Handbook of Physiology

SECTION 4:

Adaptation to the Environment

HANDBOOK OF PHYSIOLOGY

A critical, comprehensive presentation of physiological knowledge and concepts

SECTION 4:

Adaptation to the Environment

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Preface

When Maurice Visscher invited me in February 1960, on behalf of the *Handbook* Committee, to edit a section on "Adaptation to the Environment," I accepted without hesitation. The first two volumes of the Neurophysiology section then in print were proving the soundness of the concept. Visscher wrote that in addition to sections dealing with major organ systems, it was planned to have a group dealing with functional entities. One on " 'Adaptation to the Environment' would include such matters as temperature, pressure, acceleration, contamination of the atmosphere. . . ."

The scope of the volume took form by a series of approximations. A rough outline with eight main topics was submitted for review and suggestions to E. F. Adolph, D. R. Griffin, F. A. Hitchcock, A. Hurtado, and L. Prosser. On the basis of their many suggestions a more detailed outline was prepared late in 1960. This was done with the help of many environmental physiologists, particularly Adolph and Wilber; the *Handbook* Committee had agreed with my suggestion that they be invited to join me as associate editors.

This outline and a general letter intended for contributors was approved by the *Handbook* Committee. In this letter the hope was expressed that planning would be completed by the beginning of 1961 and that all manuscripts would be in hand by early 1962. This letter in part read as follows:

Several chapters will be devoted to adaptation of man to high and low temperatures, oxygen lack, low atmospheric pressure and radiation. In the broader biological field the scope will extend from bacteria to mammals, from the deep sea to the upper atmosphere, from dark caves to intense sunlight, from the arctic winter to the tropical rain forest. Such modern problems as the adaptation of insects to toxic environments will be included as well as adaptation to poisons as a problem in general physiology.

Each chapter should be written for three groups of readers: 1) the graduate student who wants to go more deeply and broadly into the meanings of current physiological concepts and their background than he can from standard textbooks; 2) the teacher who is dissatisfied with the comprehensiveness of his background in fields other than that of his own specialty; and 3) the investigator who will use it as a springboard for references and current concepts in research fields which he is beginning to explore. The contributions should be modern in viewpoint, adequately introduced and thus, emphatically, not esoteric polemics between specialists.

Each contribution should be an authoritative systematic account of the present status of the field and should contribute to physiology as a science in its own right. The contribution should be as complete and detailed as the overall space allotment will permit, including the factual evidence and the theoretical interpretations that are being seriously advocated at the present time. Recent investigations should not be dealt with merely because they are recent but only as they are constructive of current concepts.

Authors will be entirely free in choice of material, emphasis and method of presentation but since it is expected to make the section an integrated whole, it is hoped that they will be receptive of suggestions from the editors for inclusion of material omitted from various chapters which together cover a wide field and likewise for the elimination of material duplicated in closely related chapters.

In order that this kind of integration may take place smoothly, each author will be requested to submit a fairly detailed outline of the contents of his chapter. This we would compare carefully with outlines in bordering fields in order to suggest remedies for duplication or omission of important topics. An early chapter in our first volume will be a history of the development of physiological concepts in the field as a whole. Each chapter may require some highly specialized historical material but the scope of such material should be limited and its telling brief. The references should include treatises, monographs and reviews, as well as such original literature as is constructive of concepts that are widely accepted or reasonably advocated at the present time. There is not available space for the reference list to be complete or exhaustive.

We began sending this letter to prospective authors in January 1961. Each was invited to collaborate, to comment on the outline, to suggest other authors; if he declined to write a chapter, he was asked to name a competent replacement. He was asked to submit an outline soon and was informed that chapters should be within the range of 5,000 to 10,000 words, with 15,000 words and 100 references as the upper limit.

Based on replies to these inquiries and invitations the list of authors grew. Some new topics were added and some topics were dropped. Poupa of Prague first agreed to write on adaptation to aging but finally decided there was too little to justify the effort; instead he proposed writing on adaptation to injury. The topic, environmental adaptations by bacteria, was dropped, partly because it was nearer plant physiology than animal physiology. The plan to include a chapter on adaptations to diseases was dropped when no author could be found; some refused for lack of time, others asserted there was little information of interest to physiologists. Neither could takers be found for chapters on adaptation to alcohol nor for adaptation to microorganisms responsible for acute diseases. One agreed to write on adaptation to emotional stress and another on adaptation to isolation, solitude, confinement, and lowered level of stimulation. Both eventually withdrew for similar reasons. One replied, "What is needed is to do research specifically detailing how each particular type and intensity of emotion is manifested in terms of the physiological response pattern. There seems to be too little known about this as yet to put in a handbook. I believe I can best serve the field and myself by pursuing this research rather than by detailing our ignorance of these matters." The other "found the material in the field of sensory deprivation and social isolation so devoid of substantial content as to be almost embarrassing. . . . There are a bare three points which are substantially agreed upon: 1) Individual differences in response in man are great; 2) time orientation is poor; 3) the highest frequency of visual imagery occurs under conditions of moderate stimulation, decreasing under both normal stimulation and extreme deprivation. The other findings not only were not replicable in different laboratories, but not even within the same laboratory. I was led to the conclusion that the findings in this field of endeavor are too premature to warrant inclusion in a handbook of physiology."

