

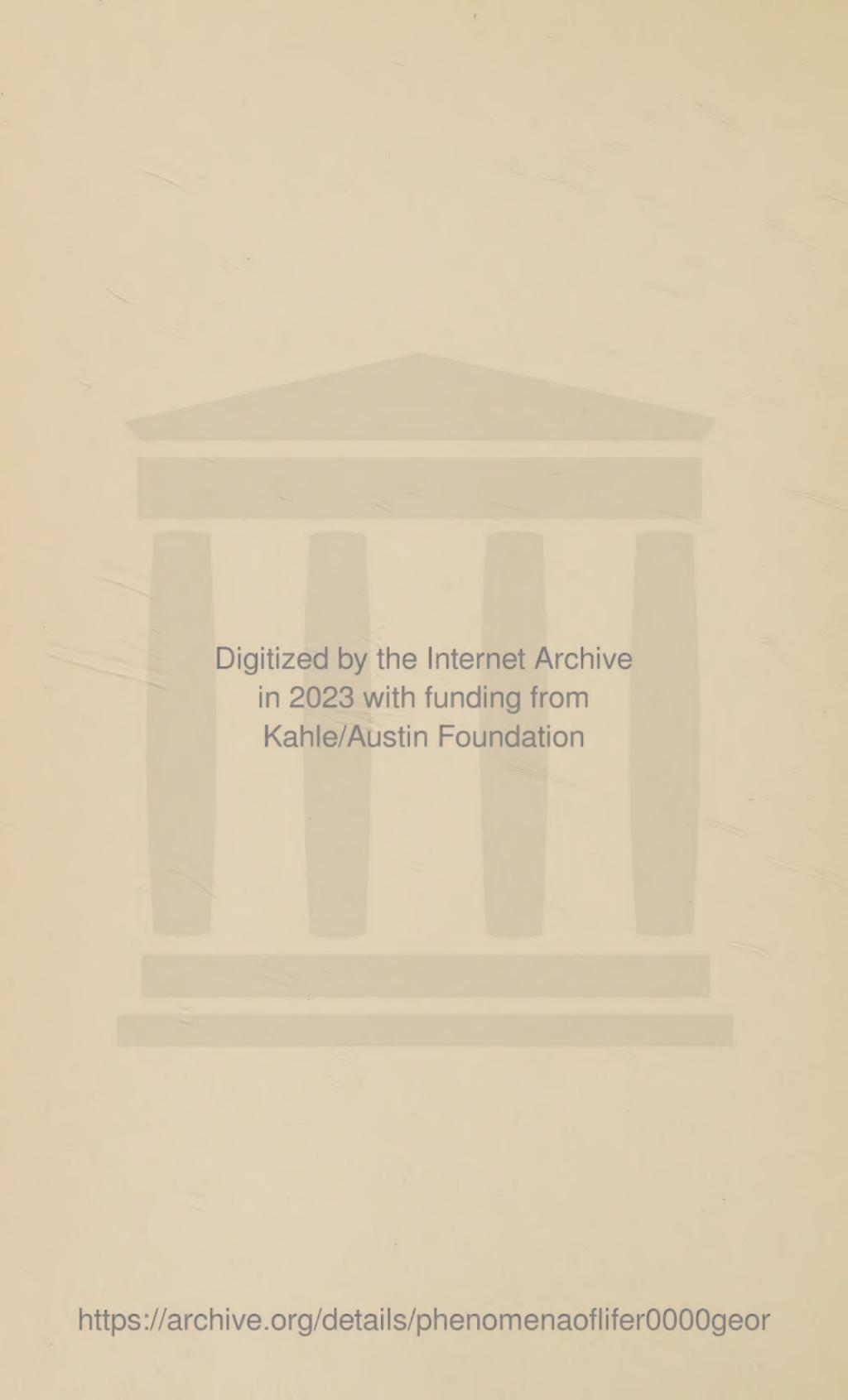
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THE PHENOMENA OF LIFE

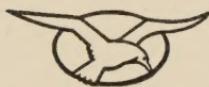
A Radio-Electric Interpretation

THE PHENOMENA OF LIFE

A Radio-Electric Interpretation

BY

GEORGE CRILE



Edited by AMY ROWLAND

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In grateful appreciation this book is dedicated to all my collaborators in the long line of researches on the phenomena of living processes which led to the conception presented here.

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INTRODUCTION

INTRODUCTION

OXIDATION produces radiant energy.

Radiant energy generates electric currents in protoplasm.

Electricity is the energy that governs the activity of protoplasm.

The normal and pathological phenomena of life are manifestations of protoplasm.

Therefore the phenomena of life must be due to radiant and electrical energy.

This syllogism represents our problem! We shall offer evidence tending to show that the living organism is specifically adapted to the formation, storage and specific use of electric energy and that the genesis of this electric energy is due to radiant energy emitted by ultramicroscopic units or furnaces in protoplasm. These furnaces we have called *radiogens*. We shall postulate that the combustion of the proteins is effected by these microscopic units and that the short wave radiation emitted by this continuous combustion has two primary and fundamental effects. (1) Short wave radiation knocks off electrons and thus disturbs the electrical state of the protoplasm, especially of the infinitely intricate network of the nervous system. (2) Short wave radiation so disturbs the architecture of the atom as to make the atoms chemically active, thereby forming the basis for the synthesis of protoplasm.

We shall describe first the long series of researches which were undertaken in the hope of discovering the nature of the energy that is lost as a result of physical injury, emotional excitation, infection, etc., that is, the search for the fundamental mechanism involved in exhaustion, shock and death.

In many years of biophysical studies we accumulated data which tended to show the validity of our syllogism as applied to protoplasm generally. We then tested whether this concep-

tion would interpret the function of the special senses, the brain, the sympathetic nervous system, the adrenal glands, the thyroid gland, the liver and the muscles; that is, we endeavored to find whether this conception would interpret the normal function of organs. We then turned from the normal to the clinical aspect to discover whether or not the play of radiant and electric energy could account for shock, exhaustion and death when produced by injury, emotional excitation, hemorrhage, muscular exertion, infection, asphyxia, lack of sleep, etc. We next endeavored to discover whether or not radiant and electric energy could account for the action of anesthetics, narcotics, stimulants and poisons. We also made an investigation to discover whether or not radiant and electric energy could account for the phenomena of such diseases as hyperthyroidism, neurocirculatory asthenia, polyglandular disease, peptic ulcer, and diabetes.

The identity of the energy that is lost in shock, exhaustion and death was not found by attacking this problem by physiological, cytological and chemical methods. Although these extensive researches failed in their primary objective, methods for the protection, conservation and restoration of protoplasm were evolved which have become common procedures in surgical clinics, and in the long series of cytological studies the electrical nature of protoplasm was glimpsed. This led our attack of the problem into the domain of physics.

As a final test of the validity of our conception we carried our reasoning to the clinic of life as well as to the surgical clinic and shall offer an interpretation of mental processes, of the emotions, of sleep, and of certain surgical emergencies.

Throughout these researches our findings have been constantly tested in the crucible of the clinic. If any finding could not stand this test it was discarded, as any theory regarding the nature of living processes must explain the vicissitudes of life that are seen daily by the surgeon.

In the following pages we shall describe first the long quest to obtain a clue to the nature of normal and pathological processes which led us at last to the radio-electric interpretation. We shall then present the argument in favor of our hypothesis and the experimental data on which the hypothesis is based.

THE ARGUMENT

PART ONE

THE THEORY

CHAPTER 1. *THE QUEST*

IN 1887, on the day after I became an interne in University Hospital, Cleveland, William Lyndman, a healthy young medical student, was brought into the hospital in the state of profound shock, both of his legs having been crushed by the wheels of a street car. He was perspiring, his face was pale and drawn, his respiration was hurried, his pulse soft and slow. He had lost but little blood. It became my duty to administer chloroform while Dr. Frank J. Weed performed an amputation at the thigh.

Following the operation, the patient exhibited a shrunken countenance, a rapid, feeble, failing pulse, pallor, cold sweat, sighing respiration, restlessness, semi-consciousness. I attended him through the night and noted his steadily failing faculties and deepening depression. In the early morning he died. This was the first death I had ever witnessed.

The postmortem showed all the organs and tissues to be normal in structure. On the known morphologic basis of his organs, *per se*, young Lyndman was not dead.

During the night I had made notes on the inexplicable phenomena of this failing mechanism. What was it that was failing? What was it that this young medical student possessed up to the moment of his accident that he lost by reason of the crushing of his limbs without material loss of blood; and why was the treatment for shock which was applied all through the night of no benefit?

The literature on shock yielded no answer to my questions, but having noted the pallor and the coldness of the skin, the shrunken face, the fading pulse, and the fact that at autopsy

the large venous trunks were well distended, especially in the abdominal area, it seemed to me that the most important factor in this death must have been the shifting of the blood from the arterial and capillary system to the venous system. I concluded, therefore, that as the result of his injury this healthy young man bled to death into his veins; in other words, that the blood failed to circulate, hence the otherwise apparently sound organs could not function. This identical conception of death from shock was proposed by physiologists many years later, during the World War.

What impressed me most in this slow fading away of young Lyndman was the failure, in concert, of every organ of the body. Looking collaterally at that time, physics and chemistry had made none of their revolutionary advances. Living energy was referred to as vital energy, as something not to be understood. Medicine was largely empirical.

In my questionings there was one favorable element—I never even suspected the extent of my ignorance with respect to the problem I was formulating for myself. The problem was: What was Lyndman? Why did he leave his habitat just because his legs were crushed and he had had an anesthetic and an amputation, since the morphological appearance of all of his essential organs showed apparently that his body was as good a habitat as before the injury? Autopsy revealed no lesion in any vital organ.

Accordingly, I began an experimental investigation which has continued until the present time. That my hypothesis, namely, that William Lyndman bled to death into his veins, was not adequate was quickly proven, for when in experiments on anesthetized animals I closed the splanchnic circulation, thus preventing the accumulation of blood in the large veins in this area, I found that death from shock could be produced almost as readily as in normal animals.

I then made a long series of investigations on anesthetized animals in which was tested the effect of injuries of every conceivable type and of stimulants, narcotics, anesthetics, and toxins upon the blood pressure, the respiration, and the significant organs and tissues of the body.

I found that the more richly a given area was supplied with

sensory and vasomotor nerves, the more rapidly was the animal exhausted when such an area was subjected to injury, and that injury of a given area produced shock in proportion to the severity of the trauma and the duration of the application of the injuring agent. I found that infection, hemorrhage, asphyxia, cold, injury, exertion, stimulation, emotional states and lack of sleep, each added to the effects of the others. The constant factor, however, was always a loss of energy.¹

After finding that the loss of energy was not due to the transference of the blood from the arteries to the veins, I tested the hypothesis that the circulation failed because the vasomotor centers were exhausted, thereby allowing the blood to become pooled in the large venous trunks of the body, thus producing the equivalent of death from hemorrhage.²

In the meantime we had devised the technique for a direct transfusion of blood,³ whereby we found that, although death may be delayed, an animal under anesthesia may be killed by traumatic shock even when its blood pressure is maintained at or higher than the normal level.⁴ Thus I disproved my second hypothesis, viz., that surgical shock is due mainly to impairment or breakdown of the vasomotor mechanism.

I then supposed that changes in the respiration, that were always present and often striking, might affect the exchange of gases in the blood and tissues, at least sufficiently to contribute largely to, or of themselves to cause death from shock. Under inhalation anesthesia, further experiments were carried out in which artificial respiration was maintained at an even rate and the blood was kept normally oxygenated, but the animal still succumbed to surgical shock, thus disposing of our third hypothesis.

We then proposed the hypothesis that if death from shock was not due to factors in the circulation or in the respiration, it must be due to fundamental changes in the chemistry of the blood itself. In collaboration with Dr. M. L. Menten, Dr. W. J. Crozier, and Dr. W. B. Rogers, I conducted experiments on the hydrogen-ion concentration of the blood, and found that the buffer substances in the blood continued to be effective up to or near the time of death, and that there was little or no variation in the hydrogen-ion concentration during the development

of shock.⁵ Even when all the other symptoms of shock were being exhibited, the hydrogen-ion concentration of the blood suffered little change. It was clear, therefore, that the changes in the hydrogen-ion concentration of the blood were not the primary factor that caused surgical shock.

During these long-continued researches, six facts had been

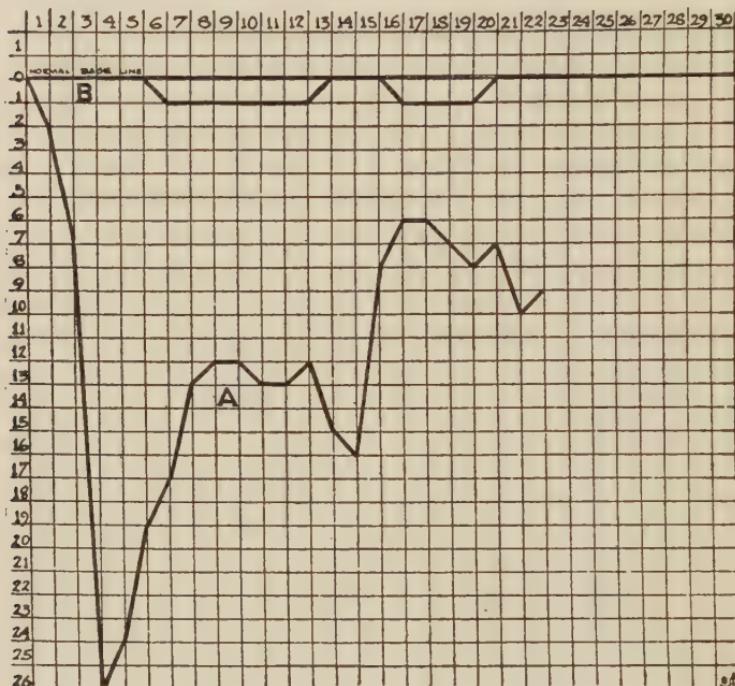


FIGURE 1. Comparative effects on the blood-pressure of intralaryngeal irritation without (A) and with (B) the application of cocaine in an anesthetized animal.

established which have been of theoretical and practical importance.

1. We demonstrated conclusively that the local application of cocaine to the laryngeal mucous membrane, before this membrane was subjected to physical irritation, prevented completely reflex inhibition of the heart.⁶ (Fig. 1.) When cocaine was applied to nerve trunks or to the spinal cord, we found that neither afferent nor efferent impulses of any kind could pass,

and no amount of traumatism in the areas peripheral to this block could cause surgical shock. Upon this principle, the first shockless operations were performed in 1897, and a new principle in surgery was established.¹

In addition to its practical value, the fact that the blocking of a nerve trunk by cocaine prevented shock had an important theoretical significance, as it showed that whatever was the mechanism that maintained the normal energy of the body in health and was lost as a result of physical injury, that mechanism was reached over the nervous system exclusively. This fact led to an attack upon the problem from an entirely different standpoint.

2. The second observation which proved to be of theoretical and practical importance was that when an inhalation anesthetic was administered, the hydrogen-ion concentration of the blood was steadily increased, and at the point at which all the buffers were overcome and the blood became acid, death inevitably and automatically occurred.⁷ This finding was in accord with the well-known fact that protoplasm ceases to function when it becomes preponderantly acid or preponderantly alkaline; that is, the acid-alkaline balance of an organism has a vital significance. Later on, we shall see how this principle reappears in an apparently unrelated but fundamental fact, namely, that when the nucleus and the cytoplasm of a cell will no longer take differential stains, the energy of the cell is lost and the cell breaks down.

3. The third practical result of our pursuit to discover the nature of the energy that was lost in death from surgical shock was blood transfusion. As far as I have been able to ascertain from the literature, the first direct transfusion of blood by the anastomosis of the blood vessel of one human individual with that of another was performed by me in 1905.⁸ This procedure immediately became of great value in the surgical clinic. Blood transfusion was used extensively during the World War, and is now used all over the surgical world as a means for the treatment of surgical shock, pathologic hemorrhage and certain depressed states.

4. The fourth observation of practical importance was the effect of the injection of adrenalin in the treatment of shock.^{4, 9, 10}

Since in surgical shock there is a progressive fall toward zero in the blood pressure, and since the injection of adrenalin (then newly discovered by Oliver and Schäfer¹¹) counteracted the lowered blood pressure in shock, I believed that adrenalin might be highly useful in the treatment of shock. Our researches proved that the injection of adrenalin raised the blood pressure regardless of the degree of shock, but that the effect was transient.

Continuous intravenous infusions of adrenalin for indefinite periods of time, however, gave results precisely opposite to that for which I had hoped; that is, adrenalin actually increased the state of exhaustion of the organism. We found that we could kill an animal by excessive doses of adrenalin alone, the animal sinking into exhaustion and death, just as in traumatic shock, infection, exhaustion from lack of sleep, etc. The significance of this surprising and disappointing observation will appear later.

5. The fifth practical observation was that the treatment of the failing energies due to shock by the administration of stimulants of any kind whatsoever hastened the death of the animal, whereas narcotization with morphine tended to prevent and diminish shock.¹² The administration of nitrous oxide anesthesia was an almost complete preventive of traumatic shock, while ether and chloroform alone effected no prevention of shock.¹³ The significance of these findings will also appear later.

6. The sixth interesting and significant observation that was made in the course of these experiments was that there is a clear distinction between surgical shock and the sudden suspension of energy which is called collapse, such as results from inhibition of the heartbeat, asphyxia, a rapid hemorrhage, and air embolism. The animals in collapse that were resuscitated by the injection of adrenalin immediately regained their normal vigor, in contradistinction to the long slow recovery of those animals that were resuscitated while in the state of shock.^{1, 4}

Having observed a wide range of variation in the resistance of the tissues and organs of the body to the influences that cause death, and having observed the damaging effects of

hemorrhage and of low blood pressure, we attempted to maintain the blood pressure by bandaging, and then devised a pneumatic suit by means of which the general blood pressure could be raised at will within a range of from 15 to 45 mm. of mercury.¹⁴ Although this was of value, the mechanical difficulties outweighed its usefulness.

It was blood transfusion that showed us the unique significance of an adequate circulation and oxidation in the maintenance of the energy of the body. Human blood is the only fluid which does not pass through the vessel walls, causes no chemical injury, carries oxygen and is always immediately available. Our researches showed that the direct transfusion of blood was the most important single factor in the treatment of surgical shock.

We then followed a line of investigation in which we temporarily deprived various organs and tissues of their circulation and found not only a great variation in the length of time various organs maintained their vitality without circulation of blood, but also variations in the time that the component parts of organs endured anemia safely.⁹

We found that organs and tissues such as the skin, bone and connective tissue at one extreme, endured anemia for many hours, while at the other extreme, the brain and the liver endured anemia for only a few minutes. Moreover the component parts of organs endured anemia unequally; the connective tissue framework was more resistant by far than the parenchymal (tissue) cells and there was strong evidence that the power to endure anemia was in proportion to the sensitivity of the function of an organ or tissue. Thus the organs that most promptly succumbed to anemia were the brain, the liver and the cortex of the adrenal glands, the heart muscle and voluntary muscle being many times more resistant. It appeared, therefore, that the brain, the liver and the adrenal glands are on the firing-line; that is, they must play a fundamental rôle in controlling the energy of a living organism, the loss of which, due to injury, emotion, infection, we call exhaustion and shock.

One fact of great significance which emerged during these researches on anemia was that different parts of the brain

endure the effects of suspended animation or apparent death in different degrees, the most sensitive being the optic areas and those areas by which consciousness is maintained. In other words, the more highly sensitive or labile the cells, the more easily is the organ broken down by loss of blood during suspended animation or apparent death.

In order to test the resistance of the brain and other tissues, we developed the technique of resuscitation of animals after apparent death. The experiments of Kuliabko,¹⁵ d'Halluin,¹⁶ Stewart,¹⁷ and others on the isolated heart in which the heart was made to beat for hours by perfusing it with various solutions, notably Locke's solution, were well known. This principle, which applied so successfully to the heart, we extended to the entire animal, and it yielded a large group of dramatic and fundamental facts: Of prime importance was the fact that up to an average period of six and a half minutes after an animal in a state of normal health had been "killed" by an anesthetic or by asphyxia, the perfusion of adrenalin in salt solution into an artery toward the heart, or the injection of adrenalin directly into the heart, while artificial respiration was maintained by rhythmic pressure upon the chest, would cause the heart to leap suddenly into activity and to circulate the blood violently. Respiration was spontaneously resumed; the animal would open its eyes, get up and move about and would soon resume its normal activities without any serious loss of energy, just as in the cases of collapse. This was in complete contradistinction to the tardy recovery after surgical shock. The fact that adrenalin *was the only agency that could bring about such a resuscitation is highly significant.* No other drug, no other hormone, no other stimulant, not even electricity, could effect the resuscitation of an apparently dead animal. Only adrenalin could effect resuscitation. Even if there were no artificial respiration, and even if the heart were filled with asphyxiated blood, adrenalin would still cause the heart to beat; but naturally, to sustain the heartbeat, respiration had to be restored. Obviously, adrenalin was the only agency that had the power to excite a sufficiently violent anaerobic oxidation—and the heartbeats were violent

—to reanimate the animal. In certain clinical cases this method was effective.

Up to this point we had shown that the active generation and control of the vital energy of the body was primarily the function of the brain, the heart and the adrenal-sympathetic system. The precise nature of this energy, however, had not been identified.

Not having found the cause of shock in the circulation, in the respiration, in the blood, and obviously not in the bony skeleton, the connective tissue, the fat or the skin, and having observed in our experiments that the use of cocaine as a local anesthetic prevented shock from trauma of the area involved and that spinal anesthesia prevented shock completely as the result of trauma of a large field, I was convinced that, in shock, nerve impulses pass from the field of trauma and enter the vast network of nerve cells and fibers, thereby affecting profoundly the brain and all the nervous tissue. If this were the case, then the brain cells must show morphologic changes analogous to the changes described by Hodge¹⁸ in the nerve cells of bees and birds at the end of an active day. Therefore, in collaboration at first with Dr. D. H. Dolley and later with Dr. J. B. Austin and Dr. F. W. Hitchings, histologic studies were made, at first of the brain^{19, 20, 21} and later of every tissue and organ of the body, and we found that if an animal were reduced to a state of depression from surgical shock, changes occurred in the structure and differential stainability of the cells of the brain, of the liver, of the adrenal cortex and to a lesser degree of the adrenal medulla, and only in these organs. (Figs. 2-4.) The cells of other organs and tissues showed no histologic change.²²

Attempted resuscitation by the injection of adrenalin failed when animals, in which the cells of the brain, liver, and adrenal glands showed such physical changes, were killed quickly by anesthetics or by asphyxia.

The original brain cell studies led to a consideration of the principal reason for the variations in the discharge of energy when different parts of the body are injured—a consideration which led to an investigation of man's phylogeny in its relation

to medical problems. Our first conclusions were expressed in the Ether Day Address delivered at the Massachusetts General Hospital on October 15, 1910.²⁰ The scope of this thesis is well expressed by the following quotations:

"When a barefoot boy steps on a sharp stone there is an immediate discharge of nervous energy in his effort to escape from the wounding stone. This is not a voluntary act. It is not due to his own personal experience, i. e., his ontogeny, but is due to the experience of his progenitors during the vast periods of time required for the evolution of the species to which he belongs, i. e., his phylogeny. The wounding stone made an impression upon the nerve receptors in the foot similar to the innumerable injuries which gave origin to this nerve mechanism itself during the boy's vast phylogenetic or ancestral experience. The stone supplied the phylogenetic association, and the appropriate discharge of nervous energy automatically followed. If the sole of the foot be repeatedly bruised or crushed by the stone, shock may be produced. If the stone be only lightly applied, then there is also a discharge of nervous energy from the sensation of tickling. The body has had implanted within it in a similar manner other mechanisms of ancestral or phylogenetic origin whose purpose is the discharge of nervous energy for the good of the individual. . . .

"The brain cells have existed during eons of time and amid the vicissitudes of change with perhaps less alteration than the crust of the earth. Whether lodged in man or in the lower animals, they are related to and obey the same general biological laws, thus binding them, that is, ourselves, to the entire past, and perform their function on the law of phylogenetic association.

"So long have we directed our attention upon tumors, infections and injuries that we have not sufficiently considered the vital force itself. We have viewed each anatomical and pathologic part as an entity, and man as an isolated phenomenon in nature. May we not find in the law of adaptation under natural selection, and the law of phylogenetic association, the master key that will open to us the explanation of many of the pathologic phenomena as they have already explained many normal phenomena?

"And may medicine not correlate the pathologic phenomena of the sick man with the forces of evolution, as the naturalists have correlated the phenomena of the sound man,—and disease as well as health be given its evolutionary setting?"

Our experiments had thus led us to the conception that the fact that part of the body or tissue is more richly supplied

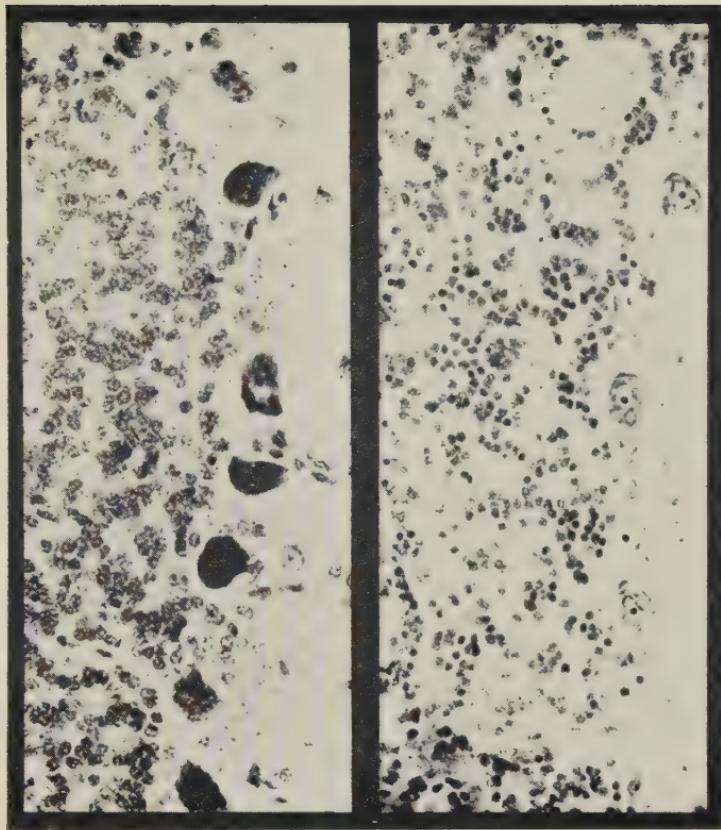


FIGURE 2. Effect of surgical trauma on the brain cells.
A, Section of the normal cerebellum; B, Section of the cerebellum of an animal after surgical trauma under anesthesia. Compare the hypochromatic appearance of the Purkinje cells in B with the deeply colored intact cells in A. (From photomicrographs X 310)

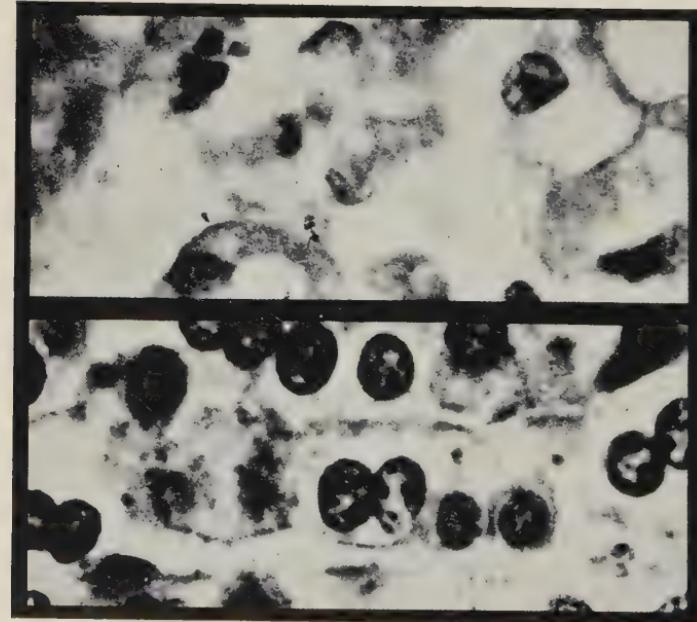


FIGURE 3. Effect of surgical trauma on the liver.
A, Section of normal liver; B, Section of liver of an animal after surgical trauma under anesthesia. Note the vacuolated spaces, the disappearance of the nuclei and general disintegration of the cells in B. (From photomicrographs X 1640)

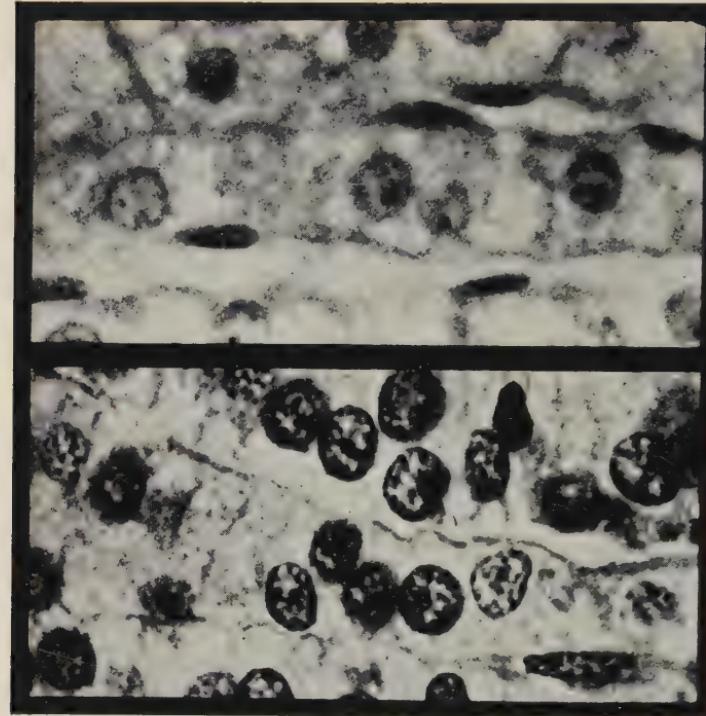


FIGURE 4. Effect of surgical trauma on the adrenals. A, Section of normal adrenal; B, Section of adrenal of an animal after surgical trauma under anesthesia. Compare A and B and note the marked signs of disintegration in B. (From photomicrographs X 1640)

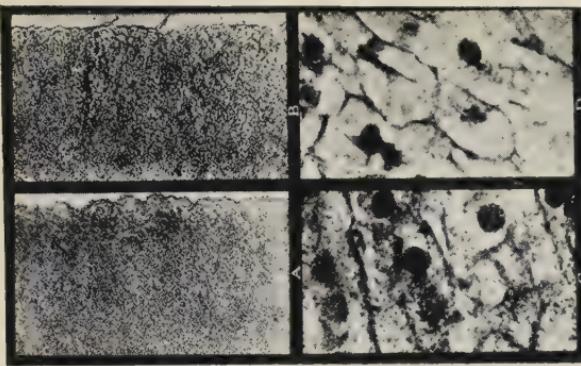


FIGURE 7. Effect of insomnia on the adrenals of a rabbit. A and C, Sections of adrenal of a normal rabbit. B and D, Sections of adrenal of a rabbit after prolonged insomnia. (A and B from photomicrographs X 100; C and D from photomicrographs X 1600)

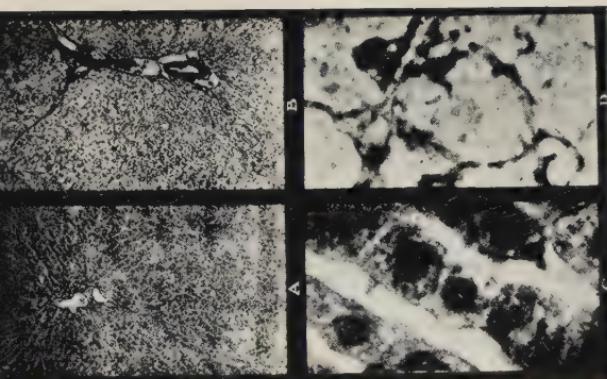


FIGURE 6. Effect of insomnia on the liver of a rabbit. A and C, Sections of liver of a normal rabbit. B and D, Sections of liver of a rabbit after prolonged insomnia. (A and B from photomicrographs X 100; C and D from photomicrographs X 1600)

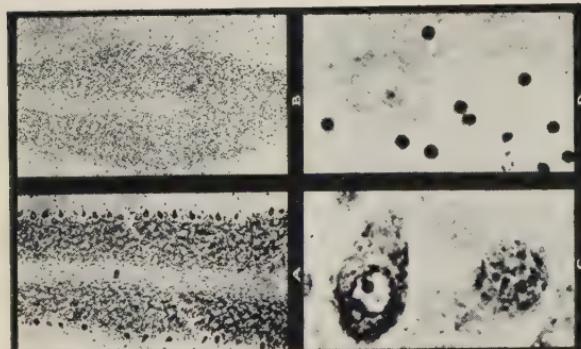
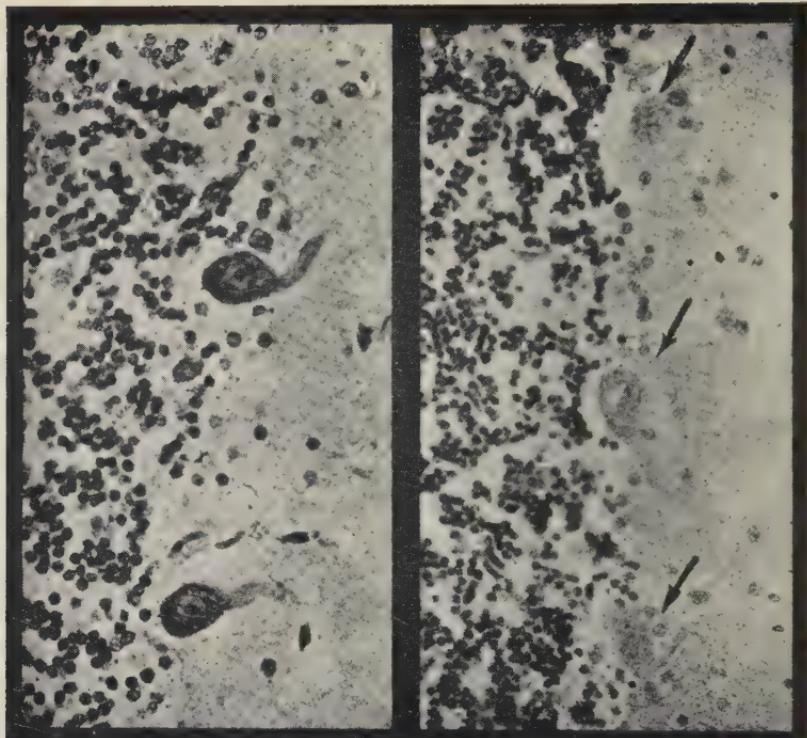


FIGURE 5. Effect of insomnia on the brain cells of a rabbit. A and C, Sections of cerebellum of a normal rabbit; B and D, Sections of cerebellum of a rabbit after prolonged insomnia. (A and B from photomicrographs X 100; C and D from photomicrographs X 1600)



A

B

FIGURE 9. Effect of a fatal infection on the brain cells of a human being. A, Section of normal human cerebellum. (The normal human cerebellum from which this section was made was secured from a healthy young man who was killed instantly by a truck.) B, Section of human cerebellum after death from an infection. Note the marked disintegration of the Purkinje cells in B. (See arrows) (From photomicrographs X 310)

with nerves, and hence when excessively stimulated by injury produces physiologic exhaustion and morphologic changes in the millions of cells of the brain, may be interpreted as due to phylogenetic or racial experience in the adaptation of animals by evolution.

Hence it is that injury of the hands, the feet, the brain and the spinal cord, the outer skin, the nerve trunks, the abdominal area, the sympathetic system, causes a greater and more rapid loss of vital energy than an equal injury of the fat, connective tissue, bones or joints. Stimulation or depression of the skin of that part of the body which through phylogeny has more often suffered injury, such as on the soles of the feet, the palms of the hands, the abdomen, neck and face, causes more injurious impulses and impressions of greater intensity to be passed on to the brain and nervous system than are passed on after equal injury of the back, the back of the thighs, the arms, that is, of those portions of the body which have been less exposed and more protected through our phylogenetic experience.

Our research was then extended to include an investigation of the cells of every organ and tissue in the body in animals whose energy was normal, whose energy was exalted, and whose energy was depressed by such various factors as injury, loss of sleep, (Figs. 5-7) emotion, exertion, hemorrhage, asphyxia, narcotics, excision of glands and organs, anaphylaxis, thyroxin, adrenalin, foreign proteins, strychnine, alcohol, ether and nitrous oxide; that is, we studied the effects of depression and death from every possible cause.²³

These experiments continued over a period of ten years and included over 2,500 animals of various kinds, mammals, birds and fishes. We examined the cells of all the organs of foxes which had been pursued by hounds; of salmon before and after they had made their long swim of approximately a thousand miles from the sea to the spawning beds in the Columbia River; of electric fish in the Marine Biological Laboratory at Naples as well as of electric fish from the Atlantic Ocean, before and after the discharge of their electric energy; of woodchucks in hibernation, (Fig. 8) of animals with natural protection such as barbs, quills, carapaces, offensive odors

or poisons; of animals in the wild state, of animals in captivity, of animals in hibernation, and of human beings killed by injury and by disease. (Fig. 9.)

During this time, and based upon these experimental facts, the principle of anoxic-association or the shockless operation was established; the principle of resuscitation by adrenalin had been put into practice and blood transfusion had been used not only in the treatment of hemorrhage and shock but

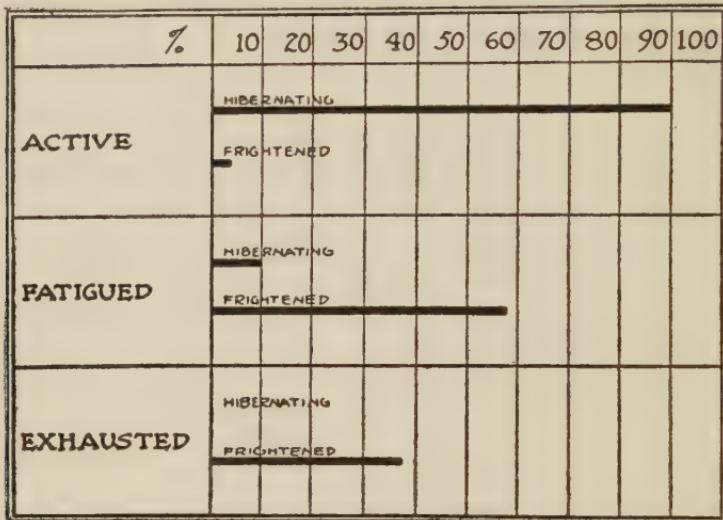


FIGURE 8. Comparison of the differential Purkinje cell counts in hibernating and in frightened woodchucks.

as a preventive against shock in patients handicapped by old age, infection, anemia, malignant tumors, degenerative disease, by the crises of hyperthyroidism, etc.^{23, 24} The observations made in the experimental laboratory were continually being tested in the crucible of the clinic; and the experimental laboratory in turn was deriving problems from the clinic, among them the extraordinary problem presented by the volatile patient with hyperthyroidism, in whom all the symptoms that are produced by the intravenous infusion of adrenalin are exhibited. When this excessive stimulation of the thyroid gland is reduced to the normal level, all of these symptoms due to the adrenal-sympathetic system disappear and the patient

returns to normal health. We found by practical experience with these patients that there were six and only six major excitants capable of aggravating the symptoms in this explosive disease. These are the same excitants that are known to cause an increased output of adrenalin, namely, pain, emotional excitation, infection, asphyxia, inhalation anesthetics, and hemorrhage. As for the injection of adrenalin itself into the volatile patient with hyperthyroidism, even a minute dose might cause a violent reaction and a normal dose might kill the patient as the result of an explosive outburst of activity. *Adrenalin seems to act as a fulminate.* On the other hand, in patients with myxedema (hypothyroidism) adrenalin has little or no effect. In myxedema, large doses of adrenalin may be given hypodermically but the patient remains cold and unmoved.

In the laboratory studies in which physiological, biochemical and cytological methods were used, with close scrutiny in the clinic of the patient's maladies, diseases, injuries and operations and of the effects of anesthesia and drugs—in this wide search for the nature of the energy that protoplasm exhibits in growth and function and for the reasons for the failure of that energy in depression and death, though we had been able to prevent shock and to treat it effectively, and through the principle of anoci-association had been able to operate more successfully on handicapped patients; though we knew that this energy depended on oxidation, temperature, and the proper balance of water and electrolytes; though we knew that energy was lost under ether or chloroform anesthesia and as the result of injury, exertion, emotion, asphyxia, hemorrhage, infection, loss of sleep, and that it was conserved by morphine, by nitrous oxide anesthesia, and by nerve-blocking, we had reached no theory that would harmonize this vast array of established facts, many of which seemed to be contradictory to each other.

Our first glimpse of a harmonizing fact had come from the long series of studies in the differential stainability of the cells of various organs.

These studies led to the conception that there is in the organism an energy-controlling or kinetic system, viz., the brain, the liver, the thyroid gland and the adrenal-sympathetic

system, which collaborate in the transformation of potential into kinetic energy to effect adaptive responses—muscular action, emotional excitation, fever, etc. In spite of our array of facts, however, we still were unable to formulate any hypothesis that would explain the significant rôle of the liver. Yet if our cytologic researches were of value, the rôle of the liver must be identified, for in our studies changes in the cells of the liver appeared equally and consistently with the changes in the cells of the brain and the cells of the adrenal glands.

In the hope of discovering the nature of this interrelationship of the brain and the liver, we considered the structure of the cells, and especially the following observations made in our laboratory:

(1) Differential stains were required to define the nucleus and the cytoplasm, the nucleus taking a basic stain, the cytoplasm an acid stain.

(2) In exhaustion or death from any cause, even including the want of sleep, the differential stainability of the cells of the brain, of the liver, and of the adrenal gland—and of these organs only—was decreased or even disappeared.

(3) After the administration of a fatal dose of an alkali, the differential stainability of the cells was lost.

(4) After the administration of a fatal dose of an acid the differential stainability of the cells was lost.

When these observations were considered together with the fact that when the alkalinity of the blood disappears, that is, when the neutral point is reached, the animal dies, it became evident that death was associated with loss of the acid-alkali balance within the cells of the organism. What could be the fundamental relation between the relative acidity of the nucleus and the relative alkalinity of the cytoplasm?

An acid colloid and an alkaline colloid separated by a semi-permeable membrane, a dielectric membrane, constitute a concentration cell, within which an electric potential exists between the positive and the negative poles. According to this conception the cells of the organism are electric cells in which the comparatively acid nucleus constitutes the positive pole and the comparatively alkaline cytoplasm the negative pole. On

this basis, therefore, we began to consider the organism as a *bipolar mechanism* and to direct our researches into the field of biophysics.

According to our cytologic findings, the maintenance of the acid-alkali balance between the nucleus and the cytoplasm of the cells—the electric potential—is essential to life and furnishes the immediate driving energy of the living process itself. Its reduction to zero or equilibrium is death.

It remained, however, to discover how this vital electric potential of the cells is maintained. We assumed that the electric potential is mainly due to oxidation and that, in turn, the electric potential within the cell governs oxidation. This assumption led us to abandon physiological, chemical and morphological methods of attack upon our problem and to turn to physics in the hope that, by the application of the principles of physics, we might identify the physical laws and forces in accordance with which the organism is constructed and operated.

Among the limitations of physiological, chemical and cytological methods is the fact that by these methods no direct observation can be made within the protoplasm itself while it is actually responding to influences that cause excitation, depression, and finally death. In other words, our studies came after the protoplasm had done its work and received its injury.

We realized that we had exhausted our physiological, cytological and biochemical methods of attack on our problem, which was the identification of the nature and the genesis of the energy by which the protoplasm of William Lyndman grew, functioned, became exhausted and died. With the clue afforded us by the cytologic studies, we embarked upon the accumulation of evidence in support of the Bipolar Theory suggested by the cell studies. At this point I received valuable suggestions from Professor Dayton C. Miller of the Case School of Applied Science as to the methods by which the physical properties of protoplasm could be studied experimentally.

Accordingly, in 1915, in collaboration with G. B. Obear of the Case School of Applied Science, Amy F. Rowland, and Helen Hosmer, formerly of the Research Laboratories of the General Electric Company, a series of researches was initiated which led to the establishment of a permanent biophysical

laboratory in which the Bipolar Theory was subjected to bio-physical investigation.

Our histological studies had indicated that in the normal state the lipoid films surrounding the nucleus and cytoplasm offer a normal resistance to the passage of ions, that in exhaustion this

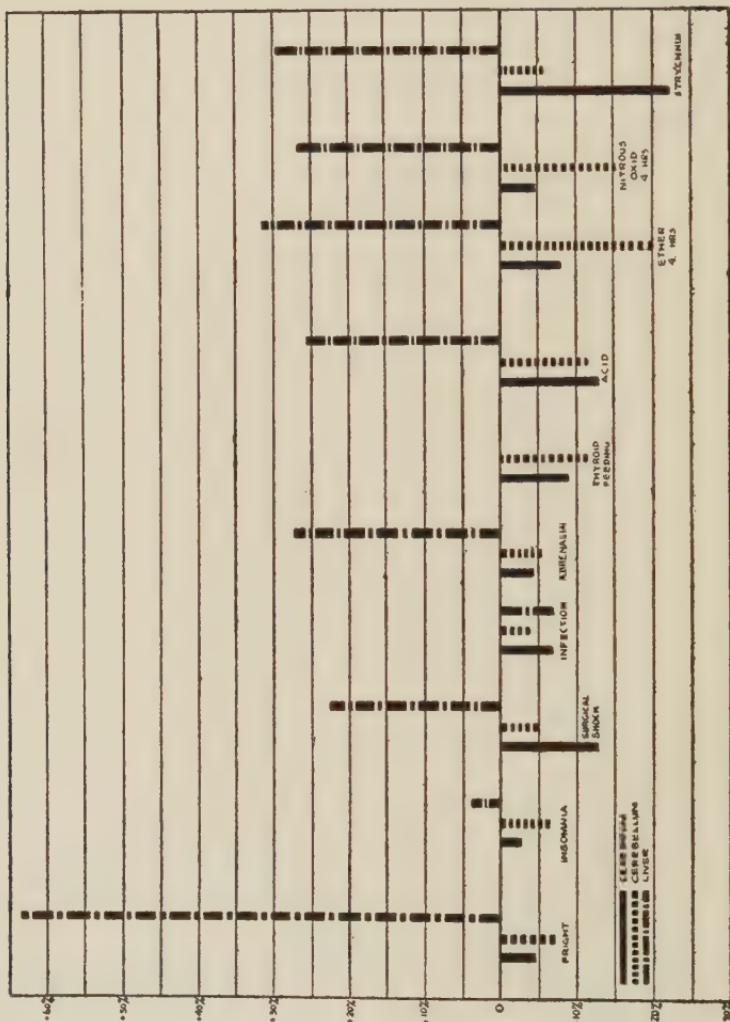


FIGURE 10. Effects of exhaustion due to various causes upon the electric conductivity of the brain and the liver. (Percentile variations from the normal.)

resistance is lowered, and that this specific resistance disappears at death. If these inferences were correct, then the changes indicated by the microscope could be more accurately identified by measurements of the electric conductivity, capacity and potential of the tissues. Such measurements were made and the findings supported this assumption. (Figs. 10, 11.)

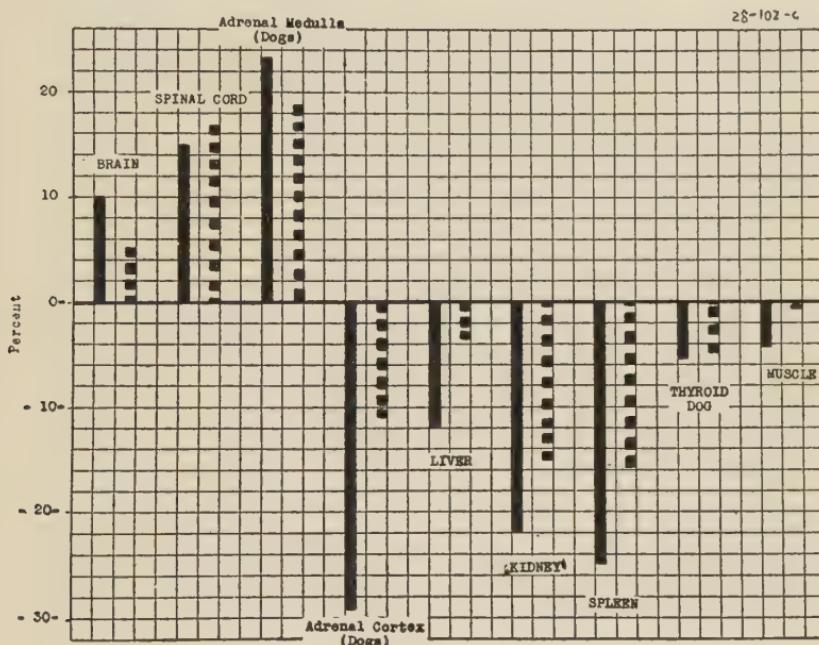


FIGURE 11. Percentile changes in the conductivity and capacity of various tissues produced by the injection of adrenalin.

If we were justified in our further assumption that the electric potential within the cells is maintained by oxidation, then variations in oxidation must accompany variations in activity and these variations in oxidation would be manifested by variations in temperature. This assumption was supported by experimental research. (Figs. 12, 13.) ^{25, 26, 27, 28, 29}

If the organism is operated by electricity, one would expect that the cells would be specifically adapted for the accumulation of electric charges. That this is the case, was in turn shown in our biophysical laboratory by Hugo Fricke who found that

the film which surrounds the red blood cells is on the order of $\frac{3}{10,000,000}$ of a centimeter in thickness and that this lipoid structure has an electric capacity of a high order, viz., 0.8 microfarad per square centimeter.³⁰

Our findings then were critically examined and correlated

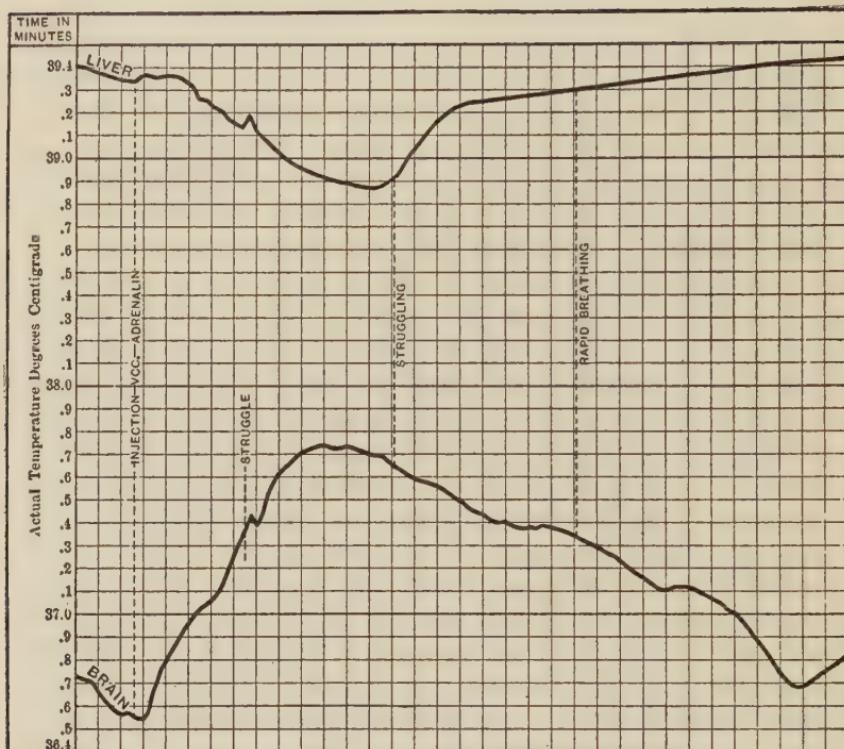


FIGURE 12. Effect of the injection of adrenalin upon the temperature of the brain and the liver.

in the hope of being able to propose a theory which would bridge the gap between the living and the non-living and suggest a physical line of ascent from the atom to man. The physical constants of temperature, electric conductivity, electric capacity and electric potential could all be estimated during life, that is, during the operation of the causes of excitation, depression and death, thereby making it possible to glimpse the transformation of biology and medicine into exact sciences.

We were in the midst of these observations upon the electric conductivity of the tissues and organs of animals that had been taken through the same gamut of excitation, depression and death as in the long series of studies that had gone before, when in 1914 I went to France, and again in 1917. In the World War I observed on a large scale all the methods of excitation,

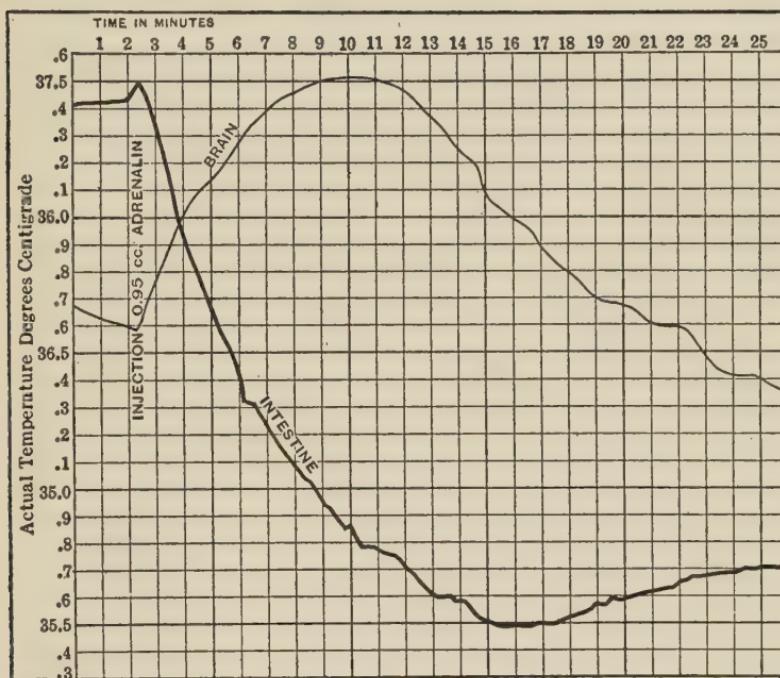


FIGURE 13. Effect of the injection of adrenalin upon the temperature of the brain and the intestines.

depression and death which we had employed during so many years in animal experimentation in the search for the identity of the energy in protoplasm which is temporarily increased in excitation, lowered in depression and finally lost in death. I saw soldiers who had been subjected to physical injury, to pain, to emotional excitation, to infection, to hunger, to thirst, to loss of sleep, to hemorrhage, to asphyxia, to the destruction of organs, to anesthetics, to cold, to shell concussion. The battle fields presented every grade and degree of injury—from the

slightest to death-producing injuries. Here the protoplasm of the soldier struggled against the protoplasm of the enemy. No investigator would dream of subjecting animals without anesthesia to a tithe of the injuries that were inflicted in battle upon each other by normal young men.³¹ (Fig. 14.)

Professor Marianesco of Bucharest joined my group in France for a time and during this period a significant discovery was made, namely, that when an oxidase stain is used, adrenalin causes a sharply defined area of increased staining in the cellular area of the brain. This stain affected only the cells of the gray matter and affected the white matter not at all. The significance of this will appear later.

During the war the most outstanding physiologists and biochemists of Great Britain, the United States, France, Italy, and other countries were engaged in intensive researches in their home universities, and many of them studied the problem of shock, exhaustion and restoration in the hospitals of France. Every opportunity was afforded to them in their search for the nature of the energy that operates the mechanism during the normal state and is depressed and lost in shock, exhaustion and death. The physiologists and the biochemists of the universities during the war and in the seventeen years following it were apparently as far from a solution of what caused the death of William Lyndman in 1887, and of millions of other young Lyndmans in the World War, as they were in 1914. It seemed, therefore, perfectly apparent that the physiological and biochemical method of attack had failed to solve this crucial problem, and that physiological and biochemical methods of approach were inadequate as a mode of attack. Classical physiology had failed.

During the vast experience of the war, a fundamental fact was disclosed, namely, that while blood transfusion was the most effective immediate treatment of shock known, its effect gradually diminished and shock deepened into prostration and unconsciousness. In other words, in an advanced state of shock the wounded soldier could be filled with blood and saturated with atmospheric oxygen, yet his oxidation failed. This is but another way of saying that when a certain depth of shock is reached, atmospheric oxygen is not ionized. The inference is

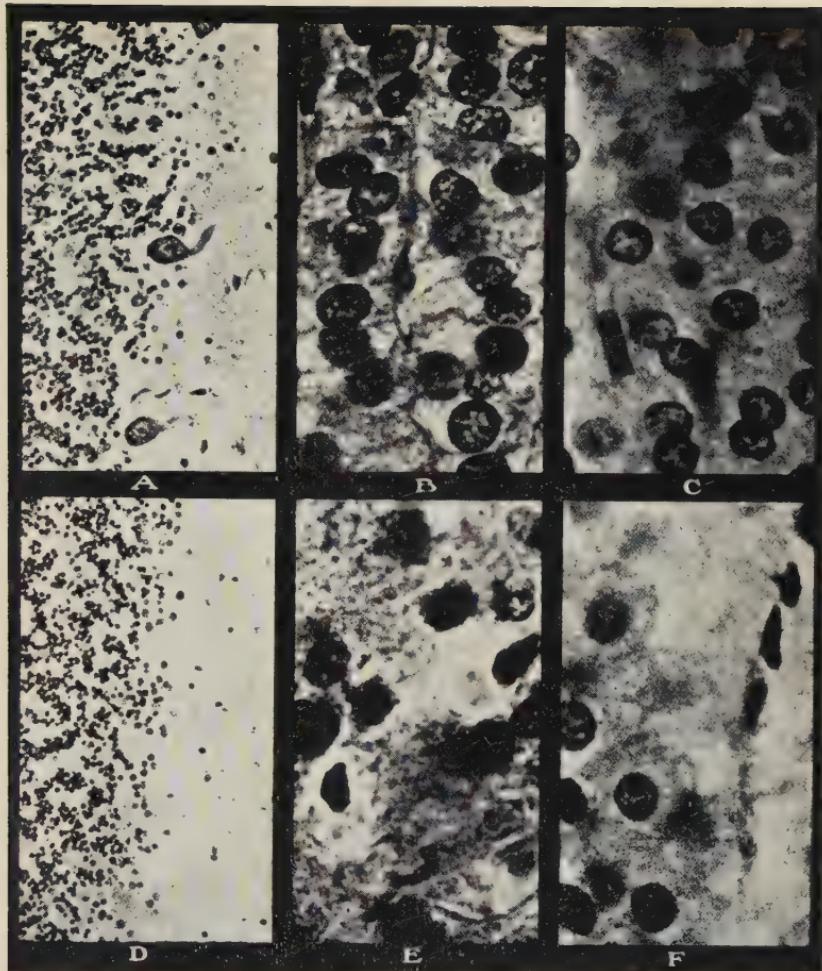


FIGURE 14. The effect of extreme exhaustion due to insomnia, exertion, emotion and infection on the brain, adrenals and liver of a soldier. This soldier was admitted to the American Ambulance after the retreat from Mons. His wound and the consequent infection would not have caused death in the absence of the other factors leading to his intense exhaustion. A, B, C, Sections from a normal human brain, adrenal and liver. D, E, F, Sections from the brain, adrenal and liver of the soldier described above. (A and D from photomicrographs X 310; B, C, E, and F, from photomicrographs X 1640)

that when oxygen is not ionized there is such an impairment of the normal mechanism within protoplasm as to produce exhaustion and shock.

Thus the whole clinical problem of shock—its cause, its treatment, its prevention, was put to a test on a vast scale during the war.^{32, 33, 34} While the war established the correctness of our position regarding the cause, treatment, and prevention of shock, as applied to the patient, it did not end the controversy as to the mechanism by which shock is produced.³⁵

The unparalleled opportunities presented by the World War eliminated large numbers of misconceptions, erroneous hypotheses and theories, and focussed the problems of the nature of protoplasm in the domain of biophysics, namely, the realm of radiation and electricity. It was a matter of the greatest importance that this phase of the nature of protoplasm was studied so intensively in laboratories and on the battle fields by the most outstanding and brilliant research workers in physiology, in biology, and in biochemistry. Classical physiology, classical biochemistry, classical biology lacked the text, not the personnel. It was the limitation of classical knowledge, not the limitation of brilliant scientists, that failed to find the mechanism that generates and operates protoplasm and is lost in depression and death.

In our researches, therefore, we turned to physics as applied to radiation and electricity for further investigation.

In the war our principle of nerve blocking as a means of preventing shock was settled beyond a question by the use of spinal anesthesia for amputations of the leg or the thigh. Even hip joint amputations under spinal anesthesia were wholly free from shock.

In the war our experimental and clinical point of view as to the value of nitrous oxide anesthesia in the prevention of shock in the course of surgical operations was also definitely settled. Nitrous oxide anesthesia alone almost as specifically prevented surgical shock as did spinal anesthesia, whereas ether and chloroform prevented pain but did not prevent the production of shock. The significance of this fact will appear later.

Since neither the inhalation of pure nitrogen nor of pure oxygen causes anesthesia, we drew the inference that the nitrogen in

the nitrous oxide molecule was not the same as the nitrogen that is free in the air. The nitrogen that is free in the air is at a low energy level. The nitrogen in nitrous oxide is at a high energy level. Therefore, we concluded that it was the nitrogen with the high level of energy that had the chemical affinity required for its substitution for an oxygen atom, thus breaking the bonds of the living molecule. These bonds being broken, the living molecule then was immune against the excitation of physical injury. Its energy could not be expended by the effects of the physical injury of an individual under nitrous oxide anesthesia, and therefore, under nitrous oxide anesthesia, no amount of injury to the tissue could cause surgical shock.

The reason why we thought nitrogen at a high energy level displaced oxygen, which was acting as a bond holding together important fractions of the living molecule, was because when oxygen is supplied to the blood and tissues in normal concentration, the anesthetic effect of nitrous oxide is accordingly diminished or lost. Pure nitrous oxide alone quickly suspends the activity of protoplasm and kills the organism. It is the play, back and forth, between ionized nitrogen and atmospheric oxygen that makes the difference between a normal state and the state of anesthesia.

In regard to the energy-nature of protoplasm, it was significant that before the close of the war, nerve blocking, blood transfusion, and nitrous oxide anesthesia were adopted by the Interallied Surgical Council as the most effective surgical methods for the prevention and the treatment of shock. It will be seen later how the rôle of local anesthesia, nitrous oxide and morphine, as preventives of shock, fits into the conception that radiant and electric energy are the forces that construct and operate protoplasm.

Two additional conclusive facts having a bearing upon our present problem were observed during our experience in the war.

(1) In patients in whom the protoplasmic energy was depressed, every organ and tissue showed a lowered resistance to infections of every kind. In a chemical sense, the protoplasm of the soldier was battling against the protoplasm of the bacteria, just as in a mechanical sense the protoplasm of the soldier was battling against the protoplasm of his human enemy.

(2) The war in its extreme activation of the emotions in the intense activities of battle, revealed a pathologic fury of the whole kinetic system, which means the brain, the sympathetic nervous system, the adrenal glands and the thyroid gland, in two special groups of soldiers, the soldiers in shell-shock, and the soldiers exhibiting intense nervousness, palpitation, tremors, sweating, excitability and exhaustion—the entire complex sometimes called “soldier’s heart,” and in civilian life designated as “neurocirculatory asthenia.”

When the energy that causes growth and function is clearly identified, then we shall be able to describe the exact mechanism of these battle injuries and modifications of protoplasm.

Our war experience in addition to adding to our former clinical observations and laboratory researches led us to the further development of the theory that the genesis and operation of protoplasm is dependent upon radiant and electric energy.

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CHAPTER 2. *THE THEORETICAL RÔLE OF ELECTRIC- ITY IN THE LIVING STATE*

ANY theory as to the nature of protoplasm must identify the primary factors in the genesis of protoplasm. It must account for the universal phenomena of living processes from the simplest to the most complex forms. It must identify the universal energy that constructs and operates protoplasm. It must identify a uniform pattern for the transformation and utilization of energy in protoplasm. It must account for the necessity for such ever-present characteristics as the acid-alkali balance, the semi-permeable membranes, the omnipresent electrolytes. It must show why continuous oxidation is necessary. It must show the mechanism of stimulation and of specific response to stimulation. It must identify the mechanism by which reason, imagination and memory operate. It must account for reproduction.

The central fact regarding living organisms is that they are transformers of energy and that they must be operated by means of one or more of the following five forms of energy: (1) heat energy, (2) mechanical energy, (3) chemical energy, (4) radiant energy, (5) electric energy.

It is obvious that the organism of a rabbit, for example, is not operated by heat or by mechanical energy alone. Since the atomic and molecular energy that characterize organic compounds is derived from radiant and electric energy, it follows that the probable organizing and driving force of living organisms is radiant and electrical energy, although chemical

energy plays a part. Therefore, plants and animals must meet the following requirements:

1. Differences of potential and the resultant electrical phenomena must be demonstrable throughout the organism as a whole and in its component parts—the cells.
2. The application of electricity to the muscles or glands, or to their nerve supply, must cause them to perform their natural functions.
3. The materials of which animals are constructed must be specifically adapted to radiant and electrical processes.
4. In structure and function the unit cells which drive the organism must be adapted to generate and to release radiation and electricity.
5. It must be possible to interpret the normal and the pathological phenomena of man and animals in terms of radiant and electric energy.
6. It must be possible to identify the mechanism by which oxidation generates radiation and electricity.

DEFINITION OF TERMS

Properly to understand the application of physical constants to the human mechanism it is necessary to have clearly in mind the electrical significance of certain physical terms such as potential, capacity and conductivity. In simplest terms, electric potential means the amount of electricity which is available for use or work in the part of a mechanism which is referred to. It is measured by taking some arbitrary point or part as a zero point and comparing the difference of potential between that arbitrary point and the part of the mechanism the potential of which is to be determined. It is necessary, of course, that these parts be in electric connection with each other. This potential difference is generally designated by the abbreviation P. D., which will be generally used throughout this volume. In commercial mechanisms the ground is generally selected as the arbitrary zero point. In our measurements of potentials in different parts of the living mechanism we usually selected the fascia immediately beneath the skin as the arbitrary zero point.

The ability of a tissue or of a chemical system to conduct an electric current from a point of higher to a point of lower potential is called its electric conductivity. The ability of a substance or of a chemical system to store electricity is called its electric capacity.

THE ELECTRICAL SIGNIFICANCE OF CERTAIN CONSTITUENTS OF THE ANIMAL ORGANISM

Water, which forms more than three-fourths of the body content, has the highest known dielectric constant. This property of water is responsible for the ionization of the infinite number of molecules which water holds in suspension or in solution. Water is one of the most important catalysts. Water possesses the highest specific heat.

Electrolytic solutions and colloids which make up the bulk of the body are especially adapted to electrical processes.

Hydrogen ions permeate all living organisms. The slightest change in the hydrogen-ion concentration fundamentally alters the organism. It is known that hydrogen ions are of high electrical significance.

Proteins hold active nitrogen in bonds from which it is released by electric forces thus producing the radiations which we postulate are the primary source of living energy.

Of high electric significance are the exquisitely thin, low-conducting *lipoid structures* which surround each of the trillions of cells which compose the body. It is a well known physical fact that an oil film has a high capacity for the accumulation of electric charges and that the thinner the film the higher its electric capacity. While the other essential constituents of the organism might play a rôle in an organism operated by some other form of energy, these lipoid structures are of the highest significance in an organism which is operated by electrical forces.

The animal organism as a whole is enmeshed in a network of highly specialized electric conductors—namely, the *nervous system*. In its physical composition, therefore, the body is not only highly adapted to electrical processes but its constituents in their inter-relations within the organism could not be of any

conceivable value in a mechanism operated by any other form of energy.

The mechanism by which oxidation within the protoplasm of the cell generates the electric charges that operate the cell and the organism we postulate is due to the short wave radiation generated and emitted by oxidation within protoplasm. According to this conception this short wave radiation knocks off electrons. These moving electrons charge up the intricate network of the nervous system as well as the infinitely thin membranes that separate the various units of structure and the network within the cells.

THE UNIT CELL AS A BIPOLAR MECHANISM

The unit of structure and of function of the living organism is the cell. Plants and animals are disperse systems of cell suspensions.

The nucleus of the cell is comparatively acid. The cytoplasm of the cell is comparatively alkaline. The nucleus and the cytoplasm are separated by a semi-permeable membrane.

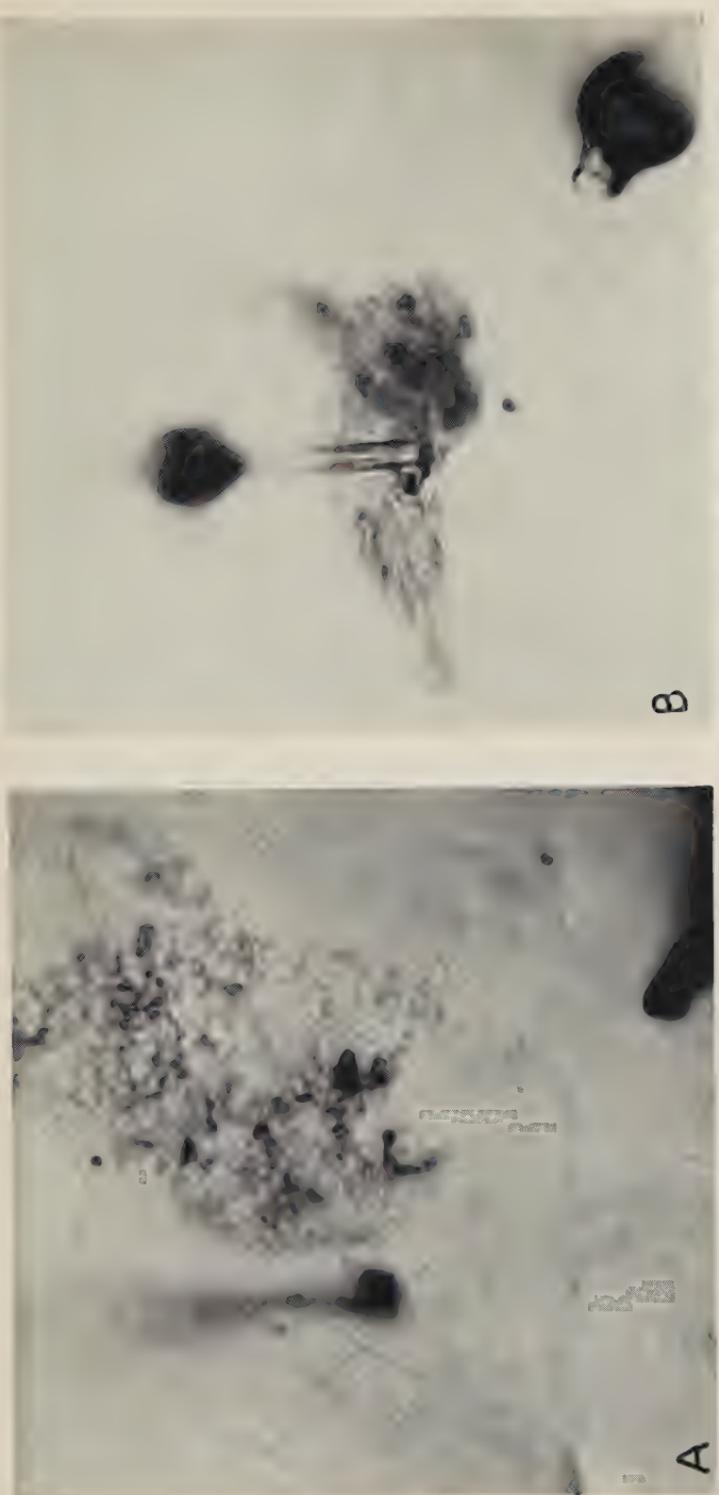
Therefore the cell is a bipolar mechanism or an electric battery, the nucleus being the positive element, the cytoplasm the negative element. The rate of oxidation in the nucleus is greater than the rate of oxidation in the cytoplasm; and therefore as the electric tension increases in the nucleus, the electricity passes through the nuclear membrane; the electric potential in the nucleus falls and in consequence the current is interrupted. Since the potential is again immediately restored by oxidation, radiation and other chemical activity, we conceive that an interrupted current passes continually from the positive nucleus to the negative cytoplasm and in consequence a charge is accumulated on the surface membranes. As we have stated, these membranes of infinite thinness and of high dielectric capacity are peculiarly adapted to the storage and adaptive discharge of electric energy.

There are two lines of evidence which indicate that the structure and function of cells are both dependent upon the maintenance of the normal electric potential.

The first line of evidence is the following: We have been able to measure the electric potential difference between an ameba and the medium in which it was suspended. One electrode was inserted into the body of the ameba and the other electrode was placed in the fluid in which the ameba was suspended. (Fig. 15.) This was done on a micromanipulator stage under direct observation through the microscope. A crucial test could thus be made with respect to the relation of the function and the structure of the ameba to the variations in its electric potential. Such changes in electric potential difference could be compared with the changes that had been noted in the organs and tissues of animals under the varying conditions described in the preceding chapter. In animals under these varying conditions we had noted a relationship between the electric conductivity, electric capacity, electric potential and the power of growth and function, but we were dependent upon mass measurements, not upon measurements of individual cells. Thus, in our studies of the giant ameba we were able to observe the phenomena in an individual cell.

Under exactly the same conditions as those in which control measurements were made, we found that the P. D. which was normally about 20 millivolts was depressed to zero by the introduction of a similar P. D. with an opposite sign of charge. This enabled us to observe astonishing changes which are probably analogous to the changes which occur in the protoplasm of organs during the processes of depression and death from any cause. The first changes noted were functional, that is, the ameboid movement was arrested; the ameba was then seen to become spherical in form and all movement ceased. Then followed a beautiful demonstration of the dependence of the structure of the ameba on its P. D. When the P. D. was reduced to zero, the outer membrane of the ameba ruptured at various places and through these rents we could see granules floating out into the surrounding fluid where they broke down. (Fig. 16.) Thus under direct observation the form and the structure of the giant ameba disintegrated. If the P. D. was increased by the introduction of an electric current when the granules began to float out before the rent in the membrane occurred, its form was reconstructed and the ameba again be-

FIGURE 15. The effect of an electric current on the structure of an ameba. A, Photomicrograph (X 400) showing one electrode in ameba and one in medium; B, Photomicrograph (X 400) showing effect of introduction of a current into the ameba with an opposite sign of charge to that between the ameba and the medium.



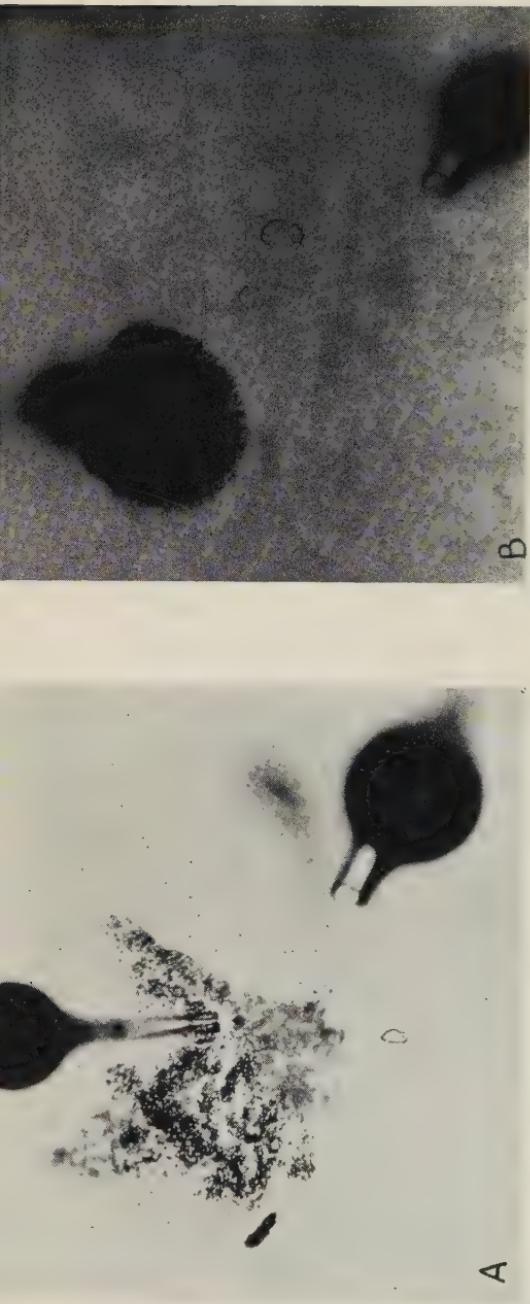


FIGURE 16. The effect of an electric current on the structure of an amoeba. A, Photomicrograph (X 400) showing disintegration of amoeba by application of a strong opposing current; B, Photomicrograph (X 400) taken just before rupture in membrane occurred; C, Photomicrograph (X 400) showing restoration of amoeba when application of destroying current was stopped.

(Note: Figures 15A, 15B, 16A, 16B, 16C, are all photomicrographs of the same amoeba, Figure 16A being the last one taken.)

came active, (Fig. 17) thus demonstrating that reconstruction of form and resumption of function are dependent upon the restoration of the potential difference.

The second line of evidence was supplied by a similar but

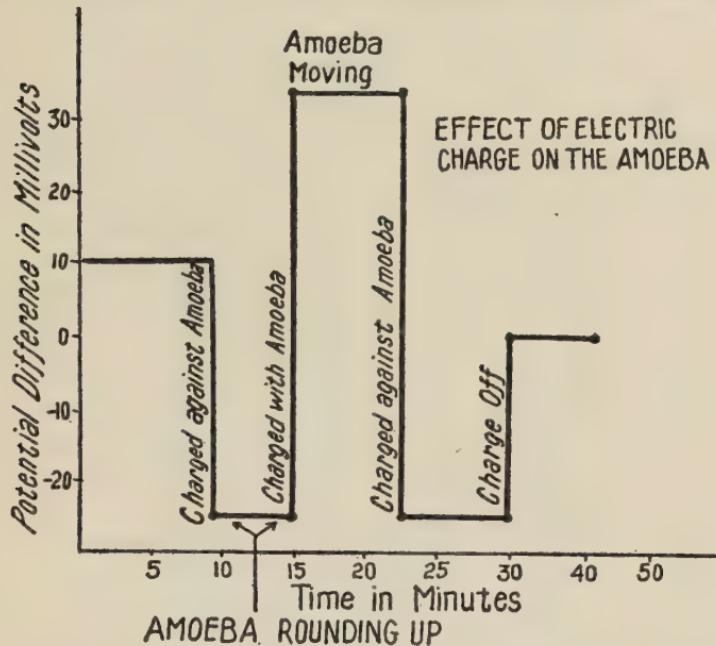


FIGURE 17. The effect of variations in the direction of the electric charge applied to an ameba.

even more interesting study of the autosynthetic cell which will be described later in the chapter.

