complex organisms, however, it is granted that organization has followed a definite pattern. At first glance, it is apparent that cells are grouped in morphologically regular ways to form tissues. Similarly, tissues are grouped to form organs and these in turn compose the organism. In this classical systematization, a complex individual would appear to be the result of a grouping of cells, tissues and organs, bound together in what has been described as an harmonious morphological relationship.

In our study of organization of the biological realm, we have emphasized the individualization of both conceptual and material entities. In some cases, entities have been simple to identify because they are easily separable morphologically. Where morphological separation has not been immediately evident, other criteria—such as structural and functional properties—have been used for identification. Besides playing its part in organization, each entity has its own individuality, and consequently can be recognized holistically as a well-defined unity. Starting with chromomeres, the entity status is easily accepted because, in addition to clear morphological and functional properties, there is a degree of independent individuality. Following up, chromonemata, chromosomes, nuclei are other entities.

The study of the organization of biological entities has shown, however, that in all cases there is a specific pattern of interrelationship which is more complex than the classically accepted pattern. In the simplest microscopically identified entities, it could be seen that a series of chromomeres are bound together through a special fibrillar formation, which stains differently from the chromomeres, to produce the chromonemata (1, 2), which can be considered holistically as a new entity. Two or four chromonematas (3), together with the chromosomal sap, form the chromosome as a new entity. Similarly, several chromosomes together with another part—this time represented by the nuclear sap and the proper nuclear membrane—form a nucleus. In turn, the nucleus, plus protoplasmic formations, cytoplasm and the cellular membrane, form the cell. Even superficial analysis indicates a common fundamental pattern in the organizational changes taking place for entities ranging from chromomeres to cells. Because of this pattern, these entities can be considered to be "hierarchically" interrelated. One entity is hierarchically "superior" to the entities which form it and "inferior" to those it will itself help form. Two immediately interrelated entities thus are hierarchically superior and inferior, respectively, just as in organization in other realms. *(Fig. 1)*

Analysis of the progression of organization from simple to more complex entities permits us to recognize other characteristics of the fundamental pattern. In order to form a hierarchically superior entity, several similar entities first join to form a group. It is the group which then will bind other constituents to bring into existence a new, hierarchically superior, biological entity. Thus, the chromomeres as a group join with a fibrillar formation to produce chromonemata; chromonemata join with chromosomal sap to form chromosomes. Groups of chromosomes plus nuclear sap form the nuclei. It has appeared evident that the parts which are bound to form each hierarchic entity do not play equal roles. In each case, the principal part is the one which is composed of similar entities acting as a group; the other part is the secondary. Figure 2 offers a graphic representation of hierarchic organization from chromomeres to cells.

In all entities, mentioned above, there is the same relationship between principal and secondary parts. The secondary surrounds the principal part. The morphological relationship has helped us to apply to those entities the hypothesis discussed previously concerning the mechanism through which hierarchic progression has taken place in nature. According to the hypothesis, several similar entities would first associate and form a group. In a second step, the group would tend to maintain around it a small portion of its immediate environment. From this portion of the environment would come the secondary part for the next superior hierarchic entity. With a boundary formation, separating this minute part from the rest of the environment, the new entity would be established. Such a process could occur, although rarely, with a single biological entity serving as principal part. Usually, several entities grouped together would be needed. This pattern explains why the secondary part can be conceived of as a part of the environment retained around the principal part, and why the establishment of a new and higher entity can be considered to occur only when this secondary part is detached from the rest of the environment and separated from it through the intervention of a boundary formation.

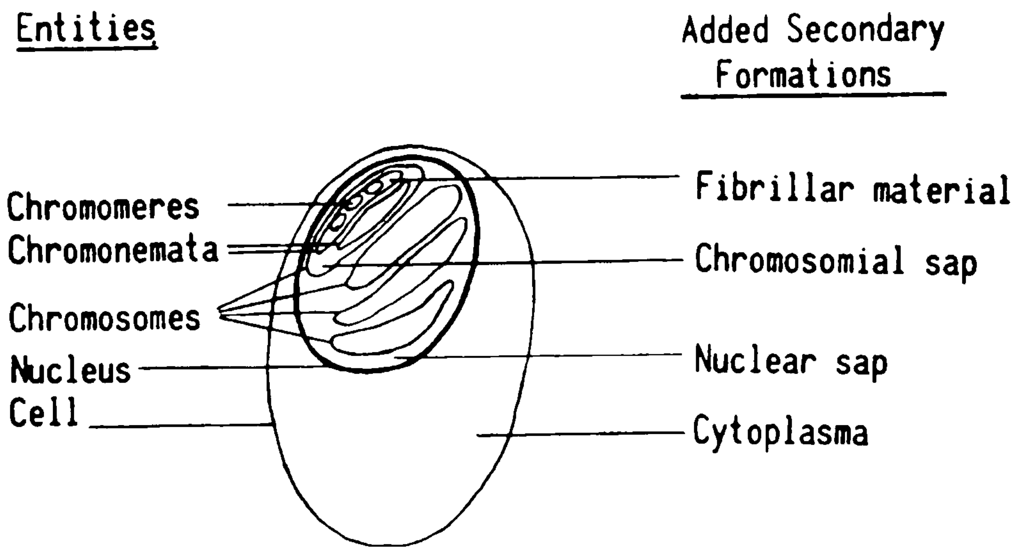

FIG. 2. *The hierarchic relationship* in the organization of morphological entities *below* cells. For each entity its principal part is recognized as being made by a grouping of entities hierarchically inferior to it. The secondary part which corresponds to a kind of environment for the principal part usually surrounds the principal part.