The response to the request for chapter outlines was gratifying. The reproduction and distribution of these among authors helped to fill gaps and to reduce duplication. Thus it became clear that there should be an introductory chapter for each major environment: despite this late decision these chapters were completed ahead of schedule. While duplication has not been avoided the editors think it will be forgiven in view of the wealth of stimulating research, original ideas and colorful accounts of living organisms brought together in this volume.

The concept of adaptation has not been standardized among physiologists. No general definition of it was recommended to our authors. Each author, interpreting the term for himself, showed by his choices of material and emphasis what it means to him. In the end, however, a general concept is built in the reader's mind by the chapters here presented. This kind of concept formation is usual in science; the specific examples are the building blocks for an abstraction. Thus, no one defines life, yet he adds to his concept of life by his daily exploration of life's manifestations. This volume designedly supplies the reader with both examples and abstractions. Whether the word adaptation can be kept as fluid as its present meanings warrant remains to be seen.

In this international venture the editors were determined to seek out experts regardless of national lines. There was some concern about delay in receipt of manuscripts from distant lands; we also realized that the Yankee tradition of hurry, hurry, is not popular in some quarters. It is a pleasure to record that the first chapters received included Barbashova's from Leningrad and Cloudsley-Thompson's from Khartoum. The friendly exchanges we have had with our fellow physiologists around the world has been rewarding. It has demonstrated once again that a kindred spirit exists among scientists, that there is only one world of science.

D. B. DILL, *Section Editor*

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Perspectives of adaptation: historical backgrounds

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CHAPTER CONTENTS

The interaction between organisms and their environment is an old but very important problem for biologists. Organisms respond to environmental change in different ways according to the time during which the environmental change persists and according to the magnitude of the stress. In living organisms those alterations which favor survival in a changed environment are said to be adaptive. Similar adaptive variations of organisms may be genetically determined or they may be environmentally induced. . . .

C. LADD PROSSER

THIS QUOTATION FROM PROSSER offers the significant current aspects of the concept of adaptation. More formally, the concept of physiological adaptation may be said to imply the capacity and process of the adjustment of living material to itself, to other living material, and to its external physical environment. The teleological inference may be avoided by stating that the greater the extent of adaptation, the more the living material will tend to survive or to reproduce itself so that its biological characteristics may persist. The concept of physiological adaptation as defined in this manner took a long while to develop. It is in the light of this concept that the survival of living species becomes understandable.

Different types of physiological study have emphasized different aspects of adaptation. As Prosser indicates, animal physiologists have been chiefly concerned with adaptive variations induced by physical factors in the environment, such as light, temperature, oxygen tension, and food. On the other hand, microbial physiologists have been interested chiefly in enzymatic changes induced by varying the nutrients in the environment, and plant physiologists have been more interested in analyzing the genetic variations shown by adaptation to varying environments than in environmentally induced variations in individual plants.

The concept of biological adaptation involves many extensive generalizations and speculations. Some of these go back to potential factors operating in the origin of life, as explored by A. I. Oparin. Harold F. Blum has offered many stimulating considerations in developing his concept of *Time's Arrow*. Further generalizations relating to adaptation are considered by Linus Pauling, J. D. Bernal, J. B. S. Haldane, C. B. Anfinson, Ludwig von Bertalanfy, M. Florkin, George G. Simpson, Harold C. Urey, and George Wald.

EARLY ASPECTS OF CONCEPT OF ADAPTATION

The development of the concept of adaptation offers an interesting perspective on human history; it is implicit in a consideration of human behavior. Primitive peoples everywhere and the ancients seemed to have observed themselves and their neighbors in relation to their environments, and to have tried with some success and much error to adapt satisfactorily to each other and to their respective environments. Empirical and pragmatic considerations seem to have resulted in their developing gradually patterns of behavior which were thought to be appropriate for getting along with each other and with the world around them.