By means of a micromanipulator,* Dr. Telkes was able to introduce one electrode into the nucleus of an autosynthetic cell and the other electrode into the cytoplasm and thus to measure directly the potential difference between the nucleus and the cytoplasm. Then by the same maneuvers as in the case of the giant ameba, the electric potential was depressed to zero or carried to the negative side, and as in the case of the ameba the cell was seen to disintegrate. It might be urged that

* A device whereby by means of fine needles, particles or organisms of microscopic size can be moved about on the stage of a microscope.

in one respect this observation lacks the validity of the observation of the changes in the giant ameba, since the protoplasm which constitutes the structure of the autosynthetic cell had been reassembled from the elements of pre-existing protoplasm.

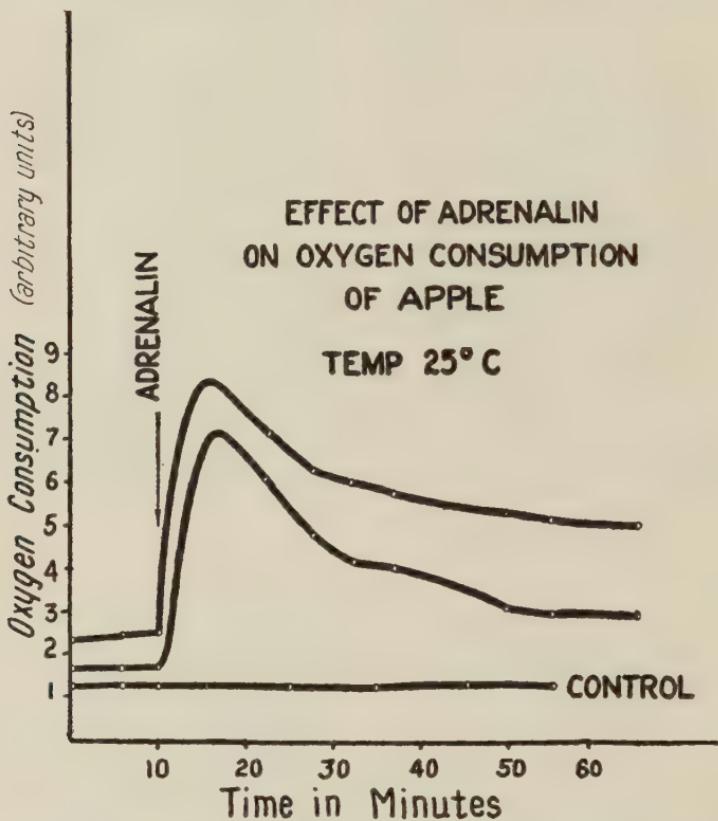


FIGURE 18. The effect of adrenalin upon the oxygen consumption of an apple.

It is, however, of great significance that these changes in the autosynthetic cell were observed.

Realizing the fundamental importance of the question as to whether the form and function of protoplasm is dependent upon electric strain, we carried our experiments into an analogous field presenting only slight technical difficulties but giving evidence that was gross and unmistakable. I refer to experiments

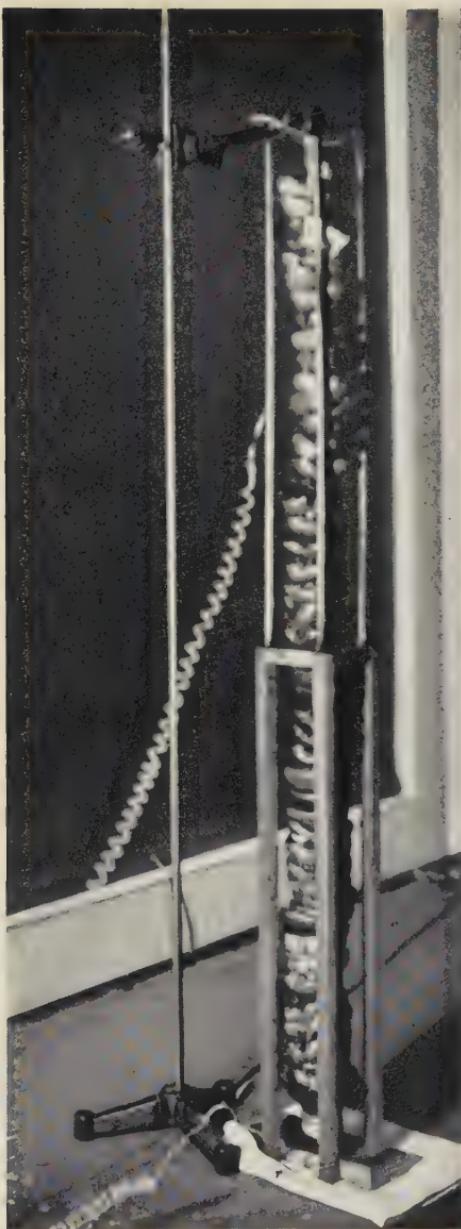


FIGURE. 19. Voltaic pile constructed of halves of apples.

with fruit and vegetables such as onions, potatoes, apples, etc. For convenience the apple was used in most of the experiments but in such studies as were repeated with other kinds of fruit and with vegetables, identical results were secured.

An apple may be compared to a single cell of simple structure. Though the skin of the apple is complex, it is an ideal membrane, serving not only the purposes of metabolism, such as the intake of oxygen and expiration of carbon dioxide, but also for the retention of fluids. The skin of the apple is apparently as effective as are the membranes of unicellular organisms or as the membranes of the cells which make up the protoplasm of an animal. In other words, the skin of the apple is an adaptive semi-permeable membrane.

Our metabolism observations showed that an average apple consumes from 1 to 3 cc. of oxygen an hour (Fig. 18) and gives off a corresponding amount of carbon dioxide. The average difference of potential across the limiting membrane or skin of an apple is from 60 to 80 millivolts. If the organic structure of the apple, like that of the ameba, the autosynthetic cell and animal cells, is dependent upon a given electric potential, then if the electric potential of the apple be reduced to zero, the apple will be unable to consume oxygen and give off carbon dioxide; in other words, the apple will be dead and will disintegrate. This was demonstrated by our experiments.

The electric properties of the apple were strikingly demonstrated when by piling halves of apples upon each other, a voltaic pile was constructed which had a potential of approximately one volt, sufficient to light a tiny electric bulb. (Figs. 19, 20.)

The electric potential of an apple is clearly dependent upon oxidation. This was demonstrated by the following experiment. When oxygen was excluded from an apple, the potential of the apple fell to zero and the apple disintegrated. When the apple was cooled, the consumption of oxygen was diminished and the potential fell. When the temperature of the apple was raised, the rate of oxidation of the apple was increased and the electric potential was increased. When ether or chloroform was injected into the apple its potential was reduced to zero, respiration ceased and the apple slowly disintegrated. (Fig. 21.)

Now an apple is a unit of the organic world. An apple obeys

the same laws as do the cells and organs of other organic forms. Therefore in the apple we have a simple example of the interrelation of oxidation and electric potential, that is, the dependence

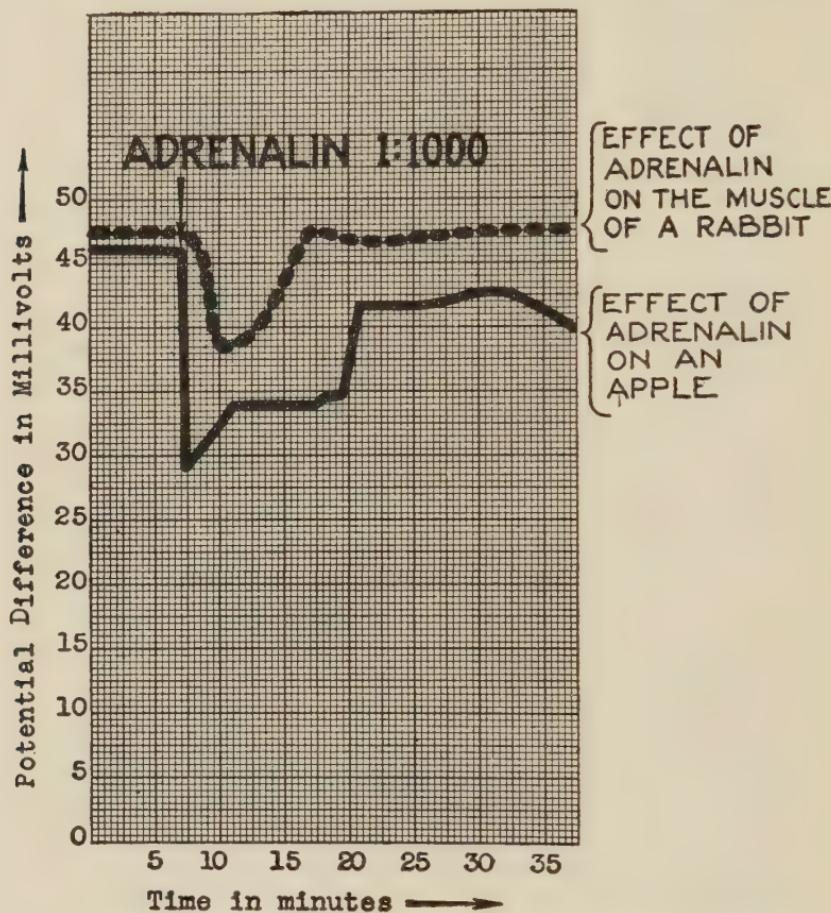


FIGURE 20. Comparison of the effects of adrenalin on the electric potential of a rabbit's muscle and of an apple.

of oxidation upon electric potential, and the dependence of electric potential upon oxidation, and also of the complete dependence of the organic structure upon the presence of electric potential and oxidation.

From these experiments upon the giant ameba, upon the autosynthetic cell and upon fruit, vegetables, etc., together with

our previous findings in studies of the differential stainability^{1, 2, 3} and the electric conductivity,⁴ potential^{5, 6, 7} and capacity^{8, 9} of tissues of animals it appears that all protoplasm

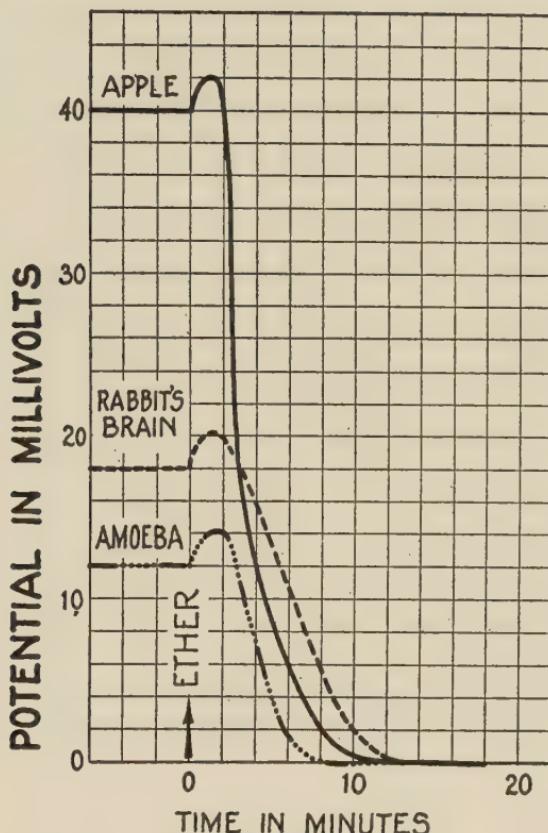


FIGURE 21. Comparison of the effects of ether upon the electric potential of a rabbit's brain, an apple and an ameba.

(Note that in each the charge is finally reduced to zero—that is, the apple, the rabbit, the ameba died.)

depends for its survival and function upon the maintenance of a potential difference in its cells and in its entire mass.

It was this long series of studies, in which the loss of differential stainability between the nucleus and cytoplasm foretold both the loss of function and impending dissolution of the brain and liver cells in particular, which gave us the clue to the

fundamental rôle of electric potential differences in the organization and function of protoplasm.

When the differential stainability between the nucleus and the cytoplasm was lost the difference in electric potential between the nucleus and the cytoplasm was lost also. Differential stainability depends upon the fact that the nucleus is relatively acid and the cytoplasm is relatively alkaline, thus indicating again that the nucleus and the cytoplasm bear opposite signs of charge.

We then devised an experiment in which we put to a supreme test the conception that electric energy can assemble and operate protoplasm. We took a mass of the most active organ of the body, viz., the brain, and separated it into an ether-soluble fraction containing the lipoid, and into a fraction soluble in dilute salt solution, containing the protein. For convenience we shall hereafter refer to these respectively as the lipoid and the protein fractions. The lipoid fraction bears a negative, the protein fraction a positive sign of charge. We argued that since the lipoid and protein fractions had opposite signs of charge, when mixed they would unite like the ovum and the sperm, which also have opposite signs of charge. Our anticipations were realized and forms which we called autosynthetic cells were immediately produced.¹⁰ This finding added validity to the fact established by our previous researches that electric energy plays a fundamental rôle in the organization, growth and function of protoplasm.

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CHAPTER 3. *OXIDATION*

OXIDATION is the most universal chemical reaction in nature. Oxidation is so predominant, so universal, that lungs are evolved by all higher animals to obtain the needed supply of oxygen. If food is withheld, life goes on for days; if oxygen is excluded for a few minutes, life ends. So critical is the oxygen necessity that an anaerobic supply * is provided. So basic is oxidation that its intake and output are used as a measure of the rate of metabolism.

What is oxidized? Is it sugar? Is it glycogen? Is it a higher hydrocarbon, a fat, a lipoid? Is it an alcohol? It is generally held that the adaptive energy of the organism is obtained exclusively from the oxidation of one or more of these carbon compounds, and disregarding the energy of the nitrogen compounds, the following question arises: At what point in the cell and in what manner is the carbon compound oxidized?

We know that the oxidation must be initiated and controlled by electric energy, for electric stimulation initiates and controls oxidation. A nerve current may be regarded as an electric current. But a nerve current—an electric current—causes no oxidation of any carbon compound outside the organism. It may be argued, however, that at the point of impact, the nerve current may be converted into heat of sufficient intensity to cause oxidation of the carbon compound.

Let us suppose that there is a carbon compound, say on the surface of the membrane of a cell, which, when subjected to stimulation at the point of nerve, hence of heat impact, would cause a change in the rate of oxidation, and that this change in

* A supply of oxygen derived from other sources than air.

the rate of oxidation would cause a change in function. What would prevent uncontrolled spreading of the oxidation?

If an electric charge is required to alter the rate of oxidation, then the continuous oxidation in unicellular as well as in higher organisms must be caused by electric strain, and this strain must be within the cell. Why does not this strain cause the burning of all the carbon compounds in the cell? Why doesn't the cell die?

How can the sun's rays falling on the retina cause oxidation of a carbon compound when there is no such delicately poised compound in the non-living compounds of carbon? If there is any such delicately poised carbon compound, it is as yet unknown.

That oxidation is the final and only process in the burning of a tallow candle, in a combustion engine, in the burning of coal and wood, is clear, and it may be said that the oxidation within the cells of the organism is analogous to oxidation within the cylinders of the internal combustion engine, since in such a mechanism the vaporized gasoline is ignited by an electric spark. This spark, however, does not take part in ordinary oxidation but indicates that oxidation is used in the process. It is an explosion that occurs. Because oxygen is consumed in the living processes in animals, it does not follow that molecular oxidation in the ordinary sense occurs at all. For example, it is now clear that the consumption of oxygen as the result of a muscle contraction does not occur in the actual contraction itself, but rather in the process of building up the compound that furnishes the energy that executes the contraction.

The spread, the finesse, the speed of the simple oxidation of carbon compounds is clearly not adequate to explain many processes. Simple oxidation of carbon compounds is too crude a tool to account for the infinitely delicate processes of the special senses, the mind, etc. These considerations led us to examine more closely the fundamental phenomena of metabolism.

Metabolism is universally accompanied by the production of carbon dioxide and water. Recent investigations indicate that the nitrogen metabolism is as constant as the carbon metabolism in organic processes.

In this connection, it is interesting to note a recent observation by Meyerhof that "in certain types of biological systems

which utilize molecular oxygen as oxidant in the respiration process, nitric oxide can be used in place of oxygen, being reduced to nitrous oxide during the process."^{1, 2} If the production of carbon dioxide and water corresponds exactly to the amount of oxygen inhaled, what is the simultaneous origin of ammonia in the blood and in the urine?

On the basis that carbohydrates are the sole source of adaptive energy transformation, the total calories are incompletely accounted for. For instance, in the items making up the total number of calories produced in the anaerobic contraction of muscle only "170 are due to the splitting up of glycogen into diluted lactic acid. There remain 210 calories of which 140 can be explained by the ionization of protein. Only 70 calories remain unexplained. I suggest that this too may be traced to the dissociation of protein."³ This fact would seem to be open to the following interpretation, namely, that the 210 calories accounted for by the dissociation of the nitrogen compounds are as essential and as adaptive as the calories obtained from the carbon compounds. With the exception of enzymic activity, glucose, in solution, is oxidized outside of the living with great difficulty. The process of the oxidation of glucose would appear to be too rigid to execute the infinite variations in the energy activities of animals, such as the creation of thought, the perception of color, the expression of an emotion, the rush of a lion, the execution of a convulsion, the "all-or-none" law of muscular contraction, overwhelming excitation, depression and death on the injection of an excessive dose of adrenalin, the speed of the wings of an insect, the exquisite sensitiveness of the entire organism in exophthalmic goiter.

Oxidation of glycogen could scarcely explain the rôle of the end organs of the special senses; it could scarcely explain the rôle of the end plates of muscles and of the synaptic junction.

Let us now consider the inner structure of the most highly evolved energy-transforming unit, namely, a Purkinje cell. The mechanism within the Purkinje cell for the utilization of oxygen has been described by Sir Frederick Mott as follows: ^{3, 4}

"The Nissl granules of basophile substance do not exist in the living cell. Nevertheless, the amount of this basophile staining substance

in the form of Nissl granules may be regarded as evidence of the amount of energy substance (neuropotential) which the cells possessed during life. In the healthy cell it is continually undergoing disintegration and automatic reintegration. . . . If the living cell be examined by direct illumination, no Nissl bodies are seen in the cytoplasm, only fine dark granules like an emulsion. If living cells are examined microscopically with dark-ground illumination, they are seen to be filled with small granules or globules, each of which after escaping from the cell remains discrete. They are refractile and appear white and luminous; this is due to a delicate covering film of a lipoid (fatty) substance which encloses a colloidal fluid, probably consisting of a solution of salts and cell globulins. When the cell dies this colloidal fluid is coagulated and the precipitated protein substance is massed together into little blocks—the Nissl granules; the intervening denser colloidal substance is continuous with the colloidal substance of the axon and dendron. The film that covers each granule is stainable by vital methylene blue, and a living nerve cell stained by vital blue presents the appearance of an emulsion of minute faintly blue globules. If the living cell thus stained be kept in an atmosphere of nitrogen in a warm chamber, the stored oxygen is used up and a leuco-base is formed, causing the globules to lose their color, and the cells appearing of a greenish tint. On admission of oxygen the cell again becomes blue. *It thus appears possible that these granules represent a large oxygen surface, like spongy platinum, within the cell.* When the cells die, the lipoidal film of the globulin-containing fluid is destroyed, coagulation occurs, and the Nissl granules are formed.

"The delicate granules filling the nerve-cells have been termed 'neuro-bions,' as if they were independent living units, but this is theory."

Sir Frederick Mott clearly recognizes that there are discrete points or ultramicroscopic units within protoplasm in which oxidation takes place. That is to say, oxidation does not take place within the mass of the cell but within definitive units. We assume that these units can be considered to be the furnaces which supply the energy of the organism.

How could one suppose the clumsy oxidation of a carbon compound to be the precise method used for the production of such manifold phenomena as those exhibited in the processes of metabolism? How would that account for the infinite delicacy of response to stimulation? How could that account for the

production of ammonia? Why does not oxygenated Ringer's solution with glucose satisfy the brain? It is clear that oxidation of carbohydrates does not offer a complete explanation of vital phenomena.

The foregoing considerations suggest, therefore, that instead of carbohydrates being the final and only source of animal energy, it is the disruption and anaerobic oxidation of the combined nitrogen and carbon fractions that is the principal final source of animal energy.

We shall next consider the source of the sensitive, high tension nitrogen fraction which forms the base of protoplasm.

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CHAPTER 4. *THE RÔLE OF LIGHTNING, BRUSH ELECTRIC EFFECTS, AND THE NITRIFYING BACTERIA IN THE GENESIS AND ACTIV- ITY OF PROTOPLASM*

THE elements from the air, oxygen and nitrogen, whose compounds are essential alike to plant and animal protoplasm, and carbon dioxide and water, which make up the carbon compounds, carry within the atoms that form their structure the greatest part of the energy of protoplasm.

It is significant that the element nitrogen is one of the most difficult to force into chemical combination. The high degree of negativity or refractoriness of nitrogen is due to the firm union that exists in the nitrogen atoms which are bound together in pairs. In nature only lightning, the brush effects of the terrestrial electricity and nitrifying bacteria can force the atoms in the nitrogen molecule apart so that they are free to combine with oxygen to form the nitro group, NO_2 . The vast scale on which the rending asunder of the nitrogen occurs in nature is indicated by the statement of Ernst and Sherman of the Fixed Nitrogen Research Laboratory in Washington that one hundred million tons of nitrogen are fixed annually by lightning and carried to the earth's soil by the precipitation of rain, snow and hail.¹

The high voltage arc has the same effect on the nitrogen atoms as has lightning. The temperature of the lightning is not precisely known. It has, however, been estimated that the

voltage of a lightning discharge 1,000 feet long is about 100,000,000 volts. We therefore have basis for the assumption that the temperature generated by lightning would far exceed that of the outer surface of the sun which is about 6,000° C. It may even exceed the highest temperature which has been measured, that of the stellar surfaces, which lie between 12,000° and 13,000° C.

The fixation of nitrogen by lightning puts into the atom of nitrogen more energy than is put into the carbon atom by the sun's radiance. Therefore, the oxidation of a nitrogen compound will emit a shorter wave than the oxidation of a carbon compound. We assume that it is the intense energy emitted by the nitrogen atom in the process of oxidation that vigorously detonates the adjacent nitrogen and carbon compounds, so that it comes to pass that the carbon compounds are burned in the intense "flame" of the nitrogen fire. Nitrogen atoms can also be endowed with chemical affinities in the dark and on a larger scale than by lightning. I refer to the action of the nitrogen-fixing bacteria which are found everywhere in the soil. According to preliminary experiments, it appears that the nitrifying bacteria emit ultraviolet radiation which is essential in making the inert nitrogen chemically active. Other facts support this assumption, namely, that in nitro-explosives the wavelength of emission—hence the energy of emission—depends on mass explosion. The larger the mass exploded, the shorter the wavelength, because the combustion, in unison, of vast numbers of nitro-compounds have additive effects, hence step up the energy, hence shorten the wavelength.

Since the most intense energy to which the air and earth are subjected is lightning, the temperature of which has been estimated to be perhaps as high as 25,000 degrees, much higher than the temperature of the sun, it would follow that the "lightning compounds" would emit a shorter wave radiance than the "solar compounds." We assume that the nitrogen group, by virtue of this fact, would become the fulminate, i. e., the controller of the oxidation of the carbon group; and that it is this dual property of the nitrogen and the carbon compounds linked together to form proteins that endows the proteins with the two properties of sensibility of release and speed of release.

In accordance with this assumption the nitrogen fraction of the protein molecule would be the sensitive, high-tension factor, or fulminate. The carbon fraction in the protein molecule would be the low-tension fraction. The carbon fraction constitutes the larger percentage of the protein molecule. The sequence of events, then, in the formation of the nitro-base of protoplasm and of nitro-explosives would be as follows: Lightning tears asunder on a vast scale the pairs of nitrogen atoms. These nitrogen atoms when thus torn asunder possess so high a degree of chemical affinity that they combine with oxygen to form the unstable oxides of nitrogen, particularly the nitro group (NO_2) which has a high energy content.

This unstable unit, NO_2 , when in contact with oxygen forms the unstable oxides of nitrogen which in contact with water form HNO_3 or nitric acid. When nitric acid falls to the ground in the rain it comes in contact with potassium compounds of the soil and forms KNO_3 (potassium nitrate).

Potassium nitrate (KNO_3) is present in the protoplasm of plants. In the plant it becomes the base of protein just as potassium nitrate (KNO_3) is the base of the nitro-explosives. In both nitro-explosives and in protoplasm it is, however, the active nitrogen that is the important fraction. Its importance is due to its state of oxidation.

It was the nitro group, NO_2 —the oxide of nitrogen, that caused the deaths in the Cleveland Clinic disaster in 1929. It was that event that led me into this field of research. Nitrogen peroxide (NO_2) was the brown gas that filled the building after the spontaneous incomplete combustion of the nitrocellulose films. Just as in the case of protoplasm, the nitrogen compounds in those films were originally built up by lightning, and just as in the case of protoplasm, the cellulose of those films was originally built up by solar radiance.

Owing to the difficulty in breaking this nitrogen linkage, specialists in the chemistry of explosives no longer write the formula for potassium nitrate as KNO_3 , but as $\text{KO}(\text{NO}_2)$, thus preserving in the formula the linkage which it is so difficult to tear asunder.

We assume that the nitro group confers unique properties upon the nitro-explosives and likewise on protoplasm. This

may well be of fundamental significance in the behavior of animals.

We have already stated that the greater amount of energy in protoplasm as well as in nitro-explosives is carried by the carbon compounds, but the carbon compounds have an outstanding characteristic which makes them incapable in themselves of functioning as an explosive. This characteristic is chemical stability, such as is exhibited in such carbon compounds as wood, coal and oil.

It is the chance fact of the physical properties of solar radiance, on the one hand, and of carbon dioxide and water, on the other hand, that is responsible for the genesis of the organic carbon compounds such as starch, oils, fats, coal, wood, etc.

It is the sun's radiance that builds up the carbon molecules, and not the nitrogen molecules. It is the lightning, brush electric effects, etc., that build up the nitrogen molecules and do not build up the carbon molecules.

The higher energy state of the nitrogen compounds and the lower energy state of the carbon compounds is the primary step in building the proteins and the lipoids in protoplasm, the primary step in building the nucleus and the cytoplasm, the primary step in setting up the acid-alkali balance, the primary step in generating a bipolar mechanism.

To be sure the carbon compounds are exploded in the combustion engine, but here explosion occurs under highly specialized conditions. There is no plant, no animal, no explosive that consists of carbon compounds alone. The carbon group, to be effective in protoplasm or in an explosive, must have the nitro group incorporated into it. We need be in no doubt as to the contrasting reactivity, sensitivity and speed of oxidation of the nitrogen and of the carbon compounds. We need only to compare nitrated compounds such as nitrocellulose, gun cotton, nitroglycerine and the chloride of nitrogen, which may be detonated by a beam of light or the touch of an oiled feather, with carbon compounds such as glucose, cellulose, coal or oil.

Where both power and sensitivity are desired, stable carbon compounds are chemically combined with the sensitive nitrogen compounds in such a way that an atom of nascent oxygen

lies chemically adjacent to every atom of carbon. This arrangement permits instantaneous detonation which furnishes maximum speed, maximum heat and maximum power over the shortest period of time. An analogous arrangement of nitrogen and carbon compounds would seem to be present in protoplasm.

NITRO-EXPLOSIVES AND PROTOPLASM—A PARALLEL

We have inferred that protoplasm and the nitro-explosives have certain characteristics in common. On the basis of this inference the parallel between them may be expressed briefly as follows:

1. Both protoplasm and nitro-explosives are constructed by the incorporation of a nitrogen group into a carbon compound.
2. Both protoplasm and nitro-explosives may be detonated.
3. Both protoplasm and nitro-explosives show a high speed oxidation.
4. Both protoplasm and nitro-explosives give off CO_2 and either free nitrogen or a nitrogen compound.
5. Both protoplasm and nitro-explosives produce short wave radiation.
6. Both protoplasm and nitro-explosives may be detonated by a beam of light, by a sound wave, by an electric charge.
7. Protoplasm like most nitro-explosives is in continuous chemical disintegration.

The maximum speed of protoplasmic disintegration is seen in the major emotions, in physical struggle, in convulsions, in the crises of hyperthyroidism, in the overwhelming explosive action provoked by the injection of adrenalin.

The activating bases of explosives are the nitrates. If exposed to the radiance of sunlight, nitric acid is in continuous disintegration. The carbon compounds such as glycerine and glucose are not disintegrated by sunlight, by an electric charge or by mechanical disturbance as are the nitrogen compounds. Glycerine by itself can be pounded, heated, given an electric shock, but glycerine can not explode. However, when an unstable nitrogen compound is incorporated into the stable glycerine by chemical manipulation, the resulting nitroglycerine

is exploded readily by radiant energy or by an electric shock. When a nitrogen compound and sulphur are incorporated into the stable charcoal, we have the unstable gunpowder. Cotton is not explosive, but when by chemical manipulation it is united with a nitrogen compound, the explosive nitrocellulose is formed. When the nitro group is added to phenol, an explosive coal tar product, picric acid, is formed; and when the nitro group is added to toluol, another coal product, the explosive, T N T, is formed.

These simple examples illustrate the contrast between the stable carbon compounds such as glycerine, charcoal, cotton fiber, glucose, and the unstable nitrogen compounds that are normally in chemical disintegration; they illustrate how, when the stable carbon compound has incorporated with it the unstable nitrogen compound, as in the nitro-explosives and in protoplasm, the energy of the whole becomes sensitively poised.

A carbon fraction and a nitrogen fraction are linked together to form protoplasm. A carbon fraction and a nitrogen fraction are linked together to form explosives. The broad inference is that the nitrogen fraction alone would be too unstable to form an animal, and that the carbon fraction alone is too stable to form an animal. In nature there is no known carbon animal, no known carbon plant, no known carbon bacterium. All animals, plants and bacteria, like nitro-explosives, are nitrogen and carbon compounds linked together. In nature, the element nitrogen and the element carbon are complementary to each other. They are in biologic union.

In nitro-explosives and in protoplasm the active nitrogen compounds confer upon the stable carbon compounds the property of sensitivity to radiant energy, to electric charges and to mechanical disturbances. These physical factors do not initiate the disintegration of the nitro-explosives or of protoplasm, but accelerate the normal continuous chemical disintegration, up to instantaneous oxidation or detonation.

Take for example a frog's muscle. The muscle consists of carbon compounds into which are incorporated nitrogen groups, just as in nitrocellulose, nitroglycerine and T N T nitrogen groups are in chemical combination with carbon compounds. When the muscle contracts it emits energy, carbon dioxide, a

nitrogen compound and water. When the nitro-explosive is detonated it emits energy, carbon dioxide, free nitrogen and water.

A common physical property possessed by nitro-explosives and by muscle is that each will either not respond at all or responds completely. Each obeys the "all-or-none law." A physical blow or an electric charge may "explode" a nitro-explosive or muscle. It is known that in a mass of nitro-explosives a definite wave of explosion passes over the mass. In the process of contraction, a wave of contraction passes over a muscle.

When a nitro-explosive is used in firearms or in industry, a still more sensitive explosive is added, viz., a primer or fulminate. The function of the primer or fulminate is that of initiating a swifter wave of disintegration throughout the main bulk of the nitro-explosive. Primers and fulminates are nitrogen compounds. These primers and fulminates are as much more sensitive to detonation than nitroglycerine, gunpowder, or nitrocellulose, as these nitro-explosives are more sensitive to detonation than charcoal, glycerine, or cotton fiber. The iodide of nitrogen, for instance, is so sensitive that it may be detonated by slight radiation, by an electric charge or by mechanical disturbance of the most delicate nature. The chloride of nitrogen is still more sensitive. It may be detonated by the sun's rays, by the closing of a distant door, by the lightest contact with the fringe of an oiled feather.

Thus we see that there are nitrogen compounds in the non-living state which are approximately as delicately poised as is the protoplasm of the brain which is detonated by the radiant energy of light in the process of seeing, or by the impact of air waves in the process of hearing.

One further and very important point is that if a given number of oxidations are executed over a considerable period, a certain amount of heat will be emitted, but if oxidation of the whole mass is instantaneous, the temperature will be far higher, which is another way of saying that oxidation by explosion generates a shorter wave radiation than oxidation by continuous burning. It would be of the greatest possible advantage in the struggle of animals for supremacy that radiation

of the shortest possible wavelength be produced, and this would be accomplished by the detonation of a nitro-explosive.

From such considerations as these, one may feel justified in thinking of protoplasm and of the nitro-explosives as analogous. In protoplasm, atoms are so accurately placed that when detonation occurs, there is emitted radiant energy, CO_2 , a nitrogen compound (ammonia, NH_3), and water. In nitro-explosives atoms are so accurately placed that when detonation occurs there is emitted radiant energy, CO_2 , free nitrogen and water.

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CHAPTER 5. THE RADIOPEN

RADIOPEN is the descriptive term which we have adopted to denote the theoretical units of protoplasm in which oxidation occurs and from which radiation is emitted. We believe that little or no oxidation takes place in the great mass of protoplasm outside of these infinitesimal units or radiogens.

Warburg¹ and many other observers have accumulated evidence that it is the element iron that is essential for oxidation in the protoplasm of animals. In the report of the Bureau of Chemistry and Soils for 1931, the following statement appears:²

"Investigations during the year have gone far toward determining the mechanism by which ammonia catalysts function. The indications are that the iron catalysts are particularly effective in ammonia synthesis because, as experiments during this last year have shown, nitrogen can react with active iron atoms on the surface of the catalysts to form a surface iron nitride. This nitride in turn is capable of reacting with hydrogen to produce ammonia and form again the catalytic iron."

We postulate, therefore, that the radiogen is a unique unit in which energy transformation takes place; that this unit is patterned after the solar system, (Fig. 22) or the atom; that the nucleus or sun of this infinitely small solar system is an atom of iron; that these atoms of iron, bearing a like sign of charge, repel each other as do metals in a colloidal suspension, and that by this radiogen, energy is continuously released and organic compounds are continuously built up. Thus in this cycle one could imagine that ultraviolet and other wavelengths are

emitted, but instead of their spreading freely, many are immediately absorbed in the neighboring atoms in the process of building them up into the higher compounds of the living state. In particular, this would account for the ionization of oxygen. Oxidation and reduction, exothermy and endothermy, would proceed in sequences of infinitely small fractions of time. The element iron, acting as a sun, would itself be in a highly excited

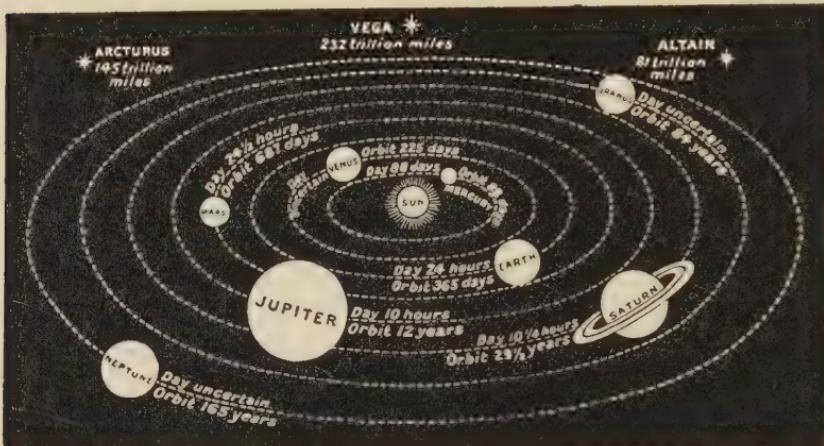


FIGURE 22. A diagram of the solar system. (From the *Outline of Science*, edited by J. A. Thomson, G. P. Putnam's Sons, New York, 1922, facing p. 11)

state, and since it does not enter into the combination of the organic molecules except in the case of growth, the iron nucleus would fulfill the definition of a catalyst, that is, an element that facilitates chemical activity but does not enter into it, itself.

This rôle of iron is supported by the work of various investigators. Thus Dr. E. S. Johnston, of the Division of Radiation and Organisms of the Smithsonian Institute, who "performed some experiments on the effect of natural and synthetic humic acids upon the growth of tomato plants," makes the following statement:

"More iron per unit of dry weight is required by Azotobacter than by tomato plants, but less dry weight is produced per unit volume of culture solution, so that the actual iron requirements per unit of cul-

ture solution are about the same. . . . In the experiments being reported upon, no appreciable growth took place unless 'iron' in some form were added."³

Wright makes the following statement:

"Cytochrome (Keilin) is the name given to a series of pigments which have been demonstrated by spectroscopic methods in many tissues. It has a very wide distribution in nature and is present in aerobic bacteria, in yeast, in plants, and in animals down to the worms. It is *absent* in *strictly anaerobic organisms*. Its distribution is related to the *activity of tissues*: Thus there is a high concentration in the wing muscles of insects (which can contract up to 300 times per second), but there is very little found in the thoracic muscles of wingless insects. . . . Cytochrome probably belongs to the haemochromagen group of compounds; like them it is believed to consist of an *iron-containing haematin* compound bound with *another nitrogenous body* of an unknown nature. The peculiar properties of cytochrome seem to be due largely to these unidentified nitrogenous bodies."

"The notable work of Warburg seems to demonstrate that an iron-containing pigment, related to haematin, but *other than cytochrome* is present in the tissues in minute concentrations and is an essential catalyst which is responsible for oxidation in the cells."

"The above experiments strongly support the suggestion that an iron-containing substance (atmungsferment) (respiratory enzyme of Warburg), probably resembling haematin, is of fundamental importance in tissue oxidation."⁴

The element iron, would be in continuous oscillation thus producing a temperature of not less than 5,000° C., just as the element iron in the sun is in continuous oscillation. The degree of this temperature is indicated by the genesis of ultraviolet, visible and infra-red radiation; in other words, a reradiation of the solar energy originally put into the organic molecule in the plant takes place within the radiogen.

In this connection the following statement is significant:

"During several chemical reactions an emission of light occurs although the temperature of the reacting mixture is far below the temperature required for the emission of visible light. We designate this phenomenon as chemical reaction luminescence (also called chemiluminescence). This cold light has been the subject of our in-

vestigations. It is correlated with fluorescence and luminescence more than was expected originally.

"There is no doubt that the energy of the reaction luminescence originates in the chemical energy of the reacting materials. Under ordinary conditions this energy appears as heat which develops during the chemical reaction. In the cases discussed here part of the energy appears as light which is not caused by the temperature but which originates in a more direct way. Since in almost all cases of reaction luminescence large chemical energies are released for changed or newly formed molecules and since therefore great dilutions of the reactive materials play an important rôle, it is to be expected that in spite of low temperatures (the average kinetic energy of the molecules in the total volume) the molecules of the reacting mixture nevertheless have high values of kinetic energy (molecular or intramolecular); that is, *the molecules partaking in the reaction show very high local molecular temperatures. The luminescence therefore may be ascribed to the local-molecular high temperatures.*"⁵ (Italics mine.)

From these theoretical considerations it would appear that the radiogen could no more become cool than could the sun become cool. The radiogen would be continuously transforming energy, or it would be cold and dead. Below the level of producing short wave or ionizing radiation the elements constituting this exceedingly hot furnace would coalesce and could never be reconstructed. Thus it is with protoplasm which can only be maintained by continuous detonations or combustion.

We postulate that there are infinite numbers of radiogens spaced equidistantly like metals in colloidal solution, and spaced like the electrons, the spacing of which has been compared to that of the stars. In regard to the inter-stellar and intra-solar-system spaces as compared with the spaces between the electrons, Jeans makes the following statement:

"Choose a point in space at random and the odds against its being occupied by a star are enormous. Even the solar system consists overwhelmingly of empty space; choose a spot inside the solar system at random and there are still immense odds against its being occupied by a planet or even a comet, meteorite or smaller body, and now we see that this emptiness extends also to the space of physics. Even inside the atom we choose a point at random, and the odds against there being anything there are immense; they are of the order of at least millions of millions to one."⁶

The chance of an x-ray collision with the proton or an electron in an atom is as improbable as would be the chance of hitting a planet or the sun by throwing a snowball through the solar system. The intense heat generated by the radiogens then would be as readily dissipated in the inter-radiogen spaces as the heat of the sun is dissipated in the interplanetary spaces.

It is the inconceivably small size of the protons, the electrons, the atoms, and the molecules that makes it impossible for our minds to appreciate it, and at best the idea can only be crudely represented by parables and analogies. Only the conception that the hot points or radiogens are infinitely small and the interspaces infinitely large in comparison can make acceptable the conception of a temperature as high as that of the sun itself in relatively cool protoplasm. The relatively free spaces between the atoms and molecules in protoplasm are relatively vast, and it is because our minds are not accustomed to think in terms of the infinite that it is difficult to grasp this fact.

Although the sun has an outer temperature of from 5,000 to 6,000 degrees centigrade, a temperature which we conceive to be less than that of the infinitely small points which we may call the "suns" or "radiogens" in protoplasm, neither the solar system as a whole nor protoplasm as a whole has a high temperature. The solar system and protoplasm alike have only a moderate temperature because of the vast relative spaces in the solar system and in protoplasm wherein is absorbed the radiation emitted from the points of high temperature. In other words, it would appear that the sun's radiance has set up infinitesimal "suns" in protoplasm which generate and emit radiation identical with the sun's direct radiance on plant cells. That is to say, the sun shines with undiminished radiance in the protoplasm of animals.

If one could look into protoplasm with an eye of sufficient magnification one might expect to see the radiogens spaced like the stars as miniature suns. We may say that protoplasm is a milky way consisting of "solar systems," each created in its own image by the sun's radiance. The nucleus or "sun" of our theoretic radiogen would theoretically, as stated above, be an atom of iron. We would suppose that these radiogens are the

exclusive mechanisms of energy transformation—exclusive centers of protoplasmic growth and activity.

The radiogens of plant and animal protoplasm can generate as much heat as can be generated by the absorption of short wave energy from lightning, from the high voltage arc, or from the sun's radiance itself.

From this point of view, it would appear that the radiogens perform the work that is usually attributed to enzymes and catalysts. Enzymes are defined as "certain substances—no doubt compounds of high molecular weight or mixtures of substances—which occur in the organic world and are able to accelerate in a pronounced manner a number of chemical reactions."⁷

Enzymes are credited with requiring no energy, but nevertheless with always contributing vast amounts of energy. As they are described, the enzymes and catalysts represent the entire mystery of living processes. Therefore they must produce their mythical effects by acting upon atoms, and we know that any alteration in atomic activity requires radiation of short wavelengths.

The activity of the enzymes is said to be increased in the springtime, when thyroxin or adrenalin is given, or as a result of stimulation, or as a result of a rise in temperature, while their activity is said to be decreased by anesthetics, narcotics, poisons, anemia, anoxemia, and asphyxia, a depression of the temperature. How can such alterations be expressed except in physical terms? Can such entities be anything else but purely physical agencies? In other words, an agency that can cause chemical combinations of high order, that can respond to temperature, to oxidation, to change in environment, to stimulants, to adrenalin, to thyroxin, to an anesthetic—such an agency must be a purely physical agency and all its requirements are met by radiation.

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CHAPTER 6. RADIATION

AS ALREADY stated in Chapter I, we made studies of long wave radiation, that is, studies of the heat changes in the brains and livers of warm-blooded animals and determined the variations under many conditions. We measured the temperature of the brains of animals in shock, during and after hemorrhage, under the influence of anesthetics and narcotics, after the excision of the thyroid and adrenal glands and of the liver, in depression and death from insomnia; and we found that these variations in temperature bore a direct relation to the structure and stainability of the cells and to the increase and decrease in the energy and function of the brain.

It was apparent that the variations in that form of radiant energy which we call heat followed closely the variations in electric conductivity, electric capacity and electric potential observed under like conditions, thus indicating the fundamental nature of these electric and radiant forces.

But it is not the long wave heat radiation but the short or ionizing wave radiation that has hitherto escaped detection as the energy that builds up protoplasm and generates the electric changes and currents that operate protoplasm.

The long wave or heat radiation affects molecules but does not affect atoms as far as the structure of the atom is concerned. To build an organic compound it is necessary to have such a powerful short wave radiation that it can affect or modify the structure of the atom by knocking off electrons or by changing their paths, thus altering the charge of the atom. When an electron is knocked from an atom, the balance of charge is shifted toward the positive side, thus making the atom more

positive and giving it a greater affinity for other atoms. In other words, short wave radiation gives chemical affinity to the atoms. Therefore to build such organic compounds as those which make up plants and animals, radiation of a certain short wavelength is essential.

Since the interior of an animal receives no radiance directly from the sun, an animal necessarily must use the sun's radiance that is stored in the atoms and molecules of the protoplasm of the plant. Just as in the non-living, for example in coal and oil, the stored radiance of the sun is present in the atoms of the carbon compounds and is released as light and heat which in turn effect mechanical activity, so in animals solar radiation is released from the atoms of the plant food and produces light and heat and animal activity. Einstein's Law of Equivalence should be cited here, viz., that the energy of an atom is given out in the same quanta as those received by the atom, so it is not a figure of speech but a fact that the sun shines again in the protoplasm of animals, endowing them with the unique power of the sun.

Is radiation merely a waste product or is this radiation an essential function of protoplasm? This question is answered in part, for the nitrifying bacteria at least, by the following quotation from a report of the U. S. Bureau of Chemistry and Soils:¹

"There are various ways of rendering the inert nitrogen molecule chemically active. Heat and electricity are effective when properly applied, and results obtained in this bureau have indicated that *ultra-violet light having very short wavelengths is an agency to this end*. . . . Spectroscopy has recently furnished detailed knowledge of the structure of the nitrogen molecule, and *it is now possible by means of ultraviolet light to alter the structure, so as to render this exceedingly inert substance chemically active.*" (Italics mine.)

Since the energy that constructs and operates animal protoplasm is derived directly from plant protoplasm and since the energy that constructs and operates plant protoplasm is derived directly from solar radiation, lightning, terrestrial electricity, and the nitrifying bacteria, what the animal specifically obtains in his food is the radiation or quanta of energy which

has been packed into the atoms of the plant protoplasm by sunlight, by lightning, by terrestrial electricity, and by the nitrifying bacteria.

Thus modern physics has given us a simple conception of the source of energy in animal protoplasm, since only short wave radiation can knock off electrons and hence confer chemical affinity of the high order demanded for synthesis and growth.

Short wave radiation accounts also for the origin of the electric charges and currents in protoplasm. The same short wave radiation which confers chemical affinity detaches electrons in infinite numbers, thereby charging up the innumerable membranes and nerve and electric circuits which are present everywhere in protoplasm. This is the origin of the electric charges by which protoplasm is operated. This is as simple as the operation of the photo-electric cell in which short wave radiance falls upon an electrode and detaches electrons, which in turn charge up the available circuits which operate robots. In protoplasm are present compounds whose electrons are detached with facility by ultraviolet, visible and short infra-red wave radiation. It would thus seem that protoplasm has the properties of a photo-electric cell.

Such a view would account for the universality of the electrical properties in protoplasm already described (Chapter 2). It would elucidate the only physiological fact that has stood the test of time in the science of physiology—the one fact that has never been successfully contested, namely, that electricity when properly applied to nerves, tissues and organs can stimulate them to perform the identical work performed by those nerves, tissues and organs in nature. Electricity outside of the living and electricity generated within the living organism are identical.

It is clear that radiation produces the electric current, which operates adaptively the organism as a whole, producing memory, reason, imagination, emotion, the special senses, secretions, muscular action, the response to infection, normal growth and the growth of benign tumors and of cancers, all of which are governed adaptively by the electric charges that are generated by the short wave or ionizing radiation in protoplasm.

Since the electric potential and the electric currents in proto-

plasm are produced by short wave or ionizing radiation, it follows that electric potential would serve as a method whereby to estimate the amount of short wave or ionizing radiation. Moreover, since the energy and activity of an animal is dependent upon the electric charge which is known to govern the activity of protoplasm, and since the electric charge itself is generated by short wave or ionizing radiation, it would follow that the activity of the animal would likewise be an estimate of the amount of short wave or ionizing radiation that the protoplasm of that animal generates.

It is apparent that there will be many limitations in the detection of the short wave ionizing radiation, for the very reason that it affects atoms and therefore is absorbed by them. It would seem as if a more correct measurement of the activity of protoplasm would be by measuring the entire spectrum of the protoplasm because, since most wavelengths are finally eliminated as heat, the long heat waves do not tell the whole story of organic activity. For example, consciousness would be associated with a certain percentage of short wave radiation. Yet the patient who is unconscious and exhibits a great loss in short wave radiation may emit an excess of long heat waves, that is to say, the patient may have a high temperature and yet be unconscious.

One would expect that when such organs as the liver and kidneys and brain are seriously degenerated, they would emit subnormal short wave radiation. On the other hand, a tissue that is growing rapidly is doing so by virtue of a corresponding abundance of the short wave radiations which are required to ionize atoms and to build the organic compounds by which growth is effected. Therefore, we would expect that the apex of a root or a bud or a fertilized ovum or a growing fetus or a hyperplastic thyroid or a cancer would exhibit correspondingly higher percentages of short wave radiation as well as increased electric conductivity, electric capacity and electric potential.

It has been stated by eminent scientists that the genesis of radiation—ultraviolet, visible and infra-red radiation—in protoplasm could have no biologic significance because such radiation is present everywhere in nature and is present in one form or another in chemical reactions. Regarding this point, one

could argue with equal logic that because everywhere in the world, oil and gasoline and wood are being burned, since oxidation and heat are common phenomena, serving any or no purpose, then in the case of organic oxidation, the combustion is a mere by-product and has no relation to the pull of the load. One might with equal logic say that the burning of the coal in the fire box and the by-product, steam, have no relation to the work of the locomotive, or that although an electric battery exhibits electricity, the electricity is a by-product because almost all matter exhibits electrical phenomena, and indeed is electrical in nature; or that because sunshine is everywhere and has always existed, or because water is everywhere, even where plants and animal life do not exist, sunshine and rainfall have no relation to the existence and growth of protoplasm.

The choice lies between accounting for the phenomena of protoplasm by the application of the laws of physics and chemistry, or accounting for these phenomena as being due to causes unknown.

On the basis of the foregoing considerations, one would expect to find that when an organ is so impaired by disease or injury that it can no longer perform its function, the loss of function must be due to a corresponding decrease of the short wave radiation. An interesting experiment indicates the validity of this assumption. When the organs of the body are oxidized by the method described in Chapter 26, visible light is produced, the radiations varying from the short infra-red to the ultraviolet. If the muscles, the kidneys, the liver, and the heart are performing their functions within the normal range, while the function of the brain is so depressed that the conscious state is lost, one would expect to find that the radiations generated by the oxidation of muscles, the liver, the kidneys, and heart would be within the normal range, while very little or no light would be produced by the oxidation of the brain. We found that this expectation was realized in the case of a human being who died after five days of unconsciousness, due to age and acute disease, while all of the other organs functioned normally.

This was probably the first instance in medical science and in medical practice in which the study of radiation has been applied to the interpretation of the mechanism by which an

organ fails to function, this failure of function in turn causing death.

In this case the inhalation of concentrated oxygen in an oxygen tent, repeated blood transfusions, the administration of the thyroid hormone and of adrenalin, did not enable the brain to reach the conscious state. We reached the conclusion that the radiogens within the protoplasm of the brain were oxidizing at so low a level that no ionizing short wave radiation was produced. In consequence, oxygen was not ionized, hence oxidation could not occur. The helpless, passive state of the muscles of the body showed that the electric potential of the brain had fallen to near the zero point, hence the muscles did not receive from the brain along the nerves the radio-electric action current which fires the nerve end-plates of the muscles—an essential factor in the maintenance of muscle tone and the performance of muscular action.

Our theoretical predictions as to the change in the wavelengths emitted by the brain in this case are supported by the science of radiation as applied to the human organism. These considerations point to the application of the science of radiation to the normal and to certain disease processes.

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CHAPTER 7. *AUTOSYNTHETIC CELLS*

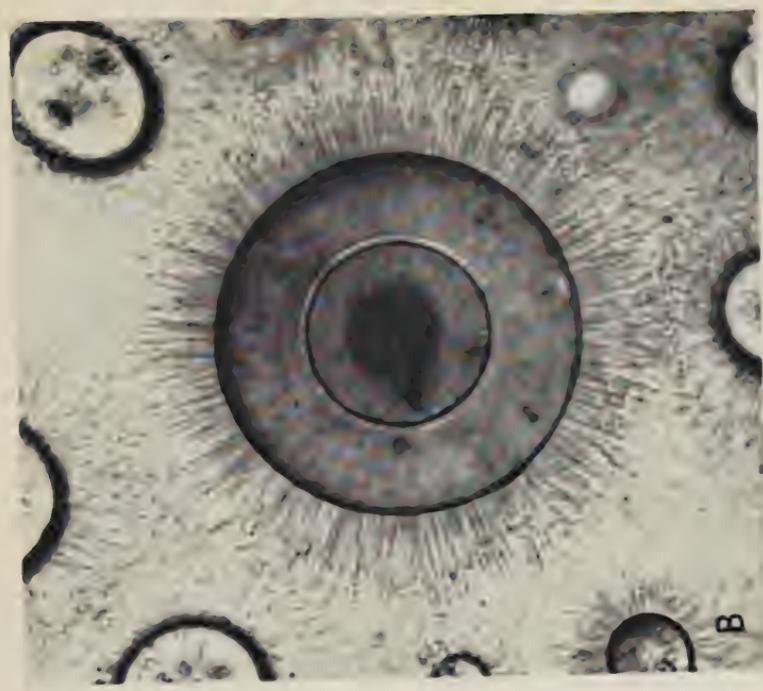
THE protein fraction separated from protoplasm bears a positive sign of charge, and the lipoid fraction, separated from protoplasm, bears a negative sign of charge.

According to Keller,¹ the ovum has a positive sign of charge and the spermatozoon has a negative sign of charge. The opposite signs of charge of the ovum and the spermatozoon supply a fundamental energy factor in effecting a union of the ovum and spermatozoon in fertilization. By analogy, we would expect that the opposite signs of charge of the protein and lipoid fractions of protoplasm would effect a union of these two fractions followed by organization and growth, analogous to that seen in fertilization.

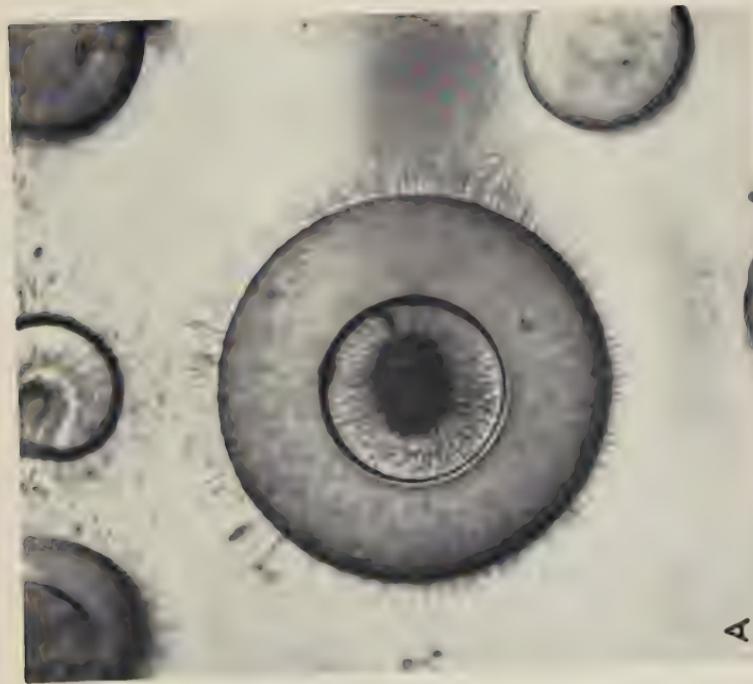
At this point, it is well to remember that the energy pattern of the protoplasm of the tissues and organs of the organism is initiated by the positive ovum and the negative spermatozoon in fertilization. Therefore, protoplasm is stamped with the pattern of positive protein and negative lipoid. Protoplasm, therefore, is a bipolar mechanism.

In the first period following fertilization, the energy of the newly formed organism is used solely for growth and cell division. At a certain time thereafter differentiation of the cells and organs for the performance of specific functions begins to appear. As energy is utilized increasingly in proportion to the development of these specific functions in the muscles, glands, nerve tissue, etc., growth is by so much diminished, until finally a balance is reached when there is no further growth and all the energy of the organism is expended in function and repair. This applies to normal tissue.

FIGURE 23. Autosynthetic cells.



B



A

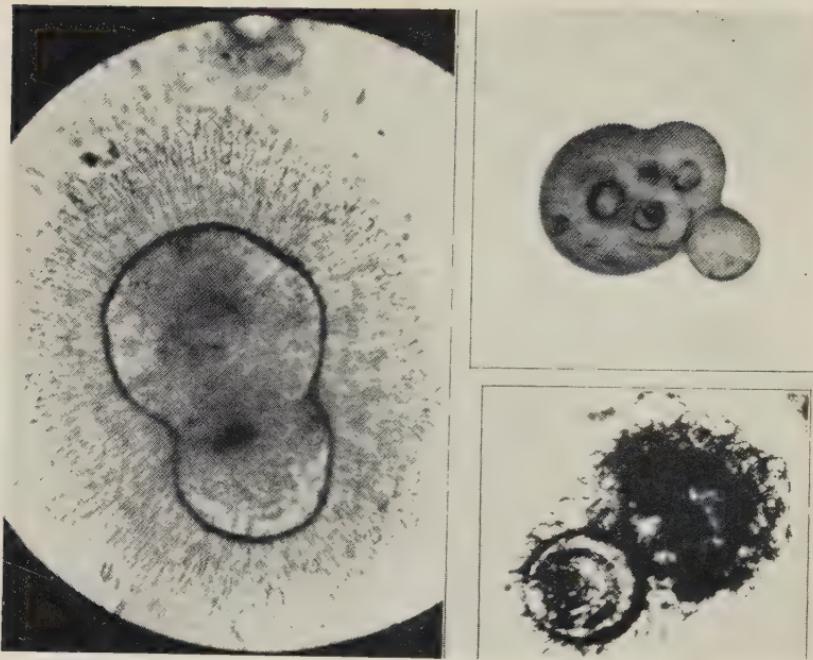


FIGURE 24. Autosynthetic cells in process of division.

Under certain abnormal conditions, however, certain cells exhibit a capacity solely for growth and exhibit no function. Such cells have the essential characteristics of cancer. It would seem as if cancer cells have been bereft of that mechanism which is present within normal cells, by the exercise of which their specific function is performed, as if the only mechanism left

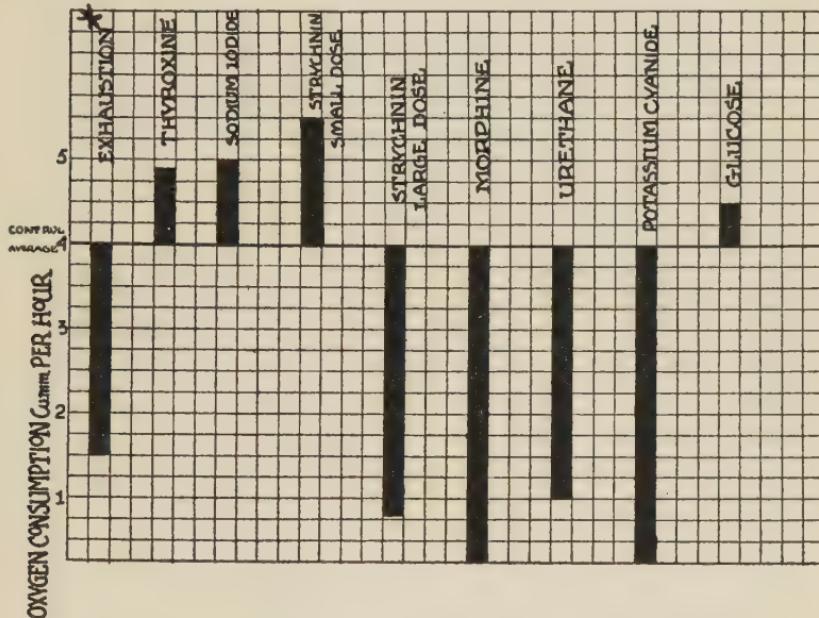


FIGURE 25. The effect of various agents on the oxygen consumption of autosynthetic cells. (The respiratory quotient of the auto-synthetic cells varied from 0.7 to 0.98)

is that which uses its energy for growth alone. To test this conception we endeavored first to discover the properties of the separate fractions of normal cells.

Since the brain is the most highly active and most highly differentiated tissue in the body, it occurred to us that if we should extract separately the lipoid fraction and the protein fraction from the brain and make a solution of the ash and should then mix these together, we would reproduce crudely the process of normal fertilization and might thus gain an insight into the genesis and growth of cancer.

We therefore separated the lipoid fraction, the protein fraction and the electrolytes from brain tissue and then united them again and thus formed models of cells which exhibited such phenomena of living cells as assimilation, respiration, growth and cell division. (Figs. 23, 24.) Upon these structures, which we called *autosynthetic cells*, anesthetics, narcotics, electrolytic solutions, iron, the thyroid hormone and adrenalin produced effects similar to the effects of these agents upon the ameba, man and other animals.² (Fig. 25.) Of particular significance was the finding that for a period of eight months cultures of these cells exhibited the phenomena listed above, provided the protein fraction extracted from the brain of the same species of animal as that from which the original extracts were secured, were added from time to time. (These experiments are described in detail in Chapter 27.)

That the autosynthetic cells could use only the protein fraction of the same species for the maintenance of their growth and physiologic activity would seem to be a significant fact. It would appear to be equally significant that the autosynthetic cells could not utilize lipoids, carbohydrates, blood serum, beef broth, agar, etc. From the consumption of the protein fraction not only were metabolism, growth and reproduction effected but ammonia, an end-product of nitrogenous metabolism, was elaborated.

The fact that proteins of the same species alone appear to maintain the cultures of autosynthetic cells for prolonged periods raises the following question: Is it possible that the apparent successive generations of cells represent merely the organization of the proteins into new cells?

Opposed to this are the following facts: First, the number of cells appeared to increase when counts were made at repeated intervals. Second, no new lipoid was added to the cultures, therefore, the cells must have elaborated the additional lipoid material required for the construction of the new cells out of the added protein material unless all the lipoid was not used in the primary reaction. Third, nuclear division and cell division occurred as shown in figure 24. From these observations it would seem probable that both growth and function of

normal tissue derive their energy and their structure principally or solely from the proteins.

The question, whether or not it is possible that the successive generations of autosynthetic cells represented merely the organization of the protein fraction into new cells, though apparently answered, requires more detailed observation.

The giving off of ammonia in a certain proportion to the giving off of CO_2 , is in agreement with the work of Emden³ and of Parnas,⁴ who demonstrated that in muscle contractions ammonia is given off. Tashiro⁵ demonstrated the production of ammonia by nerve fibers, during the passage of action currents.

If our assumption that reactions similar to these take place in the proteins and carbohydrates of our autosynthetic cells is correct, then there should be established a certain ratio between the carbon dioxide and ammonia output of the cells; and heat should be absorbed during the active synthesis of the cells.

These points were put to experimental test with the following results:

The respiratory quotient of the autosynthetic cells was found to range between 0.8 and 0.9; and it is interesting to note that this is the range of the respiratory quotient for bacteria (*B. coli*).

In an average of sixteen tests, the relation between the CO_2 output and the NH_3 production was as 33 to 1 which, within the limits of experimental error, agrees with the ratio found for bacteria (*B. coli*).

During the period of formation of the autosynthetic cells, that is, during the first 10 minutes after the mixture of the protein and lipoid solutions, heat was absorbed as demonstrated by a loss of temperature in the suspending solution—an absorption of 16 calories per 100 cc. After the period of formation of the cells there was a heat production of 46 calories for one hour.

In our study of the autosynthetic cells, as we have stated, we have had the unique opportunity of observing separately the characteristics of the protein or predominating nitrogen fraction and of the lipoid or predominating carbon fraction. We

know that alone neither the protein nor the carbon fraction can grow or multiply. We know that when united they behave, with respect to respiratory quotient and growth, like the ovum and sperm when united. We know that the maintenance of life, growth and reproduction depends on the consumption of protein. We infer, therefore, that the real intracellular "food" of animals consists of proteins which are built up from nitrogen and carbon compounds and which are probably synthesized or linked up in the cells into higher compounds by the powerful short wave radiation emitted by the radiogens.

In this and the preceding chapters we have introduced many lines of evidence that radiant and electric energy play just as basic a rôle in the operation of plants and animals as do radiant and electric energy in combustion engines and electric motors, which is to say that plant and animal life is constructed according to the law of physics.

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CHAPTER 8. *THE PHYSICAL CHARACTERISTICS OF LIVING ORGANISMS AND CELLS*

PHYSICS identifies an animal—its height and length, its mass, its weight, its specific gravity, its color, its temperature, its movements, the texture and appendages of its skin, the size, the color, the weight of every organ and tissue, and the dimensions of every cell that makes up the organs and tissues as revealed by the microscope.

The concentration of electrolytes in the fluids is measured by the physical constant, electric conductivity. The Nernst formula

$$(P. D. = \frac{0.058}{N} \log \frac{C_1}{C_2}) \text{ Volts. } C_1 = \text{more concentrated solution.}$$

$C_2 = \text{less concentrated solution. } N = \text{chemical valence.}$) expresses the potential difference between electrolytic concentrations on the opposite sides of semi-permeable membranes in living systems precisely as it expresses the potential differences in non-living systems. The Einstein mathematical formulae for the surface tension phenomena in living systems—a fundamental factor in living protoplasm—are identical with those for non-living systems.

The three physical constants, the electric conductivity, electric capacity, and electric potential of cells, of organs, and of organisms are a measure of their power of growth, of function, and of resistance to infection, etc. At death the electric potential is reduced to zero and the anatomical and the histological components of the animal are resolved into the simple elements of the earth and the air.

Not only do living cells exhibit physical characteristics in form and function but the action of the secretions of certain glands, notably of the thyroid gland and the adrenal glands, have certain physical characteristics. The thyroid secretion through its control of oxidation governs the electric conductivity, electric capacity, and electric potential of the tissues; that is, the thyroid gland governs the capacity of the organism for work. When the thyroid gland is removed, the value of these electric constants decreases, the electric potential finally reaching zero at death. Therefore, the function of the thyroid gland is the maintenance of the electric potential of the cells of the organism at adaptive levels.

When the electric potential is reduced to zero, the plant, the fruit, the ameba, the animal, disintegrates. The progressive weakness which results from unchecked hemorrhage, uncontrolled infections, overwhelming emotion, prolonged loss of sleep, surgical shock, is accompanied by a progressive decrease in electric conductivity, in electric capacity and in the electric potential, which is reduced to zero at death. Such anesthetics as chloroform, ether and nitrous oxide, and such narcotics as morphine, luminal, amyta, etc., depress the electric potential of tissues and organs.

In general, the physical well-being of the organism can be expressed in terms of electric potential.

In the majority of organs and tissues electric stimulation is the equivalent of biologic stimulation. Radiation is a fundamental example of a physical property in living organisms, as is strikingly illustrated by the luminescence of certain animals, plants and bacteria. Gurwitsch,¹ the Russian investigator, was not able to demonstrate radiation directly, but he and others have recorded radiation from cancer, blood and other biological tissues.

Evolution probably seized upon the factors that have the power of shifting the amount of radiation toward the short wave field, hence increasing the amount of electricity generated. Thus, an increase in the electrical charge-up increases the muscular and glandular activity of the animal. Our experiments have shown that thyroxin and adrenalin have the power of shifting the spectrum toward the short wave field, but the lat-

ter acts only for short periods. It would appear, therefore, that the energy characteristics of the various species of animals would be associated with this or that size of the thyroid gland and the adrenal-medulla-sympathetic complex. In other words, in a sense, given the relations between the size of the brain, the size of the thyroid, and the complexity of the adrenal-sympathetic system, with respect to each other and with respect to the body weight, one could write an equation for the energy characteristics of any animal. This fundamental conception was tested by a study of the comparative anatomy of many varieties of wild and of domestic animals, of anthropoids and of man by which this conception was definitely supported.

From the foregoing it is evident that the gross, the ultra-microscopic, the molecular, the atomic and the electron configuration of every living thing may be identified by physical constants. Every movement of ions across the countless billions of semi-permeable membranes, which governs the chemical activities of cells, is in accordance with the Nernst Law. The rôle of surface tension which fundamentally governs the action of cells is expressed by the mathematical equations of Einstein. The electric conductivity, electric capacity, and electric potential of the living organism which provide an accurate measurement of the activity of cells and organs are expressed by the same mathematical formulae as in non-living systems.

Through extra-terrestrial forces—viz., the sun's radiance, lightning, etc., carbon dioxide, water, and active nitrogen groups are linked together. When this linkage breaks down, the energy of living processes is released and the chemical units return to the neutral state, ready to be used again. Therefore, protoplasm in its construction, in its activity, in its death, and in its decay, obeys the same mathematical and physical formulae as the non-living. Plants and animals are self-perpetuating transformers of extra-terrestrial energy. Therefore the normal and pathologic growth and function of protoplasm, hence of organs and tissues and of the organism as a whole, must be accounted for on the basis of electric and radiant energy.

The surgeon, as no one else, is concerned with the problems of energy transformation as seen in shock from injury, from hemorrhage, from surgical procedures, from strong emotion and

intense infection; he is equally concerned with the abnormal changes in energy transformation as seen when there is too great or too little activity of the thyroid and the adrenal glands, in the presence of excessive action of the nervous system, in the growth energy of benign and malignant tumors, and in the modification of energy transformation by anesthetics, narcotics, etc.

On the ground that the test of the validity and the value of a theory is the number of facts it will harmonize and the number of significant problems that it suggests for further investigation, we shall apply this conception to the normal processes in certain dominant organs, in the components that govern the energy system, and in protoplasm as a whole, with especial reference to normal growth.

The most significant and the most active protoplasm is that of the special senses and the nervous system which we shall now interpret in the light of our theme.

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THE ARGUMENT

PART TWO

THE CONTROL OF THE RADIO-ELECTRIC
MECHANISM

CHAPTER 9. *THE CENTRAL NERVOUS SYSTEM*

FROM the mass of data regarding the structure, arrangement, chemical constitution and function of the central nervous system, practically all of which would be pertinent to this discussion, the following facts are presented because of their peculiar significance.

The great importance of the electrical control of the body processes is demonstrated by the infinite network of nerves—wires—in every reactive part of the organism.

The facts that the nerve connects with the muscle cells by end-plates; that, as Cajal¹ has demonstrated, in certain cells one branch of the neurone is apparently connected with the nucleus, and the other with the cell body, thus making possible the linking of the cells in series; and that the intercommunications of the cells themselves and the end organs are not continuous but are broken by synapses which serve as make-and-break mechanisms or keys (Fig. 26)—these facts present a complete picture of an electrical mechanism with central batteries and connecting wires, in which the synapses intervene as make-and-break mechanisms or keys.

The power of the nervous system to create new cells is indicated by certain functions of the nucleus which have been demonstrated by Pfeffer. In Pfeffer's experiments² the nervous system of multicellular organisms appears to have been shown in miniature, and his observations offer such convincing evidence in support of the conception of the nuclear origin and function of the central nervous system, that it has seemed well to include here the following extensive quotation:

"After having detached by plasmolysis the cell membrane of the nucleated protoplasmic body of a plant cell, and dividing the cell in halves, one containing a nucleus and one without any, he observed that only the nucleated half had surrounded itself with a new cell

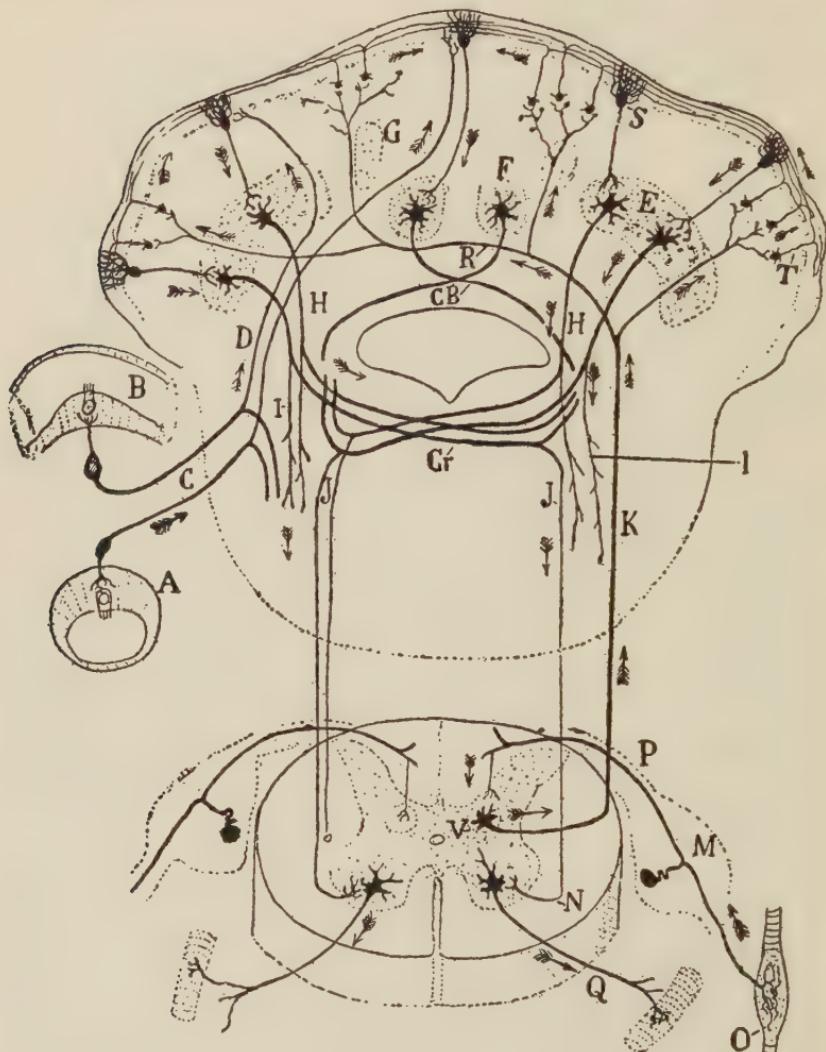


FIGURE 26. Schematic drawing of the afferent and efferent nerve paths in the cerebellum. The arrows indicate the direction of the nerve current. Note the synapses in A and B. (From Cajal: *Histologie du Système Nerveux*, Paris, 1911, Vol. II, p. 144)

membrane. If, however, the part deprived of a nucleus remained united to the nucleated fragment even by only a very fine protoplasmic filament, it also was capable of secreting its little cellulose membrane.

"Pfeffer varied his experiment also in the following manner. He prepared cells of a moss protonema in such a way that an entirely isolated, anucleate mass of protoplasm remained united to the neighboring cell which contained a nucleus by means of thin filaments piercing the cell wall. In this case a membrane was formed round the anucleate fragment. But the membrane was not formed if the neighboring cell had been itself deprived of its nucleus.

"In the formation of this cellular membrane in anucleated parts of the cytoplasm united by protoplasmic filaments with other nucleated portions, the maximum intervening distance observed by Pfeffer was 3.7 mm. 'But the nucleus can certainly exercise the membrane-forming stimulus at an even greater distance.' If the nucleus remains united with a whole chain of anucleated bits of cytoplasm 'the production of the membrane appears to advance centrifugally and so to commence a little later in the more remote portions of cytoplasm than in the bits nearer the nucleus.'

"From these experiments one is inclined to think, this author concludes, 'that the production of a cellular membrane required the continuous transmission and coöperation of certain states of motion and vibration which radiate out from cell nuclei or rather owe their origin to the reciprocal action of nucleus and cytoplasm.'

"Oscar Hertwig makes in this connection the following remark: 'This experiment proves that the stimulus necessary for membrane formation can be transmitted by thin connecting filaments, which traverse the septum interposed between two cells. Nothing hinders us then from assuming that some similar transmission goes on in other functional conditions.'

"But it is very probable that this nervous current or discharge which is conducted from the nucleated cell along the protoplasmic filaments to the anucleated fragment of the contiguous cell, also passes across into the fragment even when it contains a nucleus and so also when it is replaced by an entire cell. This leads us to the conception that wherever intercellular protoplasmic connections are present, the various nuclear currents of discharges stream through these connections and so permit a general nervous flux throughout the whole network of these protoplasmic bridges, in the meshes of which the nuclei themselves would constitute the nodal points. In this way one would have a continuous circulation or distribution of nervous electric energy throughout the entire organism.

"The augmentation of the nervous system in these ways will have as its result an augmentation of the trophic stimulus which it exercises; so that the cells situated along these ways will grow and proliferate more rapidly, thus producing a zone characterized by numerous mitoses. The augmentation of the vital processes of these cells will in consequence of increased osmotic attraction, attract a greater quantity of nutritive fluid, exactly as the wick of a lamp which is stimulated by a current of air draws up by capillarity a larger quantity of combustible fluid."

In support of this view may be cited also the findings of Kofoid and his collaborators³ in their studies of the neuro-motor apparatus of certain intestinal parasites in which the primitive apparatus of flagella and the protoplasmic areas from which they originate appear to be of a truly nervous character and to be dependent upon the nucleus both for origin and for function.

"The close physical connection between the blepharoplasts at the base of the flagella and the nucleus, the metabolic center of the cell, throughout the period of flagellar activity, is indicative of the intimate relation which the nucleus bears to these energy-expending structures. It cannot be merely the physical tug of the moving flagella which pulls the nucleus to its anterior position, for the blepharoplasts retain this anterior location when the nucleus moves posteriorly, the connection between them being retained merely by the slender nuclear rhizoplast. The rounding-up process in the cytoplasm of the encysting individual doubtless exerts some pressure leading to spatial readjustments, but the translation of the nucleus appears to be out of proportion to this single factor. *In the active phase of the organism the nucleus is nearest to the center of metabolic activity*, and in the passive phase of encystment it tends to assume a place as near as possible to the center of the cytoplasmic mass, the cytostomal pouch appearing to hold it off from the fully central location." (Italics mine.)

There is a striking analogy in the above description to the findings of Magini (cited by Cajal)⁴ who in studies of the cerebro-electric lobe of the torpedo observed that in periods of rest the nucleolus occupied a central or slightly eccentric position in the nucleus, while in periods of activity it moved in the direction of the axon to the membrane of the nucleus where it came in contact with the point of origin of the

cylinder axis, with the resultant development of the nervous (electric) wave which discharged the electric organ.

All of these facts and the conjectures suggested thereby would indicate that throughout phylogeny nerve tissue like the nucleus has been an energy-producing tissue; and that the central nervous system may justly be considered *the direct descendant of the nucleus of the original ancestral unicellular organism.*

Since in a bipolar mechanism, the electric current must flow from areas of higher to areas of lower potential, it is necessary to cite such facts as may tend to support the conception that the cells of the brain are the principal source of the electric energy that coördinates the body and to show how the direction of the fabricated current is established.

Since, according to experimental findings, the low-conducting, exceedingly thin lipoid films which surround the cell body and the nucleus have a high electric capacity, it would seem that the potential within the cells must be very high as compared with the potential within the axons which are surrounded by a thicker myelin sheath. The electric current, therefore, would pass from the highest potential within the cells through the zones of lower potential in the axons and nerves toward the points of lowest potential in the glands and muscles to be stimulated. (Fig. 27.) In accordance with this conception, when the electric charge in its passage from the cell through the axon builds up a certain "pressure" the current would pass across the synapse to the structures beyond. Thus the synapse may be in effect a projected part of the lipoid film surrounding the nucleus and the cell; and being endowed with less resistance to the passage of electric charges, after a certain pressure is reached, the current would break through.

