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by George W. Crile

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THE ORIGIN AND NATURE

of the

EMOTIONS

Miscellaneous Papers

BY

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EDITED BY

AMY F. ROWLAND, B. S.

PREFACE

IN response to numerous requests I have brought together into this volume

eight papers which may serve as a supplement to the volumes previously

published[\*] and as a preface to monographs now in preparation.

[\*] Surgical Shock, 1899; Surgery of the Respiratory System, 1899;

Problems Relating to Surgical Operations, 1901; Blood Pressure

in Surgery, 1903; Hemorrhage and Transfusion, 1909;

Anemia and Resuscitation, 1914; and Anoci-association, 1914

(with Dr. W. E. Lower).

In the first of these addresses, the Ether Day Address, delivered at

the Massachusetts General Hospital in October, 1910, I first

enunciated the Kinetic Theory of Shock, the key to which was found

in laboratory researches and in a study of Darwin's "Expression

of the Emotions in Man and in Animals," whereby the phylogenetic

origin of the emotions was made manifest and the pathologic

identity of surgical and emotional shock was established.

Since 1910 my associates and I have continued our researches through--

(a) Histologic studies of all the organs and tissues of the body;

(b) Estimation of the H-ion concentration of the blood in the emotions

of anger and fear and after the application of many other forms of stimuli;

(c) Functional tests of the adrenals, and (d) Clinical observations.

It would seem that if the striking changes produced by fear

and anger and by physical trauma in the master organ of the body--

the brain--were due to WORK, then we should expect to find

corresponding histologic changes in other organs of the body as well.

We therefore examined every organ and tissue of the bodies of animals

which had been subjected to intense fear and anger and to infection and

to the action of foreign proteins, some animals being killed immediately;

some several hours after the immediate effects of the stimuli had passed;

some after seances of strong emotion had been repeated several

times during a week or longer.

The examination of all the tissues and organs of these animals

showed changes in three organs only, and with few exceptions in all

three of these organs--the brain, the adrenals, and the liver.

The extent of these changes is well shown by the photomicrographs

which illustrate the paper on "The Kinetic System" which is included

in this volume. This paper describes many experiments which show

that the brain, the adrenal, and the liver play together constantly

and that no one of these organs--as far at least as is indicated

by the histologic studies--can act without the co-operation

of the other two.

Another striking fact which has been experimentally established

is that the deterioration of these three organs caused by emotion,

by exertion, and by other causes is largely counteracted,

if not exclusively, during sleep. If animals exhausted by the continued

application of a stimulus are allowed complete rest for a certain

number of hours, \_\*without sleep\_, the characteristic histologic

appearance of exhaustion in the brain, adrenals, and liver is not

altered notably, whereas in animals allowed to sleep for the same

number of hours the histologic changes in these organs are lessened--

in some cases obliterated even.

This significant phenomenon and its relation will be dealt with in

a later monograph.

Many of the arguments and illustrations by which the primary

premises were established are repeated--a few in all--many in

more than one of these addresses. It will be observed, however,

that the APPLICATION of these premises varies, and that their

SIGNIFICANCE broadens progressively.

In the Ether Day Address the phylogenetic key supplied by Darwin was

utilized to formulate the principle that the organism reacts as a unit

to the stimuli of physical injury, of emotion, of infection, etc.

To the study of these reactions (transformations of energy)

the epoch-making work of Sherrington, "The Integrative Action

of the Nervous System," gave an added key by which the dominating

role of the brain was determined. Later the original work

of Cannon on the adrenal glands gave facts, and an experimental

method by which Darwin's phylogenetic theory of the emotions

was further elaborated in other papers, especially in the one

entitled "Phylogenetic Association in Relation to the Emotions,"

read before The American Philosophical Society in April, 1911.

GEORGE W. CRILE. CLEVELAND, OHIO, \_February, 1915\_.

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THE ORIGIN AND NATURE OF THE EMOTIONS

PHYLOGENETIC ASSOCIATION IN RELATION TO CERTAIN MEDICAL PROBLEMS[\*]

[\*] Address delivered at the Massachusetts General Hospital on

the sixty-fourth anniversary of Ether Day, Oct. 15, 1910.

The discovery of the anesthetic properties of ether and its practical

application to surgery must always stand as one of the great

achievements of medicine. It is eminently fitting that the anniversary

of that notable day, when the possibilities of ether were first

made known to the world, should be celebrated within these walls,

and whatever the topic of your Ether Day orator, he must fittingly

pause first to pay tribute to that great event and to the master

surgeons of the Massachusetts General Hospital. On this occasion,

on behalf of the dumb animals as well as on behalf of suffering humanity,

I express a deep sense of gratitude for the blessings of anesthesia.

Two years ago, an historic appreciation of the discovery of ether

was presented here by Professor Welch, and last year an address

on medical research was given by President Eliot. I, therefore,

will not attempt a general address, but will invite your

attention to an experimental and clinical study. In presenting

the summaries of the large amount of data in these researches,

I acknowledge with gratitude the great assistance rendered by

my associates, Dr. D. H. Dolley, Dr. H. G. Sloan, Dr. J. B. Austin,

and Dr. M. L. Menten.[\*]

[\*] From the H. K. Cushing Laboratory of Experimental Medicine,

Western Reserve University, Cleveland.

The scope of this paper may be explained by a concrete example.

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--

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 a stone,

shock may be produced; if the stone be only lightly applied,

then the consequent sensation of tickling causes a discharge of

nervous energy. In like manner there have been implanted in the body

other mechanisms of ancestral or phylogenetic origin whose purpose

is the discharge of nervous energy for the good of the individual.

In this paper I shall discuss the origin and mode of action of some

of these mechanisms and their relation to certain phases of anesthesia.

The word anesthesia--meaning WITHOUT FEELING--describes accurately

the effect of ether in anesthetic dosage. Although no pain

is felt in operations under inhalation anesthesia, the \_\*nerve

impulses excited by a surgical operation still reach the brain\_.

We know that not every portion of the brain is fully anesthetized,

since surgical anesthesia does not kill. The question then is:

What effect has trauma under surgical anesthesia upon the part

of the brain THAT REMAINS AWAKE? If, in surgical anesthesia,

the traumatic impulses cause an excitation of the wide-awake cells,

are the remainder of the cells of the brain, despite anesthesia,

affected in any way? If so, they are prevented by the anesthesia from

expressing that influence in conscious perception or in muscular action.

Whether the ANESTHETIZED cells are influenced or not must be determined

by noting the physiologic functions of the body after anesthesia has

worn off, and in animals by an examination of the brain-cells as well.

It has long been known that the vasomotor, the cardiac, and the respiratory

centers discharge energy in response to traumatic stimuli applied

to various sensitive regions of the body during surgical anesthesia.

If the trauma be sufficient, exhaustion of the entire brain

will be observed after the effect of the anesthesia has worn off;

that is to say, despite the complete paralysis of voluntary

motion and the loss of consciousness due to ether, the traumatic

impulses that are known to reach the AWAKE centers in the medulla

also reach and influence every other part of the brain.

Whether or not the consequent functional depression and the morphologic

alterations seen in the brain-cells may be due to the low blood-pressure

which follows excessive trauma is shown by the following experiments:

The circulation of animals was first rendered STATIC by over-transfusion,

and was controlled by a continuous blood-pressure record on a drum,

the factor of anemia being thereby wholly excluded during the application

of the trauma and during the removal of a specimen of brain tissue

for histologic study. In each instance, morphologic changes

in the cells of all parts of the brain were found, but it required

much more trauma to produce brain-cell changes in animals whose

blood-pressure was kept at the normal level than in the animals

whose blood-pressure was allowed to take a downward course.

In the cortex and in the cerebellum, the changes in the brain-cells

were in every instance more marked than in the medulla.

There is also strong NEGATIVE evidence that traumatic impulses

are not excluded by ether anesthesia from the part of the brain

that is apparently asleep. This evidence is as follows:

If the factor of fear be excluded, and if in addition the traumatic

impulses be prevented from reaching the brain by cocain[\*] blocking,

then, despite the intensity or the duration of the trauma within

the zone so blocked, there follows no exhaustion after the effect

of the anesthetic disappears, and no morphologic changes are noted

in the brain-cells.

[\*] Since the presentation of this paper, novocain has been

substituted for cocain in operations under anoci-association.

Still further negative evidence that inhalation anesthesia offers

little or no protection to the brain-cells against trauma is derived

from the following experiment: A dog whose spinal cord had been

divided at the level of the first dorsal segment, and which had

then been kept in good condition for two months, showed a recovery

of the spinal reflexes, such as the scratch reflex, etc. Such an

animal is known as a "spinal dog." Now, in this animal, the abdomen

and hind extremities had no direct nerve connection with the brain.

In this dog, continuous severe trauma of the abdominal viscera and of

the hind extremities lasting for four <p 5-7> hours was accompanied

by but slight change in either the circulation or in the respiration,

and by no microscopic alteration of the brain-cells (Fig. 1). Judging

from a large number of experiments on NORMAL dogs under ether,

such an amount of trauma would have caused not only complete

physiologic exhaustion of the brain, but also morphologic alterations

of all of the brain-cells and the physical destruction of many

(Fig. 2). We must, therefore, conclude that, although ether anesthesia

produces unconsciousness, it APPARENTLY PROTECTS NONE OF THE BRAIN-CELLS

against exhaustion from the trauma of surgical operations; ether is,

so to speak, but a veneer. Under nitrous oxid anesthesia there is

approximately only one-fourth as much exhaustion as is produced by equal

trauma under ether (Fig. 3). We must conclude, therefore, either that

nitrous oxid protects the brain-cells against trauma or that ether

predisposes the brain-cells to exhaustion as a result of trauma.

With these premises let us now inquire into the cause of this

exhaustion of the brain-cells.