Having recognized this pattern of organization for lower entities, we went on to determine whether it remains the same for higher entities. It could be seen that groups of cells, along with interstitial formations and fluids around them serving as secondary part, create the tissue as a new hierarchically superior entity. Indeed, a proper boundary formation morphologically limits and conceptually defines the new entity. The interstitial fluids are separated by a continuous endothelium limiting the lymphatic spaces as a system closed toward the intercellular spaces. Under these circumstances, the lymphatic endothelium serves as the corresponding boundary formation that limits the tissue entity. Several tissues grouped together, playing the role of the principal part, bind the lymph, as secondary part, to form the organ, as a new hierarchic entity. Lymphatic vessels and connective tissues represent the organ's boundary formations. Furthermore, organs grouped together, with blood as secondary part, form the entity called the organism. *(Fig. 3)*

Does the same pattern apply for entities hierarchically inferior to chromomeres? For these lower entities, morphological information to define the relationship between principal and secondary parts is unavailable for

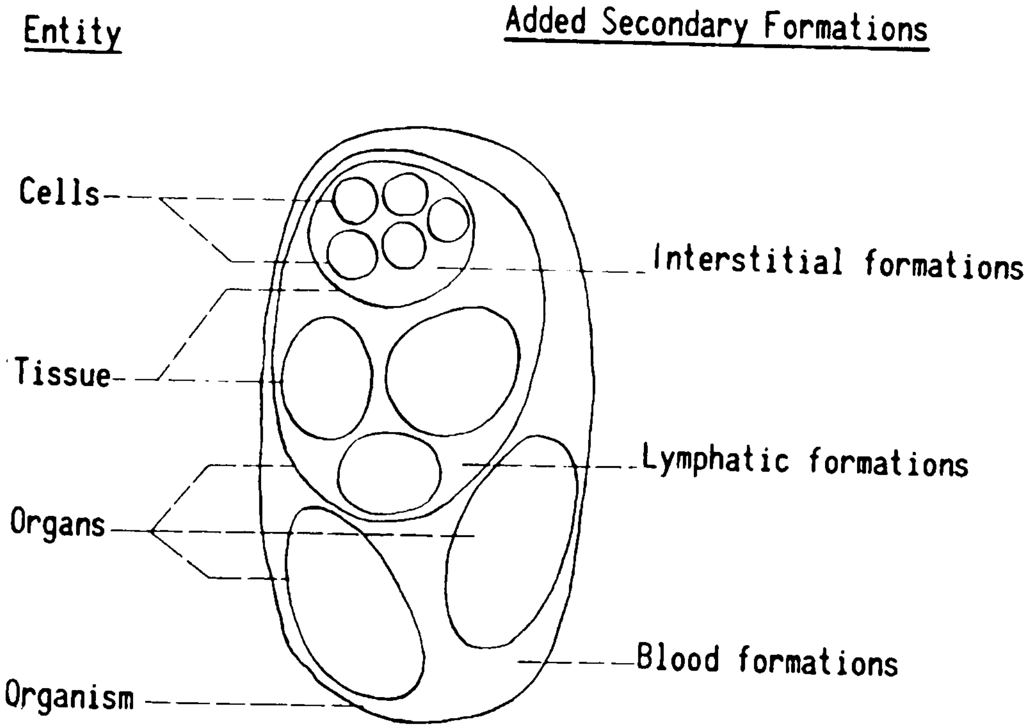

FIG. 3. *The oganization above the cells.* The hierarchic pattern of the organization in general is recognized also in the organization above the cells. Tissues, organs, organism are seen to represent hierarchic entities, each one being made by a principal part formed by the grouping of entities hierarchically immediately inferior to it. The principal part is bound to a secondary part characteristic for each entity. This secondary part would correspond to the proper environment in which the entities forming the principal part, have evolved.

the moment. Until electron microscopy and other means provide such data, we are obliged to find other criteria to indicate which, in these hierarchic entities, is principal and which secondary part. We have considered electrical characteristics of the constituents as criteria for identifying their role in the hierarchic organization of biological entities below chromomeres.

Biological Realm

Before going further in trying to analyze submorphologic hierarchic entities, one problem was to establish the limits of the biological realm

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itself. The question was, how far below the morphological formations could we go and still have entities which can be regarded as biological. With the progress of science, criteria previously used to define life have become outmoded. A separation line between the animate and inanimate no longer can be drawn. With the study of the properties of viruses, it appeared impossible to maintain the last vestige of the old vitalistic concept. According to most of the classical criteria, viruses would represent animate entities since they are able to multiply and conserve a strict identity. However, they also form salts, are crystallized, broken down, and then reconstructed in the same or another order. If the viruses are accepted as "borderline" entities, as proposed, then the concept of animate and inanimate can no longer be sustained.

Although the animate and inanimate cannot be distinguished in terms of a specific property, we cannot totally overlook the fact that an important group of entities appear quite different from others in nature. As animals and plants are different from stones, even without any vitalistic concept, we are obliged not only to recognize the difference, but also to try to establish where the difference lies. To conform to reality, we have applied the term "biological" to a group of entities, but we have given the term a new meaning.

Just as organic chemistry is considered—whether correctly or not—to comprise certain combinations of carbon, we consider the biological realm to comprise entities hierarchically developed from a specific chemical radical. This basic radical includes nitrogen and carbon atoms bound together to form the N-C-N-C group. According to this concept, starting from the basic nitrogen-carbon formation, an entire series of entities has been developed through hierarchic organization. Together they form the realm to which the term "biological" can be applied.