Another point of view here would be that waves of detonation are set up which act on the protoplasm constituting the axis cylinder, each in turn generating short wave radiation, which in its turn produces profound electric changes, giving rise to the phenomena attending the passage of an action current.

Clinically the "trigger-action" control of the body by the

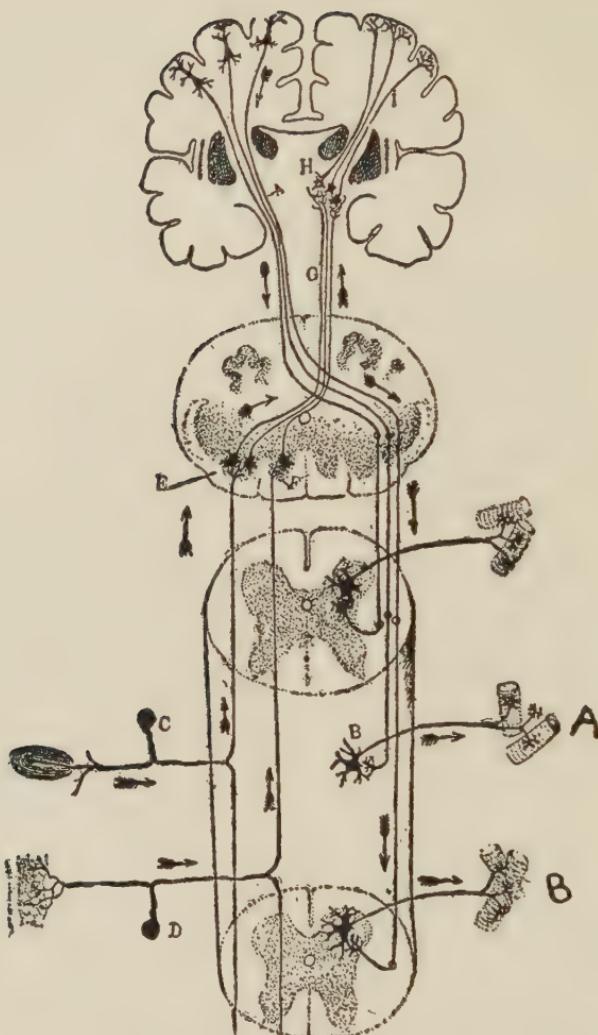


FIGURE 27. Schematic drawing representing the direction of nerve currents excited by one of the special senses resulting in voluntary movements, A and B. The arrows indicate the direction of the nerve currents. (From Cajal: *Histologie du Système Nerveux*, Paris, 1911, Vol. I, p. 540)

energy fabricated in the brain, which we believe to be radiant and electric energy, is indicated by the result of high division of the spinal cord; by the result of the suspension of the activity of the higher brain centers by inhalation anesthesia; by the result of breaking the nerve connection with any part; by the fact that when the supply of oxygen is cut off no energy is created and equilibrium or death follows.

The brain can not work continuously, but a reversible process is necessary at regular intervals to restore it. This process in the higher centers is called sleep. The more intense the activation, the more needed is sleep. The brain is the only organ that sleeps conspicuously. Of great significance is the fact that the entire man spends one-third of his time waiting for the brain to restore itself, or to put itself again in the position of being able adaptively to transform potential into kinetic energy in the form of radiant and electric energy which in turn drives the body.

From these considerations we may glimpse the actual physical process by which the normal brain exercises its function of memory, reason and imagination.

In the next chapter we shall test the validity of this conception in a consideration of the mechanical and electrical energy mechanism by which memory, reason, imagination, the expression of the emotions, muscular action, etc., are fabricated.

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3. Kofoid, C. A. and Swezy, O.: *Op. cit.* 2.
4. Cajal: *Op. cit.* 1.

CHAPTER 10. *THE PHYSICAL NATURE OF MENTAL PROCESSES*

THE entire mass of the brain that constitutes the actual mechanism of the "mind" consists roughly of two parts—the gray matter and the white matter. It is estimated that in the cerebral cortex there are 1,200 million protoplasmic units of energy-transformation, or cells. The white matter of the brain contains no cells. The white matter of the brain is not a dynamo, it is a matrix on which are recorded the patterns of action.

It is in this infinitely delicate white matter, or matrix of the brain that physical conductance paths of microscopic dimensions are established by electric charges as they pass through the matrix. These molecular paths of conductance become facilitated with the passage of certain specific electric currents which are generated in the cells of the gray matter of the brain.

Could this tangled network of facilitated pathways in the matrix of the white matter be detected by a powerful microscope, a single brain might exhibit as great a number of "hook-ups" as all the telephone wires, exchanges, and receivers in existence. (Figs. 28-30.) Could one look with an eye of sufficient magnification into the recording matrix of the brain of an individual, one would there read in the configuration of its multitude of action patterns, every act, every experience, every thought, every desire, every ideal of that individual from the moment of his birth. This infinitely intricate and interlacing network of microscopic pathways of communication we shall designate the patterns of action and memory. In every conscious moment new pathways are added, old pathways be-

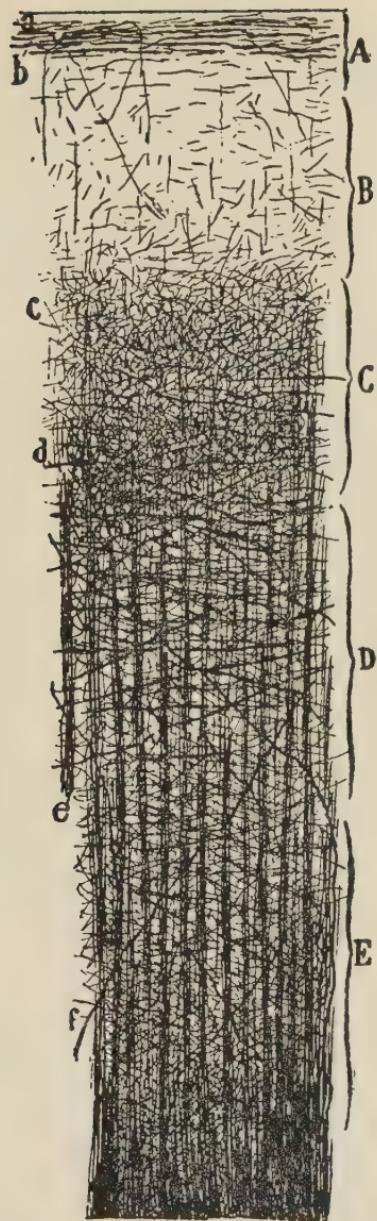


FIGURE 28. Drawing from a section of a motor center in the brain. Note the complex interlacings of the nerve fibers. (From Cajal: *Histologie du Système Nerveux*, Paris, 1911, Vol. II, p. 582)

come more facilitated, and new "hook-ups" are effected.

Since the matrix has no other function to perform, its function is changeless. Its structure is infinitely adapted to the creation of facilitated pathways. But within itself this plastic

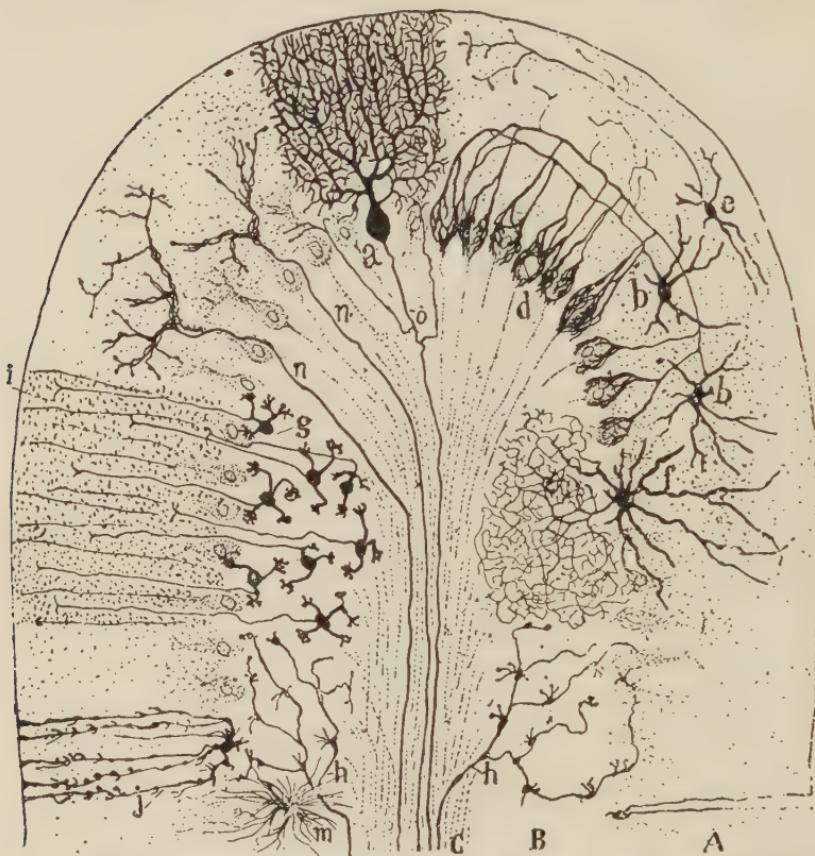


FIGURE 29. Drawing from a section from cerebellar convolution showing the possible connections and interlacings. (From Cajal: *Histologie du Système Nerveux*, Paris, 1911, Vol. I, p. 12)

and passive matrix on which the special senses have caused to be etched this network of conducting pathways of action, furnishes no power whereby it may operate its intricate system. It is in the cells of the gray matter of the brain that the energy required to operate this system is generated. As has already been stated, these cells generate and emit radiance

originally taken by the plant from the sun's radiance and from the nitrogen fraction in the protoplasm. This solar radiance and the nitrogen fraction derived originally from light-

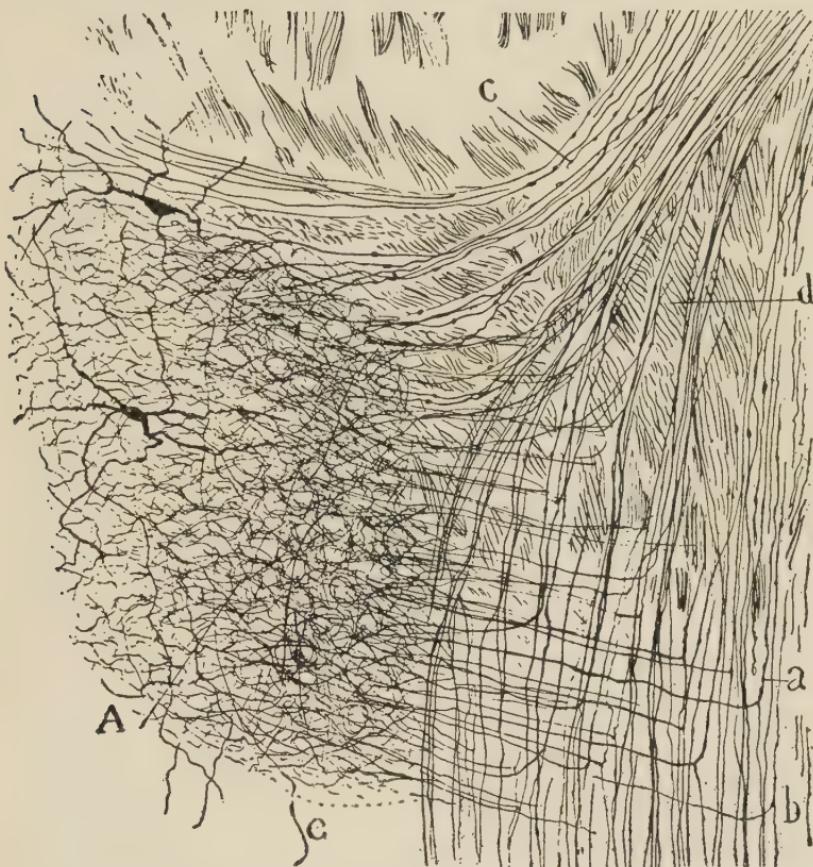


FIGURE 30. Drawing of a horizontal section in the subthalamic region. Note the complex interlacings of the nerve fibers. (From Cajal: *Histologie du Système Nerveux*, Paris, 1911, Vol. II, p. 447)

ning, from terrestrial electrical forces, and from the nitrifying bacteria are the sole source of the power of the cells to fabricate energy.

Since the only source of energy of animals is the energy, which the animal captured in the form of food from the plant, and since the energy held in the plant was captured from solar

radiance and from the nitro group in the soil, the energy that operates the brain in fabricating memory, reason, imagination, in expressing the emotions, in fighting and escaping, is not like—but is in fact—the identical radiance which is released by detonation in the radiogens of the protoplasm of the brain cells.

Since in common with the other cells of the organism, the brain cells are electrochemical radiating mechanisms; since their function is an energy function; since the structure and the function of the brain depend on electrochemical processes and radiation; then, training and education must be purely physical in nature.

Our studies of brain tissue, many of which have already been cited, may be summarized as follows: In the normal range of health there is in the brain within definite limits a constant range of temperature, electric conductivity, electric capacity and electric potential. Under excitation of the brain, these constants increase; in depressed states of vitality, these constants suffer a decline; at death, these constants reach the level of non-living material. The dynamics of the brain, therefore, seem to parallel the dynamics of the energy processes of non-living mechanisms—such as the internal combustion engine or an electric battery or the action of the photo-electric cell as exhibited by the eye.

The retina of the eye is a projection of a specialized portion of the brain through a hole in the skull. (Fig. 31.) Through the ophthalmoscope a living portion of the brain may therefore be seen in the process of receiving impressions and of creating images. These images, in turn, fabricate thoughts, memories, actions, emotions. Thus this part of the mechanism of imagery, of memory, of activity and of thought, can be glimpsed in action. Light waves which have photo-electric effects, that is, have the power of knocking off the outer electrons of the atoms, are thus able to set up fundamental biologic processes—fundamental for all protoplasm.

The electrons thus freed set up biologic currents as similar electrons do in photo-electric cells, and the atoms which are thus modified by the loss of electrons have by that change become endowed with chemical affinities.

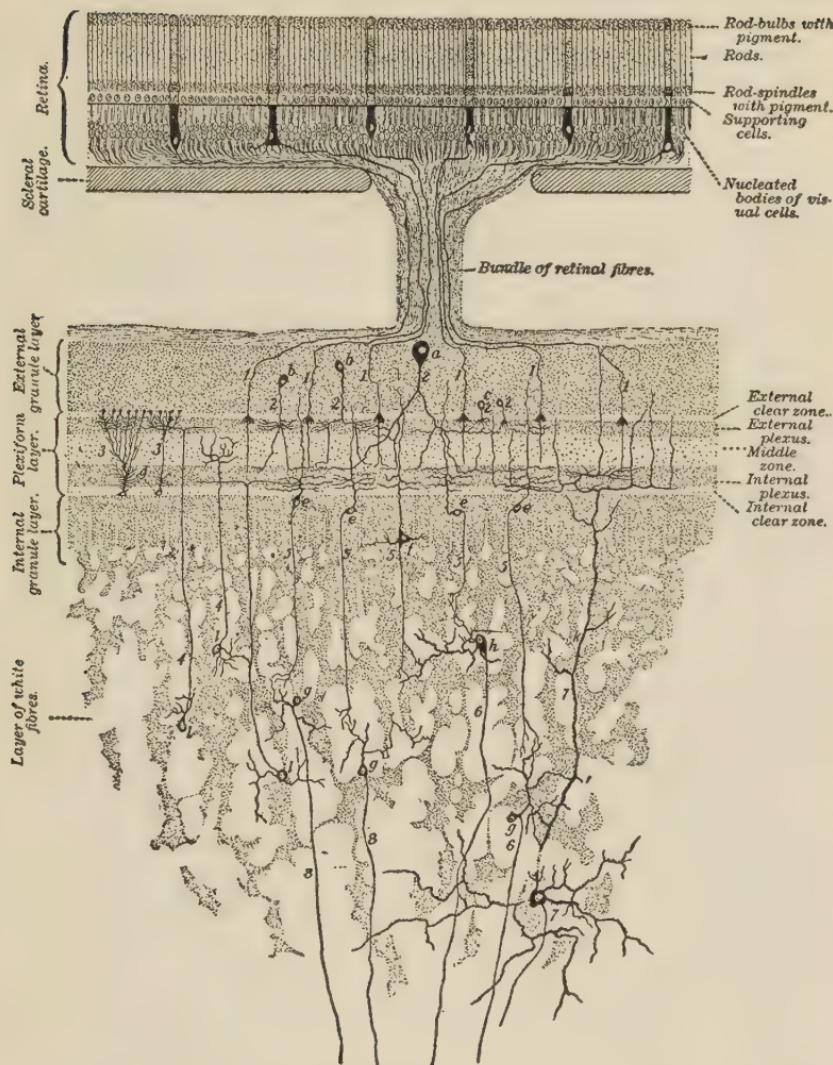


FIGURE 31. Schematic representation of the structure of the retina and visual lobe of Electrone. (After M. von Lenhossék) (From Barker, *The Nervous System*, D. Appleton and Co., New York, 1899, p. 542)

We may then suppose that this exquisitely sensitive nitrogen compound in the retina is detonated by light waves just as nitrogen chloride is detonated by a beam of light. Thus the entire chain of events from a passing image to an overwhelm-

ing emotion could be initiated and executed by the detonating impact of the radiant energy of light falling on a photo-electric mechanism—the retina.

There is nothing strange in considering the response of the eye to be a photo-electric effect since man-made photo-electric cells exhibit even better "vision" than is manifested by the human eye. These non-living automatons can initiate and execute many kinds of work, just as the eyes of animals initiate and through the release of electric and chemical energy cause to be executed muscular action, glandular work and mental processes.

Perhaps enough evidence has been cited to show that the brain is an infinitely delicate energy-transformer and receiver which responds to light waves, to sound waves, and to changes in chemical and physical stimuli, such as taste and smell, touch and pressure. It is this exquisitely sensitive mechanism that is activated by every experience of life from infancy to death.

The capacity for continuous activity is the unique characteristic of the human brain alone. A fox, a lion, an antelope, our domestic animals, show no such continuous activity as that of man. Animals divide their time into periods for securing food, for procreating, for sleeping and loafing. Man works all day and worries at night.

The practically ceaseless activity of man can not be due to a higher development of his special senses, as seeing, hearing, and smelling are not only more acute in the lower animals than in man, but many lower animals have also the power for a greater outburst of speed, and by means of keener sight, smell and hearing, are more easily excited than man.

Although our ancient progenitors developed a high outburst of speed in fight or flight, and developed their special senses more exquisitely than man, the brain of man continually grew larger, and with this increase in the size of the brain, there evolved an increased capacity for sustained activity with a corresponding decline in the keenness of the special senses.

The source of sustained energy is primarily the hormone of the thyroid gland. The larger brain capacity of man not only requires more thyroid hormone, but the enlarging brain could not have had survival value without an enlarging thyroid

gland to supply the brain with the needed increase of the oxidation-controlling secretion of the thyroid. Education obviously depends upon the thyroid gland as well as upon the brain.

The gifts of evolution to man, by which man has achieved his dominance, are the unique size of the brain, the unique size of the thyroid gland and the manipulative hand. It is the size and plasticity of the brain that makes it trainable.

Not only is the brain of man characterized by the greater mass of recording matrix, but almost as significant and lying at the very basis of education, is the fact that in the case of the lower animals, the available recording matrix has all or nearly all of its recordable capacity filled with simple action patterns at the time of birth, and there is but a small amount of blank matrix upon which action patterns after birth may be recorded. This is the physical reason why animals can be trained and educated to but a limited degree. During human fetal life only the simple action patterns peculiar to all animals are established. None of the patterns of action of man's civilized state are established in fetal life. That is, man and other animals differ fundamentally in the amount of recordable matrix which each brings from one generation to the next across the protoplasmic bridge in the process of procreation.

The bird comes over the protoplasmic bridge with all of its action patterns established in its governing matrix. Its matrix is almost completely etched. Its education is practically complete. The bird graduated in the shell. The bird can build its nest without a teacher, but it can not learn from experience how to build a better nest.

The boy comes over the protoplasmic bridge not knowing how to build a house, but he can learn how to build a better house than his grandfather. His blank matrix enables him to acquire action patterns from his wider environment; it enables him to adapt himself as he goes along. Thus is it that the matrix of man is now so large and his mechanism of civilization so complex that much of his life is set apart for training and education, in order that his matrix may be filled with the patterns of civilization. (Figs. 32, 33.)

The brain of a human being may be likened to a moving pic-

ture film which runs from birth to death. Among the infinite number of images thrown upon the film, only a few obtain possession of the final common path of action. These become patterns of action. The action pattern equipment of an individual produces the only acts he can perform. Training, therefore, consists in making action patterns. Action patterns make conduct. Action patterns are the creator of character.

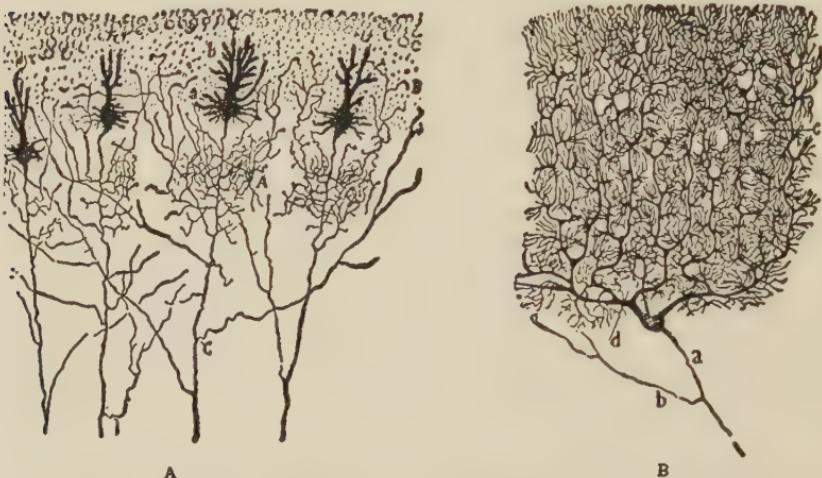


FIGURE 32. Purkinje cells from a new-born child (A) and an adult (B). Note the small number of fibers in A as compared with B and consider the infinite complexity of the patterns which may be formed by the interlacing of the fibers of B as compared with the few simple patterns which can be found in the fibers shown in A. (From Cajal: *Histologie du Système Nerveux*, Paris, 1911, Vol. II, p. 95, and Vol. I, p. 61)

Man's action patterns reflect his environment as in a mirror. If a colt grows up in the wild, it becomes a wild horse; if trained by man, its action patterns and its behavior are domestic. The young of all animals are plastic. The child is the most plastic. If the child lives in a cannibalistic web, he becomes a cannibal; if in a pagan web, he becomes a pagan; if in a civilized web, he will be a civilized man.

The steam roller can not perform the work of the automobile, but the difference between the steam roller and the automobile is less than the difference between the savage and

the scholar. The essential difference between the philanthropist and the savage is in their action patterns.

Intense fear may so condition or facilitate a simple action pattern as to cause the fear defense state to become static in the brain and cause a radio-electric pathology of the energy system. Thus the sudden breakdown caused by the tragic death of a friend or a relative, incarceration in a burning building, financial ruin, shipwreck—any of these experiences may pro-

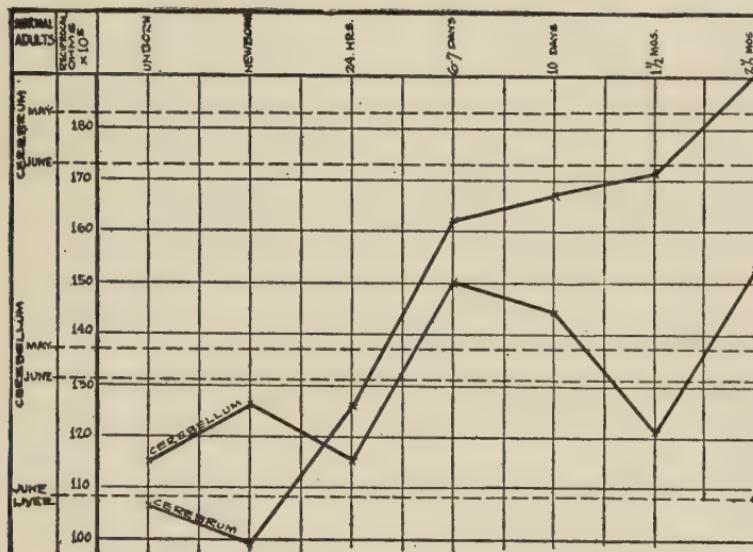


FIGURE 33. Changes in the relative conductivities of the cerebrum and cerebellum from just before birth until the age of three months.

duce in the brain for a time facilitated paths with which no other stimulus can successfully compete, thus producing a temporary dissociation of personality. Indeed in the life of everyone there are certain stimuli which for a short period completely dominate the brain so that no other stimuli can immediately dispossess them. Multiples and intensifications of these lighter, shorter civil dissociations are equal to those which occur in war, not always during shelling, not always due to explosives, but sometimes to other incidents of war as well.^{1, 2}

That this condition is not more common indicates a peculiar susceptibility of the victim. In unconscious possession of such

a susceptibility the civilian leaves his quiet civil pursuits and reaches the front line by such stages as enlistment, putting on uniform, drilling, firing, bayoneting, day and night trench duty, bomb throwing, gas attacks. Each new experience is a little more exciting than the last; he has doubts—misgivings, but he is in the stream and must go on. Finally he leaves the training ground for the real arena where the dissociation is achieved. Here he encounters such incidents as the noise of the approaching and exploding shell; the narrow escapes; the witnessing of the fragmentation of comrades. He becomes convinced that over the top is certain death and he shudders at the thought that some day he must penetrate this fateful zone; the thought of death becomes his constant companion. If he be an officer he perhaps fears that he may fail to meet his responsibility on the great day. Thus sleepless, doubting, waiting, he becomes more easily startled; he loses rest, loses appetite, loses energy, loses confidence; he contrasts his execution as a coward with the bayoneting by the enemy; these doubts tell him he has suffered a physical and moral defeat; in the sanctuary of his own conscience he stands disgraced—dishonored. At last the day comes and amid the terrifying scenes his threshold is thrust down until his duties and responsibilities toward himself and toward his officers lose command of the final common path; and the shell keeps it—holds it against all others. The man becomes an automaton—a shell-dodging automaton—oblivious to everything else; he no longer experiences fear; he exhibits only its outward mimicry. He has been dispossessed of all his brain mechanism except the auditory nerves and the nerve-muscular reaction of dodging shells; that is, he has lost speech, common sensation, understanding, reason, memory, sight, touch, taste, smell; he is divided into two parts, one a monotonous auditory nerve-muscular mechanism dissociated from the remainder of his personality; the other a suppressed remainder, now silent. Putting the finger in the eye or into the larynx can not compete with the shell-facilitated path; spoken and written language can not compete; the eyes see nothing; the nose smells nothing; in vain the skin may be pricked and pinched and cut; all the avenues leading *into the brain* are blocked except one—that of rough sound; all the

avenues leading out of the brain are closed but one—that of dodging shells.

How can the dispossessed brain paths be again placed in control? Only by strong competition with the facilitated shell-dodging mechanism—urgent persuasion, physical injury, a strong electric shock, anesthesia, impressive methods. When the barrier has once been broken at one point then usually the whole brain mechanism is reclaimed.

The complete domination of war patterns in acute shell shock and the manner in which normal brain patterns could again be placed in possession of the paths of action is well illustrated by the following case seen in a hospital in France immediately after a heavy action. The most successful method was by the use of one of the strongest mechanisms—that of speech. The patient was like a wild animal, shaking, staring, decerebrate, crouching, trembling, wild. He was constantly dodging shells, acting as if at bay—dodging his enemy. When his arm was pinched he felt no pain. His appearance was wholly abnormal; his face was earnest but portrayed not a sign of emotion—not a sign of intelligence. When asked his name he could not answer. "Do you belong to the Second?" Only a jerky respiratory sound in response, no word, no nod. "To which battalion?" A wheezing idiotic "No." "To the Third, the Fourth?" Finally when "The Tenth" was mentioned he became greatly excited and with a trembling forefinger marked "10" on a board. For half an hour the medical officer struggled to teach him to say "a." He whispered the letter in his ear; shouted it; showed his own expression while pronouncing it. Slowly and gradually he reopened the action patterns, while all the time the patient was dodging shells and enemy, constantly throwing up his arms and ducking his head. Finally he was made to cough the sound "a." As this action pattern began to open, the idiotic face began to clear. The medical officer put a laryngoscope down the throat; there was no cough, no laryngeal reflex; but finally he was made to say "a" then "e" while the larynx was irritated. This achievement marked the beginning of steady improvement. Soon he could fabricate all the vowels, then the consonants. Under patient encouragement he was made to recall the name of his regiment and his

regimental number. Gradually one after another of the normal paths of conscious action became predominant over the primal self-preservation path, and a normal expression of face and normal reactions were reestablished. It was as if an infant had grown up to a child of ten in an hour, as if a sculptor gradually put a mechanism into a marble statue until finally it climbed down from its pedestal and talked with him. In effect the life of the patient was recapitulated in an hour—in this period he was taught to speak, to count, to spell, to read; he was taken through the kindergarten, the grammar school, the academy.

Usually in acute cases of shell shock the restoration of the normal action patterns was equally acute and the soldier was soon able to return to the Front.

In other cases longer periods of restoration were required. Such patients were sent to villages established somewhere behind the lines, where conditions were made as nearly as possible like those at home. There the soldiers were released from all war association: Barbers became barbers; gardeners became gardeners; carpenters became carpenters; that is, each man worked at his peace-time trade. It is interesting to note, however, that these milder methods were not so successful as the prompt and active measures described in the above case. The brain paths having been violently dispossessed were best repossessed by violent measures.

A similar system of reeducation either short and intense or more protracted and gentle may be required to repossess the normal paths of action after a catastrophe in civil life.

Since those action patterns are found in the white matter of the brain, it becomes necessary to consider further the physical properties of the white matter.

The white matter of the brain has no cells; it has little metabolism; but the white matter of the brain is rich in lipoids, electrolytes, metal catalysts, and organic molecules. The white matter of the brain has physical properties ideally adapted to the orientation by electric charges of lines of facilitated conductance.

The white matter of the brain is not a passive mechanism like the matrix of the phonograph record or the carnauba wax

which produces the piezo electric effect; instead, in the white matter there is a constant electric strain as is indicated by the presence of an electric potential. The origin of the electric strain is the generation of electric currents in the brain cells by radiant energy released within their radiogens by oxidation. Oxidation in the brain cells is governed adaptively by the secretion of the thyroid and the adrenal glands. The thyroid gland is governed by the adrenal-sympathetic system. The adrenal-sympathetic system is governed by the brain, and the brain is governed by sight, hearing, touch, taste and smell, thus forming an automatic mechanism.

It is the specific electric currents that are generated in the brain cells that create the action patterns and activate them adaptively. The experiments by Gotch and Horsley,³ by Ferrier,⁴ and by others, show that electric stimulation of the motor centers of the cortex of the brain causes the muscles to perform the same work that electricity generated in the brain cells causes the muscles to perform. This is a well-established fact.

When an electric current is directed through the brain in such a way as to pass through the fundus of the eye, light is seen. When an electric current is passed through the center of hearing in the brain, sound is heard. These are well-known facts, and the reasons are obvious because the protoplasm constituting the cells of these centers generates electric currents which stimulate muscles and glands. Battery-made electricity is identical with protoplasm-made electricity. The muscle does not "know" to which electricity it responds.

There is no fundamental difference between muscular action, the sucking and breathing mechanism of the infant, the spontaneous running of a newly hatched quail, the closing of the Venus fly-trap, and the learning by the child that two and two equal four.

The existence in the white matter of vast numbers of facilitated ultra-microscopic lines of conductance with semi-permeable insulations provides for new combinations as these facilitated lines meet and cross, thus establishing new combinations. This would appear to be the mechanism of associative memory. The orientations of organic molecules into a line of conductance in the matrix may not be complete in the first

activation unless it be sufficiently intense, but repetition makes the conductance more nearly perfect, hence more facilitated, until at last, when the conductance is molecularly complete, repetition can do no more, memory is established.

We have offered evidence that tends to show that life, normal and pathologic, is a function of protoplasm, and that education and training are processes by which protoplasm is changed. Protoplasm is a dynamic, not a static system. The protoplasm of a plant is identical in principle, though not in pattern, with the protoplasm that executes the heartbeat in man, that sings a song, that produces offspring, that executes an emotion, that fabricates fever, that is altered by shock and injury, that is attacked by infection, or that has its action exalted or depressed or suspended by anesthetics, narcotics, and stimulants. It is the same protoplasm upon which the teacher etches the action patterns of education and training; it is the same protoplasm that is built up by a properly balanced diet, and by a proper balance between work and play, between activity and sleep, by the contributions of normal ductless glands—the hypophysis, the thyroid and adrenal glands, the sex glands, the pancreas, the liver. Each of these glands fabricates and throws into the blood stream specific molecules, and from the blood stream upon protoplasm everywhere are showered like drops of rain on the green fields or like grains of pollen in fertile fields countless millions of organic molecules, each organ and each tissue appropriating what it needs of those specific molecules required for its growth and activity, until finally the protoplasm grows old and breaks down in death. On this swiftly moving protoplasmic film there are etched the patterns of life. The teachers etch education, the church etches religion, and all the other good and evil patterns of parents and playmates and the web of life are etched not only upon this film of protoplasm of youth, but also upon that of mature estate. The teacher is in a biologic sense an engineer, whose task is the modification of energy-controlled mechanisms, viz., human beings who will be able to operate the machine of civilization.

With the rise of the empowered brain came science and invention, social order, governments, philosophies, and religions. But with the rise of the brain there also came as the result of

disuse the gradual decline of many organs and tissues, as was pointed out by Darwin.⁵ Coincident with the rise of the brain there was also a rise in the control of energy, generated within man's own organism, and a slow decline of the fighting and escaping mechanism of our simple ancestors who depended on their own muscles for defensive and offensive energy.

In our hairy ancestors, as in lower animals today, everything was settled by physical struggle. Evolution through struggle and survival has been such that when a life and death struggle was at hand there was a sharp inhibition of activity of every organ and tissue that did not contribute to the success of the attack or escape and a sharp acceleration of those organs that carried the load of the struggle. And today these inhibitions and accelerations of body-wide and fundamental importance recapitulate the reaction of our ancient ancestor, and although no blow is struck, although no attempt at escape is made, the heart pounds, the face is flushed or blanched, sweat exudes, the teeth are set, the chest heaves, the limbs tremble, the mouth is dry, digestion is arrested, the metabolism is profoundly stimulated, body waste is increased, and every cell, every organ of the body is affected. It is a phylogenetic recall. Under the emotions of fear, hate, jealousy, anger or sex excitation, the process of education, of reason, of memory, of imagination, along with digestion, is suspended. No one can fully exercise his mental faculties during phases of emotional excitement as the phylogenetic older emotions relating to procreation, to fight or flight, dispossess the newer ontogenetic processes of reason, memory, imagination.⁶

To the daily formation of action patterns in childhood, parents, brothers and sisters, uncles and aunts, and grandparents contribute. During this same period the action patterns of religion are established. But to this rapidly filling matrix of youth are also being constantly contributed action patterns produced by the radio, the movie, the theatre, the newspapers, the novel, the tale of adventure, by playmates and acquaintances, which is to say, that if the matrix of youth is not being etched exclusively with patterns of education and religion and convention, patterns of some other kind are being indelibly placed.

Important as is the placing of patterns of new facts and new experiences in the matrix of the youth, perhaps even more important is the training of the matrix by exercising it in the shifting of the action patterns in this way or that, so as to intensify or facilitate them after they are laid down, and also by exercising the matrix in the making of new combinations of action patterns. Such exercise we call reason. Reason takes the action patterns as building stones and fabricates them into a complex working mechanism, just as the artisan constructs a robot, a telephone exchange, or a comptometer by putting together a number of units in order to form a working mechanism. Thus training establishes action patterns in the brain. Education establishes "word patterns" in the brain. Training is the substance of adaptation.

Between parents and offspring there is no break in the continuity of protoplasm, as the plan and structure of the protoplasm of the parents are carried to the offspring in the protoplasm of the sex cells.

As has been stated, man comes over the protoplasmic bridge with simple animal patterns and a large blank matrix, whereas lower animals come over the protoplasmic bridge with their racial patterns etched, and possessing but little blank matrix. It is the blank matrix that is man's most important tool of civilization.

The parent or teacher does not need to give instruction in such racial acts as sucking, walking, hunting, fighting, mating, drinking and eating—patterns of which the pupil brought over the protoplasmic bridge. The parent or teacher has no problem in establishing the emotion of fear, anger, love and hate in the child. The problem of the teacher is to place patterns in the matrix of the pupil while the phylogenetic wild animal is playing and fighting and courting and mating and growing. It is while he is still a wild animal and there is only a prospect of his becoming a civilized human being that the parents and teachers must etch the way. Parents and teachers pilot the candidate for civilization in his journey through his wild animal phylogeny to the state of control of the wild animal by the action patterns of civilized man. Exercise in sports develops the "wild animal" in man; it not only coördinates the wild man and the civilized

man, but it also furnishes the much needed health and physical vigor which the brain cells, the thyroid gland, the adrenal-sympathetic system and the matrix of civilized man require. The wild man furnishes most of the power required by the civilized man. The overwhelmingly intellectual man, completely detached from the vigor and traits of the wild man, is often isolated and consumed with mental and nervous disorders and may be of little advantage to society. The web of life is the product of the activity of the action patterns of all the men and women of the past, and upon the plastic matrix of the children streaming into it is etched the pattern of this web.

THE ADOLESCENT

In the adolescent there is a crescendo of activity of the ductless glands led by the hypophysis which not only builds the bony skeleton with a great rapidity but also stimulates to greater activity the thyroid and adrenal glands and the sex glands. Rapid growth is hard work, overwhelming the organism not only with the novelty and strangeness of the development of the procreative mechanism but also by the magic change in the entire anatomy as well as in the entire emotional state. The changes of senility are as nothing compared with the transformation enacted in adolescence. The only other chemical and physical transformation that is comparable is dissolution in death. Fortunate is it that the process of adolescence is spread over several years. What if it occurred in a night!

Not only is the physical fact of this transformation a heavy load on the organism of the adolescent boy and girl, but the dominating organs themselves, new to their tasks, are in one instance too active, in another too depressed, thus adding to the overload of general growth and procreative growth the disturbance of organs and emotions. In consequence, there is a new and imperative competitor for the use of the available oxidation—a new and imperative competitor for energy that is needed for education. Therefore, when training the mind of the adolescent, the hard work of growth and the hard work of the fabrication of the mechanism of procreation as well as the hard work in the expression of the excessive emotion of the adoles-

cent should be taken into account in terms of competition for energy required in the process of training the mind.

In comparison with the brain of the normal teacher, the energy function of the adolescent pupil may be as much disturbed as in the case of an infection, a fever, anemia, chronic tonsillitis, insufficient oxygen, hunger, overeating, want of a balanced diet, thyroid deficiency or thyroid excess. Under these adverse influences, it is the electric potential of the brain that is affected. So is it in adolescence.

The most striking alterations of the brain which may occur in both an adolescent and an adult are due to too little or too much thyroid activity. The degree of activity of the brain and adrenal-sympathetic system is roughly a measure of the activity of the thyroid gland. If the thyroid gland is underactive, the individual is correspondingly slow mentally, has a diminished power of sustained attention, has a dry, inelastic skin, a slowed pulse, slowed reactions. It would be as reasonable to expect a motor car with a choked carburetor to equal the performance of a perfect mechanism as to expect concentration and mental alertness in an individual whose metabolism is below normal.

On the other hand, the exceedingly brilliant individual, who, without effort, leads his class, is on all important committees, is socially popular, and breaks down before graduation from school, who complains of a pounding heart, intense nervousness, has a good appetite, perspires excessively, and cries easily,—this brilliant personality may be due to a high activity of the thyroid gland. So high is the scholastic record among patients with hyperthyroidism and so many individuals of Phi Beta Kappa rank are to be found among them, that although hyperthyroidism may appear years after graduation, in a certain sense we may say that Phi Beta Kappa itself is a disease. Certainly there is no record of an individual with myxedema attaining Phi Beta Kappa rank. This state of overactivity appears in teachers as frequently as in pupils.

Hypothyroidism, or depressed activity of the thyroid gland, occurs more frequently in middle-aged individuals than in adolescents. Many a potentially fine individual has been sacrificed by the inconstant thyroid. What part, then, does the thyroid gland play in intellectual and emotional work?

The unique effect of the thyroid hormone upon mental and emotional activity can now be explained by the demonstrated fact that the thyroid hormone increases the percentage of radiation in the short wave or ionization field and the immediate effect of this would be that of increasing the electric potential of the brain. This increased electrical potential would confer upon the brain a corresponding increase of mental and emotional power.

Conversely, decreasing the thyroid activity diminishes the electric potential of the brain. The electric potential is the energy that drives the brain in mental and emotional activity. The electric potential bears as direct a relationship to memory, to reason, to imagination, as does the voltage in a battery to its driving power.

Therefore, if an adult or a child has too little thyroid hormone, his mental processes are slowed down accordingly. Concentration is difficult. Accomplishment is slow. If there is too much thyroid hormone, there will be a gradual stepping-up of every intellectual and emotional process, and when too high a level is reached exophthalmic goiter will develop. On the other hand, insufficient thyroid secretion results in myxedema. It is in the wide, middle range that the great mass of individuals roll along.

In certain individuals, there occurs a state of unbalance resembling exophthalmic goiter. In these individuals the heart palpitates without obvious cause, there is excessive hyperexcitability, sleeplessness and instability, the victim vacillating between excitability, exhaustion and complete breakdown. This condition is known as neurocirculatory asthenia or "soldier's heart." In this group may be found brilliant and interesting invalids of history.

Thus it would seem that the word "mind" connotes the work of the protoplasm of the brain. It would be more simple to make no use of such terms as "mind" or "psyche" and instead use the physical terms that are involved. Whether a plant, a protozoan, or a man, the protoplasm in all its forms is influenced in the same way by anesthetics, by stimulants, by narcotics, by want of oxygen, by electrolytes, by poisons, and by variation in temperature. If the plant, the protozoan, the child,

is sick, all of its protoplasm is sick. "A sound mind in a sound body" is "sound protoplasm in sound protoplasm."

Having identified the energy that operates the organism and taking into consideration the common knowledge that individuals of a species, as well as the species of animals themselves, exhibit to varying degrees the power of changing their speed of energy transformation in muscular, mental and glandular activity, we must identify the organs and the mechanisms by which these dramatic changes are wrought.

It is at once clear that there is within the organism an energy-controlling system which is activated by the special senses primarily. Theoretically, this system would consist of the special senses, the brain, the adrenal-sympathetic system and the thyroid gland. This is the system that should be proven to be responsible for extracting the energy from the nitrogen and carbon compounds in the organic molecules of food and converting them into radiant and electric energy, which in turn governs the growth, the function and the activity of the organism. This energy-controlling system, like the internal combustion engine, converts the potential energy packed in the atoms of the organic compounds into the kinetic energy represented by radiation, electricity and their consequent mental, emotional, muscular, glandular and growth activities.

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CHAPTER III. *THE SPECTRUM OF THE LIVING STATE AND ITS CONTROL*

LET us assume that there is a continuous emission of radiation through the continuous process of oxidation in the radiogens, and that in addition to the emission of long wave or heat radiation there are ultraviolet radiation, visible and short infra-red radiations which have the power of ionization, for example, the power of transforming passive atmospheric oxygen into active oxygen. Let us assume further that changes in the percentages of the ultraviolet radiation, of radiations in the different portions of the visible spectrum, and of the short infra-red radiation would change the form, structure and energy characteristics of plants and animals, thereby supplying an energy basis for the differentiation of plants and animals into species. The organic compounds, hence tissues, organs, and organisms, would vary according to this or that preponderance of ultraviolet radiation, according to this or that preponderance in the components of the visible spectrum, according to this or that preponderance in the short infra-red field, according to this or that preponderance of the long waves of ordinary heat. And finally the organic building stones or compounds, hence the tissues, organs and organisms, would also vary according to the combinations of percentages in the various bands of the spectrum.

For example, since lightning and terrestrial electricity generate a shorter wave than is found in the solar radiance, it follows that when the nitrogen compounds are detonated in protoplasm they would emit a shorter wave radiation than do the carbon compounds. Supporting evidence of this assumption is

the fact that a higher temperature attends the combustion of explosive nitrogen compounds than attends the combustion of carbon compounds. This is seen in the high temperature which attends the detonation of the nitro-explosives. Therefore, we would expect that an organ that commands and controls other organs, such as the brain, would exhibit a higher percentage in the short wave field, even in the ultraviolet, than would such organs as the liver, the spleen, the kidneys, the digestive tract, fat, bones, joints, tendons, fascia, etc. Furthermore, one would expect to find in an animal that has a preponderant brain, such as man, a correspondingly larger thyroid gland, the hormone of which would have the power of increasing the percentage of emissions in the short wave field, and this is a fact.

The mechanism of memory, reason, imagination, is dependent upon electric potential. Electric potential is in part dependent upon the rate of the emission of electrons from atoms in the process of ionization. The process of ionization is in part dependent upon the impacts of short wave radiation. It would appear, therefore, that that animal having the largest number of brain cells and the largest matrix, would have the greatest capacity for the continuous exercise of memory, reason, and imagination; that is to say, the greatest intellectual power and leadership. This again is true of the human being.

That organ which has the greatest capacity for the production of short wave radiation should exhibit the greatest rate of growth. Therefore, in the early period of differentiation of the fetus into organs and before the cells of the organs have become differentiated for the performance of their peculiar functions, the brain would have the greatest speed of growth; that is to say, in view of the unique capacity of the brain to generate short wave radiation, if this short wave radiation were expended exclusively upon growth, the brain would grow faster than any other organ, and such is the case.

The conscious state is the act of responding to impulses from the special senses, to the impulses of common sensation, and perhaps to impulses arising within the organism. Consciousness is the act of response, and the act of response means that within the brain there is that rate of oxidation and resultant short wave generation, with the consequent emission of electrons,

which will change the electric status of the cells and of the infinite numbers of nerve pathways and circuits, thereby causing muscles to contract and organs to function, memory to be awakened, reason and imagination to act.

This is the commanding or the conscious state, and the conscious state is a function of the short or ionization waves in the spectrum. If one could imagine an amount of oxidation or detonation in the brain that instead of producing a preponderance of radiation in the short wave or ionization portion of the spectrum produced a preponderance in the long wave or non-ionization part of the spectrum, then there would be a corresponding diminution in the number of electrons emitted into the nerve circuits, the membranes would be but meagerly charged, the electric potential would fall, and instead of the conscious state there would be the state of unconsciousness. The state of unconsciousness, like the state of consciousness, is the result of the percentage of the short or ionization waves in the spectrum.

When an excessive amount of the thyroid hormone is thrown into the blood, hence enters the brain cells, and causes an increase of short wave radiation above the normal, consciousness is so intensely stepped up that the subject is in a state of pathologic nervous tension, weeps emotionally, has every reaction quickened, even to the extent that it is difficult to attain the unconscious state of sleep without the use of sedatives and narcotics, all of which is but another way of saying that the unconscious state of sleep can not be attained without diminishing the production of the waves of the spectrum, which produce ionization.

On the other hand, when the organs which control the short wave radiation, viz., the thyroid gland and the adrenal glands, are removed completely, the percentage of short wave radiation is so greatly reduced that the normal conscious state is depressed to the level of drowsiness, dullness, and cold inertia. The state of the mind and the state of consciousness are a result of radiation and electric potential.

From this point of view, in an animal that possesses the mechanism by which the percentage of short wave components of the spectrum can be increased rapidly, the amount of elec-

tricity available for driving the organism would be correspondingly increased, hence would confer upon that animal high speed and greater power. On the contrary, an animal that possesses to a lesser degree the power of changing the percentage of the short wave components of the spectrum, would correspondingly generate less electricity for driving the organism, hence that animal would be slower and less powerful in attack and defense. The lion and the tiger, for instance, which possess a large and exceedingly complex adrenal-sympathetic system, would have the power of making great shifts to the short wave part of the spectrum. The alligator, the crocodile, the armadillo, the turtle, and other animals, which possess a small and exceedingly simple adrenal-sympathetic system, have far less power of shifting the radiations to the short wave part of the spectrum. In other words, the thyroid gland and the adrenal-sympathetic complex are the mechanisms that regulate the speed of the animal organism; that is, the thyroid gland and the adrenal-sympathetic complex are the chemical mechanisms that, by controlling the rate of oxidation, shift the spectrum to the short wave field, and the short or ionizing waves of the spectrum generate the electricity that operates this muscle or that muscle, this animal or that animal, at this speed or that speed. Therefore, the brain, being the greatest generator of radiant and electric energy, is endangered by the rapidly increased polarization in its infinite number of cells or batteries.

In the animal battery as in the man-made battery, when as the result of continuous action the contra-electric current equals the primary current, then the electric circuit is inactive and dead; the electric potential within the circuit and within the cells coincidentally falls to zero—and the animal is dead. Such a death is unique in that there is no struggle, there is only a continuous loss of energy, until the animal or man stops living as inconspicuously as a battery fades to zero. Just as a battery runs down by virtue of polarization and is restored by opening the circuit, so in the case of the billions of brain cells that run down by virtue of polarization as the result of adequate stimulation of the senses, if the stimuli are reduced below the threshold of action, the nerve circuits are opened and depolarization occurs. This is sleep.

The possession by protoplasm of a mechanism that can generate and emit ionizing radiation interprets most simply that hitherto unexplained phenomenon, the ionization of oxygen, since it explains by what means oxygen is ionized, hence made chemically active. It is the short wave radiation emitted by the radiogens that ionizes oxygen. The atmospheric oxygen at the low level of energy in the alveoli of the lungs, in solution in the blood stream, in the hemoglobin, in the plasma that bathes the cells of the body, in the electrolytic solutions within the cells themselves, indeed throughout its journey from the atmosphere until it reaches the ionization radiation emitted by the radiogen—this atmospheric oxygen remains at its primary low energy level and is incapable of performing its elementary fundamental rôle of energizing the organism by oxidation. *Ionization of this element, oxygen, is accomplished instantaneously by the radiation emitted from the molecular unit, the radiogen, just as the ionization of the oxygen in the air is accomplished instantaneously by lightning.*

If ionization and oxidation occur in growing tissues, as in the fertilized ovum, the fetus, or a cancer, the energy of the ionizing radiation is expended wholly for growth. Between these two extremes of function only and of growth only there are such states as those of adolescence, of repair, of physiologic hypertrophy; that is, a combination of both growth and function. Whether the state shall be exclusively one of function or exclusively one of growth, or a combination of the two, is determined by the percentages of short wave, medium wave, and long wave radiations in the spectrum.

Lightning is an aggregation of electrons travelling at a certain speed. It is the summation of the radiant energy from all the countless electrons of which lightning consists, that produces the brilliant white light. There are countless numbers of electrons travelling at the same speed which produce no visible light. The eye is not adapted to react to that infinitely transient radiation in the visible field. At the point of impact of a single electron, the electron voltage is as high as is that of each electron in the bolt of lightning and the effect produced by the single electron at its inconceivably small point of impact is as great per mass as that of the bolt of lightning.

If we could see the waves of individual electrons, we would be in a state of infinite confusion. Our adaptation is to see light in the mass. It is oxidation in the mass that makes light emitted by wood, coal and oil visible. It requires a certain mass to energize the mechanism of the eye. The photographic plate under special arrangements and equipments can "see" the collision of an electron and so in protoplasm there could be infinite numbers of the visible light wavelengths that could not be seen by the eye but could be "seen" by atoms and molecules. If the mechanism for the production of light in the firefly were located within the body of the firefly the light would be correspondingly dim or would not be visible at all.

In the case of the firefly, oxidation produces visible light and an undetermined amount of heat. The firefly has evolved a mechanism by which 91 per cent of the emitted light is in the visible part of the spectrum. In the brain the ionizing waves eject electrons and generate electricity. In the firefly, ionizing waves eject electrons and produce visible light. In both the brain and the firefly there is a fraction of emission which presumably is in the ultraviolet field and a portion which is in the short infra-red field and in the long wave field or the zone of ordinary heat radiation.

In the competition among the various species of animals for dominance, it is significant that the protoplasm of nearly every animal contains about the same percentage of water in its protoplasm, viz., about 75 per cent. In the case of the brain, the percentage of water is about 85; in the case of the bones the percentage of water is very small. It would appear that the water content maintains an optimum temperature at a certain ratio between the amount of water and the amount of radiation; in other words, protoplasm is a water-cooled system. If this be true, then it would follow that a tooth which would emit a relatively small amount of radiation per mass could dispense with water and be a solid. A bone also contains a greater amount of water than a tooth and we would conclude that it would emit a larger amount of radiation. In the tendons, cartilage, fascia, fat, hair, nails, the horny layer of the skin, hoofs, claws, beak or horn, in which there is a high ratio of solids to water, the amount of radiation would be small.

Therefore, if the amount of water corresponds to the intensity of the radiation, the brain, which is the most active tissue in the body, should have the highest percentage of water per mass, and as stated above, 85.27 per cent of the gray matter of the brain substance consists of water, a higher percentage of water than is present in any other tissue excepting the electrical organ of the electric fish. It is significant also that the percentage of water in the brain varies with age, being largest in the youngest brains.¹

Even the most conservative classical scientist would not deny that solar radiation is the source of the energy of plants or that plants are the source of the energy of animals, or that it is the release of plant energy in the animal which makes the animal function through oxidation. This is equivalent to saying that in accordance with Einstein's Law of Equivalence oxidation can do no more and no less than to release from the organic compounds taken in as food by the animal that part of the spectrum of the sun which was captured and stored in the atoms and the molecules of the proteins and carbohydrates of the plant.

Theoretically, it would be just as reasonable to deny that radiant energy plays a rôle in the growth of the plant as to say that radiant energy released within the animal plays no rôle in the growth and function of the protoplasm of the animal.

THE SOLAR SPECTRUM

If the solar spectrum consisted of but a single wavelength, there could be no plant or animal. We have seen heretofore that the various wavelengths exert totally different physical effects.

At one end of the spectrum are the long infra-red rays which have an important biological significance as they profoundly affect molecules. At the other end of the solar spectrum there are the ultraviolet rays, the physical properties of which are entirely different from those of the long infra-red rays.

In between the long infra-red and ultraviolet rays comes the visible spectrum, a significant property of which has been observed by Dr. Glasser. He has found that when sodium chloride

and other crystalline salts are irradiated by radium and the x-ray, they will emit ultraviolet radiation and that this emission is increased by exposure of the irradiated salt to visible light.²

Ultraviolet rays are absorbed in even a thin film of blood serum; they are absorbed by electrolytic solutions; they are blocked by ordinary glass; they pass through quartz. These fundamental differences between ultraviolet and long infra-red rays, though strikingly opposed to each other, are as nothing when certain great fundamental biologic effects are considered.

The long infra-red rays have no photo-electric effects; they have no power of originating bio-electric currents; they have no power of causing the carbon dioxide or nitrogen to form complex organic molecules. The long infra-red rays maintain the characteristic body temperature and, like water, they are an important factor in the living.

The nitrogen fraction of protoplasm acts as the fulminate which governs the genesis of the specific energy by which growth and electric charges are generated. Ultraviolet radiation has the unique power of conferring chemical affinity upon the most inert element, nitrogen, thus forming the basis of protoplasm. The rôle of ultraviolet radiation is that of supplying atomic electric and molecular power, of putting energy into protoplasm; and having the power of putting energy into protoplasm, it has equally the power of releasing energy from protoplasm.

Lying between the ultraviolet and the long infra-red radiation are the visible spectrum and the short infra-red radiation. The visible spectrum has an entirely different biological adaptation from the ultraviolet or the long infra-red radiation. The visible spectrum, unlike ultraviolet radiation, is more readily transmitted, especially through electrolytic solutions. This fact and the fundamental fact that the visible spectrum, like ultraviolet radiation, has photo-electric effects, hence can detach electrons and generate electric currents in protoplasm, constitute the two properties of the visible spectrum which have led to the evolution of the mechanism by which animals orientate themselves at a distance.

The photo-electric effect upon the retina of the eye initiates

the radiant and electrical stimulation resulting in the greater part of the muscular energy of the animal. Ultraviolet radiation could not have been the specific type of energy for which a mechanism for seeing could have been evolved because the ultraviolet radiation is absorbed and does not penetrate. The long infra-red radiation could not have been the specific type of energy around which the eye could have evolved, for lacking photo-electric effects, the long infra-red rays could not have generated electric currents and it is the electric currents generated by the photo-electric effect of the visible spectrum that causes the animal to be moved hither and yon. Short infra-red radiation could not have been the type of energy for which the mechanism of seeing evolved. Therefore, the structure of the eye and the orientation called seeing are adaptations to the visible spectrum.

The fundamental significance, therefore, of ultraviolet, visible, and infra-red radiation is attested by the mechanisms within the organisms that have been evolved around these bands of the spectrum. In order to regulate the percentage of ultraviolet radiation in the body, there have been evolved outstanding mechanisms, viz., the thyroid gland and the adrenal-sympathetic system.

Not only the muscular work of the animal but the work of the adrenal-sympathetic complex, the work of the circulation, in short a large part of the mass of the brain, of the muscles, and of the glands of the body is partially or completely evolved around the specific radiant properties of the visible spectrum. In the short infra-red band of the spectrum we have that wavelength which in the plant performs most of the work in the construction of the carbohydrates. The carbohydrates supply to the animal organism the largest proportion of energy. The importance of the red part of the visible spectrum and of the short infra-red radiation in their genesis of the carbohydrates and their release of energy in the organism is further attested by an important organ, viz., the pancreas, which was evolved to facilitate the carbohydrate metabolism. Insulin, the hormone of the pancreas, plays a rôle in the oxidation of the carbohydrates.

If we divide the sun's radiance into ultraviolet radiation with its unique chemical and electrical properties, the visible

spectrum with its unique power of orientating the animal, moving it hither and yon in space, making possible the finding of food and mates, the avoidance of or the overcoming of enemies, etc., and the short infra-red radiation which accumulates the vast stores of carbohydrate energy, and the longer heat waves, we see that it is visible radiation that governs man from the outside, while ultraviolet and short and long infra-red radiation govern man from the inside. Visible radiation also is generated and emitted by many animals and plants as luminescence.

What an adaptive picture! One set of wavelengths moves animals about; another, the long infra-red wavelengths, maintains and equalizes the temperature of the body. The master radiation, ultraviolet, has the greatest power of generating electricity and of ionizing atoms, hence of generating the building stones of organic compounds which, in connection with short infra-red radiation, build up protoplasm itself. It is the ultraviolet and the short infra-red radiation that build up, respectively, the proteins and the lipoids, the positive and negative fractions of cells and of protoplasm.

With these selective functions of the ever-present solar radiation—ultraviolet radiation, the visible spectrum, and infra-red radiation—innumerable animals have fitted themselves into the narrowest of advantages. The cycle of the living begins with the creative sun's radiance which forms and fills plants with these creative radiations. From the plant, atoms bearing this stored energy from the sun are taken into animals where the ultraviolet radiation, radiations in the visible spectrum, and infra-red radiation are released with the reproduction of the radiations put into the proteins by lightning, terrestrial electricity and the nitrifying bacteria, which produce the energy by which the animal in turn performs its work, produces growth and reproduction, the animal thus being a motorized plant.

Hence it is that the control of the special senses is through environmental energy—solar radiation and radiation from lightning, terrestrial electricity and the nitrifying bacteria. Sound waves, chemical reactions and the special senses in turn control the activity of the brain; the brain in turn controls the activity of the adrenal-sympathetic system, which in turn controls the activity of the thyroid and other glands. That is to

say, the entire energy system is controlled by radiant and electric forces in the environment, and radiant and electric forces within the organism are constructed by what might be termed an "internal medication."

Sight, hearing, touch or smell may cause an "internal medication" by adrenalin, by sympathin, by thyroxin, each of which adaptively shifts the spectrum toward the short wave field, thus speeding up the animal to this or that end—for attack, or escape, or embrace. And so the spectrum of the living is changing continually in consciousness, in sleep, in attack and defense, in emotion, in every adaptive reaction.

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CHAPTER 12. *THE RÔLE OF THE THYROID GLAND*

THE thyroid gland governs the electric potential of the organism, hence the power of protoplasm to grow and function.* The fact that protoplasm grows and functions through radiant and electric energy, that each band of the spectrum plays a specific rôle, that growth and electric energy depend on short wave radiation, and finally that the hormones of the thyroid and the adrenal-sympathetic system alone have the power of increasing the percentage of radiation in the short wave field of the spectrum, is another way of saying that the living spectrum is the keyboard on which variations in speed of growth and function in intra-uterine life, in infancy, in adolescence, in the emotions, in combating infections, in muscular exertion, are expressed.

We have already stated that in the animal kingdom the thyroid gland and the adrenal-sympathetic system correspond in relative size to the energy characteristics of animals.

That iodine plays a part in organic life is suggested by the fact that all plants and animals contain iodine, particularly the seeds of plants and the blood and tissues of animals. That iodine plays an especially important rôle in land animals is evidenced by the development of one of the largest ductless glands, for the purpose of concentrating iodine and of manufacturing an organic compound of iodine. This organic compound of iodine, thyroxin, governs the metabolism of animals, maintaining the metabolism constantly at this or that level. The adrenal gland also has a powerful control over oxidation in

* This, of course, includes only organisms in which a thyroid gland is present. In lower animals and plants it would appear that this rôle is played by iodine.

the body, but only in short rhythms. In these short rhythms, however, adrenalin exercises a greater control than does thyroxin.

When the thyroid gland is removed, the activities of the

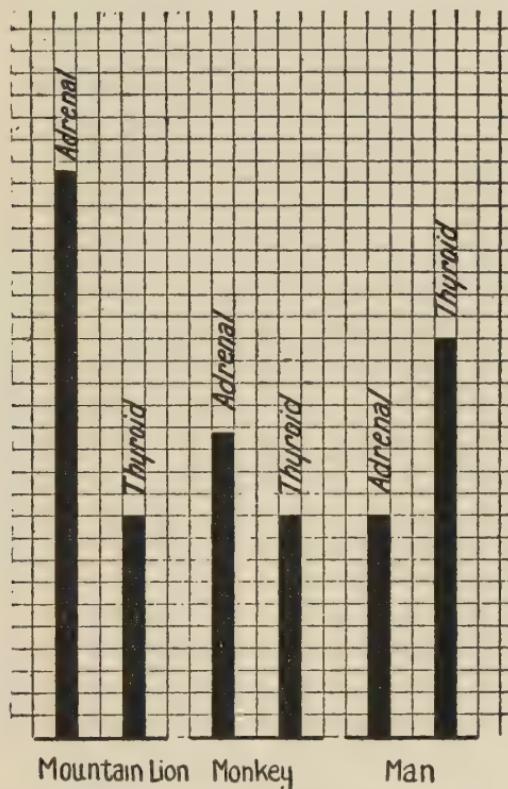


FIGURE 34. Chart showing the relative sizes of the thyroid gland in the mountain lion, monkey and man.

brain, the heart, of all of the organs and tissues are diminished to a sluggish, inactive state. When there is too much thyroid activity, excessive activity is established in the brain, the sympathetic-nervous system, the heart, and in all the cells of the body, resulting in increase of the total metabolism.

In the human being the relative size of the thyroid gland is unique, as the human being is the only animal in which the weight of the thyroid gland is greater than the weight of the

adrenal gland. (Figs. 34, 35.) There is evidence that the more highly civilized fraction of the human race has a larger thyroid than the less highly civilized fraction. The significance of this becomes apparent when taking into account certain facts concerning civilized man; first, the unique size of the brain, and second, the unique high level of mental, emotional and muscular activity. In accordance with the conception that radiant and electric energy operates protoplasm, we can readily understand in what manner the thyroid gland confers upon man attributes so characteristic.

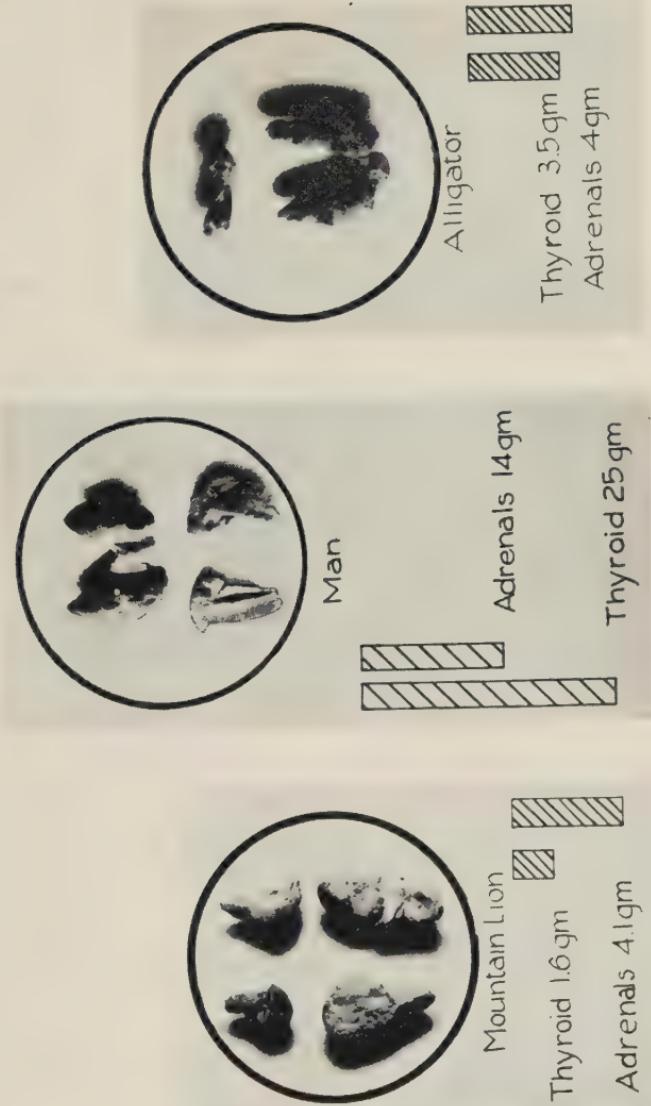
The energy of all protoplasm—in plants and animals—is based upon the presence of compounds of nitrogen and compounds of carbon, which are somewhat analogous to the components of gun-powder, nitrocellulose, etc. Protoplasm, therefore, is in the state of slow but continuous disintegration or oxidation. The thyroid hormone and the hormone of the adrenal-sympathetic complex act as fulminates to speed up this oxidation. In the case of adrenalin the speed is so great that it amounts almost to an explosion. In the absence of the thyroid hormone as in the case of cretinism, bodily growth is stunted.

The need of the organism for iodine is marked by the development of the thyroid gland as a single compact body about the time of the emergence of animals from the sea. In the fishes and Cyclostomata * the thyroid is represented only by small groups of cells hardly as large as pinheads scattered along the larger blood vessels near the heart and along the gills. The gland begins to become more compact in the amphibians, and develops progressively through the various stages of land animals until it reached its unique development in man.

The relation of the function of the thyroid gland to periods of prolonged stress is strikingly illustrated by the fact that in the lowest vertebrates and in certain of the lower vertebrates the groups of thyroid cells are connected with the ducts of the sexual organs. In the lower forms of life practically the only occasion for protracted activation beyond the needs of the moment is in connection with reproduction. This direct connection persists as far as the Cyclostomata. The relation, however, con-

* A fish-like vertebrate without a lower jaw. The lowest class of craniate vertebrates.

FIGURE 35. Photographs of the thyroid and adrenals of an alligator, a mountain lion and man.



tinues to be evidenced in the higher mammals by the enlargement of the thyroid gland in periods of sexual excitement, in menstruation, in adolescence, in pregnancy. In the winter, and in the mating season, the thyroid gland becomes hyperplastic and more active.

These facts relate solely to energy. In the Cyclostomata there is the energy of growth which is present in the fetus. In the higher terrestrial animals the rise of the thyroid gland coincides with the rise of mental and bodily energy. In the chronic infections there is the chemical energy defense against bacteria.

All of these are related in turn to the influence of the thyroid secretion upon the respective components of the spectrum of the brain and other protoplasm.

It is clear that if the speed of the mental, emotional or muscular response of an animal is to be increased, this increased speed must be produced by a mechanism that increases the amount of available nascent oxygen adjoining the carbon atoms in the organic molecule. Since iodine, like iron, plays a fundamental rôle in oxidation, one would expect that there would be mechanisms that would protect the animal against the incidental changes in the iron and iodine concentrations in the tissue. One would expect these two substances to be concentrated in organs from which, through the nervous system, they would be adaptively released to the blood and tissues. The liver concentrates iron. The thyroid gland concentrates iodine.

In our laboratories the following experimental and clinical evidence regarding the energy function of the thyroid and adrenal glands was found. After the administration of thyroxin or of iodine the electric conductivity and potential of the tissues was increased.

When the thyroid hormone was added to the protein fraction, prepared and oxidized by the methods described in Chapter 26, the percentage of short wave emissions was in every instance increased. This could well indicate the mechanism by which the thyroid hormone exerts its power. Likewise the addition of the thyroid hormone to the lipoid fraction or to a suspension of autosynthetic cells caused an increase in the short wave radiation. When Lugol's solution was added, however, in addition to the thyroid hormone, then the thyroid hormone was

not able to cause an increase in the percentage of short wave radiation. Here may well be a physical explanation for the action of Lugol's solution.

Measurements of wave emissions from the exposed brains of rabbits and of dogs under anesthesia were made and short wave and infra-red radiations were found to be present during life and to cease at death. It was found that the thyroid hormone first diminished the radiation but that later the radiation was increased. This corresponds to the physiological action of the thyroid hormone.

To what does the thyroid gland owe its power of shifting the wavelengths of the emitted radiations toward the short wave field? We believe that this is directly related to the effect of the thyroid hormone upon nitrogen metabolism. The effect of feeding thyroid extract to animals is "as if protein oxidation had been stimulated." "The protein is rapidly oxidized. There is an increased consumption of oxygen and production of CO₂ and nitrogen excretion is increased."¹

We may then sum up this consideration of the brain-thyroid gland collaboration in shifting the short wave radiation of the brain as follows:

- (a) The thyroid hormone specifically increases the percentage of short wave radiation.
- (b) This increase in short wave radiation is due to the effect of the thyroid hormone on nitrogen metabolism.
- (c) As the thyroid hormone shifts the wave emissions toward the short or powerful end of the spectrum, and as the brain and nervous tissue are especially affected by the thyroid hormone, it would appear to follow that the brain and other units of the nervous system are speeded by the thyroid hormone.
- (d) Man has a relatively larger thyroid gland than any other animal, and greater mental, emotional, and physical activity. He owes these characteristics to the relatively large development of the brain, which, collaborating with the thyroid gland, produces the required amount of powerful short wave radiation.

THE EFFECT OF THE THYROID HORMONE UPON THE
ADRENAL GLAND AND THE ADRENAL-
SYMPATHETIC SYSTEM

There is every reason to believe that the thyroid hormone exerts an effect upon the nerve cells in the adrenal gland and

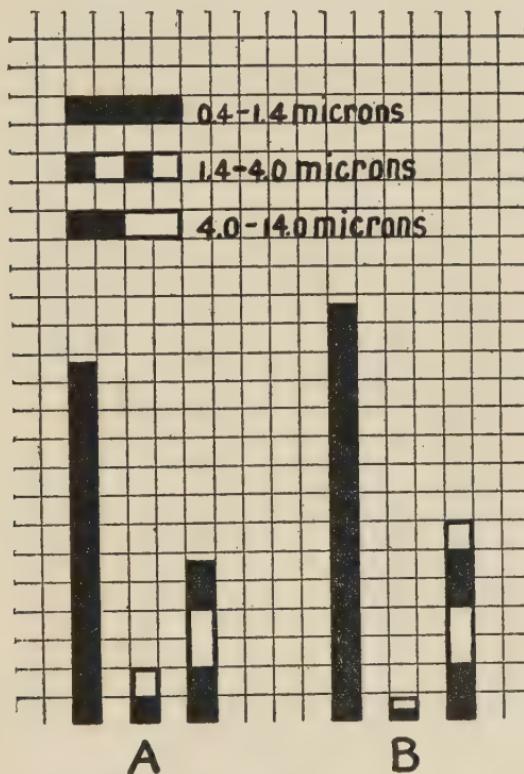


FIGURE 36. Increase in percentage of short wave radiation due to thyroxine. Radiations of short, medium and longer wavelengths produced by the oxidation of proteins; A, without and B, with thyroxine.

on the ganglion cells throughout the entire sympathetic nervous system, increasing the commanding short wave radiation, hence charging up the ganglion cells of the entire sympathetic-nervous system. This charge-up accordingly affects every tissue, every organ of the whole cerebro-spinal-adrenal-sympathetic system. Since the comprehensive nervous system controls all the rest of

the body, the organ that governs the amount of the commanding short wave radiation commands the control of the organism.

Perhaps the most characteristic inheritance in the case of

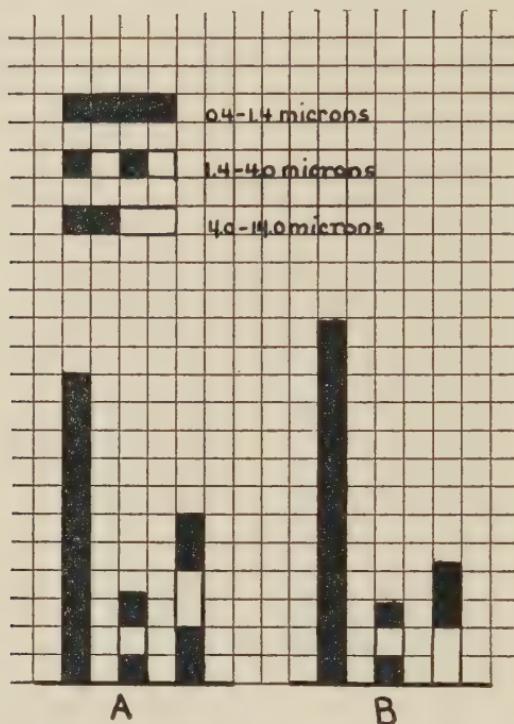


FIGURE 37. Increase in percentage of short wave radiation due to thyroxine. Radiations of short, medium and longer wavelengths produced by the oxidation of autosynthetic cells; A, without and B, with thyroxine.

man is the shift of the energy production of the spectrum. From these points of view, man could not have risen in power as he has done without a means of shifting this energy distribution, that is, without the thyroid gland. This conception explains not only the incidence but the symptoms and cure of hyperthyroidism.

From these considerations, it is clear that it is essential that the thyroid gland build up a nitrogenous compound of iodine. It

indicates that the specific action of the thyroid hormone requires the nitrogen fraction, just as explosives require the nitrogen fraction to supply the intense heat emission. This nitrogen fraction acts like a fulminate and when added to proteins causes an increase in the preponderance of the powerful short wave radiation. (Figs. 36, 37.)

From these premises, we may think of the thyroid gland as the governor of short wave radiation. The governor of short wave radiation by that fact would become the controller of the organism. It would confer the power of control upon the brain and upon all nerve ganglia and nerve tissue. The thyroid hormone would have similar effects on cells everywhere in the organism for every cell is constructed on the pattern of a diminutive brain, in so far as it possesses a lipoid and a protein fraction, and thyroid hormone, therefore, through its control of short wave radiation, would equally promote the activity of all cells. The thyro-iodine molecule, like other hormones, is everywhere present in the protoplasm of the organism. This principle as to the thyroid hormone harmonizes a great body of clinical facts.

In the absence of the adrenal glands, the thyroid hormone loses its specific effect. Likewise, in myxedema, adrenalin loses its specific effect.

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CHAPTER 13. *THE RÔLE OF THE ADRENAL-SYMPATHETIC COMPLEX*

THE medulla of the adrenal gland secretes adrenalin. The ganglia and nerves of the adrenal-sympathetic complex secrete sympathin. The physiologic action of adrenalin and sympathin is similar. Adrenalin causes increased metabolism, increased thyroid activity, increased blood pressure, increased pulse, increased respiration, leucocytosis, increased sweating, dilation of the pupils, diversion of the blood to the surface, lowering of the threshold at the myoneural junction and inhibition of the digestive and procreative processes. Adrenalin causes an immediate increase in the conductivity and the temperature of the brain and a decrease in the conductivity and temperature of all the other organs of the body.

Of no less significance are the facts that adrenalin causes hyperchromatism and later chromatolysis of the brain cells just as do emotion, injury, exertion, infection; and that when the adrenal glands are removed, the brain cells rapidly degenerate, the animal rapidly loses the power to fabricate heat, and muscular and mental action; and death follows.

Of especial importance are our experiments upon the effect of adrenalin upon the production of visible light generated by the rapid oxidation of the proteins of the various organs of the body as described in Chapter 26. If adrenalin is added to the protein solution, the oxidation is so speeded that the light is much brighter—is increased by about $33\frac{1}{3}$ per cent, and moreover, the percentage of short wave radiation is markedly increased. Here is final and definite proof that the speeding up of oxidation causes a great increase in the percentage of short

wave radiation, hence a corresponding increase in the chemical and electrical properties of protoplasm. (Figs. 38, 39.)

We know that the adrenal glands collaborate with the thyroid gland for, when the adrenal glands are excised, not only does the animal enter a state of prostration but the emission of

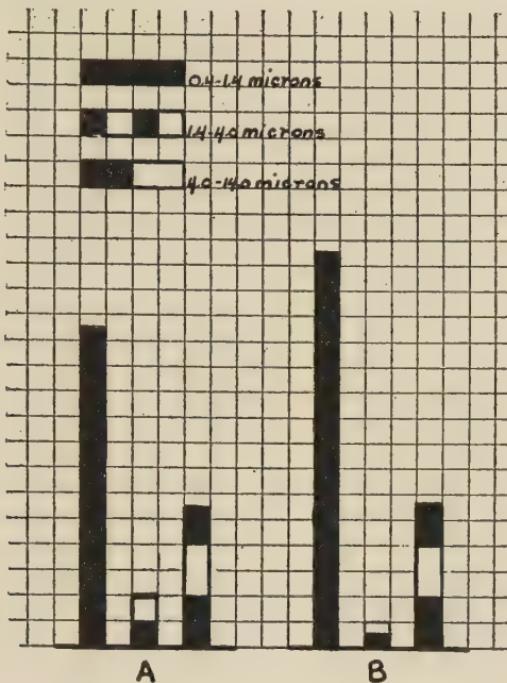


FIGURE 38. Increase in percentage of short wave radiation due to adrenalin. Radiations of short, medium and longer wavelengths produced by the oxidation of proteins; A, without and B, with adrenalin.

short wave radiance is decreased. When there is adrenal deficiency the thyroid is not able to effect short wave radiance.

On the other hand, when there is an excess of adrenalin, there is an increased output of short wave radiance. Therefore, both the thyroid and the adrenal gland contribute an organic nitrogenous chemical compound continuously to the brain, causing the rate of the power-giving radiation to vary adaptively.