The Cause of the Exhaustion of the Brain-cells as a Result of Trauma

of Various Parts of the Body under Inhalation Anesthesia

Numerous experiments on animals to determine the effect of ether

anesthesia \_per se\_, \_i. e\_., ether anesthesia without trauma,

showed that, although certain changes were produced, these included

neither the physiologic exhaustion nor the alterations in the

brain-cells which are characteristic of the effects of trauma.

On turning to the study of trauma, we at once found in the behavior

of individuals as a whole under deep and under light anesthesia

the clue to the cause of the discharge of energy, of the consequent

physiologic exhaustion, and of the morphologic changes in the brain-cells.

If, in the course of abdominal operations, rough manipulations

of the parietal peritoneum be made, there will be frequently

observed a marked increase in the respiratory rate and an increase

in the expiratory force which may be marked by the production

of an audible expiratory groan. Under light ether anesthesia,

severe manipulations of the peritoneum often cause such vigorous

contractions of the abdominal muscles that the operator is greatly

hindered in his work.

Among the unconscious responses to trauma under ether anesthesia

are purposeless moving, the withdrawal of the injured part, and,

if the anesthesia be sufficiently light and the trauma sufficiently

strong, there may be an effort toward escape from the injury.

In injury under ether anesthesia every grade of response may be seen,

from the slightest change in the respiration or in the blood-pressure

to a vigorous defensive struggle. As to the purpose of these

subconscious movements in response to injury, there can be no doubt--

THEY ARE EFFORTS TO ESCAPE FROM THE INJURY.

Picture what would be the result of a formidable abdominal operation

extending over a period of half an hour or more on an unanesthetized

human patient, during which extensive adhesions had been broken up,

or a large tumor dislodged from its bed! In such a case,

would not the nervous system discharge its energy to the utmost

in efforts to escape from the injury, and would not the patient suffer

complete exhaustion? If the traumata under inhalation anesthesia

are sufficiently strong and are repeated in sufficient numbers,

the brain-cells are finally deprived of their dischargeable nervous

energy and become exhausted just as exhaustion follows such strenuous

and prolonged muscular exertion as is seen in endurance tests.

Whether the energy of the brain be discharged by injury under anesthesia

or by ordinary muscular exertion, identical morphologic changes are

seen in the nerve-cells. In shock from injury (Fig. 2), in exhaustion

from overwork (Hodge and Dolley) (Fig. 4), and in exhaustion from pure fear

(Fig. 5), the resultant general functional weakness is similar--

in each case a certain length of time is required to effect recovery,

and in each there are morphologic changes in the brain-cells. It

is quite clear that in each of these cases the altered function

and form of the brain-cells are due to an \_\*excessive discharge

of nervous energy\_. This brings us to the next question:

What determines the discharge of energy as a result of trauma

with or without inhalation anesthesia?

The Cause of the Discharge of Nervous Energy as a Result of Trauma

under Inhalation Anesthesia and under Normal Conditions

I looked into this problem from many viewpoints and there seemed

to be no solution until it occurred to me to seek the explanation

in certain of the postulates which make up the doctrine of evolution.

I realize fully the difficulty and the danger in attempting

to reach the generalization which I shall make later and in

the hypothesis I shall propose, for there is, of course, no direct

final proof of the truth of even the doctrine of evolution.

It is idle to consider any experimental research into the cause

of phenomena that have developed by natural selection during

millions of years. Nature herself has made the experiments on

a world-wide scale and the data are before us for interpretation.

Darwin could do no more than to collect all available facts and then

to frame the hypothesis by which the facts were best harmonized.

Sherrington, that masterly physiologist, in his volume entitled

"The Integrative Action of the Nervous System," shows clearly how

the central nervous system was built up in the process of evolution.

Sherrington has made free use of Darwin's doctrine in explaining

physiologic functions, just as anatomists have extensively

utilized it in the explanation of the genesis of anatomic forms.

I shall assume, therefore, that the discharge of nervous energy is

accomplished by the application of the laws of inheritance and association,

and I conclude that this hypothesis will explain many clinical phenomena.

I shall now present such evidence in favor of this hypothesis as time

and my limitations will admit, after which I shall point out certain

clinical facts that may be explained by this hypothesis.

According to the doctrine of evolution, every function owes

its origin to natural selection in the struggle for existence.

In the lower and simpler forms of animal life, indeed, in our

human progenitors as well, existence depended principally upon

the success with which three great purposes were achieved:

(1) Self-defense against or escape from enemies; (2) the acquisition

of food; and (3) procreation; and these were virtually the only purposes

for which nervous energy was discharged. In its last analysis,

in a biologic sense, this statement holds true of man today.

Disregarding for the present the expenditure of energy for procuring

food and for procreation, let us consider the discharge of energy

for self-preservation. The mechanisms for self-defense which we

now possess were developed in the course of vast periods of time

through innumerable intermediary stages from those possessed by

the lowest forms of life. One would suppose, therefore, that we must

now be in possession of mechanisms which still discharge energy on

adequate stimulation, but which are not suited to our present needs.

We shall point out some examples of such unnecessary mechanisms.

As Sherrington has stated, our skin, in which are implanted many

receptors for receiving specific stimuli which are transmitted

to the brain, is interposed between ourselves and the environment

in which we are immersed. When these stimuli reach the brain,

there is a specific response, principally in the form of

muscular action. Now, each receptor can be adequately stimulated

only by the particular factor or factors in the environment

which created the necessity for the existence of that receptor.

Thus there have arisen receptors for touch, for temperature,

for pain, etc. The receptors for pain have been designated \_nociceptors\_

(nocuous or harmful) by Sherrington.

On the basis of natural selection, nociceptors could have developed

in only those regions of the body which have been exposed to injury

during long periods of time. On this ground the finger, because it

is exposed, should have many nociceptors, while the brain, though the

most important organ of the body, should have no nociceptors because,

during a vast period of time, it has been protected by a skull.

Realizing that this point is a crucial one, Dr. Sloan and I made a series

of careful experiments. The cerebral hemispheres of dogs were exposed

by removing the skull and dura under ether and local anesthesia.

Then various portions of the hemispheres were slowly but

completely destroyed by rubbing them with pieces of gauze.

In some instances a hemisphere was destroyed by burning.

In no case was there more than a slight response of the centers governing

circulation and respiration, and no morphologic change was noted

in an histologic study of the brain-cells of the uninjured hemisphere.

The experiment was as completely negative as were the experiments

on the "spinal dog." Clinically I have confirmed these experimental

findings when I have explored the brains of conscious patients

with a probe to determine the presence of brain tumors.

Such explorations elicited neither pain nor any evidence of altered

physiologic functions. The brain, therefore, contains no mechanism--

no nociceptors--the direct stimulation of which can cause

a discharge of nervous energy in a self-defensive action.

That is to say, direct injury of the brain can cause no purposeful

nerve-muscular action, while direct injury of the finger does cause

purposeful nerve-muscular action. In like manner, the deeper portions

of the spinal region have been sheltered from trauma and they, too,

show but little power of causing a discharge of nervous energy

on receiving trauma. The various tissues and organs of the body

are differently endowed with injury receptors--the nociceptors

of Sherrington. The abdomen and chest when traumatized stand first

in their facility for causing the discharge of nervous energy, \_i.

e\_., THEY STAND FIRST IN SHOCK PRODUCTION. Then follow the extremities,

the neck, and the back. It is an interesting fact also that different

types of trauma elicit different responses as far as the consequent

discharge of energy is concerned.

Because it is such a commonplace observation, one scarcely realizes

the importance of the fact that clean-cut wounds inflicted

by a razor-like knife cause the least reaction, while a tearing,

crushing trauma causes the greatest response. It is a suggestive fact

that the greatest shock is produced by any technic which imitates

the methods of attack and of slaughter used by the carnivora.

\_\*In the course of evolution, injuries thus produced may well have

been the predominating type of traumata to which our progenitors

were subjected\_. In one particular respect there is an analogy between

the response to trauma of some parts of the body of the individuals

of a species susceptible to shock and the response to trauma of the

individuals in certain other great divisions of the animal kingdom.

Natural selection has protected the crustaceans against their

enemies by protective armor, \_e. g\_., the turtle and the armadillo;

to the birds, it has given sharp eyes and wings, as, for instance,

the wild goose to another species--the skunk--it has given a noisome odor

for its protection. The turtle, protected by its armor against trauma,

is in a very similar position to that of the sheltered brain

of man and, like the brain, the turtle does not respond to trauma

by an especially active self-protective nerve-muscular response,

but merely withdraws its head and legs within the armored protection.

It is proverbially difficult to exhaust or to kill this animal by trauma.

The brain and other phylogenetically sheltered parts likewise give no

exhausting self-protective nerve-muscular response to trauma. The skunk

is quite effectively protected from violence by its peculiar odor.

This is indicated not only by the protective value of the odor itself,

but also by the fact that the skunk has no efficient nerve-muscular

mechanism for escape or defense; it can neither run fast nor can it

climb a tree. Moreover, in encounters it shows no fear and backs

rather than runs. The armadillo rolls itself into a ball for defense.

On these premises we should conclude that the turtle,

the armadillo, and the skunk have fewer nociceptors than has

a dog or man, and that they would show less response to trauma.

In two carefully conducted experiments on skunks and two on armadillos

(an insufficient number) the energy discharged in response to severe

and protracted trauma of the abdominal viscera was very much less than

in similar experiments on dogs, opossums, pigs, sheep, and rabbits.

It was indeed relatively difficult to exhaust the skunks and armadillos

by trauma. These experiments are too few to be conclusive,

but they are of some value and furnish an excellent lead.

It seems more than a coincidence that proneness to fear,

distribution of nociceptors, and susceptibility to shock go

hand-in-hand in these comparative observations (Figs. 6, 7, and 8).

The discharge of energy caused by an adequate mechanical stimulation

of the nociceptors is best explained in accordance with the law

of phylogenetic association. That is, injuries awaken those reflex

actions which by natural selection have been developed for the purpose

of self-protection. Adequate stimulation of the nociceptors for pain

is not the only means by which a discharge of nervous energy is caused.