The N-C-N-C group, through combination with hydrogen, would result in radicals with a strong alkaline property; that is, with strong positive electrical character. Some of these N-C-N-C groups take part in the formation of nitrogenous bases, pyrimidines and purines, while some, by acting as principal part and binding various amino acid radicals would, with the necessary electrons, build up a new group of entities, arginine and histidine as alkaline amino acids. These can be considered, hierarchically, to be the immediate superiors of the N-C-N-C group and thus to represent the first biological molecules. The alkaline positive character of these molecules is noteworthy. Following the hierarchic pattern described above, several such alkaline amino acids linked together to a series of entities of the same level (simple amino acids) will form new groups that are still electrically positive:

the alkaline histones. In a new step, these histones will act as principal part to produce nuclear entities. *(Fig. 4)*

Principal parts, by binding different secondary parts, can form not one but many new and different entities. More than one hierarchic line can be identified. An especially important line results when histones bind one or more entities of the nucleic acid group, to form nucleo-proteins. Other histones can bind various other secondary parts such as carbohydrates or lipids and, in so doing, form different biological entities. Some of these

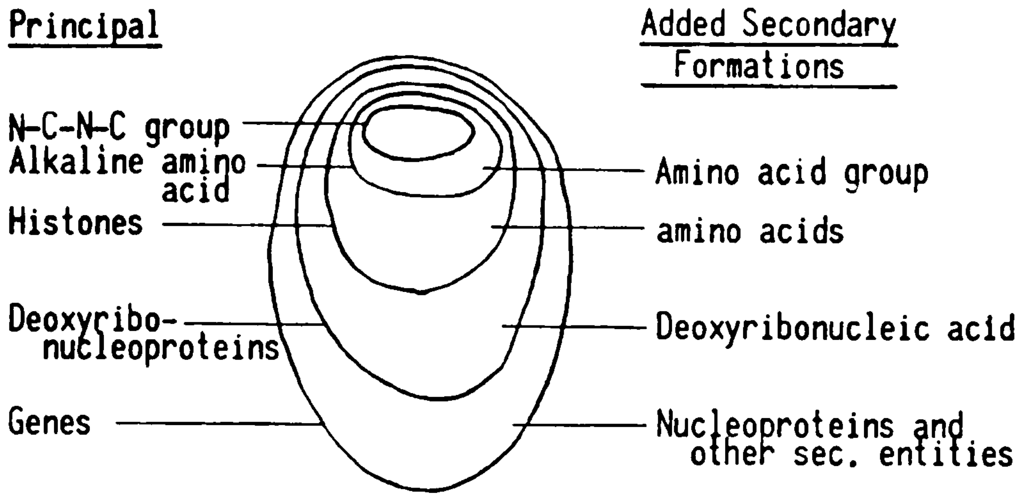

FIG. 4. *The organization of the submorphological* entities of the biological realm. The same hierarchic general pattern, with principal and secondary parts is recognized. Starting with the positive CNCN group, each entity has its principal part made by the grouping of immediately inferior entities bound to secondary parts, generally more electronegative.

entities can continue their hierarchic development. Nucleo-proteins can have ribose or deoxyribose and consequently form more complex nucleo-proteins. Through all hierarchic achievement, it can be seen that new lines are formed when groups of hierarchically lower entities, acting as principal organized part, bind different secondary parts, all more negative than the principal part. Theoretically, this would result in a series of entities all at the same level, *i.e.* entities with similar principal parts but having different secondary parts. Some would go on to develop superior hierarchic entities, others would evolve no further.

Different entities of the the same level can be grouped together in various ways to form a variety of principal parts. Always the group must be made up of entities of the same level. This requirement has been seen to be general at all hierarchic levels. Since differences can exist between the constituents forming the principal part for a new entity, the predominance of one or another constituent will make entities at the same level differ. This mechanism of differentiation through the constitution of the principal part has been extremely important throughout the biological realm.

Nucleolus

The concept that plural groupings can enter into the principal part of the nucleus puts the role of the nucleolus in a new light. It was accepted for a long time that the nucleolus represents only the reserve material necessary for metabolism of the nucleus. The strong positive electrical character of the nucleus, as recognized through its rather alkaline reaction, would give it roles more important than that of the other constituents. According to a work hypothesis which we advance, successive nucleolar formations would represent the principal parts of hierarchic organization below the nucleus level. In chromonemata, chromosome and nucleus, the parts corresponding to the nucleolus can be recognized. These formations are grouped together with genes to form the principal part of the chromonemata. Similarly, chromatine formations representing entities of the same level as the respective nucleolar formations, will form together the groups characterizing the principal part of chromosomes. In the nucleus, the nucleolus is joining the other formations to form its principal part.

Protoplasmatic Formations

In the cell, a hierarchically superior entity, a similar condition also appears to persist. The protoplasmatic formations with ribo-nucleic acid can be conceived as representing entities of a nuclear level, that is, a level similar to that of the nucleus. Together with the nucleus they would form the group corresponding to the cell. This kind of evolution of entities in relatively separate parallel lines, with their further grouping together to form principal parts for new entities, is part of the typical pattern of organization especially evident in the biological realm.