These behavior patterns were largely maintained by training procedures passed from generation to generation. Reinforcement of the conditioning was continually offered by the ritualistic repetition of various ceremonies expressing the faiths or beliefs of the group. These formed the bases of the various religions developed by different groups. Much of this involved the sort of preconscious feeling for one's self and for one's environment which have usually been ritualistically expressed. With ignorance of the actual factors operating within one's self or one's environment, there naturally arose fear of the powers in the environment and also recognition of the powers within one's self. Forces within one's self or in the environment which were thought to contribute to comfort or health were considered to be "good" and, as these powers were anthropomorphized, they were invoked and worshipped as beneficient dieties. On the other hand, corresponding powers which might produce discomfort, disease, or death were believed to be malignant dieties and offerings or sacrifices were to be made to them in order to avert their wrath or their evil influence.

Individual behavior still seems to be based largely on the hope of reward or on the fear of punishment from one's fellows or from the environment if the proper or acceptable pattern of behavior is not scrupulously followed. These conditioning factors may have given a basis for an adaptive development of "ethics."

In a more practical way various aspects of adaptation gradually became implicit in the experience which peoples acquired in the domestication of plants and animals in their respective environments. This process went far, even in antiquity. It resulted in widespread lore on the factors in an environment conducive to what we know as "survival" and even to "betterment." The adaptation or "fitness" of various crops or of various food animals to particular kinds of lands seems to have been appreciated early.

Thus, the earliest evidence of the idea of adaptation is homocentric. As the individuals in a group gradually shared their experiences with others in the group, there seems to have developed an appreciation of common opinion and a belief in the pressing need for getting along with each other and with the surrounding environment. Over many centuries the ritualistic stabilization of various faiths resulted in extensive cultural stability as found in such civilizations as characterized ancient China, India, Sumer, Egypt, Crete, Mexico, Peru, and the South Pacific islands.

In paleolithic cultures, people seem to have projected onto their surroundings their own emotional feelings, endowing everything that moves in nature with the characteristics of life. This "animism" was a convenient form of adaptation in that it helped people to feel at one with their surroundings. It also led to various kinds of sacrificial and ceremonial devices for placating the evil forces or for enlisting the support of the beneficial forces in the environment.

In interpersonal relations, paleolithic people recognized the paramount importance of women. Many ceremonial rituals were associated with the worship of women; the coincidence of the lunar and menstrual cycles resulted in a femininity being attributed to the moon and led to the development of a lunar calendar. Womanhood in general was identified with Mother Earth from which all life springs. This matriarchal culture seems to have dominated the earlier neolithic periods also. Gradually as it was learned that men have something to do with initiating childbirth, reciprocal interrelations developed between men and women which again were reflected in projected analogies with the forces of nature. Even though the ancients recognized female physiological superiority in many aspects, the general muscular strength of males in comparison with females led to the concept of male domination, not only among humans but also in the forces of nature. The threefold aspect of women as daughters, wives, and mothers with reciprocal relations with men established psychological aspects of adaptation which still survive.

The dominant adaptive characteristics of the great stable civilizations of antiquity began to fade under repeated assault from various invading peoples with differing customs who moved in accordance with population pressures and alterations in food supplies. These great migrations of antiquity were in themselves aspects of social adaptation on the part of humans.

PHILOSOPHICAL DEVELOPMENT OF CONCEPTS OF ADAPTATION

Trade has been a remarkable factor in human adaptations. Even as the great static cultures around the eastern Mediterranean decayed under repeated invasion of hostile tribes, trade developed sufficiently to permit a wealthy class to exist and to utilize time for thinking. It was then that the process of intellectual abstractions among gifted humans blossomed. This occurred explosively in the great cultural flowering in the fifth century B.C. At this time, the notion of a harmonious balance in nature arose. It is interesting that this same idea apparently developed in China at about the same time.

More systematic exploration of speculative ideas on the harmony of nature came with the collection and analysis of various kinds of reports on natural phenomena. The Greek traveler Herodotus and the Roman Pliny offer outstanding examples of the simple reporting of a great variety of observations on natural phenomena noted in traveling. The analysis of observations of this sort by such keen thinkers as Aristotle (384–322 B.C.) and his pupil Theophrastus (380–286 B.C.) gave the first systematic background for a tentative classification of living things, undertaken for animals by Aristotle and for plants by Theophrastus. The classification attempted by them, with its "ladder of life" from simple to complex forms, implies the recognition of relationships between various kinds of living material.

The Greek physician Hippocrates (460–375 B.C.) and his associates at Kos have left many records implying their growing appreciation of the role of adaptive factors in relation to health and disease. They emphasized the importance of "Airs, Places, and Waters" in regard to sickness and well-being, as well as the importance of interpersonal relations between physicians and patients, with the necessity of inspiring confidence in sick people so that they will trust physicians and thus have hope of getting well.