Nervous energy may be discharged also by adequate stimulation

of the various ticklish regions of the body; the entire skin

surface of the body contains delicate ticklish receptors.

These receptors are closely related to the nociceptors for pain,

and their adequate stimulation by an insect-like touch

causes a discharge of energy,--a nerve-muscular reaction,--

resembling that developed for the purpose of brushing off insects.

This reflex is similar to the scratch reflex in the dog.

The discharge of energy is almost wholly independent of the will

and is a self-protective action in the same sense as is the response

to pain stimuli. The ear in man and in animals is acutely ticklish,

the adequate stimulus being any foreign body, especially a buzzing,

insect-like contact. The discharge of nervous energy in horses

and in cattle on adequate stimulation of the ticklish receptors

of the ear is so extraordinary that in the course of evolution it

must have been of great importance to the safety of the animal.

A similar ticklish zone guards the nasal chambers, the discharge of energy

here taking a form which effectively dislodges the foreign body.

The larynx is exquisitely ticklish, and, in response to any adequate

stimulus, energy is discharged in the production of a vigorous cough.

The mouth and pharynx have active receptors which cause the rejection

of noxious substances. The conjunctival reflex, though not

classed as ticklish, is a most efficient self-protective reflex.

I assume that there is no doubt as to the relation between

the adequate stimuli and the nerve-muscular response of the various

ticklish receptors of the surface of the skin, of the ear,

the nose, the eye, and the larynx. These mechanisms were developed

by natural selection as protective measures against the intrusion

of insects and foreign bodies into regions of great importance.

The discharge of energy in these instances is in accordance

with the laws of inheritance and association. The other ticklish

points which are capable of discharging vast amounts of energy

are the lateral chest-wall, the abdomen, the loins, the neck,

and the soles of the feet. The type of adequate stimuli of the soles

of the feet, the distribution of the ticklish points upon them,

and the associated response, leave no doubt that these ticklish points

were long ago established as a means of protection from injury.

Under present conditions they are of little value to man.

The adequate stimulus for the ticklish points of the ribs,

the loins, the abdomen, and the neck is deep isolated pressure,

probably the most adequate being pressure by a tooth-shaped body.

The response to tickling in these regions is actively and obviously

self-defensive. The horse discharges energy in the form of a kick;

the dog wriggles and makes a counter-bite; the man makes efforts

at defense and escape.

There is strong evidence that the deep ticklish points of the body

were developed through vast periods of fighting with teeth and claws

(Fig. 9). Even puppies at play bite each other in their ticklish

points and thus give a recapitulation of their ancestral battles

and of the real battles to come (Fig. 10). The mere fact that animals

fight effectively in the dark and always according to the habit

of their species supports the belief that the fighting of animals

is not an intellectual but a reflex process. There are no rules

which govern the conduct of a fight between animals. The events

follow each other with such kaleidoscopic rapidity that the process

is but a series of automatic stimulations and physiologic reactions.

Whatever their significance, therefore, it is certain that man did

not come either accidentally or without purpose into possession

of the deep ticklish regions of his chest and abdomen.

Should any one doubt the vast power that adequate stimulation

of these regions possesses in causing the discharge of energy,

let him be bound hand and foot and vigorously tickled for an hour.

What would happen? He would be as completely exhausted as though he had

experienced a major surgical operation or had run a Marathon race.

A close analogy to the reflex process in the fighting of animals

is shown in the role played by the sexual receptors in conjugation.

Adequate stimulation of either of these two distinct groups

of receptors, the sexual and the noci, causes specific behavior--

the one toward embrace, the other toward repulsion. Again, one of

the most peremptory causes of the discharge of energy is that due

to an attempt to obstruct forcibly the mouth and the nose so that

asphyxia is threatened. Under such conditions neither friend

nor foe is trusted, and a desperate struggle for air ensues.

It will be readily granted that the reactions to prevent suffocation

were established for the purpose of self-preservation, but the discharge

of nerve-muscular energy to this particular end is no more specific

and no more shows adaptive qualities than do the preceding examples.

Even the proposal to bind one down hand and foot excites resentment,

a feeling originally suggested by the need for self-preservation.

No patient views with equanimity the application of shackles

as a preparation for anesthesia.

We have now considered some of the causes of those discharges of nervous

energy which result from various types of harmful physical contact,

and have referred to the analogous, though antithetical,

response to the stimulation of the sexual receptors.

The response to the adequate stimuli of each of the several receptors

is a discharge of nerve-muscular energy of a specific type; that is,

there is one type of response for the ear, one for the larynx,

one for the pharynx, another for the nose, another for the eye,

another for the deep ticklish points of the chest and the abdomen,

quite another for the delicate tickling of the skin, and still

another type of response to sexual stimuli.

According to Sherrington, a given receptor has a low threshold

for only one, its own specific stimulus, and a high threshold

for all others; that is, the doors that guard the nerve-paths

to the brain are opened only when the proper password is received.

According to Sherrington's law, the individual as a whole responds

to but one stimulus at a time, that is, only one stimulus

occupies the nerve-paths which carry the impulses as a result

of which acts are performed, \_i. e\_., the final common path.

As soon as a stronger stimulus reaches the brain it dispossesses

whatever other stimulus is then occupying the final common path--

the path of action. The various receptors have a definite order

of precedence over each other (Sherrington). For example, the impulse

from the delicate ticklish points of the skin, whose adequate

stimulus is an insect-like contact, could not successfully compete

for the final common path with the stimulus of a nociceptor.

The stimulus of a fly on the nose would be at once superseded by

the crushing of a finger. In quick succession do the various receptors

(Sherrington) occupy the final common path, but each stimulus is for

the time the sole possessor, hence the nervous system is integrated

(connected) to act as a whole. Each individual at every moment

of life has a limited amount of dischargeable nervous energy.

This energy is at the disposal of any stimulus that obtains possession

of the final common path, and results in the performance of an act.

Each discharge of energy is subtracted from the sum total of stored

energy and, whether the subtractions are made by the excitation

of nociceptors by trauma, by tickling, by fighting, by fear,

by flight, or by the excitation of sexual receptors, by any

of these singly or in combination with others, the sum total of

the expenditure of energy, if large enough, produces exhaustion.

Apparently there is no distinction between that state of exhaustion

which is due to the discharge of nervous energy in response

to trauma and that due to other causes. The manner of the

discharge of energy is specific for each type of stimulation.

On this conception, traumatic shock takes its place as a natural

phenomenon and is divested of its mask of mystery.

The Discharge of Energy through Stimulation of the Distance Receptors,

or through Representation of Injury (Psychic)

We will now turn from the discussion of the discharge of nervous energy by

mechanical stimuli to the discharge of energy through mental perception.

\_Phylogenetic\_ association may result from stimulation of the distance

receptors through sight, hearing, smell, or by a representation

of physical experiences, as well as from physical contact.

The effect upon the organism of the representation of injury

or of the perception of danger through the distance receptors is

designated FEAR. Fear is as widely distributed in nature as is its cause,

that is, fear is as widely distributed as injury. Animals under

the stimulus of fear, according to W. T. Hornaday, not only may exhibit

preternatural strength, but also may show strategy of the highest order,

a strategy not seen under the influence of a lesser stimulus.

In some animals fear is so intense that it defeats escape; this is

especially true in the case of birds in the presence of snakes.

The power of flight has endowed the bird with an easy means of escape

from snakes, especially when the encounter is in the tops of trees.

Here the snake must move cautiously, else he will lose his equilibrium;

his method of attack is by stealth. When the snake has stalked

its prey, the bird is often so overcome by fear that it cannot fly

and so becomes an easy victim (Fig. 11). The phenomena of fear

are described by Darwin as follows:

"Fear is often preceded by astonishment, and is so near akin to it that

both lead to the senses of sight and hearing being instantly aroused.

In both cases the eyes and mouth are widely opened and the

eyebrows raised. The frightened man at first stands like a statue,

motionless and breathless, or crouches down as if instinctively

to escape observation. The heart beats quickly and violently,

so that it palpitates or knocks against the ribs. \* \* \* That the skin

is much affected under the sense of great fear we see in the marvelous

and inexplicable manner in which perspiration immediately exudes from it.

This exudation is all the more remarkable as the surface is then cold,

and hence the term, `a cold sweat'; whereas the sudorific glands

are properly excited into action when the surface is heated.

The hairs also on the skin stand erect, and the superficial

muscles shiver. In connection with the disturbed action of the heart,

the breathing is hurried. The salivary glands act imperfectly;

the mouth becomes dry, and is often opened and shut. I have also

noticed that under slight fear there is a strong tendency to yawn.

One of the best-marked symptoms is the trembling of all the

muscles of the body; and this is often first seen in the lips.

From this cause, and from the dryness of the mouth, the voice

becomes husky and indistinct, or may altogether fail.

\* \* \* As fear increases into agony of terror, we behold, as under

all violent emotions, diversified results. The heart beats wildly,

or may fail to act and faintness ensues; there is death-like pallor;

the breathing is labored; the wings of the nostrils are widely dilated;

`there is a gasping and convulsive motion of the lips, a tremor

on the hollow cheek, a gulping and catching of the throat';

the uncovered and protruding eyeballs are fixed on the object of terror;

or they may roll restlessly from side to side. \* \* \* The pupils

are said to be enormously dilated. All the muscles of the body

may become rigid, or may be thrown into convulsive movements.

The hands are alternately clenched and opened, often with a

twitching movement. The arms may be protruded, as if to avert

some dreadful danger, or may be thrown wildly over the head.

\* \* \* In other cases there is a sudden and uncontrollable tendency

to headlong flight; and so strong is this that the boldest soldiers

may be seized with a sudden panic. As fear rises to an extreme pitch,

the dreadful scream of terror is heard. Great beads of sweat

stand on the skin. All the muscles of the body are relaxed.

Utter prostration soon follows, and the mental powers fail.

The intestines are affected. The sphincter muscles cease

to act and no longer retain the contents of the body.