Boundary Formations

We have mentioned that groupings of several entities would not be sufficient to form a new entity so long as the secondary environmental part is not isolated from the medium from which it originates. Consequently, the new entity appears only when a distinct boundary formation is formed. Progressive hierarchic development is dependent upon the appearance of such boundary formations. For the first biological entities, the radicals, the boundary seems to be more an energetic property than a morphologically organized formation. For the molecules, it can be considered to consist of molecular surface forces, recognized as the van der Waals cohesion forces. A similar but more apparent boundary formation can be found in higher molecular complexes, especially the micelles. The molecular arrangement at the surface of micelles separates them from their environment and consequently insures their identity. In the case of morphologically identifiable entities, of course, boundary formations can be easily recognized. Chromomeres are well-defined and separated from the chromosomal sap. The chromosomes, in turn, show a real membrane just as the nucleus and the cell do. The next higher entity, the tissue, is bounded by the endothelial cellular layer, separating the interstitial formations from the lymphatic spaces. Usually the boundary of organs which have tissues as principal and lymph as secondary parts is represented by organized blood vessels. As far as the organism is concerned, the mucous membranes and skin are boundary formations. *(Fig. 5)*

Hierarchic Interrelationship

Viewed as a heterotropic effect, hierarchic organization can be considered to be a method of conserving existing entities as such, in spite of changes occurring in the environment. Teleologically speaking, by entering into the formation of a new and superior entity through the system of hierarchic organization, each entity, in fact, protects its own individuality. The hierarchic organization makes it possible for each entity to continue to live in a medium which corresponds to its own environment. The constituents of the secondary part in the new entity are chosen to correspond to the environment in which the principal part of the entity has existed. The successive secondary parts, added during the hierarchic development, act as multiple protective buffers for the first entities, thus insuring their unaltered conservation in spite of continuous changes in the environment brought about by increasing homotropy.

Phylogenetic Development

Hierarchic organization, when related to time, would appear to correspond to evolution. The concept of ontogenesis reproducing phylogenesis, appears in a new light when analyzed in accordance with hierarchic organization. The parallelism between actual hierarchic organization and hierarchic phylogenetic and ontogenetic development greatly helps to increase understanding of many principal problems of biology.

In accordance with the concept of hierarchic organization, when a new level is realized through the binding of entities from a lower level, as principal part, to different secondary parts, several outcomes are possible. Some of the new entities are unable to continue to exist and disappear. Of the others, some are relatively well balanced entities and consequently can

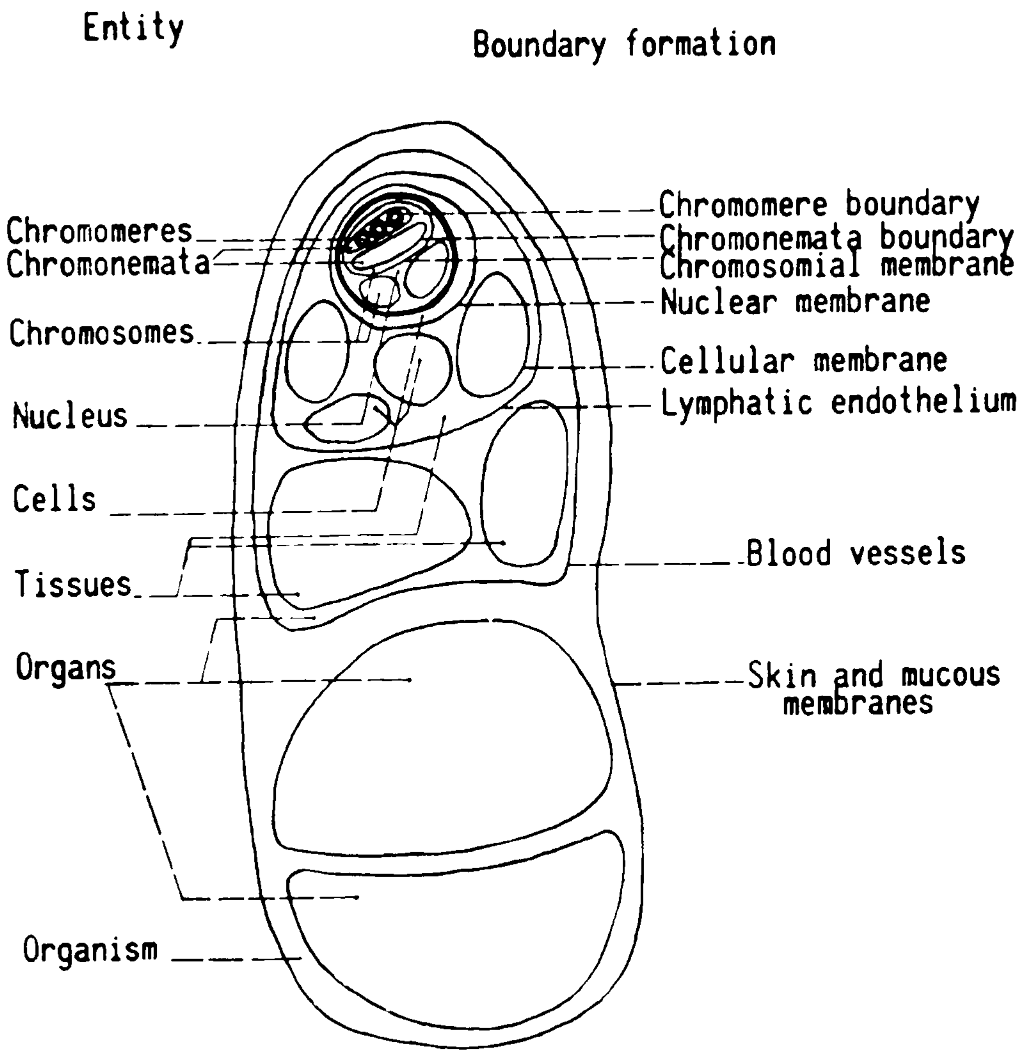

FIG. 5. *The boundary formation* in the hierarchic organization of the biological realm. *A proper boundary formation* delimits each entity, insuring thus its individuality. It is by separating each time the secondary part from the rest of the environment that the boundary formations have permitted the progressive development of the hierarchic organization. The boundary formation governs the relationship between the entity and its environment.