Titus Lucretius Carus (98–55 B.C.), in his rationalistic approach to nature in his great poem *De rerum natura*, attempted to explain the origin of life and the gradual advance of mankind from a savage to a more civilized state, suggesting various adaptive procedures in this progress. These early beginnings of adaptive biology as an empirical science were given a teleological slant by Galen (131–201 A.D.) who, as a physician and surgeon, reoriented the broader effort of Aristotle to further speculations centered around human beings.

The Galenic tradition was maintained and consolidated throughout the Medieval Period, first by the Arab philosophers and physicians and then by the scholars in Western Europe. Disease was considered to be a disturbance in the natural harmony in the body, particularly as a result of the imbalance in the four humors, an idea which had been derived in part from Egyptian speculations on Whdw, the presumed principle of putrefaction. The four humors were apparently derived by a combination of speculation and observation, with reference to the "qualities" of the four elements which were supposed to make up everything.

The most important of the four humors, the one most essential for life, was thought to be "blood" to which was attributed the qualities of warmth (from the element fire) and moisture (from the element water). This was followed by "phlegm" which combined the qualities of moisture (from water) and of coldness (from air); then by "yellow bile" with its qualities of warmth (from fire) and of dryness (from earth); and finally by "black bile," that humor which was closest to death and was formed of coldness (from air) and dryness (from earth). The theory postulated that if there were an excess of any one of these four humors, it was to be removed. On the other hand, if there was a deficiency, it was to be corrected by a diet composed of foods which would give the requisite qualities to make up the deficient humor. This dogmatic theory of adaptation to disease was followed until the nineteenth century, and echoes of it still persist in terminology (the sanguine, phlegmatic, bilious, and melancholic temperaments) and often in popular custom.

It is interesting that the initial philosophical developments on concepts of adaptation should have arisen in relation to the always pressing human problem of disease. Concepts of adaptation remained homocentrically oriented, as indeed was the case in all aspects of intellectual activity until the Renaissance.

Meanwhile, another very significant aspect of the relations of humans to each other had arisen: various intellectual speculations were systematized on principles of human behavior, depending on motivations, purposes involved, and goals to be sought. Psychology and ethics became conceptualized and began to be influential in the analysis of interpersonal relations. The various types of moral exhortation offered were guidelines to human adaptation and satisfaction. Moral injunctions, however, were tied to religious concepts and, as a result, systematic investigation lapsed.

THE RENAISSANCE

The general Galenic physiological tradition, so well stereotyped through the Medieval Period in Western culture, began to be questioned during the Renaissance. Skepticism arose as a result of the textural variations in the various manuscripts available from antiquity, many of which had recently come back into Europe from Arabic and Hebrew sources. Systematic investigations on the structure of the human body were begun by Leonardo da Vinci (1452–1519) and were brilliantly explained and illustrated by Andreas Vesalius (1514–1564). Santorio (1561–1636) inaugurated systematic studies on the physiology of metabolism, introducing exact methods of weight measurement and temperature estimations. He gave a tentative background for systematic studies on the cyclic relations of humans with their environment. The functional analyses of living phenomena were powerfully stimulated by the comparative studies on the heart and circulation made by William Harvey (1578–1657) on a variety of animals. René Descartes (1596–1650) greatly stimulated the study of animal physiology; he considered the human body as a machine and described reflex actions as related to external stimuli, thus affording a basis for studying immediate responses to environmental factors.

Meanwhile, the classification of plants had continued systematically and without the temptation of etiological speculation. Dioscorides, the Greek surgeon in Nero's Army, had extended Theophrastus' effort at plant classification. This was greatly amplified by Valerius Cordus (1515–1544). Konrad von Gesner (1516–1565) collected descriptions of all known animals and plants, and this gave background for the effort to develop a systematic classification.

During the seventeenth century various efforts were initiated for the organization of scientific information. This was accelerated by the growth of scientific societies with regular means of communication among scientists, so that a number of observations could be brought together, verified, analyzed, and classified. This process proceeded rapidly in regard to living material.

During all this time there was no clear appreciation of the concept of "adaptation"; living material in some way or other was simply a part of its environment. Nevertheless, some specific references to adjustments to environmental conditions were beginning to appear. As might be expected, these had to do with observations on diseases that might be related to environmental conditions. José de Acosta (1539–1600) first described mountain sickness and indicated that, whereas the sickness might affect individuals who came into the high mountains, those who lived there permanently were healthy and seemed to have adjusted to the altitude. George Horst wrote a treatise on sunstroke in 1665, describing the ways by which people who live in sunny climates protect themselves against the direct rays of the sun. Specific observations of this sort paved the way for a gradual accumulation of instances of adjustment to environmental conditions.