\* \* \* Men, during numberless generations, have endeavored

to escape from their enemies or danger by headlong flight,

or by violently struggling with them; and such great exertions

will have caused the heart to beat rapidly, the breathing to

be hurried, the chest to heave, and the nostrils to be dilated.

As these exertions have often been prolonged to the last extremity,

the final result will have been utter prostration, pallor, perspiration,

trembling of all the muscles, or their complete relaxation.

And now, whenever the emotion of fear is strongly felt, though it

may not lead to any exertion, the same results tend to reappear,

through the force of inheritance and association"[\*] (Fig. 12).

[\*] Darwin: Expression of the Emotions in Man and Animals.

In an experimental research, we found evidence that the physiologic

phenomena of fear have a physical basis. This evidence is found

in the morphologic alterations in the brain-cells, which are similar

to those observed in certain stages of surgical shock and in fatigue

from muscular exertion (Figs. 2, 4, 5, and 13). For the present,

we shall assume that fear is a REPRESENTATION of trauma.

Because fear was created by trauma, fear causes a discharge of the energy

of the nervous system by the law of phylogenetic association.

The almost universal fear of snakes, of blood, and of death

and dead bodies may have such a phylogenetic origin.

It was previously stated that under the stimulus of fear animals

show preternatural strength. An analysis of the phenomena of fear

shows that, as far as can be determined, all the functions of the body

requiring the expenditure of energy, and which are of no direct

assistance in the effort toward self-preservation, are suspended.

In the voluntary expenditure of muscular energy, as in the chase,

the suspension of other functions is by no means so complete.

Fear and trauma may drain to the last dreg the dischargeable

nervous energy, and, therefore, the greatest possible exhaustion

may be produced by fear and trauma.

Summation

In the discharge of energy, summation plays an important role.

Summation is attained by the repetition of stimuli at such a rate

that each succeeding stimulus is applied before the nerve-cells

have returned to the resting stage from the preceding stimulus.

If drops of water fall upon the skin from a sufficient height to cause

the slightest unpleasant sensation, and at such a rate that before

the effect of the stimulus of one drop has passed another drop

falls in precisely the same spot, there will be felt a gradually

increasing painful sensation which finally becomes unbearable.

This is summation of stimuli. When, for a long time, a patient

requires frequent painful wound dressings, there is a gradual

increase in the acuteness of the pain of the receptors.

This is caused by summation. In a larger sense, the entire behavior

of the individual gives considerable evidence of summation, \_e.

g\_., in the training of athletes, the rhythmic discharge of muscular

energy at such intervals that the resting stage is not reached

before a new exercise is given results in a gradual ascent

in efficiency until the maximum is reached. This is summation,

and summation plays a large role in the development of both normal

and pathologic phenomena.

We have now pointed out the manner in which at least

a part of the nervous energy of man may be discharged.

The integrative action of the nervous system and the discharge

of nervous energy by phylogenetic association may be illustrated

by their analogy to the action of an electric automobile.

The electric automobile is composed of four principal parts:

The motor and the wheels (the muscular system and the skeleton);

the cells of the battery containing stored electricity

(brain-cells, nervous energy); the controller, which is connected

with the cells by wiring (the receptors and the nerve-fibers);

and an accelerator for increasing the electric discharge

(thyroid gland?). The machine is so constructed that it acts

as a whole for the accomplishment of a single purpose.

When the controller is adjusted for going ahead (adequate stimulus

of a receptor), then the conducting paths (the final common path)

for the accomplishment of that purpose are all open to the flow of

the current from the battery, and the vehicle is integrated to go ahead.

It spends its energy to that end and is closed to all other impulses.

When the controller is set for reverse, by this adequate stimulus

the machine is integrated to back, and the battery is closed to all

other impulses. Whether integrated for going forward or backward,

if the battery be discharged at a proper rate until exhausted,

the cells, though possessing no more power (fatigue), have sustained

no further impairment of their elements than that of normal wear

and tear. Furthermore, they may be restored to normal activity

by recharging (rest). If the vehicle be placed against a stone wall,

and the controller be placed at high-speed (trauma and fear),

and if the accelerator be used as well (thyroid secretion?), though

the machine will not move, not only will the battery soon be exhausted,

but the battery elements themselves will be seriously damaged

(exhaustion--surgical shock).

We have now presented some evidence that nervous energy is

discharged by the adequate stimulation of one or more of the various

receptors that have been developed in the course of evolution.

In response to an adequate stimulus, the nervous system is

integrated for a specific purpose by the stimulated receptor,

and but one stimulus at a time has possession of the final common path--

the nerve mechanisms for action. The most numerous receptors

are those for harmful contact; these are the nociceptors.

The effect of the adequate stimulus of a nociceptor is like that of

pressing an electric button that sets great machinery in motion.

With this conception, the human body may be likened to a

musical instrument--an organ--the keyboard of which is composed

of the various receptors, upon which environment plays the many

tunes of life; and written within ourselves in symbolic language

is the history of our evolution. The skin may be the "Rosetta Stone"

which furnishes the key.

Anoci-association

By the law of phylogenetic association, we are now prepared

to make a practical application of the principles of the discharge

of nervous energy. In the case of a surgical operation, if fear

be excluded and if the nerve-paths between the field of operation

and the brain be blocked with cocain,[\*] no discharge of energy will be

caused by the operation; hence no shock, no exhaustion, can result.

Under such conditions the nervous system is protected against

noci-association, resulting from noci-perception or from an adequate

stimulation of nociceptors. The state of the patient in whom all

noci-associations are excluded can be described only by coining

a new word. That word is "anoci-association" (Fig. 14).

[\*] See footnote, page 4.@@@

The difference between anesthesia and anoci-association is that,

although \_inhalation anesthesia\_ confers the beneficent loss of

consciousness and freedom from pain, it does not prevent the nerve

impulses from reaching and influencing the brain, and therefore does

not prevent surgical shock nor the train of later nervous impairments

so well described by Mumford. \_Anoci-association\_ excludes fear,

pain, shock, and postoperative neuroses. \_Anoci-association\_ is

accomplished by combining the special management of patients

(applied psychology), morphin, inhalation anesthesia,

and local anesthesia.

We have now presented in summary much of the mass of experimental

and clinical evidence we have accumulated in support of our

principal theme, which is that the discharge of nervous energy is

accomplished in accordance with the law of phylogenetic association.

If this point seems to have been emphasized unduly, it is because

we expect to rear upon this foundation a clinical structure.

How does this hypothesis apply to surgical operations?

Prevention of Shock by the Application of the Principle of

Anoci-association

Upon this hypothesis a new principle in operative surgery is founded, \_i.

e\_., operation during the state of \_anoci-association\_. Assuming that

no unfavorable effect is produced by the anesthetic and that there is

no hemorrhage, the cells of the brain cannot be exhausted in the course

of a surgical operation except by fear or by trauma, or by both.

Fear may be excluded by narcotics and special management until

the patient is rendered unconscious by inhalation anesthesia.

Then if, in addition to inhalation anesthesia, the nerve-paths

between the brain and the field of operation are blocked with

cocain,[\*] the patient will be placed in the beneficent state of

\_anoci-association\_, and at the completion of the operation will be

as free from shock as at the beginning. In so-called "fair risks"

such precautions may not be necessary, but in cases handicapped

by infections, by anemia, by previous shock, and by Graves'

disease, etc., anoci-association may become vitally important.

[\*] See footnote, page 4.@@@

Graves' Disease

By applying the principle of the discharge of nervous energy by

phylogenetic association, and by making the additional hypothesis

that in the discharge of nervous energy the thyroid gland is stimulated

through the nervous system, we can explain many of the phenomena

of Graves' disease and may possibly discover some of the factors

which explain both its genesis and its cure.

In the wild state of animal life in which only the fittest

survive in the struggle for existence, every point of advantage

has its value. An animal engaged in battle or in a desperate

effort to escape will be able to give a better account of itself

if it have some means of accelerating the discharge of energy--

some influence like that of pouring oil upon the kindling fire.

There is evidence, though perhaps it is not conclusive,

that such an influence is exerted by the thyroid gland.

In myxedema, a condition characterized by a lack of thyroid secretion,

there is dulness of the reflexes and of the intellect, a lowered

muscular power, and generally a sluggish discharge of energy.

In Graves' disease there is an excessive production of thyroid secretion.

In this disease the reflexes are increased, the discharge of

energy is greatly facilitated, and metabolism is at a maximum.

The same phenomena occur also after the administration of thyroid

extract in large doses to normal subjects. In the course of

sexual activities there is an increased action of the thyroid,

which is indicated by an increase in its size and vascularity.

That in fear and in injury the thyroid, in cases of Graves'

disease, is probably stimulated to increased activity is indicated

by the increased activity of the thyroid circulation, by an increase

in the size of the gland, by the histologic appearance of activity

in the nuclei of the cells, and by an increase of the toxic symptoms.

Finally, Asher has stated that electric stimulation of the nerve supply

of the thyroid causes an increased secretion. The origin of many cases

of Graves' disease is closely associated with some of the causes

of the discharge of nervous energy, depressive influences especially,

such as nervous shocks, worry and nervous strain, disappointment in love,

business reverses, illness and death of relatives and friends.

The association of thyroid activity with procreation is well known,

hence the coincidence of a strain of overwork or of fear with

the sexual development of maturing girls is obviously favorable

to the incidence of Graves' disease. The presence of a colloid goiter

is a suitable soil for the development of Graves' disease, and I

fully recognize also the evidence that infection or auto-intoxication

may be contributing factors and must be assigned their role.

I have never known a case of Graves' disease to be caused by success

or happiness alone, or by hard physical labor unattended by

psychic strain, or to be the result of energy voluntarily discharged.

Some cases seem to have had their origin in overdosage with thyroid

extract in too vigorous an attempt to cure a colloid goiter.