The infinitesimal release of radiant and electric energy in the retina of the eye and in the nerve endings which produce the

sense of taste, touch and smell, as by a trigger action mediated by the brain, releases vast amounts of muscular energy, moving the animal in this way or that, at this speed or that. The oak requires no thyroid or adrenal gland because it needs only to grow and to maintain its vertical position. The power of command is conferred by the short wave radiance which, in turn,

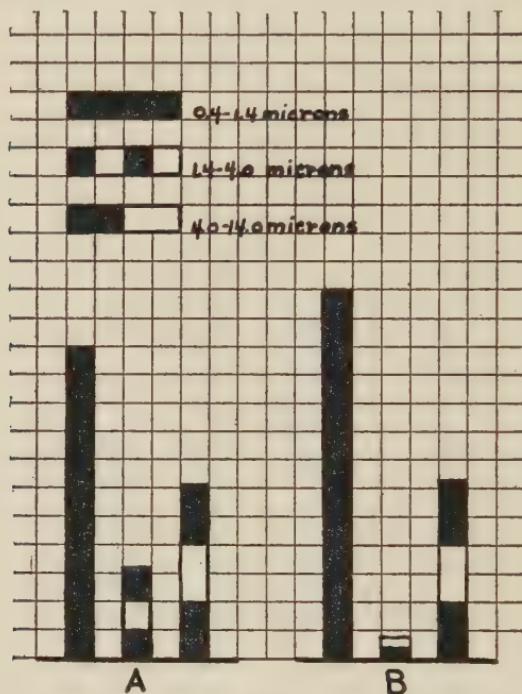


FIGURE 39. Increase in percentage of short wave radiation due to adrenalin. Radiations of short, medium and longer wavelengths produced by the oxidation of autosynthetic cells; A, without and B, with adrenalin.

commands the chemical reactions which build up the nitrogen-group whose combustion generates the short wavelength. The process then becomes that of an automatic mechanism.

Now an entire animal is a recapitulation of a single cell. In the single cell, we have proteins and lipoids. It is the nitrogen group—the proteins—that have the highest combustion. The leader, the primer, of this combustion in each cell of the organ-

ism is the thyroid hormone molecule, a compound containing the iodine and nitrogen fraction which, when in combination with protein, makes the protein easily combustible, just as fulminates render explosives more combustible. So when the highest fulminate, adrenalin, comes in contact with proteins, already supplied with the thyroid hormone, an even sharper combustion occurs. No other drug, no other hormone, has this specific effect upon protoplasm.

Adrenalin has the unique power of inducing a rapid, almost explosive development of energy in the absence of atmospheric oxygen. This was shown by experiments in which animals killed by anesthetics, asphyxia, etc., could be resuscitated within a period of six minutes or less for adult animals, and ten, or even fifteen minutes or less for young animals by the injection of adrenalin and artificial respiration.¹ During the inanimate period, oxidation had ceased. The injection of adrenalin into the blood stream or heart produced a violent anaerobic oxidation which resulted in an immediate re-animation of the animal so that immediately the animal became able to walk about the room normally. This means that adrenalin is especially adapted for the production of anaerobic oxidation in compounds in the state in which they are built up in protoplasm. It would therefore follow that adrenalin would be secreted adaptively in large quantities to meet emergencies.^{2, 3} The common emergencies among animals are those of the strong emotions, physical injury, hemorrhage, asphyxia, cold, infection. All of these emergency requirements of an animal specifically cause an increased output of adrenalin.

Adrenalin has no power of producing or of accelerating oxidation of wood or coal or oil or gasoline in the non-living state. Adrenalin has the power of inducing anaerobic oxidation at the speed of explosion only in the living.

It is exactly this emergency function that precipitates the crises of hyperthyroidism and, as one would expect, the injection of adrenalin itself into a patient with hyperthyroidism will produce an overwhelming explosive action which may even cause almost immediate death. Such fatalities occurred in the early use of adrenalin before its dangerous effects were known. As further evidence, the powerful anaerobic explosive action of

adrenalin in collaboration with thyroxin is seen in the fact that the symptoms of hyperthyroidism are essentially the same as the symptoms produced when the adrenal-sympathetic complex is stimulated.

The secretion of the sympathetic ganglia and of the sympathetic nerves themselves was first discovered by Elliott⁴ who demonstrated that the effects of the injection of this secretion were identical with the effects of adrenalin. This would suggest the reason for the development of the adrenal medulla with its great capacity for producing adrenalin as an anaerobic oxidizing agent to supplement the action of the secretion of the sympathetic complex itself.

It is obvious that the production within the sympathetic ganglia and the sympathetic nerves of an agent for the production of anaerobic oxidation could not alone and of itself, whatever may be its dimensions, equal the effects of adrenalin which is secreted through the shortest possible route directly into the vena cava and thence distributed to the entire circulation of the body.

Dr. D. P. Quiring of the Cleveland Clinic discovered a significant anatomical characteristic in the adrenal glands of the lion and tiger, an equipment which would speed up still more the action of adrenalin. He found that the medulla was surrounded by a sheath of smooth muscle fiber. This would be under the control of the nervous system and presumably would adaptively press upon the medulla in order to speed the ejection of adrenalin out of the medulla and into the circulation.

What then is the peculiar advantage to an animal of speeding up the anaerobic oxidation to such a rate that it almost resembles that of an explosion? One may suggest as a parallel the internal combustion engine, where the speed of oxidation induces rapid explosions which turn the engine, which in turn speeds electrical generators, the electricity thus generated moving the train or doing whatever work is required.

Anaerobic oxidation of the nitrogen-group is seen particularly in the high explosives in which through chemical manipulation an atom of nascent oxygen is placed contiguous to the carbon atoms and no atmospheric oxygen is used. Theoretically one would suppose that if adrenalin in an animal has the power

of speeding the rate of anaerobic oxidation, then the resultant intensive oxidation would produce shorter wavelengths and the shorter wavelengths would generate a greater amount of electric energy; a greater amount of electric energy would empower the animal to perform at a greater speed, and with greater power. Nor are we without evidence that rapid oxidation has this effect upon the resultant wavelength for, as already stated, it is a well known fact that when high explosives are detonated the resultant wavelength is shortened.

We have already cited the closer analogy to the anaerobic explosive action of oxidation in living protoplasm seen in the oxidation of the protein fractions derived from animal tissues and have shown that the addition of adrenalin to the protein fraction shifted the resultant radiation toward the shorter wavelengths. In our experiments we were using a building stone of living material in the form of the protein fraction. We introduced nascent oxygen in the hypochlorite of calcium to correspond with the nascent oxygen in living protoplasm. We added adrenalin which increased the speed of oxidation so that a higher temperature was produced and radiations of a shorter wavelength were emitted.

Another group of facts adds weight to this assumption as to the rôle of the adrenal-sympathetic complex in stimulating anaerobic oxidation. If the intravenous injection of adrenalin is preceded by the administration of a large dose of morphine, the effect of the adrenalin on the animal will be in inverse relation to the depth of the narcotization. The significance of this observation lies in the fact that under deep narcotization with morphine the effect of trauma, of surgical operation, of stimulation of the special senses of taste, hearing, sight, smell and the pain sense, are correspondingly diminished. Moreover, in our biophysical laboratory we have shown by measurements of the electric conductivity, electric potential and electric capacity of normal and narcotized animals that morphine is an antagonist to adrenalin. Moreover, the effect of adrenalin injection is diminished by nitrous oxid anesthesia and we know that under nitrous oxid anesthesia the power of producing energy is lost.

One can readily see that whether the initial stimulation be from the special senses of sight, hearing, taste, touch or smell

which would result in an emotional discharge of energy throughout the organism, or whether it be a stimulation from pain, the defense stimulation against infection, foreign proteins, etc., or whether the stimulating agent be asphyxia or hemorrhage, the great resultant stimulation of the adrenal-sympathetic complex would be in direct relation to the size and capacity of the lungs and vascular system and to the weight of the heart. That this is the case is shown by our findings in animals in which the capacity of the lungs and heart was in direct relation to the size and complexity of the adrenal-sympathetic system. (Fig. 40.)

The rôle of the adrenal-sympathetic complex as the controller of the rate of anaerobic oxidation is peculiarly supported in the Clinic by the effect of denervation of the adrenal glands. I refer to certain diseases such as hyperthyroidism, neurocirculatory asthenia, etc. These diseases are specifically ameliorated or cured by denervation of the adrenal glands. If they are cured by denervation, then the adrenal-sympathetic complex, through a pathologic activity, must have caused these diseases. This was the theoretic basis for projecting the operation of denervation of the adrenal glands.

We can now see by what mechanism a steadily increased secretion of the adrenal-sympathetic complex would cause an increased percentage in short wave radiation. This increased secretion of the adrenal-sympathetic complex, in turn, would cause an increased electric charge in the protoplasm of the various organs and tissues of the body, particularly of the brain and nervous tissue. That such an increased activity actually occurs is proven by the mental and emotional activity, the nervousness, the tachycardia, the digestive disturbances, sweating, tremors, etc., which are characteristic of these diseases and the disappearance of all of these symptoms following denervation of the adrenal glands.

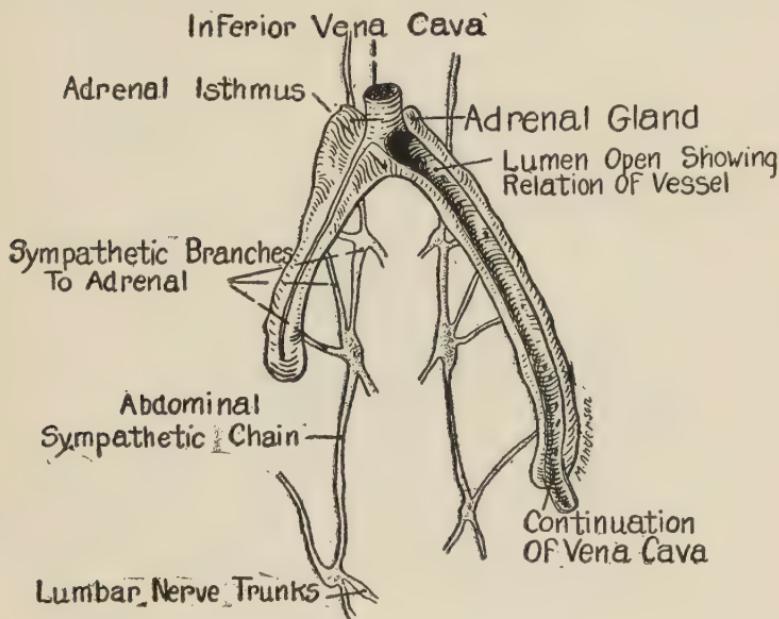
In the course of our studies on the effects of denervation of the adrenal glands and division of the splanchnic nerves, the following physiologic facts emerged: First, if the splanchnic major nerve is picked up gently between the thumb and finger and then manipulated, the blood pressure mounts with such great rapidity that it may even double itself. Second, when the



FIGURE 40. Comparative sizes of the trachea (A), Heart (B) and Adrenals (C), of the alligator (a) and tiger (b)

splanchnic nerve is divided, this acquired blood pressure falls rapidly. These two physiologic facts afford a suggestion as to a factor in the genesis and treatment of essential hypertension.

In this and the preceding chapter we have endeavored to describe the rôles of the thyroid gland and of the adrenal-sympathetic system in physical terms. The action of each upon



Alligator

FIGURE 41. The adrenal sympathetic complex of the alligator.

the biophysical system can be explained in physical terms. Each acts upon the biophysical mechanism by increasing the speed of oxidation. Increase of the speed of oxidation increases short wave radiation. Increase in short wave radiation changes the electric status of protoplasm. The thyroid hormone and adrenalin each play a specific rôle, yet their activities are correlated. Upon the relative activities of these two parts of the energy or kinetic system depends the state of activity of the species and of the individual. (Figs. 41-43.)

Anaerobic oxidation governed by adrenalin empowers the animal with a wider range of emergency response, and anaerobic oxidation supplements the oxidation supplied by the lungs

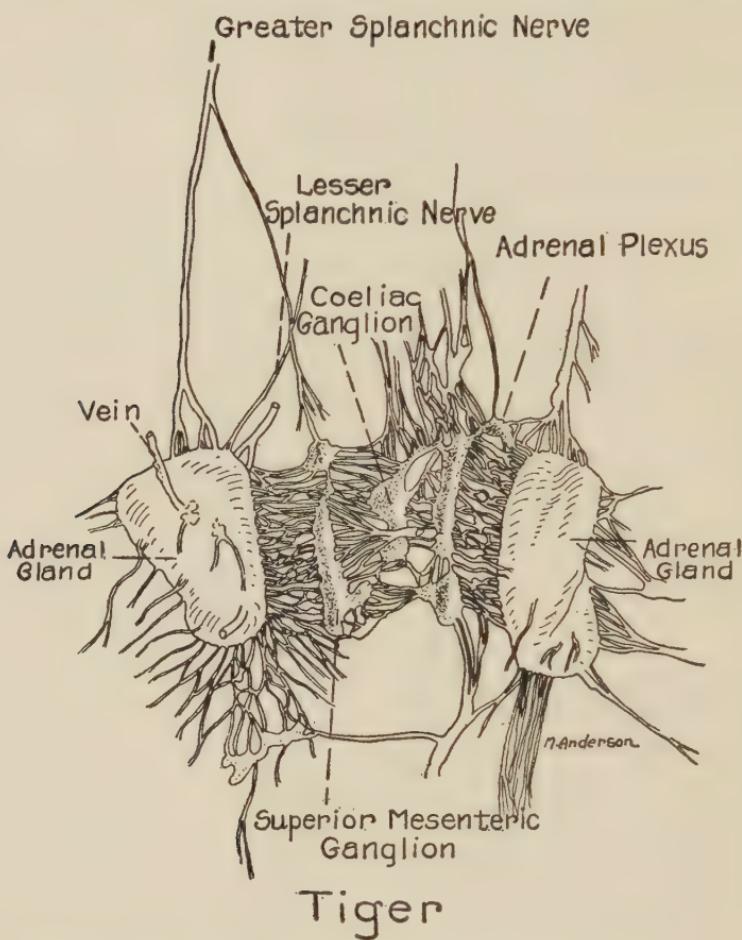


FIGURE 42. The adrenal sympathetic complex of the tiger.

and thus confers upon the animal a wider range of output of energy. From this point of view, it would seem that the size of the lungs and the heart and the blood vessels would be related to the size of the adrenal-sympathetic complex, as they are.

The commanding power of the brain is the result of the power of the short wave radiation which it generates. The short

wave radiation is due especially to the combustion of proteins; the combustion of the proteins is facilitated by the thyroid and the adrenal hormones. The adrenal gland brings to protein something whose effect is like that of a fulminate. A fulminate is an agent that is exceedingly sensitive to physical disturbance,

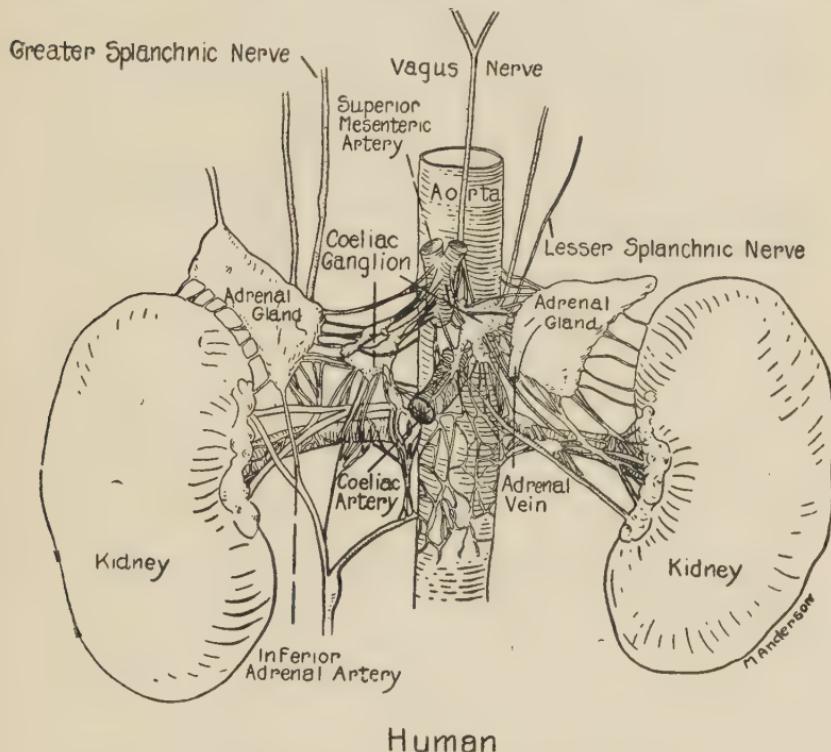


FIGURE 43. The adrenal sympathetic complex of man.

and when it is fired there is emitted short wave radiation, and a high temperature and great chemical activity are produced. Adrenalin behaves in that manner, as does thyroxin, but the latter is less sensitive. The brain, however, is an organ which requires a continuous stream of organic molecules from various sources to keep the "pyre" renewed, which is the same as saying that the brain is forever hungry and is forever being fed. The adrenal gland, the thyroid gland, and the liver, together with the processes of digestion, continually provide protoplasm

with molecular building material, thereby effecting fractional and progressive synthesis. The only example of the synthesis of entire cells is the union of the male with the female sex cell. But after the two sex cells have combined and development has been initiated the growing fetus becomes the seat of fractional syntheses produced by the products of the adrenal glands, the thyroid gland, the liver, the hypophysis, the sex cells, as well as by those from the digestive system. Growth of the fetus—growth of protoplasm—is a progressive synthesis.

Thus what is so perfectly accomplished by the ovum and the sperm in conjugation, is to a lesser degree accomplished by other glands that build up certain special molecules which complete a structure or a function.

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CHAPTER 14. *THE RÔLE OF THE LIVER AND THE ADRENAL CORTEX*

ANY theory competent to explain living processes in an animal organism must find a place for the characteristic function of every organ of the organism. Of course the obvious functions of the heart, lungs and the blood are not included in this discussion. But there are three organs, excisions of which overwhelmingly depress the organism and cause death, namely, the brain, the liver and the cortex of the adrenal gland. It is well, therefore, to consider the rôles of these three organs in an organism which we assume is operated by electric and radiant energy. The rôle of the brain is obvious but the rôle of the liver and of the adrenal cortex are enshrouded in mystery.

We are therefore introducing this theoretical chapter for the purpose of utilizing the known facts concerning the liver and the adrenal cortex in order to see how these vital organs can be fitted into the general scheme which we are presenting regarding oxidation, radiation, electricity and the living state. First of all, as reported in Chapter 1 we found long ago that when the liver is excised the organism fails rapidly and during that period of failure the interference with the normal processes of the body is somewhat similar to that which ensues when the adrenal glands are excised. There is an irremediable, progressive loss of energy—loss of muscular, mental and emotional activity ending in dissolution in a few hours.

Cytological studies of the brain have shown that after excision of the liver the brain cells show rapid morphological changes with a diminution of the differential stainability of the nucleus and cytoplasm. (Fig. 44.) In the brain there is

also a progressive diminution of the electric potential and the temperature of the brain (Fig. 45), and the electric conductivity also is progressively diminished. No means has been found for preventing these fundamental changes in the brain after removal of the liver—blood transfusion does not prevent them, saline infusions do not prevent them, the administration of glucose does not prevent them (Fig. 46), that is, nothing can

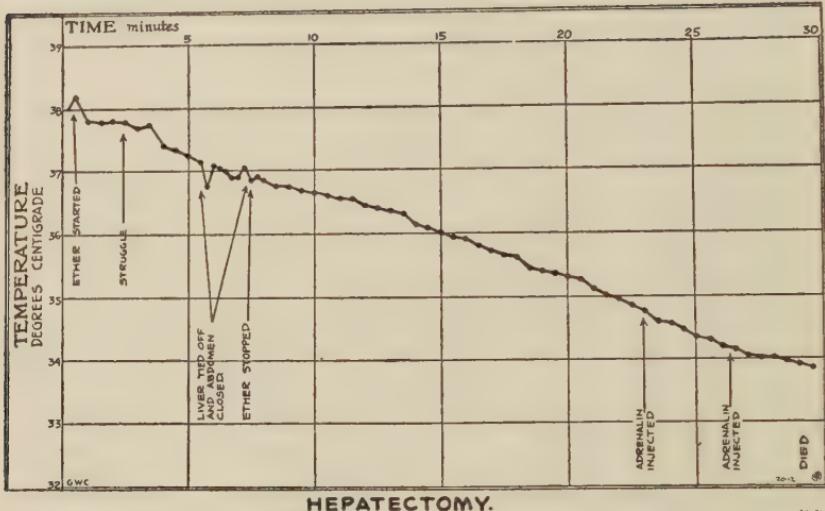
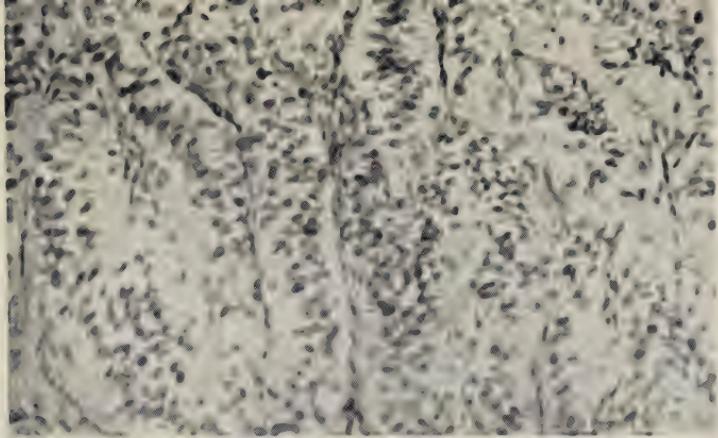


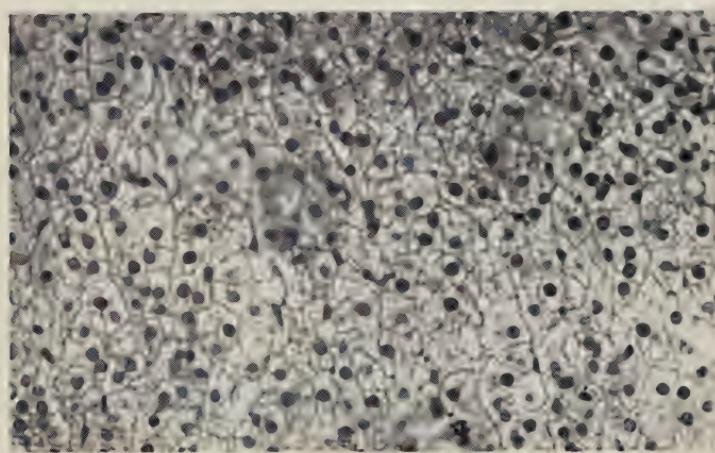
FIGURE 45. Effect of hepatectomy on the temperature of the brain. Note the lack of response to the injection of adrenalin.

prevent death and dissolution. Not only the brain but also the adrenal cortex is affected by removal of the liver. The cells of the adrenal cortex show morphological changes, they lose their differential stainability (Fig. 47), they lose their electric potential. Therefore the liver maintains a function which is essential to the life and activity of the cells of the brain and adrenal cortex. The excision of the liver does not affect any other muscle, organ, or tissue of the body, only the cells of the brain and the cells of the adrenal cortex, and this tells us that there is a vital relationship between these three organs.

Let us turn now to the adrenal cortex. We can omit discussion here of the function of the adrenal medulla because life can go on without it. When the adrenal glands are completely



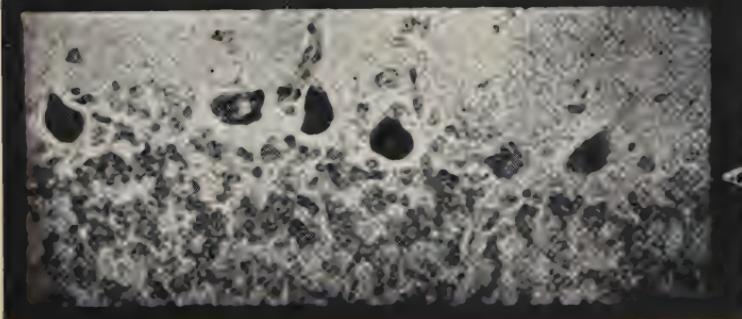
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A

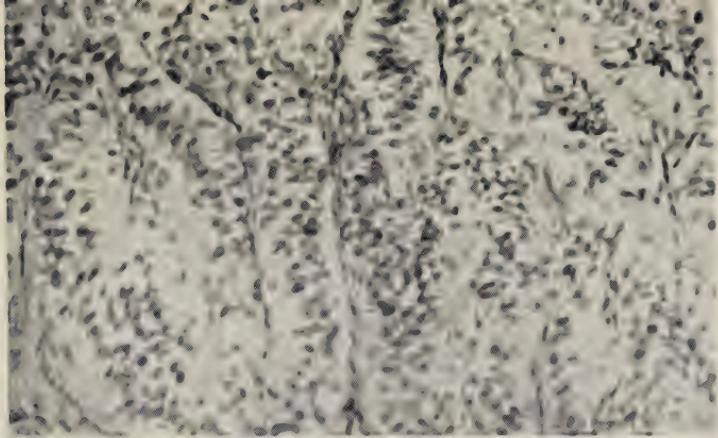


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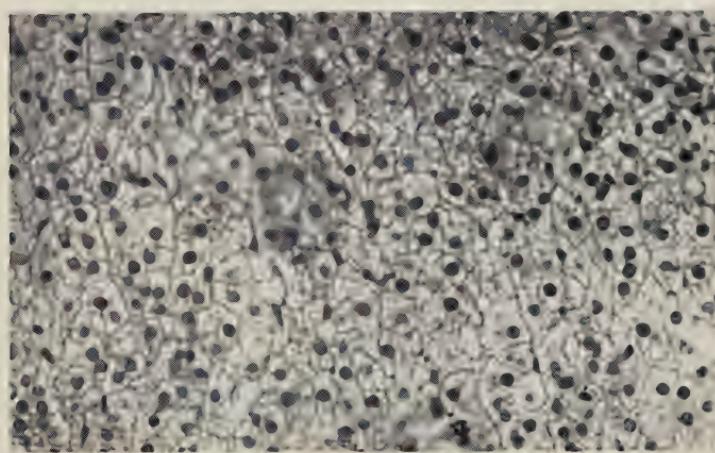


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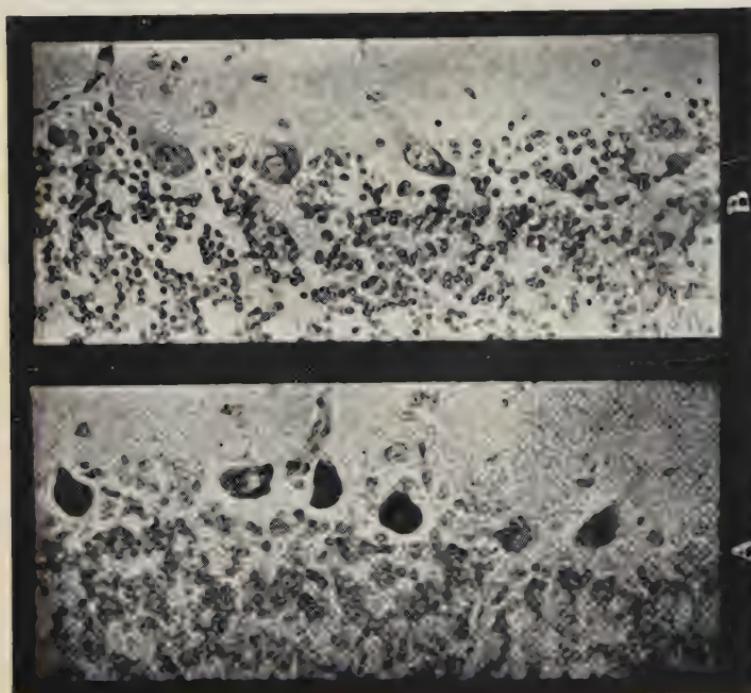
FIGURE 44. Effect of hepatectomy on the cerebellum.
A, section of normal cerebellum; B, section of cerebellum
of an animal in which a hepatectomy had been performed.
(From photomicrographs X 310)



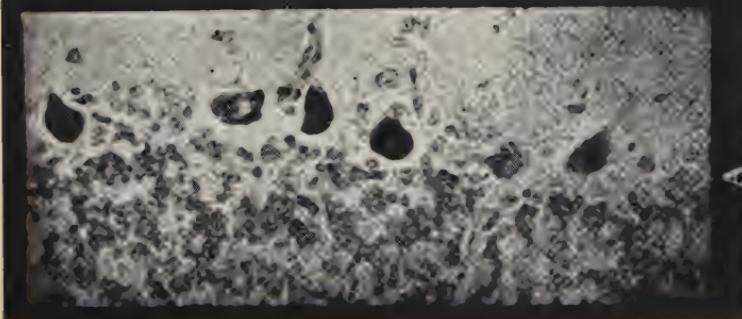
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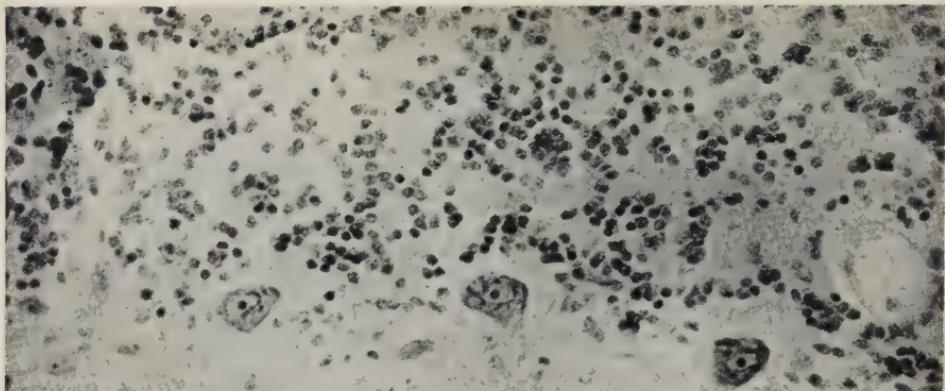


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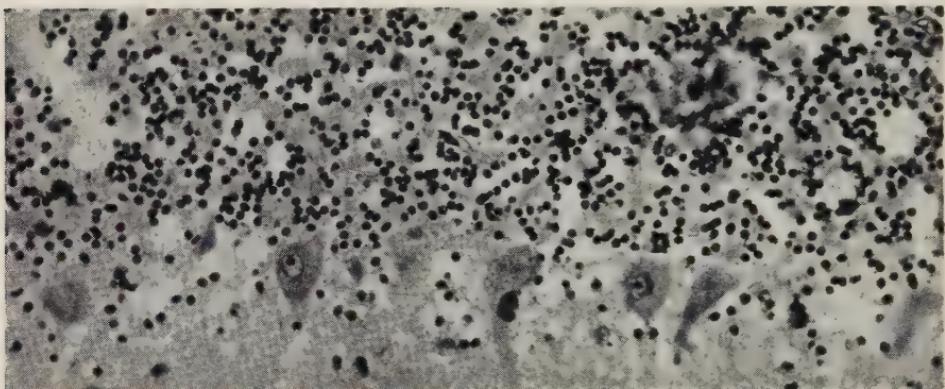


A

FIGURE 45. Effect of hepatectomy on the adrenal cortex. A, Section of normal adrenal; B, section of adrenal after hepatectomy. (From photomicrographs X 310)

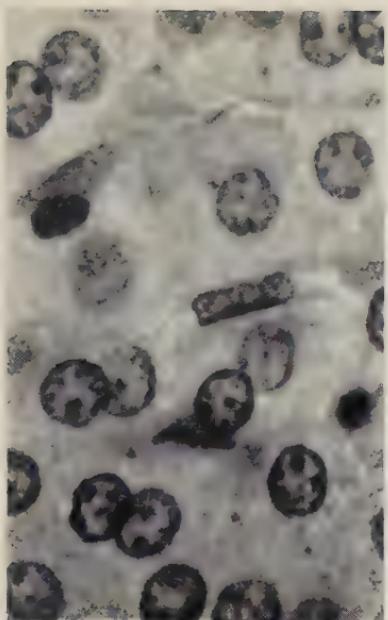


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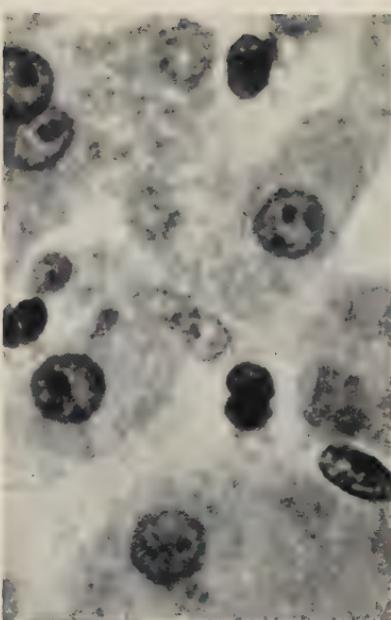


B

FIGURE 48. The effect of adrenalectomy on the brain. A, Section of normal cerebellum; B, Section of cerebellum after adrenalectomy. (From photomicrographs X 310)



A



B

FIGURE 49. Effect of adrenalectomy on the liver. A, Section of normal liver; B, Section of liver after double adrenalectomy. (From photomicrographs X 1640)

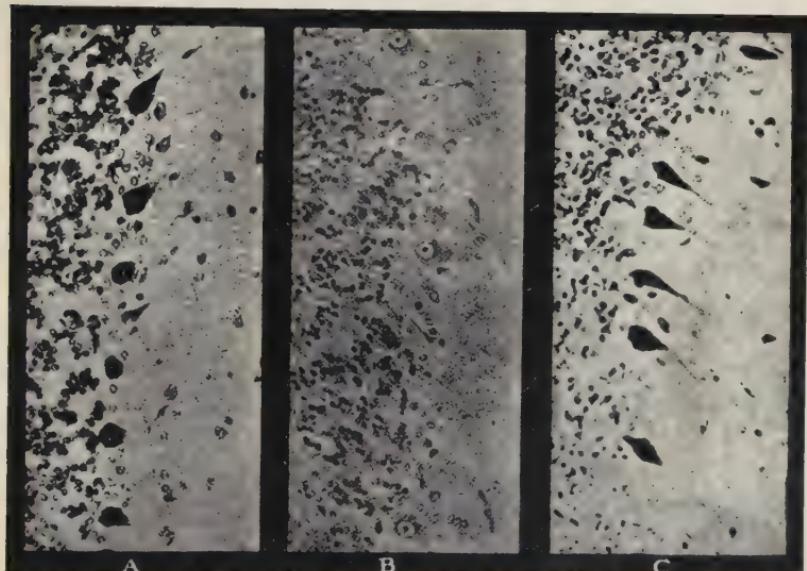


FIGURE 51. The restorative effect of sleep on the brain cells. A, Section of cerebellum of a normal animal; B, Section of cerebellum of an animal in which a state of acidosis had been induced; C, Section of cerebellum of an animal which had slept for a prolonged period after the induction of acidosis.

removed there is almost as overwhelming a change in the brain and the liver (Figs. 48–50) as that which occurs in the brain and the adrenal cortex when the liver is removed, but in this case, life can be prolonged by the administration of a cortical

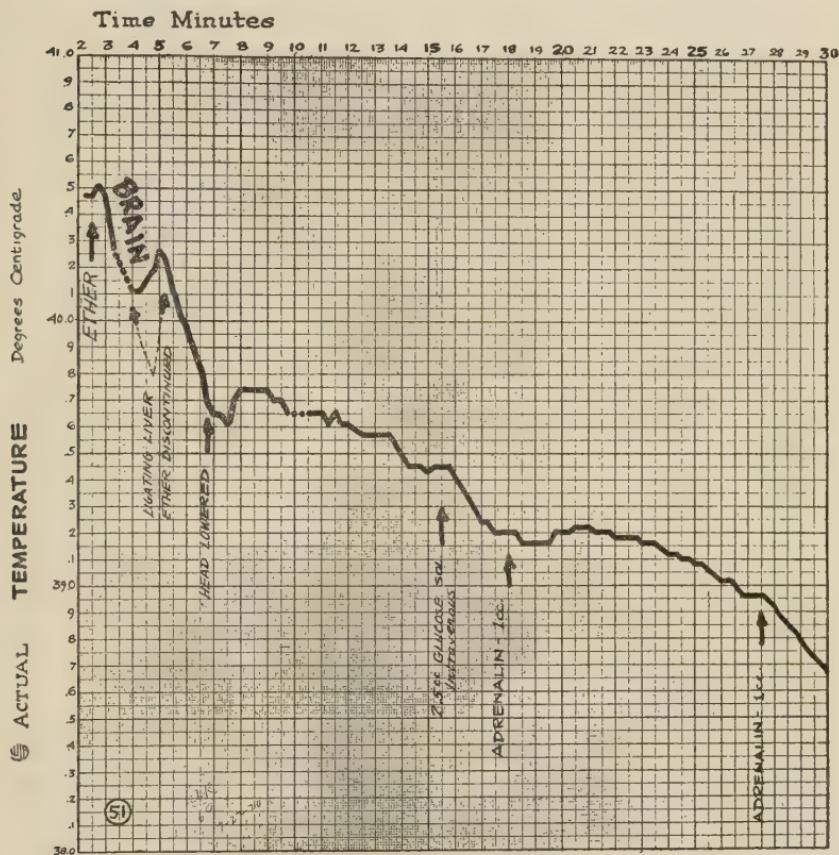


FIGURE 46. The lack of effect of the injection of glucose and of adrenalin in a hepatectomized animal.

extract—cortin or eschatin—by the administration also of large amounts of sodium chloride.

For a moment let us turn to a consideration of the contrasting effects of removal of the brain. When the brain is removed there is an immediate dramatic cessation of the activity of the body but we found that when artificial respiration and a normal

circulation were maintained we were able to keep an animal living for as long as 12 hours and we did not find in the cells of the liver, or of the adrenal cortex, any changes in their morphology or in the differential stainability such as were seen in the brain cells and in the cells of the adrenal cortex when the liver was excised or in the cells of the brain and of the liver when the adrenal cortex was excised. No hormone and no electrolyte or anything else will substitute for the brain excepting a normal circulation and normal respiration; but with a

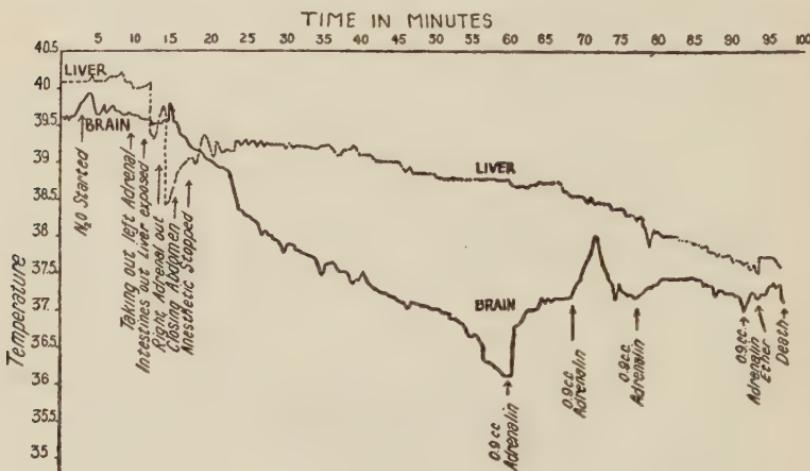


FIGURE 50. Effect of adrenalectomy on the temperature of the brain. Note marked effect of the injection of adrenalin.

normal circulation and normal respiration the functions of other organs proceed normally.

These outstanding facts concerning this triad of essential organs of the body, the most responsive organs of the body, suggest that the function of the brain is a pure energy function produced by the release of radiant and electric energy while the liver and the adrenal cortex exercise a chemical and not an energy function.

Let us first consider what the adrenal cortex does not do. First, it does not generate energy. Second, the hormone of the adrenal cortex is a lipoid structure. And third, the administration of this labile hormone of the adrenal cortex in the form of

eschatin or cortin neither increases nor decreases the metabolism of the organism. It does not increase and does not decrease the function of the normal brain or of any other organ. The cortex of the adrenal gland has no function which has to do with the control of the function of any other organ. On the other hand the mass of the adrenal cortex in the human being is increased in pregnancy, in the presence of infection and in fetal life. Moreover, the size of the adrenal cortex in relation to the medulla and in relation to body weight varies in the various species of animals.

What conception of the rôle of the adrenal cortex will harmonize all these various facts? We postulate that the rôle of the adrenal cortex is that of secreting and throwing into the blood stream the lipoid molecules which are essential in the structure of the delicate composition of the semipermeable membranes. These are lipoid membranes and they are constantly being broken down in activity and constantly being rebuilt, and therefore they require some source for the building stones or lipoid molecules. Clearly enough the brain cells have no factor within themselves whereby such molecules are generated, because the brain cells have the following characteristics which make such a function impossible:

They have within themselves no neutral factor, no buffer substance; they store nothing whatsoever, their function being purely the production of energy. Therefore it is clear that the brain can not influence its own semipermeable membranes, can not construct its own special lipoids for conduction and for insulation of the patterns of action. These compounds must be built up elsewhere in the body and taken to the brain and there fabricated into membranes. As the liver is an organ with a very high functional activity its semipermeable membranes also are rapidly broken down and have to be replaced, and it also may depend upon some other organ for the essential lipoid molecules. We postulate therefore that these molecules for the semipermeable membranes of the cells of the body might well be supplied by the adrenal cortex. The liver in part and the ductless glands in part maintain the structure of the cells. The cell as a whole is made up of the membranes of the nucleus and the cytoplasm of the cells which are dependent upon oxidation;

oxidation is dependent upon electrical strain; and the electrical strain is produced by changes in the concentration in the electrolytes in the cell, that is, chiefly by changes in the concentration of sodium chloride on the two sides of the film.

If the adrenal cortical hormone plays an essential rôle in the formation, replacement and maintenance of the semipermeable membranes of the cytoplasm and nucleus of the cells of the organs of the body and particularly of those organs whose cells are sensitive to the stimuli of life, then the adrenal cortex plays a vital rôle. How vital is this rôle of maintaining the semipermeable membranes is manifested by the overwhelming effect on all living things of a chemical agency which attacks the lipoid films, such as the lipoid-solvent anesthetics, chloroform and ether. These anesthetics produce their effects by changing the permeability of the films. The first effect of the increased permeability is to increase the electric potential of the cells, producing the stage of excitement; then as the membranes are destroyed further the electric potential decreases and if the anesthesia is sufficiently deep the electric potential reaches zero, oxidation ceases and the organism is dead. All of this is merely an expression of the results of changing the permeability of the semipermeable membranes. An increased permeability due to destruction of the films means that the electrolytic balance is altered and when that balance reaches equilibrium death ensues. Any substance that alters these semipermeable membranes alters oxidation, radiation, electricity and the living state.

From this point of view the adrenal cortex is just as vital a structure as is the brain or the liver or the heart or the lungs or the blood, because the organism must maintain an electric potential and the electric potential can not be maintained without the maintenance of a certain state of the semipermeable membranes. On the basis of experimental and clinical evidence we assume that these depend upon a constant supply of the molecules generated in the cortex of the adrenal glands. Other hormones are essential for the operation of the organism—the hormones of the parathyroids, of the pancreas, of the sex glands, of the pituitary gland, of the thyroid gland, of the adrenal medulla, but the reason why lack of these other hormones does

not cause immediate depression and death as in the case of the adrenal cortical hormone is that these other hormones do not relate directly to the maintenance of an electric potential, hence of oxidation, hence of radiation and the production of electrical changes. That is, their rôle is not so fundamental a rôle as is that of the hormone of the adrenal cortex.

As we have stated, the only way in which life can be maintained when the activity of the adrenal cortex is suppressed or lost is by the administration of the cortical hormone in the form of cortin or eschatin with the administration of sodium chloride. The latter helps to maintain the proper balance of electrolytes in the cell, the former to maintain the semipermeable membranes.

Thus the rôle of the adrenal cortex is vitally essential in the maintenance of a mechanism which is operated by oxidation, electrical forces and radiation.

CHAPTER 15. SLEEP

THE mystical state of remission of consciousness, called sleep, clearly is related to the operation, or rather to the cessation of operation, of the identical forces that generate and maintain the conscious state. The rhythms of sleep and consciousness are as definite as are the rhythms of batteries that become polarized and depolarized by the opening and closing of the circuit.

The batteries that operate a doorbell depend for depolarization on the resting period of the bell. In an electric battery the current carries positive ions to the negative pole and negative ions to the positive pole. As such elements are deposited upon the opposite poles a contra-electric current is generated. The contra-electric current is reinforced by each added ion until finally the contra-electric current arising from the elements deposited by the direct current becomes equal to the direct current; and thus the circuit of the battery is in equilibrium or "death." The battery is polarized. If the circuit be broken before polarization is complete, then the ions being freed from the power of the current of the circuit rebound from the poles and travel back into the solution or to the station from which the current brought them, thus restoring the electric power of the battery.

If the period of work, i. e., if the passage of electric current is short, as in a single heart-beat, then the degree of polarization is *proportionately slight*. The slight degree of polarization which results from a single heart-beat requires a proportionately short time for depolarization or sleep, i. e., the pause in the heart cycle may be regarded as its period of sleep. The heart, with its nerve mechanism, takes normally from seventy to

ninety naps a minute, and thus is kept depolarized or rested as it works.

We may suppose that the nerve cells which operate the respiratory mechanism become depolarized, or sleep, from sixteen to eighteen times per minute, and that thus the respiratory mechanism is kept depolarized or rested as it works. It would appear to be more than a mere analogy that such is the mechanism whereby prolonged consciousness unbroken by sleep leads to exhaustion and death.

The salivary glands, the intestinal nerve-muscle mechanism, the digestive glands, etc., we may suppose have alternating periods of *work and polarization*, and of *sleep and depolarization*. Regarded superficially, the functions of respiration, of circulation, of digestion, carry on as if they never rested, never slept; but their sum total of short periods of sleep is relatively as long as the total period of sleep of that part of the brain whose work creates consciousness, and therefore spends no more time than other organs in sleep, but sleeps more continuously.

As for the portion of the brain which governs conscious activity, the periods of work, and therefore of polarization of the cells that supply the electric power for consciousness, for emotion and for muscular action, are longer than the periods of work demanded by the heart, by the respiratory mechanism or by the digestive mechanism. Thus the option of evolution apparently has been to run the organism on long shifts or shorter ones.

If the changes in the nerve cells seen in fatigue from various kinds of work and from prolonged enforced consciousness are identical in appearance; if these physical changes are restored only during sleep (Fig. 51); and if the degree of cell change varies with the amount of work done at a stretch without sleep, that is, with the amount of electric energy that has originated in or traversed a given cell, then it would require more time and deeper sleep to restore the electrical balance of the cell after prolonged heavy muscular exertion than after a day of restful quiet. And this is demonstrated by experience. It would appear that the degree of exhaustion equals the time of consciousness multiplied by its intensity.

Let us now see whether this conception of sleep is consistent

with the known facts as to radiant and electric phenomena.

During sleep the consumption of oxygen, the use of which generates radiant energy, falls almost to one-half of that during the conscious state. If the electric potential bears a direct relation to oxidation, that is, if oxidation depends on electric potential, and electric potential depends on oxidation, then as polarization of the electric circuits increases, the resistance to the passage of the current increases, hence electric potential, electric conductivity, electric capacity would fall; that is to say, the animal would become correspondingly weak until finally if the current were not broken the resistance, that is, the polarization, would become equal to the current, and the animal organism would come to equilibrium or death, just as the battery of the doorbell reaches equilibrium or death when the bell is "pegged," closing the circuit continuously.

It is significant to remember that we found that in the state of stimulation the conductivity of the brain was increased and the conductivity of the liver was decreased, thus increasing the difference in potential between the positive brain and the negative liver. In insomnia this relation is reversed, that is, the conductivity of the brain is decreased below its normal level and the conductivity of the liver is increased, thus producing an increased difference in potential between the negative liver and the positive brain which would tend to reverse the currents and induce a negative phase. During sleep this relationship again tends to become reversed, the conductivity of the brain rising toward its normal level and the conductivity of the liver decreasing until the positive phase is again established.

Such a simple conception of sleep is a corollary of the simple conception that the conscious state is the active phase of an electric mechanism operated by radiant and electric energy. The essential facts are thus simply harmonized.

The only non-living energy mechanisms that have definite rhythms of activity and exhaustion are electric batteries. The locomotive, the internal combustion engine, the windmill, the waterfall do not exhibit such rhythms. Of man-made machines only electric mechanisms exhibit natural cycles of activity and rest.

As to the mechanism of animals, there are certain phenomena that may be used to test the validity of such a conception of consciousness and sleep.

First and most important is the energy—the life force itself—of the rabbit or of man. When a rabbit is kept awake, but given food and drink and physical and psychic repose excepting for the minimum required to keep it awake, the rabbit, like every other animal, inevitably dies, usually on the fourth or fifth day. The behavior of such a rabbit is paralleled by the “behavior” of a battery; that is, the rabbit and the battery gradually “run down” and finally come to a standstill—to equilibrium or death. The death of the rabbit from loss of sleep is unique. Life simply ceases; there is no gasp, no struggle. The mechanism of living has run down and has reached equilibrium. The closest attention is required to note the exact moment of the cessation of consciousness and life.

In a sick or an injured rabbit certain organs are changed more than other organs, yet the life of the other organs ends before they are ready, that is, before they of themselves have reached a state of equilibrium; but in death from loss of sleep, every organ reaches equilibrium at the same time. Energy has departed; the circuit is dead.

Moreover, in death from insomnia the electric potential, electric capacity, and electric conductivity are all decreased at the same time and the potential reaches zero. The reason is clear, for the radiant and electric energy created and maintained the electric potential and the electric capacity in the living.

The effect of insomnia upon the organism is also manifested by changes in the structure and the stainability of the cells of the brain, liver and adrenal cortex, and in the cells of no other organ.

Finally, as further evidence of the dependence of consciousness and sleep upon energy, we may cite the fact that autosynthetic cells could not be formed from the protein and lipoid fractions derived from the brains of rabbits which had been kept conscious for four or five days until by polarization equilibrium or death was reached; that is to say, the energy of the organic building stones of the brain had been released to the extent

that the protein and lipoid fractions of the brains of rabbits which had died from insomnia could not form autosynthetic cells.

If even so simple an electric energy mechanism as a battery becomes polarized by work and becomes depolarized when the circuit is open, how much more would the infinitely delicate and complicated electric mechanism of an animal do the same.

Sleep—depolarization, being a negative phase, can not be compelled. Consciousness—polarization, being a positive phase, can be compelled, even unto death. Normal man can not sleep unto death; he can sleep only to restoration—no more.

THE ARGUMENT

PART THREE

THE TEST OF THE THEORY

CHAPTER 16. *RADIO-ELECTRIC PHYSIOLOGY AND PATHOLOGY*

IT would appear that the specific form of energy that builds and operates protoplasm is radiant and electric energy; that radiant and electric energy is released by oxidation; that radiant and electric energy fabricates growth. It follows, therefore, that excitation, depression and death can be measured in physical terms.

When the electric potential is maintained at so high a level as to use up the factors of safety as, for example, in injury, emotion, infection, hyperthyroidism and hyperadrenalinism, then disease, exhaustion or death follow.

When the electric potential of one of the master organs—the brain, the liver, the thyroid gland or the adrenal cortex—is depressed to a degree beyond which compensation is impossible, the factor of safety is lost, and disease and ultimate death follow.

Depression and death follow asphyxia, hemorrhage, excessive cold, protracted insomnia, excessive doses of anesthetics, narcotics, or cyanides. The extent of the depression produced by each of these can be estimated accurately by measurement of the electric potential. Electricity is the energy that drives the organism. The electric potential is an important factor in the distribution of electric energy in protoplasm. The symptoms of excitation, depression and death are the external manifestation of the changes in the electric potential of the organism.

When a pathologist examines the tissues of the dead, he finds there are histological changes in the brain, lungs, heart, kidneys, liver, spleen, pancreas—they may all show changes. If the ex-

amination were made exhaustively, changes would be found wherever there is protoplasm. Autopsies show no specific changes and the pathologist in reality does little more than to say that the patient is dead, that is, he gives no information whatever as to the mechanism that has led to the changes in the protoplasm of the cells that are seen at death. The protoplasmic changes seen under the microscope are analogous to the condition of the body as a whole after death. The microscopic picture is that of a change in architecture, but it gives no information as to the forces that caused the change. The important thing for us to know is the nature of the physical forces and the physical conditions which underlie the changes that are observed by the pathologist after death.

It is of very little use for anyone to say a patient is dead; and it is not of much more use for the pathologist to say that the cells are dead. It would be a very great help to us, however, if we were able to discover the forces that have gone wrong, to discover the forces that have destroyed the cell, and to realize that in the normal man as in the soldier exhausted by emotion, exertion, injury and infection, any one of these influences may change electric potential, oxidation and reduction, and the concentration of the electrolytes inside and outside the cells and also the protein and lipoid molecules within the cell. When we consider that these vital changes must be molecular in dimension and not gross as in the microscopic picture of organs and cells, then we shall begin to visualize the influences that reduce and break up the molecular structure and arrangement in the lipoids, in the proteins, and in the cell itself. The only thing that is of importance to the surgeon or the physician is to be able to estimate properly the rôle that each one of these adverse influences plays and to know how to prevent them.

Illustrative examples of exaltation, depression and failure of function caused by pathologic physiology of the brain-thyroid-adrenal-sympathetic system in fetal life, in infancy, in adolescence, in the adult period, and in senescence will now be given.

We shall also interpret in terms of electric potential the results of physical injury, infection, stimulants, asphyxia, anesthetics, narcotics, and hemorrhage. In other words, we shall test in the clinic the science of radio-electric pathology.

FETAL LIFE, INFANCY, AND EARLY CHILDHOOD

If a mother has a deficiency of the thyroid hormone, goiter may appear in the fetus as the sole evidence of deficiency. In other instances there may be such a deficiency of the thyroid hormone in the mother and the fetus that the growth of the organs and tissues is interfered with and the child may be born a cretin. In rare instances there occurs such an increased activity in the thyroid-adrenal-sympathetic system that the child is born with exophthalmic goiter—hyperthyroidism.

In the Cyclostomata, an animal with lower order of function, hence little need of thyroid hormone, the principal need of speeding up energy is reproduction, and in these animals as already stated, the thyroid hormone enters the uterus directly by a duct. The inference from this fact would be that the thyroid hormone facilitates the genesis of radiant and electric energy and hence facilitates the growth of the fetus.

In infancy and childhood, the pathologic physiology initiated in the fetus or developed in infancy or childhood is manifested by cretinism and hypothyroidism, both of which represent a state of lowered electric potential, lowered radiant and electric energy, hence lower power of growth and function.

On the other hand, excessive activity of the thyroid-adrenal-sympathetic system brings about the genesis of excessive radiant and electric energy and hence induces excessive growth and function and differentiation, especially prominent being the precocious development of the function of the brain.

Gudernatsch's experiments on tadpoles¹ illustrate this point. He showed that when normal thyroid tissue was fed to tadpoles a precocious differentiation of the tadpole into a frog resulted. These phenomena, hypo- and hyperactivity respectively, manifested by the thyroid-adrenal-sympathetic system, we interpret as being the result of the corresponding increase or decrease in the electric potential of the affected organs, as noted in our experiments on animals in which the removal of the thyroid or the administration of the thyroid hormone specifically changed the electric potential. As has been stated the thyroid and the adrenal-sympathetic system control the rate of oxidation. The rate of oxidation controls the rate of emission of radiant energy

by the radiogens. The rate of emission of radiant energy by the radiogens governs the electric potential, and the rate of growth and functional activity.

The energy characteristics of the infant and the child, the pulse rate, respiration, the physical activity, the mental and emotional instability, the nervous tension are comparable to the state of hyperthyroidism in the adult in whom hyperthyroidism is known to be a pathologic physiology of the thyroid-adrenal-sympathetic system.

The relative weights of the adrenal and thyroid glands in fetal life, in infancy and in early childhood follow the pattern of animals in the wild state; that is, the adrenal glands are larger than the thyroid gland, and in relation to body weight, the weights of the thyroid and adrenal glands are greater in fetal life, infancy and childhood than in adult life.

The adrenal-sympathetic system exerts a powerful control over the speed of oxidation, hence over the speed of emission of radiation by the radiogens, hence of electric potential. Corresponding rhythms of emotional and muscular activity, sweating, palpitation, nervousness, crying, laughter, etc., are the characteristics of infancy and childhood.

ADOLESCENCE

Since adolescence is characterized by a rapid rate of growth and function and differentiation, one would expect to find a rapid growth of the thyroid gland itself as well as evidence of increased functional activity of the adrenal-sympathetic complex. The differentiation which is the result of the rapid development of the energy system would be seen especially in the brain, in the muscular system, in the sex glands and in the secondary sexual characteristics. The natural speeding-up during the transformation from childhood to adult life is, in a manner, comparable to the speeding up of the differentiation of the tadpole into a frog by feeding with thyroid tissue. In the adolescent and in the tadpole alike the principal factor is the thyroid hormone.

During adolescence the rate of growth of the thyroid gland by so much exceeds the rate of growth of the adrenal glands

that by the time adult age is reached, the thyroid gland is approximately twice the size of the adrenal glands.

Since the thyroid gland governs oxidation, radiation and electric potential at an even rate in contrast to the rhythmic outbursts of the adrenal glands, the behavior of the organism in adult life assumes the pattern of the thyroid, rather than the pattern of the adrenals.

On the authority of Cassan² the adrenal glands of less stable, primitive man are larger than in the more stable, civilized man.

We have already pointed out that the thyroid hormone of the mother is essential to the normal growth of the fetus and that when there is a deficiency in the amount of the thyroid hormone in infancy and childhood, growth is correspondingly diminished. In the adolescent girl also the thyroid hormone governs the growth and functional activity of an organism preparing for its prime function, namely, procreation. We would expect, therefore, that the thyroid gland in the adolescent girl would grow more rapidly than the thyroid gland of the adolescent boy, and this is a fact.

A corollary to the above statement is the fact that endemic goiter more commonly affects the adolescent girl than the adolescent boy.

A further corollary is the fact that since the thyroid gland of the adolescent girl is relatively larger than in the adolescent boy, and hence exerts a greater influence upon the adrenal-sympathetic system, the adolescent girl would be nearer to the state of hyperthyroidism than the adolescent boy. Hyperthyroidism occurs seven times as frequently in the adolescent girl as in the adolescent boy.

In adolescence the opposite state to hyperthyroidism, viz., hypothyroidism, sometimes appears. The diminished oxidation, radiation and electric potential which are present in this condition may interfere with intellectual development. The administration of the thyroid hormone will increase the metabolic rate, that is, it increases the oxidation, radiation and electric potential which are requisite for the normal function of the brain.

In this period of rapid growth and differentiation, there sometimes occurs a pathologic physiology in the sympathetic

system itself. This unique pathologic physiology owes its grotesque and dramatic manifestations to the fact that under normal conditions the sympathetic system coördinates the normal processes of growth, function, and reproduction, or the normal processes of the organism. Through influences which are not as yet understood, the adrenal-sympathetic system departs from its normal rôle of adaptive coördination and enters a state of continuous exalted activity, that is, a state of pathologic physiology.

This state is analogous to a continuous electric stimulation of this system, whereby abnormal disturbing secretions of the various ductless glands are produced—of the pituitary gland, the thyroid gland, the adrenal glands, the pancreas, the gonads. As a consequence of this pathologic physiology of the sympathetic system, there may be produced one, two, or any combination of the kinetic diseases which are characteristic of a pathologic stimulation of any part or parts of this system. Thus the following pathologic states or diseases of this system may be produced: obesity, hirsutism, amenorrhea, virilism, diabetes, hypertension, gigantism, hyperadrenalinism, hyperthyroidism. These states usually have their beginning, and often their development, in the adolescent or post-adolescent period.

The conception that one or all of these conditions are due to a pathologic physiology of the sympathetic system was put to a crucial clinical test by a surgical procedure and no other treatment. This procedure consisted in a denervation of the adrenal glands with a division of the splanchnic major and minor nerves.* On the basis that these diseases are wholly due to a pathologic activity of the sympathetic system, excluding the spontaneous increase of activity of any of the glands mentioned, the denervation would and does effect an abatement or cure of the obesity, hirsutism, hyperadrenalinism, hyperthyroidism, virilism, hypertension, etc.

ADULT LIFE

Roughly speaking, at about the age of twenty years, the brain, thyroid, adrenal-sympathetic system, pituitary and sex

* Vasomotor nerves supplying the viscera.

glands, after their turbulent passage through the fetal, childhood and adolescent periods, settle down as a smooth-working, coördinating mechanism. In the next stretch, from twenty to forty years, is carried on the routine of reproduction, work, worry, and play. The stability of this period of life is now and again disturbed by a pathologic physiology of the same thyroid-adrenal-sympathetic system, that is, hyperthyroidism, neuro-circulatory asthenia, peptic ulcer, diabetes, may occur or the even tenor of function may be interrupted by pregnancy. In pregnancy there is an actual physiological increase in the mass of the thyroid and adrenal glands and an increased physiological activity of the adrenal-sympathetic system. The increased metabolism, excitability, instability, palpitation, sweating and hunger which are present in pregnancy, attest the increased function of the thyroid-adrenal-sympathetic system.

THE FIFTH DECAENNIA

The physical and physiological preparation for reproduction that is completed during the adolescent period is demobilized between forty and fifty years of age. We shall discuss only the rôle of the thyroid gland in this demobilization. It is in this period that we see the reverse of the rapid growth and development that the thyroid gland plays in the period of adolescence.

In the adolescent and the procreative period, the pathologic physiology of the thyroid gland was similar to that of hyperthyroidism rather than of hypothyroidism. In the demobilization decade, the pathologic physiology is more frequently that of hypothyroidism rather than of hyperthyroidism. In this period there is a tendency to obesity, to mental and physical inactivity, and to a low basal metabolism which can easily be brought to normal by the administration of the thyroid hormone.

AFTER FIFTY YEARS

From the age of fifty on to senility there is a diminishing incidence of the diseases which are due to hyperactivity of the thyroid-adrenal-sympathetic system. On the other hand, from the age of fifty on, there occurs in both sexes an increasing in-

cidence of thyroid deficiency. It has been commonly thought that thyroid deficiency is associated with a tendency to increase in weight, but we now know that there are many instances of thyroid deficiency in thin people. It is becoming more and more apparent that the lassitude, the inertia, the negativity of advancing years may be dispelled in some cases by the administration of the proper amount of the thyroid hormone.

From the age of fifty on, it is worth while to be aware of the possibilities of pushing back the boundaries of colorful active life. There is evidence that in age and senility there is a lowering of the oxidation, radiation and electric potential of the organism; therefore it would be reasonable to expect that the one agent that can control oxidation, radiation and electric potential, that is, the thyroid hormone, if administered in suitable cases would tend to ameliorate the feebleness and inertia of declining years.

The driving of the organism at an abnormal speed during this period will tax not only the brain but other organs, such as the kidneys, the liver, the heart, and the blood vessels. Any-one can tell when his brain is tired because through the brain his personality is expressed, but nobody can tell when his kidneys, his heart, his sympathetic nervous system, or his liver is tired. These organs are mute and the first warning that they are tired or worn or are failing is given by the failure of their functions, and when that warning comes they may be about to be destroyed completely. The end of their life has come, and when their life comes to an end they will bear down the life of the whole man. It is these silent partners in the organism—the heart, the kidneys, the blood vessels—that must be considered during the advanced years of life. But the man can not know to what extent the factors of safety of these silent partners has been reduced.

It is here that we can take a lesson from the technique of the business man in the conduct of his affairs and have an audit made of these organs at least at yearly intervals. It is a simple matter for a physician to audit the status of these organs once a year—the organs whose breakdown, sooner or later, causes death in a high percentage of individuals. Death from such a cause, we may say, is the equivalent of bankruptcy in a business.

Now if an individual could make an audit of let us say four different departments in his business, the failure of any one of which might cause bankruptcy and the audit of which would require very little time and expenditure of very little money, then he would certainly expend that time and money. It is just as reasonable for every individual to apply that rule of business conduct to his capacity for work and to his life itself, as a means of at least deferring physical bankruptcy. If a failing condition of any of the organs listed above is discovered early enough, then a high percentage of the final disabilities and deaths due to these causes can be deferred, and, in many instances, they can be prevented altogether, so that the individuals can go on and die a natural death in old age.

When one considers the total span of life from the moment of fertilization of the ovum until death in old age, it is observed that there is a steady decrease in the rate of production of the radiant and electric energy by which growth and function are accomplished. From the time of birth on through childhood and through adolescence and maturity, the thyroid-adrenal-sympathetic system is extremely active, as may be illustrated by the fact, already noted, that the thyroid gland becomes enlarged, especially during adolescence, the period of rapid growth and development. Later in life, in normal individuals, activity is maintained at a lower and more constant level.

Those individuals, who are engaged in high competition and high activity and are successful by virtue of special gifts that they have derived from this energizing thyroid-adrenal-sympathetic system and an active brain, may find a lassitude coming over them, they become very thirsty, and want to drink more and more water. These individuals may possibly have the beginnings of diabetes, and diabetes, interestingly enough, is a disease that is most commonly found among the more active and successful people. In his scholastic standing in school the diabetic child is two or three years ahead of his average fellow. Many of the outstanding men in history have been diabetics. It isn't that diabetes makes people smart, but smart people may get diabetes.

There is an insidious and overwhelmingly disastrous condition that may steal upon the most effective of men, the most

outstanding leaders and most constructive personalities. In the latter years of life, that is, after the individual is fifty years of age, if he is in a high executive position, he is each year confronted by an increasingly dangerous and insidious encroachment upon his capacity for work and judgment and leadership and safe decisions. I refer to the stealthy onset and development of high blood pressure or cardio-vascular disease. In this discussion I am excluding organic diseases of the heart because, in the case of diseases of the heart, the disastrous consequences are not at all comparable to those of high blood pressure. In the case of the heart, so long as the blood circulates adequately, so long as the blood is pumped through the vessels in sufficient amount, the brain will function normally since it receives a sufficient supply of oxygen to maintain its normal electric potential. The executive can therefore go on at his usual pace, and when the heart stops suddenly, as it does in so large a proportion of cases, although he is dead he at least has not destroyed what he has built up. But high blood pressure induces changes so steadily and so stealthily in this type of personality, particularly in individuals of the very dynamic type, that the capacity for building up leadership, building up large affairs, building up a fortune, is endangered. It is exactly this type of individual who drives his organs on the rocks of destruction at an early age. One must keep in mind that the timid, the shrinking, the negative personality need not be considered at all because he is never in a commanding position. It is those whose brain and whose nervous and glandular systems are most active and effective who drive the organs of the body earlier to their destruction; they are the ones who, by virtue of the leadership which has been achieved, find themselves in the second half of life in commanding positions.

If, in the fifties, or sixties, or seventies, there is a gradual increase in the blood pressure, which means an increasing diminution of the amount of blood that is being pumped through the brain, which in turn means that the supply of oxygen to the brain is diminished, then the electric potential of the brain will be decreased with resultant diminution of the power of the brain to do its work. Along with this diminution in the power to

work comes a loss in the power of the brain to make decisions. Such a brain loses its ability to adjust itself to new ideas, to keep the pace in competition with younger and more active brains. Such individuals become one-track mechanisms, with one-track minds, and again and again the position of authority that has been built up by just the opposite type of mind—the active, versatile mind—is carried on by a one-track, fixed-idea mind. Again and again the fortune, the position, that has been built up through a lifetime of work, is thrown away and destroyed by this diminishing activity due to high blood pressure.

From all these considerations, it follows that in the second half of every man's life there should be at least an annual audit of the state of the blood pressure, and when the blood pressure is steadily rising and the progressive rise cannot be prevented, this should be a warning that such an executive should shift his responsibilities and should put the authority and the direction in the hands of younger brains. Such an individual should know that although he may feel sure that he himself can do what he has formerly done, he can only judge himself by a brain that is failing, not by a normal brain, and that his decision as to the disposition of his affairs, his business, should be taken at a time when he is still capable of making a wise decision.

It is clear that in the second half of life the electric potential of the elderly patient as a whole or of this or that organ has been very much reduced and that by so much the margin of safety has been dangerously diminished. Therefore, if we give to the elderly patient a general anesthetic or if the elderly patient sustains a hemorrhage or any other untoward happening, whereas most of his vital organs may not be depressed beyond the margin of safety, yet if the electric potential of only one vital organ reaches the zero point, the margin of safety of that organ is gone and the failure of that organ may cause death. Therefore, among patients in the second half of life, as compared with those in the first half of life, there will be a higher mortality. The point to be remembered is that in the case of every patient over fifty or even over forty-five years of age, it is important to take extreme care to maintain a normal temperature, a normal oxidation, a normal blood supply, a normal electrolytic con-

centration, a normal supply of food in the form of glucose in particular, and hence a normal electric potential and normal radiation in the protoplasm of the body.

We have now commented briefly on the sustained increase or decrease in oxidation, radiation and electric potential as affecting organs and the organism in the long swings of normal and pathologic physiology of the thyroid-adrenal-sympathetic system from fetal life to senility. In a later chapter we shall examine the short swings or acute changes in oxidation, radiation, and potential which are due to various causes.

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CHAPTER 17. CIVILIZED MAN— *A RADIO-ELECTRIC MECHANISM*

FROM the considerations presented in the foregoing chapters, it becomes apparent that the characteristics which differentiate the classes of animals and plants depend upon the level of energy and upon the manner in which that energy is utilized. Thus an animal like the lion or tiger would require to have its energy instantly available for attack or escape whereas the energy does not need to be kept at a constantly high level. The lion and tiger, therefore, have large and complex adrenal-sympathetic systems, to render their energy available for the needs of the moment. In the lion and tiger the stimuli received through the special senses are translated immediately into action without the intervention of the process of reasoning. In animals supplied with protective devices, such as the alligator, the porcupine and the skunk, relatively little energy is required, and the response to environmental stimuli as in the case of the lion and tiger requires no reasoning. In these animals, since relatively less energy is needed, the regulating mechanism—the thyroid gland and the adrenal-sympathetic system—is proportionately small. In contrast to the lower animals, man is in incessant activity, especially mental and emotional. Wild and domestic animals secure food, procreate, play and sleep. They require no energy for reasoning about their acts. They have no imagination and but little memory. Man acts and then reasons about his acts. His actions are directed by memories of past acts and his imagination is always busy. Primitive or uncivilized man is relatively inactive, he approaches the status of the beasts of prey. As regards its energy mechanism, the infant is allied to the wild

animals for it, too, does not reason, does not imagine. In the wild man and in the infant, therefore, the adrenal glands are larger in relation to the thyroid than in the adult civilized man, and in the infant the thyroid-adrenal relationship is reversed. (Fig. 52.) The level of energy expenditure, therefore, becomes one of the measures of the level of civilization. The more highly civilized the man, the more he reasons, the keener his memory, the more vivid his imagination, and as we have stated in the chapter on "The Nature of Mental Processes," "reasoning, imagination and memory are carried on at the expense of the energy fabricated by the cells of the gray matter of the brain especially in the frontal lobe."

The evolution of civilized man, therefore, has been coincident with the development of the thyroid gland which governs the constant expenditure of energy, and of the frontal lobe of the brain together with the development of the hands. In man, in whom the need for a constant level of energy supersedes the need for sudden outbursts of energy, the adrenal glands are smaller than the thyroid gland and, as stated above, in civilized man the adrenal glands are relatively smaller than in primitive man.

As clearly shown by Tilney in his "Master of Destiny,"¹ the rise of man by which he has harnessed the forces of nature and achieved dominance over the organic and the inorganic world, centered not in the evolution of the muscles, the bones, and the joints; not in the evolution of the digestive or the respiratory system; not in the special senses, the quality of the blood, or the organs of circulation; not in the skin or in the passive defenses, as many animals have greater prowess, fleeter limbs, better digestion, better chemical defenses, than man. Compared with man, animals have protecting hair and mane and carapace; they have barbs and scales and horns; they have pungent odors, poisonous stings, and bites. Compared with animals, man has no better sense of direction, or of equilibrium; he has no better vasomotor or respiratory centers; he has no better autonomic or ganglionic centers. In other words, man has no advantage over lower animals as to the vegetative nervous system, as to the special senses, as to muscles, bones, and joints, as to the spinal cord, or medulla, the midbrain, or the cerebellum. Evolu-



FIGURE 32. The thyroid and adrenal glands in a nude fetus of five months. The thyroid and the adrenal glands are outlined by dotted lines. The right adrenal appears to be smaller than the left because it is partially covered by the inferior vena cava. Note that either of the adrenal glands is larger than the thyroid gland.

tion centered above the cerebellum; it centered upon the cerebrum almost entirely, if not exclusively. It is the frontal lobe that is the unique gift of evolution to man.

The frontal lobe is the principal seat of associative memory. It was the frontal lobe that captured and domesticated lightning. It was the frontal lobe that devised the arrow, the wheel, the lever, the cultivation of plants. It was the frontal lobe that relieved man of hunting, and domesticated animals. The frontal lobe devised the means of providing food and clothing and shelter. The frontal lobe devised social coördination, spoken and written language, science and invention, religions and philosophies. The frontal lobe, aided by the hand and the thyroid gland, is the organ of civilization. It converted our four-footed, muscled ancestor that used only the energy released within itself to secure food, clothing, and shelter into an organism that used the energy outside itself for the same purposes. In the frontal lobe of man there has been established the capacity for holding the vast numbers of action patterns or memories that are required for the operation of the complex human state. It is the radiogens in the frontal lobe that generate the short wave radiations which have made possible the achievements of civilization.

But civilized man is still the descendant of the wild man to whom threatened danger meant the exhibition of physical prowess, and in spite of the development of the power of reasoning centered in the frontal lobe, civilized man can not completely control his racial memories.

Yet the frontal lobe is still the director of civilization. The frontal lobe is constantly changing the wild man's mechanism by building up the reason of civilized man, for although the frontal lobe can not change the protoplasm of inheritance, the frontal lobe can change the individual. It can not change the phylogeny, but it can change the ontogeny. The frontal lobe is coöperative; the wild man is non-coöperative. The frontal lobe wants peace; the wild man wants war. The frontal lobe respects property; the wild man steals property. It follows that a man is civilized to the extent that he controls the emotions by which his racial memories are expressed.

Thus the more highly civilized the man the greater is his self-

control, and the greater his provision for driving his mental processes at a constant high level, that is, the greater his power for producing the energizing short wave radiations and the greater his control of the expression of those radiations in his bodily activities.

In this very control, however, lies a danger, for if the emotions excited by racial memory—fear, anxiety, worry—break through the armor of his self-control, the brain with its high capacity for the production of energy will react upon itself and upon the organism with effects which are damaging in direct relation to the control of the outward expression of those emotions. The brain acts upon the adrenal-sympathetic system as if muscular action were to be consummated, and the resultant excessive drive of the adrenal-sympathetic system contributes to the production of such diseases as hyperthyroidism, neurocirculatory asthenia, peptic ulcer, diabetes, malignant hypertension, polyglandular disease.

What really occurs in the production of these diseases is that there has been produced an excessive amount of radiant and electric energy beyond the physiological needs as the result of the conditioning of the nervous system by the emotional state. By severing the adrenal nerves and the major and minor splanchnic nerves the effect of the adrenal-sympathetic system upon the spectrum is diminished and the percentage of short waves emitted by the radiogens is brought back to within the normal range.

As has been stated elsewhere, the action of the thyroid hormone is associated with protein metabolism. This means that the mechanism which has been evolved to sustain the high energy needed for the constant activities of civilized man centers around the use of the nitrogen compounds. As is stated in Chapter 26, the oxidation of nitrogen compounds produces radiation in shorter wavelengths than does the oxidation of carbon compounds. We may conclude therefore that the thyroid gland owes its effect upon the spectrum of the living state to its effect upon nitrogen metabolism. Since the development of the thyroid gland was coincident with the rise of the brain, we may conclude that the emotional and mental activities which are characteristic of civilized man owe their origin to the short wave

radiation generated by the nitrogen compounds metabolized by the secretion of the thyroid gland. It is certainly clear enough that the highest type of animal life is associated with a high nitrogen metabolism.

The chief difference between a plant and an animal is the preponderance of nitrogen metabolism in the animal. The chief difference between the higher and the lower forms of animals has been the development of a brain and of an organ whose activities center around nitrogen metabolism. The chief difference between civilized man and the lower animals has been the further development of the thyroid gland and of the brain which governs its activities.

It is true that civilized man is chained to the rock of evolution. But that same rock has supplied him with a tool—the power of memory and of reasoning, whereby he may loosen those chains and may to some extent free himself from the onset of those diseases which because of their origin we call Diseases of Civilization.

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CHAPTER 18. *PHYSICAL INJURY, MUSCULAR EXER- TION, INFECTION, EMOTION*

IN the inaugural phase of muscular exertion, physical injury, emotion and infection of such severity as finally to cause depression and possibly death, oxidation, radiation and electric potential are all increased. Eventually, however, the factors of safety are used up and the stage of depression ensues.

Especially in hemorrhage and asphyxia, this primary increase in oxidation, radiant and electric potential is due to the anaerobic oxidation induced by adrenalin, the output of which is increased to meet a biologic emergency.

In Chapter 8 we have presented evidence that electric potential is a true and accurate measure of the power of function and of the maintenance of the living state. We have tested the change in the electric potential in animals and when possible in fruit and in plants under the adverse influences named above. It is clear that each agent, whether injury, emotion, infection, anesthesia, etc., exerts its influence upon the oxidation, radiation and electric potential of protoplasm, the depression of which supplies the hitherto unrecognized common denominator of these various death-dealing factors. This point was well illustrated by our observations of soldiers in active service in whom every stage of stimulation and depression was manifested.

The soldier in exhaustion was able to see danger but lacked the normal muscular power to escape from it; his temperature might be subnormal, but he lacked the power to create heat; he understood words but lacked the normal power of response. In

other words, he was unable to generate radiant and electric energy adaptively despite the fact that his vital organs were anatomically intact. His mental power faded to unconsciousness and his ability to create body heat was diminished until he approached the state of the cold-blooded animal; the weakness of the voluntary muscles finally approached that of sleep or anesthesia; the blood pressure fell and most of the organs and tissues of the body lost their function.

In a heavy action neither side knew how many would be wounded. The railways were crowded with onrushing troops. There were often no means for considering the wounded. In emergencies the wounded were packed into cars—freight cars, any kind of cars—on the floors of which there might perchance be straw. Under stress it sometimes took twenty-four hours for the hospital train to make even fifty miles. After such a journey, the soldier arrived at the Base Hospital, usually at night. Up to this time he had had fragmented sleep, fragmented rest, fragmented treatment. Meanwhile the wound had become infected; the man was sallow, weak, and dejected. If left alone after his arrival at the Base Hospital he slept for one or two days, the depth and length of his sleep being a correct index of the degree of his exhaustion and the corresponding loss of resistance.

After the operation, vomiting, cold, dehydration occurred. There was little nursing care. The pulse mounted. Respiration, pulse and temperature increased. The patient was restless. Râles were heard at the base of the lungs. Little urine was secreted. The pulse became increasingly rapid and feeble. On the second or third day the patient might die with pneumonia, with suppression of urine, with a failing heart and delirium. Had the soldier not been in battle, he would have been in vigorous health. What was it that was lost? The common denominator was the result of depression of oxidation, depression of radiation, and depression of the electric potential in the dominant organs.