THE PRESENT

As increasing biological knowledge followed the rise of scientific organizations and means of communication, there were dawning suggestions of the idea of adaptation. Francesco Redi (1626–1697) offered many systematic descriptions of parasitism which is an important type of biological adaptation. His experimental studies also discredited the theory of spontaneous generation of living material, thus limiting biological development to the orderly procession of life to life.

The eighteenth century of our era was characterized by the great influence of Isaac Newton (1642–1727) whose astronomical observations and mathematical skill demonstrated an all-pervading regularity and order in the universe. His great work established the basic principles for physical theory and for directed systems of phenomena in which all factors may be interrelated.

Systematic classification of living material began with John Ray (1628–1705) who undertook a natural system of plant and animal classification which stimulated the taxonomist Carl von Linné (1707–1778). In his *Systema naturae*, Linné developed the first logical classification of plants and animals, introducing the binomial nomenclature of genus and species which gave the clue to natural relationships among living things and thus provided a sound basis for the later evolutionary theories in which the concept of adaptation as a factor in survival became apparent.

The functional interrelations of different parts of living things was further emphasized by Buffon (1707–1788) and Georges Cuvier (1769–1832) who extended the classification of existing living material to the remains of extinct fossils and thus demonstrated that the past, no less than the present, must be considered in any study of the development of living things.

The Scottish anatomist, pathologist, and surgeon John Hunter (1728–1793) collected great numbers of observations on living things in relation to their surroundings and to disease. Changes in bodily organs under the influence of disease were first systematically described by G. B. Morgagni (1682–1771). More general considerations of the adjustment of living things to environmental conditions were explored by Wolfgang von Goethe (1749–1832), the famed poet and nature-philosopher.

Jean Baptiste Lamarck (1744–1829) continued the systematic analysis of living material and introduced an important new principle involving adaptations to environmental conditions. Buffon thought that the effective results of a change in an environment are small as far as the structures of individual living things are concerned. Lamarck considered that, if the adaptation of living things to changes in the environment became constant, they would modify old organs or establish new ones. Continual changes of acquired structures might be intensified by inheritance, according to this idea. While no direct evidence for such inheritance has been given, the hypothesis remains a challenging one.

Meanwhile, the collection of comparative information on living material all over the world continued. One of the more extensive was that made by Charles Robert Darwin (1809–1882), the grandson of Erasmus Darwin (1731–1802), who had made observations on the influence of environmental circumstances on the growth of plants. In his *Journal of Researches* (1839), Charles Darwin described his observations on the round-the-world voyage of H.M.S. Beagle to investigate natural history and geology. As the late Charles Singer emphasizes, a special interest attaches to Darwin's observations on the highly specialized animals and plants associated with oceanic islands. His studies at the Galapagos Islands (where similar investigations excite interest today) revealed a remarkable wealth of living material quite different from that on the nearest land. These observations may have suggested to Darwin his theory of the processes involved in the survival of species.

Darwin himself says that he got the germ of his idea from reading *An Essay on the Principle of Population* (1798) of Robert Malthus (1766–1834). In this book, Malthus showed that humanity tends to outrun its means of subsistence. Darwin comments that his appreciation of the struggle for existence led him to the view that favorable variations in living things would tend to be preserved whereas unfavorable ones would die out. Darwin analyzed all his observations on plants and animals and brought them together in a magnificent inductive synthesis entitled *On the Origin of Species by Means of Natural Selection* (1859).

Actually, the title of this book is a misnomer. Darwin did not explain the "origin" of species; he induced the mechanisms by which species survive. The idea of genetic mutation did not come until the beginning of the twentieth century and resulted from the rediscovery of the studies of Gregor Mendel (1822–1884) which were published in 1865. Darwin showed how variations in individuals, occurring by chance or otherwise, might be conducive to survival if compatible with the environment; and if these were hereditable, the selection of variations might result in species differentiation. If the variations were not compatible with the environment, natural selection would result in the disappearance of the variant.

There has been continued popular misunderstanding of Darwin's main principle. As a result of popular discussions, chiefly by Thomas Huxley (1825–1895) and Ernst Haeckel (1834–1919), Darwinism was associated with the ruthless struggle for existence in which the strong would inevitably destroy the weak and in which nature was depicted as "red in tooth and claw." Darwin, on the other hand, stressed adaptation; those living individuals or those species of living things would survive, he indicated, in proportion to their adjustment or adaptation to their surroundings. It is this aspect of Darwinism which is even now important in Russia; in fact, Darwin is highly esteemed in Russia because he offered the scientific evidence which supports some current Russian philosophy. Indeed, Marx and Engels used Darwin's point of view as an argument to support their thesis.