persist. But with further changes in the environment, some of these entities disappear. Even among those that remain, some do not represent fully satisfactory solutions and further hierarchic development is necessary to insure their persistence. They must evolve further to correspond to the new unfavorable external conditions. This has led to the development of the complex entities present today in nature.

The multiple entity possibilities at each level have resulted in a wide variety not only of entities which, with further evolution, could produce higher complexes, but also of others which have ended their evolution at lower levels. So the existence of many varied entities appears to be the result of the existence of multiple solutions for the same problems which have been part of the mechanism of hierarchic evolution.

From this viewpoint, existing independent entities can be recognized as corresponding to the different levels of hierarchic organization. Viruses can be considered to be at the same level as genes or even the entities immediately below genes; the microbes at the same level as the nuclei; monocellular organisms at the level of cells, etc. Furthermore, in each independent organism, from simple to most complicated, the same progression in organization of successive hierarchic entities can be seen, starting with the simplest biological entities and continuing until the level at which the entity has actually stopped its hierarchic evolution.

In a further step, having arrived at the concept that the secondary part of each entity corresponds to the kind of environment in which the entity found itself at the time of its phylogenetic appearance, we tried to see what information about these environments could be obtained through study of the secondary parts.

The first biological entities, the alkaline amino acids, could have appeared in an atmosphere rich in ammonia, water and methane. Experimentally, electrical discharges through mixtures of these materials have induced the appearance of amino acids. It appears plausible that such an environment could have existed around volcanoes in times when the earth's atmosphere was formed by ammonia. With steam formed by the heat of the volcano, with methane resulting from the interactions of erupted metallic hydrocarbons with water, and with lightning so frequent around volcanoes in eruption, the necessary conditions for synthesis of amino acids may have been present. The simple amino acid molecules which would have resulted could have constituted a group needed for hierarchic development. Out of a series of such amino acids, some could have bound the group N-C-N-C which also could have been synthesized under the influence exerted by radioactive elements or radiation. *(Note 1)*

Additional information concerning the constituents of secondary parts which enter into the development of all the subnuclear entities is meager. Simple amino acids or urea are present in the chromosomial and nuclear sap which are practically free from K and Na. We could thus consider ammonium as the predominant cation for all hierarchic entities up to the nucleus. This would accord with geological data concerning a primitive atmosphere in which ammonia was predominant at the time when the first biological entities would have appeared. We can then, tentatively, in view of this cation common to all, classify the hierarchic entities below the nucleus in what we will call "the nuclear compartment."

In the same way, we analyzed the composition of cytoplasm, with the thought that it could provide information about the constitution of a second environment in the evolution of biological entities. The principal cation of cytoplasm is potassium which also represents the principal cation of the earth's crust. Curiously enough, potassium and the other constituents could be found in the same relative proportions in the earth's crust as in cytoplasm, *(Note 2)* a fact which seems to confirm the hypothesis that mud, humid earth crust, represented the environment in which entities at nuclear levels lived. The cytoplasm conserved this constitution, with potassium as principal cation, when it was separated from the environment to become the secondary part which, with the nucleus, formed the cell as the next superior hierarchic entity. The cell by itself, represents a new compartment with potassium as principal cation.

It is only for the animal cell that the environment seems to have changed again. This time the new environment was the sea. When several cells joined together to organize tissue as a new entity, they had to maintain their environment, now represented by the sea. The hierarchic entities above the animal cell show sodium as principal cation in their secondary parts, thus indicating that when they were organized the sea was their environment. This characteristic allows us to group together animal hierarchic entities above cells to form a new compartment, the metazoic, with sodium as the principal cation.

With passage from marine to terrestrial life, air is found as the new environment. Not integrated as a new secondary part, without a separating boundary formation, the part of the environment kept in the respiratory apparatus does not enter however, into the formation of a new entity. Only the presence of air in the bones of birds can be seen as such integration.

A certain fundamental further development, in the same direction can be seen in animals as well as in humans, in the area of social life. *(Note 3)*

Division of complex hierarchic organization into compartments appears to be relatively simple. There are changes in the principal cation from compartment to compartment which correspond to similar fundamental changes in the environment through which the organism passed during its phylogenetic evolution—from volcano to mud, to sea, to the surface of the earth. We tried similarly, to correlate other elements in the periodic chart with hierarchic compartments. The results will be presented in detail later. For the moment, it can be stated that elements correlated to different environments are also found in the different compartments corresponding to these environments. For example, Mg like Na represent an element of the metazoic compartment and of the sea where this compartment was phylogenetically organized. Fe, Cr, Ni, Zn, Ca, Mn, Co, As, and Se which fall into the cellular compartment, represent characteristic constituents of the earth's crust.

Constants

The concept that matter in general is the expression of the heterotropic trend permits us to explain further some of its characteristics which have been of great importance in biological development. Heterotropy can be seen working to maintain existing entities as long as possible, to conserve their characteristic properties in spite of changes in the environment. Heterotropy could result in unchanged values which would appear as constants of an entity and would indeed identify the entity. It is hierarchic organization which would tend to permit conservation of constants.