Exhaustion may follow emotional as well as physical stress since the expression of the emotions involves an increased activity of the energy system, that is, of the nervous system and of the thyroid-adrenal-sympathetic complex. The sole means by

which the thyroid-adrenal-sympathetic system can affect the energy system is by increased oxidation; and increased oxidation increases radiation, and increased radiation increases electric potential, thereby charging up the entire mechanism and effecting the preparation for a muscular attack or defense or escape. Under emotional stress, however, the gears for that part of the brain and the muscles that execute the muscular attack or escape by running are not set for action. It follows that all of the organs and processes not needed in the preparation for the muscular attack, defense or escape, such as those which function in digestion and procreation, are inhibited. In other words, the discharge of energy from the stimulated action patterns are not expressed in muscular action; therefore, emotion—fear and anxiety—holds the final common path. All of this results in a depression of the radiant and electric forces that govern the organism. As an analogy one may consider what would happen to a motor car standing still with its engine running at top speed and the clutch released.

The wounded soldier is the victim of exhaustion from intense physical exertion, intense emotion and physical trauma. Since his radiant and electric energy have been diminished it follows that he lacks the normal power of response to infection. In fact, all of his organs are abnormally predisposed to loss of function, and at death the body is well started on its way to dissolution as compared with the body of an equally vigorous soldier who is killed instantly. The underlying factor in the loss of the defense of the tissues and organs against infection is the depression of the electric potential in the tissues and organs.

Not only in war but also in civilian practice, the surgeon is familiar with the manifestations of every variety of the human emotions, in the various stations in life, from infancy to senility, in health and in disease. Not only does he come into intimate contact with the emotions displayed by the victims of disease and of accident, but he also observes those manifested by the relatives and friends of the families of his patients. Moreover he is unhappily forced to notice the emotional effect upon himself when he is waging an unequal battle against death. The strain and worry at a crisis, when a life is in the balance and a

single false move may be fatal, provide an experience which is well known to the operating surgeon.

The strongest of all emotions is fear. Fear is elicited only in those animals that utilize an energy system in defense against danger or in escape from danger. The defense of the armadillo is its shell. The armadillo does not defend itself or escape by muscular exertion; the armadillo has a most simple adrenal-sympathetic complex; the armadillo shows little or no fear. An offensive odor is the defense of the skunk; certain species of snakes are protected by venom; the porcupine is protected by its barbs—these animals possess little or no other means of defense. These animals have comparatively simple adrenal-sympathetic complexes. On the other hand, because of their superiority which is due to a large and complicated adrenal-sympathetic complex, certain other animals, such as the lion and the tiger, also show but little fear.

Although anger is similar to fear in origin, anger like fear is an integration and stimulation of the brain-thyroid-adrenal-sympathetic complex or energy system. Animals which have no natural weapons for attack experience neither fear nor anger. Animals which have weapons for attack express anger principally by energizing the muscles for attack.

What are the principal phenomena of fear? They are palpitation of the heart, acceleration of the rate and alteration of the rhythm of the respiration, cold sweat, rise in body temperature, tremor, pallor, erection of the hair, suspension of the principal functions of digestion and procreation, muscular relaxation, and staring of the eyes. The functions of the brain may be wholly suspended except those which relate to the self-protective response against the feared object.

Are any other organs stimulated by fear except those that can or do assist in making a defensive struggle? There are none. On the other hand, if an animal could dispense with his bulky digestive organs, the functions of which are suspended by fear, if he could, so to speak, clear his decks for action, it would be to his advantage. Although the versatility of natural selection apparently could devise no means of affording this advantage, it nevertheless did shut off the nervous current and

thus conserved the radiant and electric energy which is ordinarily consumed by these non-combatants in the performance of their functions.

The stimulation of this mechanism leading to a physical struggle results in action, and the stimulation of this mechanism without action results in emotion. We may say, therefore, that fear is a phylogenetic fight or flight. In accordance with this hypothesis all the organs and parts of the body are integrated and correlated for the self-preservation of the individual by the activity of his motor mechanism. We fear not in our hearts alone, not in our brains alone, not in our viscera alone—fear influences every organ and tissue; each organ or tissue is stimulated or inhibited according to its use in or its hindrance to the physical struggle for existence. By thus concentrating all or most of the action of the radiant and electric energy of the organism on the nerve-muscular mechanism for defense, a greater physical power is developed. Hence it is that under the stimulus of fear, animals are able to perform preternatural feats of strength. For the same reason, the exhaustion following fear will be increased as the powerful stimulus of fear consumes the radiant and electric energy of the organism, even though no visible action may result.

When this conception is applied to the human beings of today, certain mysterious phenomena are at once elucidated. Man has not been presented with any new organs to meet the requirements of his present state of civilization. Not only does man possess organs of the same type as those of his savage ancestors, but of the same type also as those possessed by the lower animals.

The effect of the stimulus of fear or of anger upon the body when unaccompanied by physical activity is more injurious than is an actual physical contest which results in fatigue without gross physical injury. The soldier who, while under fire, waits in vain for orders to charge, suffers more than the soldier who flings himself into the fray; a wild animal endeavoring to avoid capture suffers less than one cowering in captivity. An unexpressed smoldering emotion is measurably relieved by action. The various energizing substances needed in physical combat, such as the secretions of the thyroid, the

adrenals, etc., cause physical injury to the body when they are not consumed by action.

In accordance with this conception, worry is interrupted stimulation. Worry is a state of alternation between hope and fear. It is an alternating stimulation and depression of oxidation, radiation, and electric potential. It is a slow fading out of the molecular furnaces, or radiogens, within protoplasm.

In accordance with this conception we can understand why the man consumed with financial or family worries suffers so many bodily impairments, even diseases. We can understand the depression and slow dying of animals in captivity. We can understand the grave digestive and metabolic disturbances which appear under any strain—worry, fear, sexual love or hate, and we can understand the benefits of confidence and hope, success and happiness, a change of scene, hunting and fishing, optimistic and helpful personalities.

As has already been stated, a cell can function only when under a certain electrical strain, and this electrical strain is constantly being regenerated by the radiant energy produced by oxidation; in other words, oxidation, radiation, and electric potential go hand in hand. Whatever interferes with oxidation interferes with radiation and its consequent electric potential. It is impossible to interfere with the electric potential and not with oxidation and radiation because in the protoplasm oxidation, radiation and electric potential are tied together as a co-ordinated physical process. Thus, each of the factors that affects the soldier disturbs oxidation and radiation and therefore alters the electric potential of every cell of his body; and if oxidation, radiation and electric potential are altered, the cell can not maintain even its own structure.

Biologic stimulation is stimulation of protoplasm. Exhaustion and death are exhaustion and death of protoplasm. When we say a man is dead, we mean that his protoplasm is dead. When the activity of the protoplasm is reduced by any one agent, this reduction will be added to a reduction of the activity of the protoplasm by any other agent. When one speaks of a reduction of the activity of the human organism, in reality one is saying that there is a change in the activity of the radiogens within the protoplasm, and any change in these living furnaces

influences function, because structure and function are indissolubly tied together. When a patient has insufficient food, every cell of the protoplasm of his body from the toe to the brain has insufficient food. When a patient has insufficient water and electrolytes, every cell in his body is thirsty. When a patient has oxygen-hunger, every cell has oxygen-hunger. When a patient is too cold, the activity of the protoplasm of every cell of his body is decreased ten per cent for each degree Centigrade of loss of body temperature. When a patient has a fever, for each degree Centigrade of rise in temperature there is a rise of ten per cent in the activity of every cell of the body.

When an individual is subjected to physical injury, to exertion, to infection, to emotion, all his protoplasm is affected.

CHAPTER 19. *ANESTHETICS, NARCOTICS, POISONS, STIMULANTS*

FOR many years we have been investigating the nature of anesthesia; have been endeavoring to determine with what mechanism the anesthetic interferes; to find out why under apparently the same degree of anesthesia one patient will die and another survive. In our earlier researches we thought we had found the answer when we discovered that certain changes in the brain cells, in the liver and in the adrenals, always followed prolonged inhalation anesthesia. Later we found that the temperature of the brain decreased steadily during ether anesthesia (Fig. 53) indicating that the oxidation and electric conductivity of the brain were decreased. We found also that the electric potential of the brain decreased in anesthesia. (Fig. 54.) But none of these findings explained why, in one individual, surgical anesthesia was followed by heart failure, in another by kidney failure, in another by liver failure, etc., but more recently researches have given us the clue which we hope will solve the mystery of anesthesia.

It is not only the potential of the brain that is lowered by inhalation anesthesia, but also the potential of every organ and tissue, and as has been stated, when the potential of any organ or tissue reaches the zero point that organ or tissue is dead. That is, the general anesthetic affects not only the brain but every organ and tissue of the body, reducing its electric potential and abolishing the vital short wave radiations.

What then is an anesthetic? It is an agent that is capable of interfering with the genesis of bio-electric currents and the short wave radiation required for normal activity. A local

anesthetic interferes with the short wave radiation in the part into which it is injected. Spinal anesthesia and splanchnic anesthesia interfere with the short wave radiation from the affected nerves, which means their power of generating and transmitting nerve impulses to the respective organs and tissues.

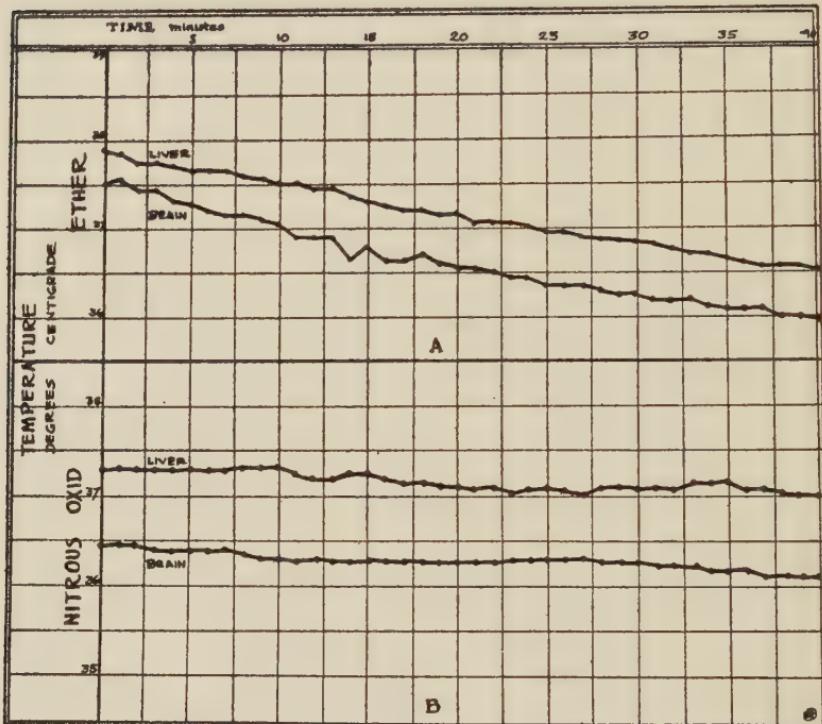


FIGURE 53. Comparative effects of ether and of nitrous oxide on the temperature of the brain.

When the nerve which supplies a tissue is anesthetized the radiation and bio-electric currents of the organs and tissues thus physiologically cut off are not interfered with. The general anesthetic, on the other hand, as already stated, affects all the protoplasm of the body.

Inhalation anesthesia, therefore, is a state which is analogous to death, and is removed from death only in inverse ratio to the depth of the anesthesia. That is, the deeper the anesthesia, the more closely is the state of the organism allied to death;

and just as all the tissues are involved in death, so are all involved in the state of anesthesia. Of course, the brain which is the most active tissue in the body is affected more profoundly and it is that profound effect which has unfortunately led us to overlook the effect upon other organs and tissues as in our earlier investigations.

Narcotics and poisons also affect every organ and tissue,

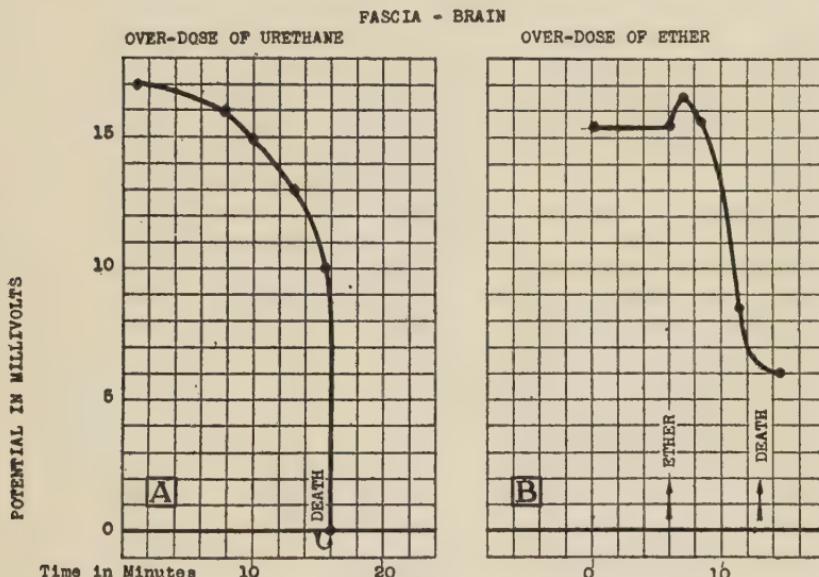


FIGURE 54. Effect of urethane and ether on the electric potential of the brain.

reducing the potential and electric conductivity, usually within safe limits when the agent is a narcotic but to zero—the death point, when the agent is a poison. (Figs. 55, 56.)

The same is true of stimulants in so far as the effect upon the whole organism is concerned, but the first effect of a stimulant is to increase the stainability of the cells of the brain, to increase electric potential, electric capacity and electric conductivity, to increase the percentage of radiation in the short wave field, thus increasing the radiant and electric energy of the whole body. This increased energy, however, is followed by a depression which is marked by decreased electric conductivity,

potential and capacity and decreased differential stainability of the brain cells, the amount of the resultant decrease bearing a direct relation to the degree of the primary increase in electric and radiant energy. That is, stimulation is followed by depression. If the upward swing goes far enough the following downward swing may carry the potential to zero with resultant

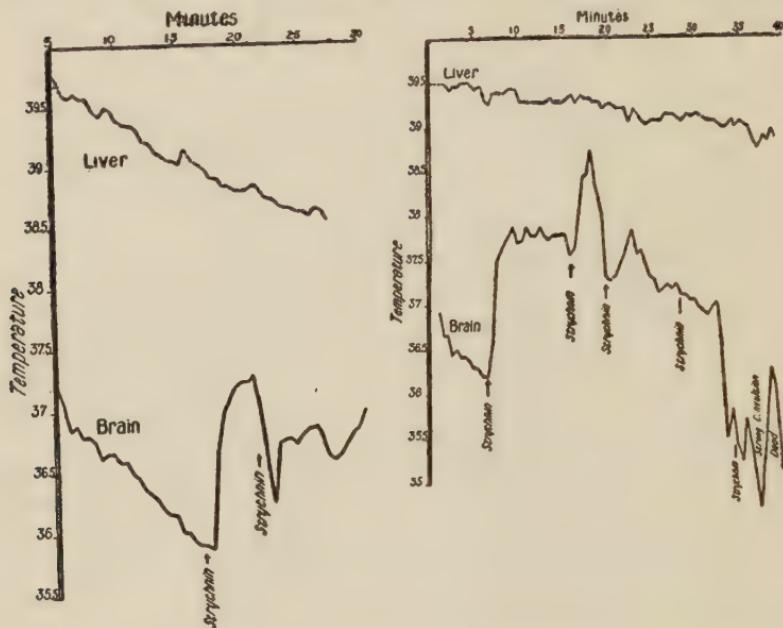


FIGURE 55. Effect of strychnine on the temperature of the brain and the liver.

death. Stimulants, therefore, may be an aid in restoring potential until other supportive measures can be applied to prevent the following depression. Thus, when the potential has been dangerously reduced by intense cold, a stimulant may temporarily increase the potential until sufficient heat—external and internal—is applied to maintain the potential within safe limits.

If an anesthetic affects every organ and tissue of the body, what happens to the patient with a degenerated or senile brain, a diseased liver, a decompensated heart, or depressed kidney function, when an anesthetic is given? Suppose that the patient

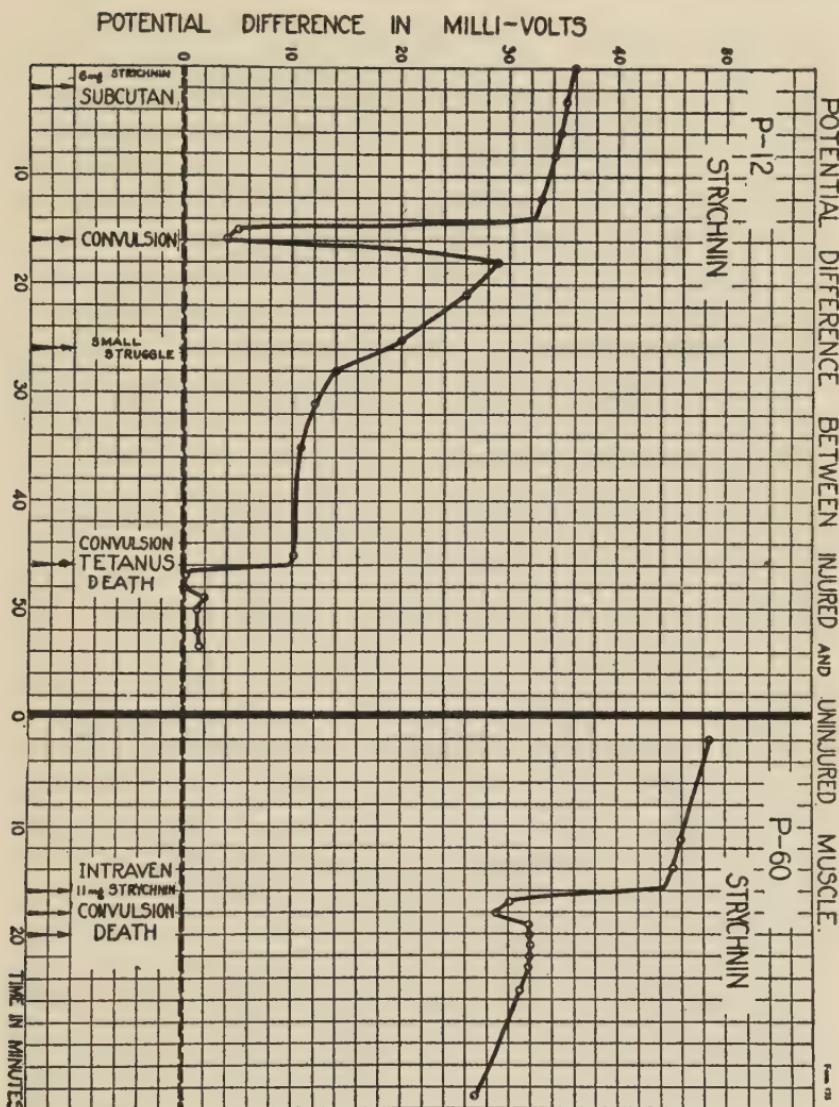


FIGURE 56. Effect of strychnine on the electric potential of the brain.

is an old man with a hypertrophied prostate. Because of the back pressure of urine the potential of the kidneys has become lowered and the vital short wave radiations are depressed. What happens when an inhalation anesthetic is given? If enough is

given to anesthetize the brain, the electric potential of the kidney—already low—may well be reduced to zero and when the operation is over, the patient may be potentially dead. It will be said that the patient died of anuria and that this was an end-effect of the patient's disease. But, in effect, the patient was dead when the anesthesia had ended.

Or suppose the patient has jaundice and the electric potential of the liver has been reduced to a low level as the result of the back pressure of bile. We have known of the dangers of operating upon the patient with jaundice but for a long time did not appreciate that the source of the danger was the anesthetic. Ether anesthesia would be given and in some instances the patient never became conscious. Death was attributed to the disease, but what really happened was that the already lowered electric potential of the liver was reduced by the anesthetic and the vital radiations ceased. Long before the potential of the brain was reduced to the danger point, the liver was dead, and the brain can not function without the liver.

In an elderly patient the electric potential of all the organs is reduced and radiations are depressed. In such people one or another vital organ may have the lowest potential and its function fails first. We say that the patient died of failure of the liver, the kidney or the brain; he really died from the anesthetic.

In an old person, the radiations of the brain may be so depressed that even a narcotic is dangerous. An elderly patient may never become conscious after a dose of morphine that would be entirely safe for a young and healthy subject.

Anesthetics and narcotics are safe enough when the processes of life are normal. When the electric potential of the brain, the myocardium, the kidneys, the liver, the adrenal glands—the essential organs of the body, is not affected by disease or injury, then a general anesthetic is safe. To be sure, a general anesthetic will reduce the electric potential of all these organs, but not to the danger point. Unless we know that there is an adequate margin of safety in the protoplasm of these essential organs a general anesthetic should not be administered.

When in the course of an operation there is a hemorrhage, the patient may die, and we say that the hemorrhage was the

cause of death. What really happens is that the hemorrhage so lowers the electric potential of the organs and tissues that they cannot bear the further depression due to the anesthetic.

It follows that before giving a general anesthetic it is essential to know something regarding the state of the protoplasm of the essential organs. If any of these organs have been affected

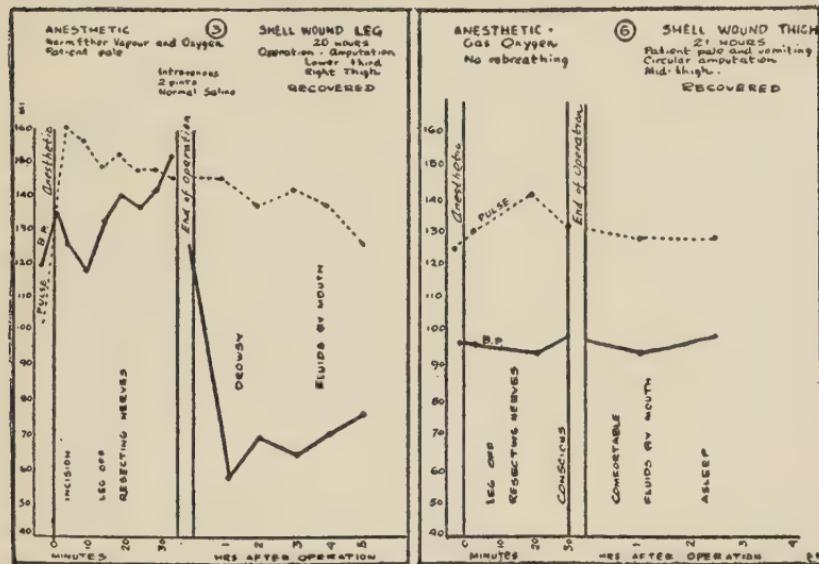


FIGURE 57. Comparison of the effects of ether and of nitrous oxide anesthesia. 3, Amputation of mid thigh under ether anesthesia, patient dead 80 hours after operation; 6, Operation under nitrous oxide anesthesia for repair of extensive shell wounds in abdomen and chest with large hole in diaphragm. Patient recovered. (Courtesy of Captain Gregory Marshall)

by the disease we know that the radiant capacity has been affected, that is, the emission of radiations and the electric potential have been reduced. In such a case, therefore, the use of a general anesthetic is contra-indicated. Local or splanchnic or spinal anesthesia should be used. Ether and chloroform should rarely be administered to a bad risk or an aged patient.

When a general anesthetic is employed, nitrous oxide-oxygen and ethylene are the safest. Their effects are the most fleeting and we have proved by experiment that nitrous oxide

changes the brain cells less than does ether (Fig. 57); and it reduces oxidation less, as is shown by the fact that there is but a slight fall in the temperature of the brain throughout the period of its administration, as contrasted with a steady and rather rapid fall in the temperature of the brain when ether is given. As nitrous oxide-oxygen interferes less with oxidation, the short wave radiations and the potential are less reduced and therefore the electric potential of the protoplasm is less reduced, a point which has been proved by direct experiment.

The safest procedure, when general anesthesia seems to be demanded, is to give nitrous oxide-oxygen until the state of analgesia is attained, and then rely upon local, regional, splanchnic or spinal anesthesia.

A special word should be said about the use of morphine. First, morphine lowers the electric potential less than do the coal tar products. In a case of hemorrhage it apparently has the power of stabilizing the excessive activity of adrenalin, the output of which is increased in hemorrhage. But morphine does depress the potential to some extent. When then should it be used? It should be borne in mind that pain or exhaustion from mental or physical activity also depresses the electric potential. When such factors are in the ascendant, therefore, morphine, which diminishes the electric potential less than do these excitants, is of value. In such cases the lesser evil tends to nullify the effects of the greater evil. When we come to consider the sick man in terms of the physical constants of his entire protoplasm, we can decide what combination of anesthetics and narcotics will best apply to each individual case.

CHAPTER 20. ANOCI-ASSOCIATION OR THE SHOCKLESS OPERATION

WE have already described the effects of fear and of physical injury upon the organism in terms of physical constants and radiation. We have described the effects of anesthetics and of narcotics; and in the first chapter we described the steps which led to the establishment of the principle of anoci-association and the development of the shockless operation. When we performed our first shockless operations, however, though we knew that we had achieved the desired results we knew only in part the basis for those results.

The extent of our knowledge at that time of the mechanism by which shock is produced is expressed in the following quotation from "Anoci-Association."¹

"There is a group of organs whose function is the conversion of potential into kinetic energy. These organs form what may therefore be designated a *Kinetic System*. Among the organs forming this system are the brain, the thyroid, the suprarenals, the muscles and the liver. The *Kinetic System* converts latent energy into motion or heat in response to adequate stimuli. If the stimuli are overwhelmingly intense, then the *Kinetic System*—especially the brain—is exhausted, even permanently injured. *This condition is acute shock*. If the stimuli extend over a period of time and are not so intense as to cause an immediate breakdown or acute shock, their repetition may cause the gradual exhaustion of the *Kinetic System*—a condition which may be called chronic shock. Either acute or chronic shock may be measurably controlled by weakening or breaking the *kinetic chain* at any point.

"In other words, shock is the result of an intense stimulation of the

Kinetic System—by physical exertion, emotion, trauma, toxins, anaphylaxis, strychnine, etc.—which leads to physical changes in the *Kinetic System* and which if carried far enough exhausts that system. The *Kinetic System* is constantly activated as long as there is life, but normal activation does not produce exhaustion. If normal activity of the *Kinetic System* be exemplified by walking, shock might be exemplified by the exhaustion caused by a Marathon race. The difference between normal processes and shock is that of intensity, not of kind. From these premises it becomes obvious that the exclusion of both traumatic and emotional stimuli will wholly prevent the shock of surgical operations."

Later we learned that the exhaustion of the kinetic system is expressed also by decreased electric conductivity, electric potential and electric capacity, and recently we have found that in the state of lowered potential, the genesis of short wave radiations and of bio-electric currents is decreased.

The fundamental principles of the shockless operation may be stated as follows: Every adequate stimulus, with or without inhalation anesthesia, whether from trauma or emotion, activates the brain-thyroid-adrenal-sympathetic system. That is, the sight of the operating room, the spoken word implying danger, the taking of the anesthetic, the instrumental injury of tissues in the course of the operation and the traction of stitches after the operation, all are adequate stimuli. As the result of this stimulation of the brain-thyroid-adrenal-sympathetic system, the electric potential falls and the emission of radiations in the short wave field are correspondingly diminished. Obviously the only way of preventing this result is by the development of a technique which will exclude from the brain the stimuli of the special senses and the stimuli of common sensation. The inhalation anesthetic in itself and narcotics, as we have shown, decrease the electric potential and the percentage of short wave radiation. There exists no single agent that is entirely harmless in itself and can produce anoci-association which is the goal of operative surgery.

Anesthetics and narcotics are necessary, however, and therefore it remains to find the anesthetic or combination of anesthetics as well as a plan of management which will exclude

all stimuli from the brain-thyroid-adrenal-sympathetic system and which will have the least possible effect upon the genesis of radiant energy and upon electric potentials.

The inhalation anesthetic which produces the least effect upon the electric potential of the brain is nitrous oxide-oxygen. This will produce subjective unconsciousness. As we have stated, stimuli from injured tissues will still reach the brain, which will respond as if no anesthetic had been administered. Local, regional and spinal anesthesia can prevent these damaging stimuli from passing beyond the operative zone. By the use of narcotics administered before the preparation for the operation, emotional excitation is prevented. By skillful management it is often possible to carry through the entire operation without allowing the patient to pass beyond the anesthetic stage of analgesia, thus diminishing the effect of the inhalation anesthetic upon the genesis of radiant and electric energy and the electric potential.

The surgeon's best assurance for the successful outcome of a serious operation would be to have the patient come under his care before the development of the disease from which relief is sought. Thus the surgeon would be able to apply constantly such methods as would keep the electric potential of all the patient's tissues at the optimum level. Even if the onset of disease could not be obviated the patient would be in the best possible condition to withstand the trauma of any operation which might be required. However, the surgeon, who too often must deal with patients heavily handicapped by factors, which, if known in time, might have been controlled, is finding that by a careful, unhastened preparation he may do much to counteract the adverse conditions.

The work of the surgeon does not begin in the operating room, nor with the immediate preparation of his patient for operation, nor does it end with the healing of the physical wound. Throughout his contact with the patient before the operation, during the operation and after the operation, the patient must be considered *as a whole*, for all of his protoplasm may be affected by the processes of his disease; all of his protoplasm is affected by the inhalation anesthetic; all of his pro-

toplasm is affected by the trauma of the operation; all of his protoplasm is affected by the psychic factors involved in any major surgical procedure.

By a reassuring preoperative environment, by the definite dulling of the nerves, by the administration of a narcotic; by the use of the least harmful anesthetic (nitrous oxide-oxygen); (See Figs. 53, 57, 60), the stage of anesthesia being kept within the limits of analgesia whenever possible; by the use of local, regional or spinal anesthesia; by gentle manipulations and sharp dissection; by blood transfusion to supply added oxygen to the taxed cells; by added fluids and nutriment in the form of saline and glucose infusions; by digitalization if there is any question of a failing myocardium; by the application of diathermy to maintain an optimum temperature—by the use of these methods the electric potential of tissues of even the most desperately ill patients may be maintained above the shock level during and after even a massive operation.

Spinal anesthesia is an almost specific preventive of surgical shock, provided the patient can be protected against the resultant fall in blood pressure (Fig. 58), which is due to the fact that nerve communication with the vasoconstrictor center to the brain is cut off from a large vascular field—the splanchnic territory and the lower limbs. It was found in war surgery that the effect of a fall in blood pressure was most severe in the recently wounded patient but that after about forty hours had elapsed after the receipt of the injury spinal anesthesia was comparatively safe. This length of time was required to stabilize the circulation by the reestablishment of the normal factors of safety.

In a front line hospital the mortality rate of major operations performed under spinal anesthesia was the same as that under nitrous-oxide anesthesia. Under ether anesthesia the mortality rate of major operations under adverse conditions was 66 per cent while under nitrous oxide and under spinal anesthesia it was 20 per cent.

Since aside from its effect upon the blood pressure spinal anesthesia does not produce any change in the brain-thyroid-adrenal-sympathetic system while inhalation anesthetics do

per se, spinal anesthesia rather than inhalation anesthesia should be used in the major shock-producing operations.

Therefore, when shock is the paramount risk, spinal anes-

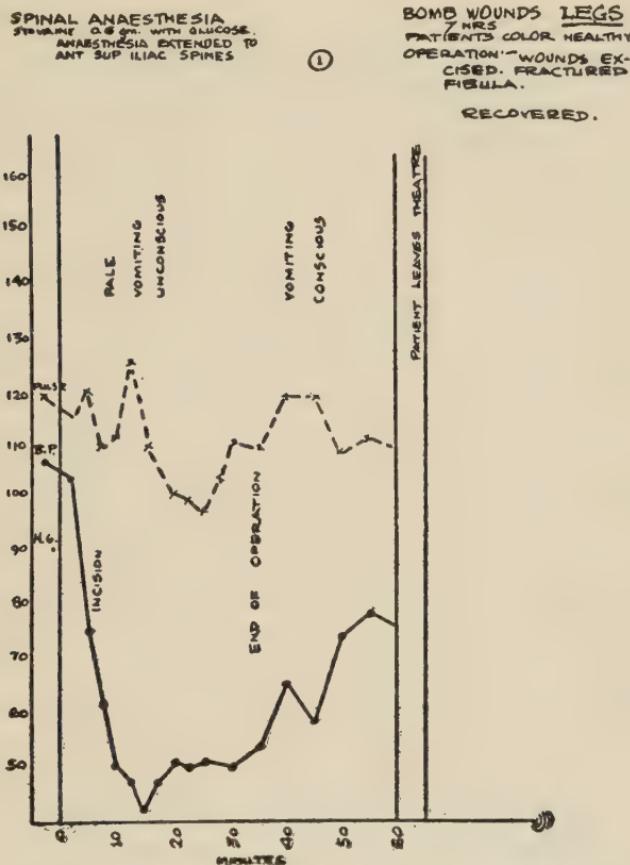


FIGURE 58. Fall in blood-pressure caused by spinal anesthesia. (Courtesy of Captain Gregory Marshall)

thesia should be used, but spinal anesthesia should be avoided when its effect upon the blood pressure will add to the hazard of the operation.

The dictum which our studies of the effects of anesthetics, narcotics, poisons and stimulants have emphasized is that the protoplasm of the sick man in relation to these agents, as in

all other respects, differs from the protoplasm of the well man; and that in considering their effects, whether upon the well man or the sick man, all the protoplasm of the individual must be considered.

REFERENCE

1. Crile, G. W. and Lower, W. E.: *Anoci-Association*, Philadelphia, W. B. Saunders Co., p. 100-101.

CHAPTER 21. *THE MECHANISM OF LIFE AND OF DEATH*

IN the preceding chapters we have summed up the researches which we have undertaken and offered the theories which we have proposed in our effort to answer the question, "Why did William Lyndman die?" We believe that that question is answered.

We know that solar radiation is the indirect generator of lightning and terrestrial electricity; that these electrical forces generate the nitrates; that the nitrates in the soil are the basis of the protein factor of protoplasm; that solar radiation falling on the plant and the nitrated soil generates plants; that plant tissue is taken up by animals; that animal tissue is taken up by plants; that long wave radiant energy or heat radiation is constantly emitted in the life of animals and of plants; that short wave radiation, identical with the short wave radiations from the sun that generate plants, have been detected in plants and animals. We know that short wave radiation could not possibly be detected as readily as heat radiation for heat radiation is not absorbed by atoms, hence heat radiation can not confer chemical affinity on atoms and of itself alone it can not produce organic compounds. Although it is difficult to detect the ultraviolet, visible and short infra-red rays being absorbed by atoms, nevertheless that these short wave radiations are present in protoplasm is demonstrated by the luminescence of numerous plants and animals, and by the detection of ultra-violet radiation or the so-called mitogenetic rays from living tissues. It is clear that plants "eat" solar radiation and nitrates

and that animals "eat" the solar radiation and the nitrates in plants.

Animals are transformed and motorized plants and, therefore, plant protoplasm and animal protoplasm naturally obey the same general physical laws of reproduction and growth. Each uses identical radiation and electric energy; each requires water, electrolytes, metal catalysts, a certain temperature. The protoplasm of each consists of identical proteins and lipoids. Each is affected by the same narcotics, anesthetics, etc. Each is generated by radiant and electric energy.

Among the outstanding characteristics of animals is the peculiar arrangement whereby energy can be released at varying speeds, as for example, in the responses to the senses of sight, smell and hearing, as manifested by the flight of a bird and the rushing attack of a lion.

There is also the great development of the proteins and lipoids in the brain into a system consisting of a recording matrix composed of conducting electrolytes and insulating lipoids and of electric generators or brain cells, the whole brain thus constituting a robot like a great telephone system, which, activated by the special senses which are detonated by radiant and chemical forces in the environment, mediate between the environment and the muscular and glandular system.

For the long constant range the rate of oxidation in the executive organ, the brain, is governed by the thyroid gland; for the short emergency range, by the adrenal-sympathetic system. The energy characteristics of species of animals are as clearly disclosed by the size and complexity of the governing organs as are the energy characteristics of a motor car by the type and size of the motor.

To a child and to a primitive man, a rainbow would seem to be an object that could be felt and measured and weighed. There is no suggestion that the individual light wave in the rainbow's composition passes as quickly in and out as does the lightning's flash.

As with the light wave in the rainbow, so life within the radiogen is the product of radiant and electric energy, and the length of time of its flash is but a single unit of the creative energy of the living in protoplasm, namely, but a single wave

length of the solar spectrum of the living. Therefore, the radiant energy that generates the living state is as fleeting as the radiant energy that generates the rainbow.

Neither the energy, nor the matter that forms the rainbow, nor the energy and the matter that form the living state, is constant. It is only the pattern that is constant. The entrance of each creative wavelength into the pattern of the living is the "birth" of that fraction of the living state; while the passing of that wavelength out of the pattern of the living is the "death" of that infinitely small fraction of the living state. So, too, is the rainbow being constantly "reborn." So, too, is the rainbow "dying"—dying in quanta or wavelengths. It is only the apparition caused by the unseen velocities of wave and electric energy which our senses express as a solid form.

Since, in animals, the protoplasm is constructed and operated by radiation, and since radiation generates electric charges and electric currents, the state of living depends on a certain amount of radiation generated by oxidation. When oxidation is so speeded by injury, pain, adrenalin, thyroxin, and electric stimulation that the available fuel is exhausted, then the state of shock exists. When the circulation of blood and the respiration are quickly arrested, although abundant combustible compounds are left but there is no oxygen to burn them, the state of collapse exists. When, for any reason, the flame of the living state burns lower, the state of depression exists. When the flame is so nearly extinguished that not enough electric energy is generated to move the mechanism sufficiently to sustain the structure of the radiogens of the protoplasm, the state of equilibrium or death exists.

Thus when radiant and electric energy decrease and finally fail in death, there follows a complete dispersion into space of the radiant and electric energy still locked in the organic molecules, and the carriers of energy, the nitrogen, the carbon, and the oxygen, return again to their neutral position in the atmosphere from which they were once captured by lightning and solar radiation. Thus the physical cycle is completed as the physiologic cycle is completed; an energy cycle and a life cycle has each run its course.

THE EXPERIMENTAL DATA

CHAPTER 22. *HISTOLOGICAL RESEARCHES*

IN the introductory chapter of this thesis have been indicated the successive investigations which led to the development of the Bipolar Theory. Of primary importance have been our histological researches, the findings in which suggested the postulate that the unit cells of the organism are electric cells. For this reason the following brief summary of these studies, which included 2,670 experiments on animals and many observations on man, is offered here.

On the basis of our earlier investigations we argued that since the vasomotor center is fatigued in shock, other parts of the brain were probably fatigued also, and following the premises established by Hodge¹ in his studies of fatigue in the bee we believed that the functional alterations in the brain cells would be accompanied by physical alterations.

To test this hypothesis, in 1900, in collaboration with Dr. D. H. Dolley, we initiated our histologic studies of the brains of animals after traumatic shock.^{2, 3, 4, 5} These studies were later extended, in collaboration with Dr. F. W. Hitchings and Dr. J. B. Austin, to include other forms of shock and exhaustion and other organs.^{6, 7, 8} Our findings may be summarized as follows:

The Central Nervous System—The cells of the brain were studied in animals which had been subjected to prolonged insomnia, to the injection of toxins, to infection, to the injection of foreign proteins. We studied the brain cells in animals which had been activated in varying degrees from the stage of excitation to that of complete exhaustion by running, by

fighting, by rage, by fear, by physical injury, by the injection of strychnine, by the injection of adrenalin. We studied the brains of salmon caught at the mouth of the Columbia River and compared our findings with those in salmon caught in the spawning season after their long swim to the headwaters. We studied the brain cells of electric fish before and after the partial or complete discharge of their electric organs. We studied

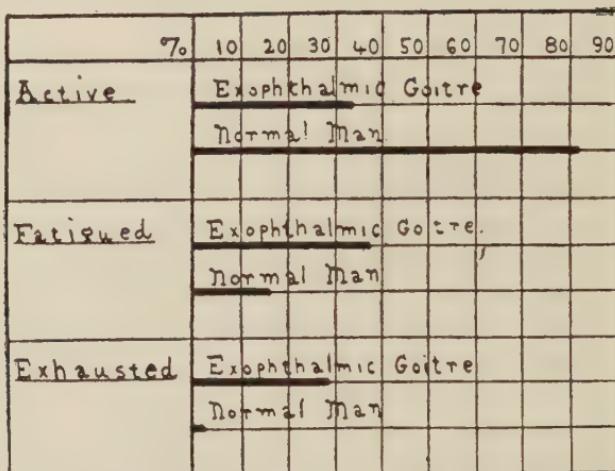


FIGURE 59. Differential Purkinje cell counts—Hyperthyroidism. The chart is made up from the average of differential counts in five clinical cases.

the brains of hibernating woodchucks. (See Fig. 8.) We studied the brains of humans who had died from hemorrhage, from acidosis, from infection (See Fig. 9), from eclampsia, from cancer, from hyperthyroidism. (Fig. 59.) We studied the brains of animals after excision of the liver and of the adrenals; and after short and long periods of anesthesia with ether and with nitrous oxide. In every instance we found identical histologic changes, chromatolysis and a *loss of differential stainability* of the nucleus and cytoplasm in the stage of exhaustion, while in animals killed in the stage of excitation, the *differential stainability was increased*.

Of especial significance was our finding that in animals, which had been subjected to prolonged insomnia and to induced aci-

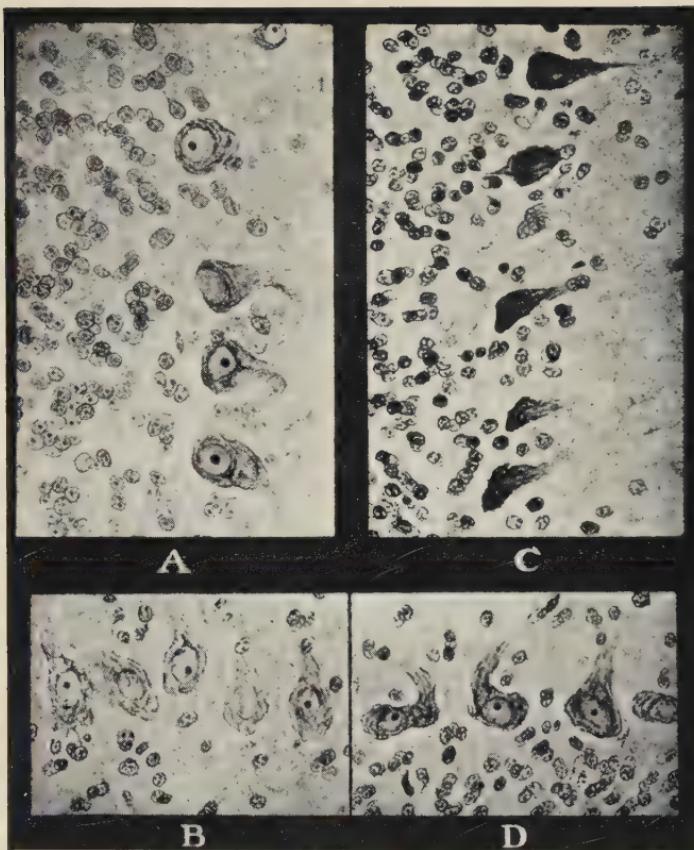


FIGURE 60. Comparison of the restorative effects of sleep and of nitrous oxide on the brain cells of rabbits exhausted by prolonged insomnia. (From camera lucida drawings). A, Section of normal cerebellum of a rabbit; B, Section of cerebellum of a rabbit after prolonged insomnia; C, Section of cerebellum of a rabbit to which nitrous oxide had been administered for one hour of each six for a period equal in length to a previous period of prolonged insomnia; D, Section of cerebellum of a rabbit which had been allowed to sleep continuously for six hours after a prolonged period of insomnia.

dosis, one period of sleep restored the brain cells excepting those in which the cell and nuclear membranes had ruptured. By making experiments in groups and killing the rabbits at various intervals after the termination of the period of insomnia we were able to follow the complete course of cell changes. The histologic evidence indicated that it took many days to restore some brain cells that were on the verge of final breakdown. The resemblance of nitrous oxide anesthesia to normal sleep is so marked that in a series of experiments, nitrous oxide was substituted for sleep in the following manner: Animals were kept awake for prolonged periods, but were given nitrous oxide anesthesia for one hour out of each six, sleep being prevented during the other five hours. The condition of the brain cells of these animals was almost as good as that of the brain cells of animals which were allowed like periods of normal sleep. (Fig. 60.)

In another series of experiments, rabbits were kept awake for prolonged periods and were then subjected to nitrous oxide anesthesia while others were allowed to sleep for an equal period of time. The histologic findings showed that the brain cells in both series were restored to approximately the same degree.

Of crucial importance in its relation to the inception of the Bipolar Theory were the findings (1) that in animals in which physical injury was limited to territories disconnected from the brain by division of the spinal cord or by local anesthetization, the brain cells showed no changes; and (2) that in animals in which the circulation of the head of one animal was anastomosed with the circulation of the body of another animal (double-crossed circulation) and one animal was subjected to severe abdominal injury, brain cell changes appeared *only in the brain of the injured animal*.

The injection of adrenalin caused immediate increase in the differential stainability of the brain cells followed by a decreased stainability. In double-crossed circulation experiments brain cell changes occurred only in the animal whose brain received the adrenalin; and the characteristic circulatory and respiratory changes *appeared first* (by a minute or more) *in the animal whose brain received the adrenalin*.

After excision of the adrenals and of the liver the differential

stainability of the brain cells progressively decreased. (See Figs. 44, 48.)

The Liver—All the stimuli which produced changes in the brain cells produced constant changes in the cells of the liver. In the stage of exhaustion the cells stained poorly, the cytoplasm was vacuolated, the nuclei were crenated, and cell membranes were irregular, the most marked changes appearing in the cells at the periphery of the lobules.

The Adrenals—The application of the exhaustion-producing factors listed above in most instances produced destructive changes in the cells of the adrenals, more marked in the cortex.

In one group of experiments, in which rabbits were subjected to protracted insomnia, the cells of every organ and tissue of the body were examined and *histologic changes were found only in the cells of the central nervous system, the liver and the adrenals.*

These histologic studies which indicated that the vitality of the animals studied was in direct relation to the differential stainability of the brain and liver cells, led to a consideration of the essential structure of the cells with the resultant conclusion that variations in stainability indicate variations in the acid-alkali balance between the colloidal content of the nucleus and that of the cytoplasm of the cells, hence to variations in electric potential. Our attention, therefore, was directed to the application of biophysical methods to the study of the function of the cells.

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CHAPTER 23. STUDIES OF ELECTRIC CONDUCTIVITY AND ELECTRIC CAPACITY

THE researches of Lillie,¹⁻³ Loeb,^(4, 5) Osterhout,⁶⁻¹⁵ Matthews,¹⁶ McClendon,¹⁷⁻²¹ Hill,²² Lucas²³⁻²⁶ and of many other biophysicists and biochemists²⁷⁻³⁵ indicate that the functions of the cells of living organisms are related to electrical processes; that the living cell, whether it exists alone or as an element in a complex organism, possesses a certain store of potential energy which is manifested by variations in polarity and by action currents; that variations in the permeability of the living cell in response to the electrically charged elements of the fluid which surrounds it parallel variations in irritability in response to stimulation; that factors which suspend or abolish irritability also suspend or abolish alterations in permeability.

Every activity of living tissue is accompanied by electric currents; and many activities are also initiated by electric currents. In fact, the work of the investigators referred to above shows how strong is the tendency to consider that vital processes are associated with electric energy.

In view of this trend of physiological conceptions, the electrical properties of living protoplasm become of vital interest. As this interest extends, the need of definite quantitative data increases. The laws which govern the action of electrical forces in inorganic systems are known exactly. It is possible to calculate exactly how much heat, or what chemical change, or how much work will result from the passage of a current of known

strength through a known resistance during a definite period of time.

The action of electric energy in protoplasm, although all the conditions are far more complicated than in inorganic substances, is governed by the same laws. In protoplasm, as in inorganic matter, electric currents will always take the path over the lowest available resistance.

The facts already established regarding bio-electric currents are sufficient to indicate the importance of further investigation, especially along certain lines. For example: What is the range of the electric conductivity of living tissue? How does that range compare with that of other electrical conductors? Is the range of conductivity the same for all types of tissue, and in each tissue does it remain constant under all conditions? Is the electric conductivity of each tissue a factor in the production of the activities of the organism, to which a fairly constant value can be assigned?

These are questions which occur at once to the most casual student of bio-electric problems, and the fact that the literature offers no clear answer is sufficient reason for a detailed study of this subject.

Various investigators have applied measurements of electric conductivity to the determination of variations in the permeability of protoplasm under varying conditions. In particular the work of Osterhout, Lillie and Loeb along these lines is too well known to be more than mentioned here.

The difficulty of measuring the electric conductivity of tissues arises from the necessity of leading an electric current through the tissues. The current is conducted by ions, which move in the electrolytes of the tissues. The numerous cell membranes offer a resistance to the ions and due to the inherent electric charges of the membranes some ions are retarded by them. Hence electric polarization occurs.

The phenomena of polarization were studied by Warburg³⁶ and by Nernst³⁷ and the theoretical formula which they obtained was verified by experiments, according to which the changes in the electrolytic concentration at a membrane

$$c_x = \text{const.} \frac{i}{\sqrt{V}}$$

in which i represents the average current in-

tensity and ν the frequency of the alternating current. We can see from this formula that the changes in the electrolytic concentration at the membrane diminish rapidly when the frequency increases. It is possible that at a very high frequency the change of concentration would be so small that it would have no appreciable influence on the membrane. Consequently, from the electro-chemical point of view, the tissue would be equal to a homogeneous electrolytic solution.

Philippson³⁸⁻⁴⁰ measured resistances of different tissues and found that between 1,000 and 3½ million cycles the resistance changes considerably. He extrapolated the values for infinite frequency and found that the resistance of frog's muscle (the current being perpendicular to the fibers) was 1,535 ohms at 1,000 cycles and only 160 ohms at very high frequencies. The resistance of guinea pig's muscle immediately after death was 1,840 ohms for 1,000 cycles and 130 ohms for very high frequencies, while two hours after the animal's death the same muscle measured only 940 ohms at 1,000 cycles, but did not change at high frequencies. The resistance of the guinea pig's liver was found to be 2,380 ohms for 1,000 cycles and 210 ohms for very high frequencies.

Philippson devised a formula for the calculation of the conductivity of inter- and intracellular spaces and of the polarization resistance of the membrane, which acts as a capacity.

Mendeleeff,⁴¹ using Philippson's method, measured the conductivity of the liver and of the mouse and found changes when the animal was treated with intraperitoneal injections of hydrochloric acid. The same investigator measured the changes produced by the x-ray in the conductivity of the liver of the guinea pig, and also the difference in the conductivity of the livers in healthy and in tumor-bearing mice.

Waterman⁴² found that the conductivity of cancerous tissues changed when they were treated with different electrolytic solutions.

Other investigators have used conductivity measurements as a means for estimating the volume of the corpuscles in blood, for determining the H-ion concentration in body fluids, for measuring the variations in the conductivity of muscle which

result from contraction. But none of these investigators attempted to determine the specific conductivity of any tissue.

Early in this century Galeotti^{43, 44} carried out a limited number of experiments for the purpose of studying the changes which occur at death. He utilized the tissues of dogs, rabbits, guinea pigs, frogs and turtles, making measurements at successive intervals after the removal of the tissue from the animal. In general, he observed a rapid decrease in conductivity during the first few minutes, followed by a more gradual de-

TABLE I

SPECIFIC CONDUCTIVITY OF CERTAIN RABBIT TISSUES AS DETERMINED BY GALEOTTI
(Expressed in reciprocal ohms)

Temperature	Liver	Heart	Muscle	
			Longitudinal	Transverse
12° C			00182	00058
18° C	000268	000799		000804
	00090			
	00053			
24° C	000269			000789

crease, which in some instances lasted for several hours. After reaching the minimum, which he considered marked the death point of the tissue, the conductivity began to rise, gradually at first, and then very rapidly until a very high value was reached.

His values for the normal conductivity of certain rabbit tissues may be of interest as compared with those observed in the work to be described later. (Tables I and II.)

For the most part Galeotti worked with the firmer tissues, sections of which he introduced directly between platinum electrodes which were clamped in place after the application of a greater or lesser degree of pressure. He used only a few animals of each species and does not state that he measured more than one sample of each tissue from any one animal.

In our original researches which were begun in 1917 in collaboration with G. B. Obear of the Case School of Applied Science, Amy Rowland and Helen Hosmer, measurements were

made of tissues immediately after the death of the animal, the measurements for each tissue being made within the survival period for that tissue.

The tissues and fluids measured included the cerebrum, the cerebellum, the spinal cord, the liver, the thyroid, voluntary muscle, the heart, the kidneys, the spleen, the lung, the spinal fluid, the blood, the bile.

Sections of each tissue were packed into small glass tubes of various sizes, each of which was accurately ground to insure uniform dimensions throughout. The tubes were packed with a

TABLE II

COMPARISON OF THE SPECIFIC CONDUCTIVITY OF RABBIT BLOOD
BEFORE AND AFTER COAGULATION AS DETERMINED BY GALEOTTI
(Expressed in reciprocal ohms)

Temperature	Before coagulation	After coagulation
38° C	00569	00566
	00679	00674
	00773	00771
	00539	00526
	00631	00590

sufficient excess of material to procure a slight projection from each end, and were placed between thin platinum electrodes, reinforced by brass backings. Sufficient pressure was applied to bring the electrodes flush with the ends of the tubes, when the electrodes were firmly clamped into place. Great pains were taken to avoid air spaces within the tubes and to insure uniform contact of the tissues with the electrodes. This was not difficult with the softer tissues, such as brain and liver, but with firmer tissues such as muscle and thyroid it was impossible to exclude considerable error from imperfect contact and other variations. The effect of these faults is plainly evident in the greater variation in the conductivity values obtained for the latter tissues.

The tubes used for the measurement of the conductivity of the brain, the liver and voluntary and involuntary muscle, were approximately 5 mm. in diameter and 5 mm. in length,

while those used in the measurement of the adrenals and the thyroid were of the same length with a diameter of approximately 2.5 mm. Special hard rubber containers were devised for the spinal cord.

The conductivity capacities or cell constants of these tubes were determined by repeated measurements of their conductivity when filled with 0.01 n KCl, at the same temperature as that used for the tissue measurements.

In the later work larger tubes, 1 cm. long \times 1 cm. in diameter, were used. These were only partially filled with tissue, and an upper electrode 1 cm. in diameter and pierced by slits was used. The tube was partially filled with closely packed material, and carefully placed in position on the lower electrode, after which the upper electrode was inserted within the tube and carried down until contact was made with the upper surface of the tissue, care being taken, however, to avoid sufficient pressure to cause the extrusion of material through the slits. This upper electrode was then clamped in place and the distance between the two electrodes was accurately measured and recorded.

Every precaution was taken to avoid any undue pressure with the consequent reduction of the fluid content of the tissue and resultant lowering of the conductivity, although this danger was lessened by the use of the pierced electrode. Various measurements of different types of tissues were made to determine the effect of varying the pressure, the results of which are illustrated by the groups of measurements shown in Table III. In each case the successive measurements were made upon the same sample of tissue, the distance between the electrodes, and consequently the pressure, being changed between each two measurements. The results indicate that a greater error is to be feared from the application of too much pressure than from too light a contact.

The cell constants for the tubes used in the later experiments, as for those used in the earlier series, were determined by measurements with 0.01 n KCl with the electrodes at different distances apart, these results being plotted for convenient use in estimating the value of the tissue measurements.

The electrodes were carefully cleansed after each measure-

ment and were replatinized at intervals with a very light coating of platinum black. The electrodes and holders were always

TABLE III

EFFECT OF VARIATIONS IN PRESSURE UPON THE ELECTRIC CONDUCTIVITY OF ANIMAL TISSUES

Tissue	Distance between electrodes (cm.)	Conductivity (expressed in reciprocal ohms)
<i>Cerebellum</i>		
Section 1	0.78	00133
	0.66	00129
	0.48	00114
Section 2	0.92	00148
	0.55	00128
Section 3	0.60	00140
	0.52	00136
	0.40	00123
	0.65	00115
Section 4	0.50	00108
	0.40	00105
	0.75	00121
Section 5	0.65	00116
	0.50	00116
	1.11	00158
Section 6	0.96	00151
	0.65	00128
<i>Cerebrum</i>		
Section 1	1.24	00183
	0.94	00167
	0.72	00159
Section 2	1.20	00183
	0.92	00170
	0.81	00169
Section 3	1.03	00172
	0.85	00164
	0.64	00145

placed in the bath long enough before use to insure the thorough warming up of the metal and glass parts, and during the insertion of tissues were exposed as little as possible to lower temperatures, and even then they were given an op-

portunity to reach the bath temperature before measurements were made. It was possible to exercise these precautions with but little loss of time by using two sets of electrodes and holders. All measurements were either made at 39° C. or were corrected to that value from temperatures not over a degree removed from it.

Our findings in these earlier studies, which included the measurement of the electric conductivity of 4,764 sections from 455 rabbits and 219 sections of pathological human tissues, may be summarized as follows: *

1. The specific normal conductivity of the cerebrum, cerebellum and liver can be determined within a narrow range; while the normal conductivity of other tissues can be determined within a sufficiently narrow range to determine the order of their relative conductivities.
2. The spinal fluid had the highest conductivity of any of the tissues studied, the lung and the liver the lowest.
3. The order of the conductivities of the following tissues was unchanged in all the animals studied, with the exception noted in (5), viz., spinal fluid, bile, blood, voluntary muscle, cerebrum, cerebellum, liver, lung. In a limited number of observations the conductivity of the heart fell between that of the cerebellum and the liver, but on account of the wide range of the individual measurements, this can not be considered as established.
4. The conductivity of normal tissues appears to vary according to the season and the general environment.
5. In every normal adult animal studied, the conductivity of the cerebrum was higher than the conductivity of the cerebellum. In fetuses and in very young rabbits this relation was reversed—the conductivity of the cerebellum being higher than the conductivity of the cerebrum until about the time when the young rabbit left the nest and began voluntary activities, when the normal adult conductivity relation of the cerebrum and the cerebellum appeared to be established. (See Fig. 33.) A most significant corollary to this observation was found

* It should be emphasized that in the measurements described here a 1,000 cycle alternating current was employed, while in the capacity measurements to be described later, currents of from 800 to 4½ million cycles were used.

in the post-mortem examination of the brains of two patients, one of whom died after days of unconsciousness resulting from a brain tumor, while the other, who died from carcinoma of the stomach, was conscious to the end. In the patient who

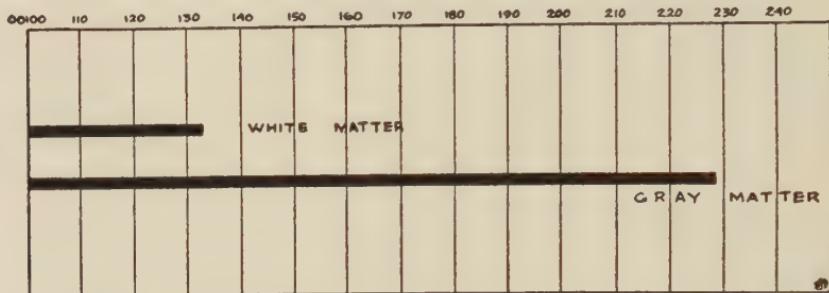


FIGURE 61. Relative electric conductivities of the gray and the white matter of the brain.

had been unconscious, the conductivity of the cerebellum was higher than that of the cerebrum. In the other patient, as in all our normal animals, the conductivity of the cerebrum was higher than that of the cerebellum.

6. The conductivity of the gray matter of the brain is higher than that of the white matter. (Fig. 61.)

7. Exhaustion from any cause—surgical shock, insomnia,

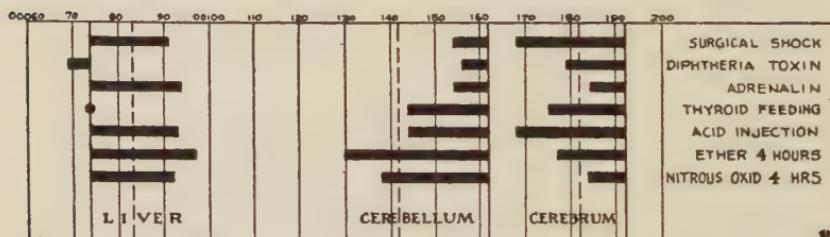


FIGURE 62. Changes in the electric conductivity of the brain produced by various exhaustion-producing agents.

emotion (fright), infection, etc.—is marked by a diminished conductivity of the brain and an increased conductivity of the liver. (Fig. 62.)

8. The immediate effect of activation appears to be an increased conductivity of the brain, tending later to decrease as

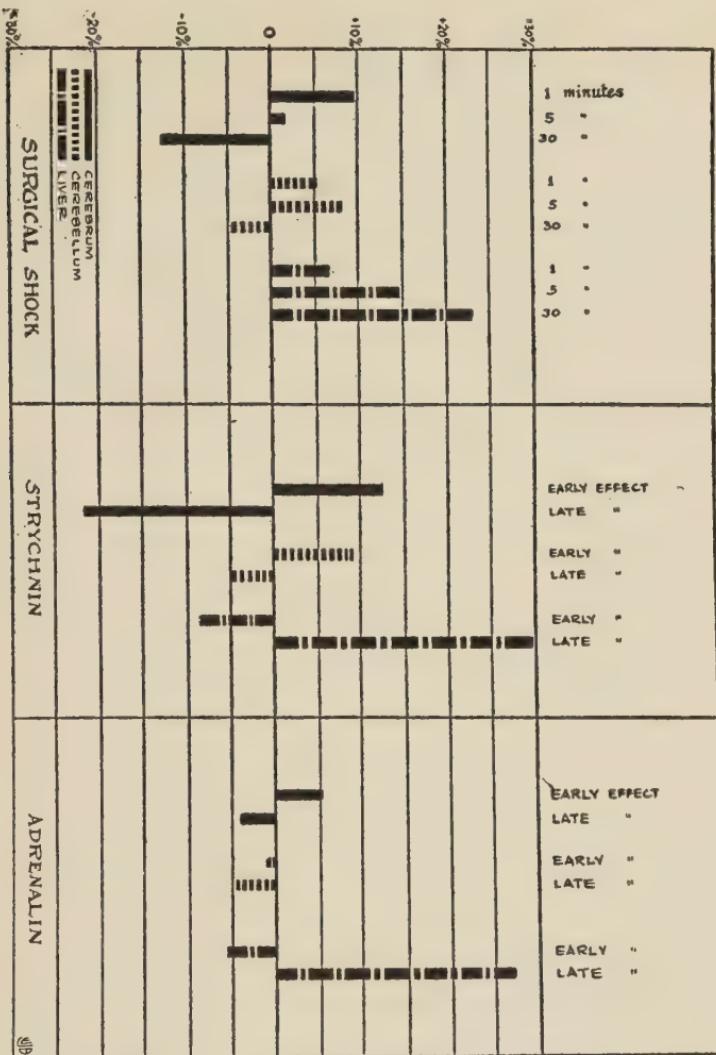


FIGURE 63. Early and late effects of stimulation on the electric conductivity of the brain and the liver.

the stage of exhaustion approaches. This has been shown to be an immediate effect of physical injury; an early effect of the injection of diphtheria toxin; an immediate effect of the injection of adrenalin. (Fig. 63.)

9. Thyroid feeding in large doses over a prolonged period

produces the typical symptoms of hyperthyroidism with ultimate exhaustion, accompanied by the changes in the conductivity of the brain typical of exhaustion from any other cause; i. e., the conductivity of the cerebrum and cerebellum is decreased.

10. Thyroid feeding in moderate doses until the symptoms

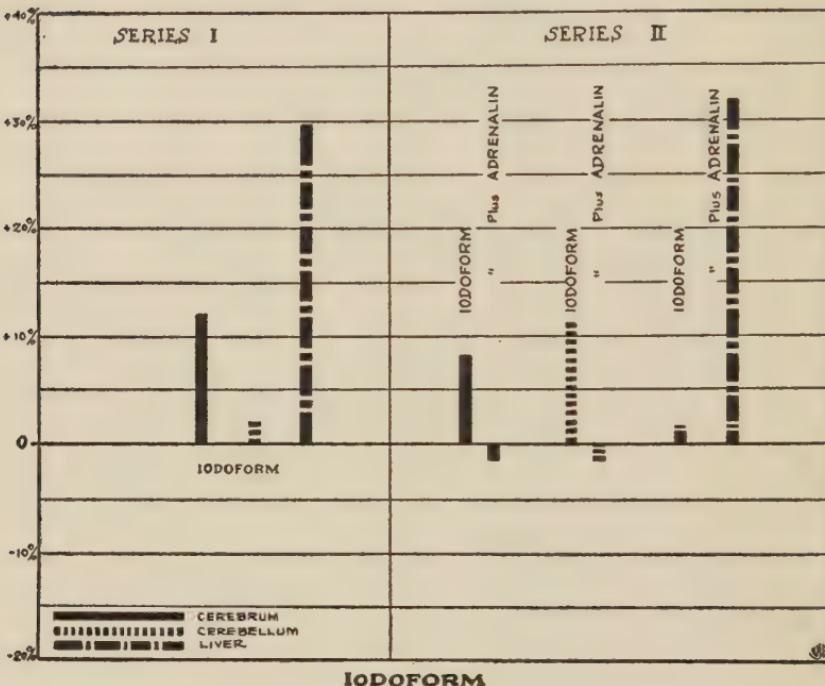


FIGURE 64. Comparison of the effects of iodoform and of iodoform plus adrenalin on the electric conductivity of the brain and the liver.

of hyperthyroidism appear, but not to the stage of exhaustion, produces conductivity changes in the brain and in the liver typical of the stage of stimulation produced by other agents; i. e., increased conductivity of the brain and decreased conductivity of the liver. These changes were diminished or reversed by the administration of adrenalin.

11. Iodoform increases the conductivity of the brain and the liver. These changes are reversed by adrenalin. (Fig. 64.)

12. The injection of hydrochloric acid produced diminished

conductivity of the cerebellum and cerebrum and increased conductivity of the liver. The injection of sodium bicarbonate produced increased conductivity of the cerebellum and cerebrum and decreased conductivity of the liver. (Fig. 65.)

13. Rabbits were kept awake continuously for a prolonged period. At the end of this period a number were killed and conductivity measurements made; others were allowed a brief

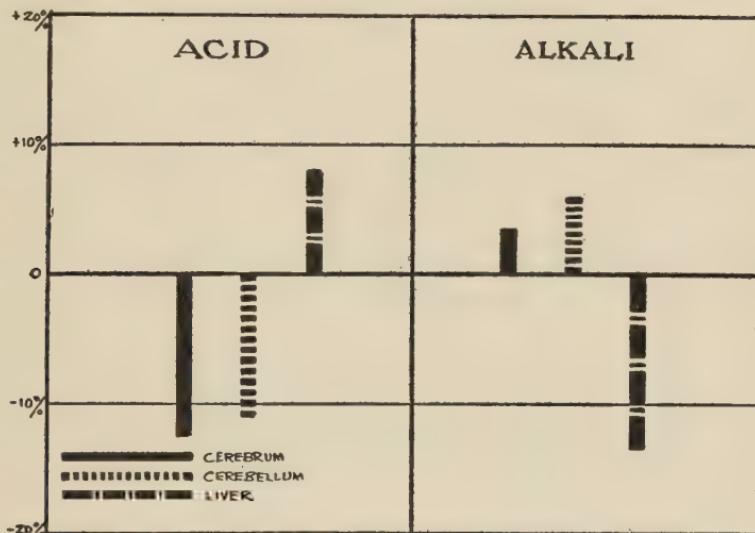


FIGURE 65. Opposite effects of the injection of an acid and of an alkali on the electric conductivity of the brain and the liver.

period of rest of from four days to a week. At the end of the insomnia period the conductivity of the brain was decreased and the conductivity of the liver was increased; at the end of the short period of rest, the conductivity of the brain and of the liver was but little changed, if at all; at the end of the longer periods of rest, the brain was again approaching its normal conductivity, while the conductivity of the liver was not affected.

14. A limited number of observations indicate that the changes produced by the injection of a toxin are minimized, provided the toxin is applied in the presence of morphine; that is, excessive doses of a toxin alone decrease the conductivity of the brain and increase the conductivity of the liver; in this

limited series of observations the conductivity of the brain remained practically unchanged when diphtheria toxin was ad-

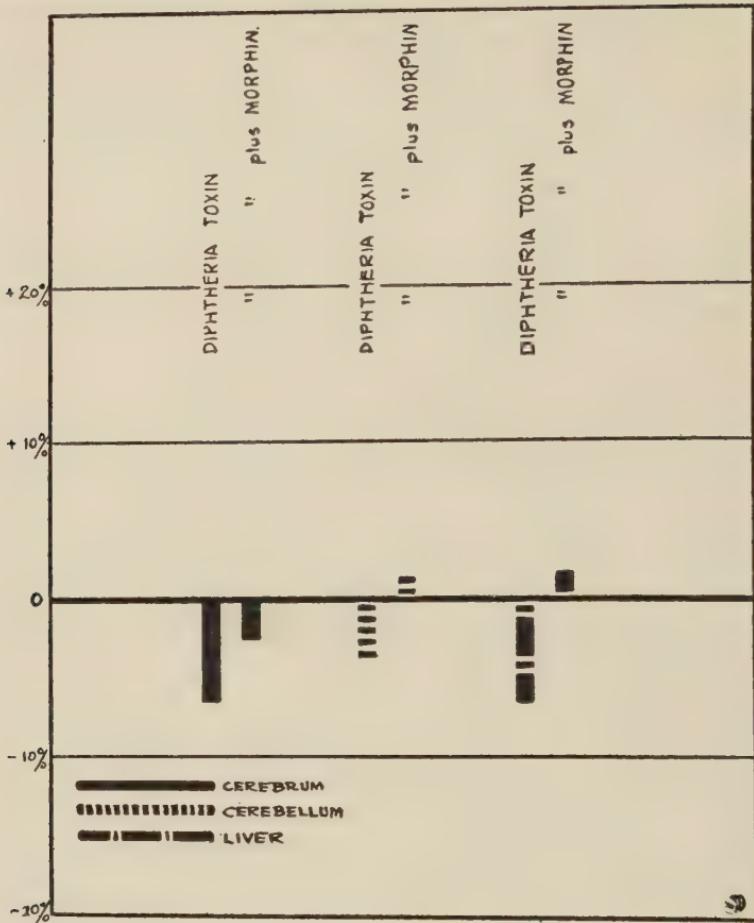


FIGURE 66. Comparison of the effects on the electric conductivity of the brain and the liver of the injection of diphtheria toxin in a normal and in a morphinized animal.

ministered in a morphinized animal, and the conductivity of the liver was but slightly altered. (Fig. 66.)

15. A limited series of observations of the influence of various agents, which produce marked clinical effects, indicate that the progress of alteration in function produced by any agent is coincident with changes in electric conductivity.

16. In the pathological specimens studied, active malignant growths have a high conductivity in comparison with adjacent normal tissue and the inactive portions of the same growth, and with growths of a non-malignant type. (Fig. 67.)

From these findings it would appear that the intracellular changes in exhaustion and shock which are revealed by the

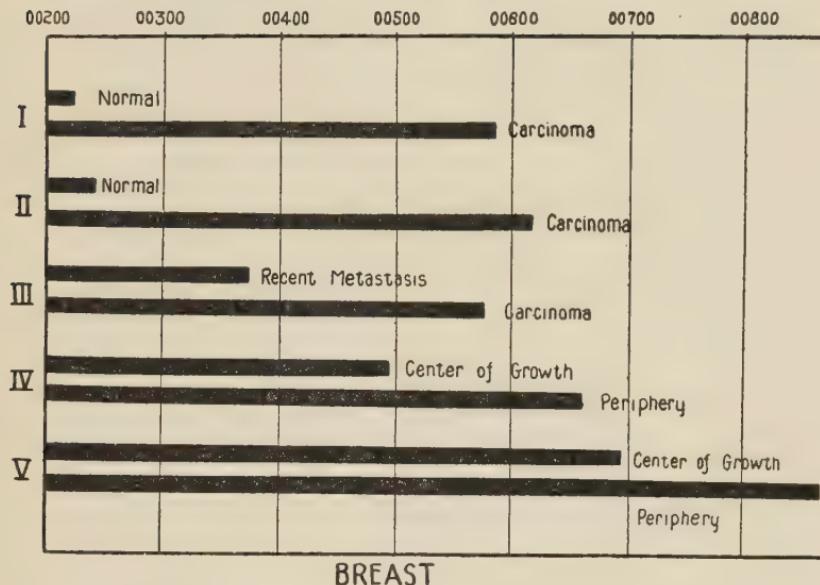


FIGURE 67. Comparison of the electric conductivity of normal breast tissue with that of carcinoma of the breast.

microscope are paralleled by alterations in electric conductivity, and that both the histologic and the electric changes bear a direct relation to the vitality of the organ.

Later in collaboration with Maria Telkes, and Amy Rowland, a second series of studies was made. At this time the conductivity and capacity of the tissues were measured in the living animal.

For such measurements the electrodes had to be sufficiently rigid to prevent any changes in their form on their insertion into the tissue and they had to be constructed in accordance with the required sensitivity of the measurements. A further requirement was that the electrodes should be so constructed

as to cause minimal injury in the tissues, because bleeding or other effects of injury would alter the physiological conditions. After a considerable number of experiments, platinum-iridium hypodermic needles of small gauge (23 to 26) were chosen. Two of these were sealed in one end of a glass tube which served as a holder. The needles had previously been welded to copper wires by means of which they were connected to the measuring apparatus. One of the wires was surrounded by a capillary glass tube to isolate it within the glass holder. The platinum needles were fused into the glass tube so as to extend beyond it for about one cm. The other end was then sealed to the glass holder by means of de Khotinsky cement and the wires leading to the measuring apparatus were carefully insulated. Before this electrode was constructed, a piece of lead glass tubing had been drawn out into a capillary to fit on the needles. Two pieces about 6 mm. in length were cut off and put aside. When the needles were fused into the glass holder and while the glass was still hot, one of the two pieces of glass capillary tubing was slipped over each of the needles and fused to it and at the same time the inside of the platinum needles was filled with glass. It is very important that the glass capillary tubes should be sufficiently thick to insulate completely the part of the needle which they cover and also that they should be fused so as to form one piece with the glass holder. On the other hand, the glass capillaries should not enlarge the needles for it should be possible to insert the needles into the tissue with a minimum of pressure. The glass should have the necessary expansion coefficient to prevent the needle from being broken off. The finished electrode is shown in figure 68. The free length of the platinum needles was 4 to 5 mm. and the distance between them was 3 to 4 mm. Electrodes, consisting of 25 or 26 gauge needles 3 mm. in length and 3 mm. apart, were used for tissues of a soft consistency, like the brain or liver; for muscle, stronger needles were generally used.

The size of the electrodes was carefully selected in order that when the current passed through them, the lines of force would require a minimum volume between and around the electrodes. To make sure that this requirement was fulfilled,

the electrodes were tried out experimentally in connection with the measuring instrument with which they were to be used. As part of the preliminary investigation, different tissues were cut into a series of small rectangular pieces and their conductivity was measured. It was found that when the block of tissue was of such a size as to surround the electrodes by 5 mm. in each direction, no change could be observed between its conductivity and that of a considerably larger piece of tissue. Even when the amount of tissue surrounding the electrodes was diminished so as to leave only enough tissue around the needles

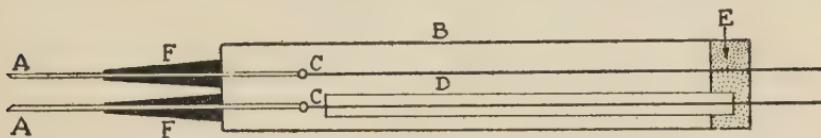


FIGURE 68. Electrode used in making measurements of electric conductivity and capacity in the living animal. A, Platinum iridium needles; B, Glass holder; C, Copper wires; D, Glass insulating tube; E, Seal of de Khotinsky cement; F, Glass capillaries.

to extend 2 mm. in each direction, the change in conductivity amounted to less than one per cent.

The cell constant was determined with n/100 KCl solution. The cell constant of the electrode couples varied from 1.5 to 3. The cell constant was determined before and after an experiment to find out whether or not the electrodes had changed in form during the experiment. After an experiment the electrodes were carefully washed with 70 per cent alcohol, dried, and kept in glass containers. When the electrodes were handled carefully, it was possible to make a series of 20 or more measurements with the same electrode before it depreciated.

Our experiments were performed on male rabbits which were all kept under similar conditions. The animal was first anesthetized by urethane (1 gm. per kg. by rectum) or ether. The electrodes were inserted into the different tissues and attached to the animal by means of holders. After the electrodes were inserted, conductivity and capacity measurements were taken for from 20 to 30 minutes, or until equilibrium was reached. The agent whose effect was to be tested was injected into the ear vein of the rabbit. After the injection, conductivity

and capacity measurements were made as often as was necessary. The time required for a single measurement was about thirty seconds in the earlier experiments and ten seconds in the later experiments. This made it possible, in the later experiments, to use an electrode in each of two different tissues of the same animal and to take almost simultaneous readings.

Throughout the experiments, specific conductivity * and capacity † were measured, the value of the conductivity just before the injection or other manipulation being considered as 100 per cent.

The effect of various injected electrolytes could be explained as due to their own electric conductivity added to that of the tissues. That this is not the case becomes evident from the results, as when various salts were injected in amounts which produced equal conductivities; some, as for example, NaCl, produced large changes in the conductivity of the tissues, while a corresponding amount of MgSO₄ either failed to produce any marked change or decreased the conductivity. (Figs. 69, 70.) The injected electrolytes are absorbed from the blood circulation and exert their physiological action on the cell membranes. The resultant change in conductivity is therefore a measure of the action of the injected material upon the physiological activity of the cell membrane.

Our findings may be summarized as follows:

1. Measurements of the electric conductivity and capacity of different tissues of a living rabbit showed characteristic changes under various physiological influences.
2. In general, changes in capacity ran parallel to changes in conductivity.
3. The injection of adrenalin produced an increase in the conductivity and capacity of the brain and spinal cord and in the medulla of the adrenal glands, and a decrease in the conductivity and capacity of the liver, kidney, spleen, thyroid gland, cortex of the adrenal glands and of voluntary muscle. (Fig. 71.)
4. The increase in the conductivity and capacity of the

* The conductivity of 1 cubic centimeter of tissue.

† That capacity in micro-microfarads which is connected in parallel with the measuring resistance box to obtain a sharp tone minimum.