It is interesting that Alfred Russel Wallace (1823–1913) came to conclusions similar to those reached by Darwin, but did so quite independently. Wallace had worked in the East Indies and had prepared a report *On the Tendency of Varieties to Depart Indefinitely from the Original Type*, and had told Darwin of his findings. The report, read before the Linnean Society on July 1, 1858, includes an abstract of Darwin's own views which were contributed by Darwin. This joint paper is a splendid example of the generous sort of cooperation in scientific endeavor that brings the finest satisfaction.

Meanwhile, important basic scientific principles for biology had been developing. Outstanding was the concept of the cell as the unit of living material, as proposed by M. J. Schleiden (1804–1881) and his friend Theodor Schwann (1810–1882). Schleiden's contribution in 1838 was largely concerned with the development of plant tissues from groups of cells which he postulated were the essential units of biological activity. This was followed the next year by Schwann's similar conclusions regarding animal tissues.

The concept of the basic significance of cells in biological phenomena stimulated a remarkable manifesto: all the activities of living material, including consciousness, are ultimately to be explained in terms of physics and chemistry. This was announced by that famed group of German physiologists, all young men working vigorously together, Carl Ludwig (1816–1895), Hermann von Helmholtz (1821–1894), and Emil du Bois-Reymond (1818–1896). In this same year, 1847, Helmholtz had announced the fundamental physical principle of the conservation of energy. Du Bois-Reymond founded electrophysiology, and Ludwig taught most of the great physiologists of the world who were active in the latter part of the nineteenth century. This manifesto was received with varying degrees of interest. It was profoundly influential in Russia as a result of the studies of I. M. Sechenov (1829–1905), one of Ludwig's pupils. Sechenov demonstrated physical and chemical factors in altering the activity of the nervous system.

The interrelations of fundamental chemistry with biology were dramatically demonstrated at about the same time by "Gold Rush Doc," California's first great scientist, James Blake (1815–1893). Blake had been a pupil at University College, London, under such great teachers as Scharpey, Faraday, and Graham. During the summer months he went to Paris to study with the French physiology teacher François Magendie (1783–1855) who had studied nerve action, founded experimental pharmacology, and stimulated the isolation of chemically pure active agents from ancient drugs. Blake announced that there must be a relation between chemical constitution and biological action, and he proposed to study it by means of chemicals having relatively better known constitutions than those of the complicated organic crystals recently isolated from crude sources. Using simple inorganic salts, Blake showed that the characteristic biological effects on injection into mammals were caused more by the electropositive element than by the electronegative element, and that if corresponding salts were used throughout, one might find the same type of biological activity reappearing, indicating that the elements can be grouped into families on the basis of their biological actions.

These families correspond with those later described in the periodic table of the chemical elements as outlined by the Russian chemist D. I. Mendeleev (1834–1907). Blake indicated that the factors responsible for the biological activity of inorganic compounds are their isomorphic properties. He also postulated that knowledge regarding the activity of chemicals on living material would give a clue to the chemical constitution and activity of the important biologically significant molecules found in or on cells.

Blake's work, which was summarized in 1848, gave a clear indication of the interrelations of physics, chemistry, and biology. However, his important contribution was overlooked and forgotten. It would seem that nothing could be more conclusive regarding the essential identity of all aspects of our world than that the periodic table of the chemical elements could be demonstrated as a result of the biological activities of inorganic compounds. Blake's work constitutes a step forward in developing the concept of the adaptation of living material to its physical environment and derivation from it.

Further significant developments relating to adaptation occurred at about the same time. Rudolf Virchow (1821–1902), another German physiological scientist, established his *Archiv* and announced his determination to establish a broad science of disease, incorporating studies on pathological phenomena ranging from cells to societies. Virchow thus gave clear expression to the importance of organizational levels of biological material. Considering cells to be the units of living material, Virchow undertook the thorough study of disease factors at a cellular level and thus established "cellular pathology" which remains dominant today. The correlation of disease symptoms with structural and functional changes in the organs of the body had previously been well developed, and it extended through the organization of living material into individuals. Virchow recognized that various types of societies constitute another level of integration of biological living material, and in his old age studied anthropology as a preliminary to a consideration of diseases of societies. We have scarcely caught up with Virchow yet.