One of the most striking characteristics of Graves' disease is

the patient's loss of control and his increased susceptibility

to stimuli, especially to trauma and to fear and to the administration

of thyroid extract. It has been shown that the various causes

of the discharge of nervous energy produce alterations in the nervous

system and probably in the thyroid gland. This is especially

true of the fear stimulus, and has been clearly demonstrated

in the brains of rabbits which had been subjected to fear alone

(Fig. 13). Of special interest was the effect of daily fright.

In this case the brain-cells showed a distinct change, although the animal

had been subjected to no fear for twenty-four hours before it was killed

(Fig. 13 C. Now, a great distinction between man and the lower

animals is the greater control man has acquired over his actions.

This quality of control, having been phylogenetically most recently

acquired, is the most vulnerable to various NOCUOUS influences.

The result of a constant noci-integration may be a wearing-out

of the control cells of the brain. In a typical case of Graves'

disease a marked morphologic change in the brain-cells has

been demonstrated (Fig. 15). As has been previously stated,

the origin of many cases of Graves' disease is associated

with some noci-influence. If this influence causes stimulation

of both the brain and the thyroid, its excessive action may cause

impairment of the brain and also hyperplasia of the thyroid.

As self-control is impaired, fear obtains an ascendency and,

\_pari passu\_, stimulates the thyroid still more actively (Fig. 16).

Finally, the fear of the disease itself becomes a noci-stimulus.

As the thyroid secretion causes an increase in the facility

with which nervous energy is discharged, a pathologic reciprocal

interaction is established between the brain and the thyroid.

The effect of the constantly recurring stimulus of the noci-influence

is heightened by summation. This reciprocal goading may

continue until either the brain or the thyroid is destroyed.

If the original noci-stimulus is withdrawn before the fear of the

disease becomes too strong, and before too much injury to the brain

and the thyroid has been inflicted, a spontaneous cure may result.

Recovery may be greatly facilitated by complete therapeutic rest.

A cure implies the return of the brain-cells to their normal state,

with the reestablishment of the normal self-control and the

restoration of the thyroid to its normal state, when the impulses

of daily life will once more have possession of the final

common path and the noci-influence will be dispossessed.

The discovery of the real cause of a given case of Graves' disease is

frequently difficult because it may be of a painful personal nature.

Of extreme interest is the fact that, in the acute stage,

the patient may be unable to refer to the exciting cause without

exhibiting an exacerbation of the symptoms of the disease.

I presume no case should be regarded as cured until reference

can be made to its cause without an abnormal reaction.

It has been established that in Graves' disease injury to any part

of the body, even under inhalation anesthesia, causes an exacerbation

of the disease. Fear alone may cause an acute exacerbation.

These acute exacerbations are frequently designated "hyperthyroidism"

and are the special hazard of operation.

In applying the principle of anoci-association in operations on

patients with Graves' disease there is scarcely a change in the pulse,

in the respiration, or in the nervous state at the close of the operation.

I know no remedy which can obviate the effect of the inflowing

stimuli from the wound after the cocain[\*] has worn off.[t] It

is necessary, therefore,

Beats 70 80 90 100 110 120

Ether \*\*\*\*\*\*\* \*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\*

N2O \*\*\*\*\*\*\* \*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\* \*

Anoci. \*\*\*\*\*\*\* \*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\* \*\* not to venture too far

in serious cases. Since the adoption of this new method

(anoci-association) my operative results have been so vastly improved

that I now rarely regard any case of Graves' disease as inoperable,

at least to the extent of contraindicating a double ligation (Fig. 17).

[\*] See footnote, page 4.@@@

[t] In later papers and in "Anoci-association" (Crile and Lower)

methods of combating postoperative hyperthyroidism are fully discussed.

If we believe that, in accordance with the law of phylogenetic association,

a continuous stimulation of both the brain and the thyroid gland,

accelerated by summation, plays a role in the establishment

of the pathologic interaction seen in Graves' disease, then it

is but the next step to assume that if the nerve connection between

the brain and the thyroid be severed, or if the lobe be excised

and the patient reinforced by a sojourn in a sanatorium or in some

environment free from former noci-associations, he may be restored

to normal health, provided that the brain-cells, the heart,

or other essential organs have not suffered irreparable damage.

There are still many missing links in the solution of this problem,

and the foregoing hypotheses are not offered as final, although from

the viewpoint of the surgeon many of the phenomena of this

disease are explicable.

Sexual-Neurasthenia

The state of sexual neurasthenia is in many respects analogous

to that of Graves' disease. In the sexual reflexes, summation leads

to a hyperexcitability by psychic and mechanical stimuli of a

specific type which is analogous to the hyperexcitability in Graves'

disease under trauma and fear; the explanation of both conditions

is based on the laws of the discharge of energy by phylogenetic

association and summation. It would be interesting to observe

the effect of interrupting the nerve impulses from the field of

the sexual receptors by injections of alcohol, or by other agencies,

so as to exclude the associational stimuli until the nervous

mechanism has again become restored to its normal condition.

Interpretation of Some of the Phenomena of Certain Diseases of the

Abdomen in Accordance with the Hypothesis of Phylogenetic Association

The law of phylogenetic association seems to explain many

of the phenomena of certain lesions in the abdominal cavity.

The nociceptors in the abdomen, like nociceptors elsewhere, have been

established as a result of some kind of injury to which during

vast periods of time this region has been frequently exposed.

On this premise, we should at once conclude that there are no

nociceptors for heat within the abdomen because, during countless years,

the intra-abdominal region never came into contact with heat.

That this inference is correct is shown by the fact that the

application of a thermocautery to the intestines when completing

a colostomy in a conscious patient is absolutely painless.

One would conclude also that there are no touch receptors in the

abdominal viscera, and therefore no sense of touch in the peritoneum.

Just as the larynx, the ear, the nose, the sole of the foot,

and the skin have all developed the specific type of nociceptors

which are adapted for their specific protective purposes, and which,

when adequately stimulated, respond in a specific manner in accordance

with the law of phylogenetic association, so, the abdominal viscera

have developed equally specific nociceptors as a protection against

specific nocuous influences. The principal harmful influences

to which the abdominal viscera have been exposed during vast periods

of time are deep tearing injuries by teeth and claws in the innumerable

struggles of our progenitors with each other and with their enemies

(Fig. 9); peritonitis caused by perforations of the intestinal

tract from ulcers, injuries, appendicitis, gall-stones, etc.;

and overdistention of the hollow viscera by various forms of obstruction.

Whatever may be the explanation, it is a fact that the type

of trauma which results from fighting corresponds closely with

that which causes the most shock in the experimental laboratory.

Division of the intestines with a sharp knife causes no pain,

but pulling on the mesentery elicits pain. Ligating the stump

of the appendix causes sharp, cramp-like pains. Sharp division

of the gall-bladder causes no pain, but distention, which is

the gall-bladder's most common pathologic state, produces pain.

Distention of the intestine causes great pain, but sharp cutting or burning

causes none. In the abdominal viscera, as in the superficial parts,

nociceptors have presumably been developed by specific harmful

influences and each nociceptor is open to stimulation only by a

stimulus of the particular type that produced it.

As a result of the excitation of nociceptors, with which pain

is associated, the routine functions, such as peristalsis, secretion,

and absorption are dispossessed from the control of their respective

nervous mechanisms, just as they are inhibited by fear. This hypothesis

explains the loss of weight, the lassitude, the indigestion,

the constipation, and the many alterations in the functions of the various

glands and organs of the digestive system in chronic appendicitis.

It readily explains also the extraordinary improvement in the digestive

functions and the general health which follows the removal

of an appendix which is so slightly altered physically that only

the clinical results could persuade one that this slight change could

be an adequate cause for such far-reaching and important symptoms.

This hypothesis explains certain gall-bladder phenomena likewise,--

indigestion, loss of weight, disturbed functions, etc.,--and it

may supply the explanation of the disturbance caused by an active

anal fissure, which is a potent noci-associator, and the consequent

disproportionate relief after the trivial operation for its cure.

Noci-association would well explain also the great functional disturbances

of the viscera which immediately follow abdominal operations.

Postoperative and traumatic neuroses are at once explained on

the ground of noci-association, the resulting strain from which,

upon the brain-cells, causes in them physical lesions.

If one were placed against a wall and were looking into the gun muzzles

of a squad of soldiers, and were told that there were nine chances

out of ten that he would not be killed outright when the volley

was fired, would it help him to be told that he must not be afraid?

Such an experience would be written indelibly on his brain.

This corresponds closely to the position in which some surgical patients

are placed. In railway wrecks, we can readily understand the striking

difference between the after-effects in the passengers who were conscious

at the time of the accident and those who were asleep or drunk.

In the latter the noci-perceptors and receptors were not aroused,

hence their immunity to the nervous shock. In the functional disturbances

of the pelvic organs, association and summation may play a large role.

On this hypothesis many cases of neurasthenia may well be explained.

From the behavior of the individual as a whole we may well conclude

that summation is but a scientific expression for "nagging."

Many other pathologic phenomena may be explained in a similar manner.

Thus we can understand the variations in the gastric analyses in a

timid patient alarmed over his condition and afraid of the hospital.

He is integrated by fear, and as fear takes precedence over all

other impulses, no organ functionates normally. For the same reason,

one sees animals in captivity pine away under the dominance of fear.

The exposure of a sensitive brain to the naked possibility of death from

a surgical operation may be compared to uncovering a photographic plate

in the bright sunlight to inspect it before putting it in the camera.

This principle explains, too, the physical influence of the physician

or surgeon, who, by his PERSONALITY, inspires, like a Kocher,

absolute confidence in his patient. The brain, through its power

of phylogenetic association, controls many processes that have wholly

escaped from the notice of the "practical man." It is in accordance

with the law of association that a flower, a word, a touch, a cool breeze,

or even the thought of a fishing rod or of a gun, is helpful.

On the contrary, all suggestions of despair or misfortune--

a corrugated brow, the gloomy silence of despair, or a doubtful word--

are equally depressing. In like manner, one could add many

illustrations of the symbolism that governs our daily lives.