Each biological entity—just as any entity in nature—can ultimately be defined by the series of characteristic properties which it is able to conserve. Constancy is the criterion which permits us to judge the importance of a property to an entity. The longer a property is kept constant despite environmental changes, the greater its fundamental importance to the entity. The progressive addition of secondary parts through hierarchic organization represents an effective means of preserving constants of the lower entities. New properties, added with the formation of each new hierarchic entity, represented new constants. This explains why considering the constants, it can be seen that those incorporated in the lower entities are the best conserved. The higher a constant in the organizational hierarchy, the less well-preserved it will be.

The idea that constants correspond to the character of the environments through which the individual has phylogenetically passed, and that they are conserved through hierarchic organization, permits us to try to extend our understanding of conditions present in past environments. Cations and even anions would represent only one type (apparently the most important) of the constants maintained through hierarchical organization. Other constants, correctly interpreted, would indicate in what direction we must search for conditions which prevailed in the environment when the respective hierarchic entities that make up a given organism were established during phylogenetic development.

As examples, let us consider the conservation of salinity and temperature as constants. Values for salinity of the metazoic compartment and of the blood and values for temperature have been seen to be constants characterizing species. Differences between these constants in different species show a succession conforming with paleontological data. In the interpretation given by Rene Quinton, constants would indicate the times when various species originally appeared in nature.

According to our concept of hierarchic organization, these constants may be interpreted otherwise. They would not indicate the moment when the lowest entities of the respective species were formed, but rather the time in the development of these species when the hierarchic entities capable of conserving the respective constants appeared. In other words, they would not indicate the earliest moments of appearance of the first entities which later developed to form the respective species, but would indicate a relatively late moment in the creation of the metazoic entity which has appeared able to conserve, as its own constant, this specific attribute of the environment. In the case of salinity, this would correspond to the constitution of the metazoic entity itself which has retained the composition of the early sea in its intercellular fluids. As far as temperature is concerned, the entity which would appear able to conserve it has to be regarded as much more complex and even to be related to the appearance of systems of organs which are sufficiently sensitive to changes in temperature and which also possess the means of insuring constancy for temperature.

The conservation of different elements in different compartments appears to be characteristic. In order to maintain its constants for elements the entity has to oppose their uncontrolled circulation. The role of hierarchic entities in conserving ancestral conditions would explain why an entity would have to oppose particularly the penetration of the constituents which characterize the succeeding environments. This has appeared evident for the cations. The boundary formations which have to play the principal role in the creation of each entity must also insure its identity by barring uncontrolled penetration of elements characterizing the new environments. Invasion by such elements would correspond to an abnormal event which must be corrected. If the invasion progressed beyond a certain limit, it would create a condition incompatible with further existence of the entity.

Water Circulation

The passage of complex organized animals into the new environment of terrestrial life brings to the fore the problem of the place of water in hierarchic systematization. It appears to us an acceptable concept that water does not circulate freely in the organism. Its appearance in hierarchic entities can be understood if, as we did for the other constituents, we relate water to its place in the environment in which phylogenetic development has taken place. In the first near-volcano environments, which applied to the subnuclear entities, water was relatively scarce, which explains the high concentration of the constituents in the nucleus. The mud of the earth's crust is richer in water, which explains the difference between the nucleus and the cytoplasm, with the latter richer in water. The sea was the environment for the metazoic compartment, which explains the richness of water in this compartment. The so-called "internal sea" consequently can be seen only in the metazoic compartment. With the passage into the terrestrial environment with its air medium, the water again becomes scarce and has to be conserved. The circulation of water between compartments is governed by osmotic forces which are determined by the original richness in water of the respective environments. The importance of water circulation appears evident when an abnormality in its distribution occurs. Water arriving in a compartment—alone or with a cation—in an amount above that corresponding to the constant for that compartment, is separated from the constituents of the entity in order to reestablish the characteristic constant value. Such separation of abnormal amounts is accomplished according to the compartment, through the appearance of vacuoles, edema, exudates or diuresis.

Animals and Plants

The concept of hierarchic organization in which each entity can conserve its own environment allows us to consider in a new light various other problems of living organisms. One concerns the fundamental differences between animals and plants. Analysis of the constituents of the metazoic secondary part provides a new criterion for distinguishing between animals and plants and gives logical meaning to its distinction. Animals can be characterized as having sodium as the cation of their metazoic compartment; from the cell level on, they have had the sea as their temporary or even permanent environment. Plants, on the other hand, have potassium as the principal cation for their metazoic compartment, indicating that, from the cell level on, they have had the earth's crust as their environment, passing thus directly from mud to air. By their actual attachment to the soil, plants continue this relationship to the mud. Their relative immobility is in accord with continuation of the terrestrial-air environment in their development. The mobility of animals, on the contrary, can be seen to have its origin in the fact that they have had the sea as their environment at least for a period of time, *i.e.*, from the cell period until the appearance of those animals which left the sea. We can interpret the appearance of cellulose and lignin as part of the plant-sustaining means which would bring to plants indispensable external protection against the hardness of the soil environment. Cellulose and lignin are not necessary for animals which experienced much of their evolution in the sea.