Meanwhile, we have extended our appreciation of the organizational levels of living material at both ends. We recognize now that certain macromolecules, particularly those concerned with genetic factors, desoxyribose nucleic acids, are definite chemicals which can crystallize and which have specific physical and chemical properties so that, as far as they are concerned, the principles of physics and chemistry apply directly to them. On the other hand, they exhibit some of the astonishing properties of life; they reproduce themselves if their amino-acid components are available and they can also provide templates for the enzyme synthesis of the basic proteins which characterize the bulk of living material. At the other end of the system of organizational levels, we are becoming more and more aware of the increasing importance of the over-all ecological milieu which is concerned with the challenging problem of the "balance of nature."

At each level of biological organization it is now appreciated that there are complex internal regulatory mechanisms with intricate feed-back systems from various parts of the living material itself and from its environment. These servomechanisms serve to maintain the steady state of the system and enable it to change appropriately to meet internal or external stresses that infringe upon it.

This concept of the internal regulatory mechanism of living material developed largely with Claude Bernard (1813–1878), another of Magendie's students. All of Bernard's studies, whether on the sympathetic nervous system, on the metabolic functions of liver, on neuromuscular mechanisms or on cardiovascular respiratory functions, emphasize the importance of the maintenance of the internal steady state of living material at any particular organizational level.

It is difficult to tell at just what level Bernard may have been thinking; it would seem that his thoughts dealt mostly with organ systems, but his ideas apply equally well to the total individual organism and to the individual cells of which the organism might be composed. From his early work on the glycogenic function of the liver, in which he emphasized the developing concept of the integrated interrelation of the parts of the organism to meet the requirements of the whole, to his last great work in 1878, he developed the idea of the "milieu interieur," that the preservation of the internal stability and constancy in an organism, despite any external change, is the essential characteristic of life. In an Aristotelian echo, he indicated that all the vital mechanisms, varied as they are, act constantly to preserve the conditions of life in the internal organization of living material. Bernard thus formulated the essential concept of adaptation.

Meanwhile, there had been further detailed investigations of the interrelations between living things and their environments. A. L. Lavoisier (1743–1794), in his development of quantitative chemistry, had measured the utilization of oxygen from the environment by humans and the production of carbon dioxide from the body itself. He thus demonstrated the analogy between respiration and combustion. This inaugurated an understanding of both the oxygen cycle and the carbon cycle between living material and its environment.

This cyclic interrelation between environments and the living things within those environments was further analyzed by Justus von Liebig (1803–1873). His studies outlining the interrelations between plants and animals in the carbon and oxygen cycle involving photosynthesis provided the basis for continuing investigation. Liebig's work also emphasized the cyclic movement of nitrogen through living material and its environment. In all of these observations, there was implicit the adaptations existing between living material and the environment.

Individual aspects of mammalian adaptations to physical factors in the environment began to be appreciated. The influence of climate was studied. With understanding of the respiratory function of the blood, as outlined later by Joseph Barcroft (1872–1947), a basis was laid for study of the effects of altitude and of changes in the oxygen tension of inspired air. As shown by my colleague, Fred Hitchcock, this approach was essential to the practical management of successful space flight as well as of deep-sea exploration and submarine navigation.

Claude Bernard's specific work on the "milieu interieur" was broadly extended by Walter B. Cannon (1871–1945). In studying digestion in mammals, Cannon observed the influence of emotional factors on digestive activities. I. P. Pavlov (1849–1936) had shown how these emotional factors relating to digestion may be conditioned. Cannon discovered the influence of the secretions of the adrenal gland in correlation with emotional states and developed the concept of "homeostasis." In his *The Wisdom of the Body* he outlines the various ways by which organisms can adjust themselves to stress situations and maintain a relative constancy of physiological behavior.

Cannon's work was profoundly influential. It stimulated his student Arturo Rosenblueth, from Mexico City, to investigate various autonomic nervous factors which are important in maintaining the internal steady state of the organism. The correlation between endocrine and nervous factors was established. The feed-back systems that began to be recognized were skillfully elaborated by Rosenblueth's mathematical associate Norbert Wiener. Wiener gave the mathematical basis for "servomechanisms" and established the new scientific field of cybernetics.

It is interesting that the concept of adaptation was so slowly accepted. The index subject headings, "Adaptation and Adaptability; see, also, evolution," appears first as late as Volume 1, Third Series, of the *Index-Catalogue of the Library of the Surgeon General's Office, United States Army*, published in 1918. C. B. Davenport in 1903 consciously refers to the "theory of adaptation."

T. H. Morgan (1866–1945) offered a careful consideration in 1910 on "Chance or Purpose in the Evolution of Adaptation." This groping analysis offers a critique of Henri Bergson's *Creative Evolution*

(Paris, 1907) which revived the vitalistic point of view which suggested purposeful adaptation. Morgan says that Bergson begs the question and a priori assumes what is impossible to verify. Morgan concludes that the process of evolution is such that organisms are carried along adaptive lines. A. P. Mathews (1871–1956) discussed adaptation in 1913 from the point of view of physiology. Again, the pathologist William Henry Welch (1850–1934) had anticipated many of the early twentieth century ideas on adaptation in his discussion of "Adaptation in Pathological Processes" which he delivered in 1897.