Thus we see that through the laws of inheritance and noci-association,

we are able to read a new meaning into the clinical phenomena

of various diseases.

Observations on Patients whose Associational Centers are Dulled,

and on Diseases and Injuries of Regions not Endowed with Nociceptors

Reversing the order of our reasoning, let us now glance at the patient

who is unconscious and who, therefore, has lost much of the power

of association. His mouth is usually dry, the digestive processes

are at a low ebb, the aroma of food causes no secretion of saliva,

tickling the nose causes no sneezing; he catches no cold.

The laryngeal reflex is lost and food may be quietly inhaled;

the entire process of metabolism is low. The contrast between a man

whose associational centers are keen and a man in whom these centers

are dulled or lost is the contrast between life and death.

In accordance with the law of adaptation through natural selection,

phylogeny, and association, one would expect no pain in abscess

of the brain, in abscess of the liver, in pylephlebitis,

in infection of the hepatic vessels, in endocarditis.

This law explains why there are no nociceptors for cancer,

while there are active nociceptors for the acute infections.

It is because nature has no helpful response to offer against cancer,

while in certain of the acute pyogenic infections the nociceptors

force the beneficent physiologic rest.

Could we dispossess ourselves of the shackles of psychology,

forget its confusing nomenclature, and view the human brain,

as Sherrington has said, "as the organ of, and for the adaptation

of nervous reaction," many clinical phenomena would appear in

a clearer light.

Natural Selection and Chemical Noci-association in the Infections

Thus far we have considered the behavior of the individual as a whole

in his response to a certain type of noci-influences. We have been voicing

our argument in terms of physical escape from GROSS physical dangers,

or of grappling with GROSS NERVE-MUSCULAR enemies of the same or of

other species. To explain these phenomena we have invoked the aid

of the laws of natural selection and phylogenetic association.

If our conclusions be correct, then it should follow that in the same

laws we may find the explanation of immunity, which, of course,

means a defensive response to our MICROSCOPIC enemies. There should

be no more difficulty in evolving an efficient army of phagocytes

by natural selection, or in developing specific chemical reactions

against \_\*microscopic enemies\_, than there was in evolving the various

nociceptors for our nerve-muscular defense against our \_\*gross enemies\_.

That immunity is a chemical reaction is no argument against

the application of the law of natural selection or of association.

What essential difference is there between the chemical defense of

the skunk against its NERVE-MUSCULAR enemies and its chemical defense

(immunity) against its MICROSCOPIC ENEMIES?

The administration of vaccines becomes the adequate stimulus which

awakens phylogenetic association of a chemical nature as a result

of which immune bodies are produced.

In discussing this subject I will raise only the question whether

or not the specific character of the inaugural symptoms of some

infectious diseases may be due to phylogenetic association.

These inaugural symptoms are measurably a recapitulation of the leading

phenomena of the disease in its completed clinical picture.

Thus, the furious initiative symptoms of pneumonia, of peritonitis,

or erysipelas, of the exanthemata, are exaggerations of phenomena

which are analogous to the phenomena accompanying physical injury

and fear of physical violence. Just as the acute phenomena of fear,

or those which accompany the adequate stimulation of nociceptors,

are recapitulations of phylogenetic struggles, so may the inaugural

symptoms of an infection be a similar phylogenetic recapitulation

of the course of the disease. A certain amount of negative

evidence is supplied by a comparison of the response to a dose

of toxins with the response to a dose of a standard drug.

No drug in therapeutic dosage except the iodin compounds causes

a febrile response; no drug causes a chill; on the other hand,

all specific toxins cause febrile responses and many cause chills.

If a species of animal had been poisoned by a drug during vast periods

of time, and if natural selection had successfully established

a self-defensive response, then the administration of that drug would

cause a noci-association (chemical), and a specific reaction analogous

to that following the administration of Coley's toxins might be expected.

Bacterial noci-association probably operates through the same

law as that through which physical noci-association operates.

Natural selection is impartial, however. It must be supposed that it

acts impartially upon the microscopic invader and upon the host.

On this ground one must infer that, in accordance with the same law

of natural selection, the bacteria of acute infections have met

by natural selection each advance in the struggle of the host

for immunity. Hence the fast and furious struggle between man

and his microscopic enemies merely indicates to what extent natural

selection has developed the ATTACK and the DEFENSE respectively.

This struggle is analogous to the quick and decisive battles

of the carnivora when fighting among themselves or when contending

against their ancient enemies. But when phylogenetically strange

animals meet each other, they do not understand how to conduct a fight:

natural selection has not had the opportunity of teaching them.

The acute infections have the characteristics of being ancient enemies.

On this hypothesis one can understand the high mortality of measles

when it is introduced into a new country. By natural selection,

measles has become a powerful enemy of the human race, and a race

to which this infection is newly introduced has not had the advantage

of building up a defense against it by the law of natural selection.

May not the phenomena of anaphylaxis be studied on associational lines?

Then, too, there may be chemical noci-associations with enemies

now extinct, which, like the ticklish points, may still be active

on adequate stimulation. This brief reference to the possible

relation of the phenomena of the acute infections to the laws

of natural selection and of specific chemical noci-association has

been made as a suggestion. Since the doctrine of evolution explains

all or nothing, I have included many phenomena to see how reasonable

or unreasonable such an explanation might be.

Recapitulation

The following are the principal points presented: In operations

under inhalation anesthesia the nerve impulses from the trauma

reach every part of the brain--the cerebrum that is apparently

anesthetized as well as the medulla that is known to remain awake--

the proof being the PHYSIOLOGIC exhaustion of and the PATHOLOGIC

change in the nerve-cells. Under ether anesthesia the damage

to the nerve-cells is at least four times greater than under

nitrous oxid. Inhalation anesthesia is, therefore, but a veneer--

a mask that "covers the deep suffering of the patient." The cause

of the exhaustion of the brain is the discharge of nervous energy

in a futile effort to energize the paralyzed muscles in an attempt

to escape from the injury just as if no anesthetic had been given.

The exhaustion is, therefore, of the same nature as that from overexertion,

but if the nerve-paths connecting the field of operation

and the brain be blocked, then there is no discharge of nervous

energy from the trauma, and consequently there is no exhaustion,

however severe or prolonged the operation may be.

Fear is a factor in many injuries and operations. The phenomena

of fear probably are exhibited only by animals whose natural defense

is nerve-muscular. The skunk, the porcupine, the turtle, have little

or no fear. Fear is born of the innumerable injuries which have

been inflicted in the course of evolution. Fear, like trauma,

may cause physiologic exhaustion of and morphologic changes

in the brain-cells. The representation of injury, which is fear,

being elicited by phylogenetic association, may be prevented

by the exclusion of the noci-association or by the administration

of drugs like morphin and scopolamin, which so impair the associational

function of the brain-cells that immunity to fear is established.

Animals whose natural defense is in muscular exertion, among which is man,

may have their dischargeable nervous energy exhausted by fear alone,

or by trauma alone, but most effectively by the combination of both.

What is the mechanism of this discharge of energy? It is the adequate

stimulation of the nociceptors and the physiologic response for the purpose

of self-preservation. According to Sherrington, the nervous system

responds in action as a whole and to but one stimulus at a time.

The integration of the individual as a whole occurs not alone in injury

and fear, but also, though not so markedly, as a result of other

phylogenetic associations, such as those of the chase and procreation.

When adequate stimuli are repeated with such rapidity that the new

stimulus is received before the effect of the previous one has

worn off, a higher maximum effect is produced than is possible

under a single stimulus, however powerful.

Sexual receptors are implanted in the body by natural selection,

and the adequate stimuli excite the nerve-muscular reactions

of conjugation in a manner analogous to the action of the adequate

stimuli of the nociceptors. The specific response of either

the sexual receptors or the nociceptors is at the expense

of the total amount of nervous energy available at the moment.

Likewise in daily labor, which, in the language of evolution,

is the chase, nervous energy is expended. Under the dominance

of fear or injury, however, the integration is most nearly

absolute and probably every expenditure of nervous energy which is

not required for efforts toward self-preservation is arrested;

hence fear and injury drain the cup of energy to the dregs.

This is the potential difference between fear and desire,

between injury and conjugation.

What is the practical application of this? In operative surgery

there is introduced a new principle, which removes from surgery much

of the immediate risk from its trauma by establishing ANOCI-ASSOCIATION;

it places certain of the phenomena of fear on a physical basis;

it explains to us the physical basis for the impairment of the entire

individual under worry or misfortune; it makes evident the physical

results of the daily noci-associations experienced by the individual

as a social unit. On the other hand, it explains the power

of therapeutic suggestion and of other influences which serve

for the time to change the noci-integration; it shows the physical

basis for the difference between hope and despair; it explains

some of the phenomena of Graves' disease, of sexual neurasthenia,

possibly of hay-fever and of the common cold. The principle is probably

equally applicable to the acute infections, in each of which chemical

noci-association gives rise to many of the phenomena of the disease

and it explains their cure by natural immunity and by vaccines.

This hypothesis should teach us to view our patients as a whole;

and especially should it teach the surgeon gentleness. It should

teach us that there is something more in surgery than mechanics,

and something more in medicine than physical diagnosis and drugs.

Conclusion

The brain-cells have existed for eons and, amid the vicissitudes

of change, they have persisted with perhaps less alteration than has

the crust of the earth. Whether in man or in the lower animals,

they are related to and obey the same general biologic laws,

thus being bound to the entire past and performing their function

in accordance with the law of phylogenetic association.

For so long a time have we directed our attention to tumors,

infections, and injuries that we have not sufficiently considered

the vital force itself. We have viewed each anatomic and pathologic

part as an entity and man as an isolated phenomenon in nature.

May we not find in the laws of adaptation under natural selection,

and of phylogenetic association, the master key that will disclose

to us the explanation of many 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 thus may not disease, as well

as health, be given its evolutionary setting?