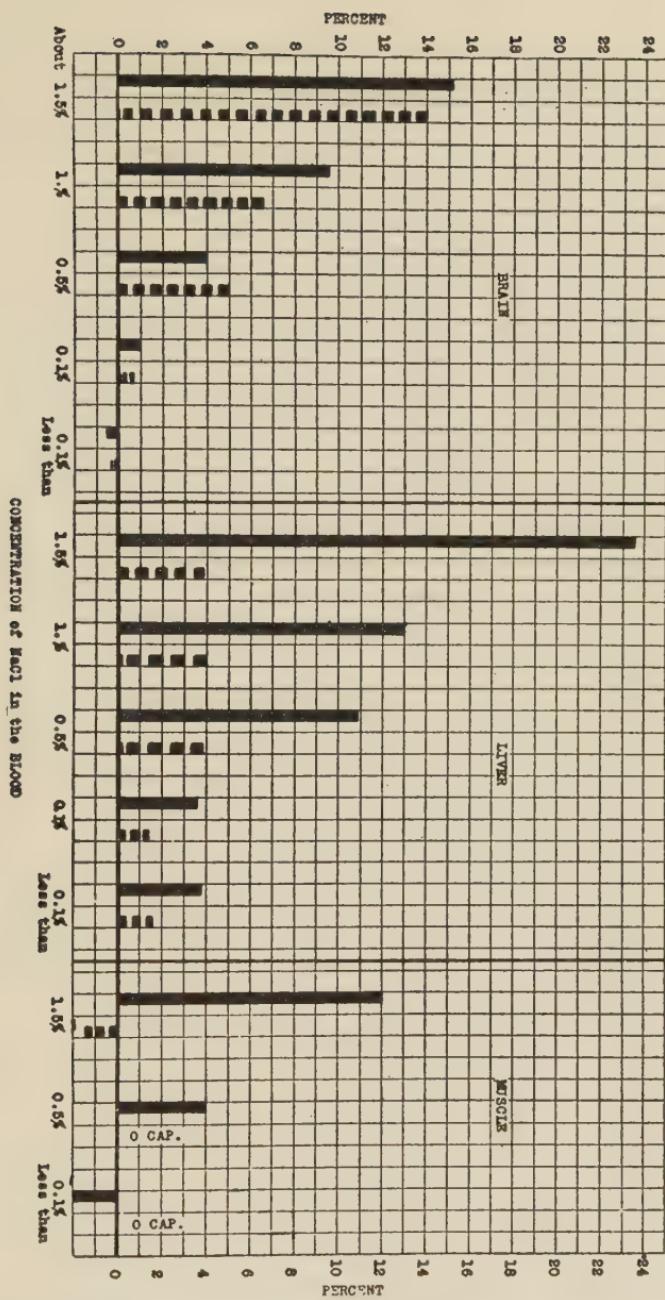


FIGURE 69. Percentile changes in the electric conductivity and capacity of the brain, liver and muscle produced by sodium chloride.

normal brain produced by adrenalin was not altered by the previous injection of sodium chloride.

5. The amount of increase in the conductivity of the brain produced by adrenalin was altered when the animal was adrenalectomized or iodized or when calcium chloride or morphine was injected previous to the injection of adrenalin.

6. The increase in conductivity and capacity of the brain

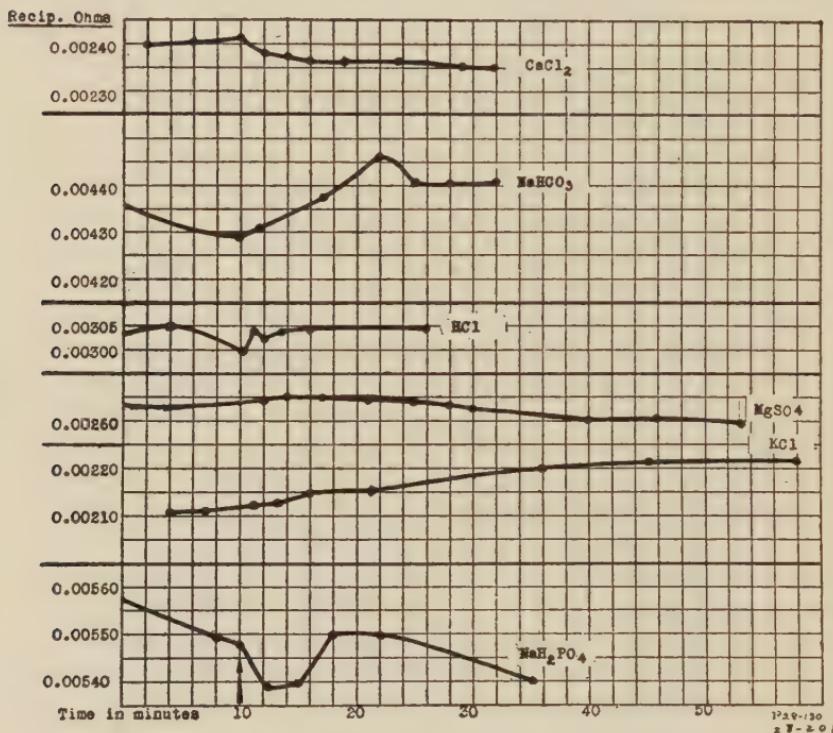


FIGURE 70. Changes in the conductivity of the brain produced by various salts.

produced by adrenalin was diminished after thyroidectomy. (Fig. 72.)

7. Scarcely any change in the conductivity and capacity of the brain was produced by adrenalin in a rabbit which had been subjected to prolonged insomnia.

8. The conductivity and capacity changes in the brain pro-

duced by the injection of adrenalin were diminished in myxedematous, hepatectomized, and thyroid-fed animals.

9. The decrease in conductivity and capacity of the normal liver after the injection of adrenalin was unaltered by previous

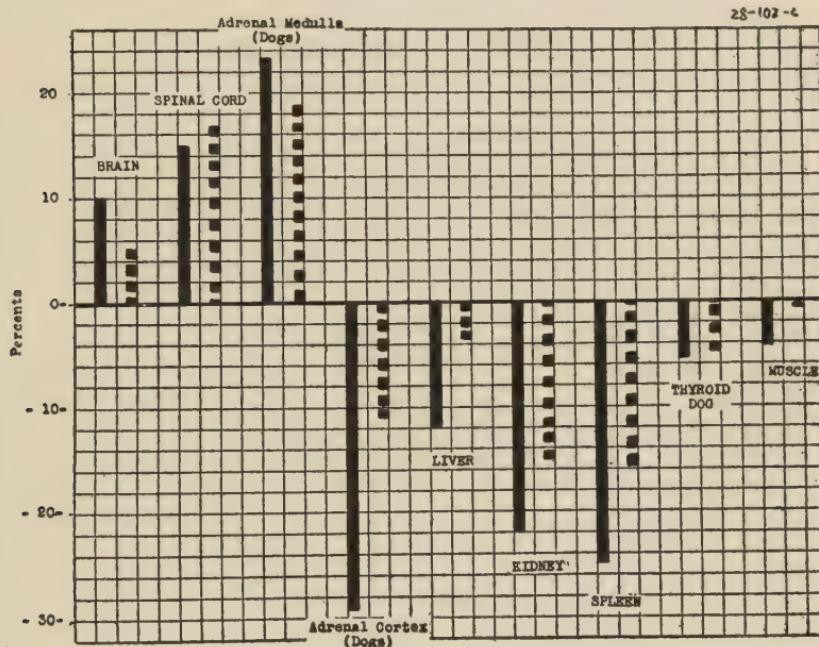


FIGURE 71. Percentile changes in the electric conductivity and capacity of various tissues produced by adrenalin.

injections of sodium chloride or when the animal was in a nephritic condition.

10. The decrease of the conductivity and capacity of the normal liver after the injection of adrenalin was diminished in iodized animals and after the injection of calcium chloride.

11. The decrease in the conductivity and capacity of the kidney of a nephritic rabbit produced by the injection of adrenalin was less than that of the kidney of a normal rabbit. (Fig. 73.)

12. The decrease in the conductivity and capacity of voluntary muscle after the injection of adrenalin was unchanged by a previous injection of sodium chloride. The conductivity

and capacity of the muscle of adrenalectomized and hepatectomized animals increased slightly after the injection of adrenalin, instead of decreasing as in a normal animal.

13. The intravenous injection of *calcium chloride* caused a slight decrease in the conductivity and capacity of the brain and a slight increase in that of the liver.

14. The hypodermic injection of *magnesium sulphate* caused

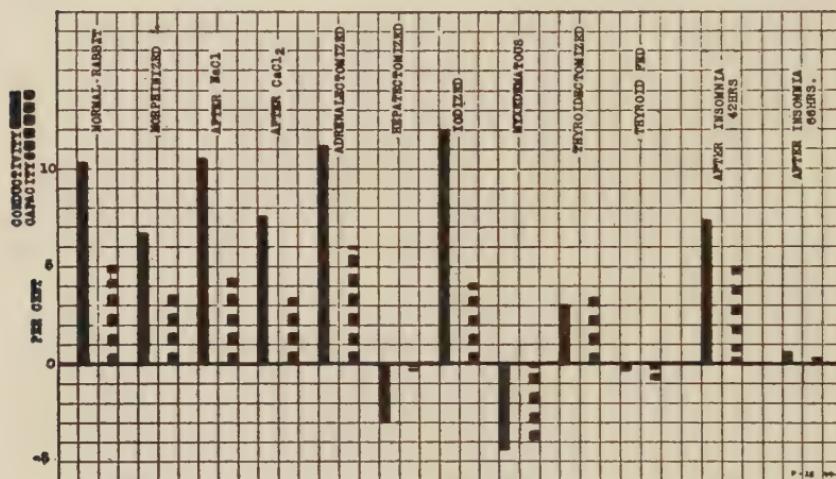


FIGURE 72. Effect of various agents and conditions on the percentile changes produced by adrenalin on the electric conductivity and capacity of the brain.

no immediate change in the conductivity or capacity of the brain or the liver but later a small decrease in the brain and no change in the liver.

15. The injection of *sodium bicarbonate* caused an increase in the conductivity and capacity of the brain and a decrease in the conductivity of the liver.

16. The injection of *potassium chloride* caused no definite change in the conductivity or capacity of the brain or the liver.

17. *Sodium acid phosphate* caused a slight decrease in the conductivity and capacity of the brain.

18. A small dose of *sodium cyanide* caused a decrease in the conductivity and capacity of the brain but a lethal dose caused an increase.

19. *Morphine* caused a slight gradual decrease in the conductivity and capacity of the brain and the liver.
20. *Alcohol* (ethyl) caused a slight increase in the conductivity and capacity of the brain 15 minutes after it was injected.
21. *Ether* caused an immediate increase in the conductivity

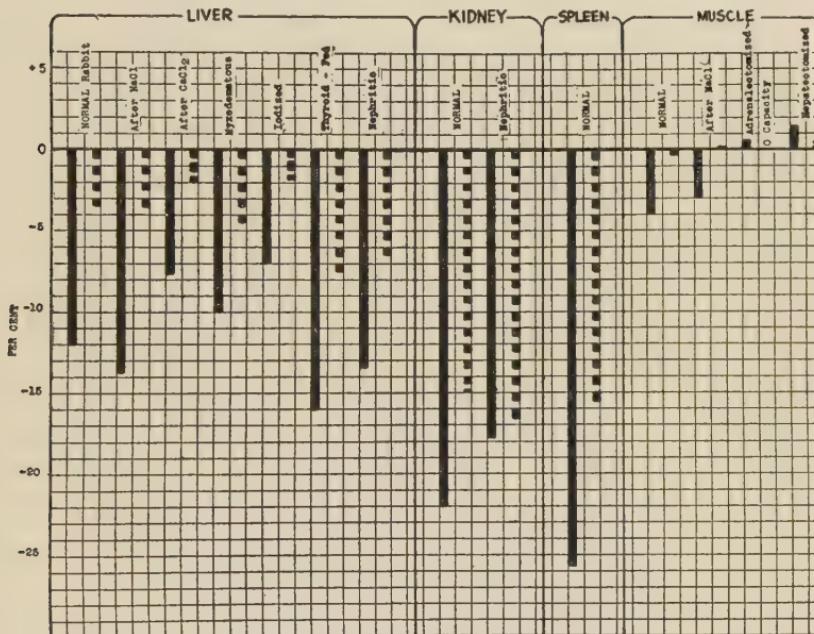


FIGURE 73. Effect of various agents and conditions on the percentile changes produced by adrenalin on the electric conductivity and capacity of the liver, kidney, spleen and muscle.

and capacity of the brain followed by a decrease as the anesthesia continued.

22. *Strychnine* (during convulsions) caused a large decrease in the conductivity and capacity of the brain followed by an immediate return toward the normal.

23. *Asphyxia* caused an increase in the conductivity and capacity of the rabbit's brain which is similar to the increase produced by the intravenous injection of adrenalin. (Fig. 74.)

24. *Asphyxia* caused an increase in the conductivity and

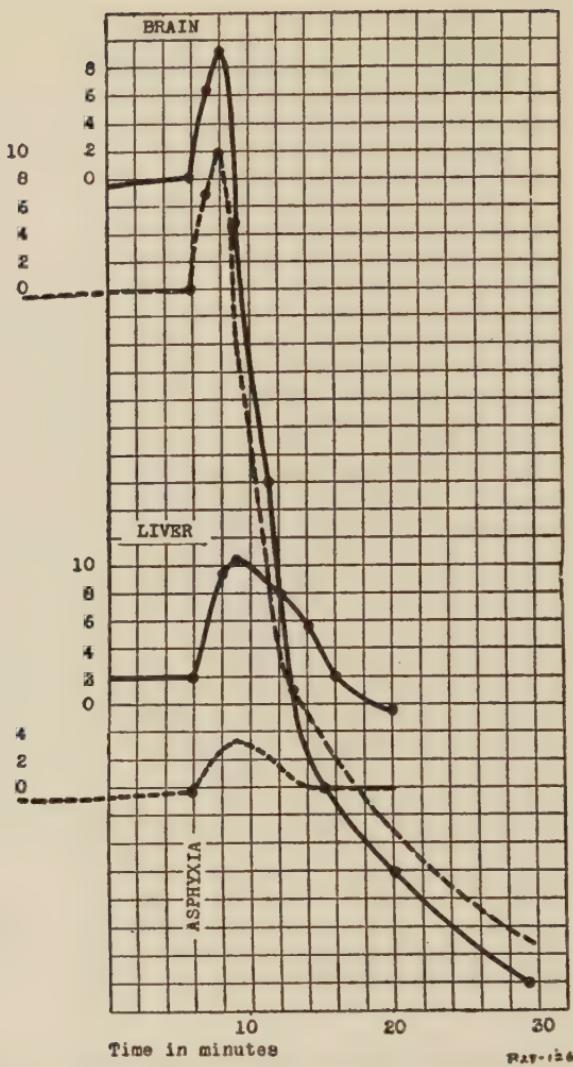


FIGURE 74. Percentile changes produced by asphyxia on the electric conductivity and capacity of the brain and the liver.

capacity of the liver, an effect opposite to that produced by adrenalin.

GENERAL CONCLUSIONS

1. Influences which affect the general physical condition of the organism produce changes in electric conductivity in the

dominating reactive tissues, these changes being uniformly and measurably manifested in the brain and the liver. Apparently these changes in conductivity appear more promptly than any gross clinical alteration.

2. Apparently the liver is more promptly and more markedly affected than any other tissue, as animals showing either no or very slight changes in the cerebrum and cerebellum will often show a marked alteration in the conductivity of the liver. On account of the wide variation in liver measurements and the apparent susceptibility of this organ to seasonal and environmental changes, the effects of applied agents are best determined by measurements of the cerebrum and cerebellum.

3. A study of the individual measurements from which the averages have been computed seems to indicate that the variations represent slightly different stages in a process that varies in rate in different animals and in the different organs of the same animal.

4. In view of the above indication and the direct evidence of the measurements we feel justified in the assumption that the first effect of stimulation within the organism is a slight and prompt increase in the conductivity of the cerebellum followed by a gradual continuous fall; a relatively slower increase in the conductivity of the cerebrum followed by a gradual continuous decrease; and a slight decrease of the conductivity of the liver followed by a rapid continuous rise to above the normal as the state of exhaustion approaches.

5. These studies indicate that electric conductivity measurements provide a means whereby to further the interpretation of the normal operation of the organism, and whereby to measure the progress of pathological processes within the various organs and tissues.

6. From our findings to date, it would appear that the intracellular changes in exhaustion and shock which are revealed by the microscope are paralleled by alterations in electric conductivity, and that both the histological and the electric changes bear a direct relation to the vitality of the organ.

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CHAPTER 24. TEMPERATURE MEASUREMENTS

VARIATIONS in functional activity indicate variations in oxidation; variations in oxidation are manifested by variations in heat production. If heat is a constant product of functional activity, then, if we could measure the progressive changes in the temperature of the various tissues and organs during the various phases of excitation and exhaustion under conditions identical with those formerly studied, we not only should be able to check our findings in the previous researches but should be able finally to link those findings with the clinical evidence.

As the first means to this end we decided to use the method of measurement employed by physicists for the measurement of minute temperature variations, that is, to employ thermocouples so constructed that they could be applied to the brain, liver, muscle, or other tissue of the living animal. These experiments were carried out with the collaboration of Amy Rowland, S. W. Wallace and Lillian Jacobson.

This method of measuring variations in the temperature of living tissues was first utilized, as far as we have been able to discover, by Becquerel and Breschet^{1, 2} in 1835, when they used thermocouples to determine variations in temperature in different parts of the body in different pathological conditions. They inserted thermocouples into various muscles of the arm, the thigh and the leg, into the abdomen and into different portions of tumorous growths. They even inserted the couples into the auricles of the heart to determine the difference between the temperature of arterial and venous blood. Their reasons for undertaking this research are significant. In their *Premier Mémoire sur la Chaleur Animale*, they state in brief that this

research was suggested as the result of certain other attempts to answer the following questions: "Are the vital forces of an electrical or chemical nature? Has the organism its own peculiar mode of action?"

In 1869 and 1870 Schiff³ published the results of an extensive research undertaken in the hope of answering the following questions:

"Is the stimulation of the nerves of sensation necessarily transmitted to the cerebral hemispheres, or is the direct transmission of the stimulation in the normal animal arrested at the spine or in the pons Varolii? Furthermore, is the transmission to the brain in accordance with the fundamental laws governing transmission along the nerves? Is the formation of a perception in the brain accompanied by phenomena which the means of investigation at our command will not permit us to regard as subject to the general laws of material movement?"

In Schiff's research thermocouples were employed which were applied directly to exposed nerves or inserted into different parts of the brain. The author felt that he had established the following points:

1. That the irritation of the nerve increased its temperature.
2. That successive irritations produced diminished response of the nerve.
3. That every peripheral irritation gave a response in the brain manifested by increased temperature.
4. That the temperature was always higher in the right hemisphere of the cerebrum.
5. That there was no temperature change in the cerebellum.
6. That no response to peripheral irritation was noted in the brains of animals under morphine. "These preparations (of opium) especially of morphine do not permit any manifestations to an appreciable degree of the effect of sensory irritation on the temperature of the brain."
7. That not only tactile sensation but stimulation of all the organs of special sense produced an increase in the temperature of the cerebrum.
8. That repeated excitation of the special senses—sight, hearing—produced progressively lessening effects as manifested by temperature changes in the brain. "It is seen, consequently,

that this last series of experiments is perhaps the most important for our conclusions."

9. That psychic excitation, independent of the sensations which produced it, was accompanied by a production of heat in the nerve centers, which was quantitatively greater than the heat engendered by less complex sensations.

The author believed that his observations definitely excluded the possibility that the temperature changes noted were due to circulatory changes; and that his experiments were sufficient "to establish, with all the desirable precision, that the production of heat which we have observed is really the result of excitation which is peculiar to and an intrinsic part of the nerve elements."

In 1868 Rosetti⁴ recorded an attempt to construct thermocouples for the measurement of body temperature and reported one practical application.

Also in 1868, Lombard⁵⁻⁹ described a thermopile devised by him for the study of external temperature changes. In particular he studied the relation of heat to mental work as manifested by temperature changes of the outside of the head, which he believed could be referred to changes in the temperature of the brain. Albutt¹⁰ in 1875 employed similar apparatus to that of Lombard in an attempt to discover the relation between internal and external heat.

From that time the literature records the occasional use of thermo-electric apparatus for the measurement of changes in bodily heat, but no especially noteworthy researches are recorded until within recent years. A bibliography of these intermediate studies is offered by Benedict and Snell¹¹ in their description of a resistance thermometer devised by them for the observation of variations in the rectal temperature of subjects in a calorimeter chamber.

In 1909 Gamgee¹² devised a clinical apparatus in which thermocouples were employed for the continued measurement and registration of diurnal variations in temperature, and following his lead, Woodhead and Varrier-Jones¹³ produced a thermo-electric apparatus which could be used consecutively for 24 hours or more without disturbing the patient.

In 1912, A. V. Hill¹⁴ utilized the thermo-electric method in

an investigation to determine the presence or absence of temperature changes during the transmission of a nervous impulse. He offers the following conclusions:

"Tetanus up to 25 secs., of a live nerve, does not cause a change of temperature (other than at the seat of excitation) of more than about $\pm 6 \times 10^{-6}$ ° C. There is no evidence of any change at all, but the method does not allow conclusions beyond this limit. For every single propagated disturbance, the change of temperature, therefore, can not exceed about 10^{-8} ° C., a hundred millionth of a degree. This corresponds to an oxidative process in which only one molecule of oxygen is used in a space of visible size, viz., a 3.7μ cube. This suggests very strongly, though of course it does not finally prove, that the propagated nervous impulse is not a wave of irreversible chemical breakdown, but a reversible change of a purely physical nature."

A thorough search of the literature, however, has discovered no reference to the measurement of variations in the temperature of the brain and other internal organs under diverse conditions, with the exception of the work of the investigators cited above, that of Stengel and Hopkins¹⁵ on the intragastric temperature and the work of MacLeod¹⁶ on the effects of hot and cold applications on the superficial and deep temperatures.

By the invitation of Dr. E. P. Hyde and with the active coöperation of Dr. W. E. Forsythe, our initial experiments were performed at the Nela Research Laboratory. A copper-constantan thermocouple, the wires passed through a glass tube in the end of which the couple was sealed, was used, the "cold" junction being placed in melting ice in a thermos bottle. (Fig. 75.)

Three anesthetized rabbits were used and as the purpose of this test was only to determine the feasibility of proceeding further, a series of rapid tests was made with most gratifying and encouraging results. This preliminary experiment proved:

1. That it is possible to insert a thermocouple directly into the brain, the liver, the muscle, the pleural cavity, for a prolonged period without any noticeable effect upon the general condition of the animal.

2. That practically any alteration in the general condition

of the animal is accompanied by a measurable change in the temperature of the brain.

3. That the temperature of the brain decreases progressively under ether anesthesia.

4. That the injection of adrenalin produces a characteristic

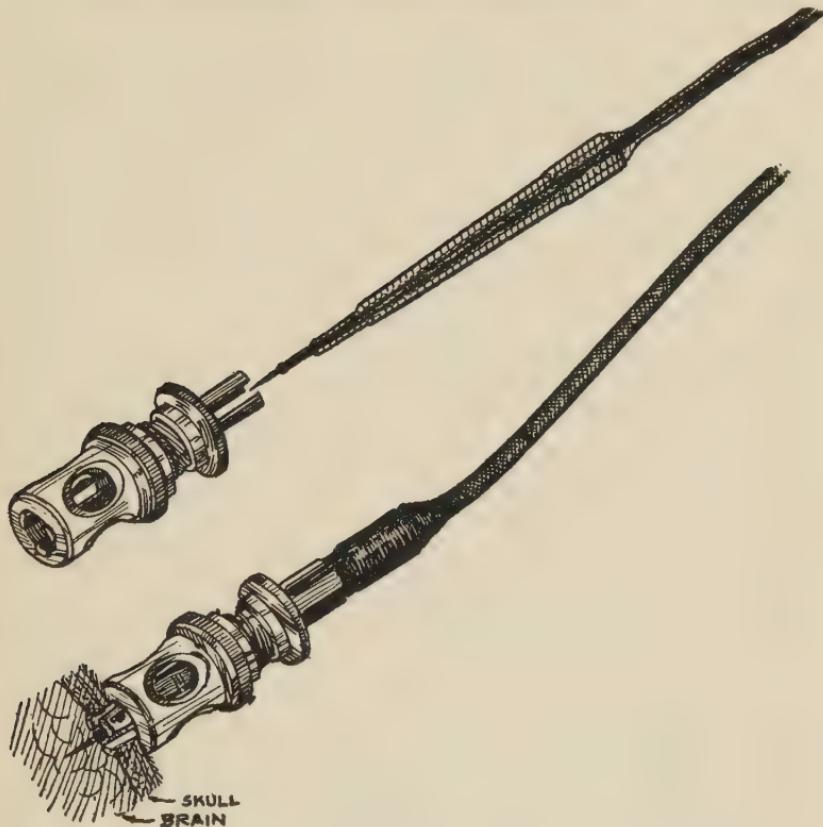


FIGURE 75. Thermocouple designed for measurements of temperature variations in animal tissues.

rise and fall in the temperature of the brain closely related to the clinical phenomena—a finding of extreme significance in view of our later studies.

These curves were not plotted, nor was any attempt made to translate the galvanometer readings into actual temperature variations, but the purpose of this preliminary experiment hav-

ing been attained, we proceeded to devise the essential apparatus for an extensive investigation. We wish at this point again to express our appreciation to Dr. Hyde and Dr. Forsythe for their interest and active coöperation in securing this first evidence.

Apparatus: The essential apparatus consisted of Leeds and Northrup galvanometers of types R and H with especially constructed copper-constantan thermocouples made of 5 mil wire twisted together and soldered. The recording junction was exposed, the leads being separated from each other and protected by concentric glass tubes, the ends of which were joined by dental cement. The junction was kept as small as possible and the protecting glass tubes were of the smallest possible caliber. These tubes were bent into such shapes as could be most easily and firmly secured in the tissue for which each was designed. This is a vitally important point, as closeness and constancy of contact of the thermo-junction with the tissue under examination is essential to the attainment of dependable records.

The use of any metal in the construction of the thermocouples was avoided, for fear it might conduct the heat away from the area of insertion and lead to local cooling. This is an essential precaution in working with an instrument so sensitive to small temperature changes; moreover, it is very important to remove any material which would produce a lag in the response of the indicating instrument to the local changes of temperature.

The "cold" or constant junction of the thermocouple was immersed in a tube of oil suspended in a constant temperature bath, the temperature of which was maintained at 38° C., thus bringing the whole range of temperature in the tissue studied upon the scale of the galvanometers. As the extreme range of temperatures involved in living rabbit tissues does not exceed 7° C., it is possible to measure variations by the direct deflection of a galvanometer of suitable sensitivity.

The circuit was of very low resistance with all wire connections soldered and symmetrical, and with all contacts non-frictional and of low resistance. The galvanometers were short-circuited when not in use and were protected from extreme deviations.

Calibrations were made immediately after the measurements

to which they applied, as there is always a tendency for the instruments to drift from day to day. The calibrations were made by immersing the active junctions along with a standard thermometer in water in a thermos bottle. To avoid error due to the lag in the response of the large bulk of mercury in the standard mercury thermometer, the readings were always made on a falling temperature, as the decrease was so gradual as to minimize error. With this apparatus, temperature variations could be measured to within 0.01° C.

Technic: As far as possible in each group of experiments rabbits of approximately equal size and age were used. This point was not as essential, however, as in our earlier conductivity studies—as in these experiments each animal acted as its own control.

In the anesthetized animal, a small hole through the skull over the cortex at the right of the median ridge was made by an especially constructed trephine, the size of the hole being just large enough to admit the glass tube containing the thermo-junction. This tube was bent at an angle, one arm of which was just long enough to enter the brain to a depth of approximately one-third to one-half a centimeter, the other lying along the top of the head. Absorbent cotton was placed over this to eliminate the chance of chilling, the whole being firmly secured in place by strips of adhesive. By this means the thermo-junction was held securely in place even when the animal moved violently.

In the early experiments only one galvanometer was used. As this precluded the possibility of simultaneous readings of the variations in temperature in different organs, another galvanometer was installed. Thus two observers could make synchronous readings at 15-second intervals or less.

Seventy-seven rabbits were used in these preliminary studies, consistent records being secured in sixty-three. Any experiment was discarded if at the termination of the experiment any fault in contact was found, the insertion of the thermo-junction being examined at the conclusion of every experiment. As noted above, calibration at the conclusion of each group of experiments and repeated testing of the constant temperature checked the findings throughout.

In these studies, the effects of various agents and procedures was observed, the temperature variations in the brain being measured in every instance, in the liver in most of the animals, and in the muscle and thyroid each in two instances.

In the first experiments, as noted above, the galvanometer readings were recorded at 30-second intervals, readings being made alternately when more than one thermocouple was employed. Later by the use of two galvanometers and two observers simultaneous readings were made at 15-second intervals.

Fifteen-second intervals, however, are not sufficiently short to assure the recording of every variation in the temperature of the brain. Frequently a rapid deflection of the galvanometer was observed between the recorded readings, but to assure the greatest possible accuracy by the undivided attention of the observers to the 15-second readings, they were told to allow no other observation to interfere with the correct reading of these—an important injunction in experiments which in many instances were 1½ to 2 hours or more in length, requiring the accurate reading and recording of 300 and more galvanometer readings by each observer. It early became apparent that a method of continuous record is required to register all the temperature changes in the infinitely sensitive brain.

These studies have yielded the following results:

1. From the very beginning it was evident that variations in the temperature of the brain under varying conditions parallel variations in the histologic picture and in the electric conductivity of the brain under the same conditions. Thus the progress of exhaustion from any cause was marked by a progressive decrease in the temperature of the brain and the liver, the rapidity of which was in direct relation to the rate at which the degree of exhaustion advanced.

2. The stage of excitement of ether anesthesia was marked by an increase in the temperature of the brain; but during surgical anesthesia the temperature fell continuously until death. On the other hand, in an animal under nitrous oxide anesthesia, the temperature of the brain remained practically unchanged even during prolonged anesthesia. See Fig. 53.

3. After hepatectomy the temperature of the brain declined progressively until death.

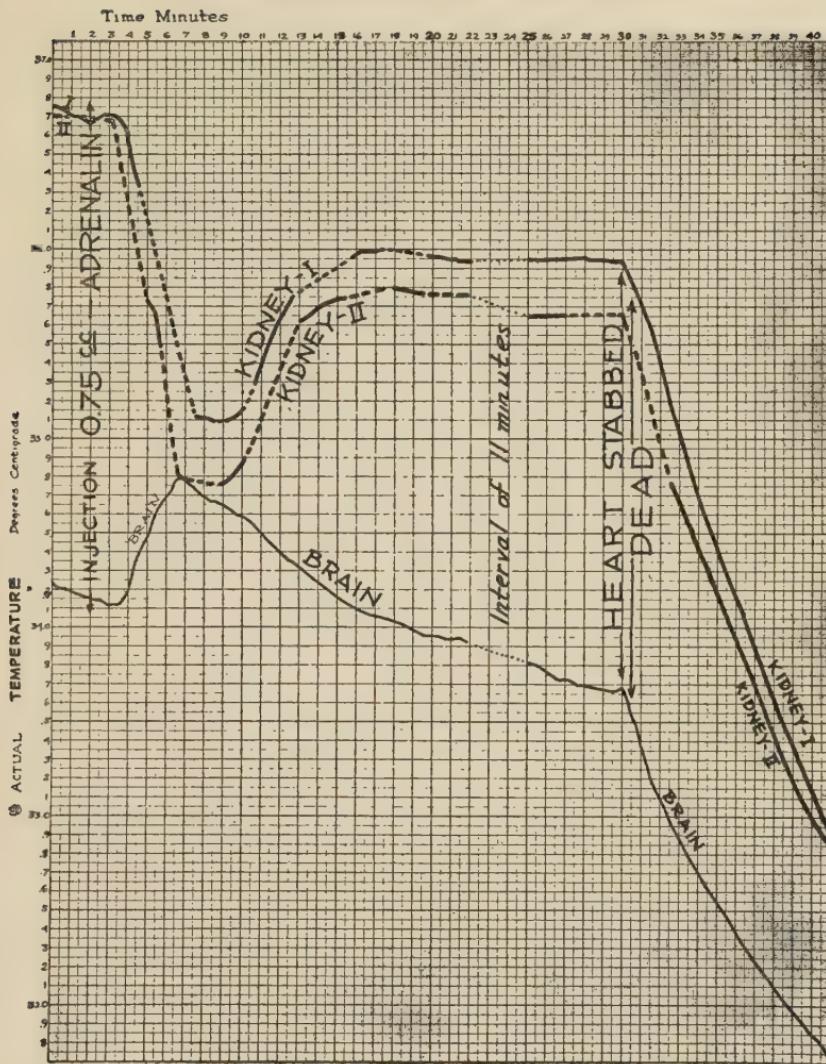


FIGURE 76. Effect of the injection of adrenalin on the temperature of the brain and the kidneys.

4. Muscular activity, produced by direct electric stimulation of a nerve, was accompanied by rapid alterations in the temperature of the brain and the liver corresponding to the phases of the muscular activity—these alterations, however, *being in opposite directions*.

5. No significant alteration in the temperature of the liver was produced by the injection of strychnine, of an acid or of an alkali, although marked and characteristic changes, corresponding in each case to the clinical phenomena, were produced by each in the temperature of the brain. See Fig. 55.

6. Exposure of the viscera and abdominal trauma alike produced a rapid fall in the temperature of the brain and the liver, the change in the latter being in part but not entirely accounted for by the direct chilling of the liver substance.

7. The restorative effect of the introduction of hot water into the stomach was marked by an immediate elevation of the temperature of the brain which *measurably preceded—in some instances by a minute or more—the resultant elevation in the temperature of the liver.*

8. Of especial significance were the temperature changes which followed the injection of adrenalin under varying conditions.

(a) In normal animals the temperature of the brain was *increased* by adrenalin, but returned immediately to or below the preceding level.

(b) In normal animals the temperature of the liver was usually decreased by the injection of adrenalin.

(c) A limited number of observations indicated that the temperature of the spleen, the kidneys, voluntary muscles and intestinal walls was decreased by the injection of adrenalin. (Fig. 76.)

(d) In the absence of the liver the injection of adrenalin produced a diminished or no change in the temperature of the brain.

(e) In the absence of the thyroid the reaction of the brain to adrenalin was less than in normal animals.

(f) In iodized animals the reaction to adrenalin appeared more promptly and was greater than in normal animals. (Fig. 77.)

(g) After adrenalectomy the reaction to adrenalin was approximately the same as in normal animals.

(h) In morphinized animals adrenalin increased the temperature of the brain but this increase was less than in normal animals and was maintained for prolonged periods.

(i) After the administration of strychnine adrenalin caused an abrupt rise in the temperature of the brain and an abrupt fall in the temperature of the liver.

(j) The transfusion of blood after hemorrhage did not affect the normal reaction of the brain to adrenalin.

Of particular significance were the following findings:

(a) In voluntary muscular activity and as a result of the

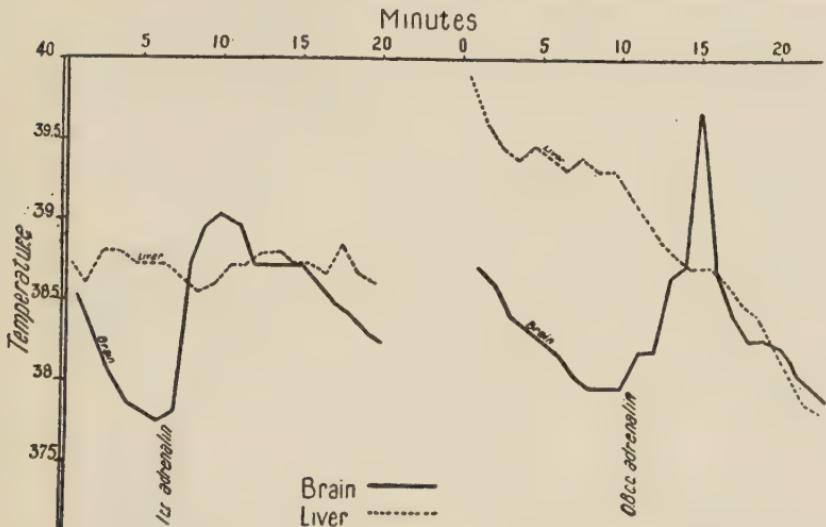


FIGURE 77. Effect of the injection of adrenalin on the temperature of the brain and the liver in an iodized animal.

direct electric stimulation of a nerve the temperature of the brain and of the liver varied in opposite directions.

(b) Upon the introduction of hot water into the stomach the reaction of the brain in increased temperature preceded that of the liver.

(c) The temperature of the liver was but little altered or was unchanged by the injection of adrenalin; of an acid; of an alkali.

An attempt was made to establish our assumption that the changes in the temperature of the brain after the injection of adrenalin may be justly ascribed to variations in oxidation. Preliminary experiments have shown that after the injection of adrenalin the temperature of the venous blood coming from

the brain was increased to above that of the arterial blood to the brain. This finding, if confirmed, will be a strong indication that the temperature changes within the brain can not be entirely, if at all, due to variations in the blood supply to the brain.

The findings in these studies which accord with the histological studies and the electric conductivity measurements support the following conclusions:

(1) The brain is the tissue upon which depend the reactions of the organism to stimulation.

(2) The thyroid and the adrenals play essential parts in the production and maintenance of these reactions.

(3) In the performance of its function the brain is indissolubly linked with the liver.

The lack of response of the brain to adrenalin in the absence of the liver, together with the opposite reactions of the brain and the liver, form vital links in the chain of evidence, whereby we may determine the function of each in the operation of the animal mechanism.

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CHAPTER 25. STUDIES OF ELECTRIC POTENTIAL

Maria Telkes, Ph.D.

THE science of electrobiology can be divided into two chapters.

1. The production of electric energy by the resting or working organism.
2. The response of the organism to applied electric energy.

The second chapter comprises the extensive studies of electrical variations in muscles and in other tissues, as a response to the application of various forms of electric energy to the tissues. The theoretical considerations of Nernst¹ serve to characterize this phenomenon. The applied electric energy changes the concentration of the electrolytes at the cell membranes and essentially the action of applied electric energy is exercised upon the cell membranes.

But the first of the two divisions of electrobiology is perhaps of even greater significance, because it includes all observations concerning the manifestations of electric energy in organisms, including the connection between electric energy with other physiological phenomena, such as metabolism, action of physiological agents, poisons, etc. It also includes the theoretical explanation of the production of electric energy in the organism and a study of potential differences at membranes composed of various materials.

PRODUCTION OF ELECTRIC ENERGY BY CELLS AND TISSUES

As the unit of structure of living organisms is the single cell, it was essential for the explanation of the electric energy pro-

duction of the whole organism to obtain first a clear picture of the electric energy of the single cell. Only comparatively recently have such studies been pursued by Loeb,² Beutner,³ Osterhout,⁴ and others. Their results can be explained on the basis of membrane potentials and concentration potentials.

One of the best known facts in electrochemistry is the production of electricity by two different metals immersed in a salt solution, the chemical energy of the resultant processes furnishing the electricity of galvanic batteries. The presence of metals, however, is not absolutely essential to the production of electric energy, as such energy can be obtained by arrangements in which no metallic ions are present. If solutions of two different salts are separated by a membrane (which serves to prevent the gross mixing of the two solutions), a potential difference between the two solutions can be measured. The electric energy is the result of the diffusion energy, and lasts as long as the two different salt solutions are maintained on the two sides of the membrane (diffusion potential).

It is not even necessary to use two different salts, as different concentrations of the same salt on the two sides of the membrane will also produce a potential difference (concentration potential). The chemical nature and physical characteristics (thickness, porosity, etc.) of the separating membrane are partly responsible for the magnitude of this potential difference. Various theories ascribe different rôles to the membranes in the production of electric energy. It is said to be due to the differences of ionic mobilities in the membrane; or to the electric charges of the particles or pores of the membrane (Höber⁵); or to chemical interaction between the phase boundaries of the solution and membrane (Beutner⁶). It is sufficient to state that most of these potential differences can be expressed by the formula of Nernst according to which the potential difference E is a function of the concentrations C and c , of the solutions on the two sides of a membrane. In Nernst's formula $E = A \cdot 0.058 \log C/c$, A indicates a variable representing the chemical and physical nature of the membrane.

It was found that this formula can be applied to a great number of physiological membranes or uninjured tissues including plants, intact skin, muscles, etc.

It is evident that the membrane of a single cell, which separates the inside of the cell with its electrolytic content from the outside medium with a different electrolytic content, must be instrumental in producing a potential difference. Measurements of the potential difference in single cells are of fundamental importance in aiding our understanding of the electrical processes in large agglomerates of cells—the tissues. Electrical measurements on single cells have been made rather recently on the larger plant cells Valonia and Nitella, by Damon,⁷ Osterhout⁸ and others, and on *Halocystis* by Blinks⁹ and others. In this laboratory observations were carried out on amebae.¹⁰ All these experiments have shown that there is a potential difference between the inside and outside of the cell of a magnitude of some 10 to 80 millivolts, and that when the cell is subjected to the effect of stimulants or poisons, the potential difference across the membrane is increased or decreased and sometimes disappears, the disappearance of the potential difference being generally followed by the death of the cell.

Although these facts have only become known rather recently, it has been recognized for a long time that injured tissues, such as muscles, show a phenomenon called the "current of injury." The injured tissue is galvanometrically negative as compared with an uninjured part of the same tissue. In figure 78 this current of injury is illustrated, the potential difference being shown between the outside circuit of the measuring instrument and the inside circuit of the tissue, where the polarity obviously is reversed. For the sake of comparison the potential difference of the ameba is schematically indicated also. The potential difference of the inside of the ameba is galvanometrically negative, and that of injured tissue is also negative. During injury obviously the inside of the cell becomes exposed and one may regard the current of injury as a measurement of the potential difference between the inside and outside of the tissue cells. However, the injury of tissues can not be compared directly to the slight injury caused by the introduction of a micro-electrode into the inside of the ameba or of other single cells. Nevertheless it is the only available method for measuring changes of the potential of tissues, until the micro-manipulative technic develops to such an extent as to permit

the introduction of electrodes sufficiently fine for the measurement of the potential difference of single muscle cells.

Whatever may be the theoretical explanation of the "injury current" it has been used to advantage to explain the effect of physiological agents—salts, drugs, etc., on the surviving frog's muscle and other tissues. The method generally employed was to lead off the current from the injured part of a muscle

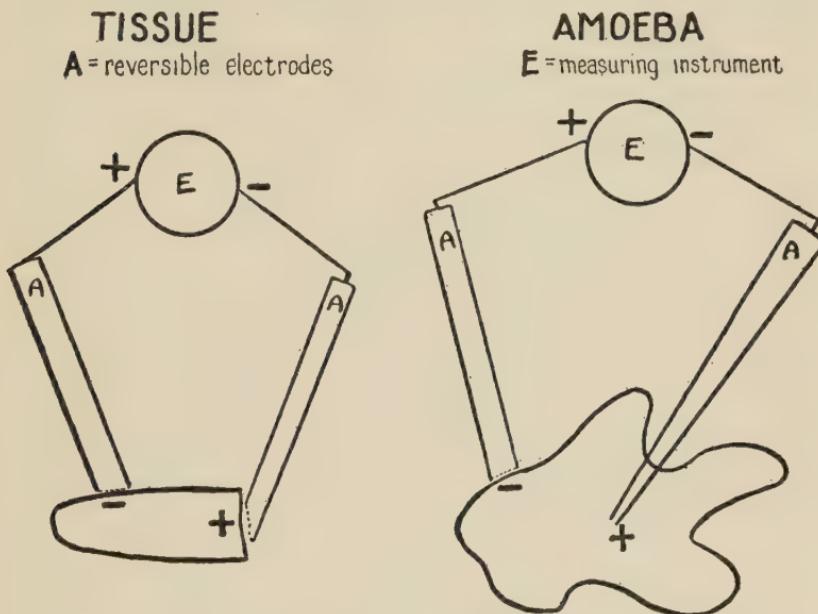


FIGURE 78. "Injury current" in a tissue and in a simple cell.

and to immerse the uninjured part in various solutions, the effect of which was to be determined.

EXPERIMENTAL INVESTIGATION OF POTENTIAL DIFFERENCES IN LIVING ANIMALS

Many experiments have been made with frog's stomach (Mond¹¹), with the kidney (Gesell¹²) and various glands (Cannon¹³) of living animals. No systematic attempt has been made, however, to compare the "current of injury" of different tissues in a living anesthetized animal. Obviously such a study

may reveal the potential differences existing between various tissues. Measurement of the current of injury in a living animal may reveal the effect of the intravenous injection of any agent and the electrical response of the tissues to its action.

If we place one irreversible electrode on the surface membrane of one tissue and have a similar electrode on the surface of another tissue, we are able to measure a potential difference, which will naturally depend on the general physiological conditions of these tissues and especially on the condition of the different tissue membranes and the solutions which are in immediate contact with these membranes. When the animal as a whole is influenced by a physiological change (produced by nervous irritation, injury, injection of different drugs, etc.) this change is communicated to each organ and tissue and in turn changes the condition of the membranes of the cells and of the solutions which are in contact with them, thus changing the potential difference between the different organs. If we could isolate a certain tissue, which is relatively inactive or which is influenced very slightly by the above mentioned physiological actions, we could measure the changes for each organ separately. The subcutaneous fascia was successfully used by Cannon¹³ as an inactive tissue. The question which now arises is: What conditions would be present if we were to measure the P. D.* between the fascia and freshly injured part of a tissue or organ? In a living animal a deterioration of the injured red cell membranes would set in gradually and the P. D. might fall to a constant value. In such a case if the physiological conditions are artificially changed, the P. D. changes would again depend upon the changes at these membranes.

Experimental Method: In this investigation the measurements of the P. D. have been made by the compensation method, using a Leeds and Northrup potentiometer, of sufficient accuracy to measure 0.1 millivolt. The zero instrument was a Leeds and Northrup galvanometer of high sensitivity. The connection between the instrument and the tissues was made by means of reversible calomel electrodes which made it possible to obtain undistorted measurements. The calomel electrodes

* Hereafter the usual manner of designating potential difference will be used, viz., the use of the initial letters, P. D.

were filled with a saturated solution of potassium chloride. A rubber tubing about 20 inches long was connected to the calomel electrodes. The rubber tubing was filled with a saturated solution of potassium chloride and in the end of the tubing was inserted a short piece of glass tubing which was sealed with a plug of filter paper. Several calomel electrodes were placed in a rack and were constantly short-circuited so that the potential difference between them was maintained at zero. Contact with the tissue was made by means of another glass tube filled with Ringer's solution and also sealed with a plug of filter paper. Several of these tubes were constantly kept in Ringer's solution in order to be ready for use. The whole system was assembled shortly before an experiment was begun and measurements were made to ascertain that no potential differences existed between the electrodes themselves.

Generally three or four electrodes were used in each experiment. They were connected to a switchboard so that the P. D. could be measured between any two tissues in which the electrodes were inserted or which they were touching. Suitable holders were used to keep the electrodes firmly in place within or on the tissue to be measured.

A suitably shaped electrode was usually placed on the subcutaneous fascia which was the arbitrary zero point. The skin was brought together over this tube and secured with clips. (Fig. 79.)

Other electrodes were used on the injured or uninjured surfaces of different tissues. These were held in position by means of suitable holders. (Fig. 80.)

Experiments were made on anesthetized male rabbits weighing from five to eight pounds. These animals were of the same breed and were always kept under similar conditions.

Experimental Results. A few preliminary experiments were made to determine what influence the size of the electrodes may have on potential difference measurements, and also to determine whether or not the size of the injured surface has any influence on the P. D. when this tissue is measured for different lengths of time. To determine these points the following experiments were performed:

The zero electrode was placed on the subcutaneous fascia

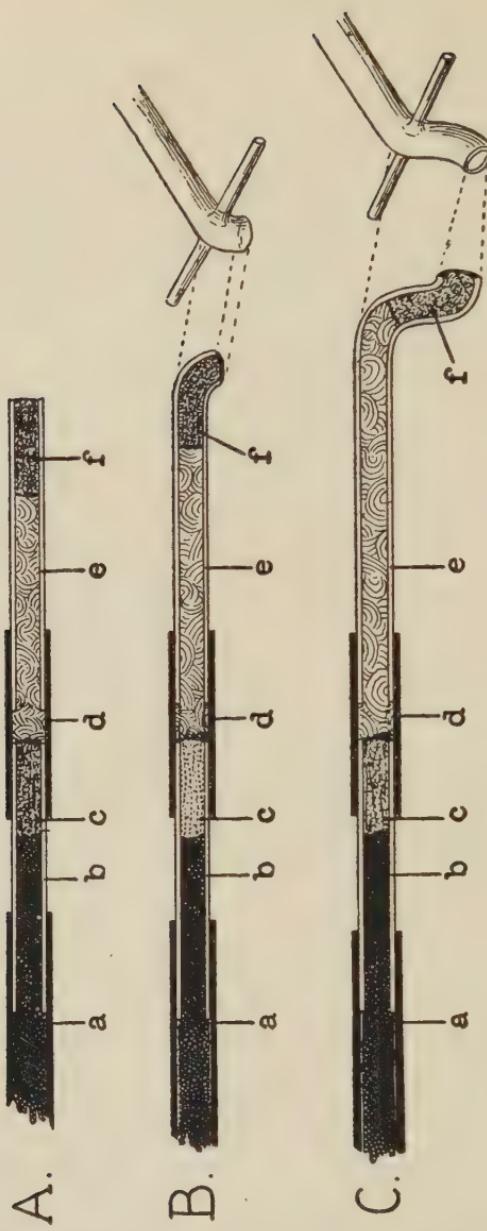


FIGURE 79. Electrodes designed for measuring the potential difference of different tissues. A, Electrode used for various tissues; B, Electrode used on fascia; C, Electrode used on muscle. (a) Rubber tubing filled with saturated KCl; (b) glass tubing filled with saturated KCl; (c) filter paper plug impregnated with saturated KCl; (d) connecting rubber tubing filled with Ringer's solution; (e) glass tubing filled with Ringer's solution; (f) filter paper plug impregnated with Ringer's solution.

above the latissimus dorsi muscle, the end of another electrode was drawn out to a capillary needle and was inserted into the latissimus dorsi to a depth of 1 cm. A third electrode had a diameter of 3 mm., the size generally used. This last electrode was inserted through a small incision into the same muscle, 1 cm. distant from the capillary electrode. In figure 81 a typical measurement is shown, the P. D. being given in millivolts and plotted against the time in seconds. It can be seen that the P. D. between fascia and the capillary electrode which was inserted with very little injury to the muscle, decreased very rapidly. On the other hand, the P. D. between the fascia and

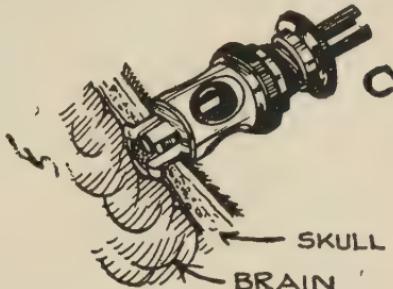


FIGURE 80. Holder for applying electrode to brain.

the larger electrode decreased more slowly. In these experiments the fascia was positive and the injured muscle was negative.

Potential differences between different tissues in living rabbits. Rabbits were anesthetized with urethane (1 gm. per kg.) or with ether. The tissues to be measured were exposed with as little injury as was possible. The zero electrode was always placed on the subcutaneous fascia above the latissimus dorsi; a second electrode was placed on the uninjured surface of the tissue to be measured; and another electrode was placed on an injured surface of the tissue. The injured surface was as small as possible, the injury being produced in such a way as to cause the least possible hemorrhage.

It was found that the injured surface of different tissues and glands was in all cases negative to the fascia. The outside (uninjured membrane) of the tissues or glands was occasionally positive but more often it was negative to the fascia. The value

of the P. D. varies somewhat between different parts of the same tissue of the same animal. On account of the complex structure of the organs, we can only give an average value of the P. D. existing between the fascia and the organ, gland or tissue as a whole. But this is no disadvantage because in these experiments the purpose has been to determine whether or not

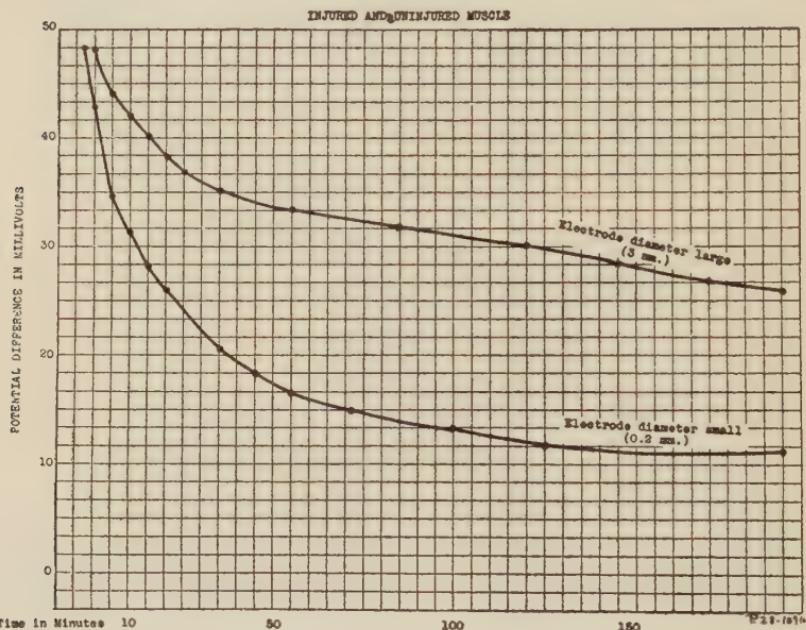


FIGURE 81. Typical measurement of potential differences of injured and uninjured muscle.

changes in potential difference are caused by physiological actions.

Figure 82 shows the P. D. between different parts of the brain tissue. These measurements were performed in the following way: A trephined hole about 3 mm. in diameter was made in the anesthetized rabbit's skull close to the medial line. The end of the electrode filled with Ringer's solution was drawn out into a capillary 1 mm. in diameter and ground into the form of the end of a hypodermic needle. This was inserted into the brain to different depths. These measurements show clearly that

there are potential differences between the different parts of the brain.

The potential differences obtained are characteristic for the living animal as compared with measurements made on the same animal one and two hours after death. In the dead animal the potential differences decrease toward zero more or less rapidly.

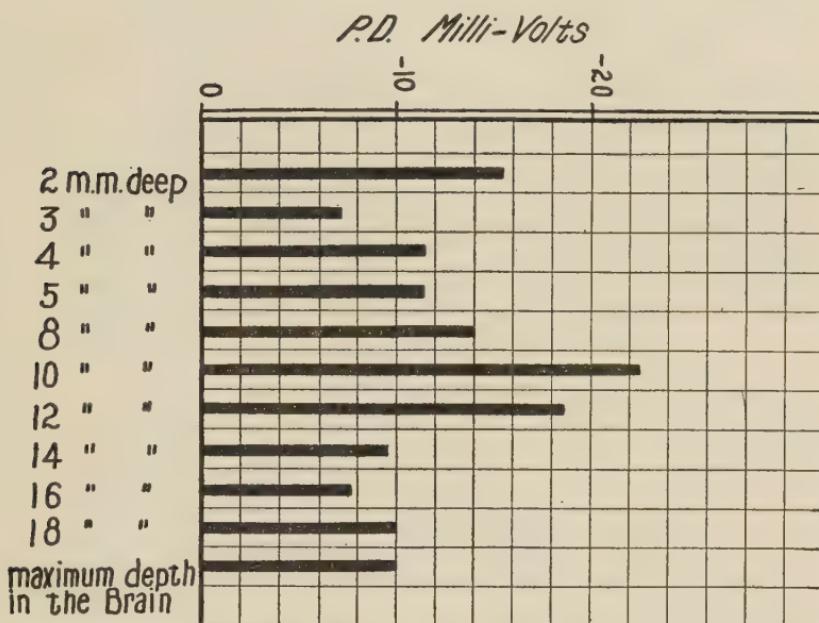


FIGURE 82. Potential differences at different depths in the brain tissue.

The average value of the potential differences for various tissues is shown in figure 83.

Potential Differences in Tissues Changed by Physiological Agents. After the tissues as measured by the procedures outlined above showed a fairly constant P. D., the various substances to be tested were injected intravenously and the changes in the P. D. were measured until the P. D. again remained constant.

In figure 84 the values of the P. D. after the injection of adrenalin are shown. The measurements were made on anes-

thetized rabbits. The zero electrode ^(I) was placed on the fascia; one electrode was in the injured brain,^(II) another in the liver,^(III) so that the measurements could be made between the fascia and brain, fascia and liver, and brain and liver. A single observation could be made in about 20 seconds, so that in one minute the three measurements could be made. It is evident

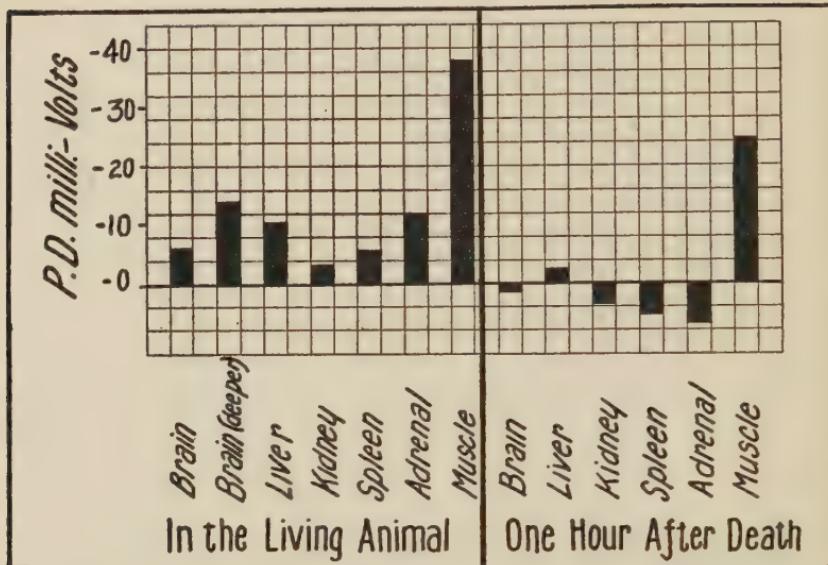


FIGURE 83. Potential differences of various tissues in an anesthetized living animal and in the same animal one hour after death.

that the potential differences between the three electrodes should have the following relationship: The difference between I and III should be the algebraic sum of the potential differences between I and II, and II and III. We found this to be true in our measurements. At the point indicated by the arrow the injection took place.

Our findings may be summarized briefly as follows:

The injection of adrenalin is followed by an immediate decrease in the P. D. which reached its minimal value in about 4 minutes. It then increased again to its original value which was reached in about 8 minutes. It then fell again to a lesser degree than at first and gradually rose again to almost its original value. The period covered by these successive changes in the

P. D. was from 30 to 40 minutes. It is interesting to note that in the time relation the changes in P. D. coincide with the physiological changes.

The effect of the administration of adrenalin under various pathological conditions was as follows:

Iodism: Rabbits were iodized by introducing 75 gr. of iodoform into the peritoneal cavity 24 hours before the experiment.

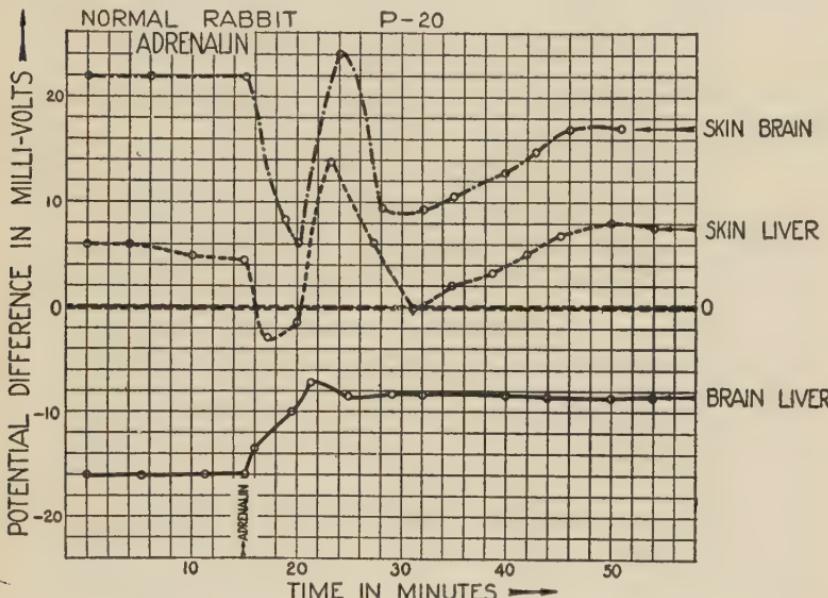


FIGURE 84. Changes in potential difference produced by the injection of adrenalin.

Figure 85 shows the changes produced by adrenalin in the P. D. between the fascia and the liver, the fascia and the brain, and the brain and the liver. The changes are similar to those observed in the normal animal, but the value of the potential of the brain is higher.*

Myxedema: Rabbits were thyroidectomized a week before

* The values of the P. D. between the fascia and liver sometimes reached below the zero line. This does not mean that the potential at this point became actually negative, because the P. D. value of the fascia was arbitrarily set at zero, as we were unable to obtain an absolute zero-point. An absolute zero-point would be assumed to exist between the injured part of certain tissues and a certain point in the animal as yet unknown to us.

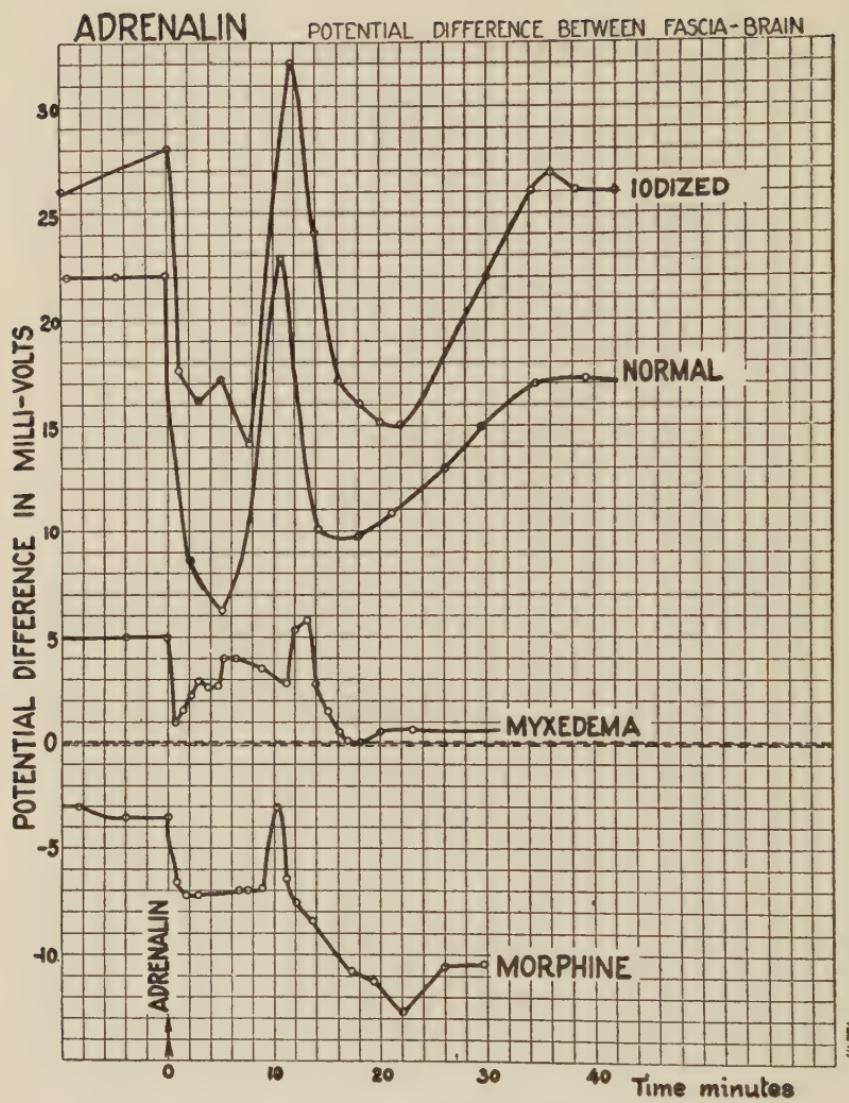


FIGURE 85. Changes in the potential difference of the brain produced by adrenalin in a normal, an iodized, a myxedematous and a morphinized animal.

POTENTIAL DIFFERENCE BETWEEN FASCIA-INSIDE BRAIN

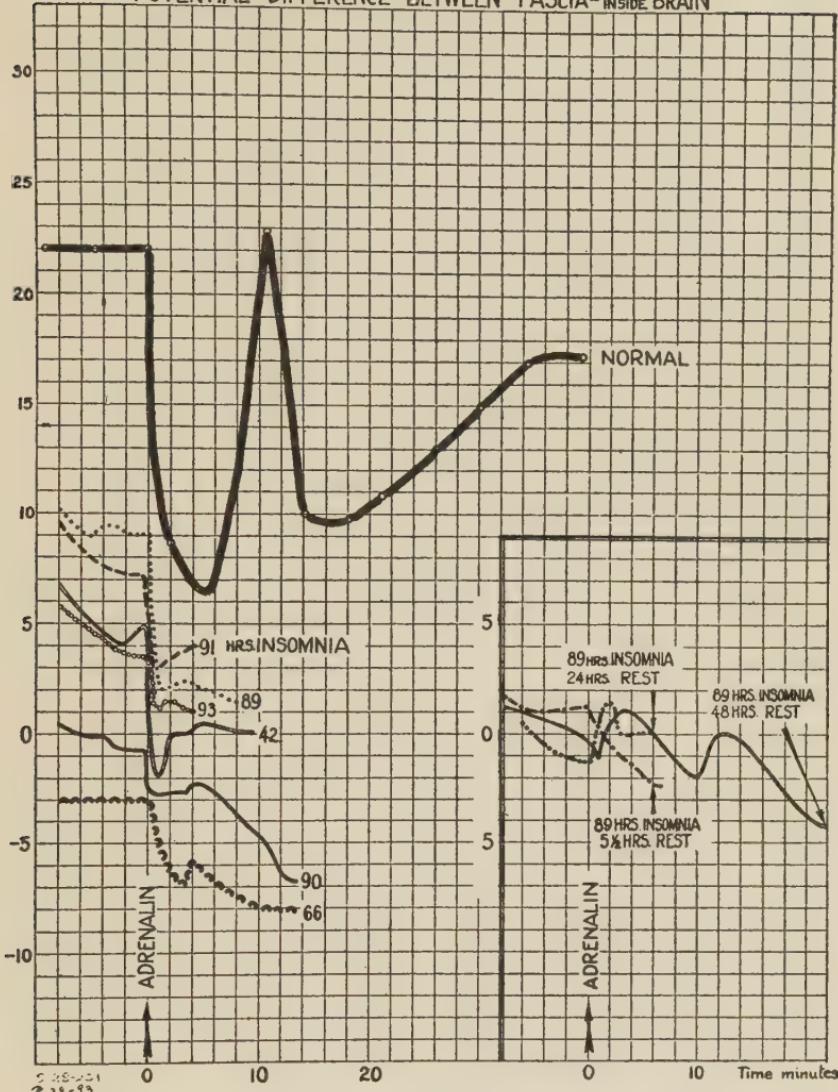


FIGURE 86. Changes in the potential difference of the brain produced by the injection of adrenalin in animals after various periods of insomnia.

the experiment. Figure 85 shows the change produced by adrenalin in the P. D. between the fascia and brain of these animals. In this figure the changes in the myxedematous rabbits are shown to be obviously smaller than those produced by the injection of adrenalin in normal and in iodized animals.

Thyroid Feeding: Rabbits were fed thyroid extract (5 gr. daily) for a week. In such animals the change produced by adrenalin in the P. D. between fascia and brain amounted to only 2 millivolts. The change in the P. D. between uninjured and injured liver was also very small, as well as the change between the brain and liver.

Morphine: When morphine was injected subcutaneously previous to the injection of adrenalin, the P. D. between the fascia and the brain became much lower than in normal animals, and after the injection of adrenalin the changes in the P. D. were the same in direction but were much smaller and the P. D. never returned to its original value. In figure 85 the changes produced by adrenalin in morphinized rabbits are compared with the changes under other conditions. It will be noted that in the morphinized animal as well as in the myxedematous, the absolute value of the P. D. before the injection is much less than that in the normal animal.

Insomnia: Ten rabbits were kept awake for prolonged periods. During this time they were kept in a large airy room and were given abundant food and water. The animals were not hurt in any way. In different animals the P. D. between the fascia and the brain was measured after the periods indicated in figure 86. We found that in all these animals the P. D. changes produced by the injection of adrenalin were much less than those in normal animals and that the absolute value of the potential before the injection of adrenalin was also much lower than that of normal animals. In figure 86 the numbers on the right-hand side of each curve indicate the number of hours of insomnia. The experiments were made after 42, 89, and 90 hours of insomnia and after 89 hours of insomnia and 24 and 48 hours of rest.

Insomnia followed by Rest: Animals kept awake for 89 hours were permitted to rest for $5\frac{1}{2}$, 24 and 48 hours. Figure 86 shows that in the rabbit that rested for $5\frac{1}{2}$ hours the P. D.

decreased after the injection of adrenalin. In those that rested for 24 and for 48 hours, the P. D. increased after the injection of adrenalin. The first two rabbits died shortly after the injection. In the one that rested for 48 hours, the changes in the P. D. were the same in general character but far less in value than in normal animals. The absolute value of the P. D. in the animal which rested for 48 hours was still very small,

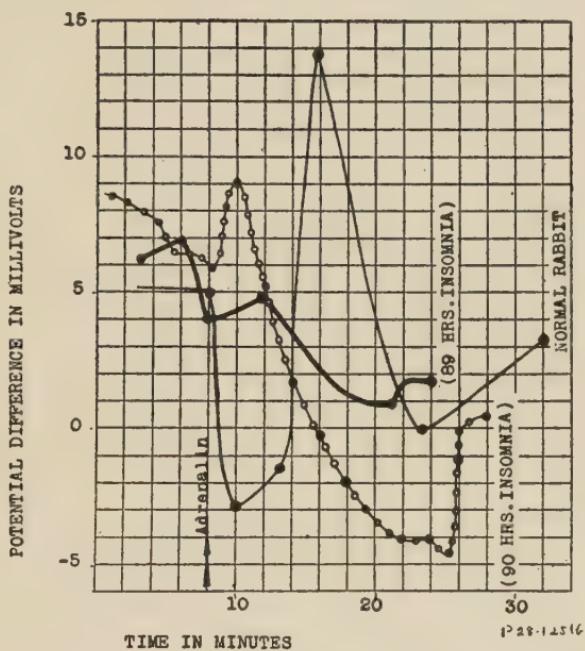


FIGURE 87. Changes in the potential difference of the liver produced by adrenalin in a normal animal and in animals subjected to insomnia.

which indicates that even a 48-hour rest is not sufficient to overcome the pathological injuries suffered from insomnia.

Insomnia—Liver: Measurements of the P. D. of the liver were made in the rabbits which had been kept awake for 89 and 90 hours. The P. D. between the fascia and liver is shown in figure 87. It will be noted that after 89 hours of insomnia, the P. D. increases very slightly when adrenalin is injected; and that after 90 hours of insomnia the P. D. increases to a greater

extent. The changes in these two experiments do not resemble those in normal animals.

As can be seen in figure 87, the P. D. between the brain and liver decreases (goes toward zero) in the normal rabbit but increases in rabbits which have been kept awake for a prolonged period.

Effect of Various Salts: When salts were injected into the animal, their effects were characteristic and depended upon the amount of salt injected. The doses used were generally from one-half to the minimum fatal dose. Some of these effects are shown in figure 88.

Large amounts of *sodium chloride* produced a decrease in the P. D. between the fascia and brain and small amounts produced a small decrease followed by an increase.

Alkalies increased the P. D.; *acid* decreased it.

Small amounts of *potassium chloride* increased the P. D.; lethal doses increased it.

Calcium chloride produced a characteristic change which was modified when magnesium sulphate was previously injected.

Magnesium sulphate caused a very gradual decrease in the P. D., which was counteracted abruptly by the injection of calcium chloride.

Sodium cyanide decreased the P. D.

Alcohol caused an increase in the P. D. followed by a decrease. *Ether* had the same effect. Lethal doses of *urethane* or of *ether* produced a steady decrease in P. D. until the animal died.

Trauma and *nerve irritation* both caused an immediate decrease in the P. D. followed by an increase.

The studies of the electric potential of the giant ameba have been described in Chapter 2 and those of the electric potential of the autosynthetic cells will be described in Chapter 27.

An examination of the results summarized above shows clearly that the electric potential bears a direct relation to the physical state of the tissue; that is, the more active the state of the tissue the higher its potential. When the tissue is activated as by the injection of adrenalin the consequent discharge of energy brings about a fall in the potential which under normal conditions quickly returns to a point near its former level. In

depressed states, on the other hand, the potential being already depressed changes but little, the amount of change being in inverse relation to the degree of depression.

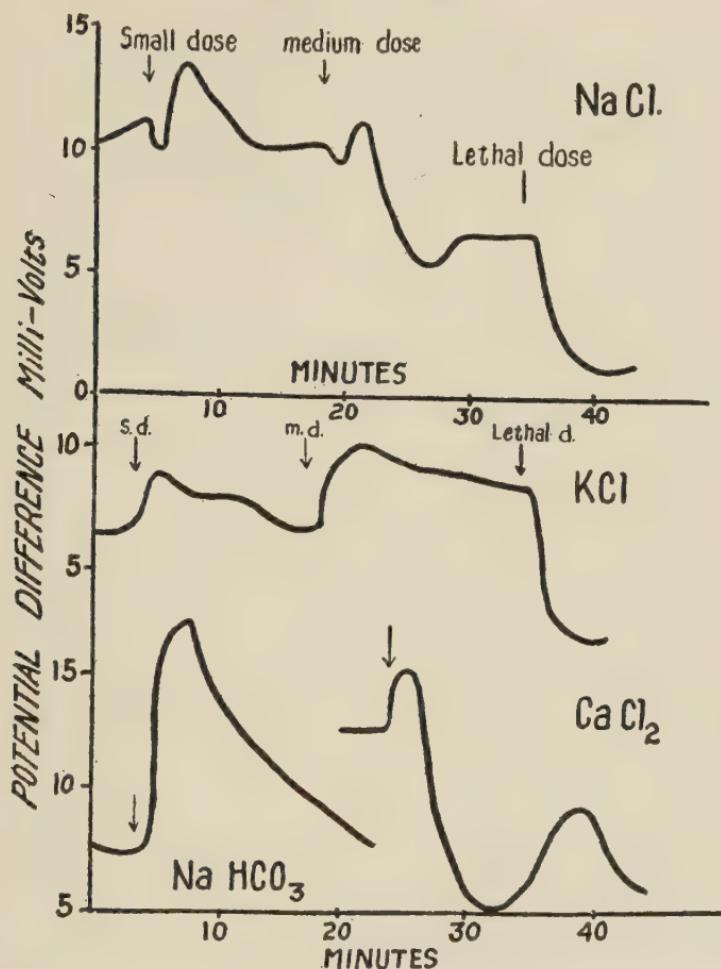


FIGURE 88. Effect of the intravenous injection of various salts on the potential difference of the brain.

The findings described in these last four chapters show clearly that the histological picture, the electric conductivity, the electric capacity and the electric potential parallel the physiological

status. These physical findings could not be so uniform in a mechanism operated by any but electric energy.

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CHAPTER 26. LIPOIDS, PROTEINS, GLUCOSE

LIPOIDS

THE lipoids which are essential constituents of all protoplasm are found in the films which form cell membranes, and in the cytoplasm of the cells, the electric charge of the membranes giving to the cell its stability of structure and contributing to its function. Lipoids also constitute the myelin sheaths which surround the axis cylinder of nerve fibers. Therefore, a study of the principal phenomena exhibited by the lipoids and of their physical properties is essential for a proper interpretation of the phenomena of protoplasm and of those presented by the autosynthetic cells.

Formation of Myelin Structures: Leathes¹ and others have shown that lipoids are able to produce peculiar structures under certain conditions. In our investigations we produced similar structures and studied the conditions under which these growths are promoted, inhibited or altered.

In our investigations, which were carried out by Maria Telkes, lipoids extracted from calves' brains were used. The tissue was thoroughly minced and rapidly dried at a temperature not exceeding 40° C. The dried tissue was pulverized, the lipoids extracted with ether, and the ether solution was filtered. This solution could be kept for several weeks. Extracts which were over a month old were not used. The concentration of the ether solution was determined by evaporating a known amount of the solution to dryness under vacuum. Generally the ether solution was so diluted as to contain one per cent lipoid.

The growth of myelin structures was observed in the fol-

lowing way. A well slide (similar to those used in tissue cultures) was thoroughly cleaned and a drop of ether solution of the lipoids was deposited on it by means of a glass rod. The drop, of such dimensions that it contained about 1 mg. of lipoid, was deposited so that it formed a round, thin film about 5 to 7 mm. in diameter. The ether evaporated very rapidly, leaving a very thin film, which was generally somewhat thicker around the edge. This film was covered with the solution, the effect of which was to be tested, and a cover glass was placed over it. Slight pressure on the cover glass expelled the excess of liquid, which was blotted off, leaving a preparation which without drying could be observed over a period of several days.

On account of the thinness of the film, the growth of myelin structures could be observed not only on the edge of the film, but throughout its surface. The control growths were made in a solution which contained the salts found in the brain, dissolved in distilled water in the same proportion as they are present in the brain.*

Immediately after a lipoid film was covered with this solution, small myelin growths appeared all over the surface of the film. With a magnification of 600, the growth of the structures could be observed and with the aid of an ocular micrometer the growth could be readily followed.

The fact that electric potential differences play an important rôle during this process was shown by the application of an electric current under the influence of which these structures formed rapidly, the growth extending toward the positive pole. Of special significance was the observation that in the presence of an anesthetic or a narcotic the organization of the myelin structures was interfered with, while in the presence of potassium iodide, this organization was increased.

* The composition of 1,000 cc. of this "brain-salt" solution was as follows. The pH of this solution was adjusted to meet the requirements of the experiment.

KCl	2.33 gm.
Na ₂ PO ₄	2.21 gm.
K ₂ PO ₄	0.89 gm.
Na ₂ CO ₃	0.11 gm.
K ₂ SO ₄	0.24 gm.
CaCl ₂	0.026 gm.
MgCl ₂	0.55 gm.
Water to make	1,000 cc.

This organized material had the power of oxidation as shown by measurements with Warburg's apparatus which showed a small and rapidly decreasing oxygen consumption.

In order to compare the effects of solutions of various salts in distilled water, a number of well slides were covered with the thin lipoid film; the various solutions were superimposed as quickly as possible and the growth of the myelin structures was observed under the microscope at intervals of 5, 10 and 30 minutes. The results are given in Table IV in which the best growths (that is, those comparable to the growth in the brain-salt solution) are indicated by xxx, medium growths by xx, slight growths by x and no growth at all by —.