Multiplication

The hierarchic organization of organisms, with the conservation of successive entities, puts the problem of entity multiplication in a new light. According to the hierarchic organization concept, the multiplication of a complex entity means the reproduction of the entire series of hierarchic entities forming it. In this process, the intervention of each hierarchic entity appears highly individualized. And this applies not only for the morphologically identifiable entities, but even for the most primitive entities. The difference between the role played by the principal and secondary parts becomes capital for these processes. While for each entity the principal part has to be built as such, the parts corresponding to the secondary parts are taken from the immediate environment. The quantitative disproportion between some principal and secondary parts makes the role of the first difficult to be recognized. The complex entity, through changes that are the reverse of those of ontogenetic and phylogenetic hierarchic development, separates the successive principal parts which characterize it. With the replication which takes place the division occurs successively for these hierarchic entities. In scissiparity the division morphologically occurs at the cell level; in karyokinesis, it can be identified at the chromomere level and certainly takes place much lower in the hierarchic entities. In replication in general, different constituents available are adequately changed by the respective principal part to form the necessary secondary parts. Through these changes the same processes are reproduced which originally occurred when the entity had been phylogenetically organized.

With the individualization of the low hierarchic entities the problem of replication is simplified. Once replication occurs, the same process takes place successively for the progressively higher levels. Above chromomeres this appears very clear in karyokinesis.

After the chromomeres divide, two or four chromonemata appear. The process goes on within the chromosome, nucleus and cell. In order to protect its individuality each hierarchic entity is protected during its division. The chromosomial membrane, the cellular cytoplasm and the cellular membrane continue to protect the respective entities as they divide. The cell itself divides only when the two nuclei have had their protecting membranes rebuilt.

In the division and multiplication of a complex entity, the return to entities as low as subnucleic parts indicates the relative importance for the characterization of the complex entity and for the conservation of its particular properties of the parts added during the hierarchic development. The entity must, in fact, rid itself of these added parts which, although they have other importance, have a secondary role even in the processes of multiplication.

It is interesting to note that a similar return to more primitive component entities also occurs, although it is less pronounced, when an entity, tissue, organ or organism has to fight a noxious intervention. The defense is passed progressively from the organ to the tissues and from these to the cells. In effect, there is a renunciation of added parts during these moments of crisis. Even at the cell level, a similar process is seen. The added parts, represented by the protoplasmatic formations, disappear. The almost non-differentiated cell fights the noxious factor at the lowest levels of its organization.

Life and Death

We have seen that the term "biological realm" can be applied to hierarchic development starting from the N-C-N-C radicals. We have employed this term for didactic convenience although it is unrelated to the commonly accepted concept of life. The study of hierarchic organization also led us to consider a concept of life and death which, while retaining some of the common meaning, also accords with the phenomena of hierarchic organization.

In the complex entity, each lower level entity lives and dies with relative independence. An organ can be dead and yet have living cells in it for a time. There are always dead cells to be found in living tissues and organs. It is the relative independence of the different hierarchic entities making up a complex entity that explains these seeming peculiarities.

Our concept of life and death stems from consideration of the nature of hierarchic entities. We have seen that all matter in nature, from the simplest to the most complex entity, is a result of heterotropy. The persistence of constants proper to each entity is distinctly opposed to homotropy. Life in its broadest sense, corresponds to the capacity of an entity to maintain heterotropy by conserving its characteristic constants. The life of any entity appears to be synonymous with conservation of its constants. An entity dies when it has permanently—that is, irremediably—lost its capacity to conserve the constants which characterize it. Death then represents exhaustion of heterotropy for the specific entity.

The fact that, in essence, life appears to be synonymous with the conservation of constants and is heterotropic, relates it, and especially its origin, to one of the important sources of heterotropic force, solar energy. A distinction has to be made between heterotropy as one of the fundamental laws of nature and the means by which it is exerted. Solar energy, with all of its quantas, would greatly increase the effects of heterotropic forces in nature. It would not create such forces but would simplify them and extend their applications. The origin of matter and, as we have seen above, of entities, biological or nonbiological, is in the final analysis the result of heterotropic forces. External conditions qualitatively and quantitatively influence operation of heterotropic forces.

The sun's heterotropic contributions have to be considered under this aspect. Through the quantas it disposes of, solar energy has not created life, as conceived above, but by permitting more and more entities to appear, has greatly facilitated their extension. Its effect, although certainly not limited to any group of entities, seems to be especially important to those forming the biological realm. Similarly, the effect, of a special type of energy, radiation, also must be considered. Radiation appears to be related to the elements, and will be discussed in a later chapter devoted to the elements.

Since life itself is related to changes directly aimed at conserving constants, in this broadest sense it is no longer limited to the specific group of entities found in the "biological" realm. Life has the same meaning for an atom, crystal or micelle, as for a cell, organ or organism. It is for this reason that knowledge of the mechanism through which constancy is achieved becomes of great importance in the study of all matter and especially of the biological realm.

Maintenance of Constants

To study the mechanism used to maintain constants, we must define exactly what constancy means. According to Cannon's principle of homeostasis, constants have been considered to correspond to a dynamic balance that results from the continuous operation of two opposing factors. And

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it was conceived that by acting concomitantly as coupled antagonists, these factors or groups of factors insure constants. The intervention of these two opposite factors becomes apparent only if an exterior cause upsets their balance.

However, our study of the processes through which dynamic balance is maintained has permitted us to recognize a different mechanism than the one which is commonly accepted.