In 1913, L. J. Henderson (1878–1942) issued his provocative book *The Fitness of the Environment* in which he emphasized the reciprocal relations in "fitness" between living things and their environment. He later emphasized the functional reserve in living material which enables it to meet changing conditions without too great distortion. This is well exemplified in the buffering power of blood and body fluids. Individual nerves and muscle fibers, however, respond "all-or-none" to appropriate stimuli, but there is nevertheless a functional reserve in their aggregation.

One of the interesting aspects of pathological adaptation is the tendency of living material to overcompensate for distortions induced by stress. This aspect of adaptation was emphasized by W. de B. MacNider (1881–1951) in studies on repair in kidneys and liver resulting from the toxic action of anesthetic agents and uranium salts. He published many reports dealing with acquired resistance of tissue cells to various types of toxic agents. This sort of adaptation by tolerance had long been recognized in reactions to such drugs as alcohol and morphine.

Currently this tendency of overcompensation in physiological processes as a form of adaptation to stress factors has been emphasized by Hans Selye. In his extensive studies on the physiology and pathology of exposure to stress, he has outlined a clinical condition which he calls the "stress syndrome." Measurements of various physiological processes indicate overcompensation on the part of various cells, tissues, and organs of the mammalian body to environmental stress factors.

It is significant that the systems theory remains widely applicable in all aspects of science and, indeed, in culture generally. The physical principle of stress is currently being extended to all phases of biology, including sociology. As my colleagues in psychiatry, Harold Goldman and Lewis Lindner, emphasize, the physical concept of stress is appropriate to all systems phenomena; stress is a force producing deformation in a system. The concept of adaptation became clearly evident in the principle formulated by the chemist H. L. Le Châtelier (1850–1936): If a system at equilibrium is subjected to any stress, a change which reduces the stress will occur; or, more generally, if a system is in stable equilibrium and one of the conditions changes, then the equilibrium will shift in such a way as to tend to restore the original condition. With increasing appreciation of the operation of the physicochemical properties in living systems, these considerations assume increasing importance, as F. W. Schueler is indicating in various isomorphic situations.

Many aspects of adaptation are currently being explored at various levels of biological organization and with particular reference to genetics. Some bacteria survive exposure to antibiotics and develop into antibiotic-resistant strains. Some insects survive exposure to insecticides, and resistant strains arise.

We are becoming aware of the importance of adaptations at social and ecological levels in such matters as overpopulation and the stresses associated with it as well as with extensive changes in the balance of nature, with air and water pollution, and with the destruction of native ecological areas. Indeed, so blind are we to what we do, that we are in danger of destroying forever the environments in which we took so long to evolve.

Julian Huxley returns to the basic Darwinian point of view in concluding that "natural selection will be constantly adjusting the organism to its environment, biological as well as physical; in other words, tending to produce more and more complete adaptations."

One of the major problems in adaptation, one not as popularly appreciated as it deserves to be, is population pressure which can be devastating to the environment. Many instances are available of the destruction of natural habitats by the introduction of exogenous species, and while these instances usually refer to isolated communities or small islands, the situation is becoming much more general with human population pressures.

Population pressures involve many problems of adaptation, including increased irritability, aggressiveness, and maladjustment. In human societies these require increasing regulation which calls for increasing bureaucracy with resulting loss of individual responsibility and freedom. Human population pressures entail serious air and water pollution and, indeed, are putting a severe strain on our water resources. Human population pressures are responsible in many parts of the world for the destruction of the ecological environment in which humans have themselves evolved. The development of nuclear energy, whether for peaceful or for military uses, increases the natural hazards of radiation and is producing a situation extremely alarming to some people. Further increase in radiation hazards may increase the incidence of mental and physical defects, thus seriously threatening the human genetic pool.

Nevertheless adaptations are to be expected. The challenge is always offered to living material by slight changes in its environment. Those organisms which have the capacity to adapt to such changes and which do so in an effective way will survive.

Specific references to various aspects of the development of the concept of adaptation may be found by utilizing the second edition of *Garrison and Morton's Medical Bibliography* (New York: Argosy Bookstore, 1954). One may further find references to the work of specific individuals by consulting the *Index-Catalogue of the Surgeon General's Office* for the classic reports. A general discussion of physiological adaptation was edited by C. Ladd Prosser (*Physiological Adaptation*. Washington, D. C.: American Physiological Society, 1958).