The effect of alcohol is shown in figure 89. The inhibiting effect of a 50 per cent solution (C), and the accelerating effect of a 25 per cent solution (B) is evident. The inhibiting effects of some of the other agents in relatively low concentrations are remarkable.

Electrical Measurements: A slightly modified Northrop cataphoresis apparatus was used to determine the electric charge of lipoid particles. The current was conducted through reversible electrodes. The charge of the particles was calculated from the Helmholtz-Smoluchowski formula. With concentrated solutions the viscosity of the solution was also taken into account.

The ether solution of the lipoid was mixed with distilled water or with the solution the effect of which on the electric charge was to be tested. As much of the ether as possible was evaporated under reduced pressure at a temperature of 40° C. In this way a suspension of round globules was obtained in which a rapid growth of myelin structures could be seen.

The emulsion of lipoid particles was placed in the cataphoresis apparatus and the velocity of the particles in an electric field was measured with a stop watch. The necessary precautions in regard to differences in the charge in the capillary tube were taken by always measuring the velocity at the same level of the capillary; in this way all the observations could be compared.

In Table V are given the charges in millivolts of the lipoid particles in the various solutions. The charge of the lipoid in

distilled water alone is -78 millivolts. Very dilute salt solutions increase the charge, while concentrated salt solutions generally decrease the charge until the particles become discharged or their charge is even reversed. The best method of observation was to fill the cataphoresis cell with the emulsion and determine the velocity of the particles; then to introduce a sufficient amount of salt solution into an attachment of the cataphoresis cell and mix it with the emulsion by shaking, after which the velocity could be determined again without removing the emulsion from the apparatus. In this way the effects of successive concentrations of the same salt could be determined. (Fig. 90.)

The peculiar changes observed are similar to those found by Heesch² and by Remesow³ in observations of cholesterol particles and by Brown and Broom⁴ in observations of bacteria. Nevertheless such changes are not characteristic of lipoid alone, as various other suspensions show similar changes in the charge during the influence of bivalent and trivalent salts. Obviously, a surface charge or a potential difference will not produce myelin structures in most substances, but naturally the conclusion will be drawn from Table V that *the growth of the myelin structures is proportional to their negative electrical charge in the solutions which were used in our experiments.*

Influence of Galvanic Current on the Growth of Myelin Structures on a Lipoid Film: If the growth of myelin structures in various salt solutions is proportional to the electric charge or electric potential difference between the film and the salt solution, then it should be possible to increase this potential difference by applying a constant galvanic current through the film. In such a case an electric polarization will result on the film, which will act as an increased charge. To test this point the following experiment was performed.

A microscopic slide was equipped with two reversible electrodes (silver needles covered electrolytically with silver chloride), which were separated by an interval of about 1 cm. A small drop of lipoid was placed between the electrodes, and a few drops of "brain-salt" solution were superimposed, so that the solution covered the electrodes. An electric current of about 1.5 volts was then passed through the solution. The myelin structures immediately began to grow rapidly all over the drop



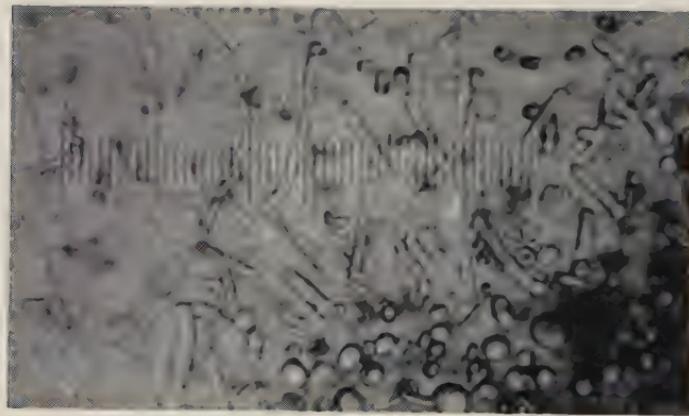
FIGURE 89. Photomicrographs showing the effect of different solutions of ethyl alcohol on the growth of myelin structures. A, Alcohol, 10 per cent, growth, xxx; cataphoretical charge, -62 millivolts B, Alcohol, 25 per cent; growth xxx; cataphoretical charge, -75 millivolts C, Alcohol 50 per cent, growth x, cataphoretical charge, -18 millivolts.



A



B



C

FIGURE 90 Photomicrographs showing the effects of different solutions of sodium chloride on the growth of myelin structures. A, 0.1 n NaCl; no growth, cataphoretic al charge, 0 millivolts; B, 0.001 n NaCl; growth xx; cataphoretical charge, -51 millivolts; C, 0.001 n NaCl, growth xxx; cataphoretical charge, -87 millivolts.



A



B



C

FIGURE 91. Photomicrographs showing the effect of the passage of an electric current on the growth of myelin structures. A, Myelin growths in "brain salt" solution; B and C, Effect of application of an electric current upon growths shown in A. Note the direction of the growth toward the positive pole.

of lipoid bending toward the positive pole of the applied current. The growth was compared with that observed in an entirely identical drop in an experiment which was made under the same conditions and at the same time, except that in the latter experiment the electrodes were omitted. B and C in figure 91 show the growth with and A without electrical polarization. It will be noted that the structures point directly toward the positive pole. These experiments show not only that the growth is proportional to the negative charge of the myelin structures in the various salt solutions, but also that in the same salt solution an artificially increased charge will produce a very much increased growth.

Measurements of Surface Tension and Viscosity: The surface tension of the lipoid suspension was measured with Traube's stalagmometer and parallel measurements of viscosity were made with a capillary viscosimeter. The procedure was as follows: The viscosimeter was filled with the lipoid suspension (1 per cent lipoid in distilled water). The determinations were made, and the same sample was then transferred to the stalagmometer and surface tension readings were taken. The solution, the effect of which was to be tested, was then added to the suspension and the surface tension and viscosity determined again on the same sample.

The relative values of the viscosity, surface tension, the electric charge in millivolts and the observed growth of myelin structures are compiled in Table VI. Values are given only for a lipoid suspension in NaOH solutions, as this is sufficient to illustrate that there is no relation between the surface tension or the viscosity and the growth of myelin structures. Other measurements were made with electrolytes and non-electrolytes.

Iodine Number: The iodine number of a fat or oil is the number of centigrams of iodine absorbed by one gram of the substance and indicates the amount of unsaturated acids that are present. It is, therefore, an index to the oxidative capacity of the substance.

"The unsaturated fatty acids have the property of adding atoms at the double bond. Thus iodine, bromine, oxygen, and hydrogen may be added here. Hence these fats have reducing powers, in that they readily oxidize themselves at the double bond going over into

the hydroxy-acid, or even into a ketone acid; they also have oxidizing powers in that they will take up hydrogen and be converted into the more stable saturated fats. By reduction or by oxidation with bromine or iodine, the number of unsaturated bonds may be discovered, since each such bond adds two atoms of iodine or bromine, two of hydrogen and presumably two oxygen atoms.”⁵

In our investigation we used the Hübl method. The following is a summary of our findings:

1. The iodine number of brain lipoid varied according to the age of the extract. In fresh extracts the iodine number was the highest, while old extracts became more saturated by autoxidation. The average iodine number of fresh dry brain lipoid was 50.2 ± 1.2 per cent.

2. The emulsification of brain lipoid in “brain-salt” solution changed its iodine number to 79.8 ± 4.1 per cent.

3. The iodine number of brain lipoid was unchanged in a one-tenth normal solution of KCl, CaCl₂, MgCl₂ and KH₂PO₄. It is interesting to note that these solutions destroy autosynthetic cells and prevent their formation and the formation of myelin growths.

In solutions in which myelin structures grew well the iodine number was increased, proving conclusively that the growth of myelin structures and the degree of the desaturation of the lipoid are correlated phenomena.

Oxygen Consumption: Warburg’s manometric method was used for the measurement of the oxygen consumption of the lipoids. The greatest care had to be taken to avoid bacterial contamination. Therefore the vessels were sterilized by heat before they were used and sterile technic was employed during the filling of the vessels. The volume of the vessels was about 15 cc.; they contained 2 cc. of the material to be tested and 0.3 cc. KOH solution, 20 per cent, was put in the attachment.

It has long been known that unsaturated fatty acids are oxidized slowly and that this oxidation can be increased by the addition of catalysts. As the lipoid contains unsaturated fatty acids, some emulsions of the highly unsaturated ricinoleic acid and of the less saturated olive oil were prepared. The oxygen consumption of such emulsions was measured in exactly the

same way as that of the lipoid emulsions. The ricinoleic acid was shaken with four times its volume of the "brain-salt" solution. Sufficient NaOH was added to emulsify it, the pH of the mixture being rendered alkaline. Some of the emulsion was prepared in such a way that the pH was 7.4.

Olive oil emulsions were prepared by shaking a mixture of 20 per cent olive oil in 14 per cent Na_2CO_3 or NaOH. The emulsion was used directly or was washed several times with the "brain-salt" solution.

At pH 11.4 the oxygen consumption per 1 cc. of the ricinoleic acid for the first 26 hours was 4.6 mm.³ per hour. At pH 7.5 the corresponding values were 1.6 and 0.4 mm.³ per hour. That is, the oxygen consumption decreased rapidly and it was very small at pH 4.4.

In the olive oil mixtures a definite although slight oxygen consumption was measurable. This decreased rapidly in a few hours. The washing of such emulsions did not change these findings.

From 0.1 to 0.2 gram of dried lipoids was placed in the apparatus and the experiment was continued for 24 hours. No oxygen consumption could be detected in 10 experiments on brain lipoid and 17 experiments with various other lipoids.

Measurements were then made of the oxygen consumption of emulsions of lipoid in the "brain-salt" solution at pH 11.4. During the first few hours a 10 per cent emulsion showed an oxygen consumption of as much as 7 to 8.5 mm.³ per hour per cc. of the emulsion. After the first few hours the oxygen consumption decreased rapidly. Further experiments were made with similar emulsions at pH 7.5 in which the oxygen consumption was only 2 to 2.5 mm.³ per hour per 1 cc. of the emulsion. At pH 4.4 no oxygen consumption was measurable. When the lipoid was emulsified in distilled water a very small and rapidly decreasing oxygen consumption was noted.

Radiation: To determine the quality of the radiations produced on the oxidation of the different materials of which protoplasm is composed and of protoplasm itself, an apparatus was assembled by means of which radiations of short (0.4 to 1.4 microns), medium (1.4 to 4.0 microns) and longer (4.0 to

14.0 microns) wavelengths could be separated, and the percentages of each emitted during any period of time were determined.

This apparatus consisted of a thermopile so constructed as to permit a filter to be placed approximately 1 cm. from the end of the thermopile which could be placed over the oxidizing

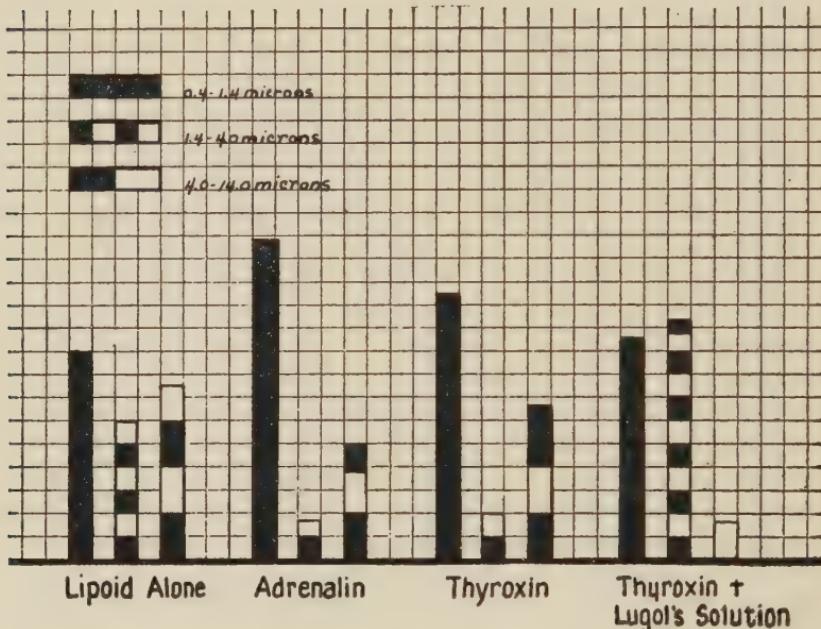


FIGURE 92. Effects of thyroxin, adrenalin and Lugol's solution upon the percentages of radiations of short, medium and longer wavelengths produced by oxidation of lipoids.

liquid 1 cm. above the surface. This thermopile was connected with a galvanometer the deflections of which could be measured on an appropriate scale. Water, glass and salt filters were used which permitted the transmission of wavelengths in the ranges indicated above.

Calcium or sodium hypochlorite (bleach) was used as the oxidizing medium. This was added to the suspension of the lipoid, and galvanometer readings were taken at 30-second intervals until the maximum deflection was attained. The conditions for each reading were identical, the three filters being

used consecutively. The hypochlorite solution was made fresh each day; and exactly identical amounts of the solution to be tested and of the bleach were used in all the experiments, viz., 100 cc. of material to be tested, 50 cc. of the hypochlorite solution. By subtracting the galvanometer deflection when the glass filter was used from the total deflection when salt was used the portion of the deflection produced by radiations of wavelengths between 4 and 14.0 mm. could be determined;

TABLE IV

GROWTH OF MYELIN STRUCTURES IN VARIOUS SOLUTIONS *

<i>Solution</i>	<i>Concentration of Solutions in Mols.</i>					
	1	0.1	0.01	0.001	0.0001	0.00001
NaCl	—	x	xx	xxx	xxx	xx
KCl	—	x	xx	xx	xx	xx
CaCl ₂	—	—	—	x	xx	xx
MgCl ₂	—	—	—	x	xx	xx
CuCl ₂	—	—	—	x	xx	xx
FeCl ₃	—	—	—	—	x	xx
HCl	—	—	—	—	x	x
NaOH	x	xx	xx	xxx	xx	xx
K ₃ PO ₄	x	xx	xx	xxx	xxx	xx
K ₂ SO ₄	x	xx	xxx	xx	x	x
KCN	x	xx	xxx	xx	x	x
NaI	x	x	xx	x	x	x
Na ₂ CO ₃	x	xx	xxx	xx	x	x

* In this and the following tables — indicates no growth; x a slight growth; and xx, xxx respectively increased growths.

and by using the water filter the radiations between 0.4 and 1.4 mm. could be determined. The findings in the measurements of the radiations produced by the oxidation of brain lipid are given in Table VII, figure 92.

These findings and charts should be compared with the findings on pp. 287 and 312.

It is interesting to note that the percentage of short wave radiations (44) is notably smaller than that produced by the radiation of proteins (63).

TABLE V

GROWTH OF MYELIN STRUCTURES IN VARIOUS SOLUTIONS COMPARED WITH THEIR ELECTRIC CHARGE (MILLIVOLTS)

Solution	Concentration of Solutions in Mols.							
	1	0.5	0.1	0.01	0.001	0.0001	0.00001	H ₂ O
NaCl	{ 0	— —11	x —51	xx —85	xxx —87	xxx	xx	xx
KCl	{ 5	— 0	x —43	xx —63	xx —73	xx	xx	xx
CaCl ₂	{ 7	— 0	— 0	— 17	x —49	xx	xx	xx
CuCl ₂	{ —	— —	— —	— 0	x —46	xx —61	xx —70	xx —68
FeCl ₃	{ —	— 0	— 38	— 66	— 0	x —49	xx —51	xx —70
NaOH	{ x —12	xx —48	xx —91	xx —108	xxx —84	xx —89	xx —98	xx
K ₃ PO ₄	{ x —15	xx —36	xx —62	xx —111	xxx —94	xx —78	xx —100	xx
Ethyl alcohol	{ x —18	xxx —75	xxx —62	xx —43	— —	— —	— —	— —
Urethane	{ —	x —36	x —47	— —18	— —	— —	— —	— —

TABLE VI

GROWTH OF MYELIN STRUCTURES COMPARED WITH THE ELECTRIC CHARGE OF THE LIPOID AND THE SURFACE TENSION AND WITH THE VISCOSITY OF THE LIPOID EMULSION

Material	Relative Surface Tension	Relative Viscosity	Electric Charge in Millivolts	Growth
Lipoid suspension in distilled water	0.76	1.00	-98	xx
Same in 0.0001n NaOH	0.89	1.08	-84	xx
Same in 0.001n NaOH	0.93	1.00	-108	xxx
Same in 0.01n NaOH	0.88	0.95	-91	xx
Same in 0.1n NaOH	0.83	0.92	-48	xx
Same in 0.2n NaOH	0.92	0.95	-40	xx

PROTEINS

"This organic, nitrogenous, amorphous matter, since it makes by far the greater portion of the organic substance of living matter proper, exclusive of cell walls is called *protein*, a word meaning 'of the first importance.'" "Protein substances are found, like the fats and carbohydrates, nowhere else in nature than in living matter or as the products of the action of living matter. In plants more or less carbohydrate is associated with the protein; but in animals by far the greater part of the tissue solids are generally protein." ⁶ (Mathews)

TABLE VII

	Filters		
	Water 0.4 to 1.4 μ	Glass 1.4 to 4 μ	Salt 4 to 14 μ
Brain lipoid—3% suspension in 0.01n NaOH	44%	25%	31%
Same as above plus adrenalin	67%	8%	25%
Same as above plus thyroxin	56%	11%	33%
Same as above plus thyroxin plus Lugol's solution	47%	46%	7%

It is obviously important, in view of our thesis, that the electric charge of proteins and the radiations emitted on the oxidation of this nitrogenous constituent of all protoplasm be studied.

Method of Preparation: The residue remaining after the lipoid has been extracted in the manner described above.

The powdered residue is weighed and thoroughly mixed with 50 times as much of the "brain-salt" solution. This mixture is allowed to stand for several hours with occasional stirring and shaking. It is boiled for half an hour in the water bath and filtered.

The pH of the filtrate which is generally about 9.0 is changed to pH 7.8 by the addition of 0.2n HCl. The solution is then brought to the boiling point and refiltered, this process being repeated several times.

Hardened filter paper is used for the last filtering. During this operation care is necessary to avoid evaporation; if any evaporation takes place the evaporated fluid is replaced by distilled water. The clear filtrate is then autoclaved. Occasionally some precipitate is formed during the autoclaving in which case the solution is refiltered and reautoclaved. If desired the solution may be poured into culture tubes which are autoclaved and handled like any bacteriological culture medium. The final solution is generally at pH 7.4.

A second method for extracting the protein is to mix the residue remaining after the ether extract of the lipoids has been filtered off with 10 per cent NaCl solution; the mixture is shaken for some time and filtered. The filtrate is then slightly acidulated by the addition of acetic acid and saturated with ammonium sulphate. This mixture is left in the refrigerator for several hours and is then centrifuged carefully so as to separate completely the solution from the precipitate. The precipitate is then redissolved and reprecipitated and finally dissolved in "brain-salt" solution. This procedure is repeated as described in the first method. This final solution should contain about one-half per cent of protein. (It is understood, of course, that the "protein" solution contains other materials besides protein, but for the sake of brevity we shall refer to it always as protein solution.)

Electric charge of proteins. The electric charge of proteins has been investigated by various methods. Loeb⁷ used membranes which were immersed in different solutions, and measured the potential differences across the membrane. Abramson⁸ used the cataphoresis method, depositing the protein over solid particles.

In our measurements the cataphoresis method was used. The protein fraction was extracted from the brain after previous extraction of the lipoid fraction. The protein and some protein split products were precipitated from the extract with saturated ammonium sulphate solution. This was washed with the "brain-salt" solution and finally suspended in "brain-salt" solution. In this way fine suspended particles were obtained, the electric charge on which could be measured in the cataphoresis apparatus. The cataphoretic charge for such protein suspensions varies

according to the pH of the solution, the electrolyte concentration, and the addition of various agents. At pH 7.4 the electrical charge of such protein particles was very small, around -4 millivolts. At pH 11.4 the charge was only -2 millivolts. As the charge of lipoid particles under the same conditions is -63 millivolts it is evident that a cataphoretically measurable potential difference exists at pH 7.4 between the protein and the

TABLE VIII

RADIATIONS PRODUCED BY THE OXIDATION OF PROTEINS FROM
VARIOUS ORGANS
(*Proteins dissolved in distilled H₂O*)

	Filters		
	Water 0.4 to 1.4 μ	Glass 1.4 to 4 μ	Salt 4 to 14 μ
Thyroid protein	65%	4%	31%
Brain protein	63%	9%	28%
Adrenal protein	58%	5%	37%
Voluntary muscle protein	56%	18%	26%
Heart protein	45%	16%	39%
Kidney protein	35%	17%	48%
Liver protein	30%	18%	52%
Spleen protein	25%	43%	32%

lipoid fractions, the protein fraction having a positive charge in relation to the lipoid fraction.

Radiation: If, as we suppose, radiations in the living organism are produced by detonation of the nitrogen compounds within the cells, then since the proteins are the principal purveyors of nitrogen it became of interest to see what radiations might be produced by the combustion of the proteins. Accordingly, proteins were oxidized and the resultant radiations were measured by the method described above.

The results are given in Tables VIII to IX. In each experiment, 100 cc. of a 2 per cent solution of the protein and 50 cc. of a saturated solution of sodium or calcium hypochlorite was used. (Fig. 93.)

It is impossible to tell from the foregoing experiments what proportion of the radiation that passes through the water filter

falls in the near ultraviolet, the visible, and the near infra-red ranges. Later we studied the complete spectrum emitted by the various substances the oxidation of which we have studied. (See Chapter 28.) In addition, Dr. Glasser has endeav-

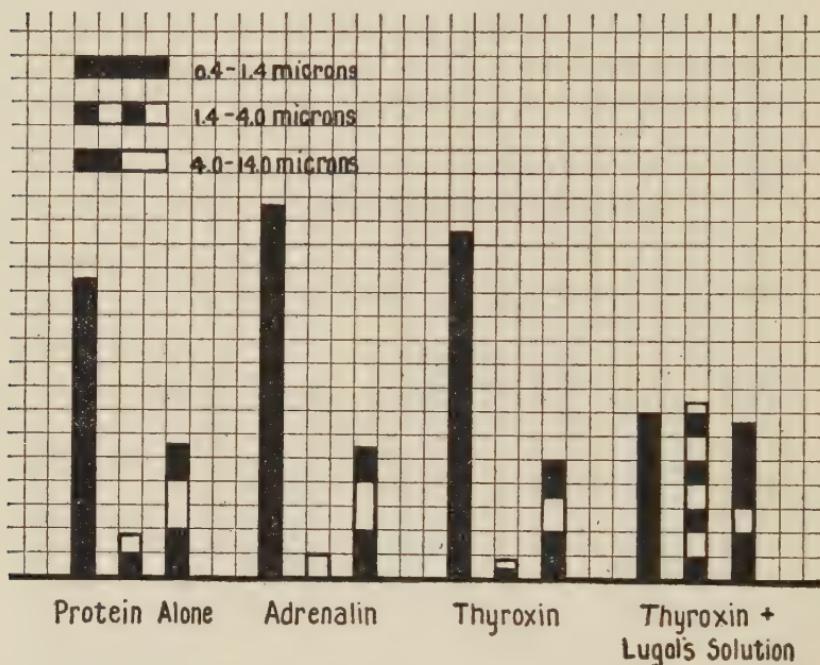


FIGURE 93. Effects of thyroxin, adrenalin and Lugol's solution upon the percentages of radiations of short, medium and longer wavelengths produced by oxidation of proteins.

ored to detect radiations in the ultraviolet field by the yeast method and the Geiger counter. (Chapter 29.)

GLUCOSE

In view of the generally accepted view that "it is, indeed, largely by the combustion of carbohydrate that we derive our energy" ⁹ a study of the radiations emitted on the oxidation of glucose and a comparison of these radiations with those emitted on the oxidation of proteins are of peculiar significance.

TABLE IX

RADIATIONS PRODUCED BY THE OXIDATION OF PROTEINS FROM
VARIOUS ORGANS

(Proteins dissolved in "brain-salt" solution)

	Filters		
	Water 0.4 to 1.4 μ	Glass 1.4 to 4 μ	Salt 4 to 14 μ
Thyroid protein	65%	4%	31%
Brain protein	50%	18%	32%
Adrenal protein	48%	15%	37%
Kidney protein	45%	16%	39%
Liver protein	45%	15%	40%
Heart protein	40%	34%	26%
Spleen protein	35%	32%	33%
Muscle protein	32%	40%	28%

The percentages of radiations in the short (0.4 to 1.4 microns), medium (1.4 to 4.0 microns) and longer (4.0 to 14 microns) wavelengths were measured by the method described above.

Our findings are given in Table XI and illustrated in figure 94.

These findings should be compared with those given in the sections on lipoids and proteins.

TABLE X

EFFECT OF THYROXIN, LUGOL'S SOLUTION AND ADRENALIN UPON
THE RADIATIONS PRODUCED BY THE OXIDATION OF BRAIN PROTEIN(Protein dissolved in distilled H₂O)

	Filters		
	Water 0.4 to 1.4 μ	Glass 1.4 to 4 μ	Salt 4 to 14 μ
Brain protein alone	63%	9%	28%
Brain protein plus thyroxin	73%	2%	25%
Brain protein plus thyroxin plus Lugol's solution	32%	36%	32%
Brain protein plus adrenalin	78%	5%	17%

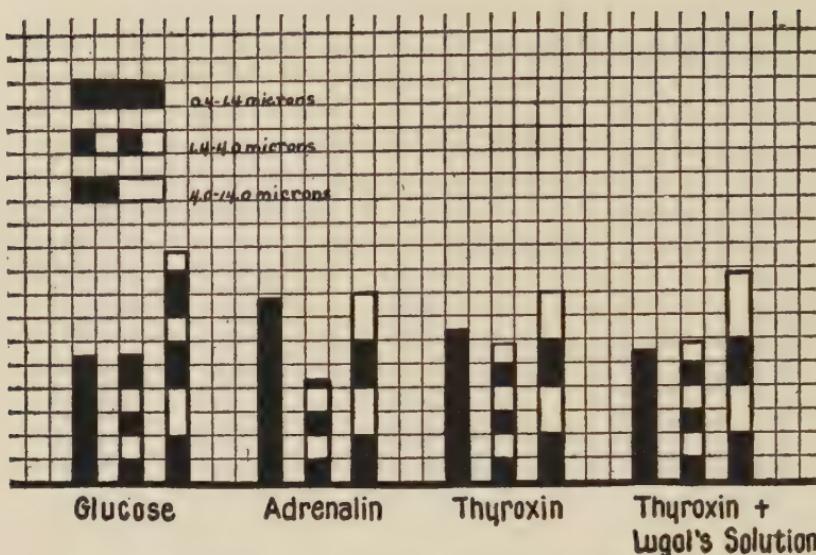


FIGURE 94. Effects of thyroxin, adrenalin and Lugol's solution upon the percentages of radiations of short, medium and longer wavelengths produced by oxidation of glucose.

TABLE XI

EFFECT OF THYROXIN, LUGOL'S SOLUTION AND ADRENALIN UPON THE RADIATIONS PRODUCED BY THE OXIDATION OF BRAIN PROTEIN

	Water 0.4 to 1.4 μ	Glass 1.4 to 4 μ	Salt 4 to 14 μ
100 cc. Glucose—10% solution in water	26%	26%	48%
Glucose plus adrenalin	39%	21%	40%
Glucose plus thyroxin	32%	28%	40%
Glucose plus thyroxin plus Lugol's solution	27%	29%	44%

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CHAPTER 27. STUDIES OF AUTO-SYNTHETIC CELLS

THE formation and investigation of the properties of auto-synthetic cells was done in collaboration with Maria Telkes, and Amy Rowland. The review of the literature and a bibliography appeared in a previous paper.¹

THE FORMATION OF AUTOSYNTHETIC CELLS

To 10 cc. of sterile protein solution (See p. 285), 0.2 to 0.5 cc. of the lipoid solution (see p. 275) is added with a glass dropper and the mixture is stirred thoroughly with a glass rod. (The protein solution contains approximately $\frac{1}{2}$ per cent solid material, the lipoid extract contains 1 per cent of lipoid in ether.) When a drop of this mixture is observed under the microscope, round structures may be seen having a distinct smaller globule inside, which resembles a nucleus. On the periphery very short, fine cilia-like structures appear at once which in a few minutes grow considerably. (See Figs. 23, 24.) Some of the cell-like structures are formed incompletely, that is, with a small dent instead of a complete nucleus-like part. If too much of the lipoid solution has been added some of it will be in larger clumps. The diameter of the cell-like structure varies from $50\ \mu$ to $150\ \mu$.

A sterile method for obtaining larger amounts is as follows: A large test tube (100 cc.) is used which is closed with a rubber stopper in which are two holes. Through these holes two glass tubes are passed, the lower ends of which have been drawn into a capillary. One of these tubes is long enough to reach to the bottom of the test tube, the other reaches to just below the stopper. The upper ends of these tubes are plugged with cotton

and the apparatus is sterilized. The large test tube is filled to about one-third with the sterile protein solution. The cotton plug of the long tube is then removed and the necessary amount of the lipoid-ether solution is introduced with a sterile pipette. The cotton plug is replaced and slight suction is applied on the short tube which forces the ether solution to run down and mix thoroughly with the protein solution. The suction is continued so as to remove the excess of ether gradually. If the excess of ether is not permitted to evaporate completely the cilia-like structures will be incomplete.

Preparations made by mixing dry lipoid with the protein solution will form cell-like structures very much more slowly and they will be less complete, sometimes not showing a nucleus or cilia-like formation. In such structures a distinct cell-wall and internal granules can be seen.

The presence of bacteria in the solution prevents the formation of perfect ciliated structures. If the already formed cell-like structures in their solutions are permitted to become contaminated by bacteria, the cilia perish very rapidly and gradually the cell-like structures change into fatty droplets, without any internal structure. If the cell-like structures are kept sterile in their protein solution it is possible to preserve them for a longer time. These "cultures" have to be subdivided and sterile protein solution has to be added from time to time.

STRUCTURES FORMED BY LIPOID AND PROTEIN MIXTURES UNDER VARYING CONDITIONS

Mixtures made with brain lipoid: The most remarkable structures are formed in a solution at pH 7.4. Structures of a very interesting type continue to appear if the pH of the protein solution is rendered more alkaline. The cilia-like structures vanish under pH 7.2 or above pH 7.8, but the nucleus-like structure is maintained even at pH 8.5, or at pH 4.0 to 7.0, although it is incomplete, that is, open to the medium. The protein extract of the brain can be partly replaced by dilute solutions of peptone, albumin, etc., without changing the formations to a very great extent. Protein extracts made of other tissues in exactly the same way as described above for the brain

tissue may replace the protein solution of the brain entirely. This type of structure can be maintained for a considerable length of time by the repeated addition of protein solution and by the subdivision of "cultures." Some of these cultures were continued from October, 1930 to August, 1931.

Very different structures are obtained in more alkaline solutions (pH 9 to 10.5), especially when a protein solution prepared from adrenals is used. These structures resemble amebae. (Fig. 95.) They have a distinct (although very slow) motion, thrusting out pseudopodia-like loops and again retracting them. A series of photomicrographs is shown in the figure picturing the same "cell" at different times. The ocular micrometer helps to determine the apparent growth of the structures.

Mixtures made with lipoids from various tissues (exclusive of the brain): Using the methods described above, the lipoids and protein extracts and the salt solutions of the following other tissues were prepared: Adrenal, thyroid, heart, voluntary muscle, stomach, spleen, liver, pancreas, kidney, testis, ovary, and malignant tumors. The aim of this work was to ascertain whether the lipoid of the brain is the only one that can form autosynthetic cells. The following mixtures were made with each of the twelve different tissues:

1. The lipoid of the tissue was mixed with the protein and "brain-salt" solution, the pH of the latter being at 7.4. The following structures were found: round globules with imperfect cilia-like protuberances when lipoids from the adrenal, thyroid, or testis were used; the other mixtures produced only fatty globules of various shapes and sizes.

2. The lipoid of the tissue was mixed with a solution of its own protein and electrolyte, at pH 7.0 to pH 7.4. In most of the mixtures only round fatty globules could be seen. In a few cases fatty structures of various shapes and sizes with an uneven surface were obtained. Only in the case of extracts of the liver did structures appear which resembled an autosynthetic cell with nucleus-like inner structure, but they had no cilia-like projections.

When mixtures of several lipoids in a solution of several kinds of proteins were used, only very simple fatty structures were obtained.

The lipoids extracted from malignant tumors (postoperative material) require special notice as they produced only structures which resembled an emulsion of oil in salt solution. (Fig. 96.)

Effect of various salts on the formation of cell-like structures: Omission of the potassium and the phosphate ions from the salt solution used for the preparation of the protein extract delayed or completely prevented the formation of autosynthetic cells; the addition of an excess amount of some of the salt constituents caused a complete change in the usual structures, the change depending on the concentration of the added solution. Deformation of the cilia-like structures is caused by the addition of n/10 KCl and n/10 NaCl. A complete breaking up of the structures is caused by n/10 CaCl₂. If the protein solution is prepared with any of these salts, only round fatty globules will be obtained if the brain lipoid solution is added to it in the usual way. At the suggestion of Dr. W. J. Maloney a salt solution was prepared from the ash of milk containing the salts in the same proportion as they are present in milk. When this was mixed with the lipoid extract fairly complete cell-like structures were produced. Excessive dilution of the salt solutions used entirely changed the appearance of the autosynthetic cells. The addition of distilled water to already formed structures changed them, and in an excess amount destroyed them.

Salts of heavy metals were added either to suspensions of autosynthetic cells or to the brain-lipoid before it was mixed with the protein solutions with the following results:

Ferric chloride in n/10 concentration transformed the auto-synthetic cells into round fatty droplets. In n/100 concentration the autosynthetic cells were transformed into round structures which contained a structure somewhat resembling a nucleus. These cells had a rough surface and were not ciliated. In n/1000 to n/100,000 concentration the autosynthetic cells were altered little if at all; a precipitate appeared between the cells. Ferrous iodide was dissolved in the ether solution of brain lipoid which was then mixed with the protein and "brain-salt" solutions in the usual manner and prevented the formation of the usual structures. Copper chloride added in great dilutions to the ether solution of the lipoid similarly prevented the usual formation. When copper chloride was added to suspensions of autosynthetic

cells the following result was observed: A 0/100% solution transformed the autosynthetic cells into structures of many different shapes and sizes surrounded by a halo and containing partly-formed nuclei.

Effect of various substances on the formation of autosynthetic cells:

Ether: When the ether is not entirely evaporated from the mixtures the formation of cells may be prevented. The addition of an excess amount of ether to a suspension of the cells destroys them.

Alcohol: The addition to a suspension of cells of alcohol, in sufficient quantity to make a concentration of 10 per cent, gradually destroys the cells. The cilia crumple, the nuclei enlarge and the cells change into dark clumps.

Strychnine, morphine, cyanides and adrenalin in very low concentrations do not affect the autosynthetic cells, but in larger doses destroy them.

Spinal fluid: When brain lipoid is mixed with spinal fluid, autosynthetic cells are formed. The cilia are somewhat curled or crumpled in appearance and the cells do not maintain their form for any length of time.

Effect of temperature on the formation of autosynthetic cells: The best formed cells were formed at room temperature 20 to 28° C. When the lipoid of the brain was added to a cold protein solution (0° C.) the ether evaporated very slowly. No autosynthetic cells were formed and most of the lipoid appeared in small fragments. When the suspension was then warmed up to room temperature very few ciliated autosynthetic cells appeared. When the lipoid was added to warm protein solution (50° C.) very few autosynthetic cells were formed. The ether evaporated almost immediately and most of the lipoid appeared in small fragments. When a suspension of autosynthetic cells was heated to 50° C. and this temperature was maintained for 10 minutes the cells were completely destroyed; only disintegrated masses could be seen. When a suspension of cells was cooled to 0° C., the cells did not show any change.

The temperature does not affect the protein solutions as this can be boiled without changing its effect when mixed with lipoid. (The protein solution is sterilized in an autoclave.) It is

the lipoid that is affected by the temperature. When the ether was evaporated and the dry lipoid was heated to 50° C. and then redissolved in ether and mixed with the protein solution no autosynthetic cells were formed, but the lipoid appeared in clumped masses.

Effect of exhaustion and disease on the formation of autosynthetic cells: The lipoids and proteins were extracted from the brains of dogs which had died of distemper and of rabbits which had been kept awake for prolonged periods. When the lipoid of the brain secured from these animals was mixed either with a solution of proteins from the same animal or from a healthy animal, dark fatty droplets appeared. (Fig. 97.) The appearance of these droplets did not even approximate that of the autosynthetic cells formed when lipoid from the brain of a normal animal was used. That this result is due to some change in the lipoids of the diseased or exhausted animals is shown by the fact that when protein extract from the brains of these animals was mixed with lipoid from a healthy animal perfectly formed autosynthetic cells were produced. Lipoids from the brains of rabbits which had died after a shorter period of insomnia, when mixed with the protein solution, produced autosynthetic cells which, however, were imperfect in form, had short crumpled cilia and contained imperfectly formed nuclei. If the brains of healthy animals were kept in the icebox for several days the lipoid gradually lost its ability to form autosynthetic cells.

Effect of various constituents of brain-lipoid upon the formation of autosynthetic cells: The term brain-lipoid as used throughout this presentation indicates the entire ether extract of dried brain tissue. It was of interest and importance to determine whether or not any one of the constituents of this extract was of any more importance than the others in the formation of autosynthetic cells. For this purpose the phospholipins, cephalin and lecithin and the cholesterol were separated in the following manner:

The total brain-lipoid was dissolved in the smallest possible quantity of ether, and acetone was added. The acetone precipitated the phospholipins, the filtrate containing fats and cholesterol. The precipitate was redissolved in a small amount

of ether and reprecipitated with acetone. This precipitate when washed was again dissolved in a small amount of ether. This solution contained the phospholipins.

To obtain cephalin and lecithin the phospholipins were mixed with absolute alcohol. The precipitate contained chiefly cephalin; the filtrate contained lecithin. These four fractions, the cholesterol and its associated fats, the phospholipins, the cephalin and the lecithin were dried in vacuum and redissolved in small amounts of ether. Each of these fractions was then mixed with the protein solution with the following results:

Cholesterol: With the cholesterol fraction long, thin, crystal-like forms were produced such as are characteristic of cholesterol.

Phospholipins: With the total phospholipin fraction, small transparent globules were produced, projecting from which could be seen pseudopodia-like structures. No nuclei could be seen.

Cephalin: With the cephalin fraction larger globules than those produced by the total phospholipin fraction were formed. Neither cilia nor nuclei could be seen.

Lecithin: With the lecithin fraction an opalescent fluid appeared within which no particles could be seen under the microscope.

Mixtures of the four fractions in varying proportions result in the formation of globules of varying size. When the cholesterol fraction was predominant in these mixtures globules were formed, in the interior of which could be seen structures like cholesterol crystals.

With none of these fractions and with no combination of them were autosynthetic cells produced. Even with a mixture of the fractions in the proportions in which they were present in the original material no structure was formed which in any way resembled that produced when whole brain lipoid was used.

Effect of lipoids from different portions of the brain and spinal cord on the formation of autosynthetic cells: A human brain was obtained and lipoids and proteins were extracted from all parts of the brain, from the cerebellum, the medulla oblongata and the spinal cord. When the extracts of each of these parts were combined with protein solution the following results were



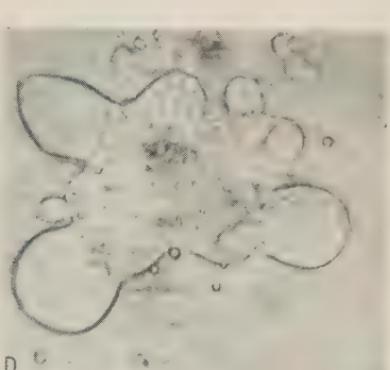
A



B



C



D

FIGURE 95. Ameba-like autosynthetic cell exhibiting growth and movement. B, C, and D, appearance of cell shown at intervals of 3, 6, and 9 hours respectively. (From photomicrographs X 400)

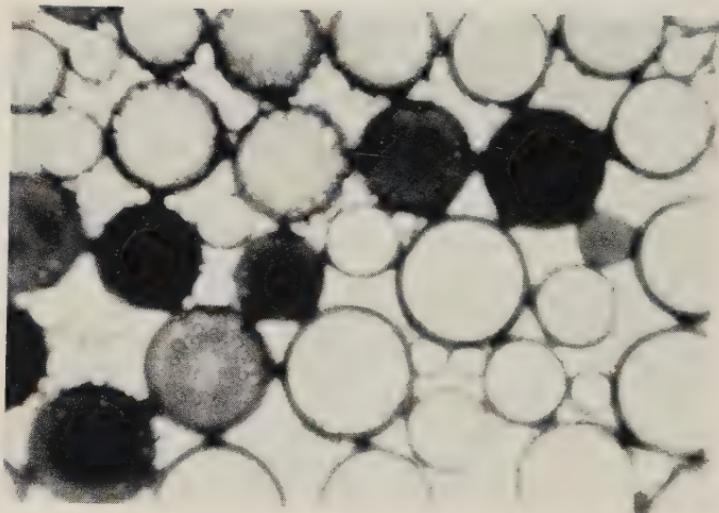


FIGURE 96. Fatty globules found when lipoid and protein fractions obtained from a cancerous growth were mixed. (From photomicrograph X 200)



FIGURE 97. Dark globules obtained when lipoid and protein fractions obtained from the brains of exhausted or diseased animals were mixed. (From photomicrograph X 200)

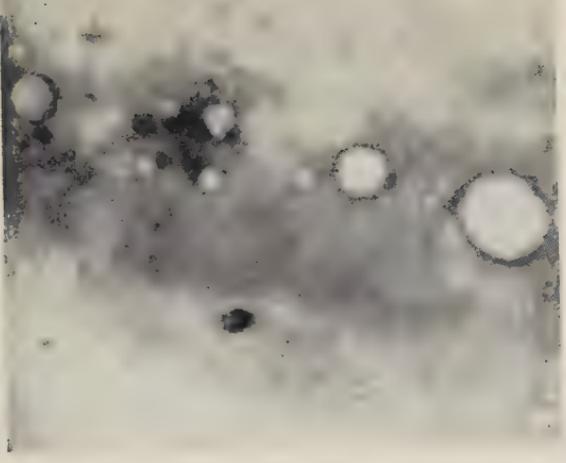


FIGURE 100. Destruction of autosynthetic cells by lack of oxygen. (From photomicrograph X 200)



FIGURE 99. Effect of radium on autosynthetic cells. (From photomicrograph X 200)

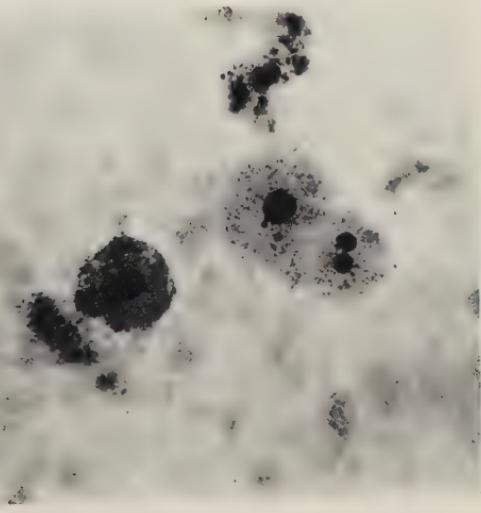


FIGURE 98. Stained autosynthetic cells (From photomicrographs A, X 200; B, X 250)

observed. *Whole brain*: very well formed autosynthetic cells were produced. *White matter*: autosynthetic cells were produced which, however, were not quite so well formed as those from whole brain. *Cerebellum*: cells were not produced but myelin structures were present. *Medulla oblongata*: cells were not produced. *Spinal cord*: irregular round structures with short and irregular cilia were produced.

Staining of autosynthetic cells: An attempt was made to stain autosynthetic cells using various methods in the same way as they are applied for the staining of protozoa. The structures stained very well with rhodamin, sudan, and nile blue. The most successful method for bringing out structural differentiation was the method of fixing with Zenker's fluid or with a mixture of osmic acid and potassium bichromate. Subsequent staining with hematoxylin-eosin gave the appearance shown in figure 98 in which dividing autosynthetic cells are seen. During the fixing and staining operations the cilia-like structures perish.

METABOLISM OF AUTOSYNTHETIC CELLS

Oxygen consumption: Warburg's manometric method was employed for measuring the oxygen consumption. The importance of avoiding bacterial contamination has already been stressed. In order to judge the sterile condition of the suspension a control experiment was carried out in one of the vessels with the same protein solution as was used in the preparation of the autosynthetic cells. Only those experiments were considered in which the control protein showed no oxygen consumption. The autosynthetic cells were prepared as described above and were kept in sterile culture tubes or flasks until the measurements were required. The mixtures usually contained 0.5 to 1 per cent protein and 0.1 to 0.5 per cent lipoid. Experiments were made during consecutive days with mixtures at pH 9.0 at which pH ameba-like structures are formed. A large number of autosynthetic cells were prepared and under sterile conditions were placed in sterile test tubes or flasks, which were kept at room temperature. Each day one of these tubes was used, 2 cc. of the mixture being put into each respiratory vessel. Five parallel experiments were carried out with each specimen. The tempera-

ture was as usual at room temperature. The O_2 consumption, as can be seen from Table XII, gradually increases with the age of the mixture, reaching its maximum at the end of one to two weeks and decreasing afterwards to a very low level at the end of 4 weeks. Two series of experiments were carried out with extracts made with the brains of different animals during an interval of two months. The variations in the results of the experiments made in the different respiratory vessels, but with the same material, agreed to 4 per cent. A somewhat larger deviation was found in experiments made on several consecutive days. (Table XII.)

These values represent the oxygen consumption in mm^3 per hour per 2 cc. of the mixture. It is evident that in comparison with the relatively small oxygen consumption of the 10 per cent lipoid emulsion mentioned in Chapter 26, this mixture has almost as great an oxygen consumption, although it contains about twenty times less lipoid. If an emulsion is prepared containing about one per cent lipoid in salt solution (that is, about twice as much as is contained in the autosynthetic cell emulsion) it will show practically no oxygen consumption within the experimental limits, even if the experiment is carried on for more than one day. Therefore, it must be concluded that the autosynthetic cells are able to use the protein solution for metabolic purposes.

Such mixtures as those mentioned above gradually lose their ability to consume oxygen. If, however, a sterile culture over a month old is mixed with some sterile protein solution, the oxygen consumption is immediately resumed, the values reaching $20 mm^3$ per hour per 2 cc. of the mixture or even higher.

The effect of the pH on the oxygen consumption was definite. Autosynthetic cells at pH 7.4 showed an oxygen consumption of 7 to $10 mm^3$ per hour per 2 cc. cell mixture (containing 0.5 per cent lipoid in a 0.5 per cent protein solution). At a definitely acid reaction, pH 2.6, the oxygen consumption ceased; at this pH naturally the morphological structure of the cells was destroyed also.

The question as to the rôle of enzyme action in this metabolism-like process must be left open.

Effect of various agents on the oxygen consumption of autosynthetic cells: The addition of concentrated salt solution not

only destroyed the morphological structure of the autosynthetic cells, but lowered or abolished their oxygen consumption. Very dilute salt solutions, however, increased it or did not change it. Especially large increases in oxygen consumption were obtained with autosynthetic cell mixtures (at pH 7.4 or at pH 10.0) to which a diluted solution of FeCl_3 or FeI_2 was added. The attachment of the respiratory vessel was filled with a certain amount of the solution which was to be tested. The main compartment was filled with the sterile autosynthetic cell mixture. First, the oxygen consumption of the mixture alone was tested, then the apparatus was inverted to mix the two solutions and the oxygen consumption determinations were continued. With a 0.0001 n to 0.001 n solution of the iron salts the oxygen consumption was increased 20 to 70 times. (Table XIII.)

A further study was made which seems to indicate the importance of the lipoid in the oxygen consumption. Autosynthetic cell mixtures were radiated with large doses of radium (10–20 erythema units). They showed the usual amount of oxygen consumption before radiation, which, however, was completely abolished by radiation. The interesting changes due to the radium are shown in figure 99. As will be seen the cilia are absent and the structure is radically changed. Radiation of the lipoid alone prevented the formation of autosynthetic cells, while the radiated protein did not show any change in its behavior.

Mixtures prepared with solutions extracted from the brains of animals which had died of exhaustion or disease, similarly did not show any oxygen consumption in addition to the inability to form the usual structures. This fact again indicates the importance of the lipoid fraction as far as the oxygen consumption is concerned.

Oxygen consumption is necessary for the maintenance of the structures. If autosynthetic cells are kept in an atmosphere of nitrogen, or if they are kept in tubes which are completely filled with the emulsion and then sealed, a gradual disintegration of the structures takes place, the cells seemingly undergoing degeneration, until finally only a grayish colored mass remains, in which large yellowish droplets are present. (Figs. 100, 101.)

Oxygen consumption of other lipoid and protein mixtures:

With exactly the same methods as described above, various other mixtures of lipoid and protein solution were made with extracts obtained from other tissues. Only simple fatty droplets, or very primitive round, granular structures were obtained, as was mentioned above. These mixtures showed no oxygen

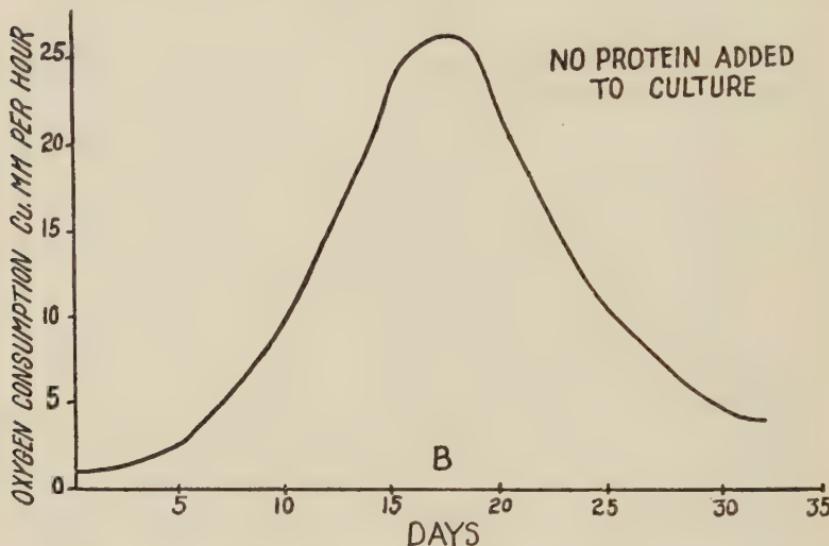


FIGURE 101. Effect of age on the oxygen consumption of autosynthetic cells.

consumption whatsoever, or to such a very slight degree as to be practically within the experimental limits.

Measurements of the "respiratory quotient": The determinations of the relation of CO_2 output to O_2 consumption were made according to the method of Richardson. The experimental limit of this method is ± 0.02 . Experiments made on various fatty acid emulsions, in the same way as those which were done to show oxygen consumption, showed no CO_2 output, or only a very small one (0.04). Experiments made with autosynthetic cells, however, showed an average R. Q. of 0.81, the experimental data varying between 0.70 and 0.86 (see Table XIV). On the addition of glucose the R. Q. increased to 0.96. Most of these measurements were made on autosynthetic cell mixtures at pH 8.0. (Fig. 102.)

Decomposition of Protein by autosynthetic cells: A large quantity of autosynthetic cell mixture was prepared and placed in several sterile test tubes each containing 10 cc. On each consecutive day the mixture in one of the test tubes was used for the determination of ammonia according to the aeration method of Myers, three parallel experiments being done each time. The protein used for the preparation of the autosynthetic cells was

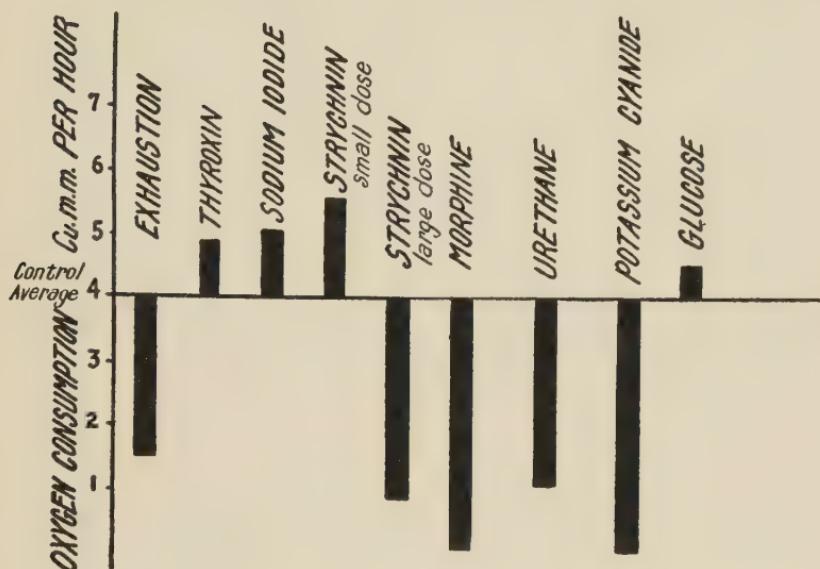


FIGURE 102. Effect of various agents on the oxygen consumption of autosynthetic cells.

also divided into sterile test tubes and the same determinations were made with it each day, as in the case of the autosynthetic cell mixtures. The experiments were carried on for two weeks, during which time the control protein solutions did not show any increase in ammonia production, whereas the autosynthetic cells showed an increase of 28 per cent. After a period of about seven days the ammonia production ceased to increase. These findings serve to indicate that protein is actually decomposed by the autosynthetic cells.

MULTIPLICATION OF AUTOSYNTHETIC CELLS

An emulsion of autosynthetic cells at pH 7.4 kept in a culture-flask for several hours will show figures resembling cell division. (See Figs. 24, 98.) If such an emulsion is placed in a hanging drop under the microscope the changes can be observed until complete division takes place. The changes in a sealed hanging drop will continue for from twenty to thirty hours. The observation of this process presents the same difficulties as similar observations on amebae, for instance. Care must be taken to avoid evaporation of the solution and lack of air, as in a sealed drop the division will very quickly cease. Observations made in a moist chamber are the most successful.

The division of autosynthetic cells in mixtures at pH 9 (ameba-like types) is somewhat more easily observed. Many series of observations were made in hanging drops placed on a counting cover glass. Increases in the number of cell-like structures were observed ranging from 10 to 30 per cent during twenty-four hours. In some mixtures changes resembling budding can be observed.

ELECTRIC CHARGE

The apparatus used in the cataphoresis measurements was similar to that described by Northrop and Kunitz. The electric charge of the particles was calculated from the Helmholtz formula. The suspensions of autosynthetic cells were prepared according to the methods described earlier in this chapter.

As a preliminary experiment, suspensions of the lipoid extract of brain were prepared and their electrical charge was determined. The electrical charge of lipoid emulsion particles was measured. (See p. 277.) These particles were suspended in the "brain-salt" solution used for the preparation of the protein solution, which was brought to different degrees of pH. (Table XV.) At pH 4.0 the particles were discharged. The lipoid, without the addition of the protein, has a relatively high negative charge, which changes at various degrees of pH. The charge of the protein solution was also measured (p. 286) in

order to see if there might be some interaction (possible absorption, etc.) between the lipoid suspension particles and the protein solution. From these findings it might be inferred that an electric potential difference (P. D.) must exist between the particles of lipoid (-63 millivolts) and protein (-2 millivolts) at pH 11.4. This P. D. might be present when the protein is in some way absorbed by or combined with the lipoid particles. The effect of the pH of the protein solution on the electric charge of auto-synthetic cells is shown in Table XV. The values are given as millivolts.

It may be seen from this table that the autosynthetic cell mixture has a lower charge than the corresponding lipoid emulsion at all degrees of pH with the exception that the discharging point for the autosynthetic cell mixture is more on the acid side.

The electrical charge of freshly prepared autosynthetic cells (at pH 7.4) depends somewhat on the method of preparation, but generally is around -40 to -45 millivolts. On standing in sterile culture flasks the electric charge of the autosynthetic cells decreases about 10 per cent in a few days, while in cultures two to four weeks old the charge is about 30 per cent lower.

Various salts and other agents have a decided influence on the electric charge of the autosynthetic cells. (Fig. 103.) To obtain a definite picture of the influence of some agents, the cell-like structures had to be washed several times with distilled water in order to free them of most of the protein and salt in the solution, as the agents (heavy metal salts, etc.) might form a precipitate with these. Such repeated washing increases the electric charge from -40 or -45 to above -55 millivolts. The addition of diluted salt solutions generally causes an increase of the electric charge of autosynthetic cells washed with distilled water. Addition of concentrated salt solutions decreases the electric charge, together with precipitation or general destruction of the morphological appearance. The effect of these agents was generally investigated with freshly prepared autosynthetic cells (mostly pH 7.4). The cells were washed several times with distilled water, their electric charge determined, the agent added, and the charge determined immediately afterwards and some time later. Some of the changes are shown in Table XVI.

Especially great effects are noted with trivalent salts, the charge being reversed. With iron salts in very great dilutions an increasing effect can be observed. Typical changes, measured many times, are cited in Table XVII.

It is interesting to note that with the addition of diluted iron salts a large increase in the oxygen consumption of autosynthetic cells can be measured.

If the salt solutions are added to mixtures which have not

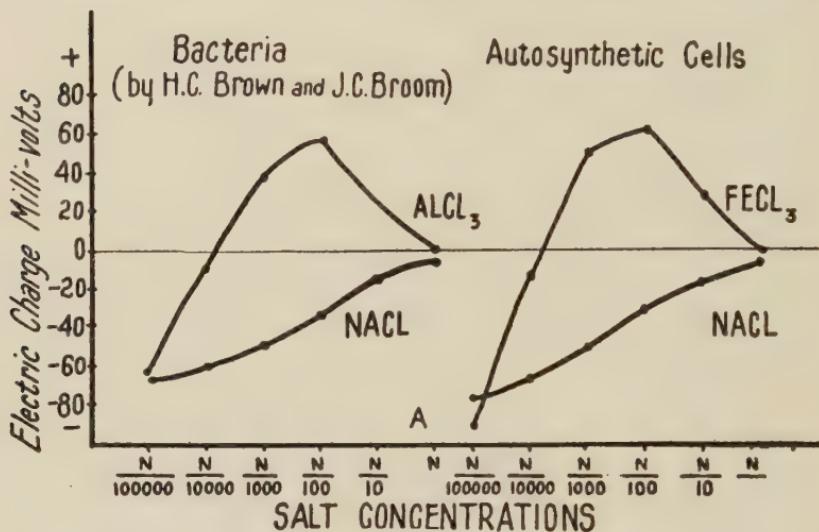


FIGURE 103. The effects of varying concentrations of sodium chloride and of ferric chloride on the electric charge of autosynthetic cells. Compare the curve for the autosynthetic cells with that for bacteria established by Brown and Broom.

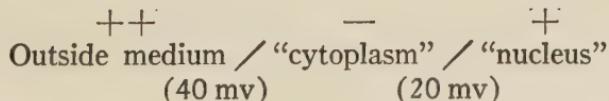
been washed, they have a distinct effect, but this is more or less a time effect—the change in charge being only temporary or decreasing or increasing in time. The addition of concentrated salt solution has a distinct decreasing effect, however.

The addition of various agents alters the electric charge greatly. Mixtures contaminated with bacteria show a rapid decrease of the charge. The addition of tuberculin toxin completely discharges the mixture. Among other agents, strychnine, morphine and urethane cause definite changes the nature of which is indicated in the following example: The original charge of the

autosynthetic cells at pH 7.4 was -50 millivolts. The addition of strychnine to make the concentration in the mixture 0.001 per cent immediately decreased the charge to 47 millivolts; 5 minutes later the charge rose to 54 millivolts, in 10 minutes to 60 millivolts, 20 minutes later it was 62 millivolts, a total increase of 24 per cent as compared with the original charge. The addition of a larger concentration of strychnine (0.01 per cent in the solution) after some time caused a 33 per cent decrease of the charge. Larger concentrations discharge the cells completely.

In comparison with the above values, the electric charge of lipid emulsions and mixtures with protein solution was measured with extracts of other tissues. It was found that such particles never had higher charges than 40 millivolts (at pH 7.4) and the average charge was around 28 millivolts. Whether a comparison can be made between the low charge and the inability of showing autosynthetic cell-like structures is open to question.

Direct measurements of P. D. of autosynthetic cells: By means of micro-electrodes and the binantenelectrometer static potential differences were measured on amebae. This method was applied to autosynthetic cells at pH 7.4. Reversible electrodes having a fine opening of about 10μ and filled with KCl were used. The end of the electrode was filled with the same solution as that in which the autosynthetic cell was suspended. On introducing one electrode into the cytoplasm-like part of the cell this part was found to be negative against the outside medium, corresponding to the negative charge found by cataphoresis. On introducing one electrode into the nucleus-like part this was found to be positive against the cytoplasm-like part. In very large autosynthetic cells this can be done without too much danger of injuring the cells. The scheme of the electrical potential differences is as follows:



Touching and manipulating the autosynthetic cell with micro-needles reveals the fact that the outside is somewhat more resistant to piercing than the outside of amebae, but they are less

hard than some eggs. Long strings can be pulled out with needles, which show mechanical properties similar to the strands of protoplasm which may be pulled out of eggs.

RADIATION

The radiations emitted on the oxidation of suspensions of autosynthetic cells were measured by the method described in Chapter 26.

Table XVIII gives the radiations of the autosynthetic cells in

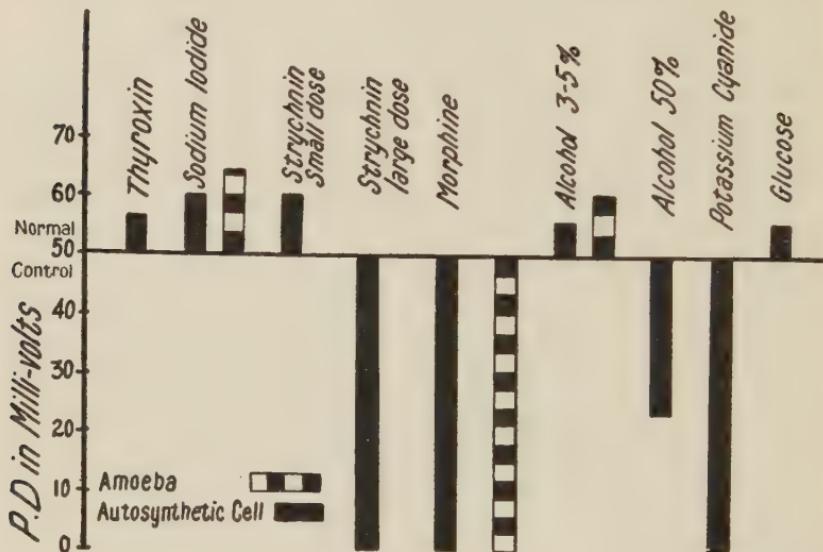


FIGURE 104. The effects of various agents on the electric charge of autosynthetic cells. The broken line represents the changes produced by the indicated agents in the potential difference of the ameba.

the short, medium and longer ranges measured by the filter method. This table also shows the effect of various agents upon the radiations. In every case the cell suspension to which agents were added was made by the same method as that by which the control suspensions were made. (Fig. 104.)

Of special significance in this table are the opposite effects of thyroxin alone and of thyroxin with Lugol's solution.

Of interest also is a comparison of the radiations from sus-

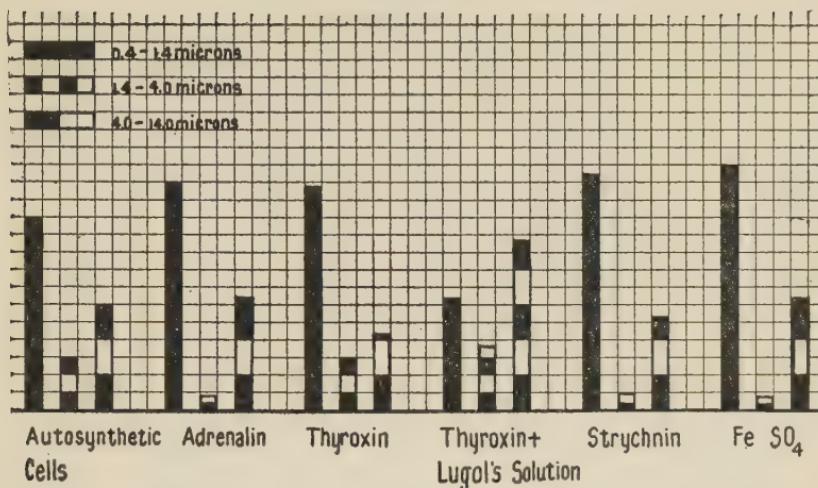


FIGURE 105. Effects of various agents upon the percentages of radiations of short, medium and longer wavelengths produced by the oxidation of autosynthetic cells.

pensions of cells made with the proteins derived from different tissues. (Fig. 105.) These findings should be compared with Table X in which are given the radiations from the proteins of the same tissues.

TABLE XII

OXYGEN CONSUMPTION OF AUTOSYNTHETIC CELL MIXTURES AT pH 9

Age of mixtures days	O ₂ consumption mm ³ / hour	Deviations mm ³ / hour	Age of mixtures days	O ₂ consumption mm ³ / hour	Deviations
2	0.4	0.2	5	1.9	0.2
8	3.8	0.9	6	4.3	0.2
9	3.9	0.1	7	6.6	0.1
10	20.3	1.1	11	2.9	0.4
13	22.0	0.4			
14	16.3	1.6			
15	17.6	1.0			
17	23.8	4.5			
18	19.5	4.5			
20	7.5	0.1			
25	4.4	0.1			
36	0.2	0.1			

TABLE XIII

EFFECT OF VARIOUS AGENTS ON THE OXYGEN CONSUMPTION OF AUTOSYNTHETIC CELLS

<i>Experiment Number</i>	<i>pH</i>	<i>Concentration of added agent or condition of the cell suspension</i>	<i>Oxygen consumption pressure mm³ / hr.</i>	<i>per cent change</i>	<i>Duration of experiment hours</i>
I a	7.4	Radiated	0		6
b	7.4	"	0		6
II a	7.4	Exhausted	0		5
b	7.4	"	0		5
c	7.4	"	0		5
d	7.4	"	0		5
III	7.4	Control 0.001 n FeI ₂ added second reading	2.0 7.0 0	+250	6 1.5 2.5
IV	7.4	Control 0.0001 n FeI ₂ added second reading third reading	1.8 10.6 11.4 14.3	+490 +530 +690	6.0 1.5 1.75 0.75
V	7.4	Control 0.00001 n FeI ₂ added second reading third reading	2.1 35.0 40.0 47.0	+1570 +1800 +2140	6.0 1.5 1.75 0.75
VI	7.4	Control 0.001 n FeCl ₃ added second reading 2 hours later	8.2 186.0 300.0	+2170 +3560	7.0 0.5
VII	7.4	Control 0.001 n FeCl ₃ added second reading 2 hours later	5.3 84.0 160.0	+1490 +2920	19.0 0.5
VIII	7.4	Control 0.001 n FeCl ₃ added second reading 2 hours later	2.2 70.2 160.0	+3090 +7170	19.0 0.5
IX	7.4	Control 0.0001 n FeCl ₃ added second reading 2 hours later	7.6 214.0 190.0	+2580 +2400	19.0 0.5

TABLE XIV

	<i>R.Q.</i>	<i>Error</i>
7 day old suspension, pH 8.0	0.70	0.01
7 day old suspension, pH 8.0 fresh protein added	0.84	0.01
14 day old suspension, pH 8.0	0.82	0.02
11 day old suspension, pH 8.0	0.86	0.02
2 day old suspension, pH 7.4	0.85	0.02
	av. 0.81	
13 day old suspension, pH 8.0 glucose added	1.00	0.03
8 day old suspension, pH 8.0 glucose added	0.98	0.02
	av. 0.99	

TABLE XV

THE EFFECT OF pH ON THE CATAPHORETIC ELECTRICAL CHARGE OF SUSPENSIONS OF LIPOID AND OF AUTOSYNTHETIC CELLS

pH	11.4	10.9	10.2	9.0	8.0	7.0	6.0	5.2	4.2	3.2
	<i>mv</i>									
Lipoid emulsion	-63	-52	-53	-43	-41	-48	-40	-29	0	0
Suspension of Auto- synthetic cells	-48		-44	-31	-33	-38	-42	-30	-28	0

TABLE XVI

THE EFFECT OF VARIOUS SALTS ON THE CATAPHORETIC ELECTRIC CHARGE OF AUTOSYNTHETIC CELLS

Solution	nNaCl	nKCl	0.2 CaCl ₂	0.2 MgCl ₂	0.02 MgCl ₂	0.002 AlCl ₃	0.05 AlCl ₃
	<i>mv</i>	<i>mv</i>	<i>mv</i>	<i>mv</i>	<i>mv</i>	<i>mv</i>	<i>mv</i>
Per cent decrease of elec- tric charge	-63	-78	-100	-100	-71	-158	-117

TABLE XVII

<i>Concentration FeCl₃ in mols</i>	<i>Cataphoretical charge in millivolts</i>
(without addition of FeCl ₃)	<i>mv</i>
0.000001	-70
0.00001	-71
0.0001	-78
0.001	-85
0.01	-64
0.05	-23
0.01	0

TABLE XVIII

EFFECT OF VARIOUS AGENTS ON THE RADIATION EMITTED BY THE OXIDATION OF AUTOSYNTHETIC CELLS

	<i>Filters</i>		
	<i>Water</i> 0.4 to 1.4 μ	<i>Glass</i> 1.4 to 4 μ	<i>Salt</i> 4 to 14 μ
Autosynthetic cells made from brain protein	55%	16%	29%
Autosynthetic cells plus thyroxin	64%	14%	22%
Autosynthetic cells plus thyroxin plus Lugol's solution	32%	19%	49%
Autosynthetic cells plus adrenalin	65%	3%	32%
Autosynthetic cells plus strychnine	68%	4%	28%
Autosynthetic cells plus FeSO ₄	64%	4%	32%

TABLE XIX

COMPARISON OF THE RADIATIONS EMITTED BY AUTOSYNTHETIC CELLS MADE FROM THE PROTEINS FROM VARIOUS TISSUES

	<i>Filters</i>		
	<i>Water</i> 0.4 to 1.4 μ	<i>Glass</i> 1.4 to 4 μ	<i>Salt</i> 4 to 14 μ
Voluntary muscle	69%	9%	22%
Liver	61%	15%	24%
Heart	59%	17%	24%
Spleen	59%	5%	36%
Kidney	57%	13%	30%
Brain	55%	16%	29%
Adrenal	47%	10%	43%

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CHAPTER 28. *THE EMISSION OF RADIATION FROM ANIMAL TISSUES*

Maria Telkes, Ph.D.

THE recent interest in the study of the emission of radiation from living organisms suggests an inquiry as to the physical basis of such phenomena. Radiation is emitted in the visible part of the spectrum by luminous organisms such as the firefly, a phenomenon which is called bioluminescence. Of course, all organisms which have a higher temperature than the surrounding medium emit heat radiation, or more precisely, infra-red radiation. Recent investigators of the mitogenetic radiation have stated that they have observed the emission of ultraviolet light by some living organisms. Therefore there is an indication that living organisms may emit radiation in the ultraviolet, visible, and infra-red parts of the spectrum.

PHYSICAL LAWS CONCERNING THE EMISSION OF RADIATION

The radiation emitted by heated objects is indicated by the term "*temperature radiation*." This may extend to the infra-red, visible or even the ultraviolet part of the spectrum, according to the temperature, and the emission, absorption and reflection coefficients of the heated object. The higher the temperature the greater the proportion of visible and ultraviolet radiation. The laws of Kirchhoff, Stefan-Boltzmann, Lummer-Pringsheim and Planck express physical constants as a function of the temperature radiation.

Many substances, however, exhibit another type of radiation,

which includes the ultraviolet, visible, and probably the short infra-red part of the spectrum, without the additional increased temperature effect of the temperature radiation. This is indicated by the term *chemiluminescence*, that is, light emission during chemical reactions, without any appreciable rise of temperature during the reaction.

From the biological point of view the most important chemiluminescent reactions are those which occur in aqueous solutions during the oxidation of organic chemical compounds. Einstein's law ($U = Nh\nu$, or $U = \text{constant } \nu$) is applicable to the chemiluminescent reactions. In this formula, U represents the heat evolved during the chemiluminescent reaction of one gram molecule of the substance, N is the number of molecules, h is the Planck constant and ν is the frequency of the radiation. As shown by this formula the greater the heat evolved during the reaction (produced by one gram molecule of the substance), the shorter is the wavelength of the emitted radiation. Harvey¹ calculates that a reaction must evolve at least 37,000 calories per gram molecule in order to produce visible red light and 71,000 calories to produce violet light. Indeed the "evidence is that most of the few chemiluminescent reactions whose molecular heat is known fall within that range."¹

An example of the difference between temperature radiation and chemiluminescence is the following: when a piece of solid gelatin burns, that is, unites with oxygen, it emits heat, visible light and even very small amounts of ultraviolet. This radiation is chiefly temperature radiation. If the same amount of gelatin is dissolved in water and oxidized with a powerful oxidizing agent, it will emit some visible light, although the increase in temperature will be almost negligible. This is chemiluminescence. In burning with flame the temperature is increased while during chemiluminescence the temperature change is very slight in comparison. On the basis of the kinetic theory it is not possible to speak of the temperature of a chemiluminescent reaction in the ordinary sense. The assumption was made some time ago by P. Lenard² that all phenomena showing visible light at a relatively low temperature (so called "cold light") show this light because points of molecular dimension ("centers") are at a sufficiently high temperature to produce

the emission of visible light. The volume of these "hot points," however, must be very small in comparison with the volume of the surrounding medium. Ultimately part of the visible light and possibly the ultraviolet and short infra-red radiation would be transformed into heat which would increase the temperature of the chemiluminescent reactant by a few degrees centigrade.

Another important difference between temperature and chemiluminescent radiations is the fact that temperature radiation is a surface phenomenon; that is, the light is generally emitted from the surface of the heated object, and the volume of the object generally does not influence the intensity of the emitted radiation. Chemiluminescence, however, occurs throughout the volume of the solution which is undergoing chemical change, and hence the brightness of the emitted radiation is influenced by the volume of the reacting substances. If chemiluminescence occurs in an opaque medium, that is, in a medium which is not transparent to the wavelengths of radiation produced during chemiluminescence, most of the radiation would be absorbed in the solution, and could be emitted only from a very thin surface layer of the solution, with greatly reduced brightness.

In general, temperature radiation is a surface phenomenon, emitted from substances opaque or black to the emitted rays. The intensity of chemiluminescent radiation depends upon the layer thickness of the radiating medium and *only those wavelengths to which the medium is transparent can be emitted.*

The physical laws of radiation emission must govern the radiation emitted by living organisms. Based upon these laws it should be possible to measure the temperature radiation emitted from warm blooded animals and express it as a function of temperature. It is possible also to indicate which wavelengths might be emitted as a chemiluminescent radiation, on the basis of the transmission of the tissues to the wavelengths concerned.

TEMPERATURE RADIATION FROM LIVING ORGANISMS

It is known from the measurements of Cobet and Bramigk,³ Aldrich,⁴ Zeiss,⁵ Philipp,⁶ Bohnenkamp and Ernst,⁷ Hardy⁸ and others that warm-blooded animals emit infra-red radiation.

In order to obtain a clear picture concerning the emission of infra-red radiation by human tissues, the infra-red emission spectrum of the human hand was measured by means of a rock salt prism spectrometer and vacuum thermopile with thermo-relay amplifier. These measurements were performed at the

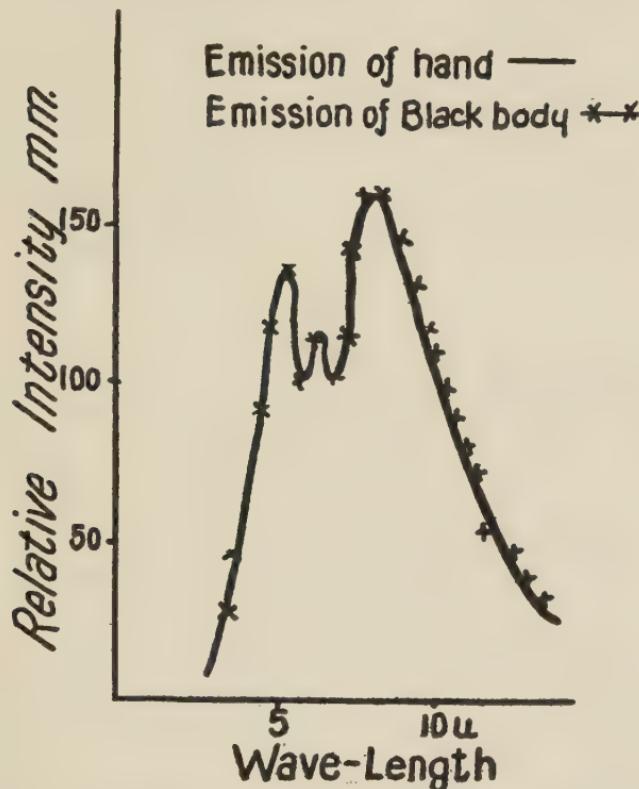


FIGURE 106. The emission of infra-red radiation from the human hand compared with that from a "black body."

University of Michigan, Ann Arbor, Michigan, in the Institute of Physics with the kind permission of Professor H. M. Randall and through the coöperation of N. Wright, Ph.D. It was found that the emission of radiation by the human hand is identical with that from a perfect radiator "black body" of the temperature of the human body. The emission curve is shown in figure 106. The absorption band at 5 to 7 μ is due to water

vapor present in the air. No radiation shorter than 26μ could be ascertained within the accuracy of the method and the maximum of the radiation was found to be around 8μ . Similar results were obtained by Hardy.⁸

These experiments, however, do not show that no other than the infra-red radiation which is due to the body temperature is emitted by the tissues. It is possible that the body temperature is the end result of a series of absorption of shorter wavelengths to which the tissues are not at all or only slightly transparent. It would appear to be probable that the radiations of shorter wavelengths are used in the tissues to synthetize or build up compounds which are needed for metabolism and growth.

BIOCHEMILUMINESCENT RADIATION

According to the definition of temperature and chemiluminescent radiation all radiations emitted by living organisms of a wavelength shorter than 20,000 Ångström are chemiluminescent radiations. The possible range of wavelengths in which such radiation could be expected to occur might reach from about 20,000 Ångström in the infra-red through the visible into the ultraviolet region. If any radiation is emitted at all in this large range it must originate in the whole volume of the living organism and not only in a very thin surface layer, because in that case its intensity would be too small to be detected at all.

Hence the transmission of the tissues to various wavelengths will give a reasonable indication of the possibility of finding any chemiluminescent radiation.