PHYLOGENETIC ASSOCIATION IN RELATION TO THE EMOTIONS[\*]

[\*] Address before the American Philosophical Society, Philadelphia,

April 22, 1911.

The surgeon is familiar with the manifestations of every variety

of the human emotions in the various stations of 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 accidents, 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, is an experience known only

to the operating surgeon.

For the data for this paper, therefore, in which I shall for the most

part limit my discussion to the strongest of all emotions--FEAR--I have

drawn largely from my personal experience as a surgeon, as well

as from an experimental research in which I have had the valuable

assistance of my associates, Dr. H. G. Sloan, Dr. J. B. Austin,

and Dr. M. L. Menten.

I believe it can be shown that it is possible to elicit the emotion

of fear only in those animals that utilize a motor mechanism

in defense against danger or in escape from it. For example,

the defense of the skunk is a diabolic odor which repels its enemies;

the skunk has no adequate equipment for defense or escape by

muscular exertion, and the skunk therefore shows little or no fear.

Again, certain species of snakes are protected by venom;

they possess no other means of defense nor have they adequate

motor mechanisms for escape and they show no fear. Because of

their strength other animals, such as the lion, the grizzly bear,

and the elephant, show but little fear (Fig. 6). Animals which have

an armored protection, such as the turtle, show little fear.

It is, therefore, obvious that fear is not universal and that the

emotion of fear is felt only by those animals whose self-preservation

is dependent upon an uncertain adequacy of their power of muscular

exertion either for defense or for flight (Fig. 7).

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, muscular relaxation, and staring of the eyes

(Fig. 12). The functions of the brain are wholly suspended except those

which relate to the self-protective response against the feared object.

Neither the brain nor any other organ of the body can respond

to any other lesser stimulus during the dominance of fear.

From these premises it would appear that under the influence

of fear, most, perhaps all, of the organs of the body are divided

sharply into two classes: First, those that are stimulated,

and, second, those that are inhibited. Those that are stimulated

are the entire muscular system, the vasomotor and locomotor systems,

the senses of perception, the respiration, the mechanism for erecting

the hair, the sweat-glands, the thyroid gland, the adrenal gland

(Cannon), and the special senses. On the other hand,

all the digestive and procreative functions are inhibited.

What is the significance of this stimulation of some and inhibition

of other organs? As far as we know, the stimulated organs

increase the efficiency of the animal for fight or for flight.

It is through skeletal muscles that the physical attack or escape

is effected; these muscles alone energize the claws, the teeth,

the hoofs, and the means for flight. The increased action of the

muscles of the heart and the blood-vessels increases the efficiency

of the circulation; the secretion of the adrenal gland causes a rise

in the blood-pressure; the increased action of the thyroid gland causes

an increased metabolic activity; there is evidence that glycogen

is actively called out, this being the most immediately available

substance for the production of energy; the increased activity

of the respiration is needed to supply the greater need of oxygen

and the elimination of the increased amount of waste products;

the dilatation of the nostrils affords a freer intake of air;

the increased activity of the sweat-glands is needed to regulate

the temperature of the body which the increased metabolism causes to rise.

The activity of all the organs of perception--sight, hearing, smell--

is increased in order that the danger may be more accurately perceived.

It cannot be a mere coincidence that the organs and the tissues

that are stimulated in the emotion of fear are precisely those that

are actually utilized in a physical struggle for self-preservation.

Are any other organs stimulated by fear except those that can

or that do assist in making a defensive struggle? I know of none.

On the other hand, if an animal could dispense with his bulky

digestive organs, whose functions are suspended by fear, if he could,

so to speak, clear his decks for battle, it would be to his advantage.

Although the marvelous versatility of natural selection apparently

could devise no means of affording this advantage, it nevertheless shut

off the nervous current and saved the vital force which is ordinarily

consumed by these non-combatants in the performance of their functions.

Whatever may be the origin of fear, its phenomena are due to a

stimulation of all the organs and tissues that add to the efficiency

of the physical struggle for self-preservation and an inhibition

of the func-

{illust. caption = FIG. 19--THE BROAD JUMP. Note the similarity

of the expression to the facial expression of fear and of anger

(Figs. 12 and 21). (Wm. J. Brownlow, drawn from photo.)

tions of the leading organs that do not participate in that struggle--

the non-combatants, so to speak. Fear arose from injury,

and is one of the oldest and surely the strongest emotion.

By the slow process of vast empiricism nature has evolved the

wonderful defensive motor me-chanism of many animals and of man.

The stimulation of this mechanism leading to a physical struggle is action,

and the stimulation of this mechanism without action is emotion.

We may say, therefore, that fear is a PHYLOGENETIC FIGHT OR FLIGHT (Fig.

18). On this hypothesis all the organs and parts {illust. caption

= FIG. 20.-FINISH OF RELAY RACE.

Compare the facial expression of the runners with those in Figs.

12, 19, 22. These pictures illustrate the fact that the same

mechanism is stimulated in emotion as in physical action.

(Photo by Underwood and Underwood, N. Y.)}

of the body are integrated, connected, or correlated for the

self-preservation of the individual by the activity of his motor mechanism

(Figs. 12, 19, and 20). 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 or hindrance in the physical struggle for existence.

By thus concentrating all or most of the nerve force 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 drains

the cup of nervous energy even though no visible action may result.

An animal under the stimulus of fear may be likened to an automobile

with the clutch thrown out but whose engine is racing at full speed.

The gasoline is being consumed, the machinery is being worn,

but the machine as a whole does not move, though the power of its

engine may cause it to tremble.

When this conception is applied to the human beings of today,

certain mysterious phenomena are at once elucidated. It must be borne

in mind that man has not been presented with any new organs to meet

the requirements of his present state of civilization; indeed, not only

does he possess organs of the same type as those of his savage fellows,

but of the same type also as those possessed by the lower animals even.

In fact, man has reached his present status of civilization with

the primary equipment of brutish organs. Perhaps the most striking

difference between man and animals lies in the greater control

which man has gained over his primitive instinctive reactions.

As compared with the entire duration of organic evolution,

man came down from his arboreal abode and assumed his new role

of increased domination over the physical world but a moment ago.

And now, though sitting at his desk in command of the complicated

machinery of civilization, when he fears a business catastrophe

his fear is manifested in the terms of his ancestral physical battle

in the struggle for existence. He cannot fear intellectually,

he cannot fear dispassionately, he fears with all his organs,

and the same organs are stimulated and inhibited as if, instead of it

being a battle of credit, of position, or of honor, it were a physical

battle with teeth and claws. Whether the cause of acute fear

be moral, financial, social, or stage fright, the heart beats wildly,

the respirations are accelerated, perspiration is increased,

there are pallor, trembling, indigestion, dry mouth, etc.

The phenomena are those which accompany physical exertion

in self-defense or escape. There is not one group of phenomena

for the acute fear of the president of a bank in a financial

crash and another for the hitherto trusted official who suddenly

and unexpectedly faces the imminent probability of the penitentiary;

or one for a patient who unexpectedly finds he has a cancer

and another for the hunter when he shoots his first big game.

Nature has but one means of response to fear, and whatever its cause

the phenomena are always the same--always physical.

If the stimulus of fear be repeated from day to day, whether in

the case of a mother anxious on account of the illness of a child;

a business man struggling against failure; a politician under contest

for appointment; a broker in the daily hazard of his fortune;

litigants in legal battle, or a jealous lover who fears a rival;

the countless real as well as the baseless fears in daily life,

in fact, all forms of fear, as it seems to me, express themselves

in like terms of ancestral physical contests. On this law,

fear dominates the various organs and parts of the body.

Anger and fear express opposite emotional states. Fear is the

expression of a strong desire to escape from danger; anger, of a

strong desire to attack physically and to vanquish opposition.

This hypothesis is strongly supported by the outward expressions

of fear and of anger. When the business man is conducting a struggle

for existence against his rivals, and when the contest is at

its height, he may clench his fists, pound the table, perhaps show

his teeth, and exhibit every expression of physical combat.

Fixing the jaw and showing the teeth in anger merely emphasize

the remarkable tenacity of phylogeny. Although the development

of the wonderful efficiency of the hands has led to a modification

of the once powerful canines of our progenitors, the ancestral use

of the teeth for attack and defense is attested in the display of anger.

In all stations of life differences of opinion may lead to argument

and argument to physical combats, even to the point of killing.

The physical violence of the savage and of the brute still lies

surprisingly near the surface (Fig. 21).

We have now presented some of the reasons based largely on gross animal

behavior why fear is to be regarded as a response to phylogenetic

association with physical danger. In further support of this hypothesis,

I shall now present some clinical and experimental evidence.

Although there is not convincing proof, yet there is evidence that

the effect of the stimulus of fear 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.

It is well known that the soldier who, while under fire,

waits in vain for orders to charge, suffers more than the soldier

who flings himself into the fray; and that a wild animal endeavoring

to avoid capture suffers less than one cowering in captivity.

An unexpressed smouldering emotion is measurably relieved by action.

It is probable that the various energizing substances needed in

physical combat, such as the secretions of the thyroid, the adrenals

(Cannon), etc., may cause physical injury to the body when they

are not consumed by action (Fig. 22).

That the brain is definitely influenced--damaged even--

by fear has been proved by the following experiments:

Rabbits were frightened by a dog but were neither injured nor chased.

After various periods of time the animals were killed and their

brain-cells compared with the brain-cells of normal animals--

wide-spread changes were seen (Fig. 13). The principal clinical phenomena

expressed by the rabbit were rapid heart, accelerated respiration,

prostration, tremors, and a rise in temperature. The dog showed

similar phenomena, excepting that, instead of such muscular relaxation

as was shown by the rabbit, it exhibited aggressive muscular action.

Both the dog and the rabbit were exhausted but, although the dog

exerted himself actively and the rabbit remained physically passive,

the rabbit was much more exhausted.

Further observations were made upon the brain of a fox

which had been chased for two hours by members of a hunt club,

and had been finally overtaken by the hounds and killed.