A value considered to be a constant for an entity is not fixed or static. It represents, rather, a statistical value, the result of a series of dynamic changes which must also be considered in terms of time. Consequently, a constant has to be seen not only as the average value of a series of organized changes, but also must be identified by the characteristics of the variations. An average value around which variations occur thus represents the first attribute of a constant. The second attribute is the existence of a rhythm in the variations, the third involves intensity of variations. For instance, when we say that human body temperature is constant, we mean that 37°C is average value for oral temperature, and also that body temperature presents characteristic variations having a 24-hour rhythm and also that the occurring changes consist of variations of a few tenths of a degree above and below the average value.

The two antagonistic intervening factors do not operate concomitantly to maintain a constant value, but rather act alternately, each being predominant for a period of time. The result is not a continuously steady value for the constant, but an oscillatory movement with successive passages from one side to the other of the average value. This oscillatory movement appears to be the general rule throughout nature, prevailing in everything from the waves in the smallest subatomic particles to the pulsation of the universe. The rhythm periods appear to correspond to environmental rhythms. A rhythm related to the day, for instance, is seen for temperature. In other constants we recognize a 12-hour rhythm which could correspond to that of the ocean tides. Other rhythms, with periods ranging from two hours to a few minutes are seen for several changes occurring in blood. There are also some in which the influence of the moon is evident; for example, the hypophysis-ovarian cycles; and for others, the influence of the seasons is apparent.

Teleologically speaking, balance represents a very effective method for maintaining constants. Any deviation in any direction as a result of an external intervention will be counteracted by the opposing phase of the oscillatory balance. This occurs because of the existence of two phases of the oscillatory movement itself. Such would not be the case if there were fixed values for constants.

Related to the pattern of the organization of matter in general, this oscillatory movement can be considered to be another instance in which the two opposite fundamental forces of heterotropy and homotropy, which are basic to progressive hierarchic development itself, also operate. This oscillatory balance can be related ultimately to the alternate successive intervention of the heterotropic and homotropic trends in the organization and the manifestations of entities existing in nature.

Dualism

The concept of dynamic oscillatory balance is of great importance in the study of biological phenomena. Coupled factors with opposite properties characterize all constants and are involved both in the processes through which constants are maintained and in their manifestations as well. Recognition of this dualism in all biological phenomena has been of great value in the investigation of normal and abnormal physiology.

According to our concept, dualism results from the alternate, not concomitant, operation of two opposing factors. And, as we have seen, these factors ultimately can be related to the two fundamental forces in nature, homotropic and heterotropic. Thus, in a unified concept, in every phenomenon in which dualism appears, one force will be homotropic the other will be heterotropic. Homotropy is related to fulfillment of electrostatic forces, and has general coulombian electric character. Heterotropy is quantum-like and organizational. Homotropy would keep entities simple. Heterotropy would lead to more organized bonds and to more complex synthesis. In every phenomenon studied, these characteristics of the two fundamental forces have permitted dualism to be recognized and interpreted. The dualistic view has become our basic approach for all of the problems related to matter and, more specifically, to biological entities.

The dualistic concept of intervening forces brings an entirely new light in any analysis in which a graphical representation is different from a straight line. From the curves of spectral analysis of constituents to those of complex phenomena, the existence of oscillations reveals the intervention of opposed forces and offers a valuable mean to study them. This broad approach has a special field of application in biology.

Dualism can be further recognized easily in the manifestations of the biological entities, in their function and in the substances composing them. In the case of the elements, such a dualism can be related to atomic structure and the properties of the electronic shells, as will be seen below. In complex molecules, a simple form of dualism can be seen in acidity and alkalinity, electrophily and nucleophily or, furthermore, in positive and negative electrical characteristics. We will see later, how important dualism is for the different groups of constituents and how, without this dualistic concept, it would be difficult to understand the roles of most of these constituents in biology.

In part, as a consequence of the separation of the constituents into two groups, dualism can be observed easily in the hierarchic organization of higher entities. Dualism appears in the relationship between primary and secondary parts, the first having a more positive character than the second. The study of cancer manifestations under this dualistic aspect has been highly rewarding and is the subject of the following chapters.

In a more concrete step, the dualistic concept has provided new understanding of abnormality.

Normal and Abnormal

A normal entity can be conceived of as one which is able to maintain its constants with their characteristic values, rhythms and intensities by means of the alternate operation of homotropic and heterotropic forces. A normal entity, thus, can be defined as one having constants within the limits that statistically characterize this particular kind of entity. We can define the abnormal entity as one in which a constant's characteristics—average value, rhythm, intensity—are altered. It is alteration, without complete loss of the characteristics of constants, that differentiates abnormality from death. In death the constants themselves are irremediably lost. This definition also distinguishes abnormal from physiological manifestations. In the physiological manifestation, oscillatory movement persists and only its intensity is influenced, usually becoming exaggerated.

As expected from the dualistic concept, abnormal changes can take place in either of two opposite directions and this is a significant fact of abnormality. The two possibilities are inherent in the oscillatory balance characterizing the constant itself. It is the offbalance, resulting from the exaggerated predominance of one of the coupled factors over its antagonist, which leads to the abnormal. Persistent predominance of one factor abnormally affects, and even suppresses, normal oscillatory rhythm.

For each normal condition, then, two opposite abnormalities are possible. By relating the abnormal condition to one or more altered concepts, and the alteration in each constant to one of the dual changes possible, a new systematized analysis of the abnormal becomes feasible. The large number of constants which compose each entity and which can become abnormal help not only to explain the great variety of abnormalities but also offer a means of obtaining analytical pictures of disease.

It is with this approach that we have tried to study pathological conditions, with special emphasis on cancer. This study is presented in the following pages.

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