The transmission of various wavelengths by the different tissues has been studied by Bachem,⁹ Cartwright,¹⁰ Gaertner¹¹ and others with spectrophotometers and by Gigon¹² and others with infra-red photographs. The transmission of blood serum and tissue extracts was studied by Müller,¹³ Guthmann and Schwerin¹⁴ and others, chiefly in the ultraviolet. Their results are indicated in figure 107. One can conclude that even thin layers of tissues or of tissue extracts completely absorb any radiation shorter than 3,000 Ångström (0.3μ) in the ultraviolet. The human cheek, in a layer about 5 mm. thick does not transmit any appreciable amount of ultraviolet radia-

tion; even in the visible range it transmits only wavelengths longer than 5,300 Ångström. In the infra-red part of the spectrum the transmission is practically nil for wavelengths longer than 20,000 Ångström (2μ) for thin layers of tissues and for the human cheek the transmission falls to zero at about 1.4μ .

The conclusions can be reached, that only radiation between

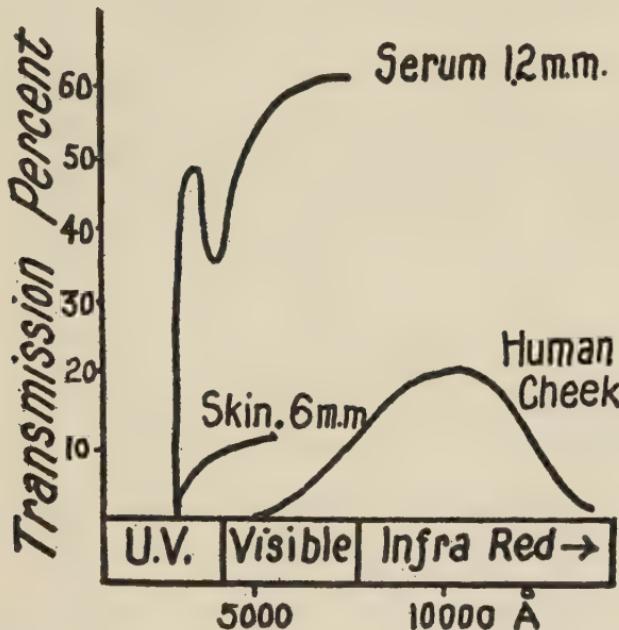


FIGURE 107. The transmission of radiation of various wavelengths by serum, skin and cheek.

5,300 and 14,000 Ångström could emerge from a thick layer of tissue and the thin layers do not transmit any radiation except between 3,000 and 20,000 Ångström. Any radiation produced in the tissues and not included in this range is completely absorbed by the tissue and transformed into body heat. It might be assumed that some amounts of radiation slightly beyond the transmission limits might be emitted from the surface layers, but the intensity of such a radiation would be correspondingly extremely weak.

The bioluminescence of the firefly is made up of such visible wavelengths as those to which the tissues of the firefly are

transparent and hence it can be detected with ease by the very sensitive human eye. Whether non-luminous organisms emit any radiation in the ultraviolet field at wavelengths longer than 3,000 Ångström, or in the short infra-red range, is a problem which presents great experimental difficulties.

In order to find some definite indication of the production of chemiluminescent radiation by the tissues it was necessary to devise some method whereby (1) the tissues or their extracts could be oxidized very rapidly in order to increase the radiation emitted during this process; and (2) to increase the transparency of the tissues so that the radiation should not be absorbed by the opaque cell elements. This we believe we have achieved by the following method which is essentially a chemiluminescent analysis of tissue extracts or tissue suspensions.

RADIATION (CHEMILUMINESCENCE) DURING OXIDATION OF TISSUE EXTRACTS

It has been known that some materials of animal origin give visible light when their aqueous solutions are rapidly oxidized. Mallet¹⁵ found that when a solution of gelatin was oxidized with calcium hypochlorite it emitted a very faint light, visible in a photographic dark-room when viewed with eyes adapted to the dark.

We therefore adopted the following procedure: A suspension of minced tissue in dilute salt solution or a solution of tissue extract, was oxidized rapidly by the addition of a solution of calcium hypochlorite and the resultant radiation was identified by photographing the emitted light. The mincing of the tissues and the preparation of tissue extracts made it possible to obtain more transparency. The calcium hypochlorite furnishes nascent oxygen. The process leads to the destruction of the suspended tissue. Although a comparison with the oxidation and other chemical processes in the living tissues cannot be regarded as ideal, nevertheless a comparison between the visible and ultraviolet radiation resulting from the oxidation of various tissues and of tissues after the addition of various physiological agents is permissible.

The method itself may be briefly summarized as follows:

The tissues from freshly killed animals are minced finely and 2 grams of each tissue is weighed out and placed in a 250 cc. pyrex electrolyte beaker, tall form. Twenty cc. of a 0.9 per cent solution of sodium chloride is added. This makes a layer 1 cm. in thickness. The beaker is then closed with a rubber stopper to which is fastened a small vial containing 5 cc. of a 30 per cent solution of calcium hypochlorite. In a perfectly dark room the beaker is placed in a suitable holder so that its bottom is only 1 mm. from the photographic plate. The rubber stopper with the vial containing the oxidizing material is inverted over the beaker and the solutions are permitted to mix. The visible light produced can be observed and the radiation to which the photographic plate is sensitive leaves an impression upon the plate. It was possible to obtain 6 or 12 pictures on a single 5" by 7" panchromatic Eastman film. The development of each film and the measurement of the density (or blackness) of the photographic impressions with a photoelectric densitometer were carried out according to standard procedure. In the tables the density (D) is expressed as the logarithm of the ratio of the intensity of the light passed through the unexposed (I_b) film to the intensity of the light passed through the exposed part (I). ($D = \log I_b/I$.)

Preliminary tests showed that to secure sufficient blackening of the films the oxidation of the 10 per cent tissue suspensions in the above described manner had to be repeated at least 10 times, the beaker being each time superimposed on exactly the same portion of the photographic film. If, however, some fluorescent material was added to the solution (such as fluorescein, esculin, rhodamin, or quinine sulphate) the intensity of the light was increased to such an extent that a single exposure produced a sufficient impression. The optimum amount of tissue in the solution and the optimum amount of fluorescent material have been determined by experiment.

In our first experiments which were performed with the use of fluorescein the total radiation from the oxidized material was measured, no attempt being made to determine what portion, if any, was in the short wave portion of the visible spectrum and in the ultraviolet field.

COMPARISON OF THE INTENSITY OF RADIATION (BRIGHTNESS OF CHEMILUMINESCENCE) FROM VARIOUS TISSUES

Experiments made with the tissues of two healthy rabbits showed that the darkening produced on the photographic plate by the oxidation of various tissues could be arranged in the following order from darkest to lightest:—

Rabbit No. 1: Muscle, liver, stomach, kidney, brain, heart, lung, spleen.

Rabbit No. 2: Muscle, liver, stomach, kidney, heart, brain, lung, spleen.

Thus with one exception the sequence in both cases was the same. The measurements with the densitometer showed that the oxidation of the muscle produced about 20 times as much light as the oxidation of the spleen.

Since these results showed sufficient constancy, a series of experiments was done with other animals. The tissues were excised, dissected free, minced and used at once. In case of repeated experiments the tissues were kept in the icebox as it had been found that the intensity of the chemiluminescence was not greatly changed when the tissues were kept for a few days.

The limit of error for exposures on the same photographic plate was 3 per cent. The variation between two different plates was 6 per cent. The agreement between the same tissue of different normal animals was generally within 25 per cent. The order of magnitude and the sequence of chemiluminescence produced by the oxidation of the various organs was very consistent. (Fig. 108.) The results of the experiments with normal animals are given in Table XX.

A second group of animals was subjected to various surgical procedures under anesthesia to detect whether or not there was any relation between these procedures and the chemiluminescence produced by oxidation of the tissues. The results are given in Table XX and may be summarized as follows:

Effect of Surgical Shock. Two animals were subjected to surgical shock under ether anesthesia. In comparison with the chemiluminescence produced by the oxidation of the tissues of

normal animals the chemiluminescence produced by oxidation of the thyroid, liver, kidney and adrenals was decreased while that of the brain was increased.

Effect of Adrenalectomy. The most striking changes in the chemiluminescence produced by the oxidation of the various

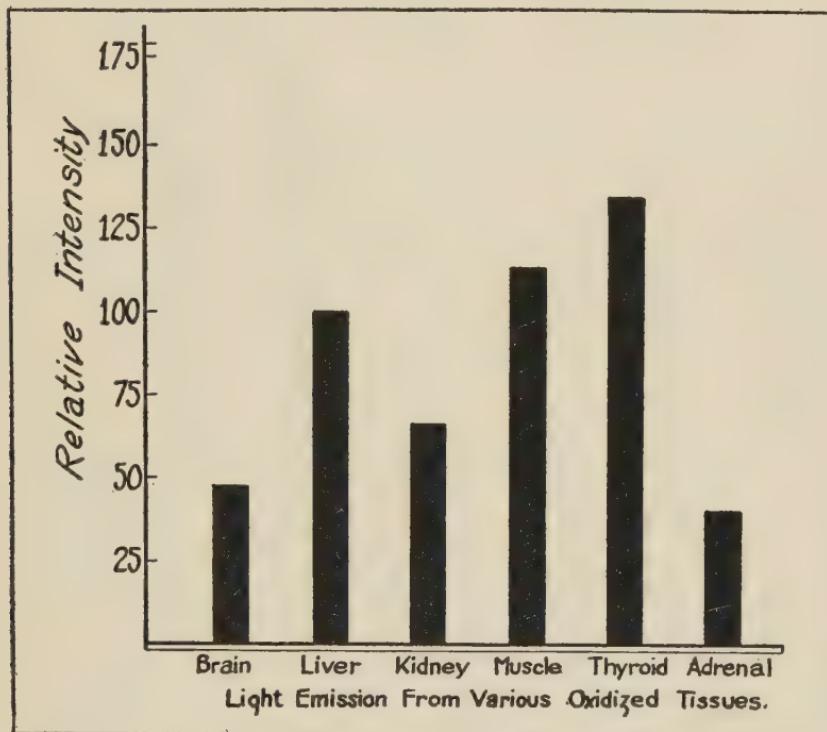


FIGURE 108. Relative intensities of the radiation (chemiluminescence) during the oxidation of various tissues with fluorescein as the fluorescent agent.

tissues were produced by adrenalectomy. Three animals were subjected to this operation. In two cases the animals died in from 24 to 36 hours after a bilateral adrenalectomy. In the third case a unilateral adrenalectomy was performed, followed a week later by the removal of the second adrenal. This operation resulted in the almost complete cessation of radiation, i. e., chemiluminescent light production, on the oxidation of the

liver, kidney, and heart, while but little change was observed in the chemiluminescence produced by the muscles and brain. (Fig. 109.) The changes in chemiluminescence from the liver, kidney and heart were far greater than those produced by surgical shock. It would appear, therefore, that the adrenals are responsible in part for the brightness of chemiluminescence

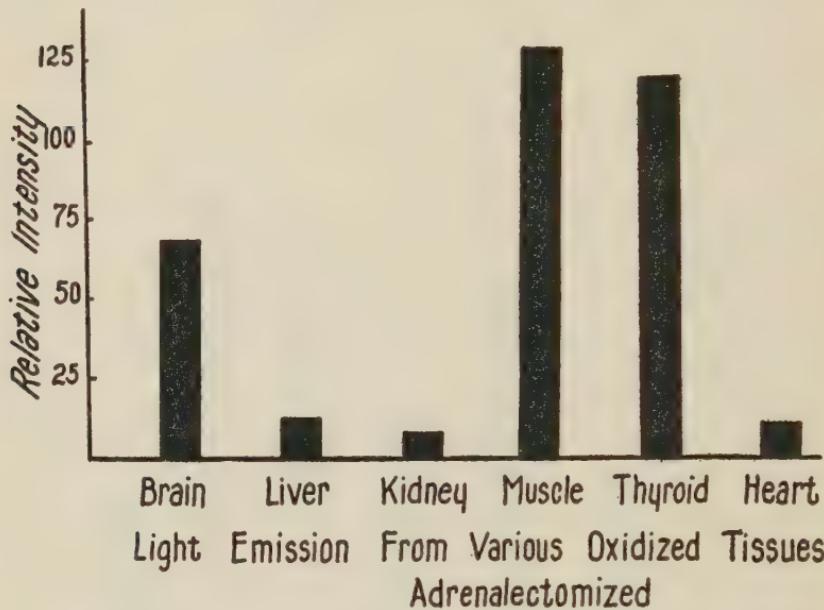


FIGURE 109. Relative intensities of the radiation (chemiluminescence) during the oxidation of various tissues from an adrenalectomized animal. (Compare with figure 108)

on oxidation of the kidney, heart and liver; but this matter requires further investigation. In addition to the above experiments single experiments were performed in which animals were subjected to hepatectomy, hemorrhage (exsanguination) and chloroform anesthesia. In each of these experiments the results were similar to those cited above for surgical shock.

EFFECT OF PHYSICAL SEPARATION OF CONSTITUENTS OF TISSUES

A method whereby to obtain some indication concerning the substance which is responsible for the emission of radiation on

the oxidation of tissues is the oxidation of the separate constituents of the tissues. The tissues were thus divided into an ether-soluble fraction which for convenience we designate the lipoid fraction and a fraction soluble in dilute salt solution which we call the protein fraction. On oxidation of these fractions the lipoid fraction showed no chemiluminescence at all, while the protein fraction showed as much chemiluminescence as the total tissue.

EFFECT OF VARIOUS AGENTS ON RADIATION (CHEMILUMINESCENCE) PRODUCED BY THE OXIDATION OF TISSUES

As previously stated, on the addition of fluorescent materials to the suspension to be oxidized the brightness of the resultant chemiluminescence is notably increased. In the following experiments in which we attempted to discover the effects of various physiological agents upon radiation chemiluminescence, fluorescein was used. The agents tested were the following: strychnine, caffeine, novocain, adrenalin, thyroxin, ethyl alcohol, ethyl ether, Lugol's solution. The amount of the agent to be employed was calculated on the basis of the minimum fatal dose of the agent when administered subcutaneously to rabbits. (Fig. 110.)

Stock solutions of the agents were prepared in such concentration that the addition of one cc. of the solution to the 20 cc. of the tissue extract employed in the experiment would be equivalent to the presence of the minimal fatal dose of the agent. Thyroxin was used in crystalline form, the maximum therapeutic dose being administered. Alcohol and ether were added directly to the solution. In some cases ten times the minimum fatal dose was employed for purposes of comparison, and in some cases the optimum therapeutic dose was also tested.

The results are given in Table XXI and may be briefly summarized as follows:

Adrenalin in a minimum fatal dose and in ten times the minimal fatal dose produces a slight increase in the brightness of the chemiluminescence.

Thyroxin similarly increases the chemiluminescence.

Novocain in a minimum fatal dose produces a definite decrease in the brightness of the chemiluminescence and a ten times stronger dose completely inhibits chemiluminescence. Doses of intermediate strength cause gradual diminution in the brightness of the chemiluminescence.

Caffeine causes a definite increase in the brightness of the chemiluminescence reaching a value as high as 150 per cent of

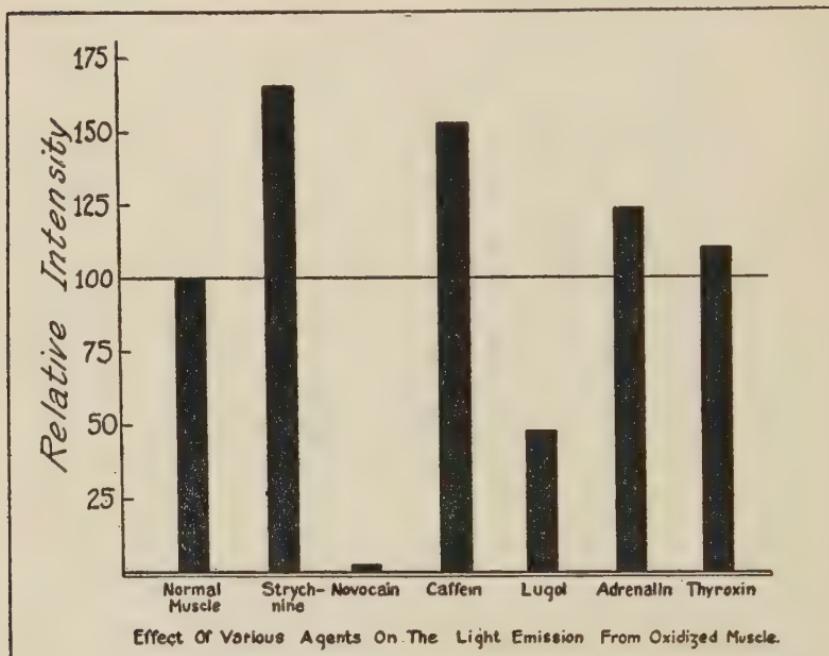


FIGURE 110. Effect of various agents on the radiation (chemiluminescence) during the oxidation of muscle.

the normal for ten times the minimum fatal dose.

Alcohol, even in small doses, decreases slightly the brightness of the chemiluminescence.

The greatest increase in chemiluminescence produced by any agent was produced by *strychnine*. When ten times the minimal fatal dose was administered the increase in chemiluminescence reached 180 per cent of the normal.

Lugol's solution caused a definite decrease in chemilumines-

cence even in concentrations used for therapeutic purposes, and ten times the minimum fatal dose almost abolished all chemiluminescence.

Experiments were also performed in which various salts in varying concentrations were used.

From these preliminary experiments the following conclusions may be drawn. The material of tissues which causes chemiluminescence when oxidized is not present in the ether soluble fraction. At least part of it is in the heat coagulable protein fraction, but this part is destroyed by heat. Chemiluminescence is completely inhibited by protein- (and protein-split-product-) precipitating agents, such as ammonium salts. Most of the chemiluminescent material can be separated by alcoholic precipitation of the extract.

Salts in large concentration and some physiological agents decrease and some increase the brightness of the chemiluminescence. One can conclude that chemiluminescence therefore is due to the protein- (and protein split-product-) fraction of the tissue extract although it does not follow that these experiments show which constituent of this fraction is responsible for the chemiluminescence.

These observations were further corroborated by various experiments in which fats, lipoids, starch, glucose, saccharose, glycogen and nucleic acid were oxidized. No chemiluminescence was observed in any case.

Similar experiments in which commercial gelatin and pep-
ton were used showed chemiluminescence, which was sometimes very bright.

A few available amino-acids were tested, but no chemiluminescence was manifested. It would appear, therefore, that the radiation- (chemiluminescence-) producing material is present in the protein or protein split-product fraction of the tissue extract. Whether the protein (and protein split-product-) fraction in itself or some part of it is responsible for the chemiluminescence has not yet been ascertained.

Physiological agents such as strychnine, thyroxin, adrenalin, Lugol's solution produce effects on the radiation- (chemiluminescence-) producing power of tissues comparable with their physiological effects.

ULTRAVIOLET AND VISIBLE RADIATION (CHEMILUMINESCENCE)
FROM TISSUE EXTRACTS

What is the spectrum of the chemiluminescent reaction which has been described above; how do fluorescent compounds increase the brightness of the chemiluminescence?

Fluorescent materials absorb ultraviolet or in some cases shorter visible light, this is the "exciting light"; they emit radiation generally in the visible part of the spectrum; this "fluorescence light" is characteristic for each substance and forms the "fluorescence band." The fluorescence band varies in wavelength only very slightly or not at all when the wavelength of the exciting radiation is changed. The intensity of the fluorescence light varies according to the concentration of the fluorescent substance present in the solution. The intensity of the exciting light in relation to the intensity of the fluorescence light gives the efficiency of fluorescence, which is generally very small; that is, only a small amount of visible light is emitted, a fraction of one per cent, as a response to the exciting light.

The fluorescence light can be demonstrated by illuminating the solutions with pure ultraviolet light, obtained through Wood's filters from a Mercury lamp. Under the influence of this "black light" the fluorescent solutions will exhibit various colors, corresponding to their fluorescence bands. Tissue extracts or tissues themselves show fluorescence; that is, if they are illuminated with pure ultraviolet light, they become visible in the dark.¹⁶ Tissues show this effect in varying degrees and some do not show it at all.

Mallet¹⁵ surmised that during the chemiluminescent oxidation of gelatine, ultraviolet light is emitted and that the addition of fluorescent materials would make this ultraviolet light visible just as the ultraviolet light of a Mercury lamp is changed into visible light by the fluorescent materials. Mallet, however, did not attempt to prove this.

The fact that ultraviolet light is emitted during a few chemiluminescent reactions was proved photographically by Bufford, Calvert and Nightingale.¹⁷ Grignard compounds dissolved in ether were oxidized and the resultant light was photographed through a series of filters. It was found that some of the com-

pounds emitted a considerable amount of ultraviolet radiation.

When the tissue suspensions or tissue extracts are oxidized with calcium hypochlorite, the reacting molecules are able to "excite" the molecules of the fluorescent materials present. The resultant light is emitted chiefly in the fluorescence band which is characteristic of the fluorescent material. The color of such a light can not be determined by looking at it, because faint light always presents the same color to the unaided eye (Purkinje phenomenon). However, when looking at the light with a small direct vision spectroscope it is possible to see that the light is emitted in a definite spectral band. An even better method for determination is by the use of color filters. A series of nine filters (Wratten filters no. 0, 2, 8, 12, 16, 21, 23, 24, 29) which cut off various parts of the spectrum were mounted to form sectors of a circle. The chemiluminescent light was then photographed through this color wheel and the density was measured to determine the brightness of the light, as transmitted by the various filters. In this way the spectral distribution of the light could be determined.

The following fluorescent substances were used: fluorescein, eosin, esculin, rhodamin and quinine sulphate.

As we were anxious particularly to determine the presence of ultraviolet radiations we shall describe only our findings in experiments in which quinine sulphate and fluorescein were used. Quinine sulphate has fluorescent bands in the violet and ultraviolet, according to L. J. Heidt and G. S. Forbes.¹⁸ The intensity of its fluorescence is much less than that of fluorescein. Fairly good photographic densities could be obtained by superimposing the oxidized tissue or tissue extract on the photographic plate for from 10 to 20 exposures. The optimum concentration of quinine sulphate was found to be 0.2 per cent, an amount which forms a saturated solution in water or in dilute salt solution.

The exciting spectrum and the fluorescent response of fluorescein and quinine sulphate show the following comparative characteristics. Fluorescein transforms ultraviolet and visible (violet, blue, green) into greenish-yellow visible light, the intensity of which is the greater the longer the wavelength of the exciting light. Quinine sulphate on the other hand responds

only to ultraviolet light, transforming it into ultraviolet and violet light and it responds equally to ultraviolet radiation of different wavelengths. When illumined with pure ultraviolet radiation from a Mercury lamp, fluorescein shows a much stronger fluorescence than does quinine sulphate.

In studying the ultraviolet chemiluminescence of tissue extracts the following considerations must be borne in mind: Tissue suspensions and extracts are opaque to radiation shorter than 3,100 Å. If any radiation shorter than 3,000 Å were produced during the chemiluminescent reaction its emission could not be verified because it is absorbed in the solution. Radiation longer than 3,100 Å could pass through the solutions and hence it should be possible to detect its emission by the photographic method.

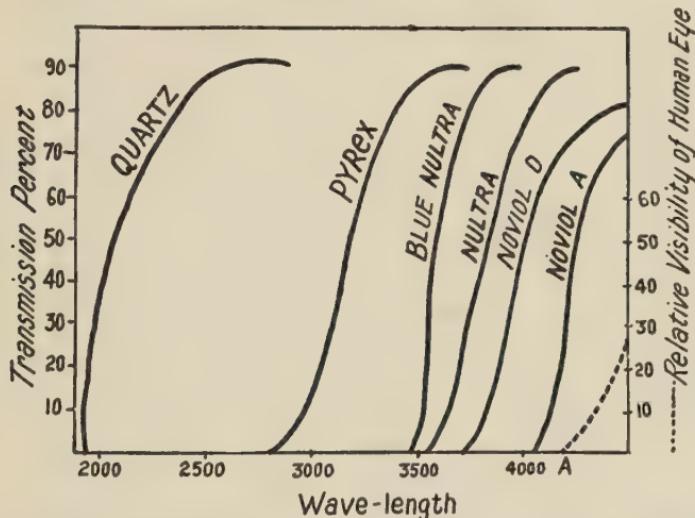
Tissues themselves have fluorescence, that is, some compounds present in tissues are able to transform part of the ultraviolet light into visible. Hence, if tissues emit ultraviolet radiation during the chemiluminescent oxidation, part of it is lost because the fluorescent materials normally present in tissues transform it into visible radiation. This phenomenon can not be prevented, unless the fluorescent materials could be removed from the tissues, before they are oxidized.

As we have stated, when quinine sulphate is added to the tissue extract and suspension it responds to short and long ultraviolet radiation alone and transforms it into partly visible and partly long ultraviolet radiation to which the tissue suspension is quite transparent. The fluorescent substance therefore "catches" the ultraviolet radiation produced during the chemiluminescent oxidation of tissues, fluorescein responding preponderantly to the longer ultraviolet and visible, quinine sulphate to the entire ultraviolet range.

Experimental method. The separation of the ultraviolet and visible part of the spectrum can be accomplished by means of filters. The following filters of the Corning Glass Works were used: Noviol A, Noviol O, Nultra and blue Nultra. The chemiluminescent reaction was induced in vessels of chemical pyrex. The characteristic transmission curves of the filters, pyrex and quartz are shown in figure 111.

The filter was made of quartz about 1.5 mm. thick and

Noviol 2.5 mm. thick. Quartz transmits all visible radiation and the ultraviolet radiation which may be emitted from the chemiluminescent reaction. There is no sharply defined demarcation line between the ultraviolet and visible part of the spectrum on account of the spectral sensitivity of the eye. Noviol, however, transmits only the visible radiation, absorbing the ultraviolet, the separation being complete within a few per cent. The filters



Transmission of Various Materials for Ultra-Violet

FIGURE 111. Transmission curves of various filters.

were mounted to form two halves of a circle in a holder made to fit over a photographic plate. The chemiluminescent reaction was induced in the pyrex beakers, which were placed directly over the filters. The tissue extracts were prepared as before, 10 per cent of the tissue being suspended in a 0.9 per cent NaCl solution.

Calibration of the filters. The quartz and Noviol filters did not transmit visible light equally, quartz being slightly more transparent than Noviol. It was necessary, therefore, to calibrate the filters. This was done with a lamp fed by a constant current, and covered with a ground glass plate and Noviol filter to remove the small amount of ultraviolet emitted by the lamp. The Noviol and quartz filters to be used in the experi-

ment were mounted in the cover of a photographic plate holder and exposures of various durations were made. In this way four sets of calibration curves were taken (H and D curves). The densities were measured and the per cent difference in visible light transmission for the quartz and Noviol filters was obtained. This difference amounted to about 4 per cent for greater and slightly more for smaller light intensities. This correction had to be applied as a correction to the densities secured when photographing the chemiluminescence which results from the oxidation of tissues.

The photographic impression obtained through the filters was measured with the densitometer. In Table XXII the density of the image through the quartz filter is indicated by D_q , that through the Noviol filter is D_n . The difference in densities through the quartz and Noviol filters ($D_q - D_n$) is expressed as per cent of the total emission, D_q . The radiation through the quartz filter represents the total radiation, to which the photographic plate is sensitive, that is, visible and ultraviolet. The image through the Noviol filter is caused by visible light alone. Therefore the difference $D_q - D_n$ indicates the ultraviolet radiation emitted during the chemiluminescent reaction. From this amount the small correction factor had to be subtracted.

Experiments using tissue extracts without any fluorescent substance. As has been mentioned before, tissue extracts give very faint visible light without any addition of fluorescent substances. Several experiments were made with blood serum, blood plasma, liver, brain, and thyroid. From the values obtained in these experiments, the following conclusions can be drawn: The order of brightness of the chemiluminescent reaction is different when no fluorescent substance is added as compared to the reaction with the presence of fluorescein. When no fluorescein is present only that part of the ultraviolet to which the solution is transparent is registered on the photographic plate, that is, wavelengths of 3,100 Å and longer. The order of brightness is as follows: Brain, blood serum, blood plasma, liver, thyroid. The chemiluminescence of the brain and blood serum is almost twice as bright as that of the rest of the tissues mentioned. The order of the tissues in relation to ultraviolet radiation is the blood serum, blood plasma, brain,

thyroid, liver, the last of which shows practically no ultraviolet radiation. (Fig. 112.)

Experiments with tissue suspensions and quinine sulphate as fluorescent material. As has been pointed out, quinine sulphate responds to ultraviolet of various wavelengths and emits ultraviolet radiation of long wavelengths and visible violet. When, therefore, quinine sulphate is added to the tissue suspension

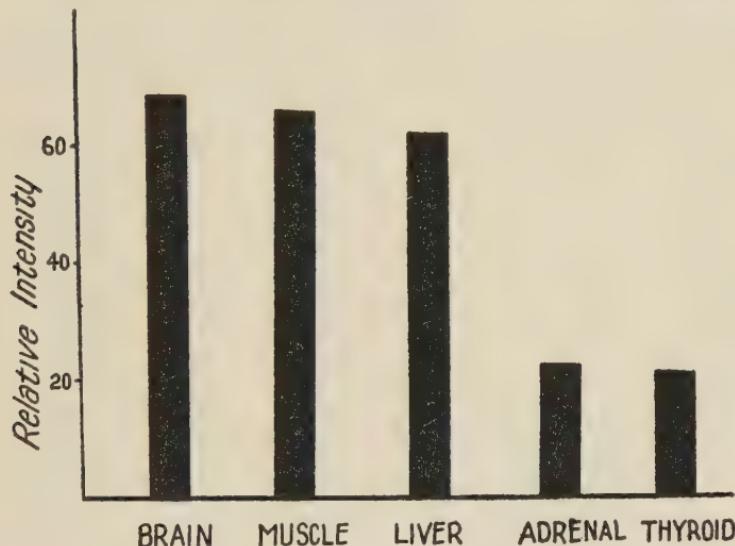


FIGURE 112. The transmission of radiation (chemiluminescence) during the oxidation of various tissues with quinine sulphate as the fluorescent agent (compare with Figure 108).

(forming a 0.2 per cent solution) the ultraviolet radiation produced during the chemiluminescent oxidation is changed into long ultraviolet and visible violet radiation. The efficiency of quinine sulphate to transform the ultraviolet is very low but the quinine sulphate is able to transform that part of the ultraviolet radiation which is absorbed by the tissue extract or which is shorter than 3,100 Å. This radiation is "caught" by the quinine sulphate and emitted in its characteristic fluorescent band. The average density caused by 17 to 19 exposures of suspensions of brain tissue with quinine sulphate is increased as compared with the density caused by like suspensions without any fluorescent material. The percentage of ultraviolet

radiation is about 18 as shown in Table XXII. During the chemiluminescent oxidation of liver and muscle suspensions the proportion of ultraviolet remains low, about 5 to 7 per cent. The order of brightness is: brain, liver, serum and plasma, thyroid, adrenal. (Fig. 113.)

SUMMARY

The temperature radiation of the human hand was measured and found to be the same as that of a perfect radiator ("black

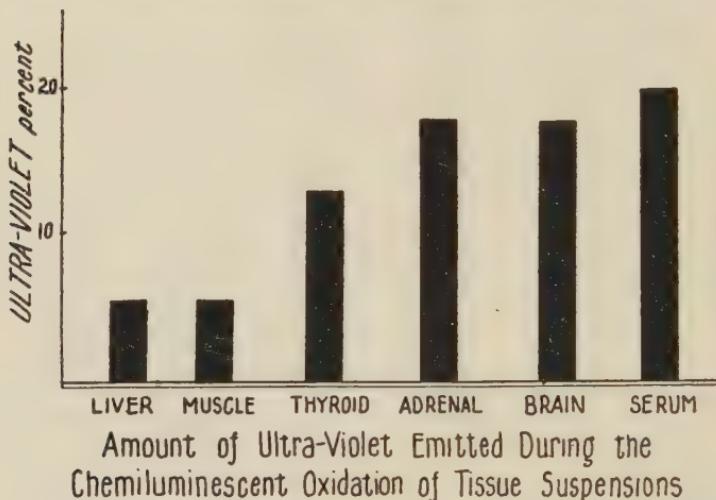


FIGURE 113. Relative amounts of ultraviolet radiation emitted during the oxidation of various tissues.

body") heated to human body temperature, the shortest wavelength emitted being 2.6μ in the infra-red.

From physical considerations of the transmission of tissues it is most probable that no radiation could emerge from a tissue of shorter than 3,000 and longer than 20,000 Ångström, as such radiation would be absorbed by the tissue itself. If any radiation is emitted outside these limits it must be of extremely small intensity.

In order to increase the rate of oxidation and also the transmission of tissues, extracts were prepared and oxidized *in vitro* with powerful oxidizing agents. From these results of experi-

ments it can be stated that tissue suspensions emit ultraviolet radiation and visible radiation during their chemiluminescent oxidation. Muscle, liver and kidney emit very little ultraviolet radiation while thyroid, adrenal and brain emit much more, in

TABLE XX

RELATIVE DEGREES OF RADIATION (CHEMILUMINESCENCE) FROM
OXIDIZED TISSUE SUSPENSIONS, AS DETERMINED FROM
MEASUREMENTS WITH THE DENSITOMETER

(The values given are photographic densities $\times 100$)

<i>Animal</i>	<i>Brain</i>	<i>Liver</i>	<i>Thyroid</i>	<i>Adrenal</i>	<i>Muscle</i>	<i>Kidney</i>	<i>Heart</i>
Normal	30	84	49	45	131	58	32
Normal	54	104	142	36	117	70	
Normal	16	95	114		92	55	19
Surgical Shock	49	41	90	3	95	16	16
Surgical Shock	51	61	81	4	106	34	29
Adrenalectomy	68	3	120		130	5	
Adrenalectomy	57	8			98	9	9
Adrenalectomy in two stages	33	17	45		131	36	25

TABLE XXI

RELATIVE AMOUNTS OF RADIATION (CHEMILUMINESCENCE) FROM
OXIDIZED MUSCLE SUSPENSIONS AS MODIFIED BY THE
ADDITION OF VARIOUS AGENTS

<i>Agent</i>	<i>Percentile Changes</i> (Normal considered as 100)			
	<i>Animal 1</i> MFD *	<i>10 X MFD *</i>	<i>Animal 2</i> MFD *	<i>10 X MFD *</i>
Adrenalin	102	126	108	92
Thyroxin			105	110
Lugol's solution	48	20	60	20
Novocain	85	3	78	3
Caffeine		136	117	120
Alcohol		97		87
Ether	109		105	89
Strychnine	154	171	136	149

(The values are percentages of the normal)

* MFD = Minimum fatal dose.

the oxidation of the brain and of the thyroid as much as 18 per cent of the total radiation being in the ultraviolet field. On account of the limitations of transmission in the tissue suspensions, this detectable ultraviolet emission must be longer than 3,100 Å.

The addition of fluorescent substances increases the emission

TABLE XXII

DENSITY OF PHOTOGRAPHIC PLATE EXPOSED TO THE CHEMILUMINESCENCE FROM OXIDIZED TISSUE SUSPENSIONS AND THE PERCENTAGE OF ULTRAVIOLET RADIATION

(D_Q , quartz filter, D_N , Noviol filter)

Oxidized tissue suspension	D_Q	D_N	$D_Q - D_N$ per cent	Ultra-violet per cent *	Number of experiments
Brain	0.459	0.358	22	17	1
Brain with 0.2 per cent quinine sulphate	0.740	0.561	24.2	18 ± 5	5
Liver	0.262	0.235	10	3 ± 1	2
Liver with 0.2 per cent quinine sulphate	0.626	0.546	13	6 ± 1	2
Muscle with 0.2 per cent quinine sulphate	0.659	0.589	11	6	1
Thyroid	0.251	0.189	25	18	1
Thyroid with 0.2 per cent quinine sulphate	0.221	0.176	20	13 ± 2	2
Adrenal with 0.2 per cent quinine sulphate	0.224	0.166	26	19 ± 3	3

* Corrected according to H and D curve (see text).

of radiation during the chemiluminescent oxidation of tissue suspensions. This increase varies according to the fluorescent efficiency of the fluorescent materials and also according to their excitation and fluorescence bands. As the increase in intensity is very considerable, with some fluorescent material one can conclude that considerable ultraviolet radiation of wave-

lengths shorter than 3,100 Å might be present, which ordinarily could not be emitted by the tissues, as they are opaque to it and would absorb it.

Various tissues emit different amounts of chemiluminescent radiation. The pathological condition of animals and the effect of various surgical procedures change the brightness of the chemiluminescence.

Various inorganic and organic materials affect the brightness of the chemiluminescence.

The question whether these *in vitro* experiments with oxidation of tissue suspensions or tissue extracts can be compared with the oxidation occurring in the living animal and whether any conclusions can be drawn as to the possibility of ultraviolet radiation of extremely small intensity, cannot be decided with certainty. Certainly, however, the analogy to oxidative processes in the living may be inferred.

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CHAPTER 29. *MITOGENETIC RADIATION*

Otto Glasser, Ph.D., and Margaret Schott, M.A.

THE discovery almost a century ago that all plants and animals are constructed of similar units, cells, led to a great deal of biological study which was focussed on the phenomena occurring within the cells. Painstaking observations through the microscope have revealed the succession of events taking place in the division of cells to form new individuals or to build tissues and organs. Such cytological studies have left unanswered the inevitable question as to what factor causes the cell to divide. A means of discovering this causative factor was suggested to the Russian cytologist, A. Gurwitsch,¹ in 1923 by the rapid cell proliferation which occurs in the repair of damaged tissue. When circular wounds were inflicted on the cornea of the frog's eye, which was later removed and stained, the area surrounding the wound was seen to contain many more mitotic figures than the unaffected regions. This increase in the rate of cell division was explained by Haberlandt² as being due to the diffusion from the site of the wound of a substance, or hormone, which stimulates cell mitosis in contiguous cells. However, this hypothesis did not explain to the satisfaction of Gurwitsch a further phenomenon observed by him. If he made a second linear wound in the neighborhood of the first deep wound he found that the area of increased mitosis spreading from the deep wound did not extend beyond the linear wound. The second wound acted as a barrier to the stimulus to cell division originating in the first wound and cast a distinct "shadow." This shadow effect suggested to Gurwitsch that the

stimulus must be oscillatory in character, rather than a chemical diffusion, since it appeared to travel in straight lines.

Further experiments were conducted with the root of *Allium cepa* which because it is remarkably straight would presumably give definite direction to the passage of the stimulus. The actively growing end-portion of the root was selected as the most suitable place for determining the effect of a stimulus to division.

The experiment which became the foundation of all later work on this problem was performed with two onion roots, one as sender, the other as detector of the stimulus. The tip of the sender root was directed at a right angle toward but not touching the meristematic lower portion of the other. When the induced region of the detector root was later fixed, sectioned, and stained, it was found that there was an increase in the number of mitotic figures on the side exposed to the sender root. It was evident that the stimulative effect had been exerted without direct contact. In order to exclude the possibility of the diffusion of volatile substances, glass and quartz plates were interposed between the sender and detector roots.

The results of these experiments not only confirmed the hypothesis that the stimulus was oscillatory in character but gave evidence regarding its wavelength. Since the radiation was found to pass easily through quartz and to be absorbed by glass and by thin layers of gelatine, Gurwitsch³ concluded that it lay in the ultraviolet region of the spectrum, around 2,000 Å.

Following Gurwitsch's original publication numerous investigations have been conducted to study the various aspects of the phenomenon, biological, chemical and physical. These experiments have their foundation in the hypothesis proposed by Gurwitsch, which may be stated briefly as follows: The stimulus which acts on cells specifically to induce mitotic division is a radiation which has its source in the cells and tissues of the organism. Gurwitsch named this stimulus "mitogenetic radiation."

BIOLOGICAL INVESTIGATIONS

Extensive studies have been made on biological materials to determine their response to mitogenetic radiation and to find

the origin of the radiation. The first materials used to detect the radiation were the onion root tip and the corneal epithelium of the frog's eye. In both tissues the effect was observed by counting the mitotic figures in stained preparations, an increase in mitosis in the exposed portions indicating that stimulation had occurred.

In 1926 Baron⁴ demonstrated that a mitotically reproducing organisms, beer yeasts, were sensitive to mitogenetic radiation. In these organisms an increased rate of budding, with a consequent increase in the total number of individuals, was observed after exposure to onion root or pulp. The yeast also served as a source of radiation for the growth stimulation of onion roots, or of a second yeast culture. Baron concluded that the mitogenetic phenomenon is not restricted to mitotic division but that it is universally applicable to all types of cell cleavage. Since this discovery indicated that yeast cultures were suitable detectors of the radiation, the yeast method has almost entirely replaced the more laborious method of preparing sections and counting mitoses.

The modifications of Baron's original method used by investigators to detect mitogenetic radiation may be illustrated by a description of those which have been employed in the Biophysical Laboratory of the Cleveland Clinic Foundation. Pure cultures of *Saccharomyces cerevisiae* and *ellipsoideus* in liquid beer-wort and a peptone-glucose medium are used. Equal quantities, 0.5 to 2.5 cc., of the yeast suspensions are measured accurately into quartz and glass test tubes. The lower ends of the test tubes are then placed in direct contact with the various radiators and rotated continuously during the irradiation in order to prevent settling of the yeast. After the irradiation, the tubes are placed in an incubator and kept at 26° C. for periods up to 24 hours. Then sulphuric acid is added to kill the yeast cells and after the tubes are thoroughly shaken, the amount of yeast present is determined in the following way: The suspensions are introduced into small haemotocrit tubes which are rotated rapidly in the centrifuge for five minutes. The height of the packed yeast cell columns in the haemotocrit tubes, which had previously been calibrated carefully, is then determined, and the percentile differences between the columns of

cells irradiated in the quartz tube and in the glass tube are calculated.

Numerous control experiments indicated that the accuracy obtainable with this method is satisfactory.

Experiments in which the yeast suspensions were counted with the haemocytometer showed greater errors than the centrifugation method. The counting method is useful nevertheless in determining the cell concentration of the suspensions and in estimating the percentage of budding individuals in the culture.

Numerous determinations were made with both methods on control sets of yeast suspensions and showed that there is considerable normal variation in growth rate and in the percentage of buds. These fluctuations, which have been observed by other investigators (Richards and Taylor⁵), can not be entirely eliminated in experiments with biological material nor should they be disregarded. Nevertheless, a consistent difference between exposed and control cultures, which is unmistakably outside the limits of normal variation, may be considered sufficient evidence for a stimulation effect.

With yeast methods similar to those described, the emission of radiation from various biological tissues and organisms has been studied by numerous investigators. The results compiled by Gurwitsch⁶ may be summarized briefly. Mitogenetic radiation has been found to be given off by simple organisms, bacteria and yeasts; by plant tissues; by embryonal animal tissues; by skeletal and cardiac muscle in contraction; by nerve fibers, spleen, corneal, ciliated and gut epithelia; by blood and urine; by tumors. The study of tumor tissue is of especial interest, since the radiation from malignant tumors is said to be stronger than that from benign tumors. Moreover, in a cancerous condition the normally-appearing blood radiation is absent. These properties peculiar to tumors suggested the possibility of utilizing the methods of mitogenetic study for the early diagnosis of cancer.

Although the majority of experiments have confirmed the observations reported by Gurwitsch, a number of investigators have failed to reproduce them. For example, no evidence of increase in yeast growth was obtained after exposure to bacteria, onion roots (Richards and Taylor⁵) or to yeast (Kreuchen

and Bateman,⁷ Nakaidzumi and Schreiber⁸). Negative results have been obtained also in experiments in which bacteria (Sulmann⁹) and onion roots were used as detectors.^{10, 11}

Attempts to demonstrate the mitogenetic radiation from some of the materials enumerated by Gurwitsch have been made in this laboratory using the detector method described above. Yeast, cultures of *Azotobacter vinelandi* and *chroococcus*, growing rat tumors, and human tumors obtained by operation were used as senders. The results with yeast and bacteria were inconclusive. The experiments with tumors showed tendencies to stimulation with short exposures, and inhibition of growth when the exposure time exceeded three minutes. These observations appear to be in agreement with some of those reported by Russian workers. The experiments are being continued in order to obtain more definite data.

CHEMICAL FACTORS IN MITOGENETIC RADIATION

The mitogenetic radiation, as we have seen, is said to be emitted by many tissues differing widely in form and function. The underlying cause of the radiation must be some substance or activity which these tissues possess in common. Harvey's discovery that visible luminescence of organisms was produced by the reactions between luciferin and luciferase led Gurwitsch to assume that a similar reaction might account for the emission of mitogenetic rays.⁶

Which of the many complex processes occurring in the cells are associated with the radiation? Since highly-specialized, non-dividing tissues like muscle and nerve had been found to give off radiation, Gurwitsch concluded that the radiation was not peculiar to cleavage processes, but characteristic of functional metabolism.¹² Moreover, in the onion it had been shown that the rays have their origin in the sole, even though the site of their action is in the root tip. Although the emission of radiation from contracting muscle and stimulated nerve may be explained as a by-product of energy release, the significance of radiation from blood and urine, with relatively low metabolism, is not clear.

There are three classes of tissue which apparently give off

rays in process of division, bacterial and yeast cultures, embryonal tissues, and neoplasms. It is claimed, however, that the emission of radiation from unicellular and embryonic forms alternates with periods of cell cleavage. If this be true only the tumors are distinguished by a mitogenetic radiation originating in rapidly proliferating tissues.

Gurwitsch concluded¹² that with the exception of tumors, mitogenetic radiation is produced in actively metabolizing rather than in meristematic tissues. It was hoped that the reactions involved would be revealed by a study of the commonly occurring metabolic processes. In experiments with blood it was found that the emanation tended to disappear after fasting or bodily exertion and could be restored by the addition of glucose. It appeared, therefore, that glycolytic processes were necessary to the radiation from blood.⁶

The problem of discovering the nature of the reactions was then approached indirectly by Kannegiesser, Siebert, F. and M. Magrou, Braunstein and Potozky, and others, by studying simple chemical models.^{6, 13} Since they found that the yeast detectors responded readily to these test tube reactions, they conclude that the production of mitogenetic radiation is not confined to living protoplasm or even to protoplasmic constituents.

The many reactions which were found to effect the induction of yeast cultures belong to two general types: organic enzymatic reactions, and inorganic oxidation-reduction reactions. The digestion *in vitro* of proteins and of carbohydrates and the action of urease, phosphatase, and creatinine-phosphatase are examples of the first group. A number of simple inorganic reactions, the oxidation of cuprous, mercurous, ferrous, and other metallic ions, acid-alkali neutralization, the action of acids on metals, have likewise been found to stimulate yeast.¹³ It may be concluded briefly that the property of emitting mitogenetic radiation is characteristic of molecule-splitting and of oxidative reactions. The radiation from animal tissues may be ascribed, by analogy, to similar reactions in the organism.

Two reactions representative of these two classes have been studied in this laboratory, the digestion of fibrin with pepsin

at 37° C. and oxidation of tissue extracts or yeast with calcium hypochlorite. The results did not show any stimulative effect on the growth of the yeast.

A few investigators have made attempts to show that certain chemical systems are sensitive to mitogenetic radiation from external sources. It has been claimed that colloidal systems, i. e., Liesegang rings¹⁴ and sol suspensions,¹⁵ respond to radiations with visible changes in structure. Since these results have not been substantiated by the observations of other investigators, the usefulness of these chemical detectors is questionable.

PHYSICAL INVESTIGATIONS

The early experiments already cited in which glass, quartz, and gelatine plates were interposed between the sender and detector onion roots indicated that the mitogenetic radiation lay in the ultraviolet region of the spectrum. Numerous experiments have been carried out to investigate further the physical properties of the mitogenetic radiation. Determinations of the wavelengths have been made with the quartz spectrograph, employing as detectors in place of a photographic plate onion roots or yeast agar blocks, subdivided into units corresponding to several Ångström. Most of the experiments with the spectrograph have been performed using as sources of radiation the biological material or chemical reactions already enumerated.

The investigators reported that the mitogenetic effects were obtainable only in sharply delimited regions of the ultraviolet spectrum. In some experiments it was claimed that a division of the spectrum into units as small as 3 Å had been attained.¹³

With such an arrangement a series of spectra with wavelengths lying between 1,900 and 2,500 Å have been obtained for the materials studied. The spectra collected by A. and L. Gurwitsch¹³ show characteristic bands or groups of bands for various sources of the radiation. The individual spectra present certain similarities and dissimilarities between the members of a group, such as the oxidation-reduction systems. The authors suggest that the delicacy of the biological detectors makes it possible to apply this method to the analysis of spectra difficult

to study by other means, or even to the discovery of the more obscure reactions occurring *in vivo*. There is, however, no evidence from other sources to substantiate these results.

The desirability of supplementing the biological evidence for the existence of the mitogenetic radiation with evidence obtained by physical means for detecting ultraviolet light is obvious. Two methods have been employed, photography and the photo-electric cell.

The photographic method has two outstanding advantages, sensitivity to low intensities of light and the ability to summate stimuli over a period of time. Accordingly, in the attempts to photograph this radiation, continuous or repeated exposures were made, on plates sensitized to ultraviolet light. Although some positive results were obtained, as many negative experiments were reported by other workers.¹⁰ It has been pointed out that in prolonged exposures to chemical substances a darkening of the plate may be produced by vapors. In explanation of the negative results, Gurwitsch has emphasized the low intensity of the mitogenetic radiation. In the early experiments of Frank and Gurwitsch³ they estimated that the radiation sufficient to produce an effect on onion roots was one two-hundredth of that necessary to blacken a plate. Inasmuch as a quantity of light of 2×10^8 quanta per cm.² will produce a just perceptible darkening, the longest exposures made, 89 days, must have yielded less than that necessary to affect the plate.¹⁰ Counting the reduced grains of silver in the exposed plate has also been attempted, but with negative results. Since several hundred quanta are required to reduce a single grain,¹⁶ it is again possible to claim that the ultraviolet ray production was not sufficient. At any rate it is evident that the photographic method has not proved successful in the detection of mitogenetic radiation.

Several types of photo-electric cells known to respond to ultraviolet light have been employed as detectors. An improved method of detection is a combination of the photo-electric cell with the principle of the Geiger-Müller counter. Rajewsky, Frank and Rodionow, Audubert, and Barth, who used this type of detector for mitogenetic radiation, claimed that various materials, including onion bulb, cancer tissue, frog sartorius mus-

cle in contraction, the peptic digestion of fibrin, and the oxidation of FeSO_4 , gave an increase in the counts, indicating the emission of rays. Siebert and Seffert also reported positive results based on the simultaneous use of two counters with alleged equal dark counts.¹³ Other investigators, Lorenz,¹⁷ Gray and Ouellet, Kreuchen and Bateman, Schreiber and Friedrich,¹⁰ have obtained negative results with the photo-electric Geiger counter. In this laboratory extensive studies have been made to detect radiation from onion root and pulp, bacteria, cancerous tissue, from oxidations of organic material, from the peptic digestion of protein, but as yet no satisfactory or reproducible positive results have been obtained. Experience with these highly sensitive devices has shown that extreme caution must be exercised in order to obtain indisputable results.

These failures to obtain physical evidence for the existence of mitogenetic radiation may be interpreted as significant evidence, not that the rays do not exist, but that their intensity is below the sensitivity of the most delicate instruments employed. To what light intensity will the Geiger counter respond? As an example we refer to the recent experiments of Lorenz.¹⁷ This author estimated that the counter used by him could detect 10 to 15 quanta per cm^2 per second, using the wavelength 2,536 Å. Other authors estimated the sensitivity of their instruments to lie between 10^4 and 10^2 quanta per photo-electron for the wavelength 2,540 Å.⁷ If, then, the intensity of the mitogenetic radiation is less than these figures, it can not be more than 300 quanta per cm^2 per second, according to Kreuchen and Bateman,⁷ or 10–15 quanta per cm^2 per second according to Lorenz.¹⁷ It is evident that the results with the photo-electric Geiger counters are contradictory.

From the results with physical detectors it must be concluded that the mitogenetic radiation is of an extremely low intensity. Yet, according to Gurwitsch,¹⁸ this weak radiation can be further diminished in intensity by passage through the optical system of a spectrograph without an appreciable reduction in its effect on biological detectors. The question naturally arises how these light stimuli, so weak they can not be detected by the most delicate instruments, can nevertheless influence biological systems. The only explanation is that the biological

detectors must be incomparably sensitive to these radiations.

Furthermore, Gurwitsch suggested that the quantity of radiation falling on the detector may be decreased by a device providing for intermittent irradiation without diminishing the stimulative effect. The experiments showed that the relative effectiveness of interrupted stimulation is apparently greater than that of continuous irradiation. According to Gurwitsch, this result was to be expected as a corollary to the natural rhythmicity of vital processes. Presumably only those stimuli which strike a cell at a certain time would produce an effect, while all those impinging during the refractory periods would be wasted.⁶

In order to confirm the hypothesis that the mitogenetic stimulus is ultraviolet light, several attempts have been made to reproduce the mitogenetic effect with ultraviolet light from artificial sources, the light being separated into its component bands with a monochromator. Frank and Gurwitsch reported that they were able to obtain a response in onion roots with radiations of wavelengths between 1,930 and 2,370 Å.³ Reiter and Gabor found positive results in the region 3,340 to 3,400 Å but none below 2,800 Å. Chariton, Frank and Kannegger were able to demonstrate an inductive effect with light of wavelengths 2,060 to 2,650 Å, but none around 3,400 Å.⁶

On the other hand, similar experiments by other investigators have failed to confirm these positive results. Schreiber, employing the three wavelengths 2,290, 2,540 and 3,340 Å of a low intensity, which was, however, not measured, was unable to find any evidence of cell stimulation in yeast cultures.¹⁸ Kreuchen and Bateman⁷ using both mercury ultraviolet and monochromatic light of wavelengths 2,140 to 2,540 Å found no evidence of stimulation or depression. Their lowest intensity was estimated to be about 10^{-10} quanta per cm.² per second.

In order to obtain a radiation of an extremely low intensity, experiments were conducted in this laboratory with a known source of weak ultraviolet light. Sodium chloride crystals previously irradiated with roentgen rays have been found to release stored energy in the form of ultraviolet light in the presence of visible light. Although this radiation with an emission maximum at 2,450 Å is extremely weak, it can be detected easily

with the photo-electric Geiger counter. Yeast cultures exposed to crystals of irradiated sodium chloride with the method described previously, did not show increased growth. The failure to obtain stimulation with ultraviolet light may indicate that the biological detectors, because of their unique sensibility, may be refractory to doses of radiation in excess of the optimum for cell division.

The investigator is driven to the necessity of assuming that only extremely low light intensities have the property of inducing mitosis or budding. It is conceivable that the efficiency of the biologic effect is very high in contrast to physical, i. e., photo-electric effects. It is more difficult, however, to imagine a mechanism which enables such weak radiations to penetrate biological material. Fluids, serum and nutrient media absorb radiation of these wavelengths rapidly, and cell membranes and protoplasmic constituents undoubtedly present further barriers to the passage of ultraviolet light. The problem of explaining how the few quanta surviving the process of absorption are able to produce widespread effects is not altogether simple.

This apparently insurmountable difficulty has been overcome, on paper at least, by Gurwitsch's theory of "secondary radiation."⁶ This hypothetical radiation may be described as being comparable to a chain reaction, in which the products of the first reaction initiate a second, this in turn a third, and so on, with this difference, that all the reactions and their products are the same. An adequate unit of radiation striking a cell may either cause that cell to divide, or enable the cell to release a radiation or both. The lipoid membranes which may prevent penetration of the cell by ultraviolet light, may nevertheless by resonance emit a "secondary radiation."¹⁹ This radiation falling on a neighboring cell produces a similar effect, cell division or re-radiation. In other words, the properties of the "secondary radiation" are essentially those of the primary radiation. In this way the original stimulus from an external source can be propagated through the interior of the culture or tissue.

To what extent does this relaying of the mitogenetic impulse proceed with decrement? The answer given by experiment is not clear. It will be recalled that in the early experiments a difference in the mitotic index on the exposed as compared

with the control side of the root was interpreted as evidence of induction. Evidently the root in cross section was only slightly transparent to the radiation. On the other hand, it was found that the radiation emanating from the root tip originated in the onion sole. The transmission of these rays lengthwise through the root apparently did not impair their power to stimulate cell division, even beyond the tip of the root.¹⁶ Even if this effect is due to secondary radiation, we can only conclude that the onion root is penetrable in one direction and opaque in another to the same radiation.

The relation of the wavelengths of the secondary to those of the primary radiation is of interest. With the spectrograph the radiations emitted by nerve, or by chemical solutions subjected to mitogenetic rays from an external source, have been studied. The results may be summarized in the following quotation from A. and L. Gurwitsch:¹³

“Les corps qui, en subissant une décomposition par voie fermentative ou hydrolytique, émettent à ce moment un rayonnement, d'un spectre défini, sont sensibles à l'irradiation d'un spectre *identique*, en émettant en guise de rayonnement secondaire, le même spectre.

“En cas d'irradiation d'un spectre différent, le rayonnement secondaire est nul ou du moins très faible.

“Ce fait, assez inattendu par lui-même, devient encore plus difficile à interpréter, si on envisage les suites d'une irradiation monochromatique. Ce n'est pas seulement le raie en question qui réapparaît dans le spectre secondaire, mais ce dernier en sa totalité, en faisant infraction au principe de Stokes. Si nous prenons, par exemple, la raie 2170–2180 Å du spectre glycolytique en qualité d'irradiateur d'une solution de la glucose, le spectre secondaire, émis par cette dernière, contient aussi la raie la plus courte (1900–1920), appartenant au spectre glycolytique.” *

* “The substances which, in undergoing decomposition by fermentation or hydrolysis, emit at that moment a radiation of a definite spectrum, respond to irradiation by an identical spectrum, by emitting the same spectrum, as a secondary radiation.

“In case of irradiation with a different spectrum the secondary radiation is absent or at any rate very weak.

“This fact, unexpected enough in itself, becomes more difficult to interpret if one considers the results of monochromatic irradiation. It is not merely the band in question which reappears in the secondary spectrum, but the latter in its entirety, in infraction of Stokes' law. If we take, for example, the band 2170–2180 Å of the glycolytic spectrum as irradiator for a solution of glucose, the

This paradoxical behavior of mitogenetic radiation and its "secondary radiation" does not agree with some of the known laws governing light. These contradictions make it difficult to accept these theories of mitogenetic radiation at the present.

Moreover, from a survey of the representative experiments reported from 1923 up to the present time, it is clear that the evidence for such behavior is inconclusive. The discrepancies in results obtained by different investigators cannot be ignored. Gurwitsch's original experiment with the onion root has been repeated many times. Some investigators failed to find any evidence of an induction effect. The positive results obtained show a wide divergence in the actual distribution of the observed increase in mitoses.¹⁰ As a consequence, the validity of conclusions based on the early onion-root experiments has been questioned. Many investigators have emphasized the importance of determining the reliability of the detectors used in induction experiments.

In spite of the unfavorable criticism directed against the use of biological detectors, Gurwitsch and his collaborators have not considered it necessary to repeat their basic experiments. While some investigators question the firmness of the foundation, others continue to erect an elaborate structure of experiment and theory. Numerous investigations are carried out which concern themselves chiefly with the discovery of new phenomena. The mitogenetic studies are being extended into related fields, spectral analysis of chemical reactions, the diagnosis of cancer.

The important task of the immediate future does not lie in any one of these fields. It is necessary first to establish beyond reasonable doubt that the mitogenetic radiation exists. The skeptical attitude which has been expressed by not a few investigators does not necessarily indicate that the existence of these rays is considered improbable. There is little doubt that much of the evidence points to the operation of a division-stimulating factor and its transmission from one cell to another. With careful attention to experimental procedures it should be possible to demonstrate this phenomenon convincingly. It is to be hoped

secondary spectrum emitted by the latter contains also the shortest band (1900-1920) belonging to the glycolytic spectrum."

that future work will reveal the nature and properties of the mitogenetic factor, to the satisfaction of the critics as well as of the proponents of the hypothesis. With a clear conception of the mitogenetic rays as a foundation, the further investigation and the application of this phenomenon in branches of chemistry and medicine may progress unhampered.

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GENERAL SUMMARY

CHAPTER 30. *THE RADIO-ELECTRIC THEORY OF LIVING PROCESSES*

IN my quest to find what William Lyndman was and what caused William Lyndman's death, I found that the slow fading away of every organ to death from shock was not due to failure of the heart, nor to failure of the arteries or of the capillaries, nor to the pooling of the blood in the large veins, nor to the loss of any elements in the blood stream. It was not due to accumulation of poison in the blood. It was not due to changes in the respiration nor to changes in the capillaries of the lungs. It was not due to fat emboli in the lungs. It was not due to changes in the hydrogen-ion concentration of the blood. We demonstrated that the cause of William Lyndman's death was an excessive physical stimulation of the sensory nerves.

No amount of trauma, no amount of physical injury in an area where the sensory nerves are blocked by local, regional or spinal anesthesia can cause excitation, depression or death. That is to say, the impulses that finally killed William Lyndman passed over the nerve pathways to the brain and thence were broadcast throughout the body, activating the identical mechanism used in struggle or in the emotions so excessively that complete exhaustion resulted. We found that injury of the different regions of the body produced excitation, depression and death according to the extent of the injury, according to the exposure of the part, throughout man's long phylogeny, to the

injuries of physical environment and of combat with fellow man and animals.

Thus the abdomen and chest when traumatized stand first in their facility for causing the discharge of nervous energy; that is, injury of these parts most readily produced shock showing that primitive man faced his enemies and fought his battles.

We also found that the response to trauma itself had a relationship to the type of injuries received in our long phylogeny; that is, one type of contact would cause pain, another, a tickling sensation, and either of these would tend to cause exhaustion. The ticklish points of the soles of the feet suggest the stony trail which barefoot man trod in the millenniums of time in his evolution.

In other words, we found that excessive stimulation of the receptors of the special senses and common sensation, singly or in any combination, causes excitation, depression and death. It is as if phylogeny implanted within man innumerable receptors, upon which the hostile environment plays a symphony of life as the musician plays upon the keyboard of the organ. But even these findings gave us no understanding as to the source and nature of the energy which was present in life and was lost in death.

We then tested the variations in the vitality of organs by excluding from them the circulation of the blood. We already knew with what rapidity death could occur as the result of physical injury. Therefore the fact that some organs could endure complete loss of blood for a longer time than the animal under anesthesia could survive shock-producing trauma proved that there was no mechanism in these organs, the failure of which would be the sole cause of death by traumatic shock.

We then removed the various organs of the body to ascertain how long an animal could survive without them. By these two methods we could exclude those organs the failure of which could not of itself cause death within the time in which fatal shock could develop.

The primary cause of death from shock was not to be found in the circulation, in the respiration, or in the blood. Our experiments in which the blood supply of organs and tissues was excluded proved that the excitation, depression and death due

to physical injury, emotional excitation, toxins, etc., was not due to failure of the kidneys, the stomach and intestines, the pancreas, the spleen, the thyroid gland, the muscles, the tendons, the connective tissue, the bones or the joints.

We then embarked upon a long series of researches that lasted for ten years and involved over 2,500 animals. In these researches animals were subjected to physical injury under anesthesia, emotion, exertion, infection, inhalation anesthesia alone, stimulation, narcotics, excision of organs, prolonged loss of sleep, hemorrhage, asphyxia, in order to determine the effects of these agents on the structure of the cells of the various tissues and organs of the body. In this long quest we found a clue to the fundamental nature of living processes.

Though the cells of all the tissues and organs of the body were examined microscopically, changes were found only in the cells of the brain, the liver and the adrenal glands in the last of which the most marked changes appeared in the cortex. The stage of excitation produced increased differential stainability, the cells exhibiting a deeper stain than normal, the cell itself appearing to be shrunken.

The stage of exhaustion was characterized by an increase in the size of the cell, and by the diminution or disappearance of the differential stainability. These three organs provided the Rosetta stone. They seemed to provide the clue to the control of the energy that most immediately governs life, the failure of which causes death.

Considering that all life exists in the form of cells with a comparatively acid or positive nucleus, and a comparatively alkaline or negative cytoplasm, we postulated that living cells were electric cells and this consideration led to the formation of the electrical or Bipolar Theory of living processes. At this point we abandoned physiology, biochemistry and morphology, and established a laboratory of biophysics, in which we ran the entire gamut of all the previous experiments that caused changes in the cells of these master organs. We made measurements of the changes in temperature, in electric conductivity, electric capacity, and electric potential under the same conditions as before; that is, the animals were subjected to injury, emotion, hemorrhage, asphyxia, infection, anesthesia, stimulants, narcotics, in-

somnia, thyroxin, adrenalin, etc., and the thyroid, the adrenal glands and the liver were excised. We carried these researches into a study of fruits and vegetables, which were subjected to loss of oxygen—asphyxia—and to the action of anesthetics and stimulants, and we found that the changes in temperature, electric conductivity, electric capacity and electric potential roughly paralleled the changes in the structure of the cells of the master organs of animals.

Since all matter is electrical in nature and since in the final analysis all energy is radiant and electric energy, we conceived that protoplasm must be generated and operated by radiant and electric energy.

In accordance with this conception, protoplasm would be a system of generators, conductance lines, insulators and infinite numbers of infinitely thin films for holding electric charges.

Lightning and terrestrial electricity which fix nitrogen, form the nitrates. The nitrates in the soil represent a pre-plant phase of living things. Solar radiance added to the nitrates generates plants. Plants generate animals. Thus solar radiation generates man.

The generation of radiant and electric energy in animals is made through oxidation of the organic compounds of the plant; that is, solar radiance is released in the animal by oxidation.

Animals are adapted to oxidation, just as a combustion engine is adapted to oxidation. Much of the body of animals, the lungs and the circulatory system, is related to the fact that it is through oxidation in animals that the sun's radiance is re-radiated in protoplasm; that is, oxidation causes the sun to "shine" again in protoplasm. Animals, like plants, grow by virtue of solar radiation and re-radiate solar radiation.

The intensity of the re-radiation of solar energy in animals is increased by thyroxin, by adrenalin, by nerve impulses. The sun's radiance is dimmed at night and in the winter but the identical solar radiation in animals shines as brightly at night as in the day; as brightly in the winter as in the summer. The intensity of the solar radiance of protoplasm is governed adaptively, and is altered, increased or diminished swiftly, as in the flight of a bird, the hum of an insect's wings, the rush of a lion, the quickness of the mental and emotional processes. These

delicate and massive oxidations could be only the product of the high energy content of the nitrogen or pre-plant group formed by the highest energy that reaches the earth, namely, lightning. The nitrogen fraction, an essential of all protoplasm, then, is the fulminate, which was generated under a higher temperature than the surface of the sun; that is, the nitrogen fraction of the proteins is the fulminate that ignites the fraction which contains the slower burning but greater source of solar energy, namely, the carbohydrates.

Animals are exquisitely sensitized to radiant and electric energy, and therefore they are detonated, oxidized and exhausted readily by physical injury, by emotion, by infection. Animals are profoundly modified by changes in the mechanism that governs the rate of internal combustion; that is to say, the rate of the re-radiation of "sunshine" in the protoplasm.

The chief organs that normally govern the protoplasmic sunshine in health and alter it in a state which we call disease, are the brain, the thyroid, the adrenal-sympathetic system. The thyroid gland and the adrenal-sympathetic system energize the system by shifting the emitted radiations toward the short wave field.

The same radiant and electric energy that effects fertilization and normal growth, also, through abnormal influences, presumably would generate tumors and cancers.

Not only are radiant and electric energy governed by the neuroglandular system, but radiant and electric energy are diminished and suspended by agencies that interfere with oxidation, or with the infinitely delicate dielectric films that hold electric charges; that is to say, agencies that interfere with the normal range of electric potential, electric capacity, and electric conductivity. Such agents are anesthetics and narcotics.

One recognizes three phases of the energy mechanism of protoplasm. The first is the nitrogen or pre-plant phase; the second, the carbon or plant phase; the third and last, the oxygen or disintegration phase—the animal phase, each of which plays its rôle in the production of normal life, disease, senescence and death.

If one could imagine a physicist who had never seen light and had no knowledge of the solar system, and if that physicist

should make measurements of radiant energy and should determine the solar spectrum, he would logically reach the conclusion that there was at a long distance a radiator of vast power; and finding by comparison only a slight amount of radiation from other sources, from the moon and stars for example, he would appropriately name this great source of radiation the "primary radiogen." If this imaginary physicist had found radiation of the same wavelength in the same bands emitted by the protoplasm of plants and animals while alive and absent at death, he would conclude that there were secondary radiators in protoplasm. Continuing his quest further, this physicist would find that the secondary or re-radiation in protoplasm was related to oxidation solely; that oxidation was controlled by the nerve cells of the brain and the nerve cells of the sympathetic system, and that the nerve cells of both systems were adaptively speeded up or lessened in activity by the thyroid and the adrenal glands, which in turn are controlled in their adaptive activity by the brain and adrenal-sympathetic system, while the brain, in turn, is controlled by the special senses. The special senses, in turn, are controlled by light waves, sound waves, chemical influences, etc.; that is to say, the physicist would find that the special senses were the primary controllers of adaptive variations in the rate of oxidation, which is the same as saying, of the number and the length of the waves of radiation generated in the protoplasm. The physicist would then endeavor to find the exact mechanism that could generate radiant energy equal to that of the sun, though infinitely small in amount; he would see that bones and tendons and fascia and skin and fat could emit but negligible amounts of radiant energy; that water and electrolytes and metals of themselves alone could emit but little; he would be struck by the most significant fact, that when life ends radiation ends; he would be struck by the fact that at the moment life ends although the cell membranes are intact no oxidation occurs, hence surface tension is not a primary factor; he would be struck by the fact that the characteristics of oxidation had been inherited over vast periods of time; hence, a persistent pattern of energy transformation exists.

He would then realize that there are continuing forces at work which keep the pattern of the mechanism of energy transforma-

tion as constant as the energy that produces those forces is constant. Such a constant source of energy transformation could not be so haphazard as surface tension, or as enzyme action, for the infinite niceties of the mind and of emotion demand energy levels as high as the outer surface of the sun, for ultraviolet, visible, and infra-red radiations are thermometers which indicate the heat at the point—molecular point—of generation.

These considerations would lead our physicist to investigate the chemical and physical nature of protoplasm and he would first note that the surface films could not generate adaptively the intense energy of radiation, and would consider what would be the physical nature of a hitherto undescribed molecular furnace.

Short wave radiation results from oxidation of nitrogen and carbon compounds—an oxidation at high speeds as in the detonation of explosives. It would be evident that there is in protoplasm the constant re-radiation of the energy put into the nitrogen compounds and the carbon compounds; but the temperature of the protoplasm is at almost a cold level, though higher than the environment. Our physicist therefore would ask himself what would become of the intense heat of combustion since it is not manifested in the organism as a whole? He would see clearly that it is the great preponderance of water which dissipates it. The physicist would then see what the fuel that energizes protoplasm is. He would see that protoplasm is water-cooled. He would see how it is made to flare up adaptively. He would then consider the number and size of these generators of radiation—these radiogens. It would be clear that if the radiogens should coalesce they would either extinguish each other or would fail to be water-cooled. Therefore, the radiogens would be spaced by some form of energy analogous to that which spaces colloidal particles. The physicist, knowing that animal protoplasm contains a constant but small amount of iron-bound iron—and knowing that iron promotes oxidation, would think that while cold iron like cold oxygen, cold nitrogen, cold carbon, from the standpoint of energy is one thing, on the other hand a molecule of iron at a temperature of from 3,000 to 6,000 degrees Centigrade would be “excited” iron and a vastly

different thing. Our physicist would then glimpse the fundamental rôle of iron; namely, in the "excited" state the molecule of iron would be the luminous sun of the radiogen—the center of the protein fire which would hold the atoms of the proteins in its "energy field" as the primary radiogen, the sun, holds in its "energy field" the planets. And so the physicist would consider that these theoretic radiogens would space themselves through the "energy fields," thus making a uniform distribution for the genesis of energy; and also a uniform division of the water-cooled system.

It would then be clear to the physicist what factors have maintained a constancy of the protoplasm through eons—the constancy of the wavelengths of solar radiation; the constancy of iron; the constancy of water and electrolytes; the constancy of electricity; the constancy of the wavelength that each atom of nitrogen, carbon, and oxygen brings to the radiogens where it is released to maintain the flame of life—to produce and maintain the spectrum of the living state.

It would be easy for our physicist to see how molecules of thyroxin, adrenalin, theelin, Eschatin, Prolan A, the molecules of digested food, organic iron, of alcohol, molecules of morphine, of atropine, molecules of the vitamines, of nitrous oxide, and of ether can reach and influence the infinite numbers of radiogens which are the essence of the living. He would see how the radiant energy emitted by the radiogen can not only bind water to its energy sphere, but can change and maintain differences of electrolytic concentration across semi-permeable films. He would see how protoplasm grows by the accumulation of non-living elements and forms from them living units or radiogens.

Theoretical as the conception that the radiogen is the primary source of protoplasmic energy may seem, how could our physicist accept the proved facts that radiations are received by protoplasm and that they must therefore be and are re-radiated in the same wavelengths as those which were received, without postulating that there are central points or "furnaces" for such re-radiation?

In his consideration of the Radio-Electric conception as an explanation of living phenomena our physicist would find that

although it can not be proven, since protoplasm has not been generated in the laboratory, it nevertheless harmonizes many phenomena of the living state. It offers many parallels and analogies between the living state and non-living phenomena. It has suggested a solution of certain problems pertaining to the normal and the pathological states of living organisms. The radio-electric conception explains our failure to show that the loss of the energy of the living state in surgical shock was not due primarily to failure of the circulation or of respiration or to changes in the chemistry of the blood. It has shown why living matter can exist only in cells. It has given a simple explanation for the universal pattern of cells with respect to their exhibition of a nucleus and a cytoplasm and has also explained why the nucleus and cytoplasm exhibit differential stainability and opposite signs of charge. It shows why the cell loses its power of function and of maintenance of its structure when the differential stainability of the nucleus and the cytoplasm is lost. It explains the presence in living organisms of electric potential and of electric currents. It shows the necessity of continuous oxidation for the maintenance of radiant and electric properties. It shows the reason why the electric conductivity, capacity and potential vary with the speed of function and the rate of growth. It explains the universal presence in living matter of insulating lipoids. It explains the universal presence in protoplasm of water which has the highest dielectric constant, the greatest specific heat, is the greatest solvent. It explains why iron is present in greater concentration in the muscles of insects, in which energy is liberated at high speed, than in the muscles of mammals. It explains the fact that proteins with their relatively positive sign of charge when mixed with lipoids of the same species with their relatively negative signs of charge form models of living cells that exhibit the simpler fundamental phenomena of living cells, such as cell division, the presence of an electric potential difference, the taking of differential stains, the exhibition of metabolism, and a response to anesthetics, narcotics, thyroxin, and to changes in the hydrogen ion concentration identical with that manifested by living organisms. It explains why this protein fraction, when oxidized rapidly, emits ultraviolet, visible, and infra-red radiation. It explains the fact that the protoplasm

of animals can perform much of the function and growth exhibited by plants by utilizing the energy derived by the plant from solar radiation. It explains how the presence of radiation can account for the ionization of the atmospheric oxygen. It explains why in the living state, where the radiogens are burning too low to emit the ionizing short wave radiation, the ionization of oxygen ceases. It explains the fundamental rôle of heat. It identifies the rôle of the thyroid and of the adrenal-sympathetic system as controllers of the percentage of short wave radiation, hence, as regulators of the power of this or that animal to alter adaptively this or that speed of action; this or that emotion; this or that mental process.

The Radio-Electric Theory identifies the mechanism by which the conscious state is established and maintained by short wave or ionizing radiation. It also shows that the unconscious state is due to the absence of the short wave or ionizing radiation. The Radio-Electric Theory offers a physical explanation of the mechanism of memory, reason, imagination and the expression of the emotions. It assigns to the insulating lipoids and the highly sensitive proteins, which together constitute the brain, their respective rôles. It assigns to the white matter the rôle of a recording matrix, on which the lines of facilitating conductance are not only etched but whose permanency depends on the completeness of the etching. It shows why the millions of cells or dynamos are placed in close relation to the infinitely fine and complex switchboard—the white matter. It harmonizes the complete dependence of the function of the brain upon oxidation and equally upon electric potential. It explains conditioned reflexes as being due to the production of action patterns which are more completely facilitated than are the competing ones. The Radio-Electric Theory explains the specific rôle of the thyroid in the control of mental and emotional activity on the ground that thyroxin increases the percentage of radiation in the short wave part of the spectrum of the living.

In accordance with this conception, inasmuch as man possesses the largest mass of brain, the thyroid gland which maintains its metabolism at a constant level would be expected to be relatively larger in man than in any other animal. An extensive survey of most species of animals shows that in animals in the

wild state the adrenal-sympathetic complex has a larger mass than that of the thyroid gland while in man the thyroid gland is double the weight of the adrenal-sympathetic complex. In accordance with the Radio-Electric Theory, therefore, one would expect that the energy equation of animals and man could be expressed by the relative sizes of the brain, thyroid and adrenal-sympathetic complex.

The Radio-Electric Theory explains why this peculiar energy equipment of man predisposes man to certain diseases and infirmities. It associates this or that development of the energy-controlling glands with this or that length of life.

The Radio-Electric Theory suggests how a high energy level of the nitrogen fraction in protoplasm, which is always present in combination with the lower energy level of the carbon fraction, parallels the relationships of the nitrogen and carbon compounds in the nitro-explosives and supplies a simple explanation of the manner in which energy is released at a peculiarly high speed in mental and emotional processes, or in the speed of an insect's wings, by a process which resembles a detonation. It explains simply that broad, unchallenged, universal fact that all protoplasm, plant and animal, can be made to exercise its function by electric stimulation because the electricity generated in protoplasm is identical with the electricity generated by batteries and dynamos.

In the domain of disease and injury, it explains the conduction of injury currents along nerves by progressive detonation which generates radiant and electric energy as it travels, thereby causing exhaustion of the whole animal by its bodywide effects.

The Radio-Electric Theory has been proved clinically as far as the diseases due to a chronic excessive drive of the neuro-glandular system are concerned, just as anoxia-association has become a clinical fact as far as surgical operations are concerned. In a broader sense the Radio-Electric Theory is pointing the way to an explanation or rationalization of the emotions.

It is obvious that the rôle played by radiation and electricity in living processes is no more mystical than that played by radiation and electricity in man-made mechanisms. Electricity brought over a single feed wire may light an electric lamp, operate a dynamo or turn an electric drill. Radiation may operate

a radio or a robot, the final manifestation of the electric power or of the radiation depending upon the receiving instrument. So in living processes the final manifestation depends upon the end organ or the receiving mechanism. The effect on the receiving mechanism in an ameba would differ from that in a lion; the effect if the thyroid gland received the electric current or radiation would vary from that if the pancreas received it. Like the receiving mechanisms made by man, each produces its specific response.

Thus we have sketched the long road which we have travelled to arrive at the conception that not only this or that but every phenomenon of life can be identified in the terms of physics and can be explained in the light of a Radio-Electric Theory. The Radio-Electric Theory suggests that plants are generated by radiant and electric energy; that animals are constructed and operated by the radiant and electric energy stored in the plant; that the energy of the body is released by oxidation in the radiogens which are patterned after the solar system; that as the result of this oxidation radiations of different wavelengths are released; that the genesis of radiation is the first step in the genesis of tissues; that organisms can exist and function only in the presence of mechanisms that maintain differences of potential. Thus according to the Radio-Electric Theory living organisms are bipolar mechanisms constructed and energized by radiant and electric energy.

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