Most of the brain-cells of this fox, as compared with those of a

normal fox, showed extensive physical changes (Fig. 4).

The next line of evidence is offered with some reservation,

but it has seemed to me to be more than mere idle speculation.

It relates to the phenomena of one of the most interesting diseases

in the entire category of human ailments--I refer to exophthalmic goiter,

or Graves' disease, a disease primarily involving the emotions.

This disease is frequently the direct sequence of severe

mental shock or of a long and intensely worrying strain.

The following case is typical: A broker was in his usual health up

to the panic of 1907; during this panic his fortune and that of others

were for almost a year in jeopardy, failure finally occurring.

During this heavy strain he became increasingly nervous and by

imperceptible degrees there developed a pulsating enlargement of

the thyroid gland, an increased prominence of the eyes, marked increase

in perspiration--profuse sweating even--palpitation of the heart,

increased respiration with frequent sighing, increase in blood-pressure;

there were tremor of many muscles, rapid loss of weight and strength,

frequent gastro-intestinal disturbances, loss of normal control

of his emotions, and marked impairment of his mental faculties.

He was as completely broken in health as in fortune.

These phenomena resembled closely those of fear and followed

in the wake of a strain which was due to fear.

In young women exophthalmic goiter often follows in the wake

of a disappointment in love; in women, too, it frequently follows

the illnesses of children or parents during which they have had

to endure the double strain of worry and of constant care.

Since such strains usually fall most heavily upon women, they are

the most frequent victims of this disease. Now, whatever the exciting

cause of exophthalmic goiter, whether it be unusual business worry,

disappointment in love, a tragedy, or the illness of a loved one,

the symptoms are alike and closely resemble the phenomena of one

of the great primitive emotions. How could disappointment in love

play a role in the causation of Graves' disease? If the hypothesis

which has been presented as an explanation of the genesis and

the phenomena of fear be correct, then that hypothesis explains

also the emotion of love. If fear be a phylogenetic physical

defense or escape which does not result in muscular action,

then love is a phylogenetic conjugation without physical action.

The quickened pulse, the leaping heart, the accelerated respiration,

the sighing, the glowing eye, the crimson cheek, and many other

phenomena are merely phylogenetic recapitulations of ancestral acts.

The thyroid gland is believed to participate in such physical activities.

Hence it may well follow that the disappointed maiden who is intensely

integrated for a youth will, at every thought of him, be subjected

by phylogenetic association to a specific stimulation analogous

to that which attended the ancestral consummation. Moreover, a happy

marriage has many times been followed by a cure of the exophthalmic

goiter which appeared in the wake of such an experience.

The victims of Graves' disease present a counterpart of

emotional exhaustion. That the emotions in Graves' disease are

abnormally acute is illustrated by my personal observation

of the death of a subject of this disease from fear alone.

Whatever the exciting cause of this disease, the symptoms are the same;

just as in fear, the phenomena are the same whatever the exciting cause.

Figures 12 and 16 show the resemblance between the outward appearances

of a patient with Graves' disease and of a person obsessed by fear.

Fear and Graves' disease have the following phenomena in common:

Increased heart-beat, increased respiration, rising temperature,

muscular tremors, protruding eyes, loss in weight; Cannon has found

an increased amount of adrenalin in the blood in fear and Frankel

in Graves' disease; increased blood-pressure; muscular weakness;

digestive disturbances; impaired nervous control; hypersusceptibility

to stimuli; in protracted intense fear the brain-cells show marked

physical changes, and in Graves' disease analogous changes are seen

(Figs. 13 C and 15). In Graves' disease there seems to be a composite

picture of an intense expression of the great primitive emotions.

If Graves' disease be a disease of the great primitive emotions,

or rather of the whole motor mechanism, how is the constant flow

of stimulation of this complicated mechanism supplied? It would

seem that there must be secreted in excessive amount some substance

that activates the motor mechanism. The nervous system in Graves'

disease is hypersusceptible to stimuli and to thyroid extract.

It might follow that even a normal amount of thyroid secretion would

lead to excessive stimulation of the hypersusceptible motor mechanism.

This condition of excessive motor activity and hyperexcitability may

endure for years. What is the source of this pathologic excitation?

The following facts may give a clue. In suitable cases of Graves'

disease, if the thyroid secretion is sufficiently diminished by a removal

of a part of the gland or by interrupting the nerve and the blood supply,

the phenomena of the disease are diminished immediately, and in favorable

cases the patient is restored to approximately the normal condition.

The heart action slows, the respiratory rate falls, the restlessness

diminishes, digestive disturbances disappear, tremors decrease,

there is a rapid increase in the body weight, and the patient gradually

resumes his normal state. On the other hand, if for a period

of time extract of the thyroid gland is administered to a normal

individual in excessive dosage, there will develop nervousness,

palpitation of the heart, sweating, loss of weight, slight protrusion

of the eyes, indigestion; in short, most of the phenomena of Graves'

disease and of the strong emotions will be produced artificially

(Figs. 15 and 23). When the administration of the thyroid extract

is discontinued, these phenomena may disappear. On the other hand,

when there is too little or no thyroid gland, the individual

becomes dull, stupid, and emotionless, though he may be irritable;

while if a sufficient amount of thyroid extract be given to such

a patient he may be brought back to his normal condition.

Hence we see that the phenomena of the emotions may within certain

limits be increased, diminished, or abolished by increasing,

diminishing, or totally excluding the secretion of the thyroid gland.

Graves' disease may be increased by giving thyroid extract and by fear.

It may be diminished by removing a part of the gland, or by

interrupting the blood and nerve supply, or by complete rest.

In addition, at some stage of Graves' disease there is an

increase in the size and in the number of the secreting cells.

These facts regarding the normal and the pathologic supply of thyroid

secretion point to this gland as one of the sources of the energizing

substance or substances, by means of which the motor phenomena

of animals are executed and their emotions expressed.

Anger is similar to fear in origin and, like fear, is an integration

and stimulation of the motor mechanism and its accessories.

Animals which have no natural weapons for attack experience neither

fear nor anger, while the animals which have weapons for attack

express anger principally by energizing the muscles used in attack.

Although, as has already been stated, the efficiency of the hands

of man has largely supplanted the use of the teeth, he still shows

his teeth in anger and so gives support to the theory that this

emotion is of remote ancestral origin and proves the great persistence

of phylogenetic association. On this conception we can understand

why it is that a patient consumed by worry--which to me signifies

interrupted stimulation, a state of alternation between hope

and fear--suffers so many bodily impairments and diseases even.

This hypothesis explains the slow dying of animals in captivity.

It explains the grave digestive and metabolic disturbances which

appear under any nerve strain, especially under the strain of fear,

and the great benefits of confidence and hope; it explains the nervousness,

loss of weight, indigestion--in short, the comprehensive physical

changes that are wrought by fear and by sexual love and hate.

On this hypothesis we can understand the physical influence

of one individual over the body and personality of another;

and of the infinite factors in environment that, through phylogenetic

association, play a role in the functions of many of our organs.

It is because under the uncompromising law of survival of the fittest

we were evolved as motor beings that we do not possess any organs or

faculties which have not served our progenitors in accomplishing their

survival in the relentless struggle of organic forms with one another.

We are now, as we were then, essentially motor beings, and the only way in

which we can meet the dangers in our environment is by a motor response.

Such a motor response implies the integration of our entire being

for action, this integration involving the activity of certain glands,

such as the adrenals (Cannon), the thyroid, the liver, etc., which throw

into the blood-stream substances which help to form energy, but which,

if no muscular action ensues, are harmful elements in the blood.

While this motor preparation is going on, the entire digestive

tract is inhibited. It thus becomes clear why an emotion is more

harmful than action.

Any agency that can sufficiently inspire faith,--dispel worry,--

whether that agency be mystical, human, or divine, will at once

stop the body-wide stimulations and inhibitions which cause

lesions which are as truly physical as is a fracture.

The striking benefits of good luck, success, and happiness;

of a change of scene; of hunting and fishing; of optimistic

and helpful friends, are at once explained by this hypothesis.

One can also understand the difference between the broken body

and spirits of an animal in captivity and its buoyant return to its

normal condition when freed.

But time will not permit me to follow this tempting lead, which has

been introduced for another purpose--the proposal of a remedy.

Worries either are or are not groundless. Of those that have

a basis, many are exaggerated. It has occurred to me to utilize

as an antidote an appeal to the same great law that originally

excited the instinctive involuntary reaction known as fear--

the law of self-preservation.

I have found that if an intelligent patient who is suffering from

fear can be made to see so plainly as to become firmly convinced

that his brain, his various organs, indeed his whole being,

could be physically damaged by fear, that this same instinct of

self-preservation will, to the extent of his conviction, banish fear.

It is hurling a threatened active militant danger, whose injurious

influences are both certain and known, against an uncertain,

perhaps a fancied, one. In other words, fear itself is an injury

which when recognized is instinctively avoided. In a similar manner

anger may be softened or banished by an appeal to the stronger

self-preserving instinct aroused by the fear of physical damage,

such as the physical injury of brain-cells. This playing of one

primitive instinct against another is comparable to the effect

produced upon two men who are quarreling when a more powerful enemy

of both comes threateningly on the scene.

The acute fear of a surgical operation may be banished by the use

of certain drugs that depress the associational power of the brain and

so minimize the effect of the preparations that usually inspire fear.

If, in addition, the entire field of operation is blocked by local

anesthesia so that the associational centers are not awakened,

the patient will pass through the operation unscathed.

The phylogenetic origin of fear is injury, hence injury and fear cause

the same phenomena. In their quality and in their phenomena psychic

shock and traumatic shock are the same. The perception of danger

by the special senses in the sound of the opening gun of a battle,

or in the sight of a venomous snake, is phylogenetically the same

and causes the same effects upon the entire body as an operation under

anesthesia or a physical combat in that each drives the motor mechanism.

The use of local anesthetics in the operative field prevents

nerve-currents from the seat of injury from reaching the brain and there

integrating the entire body for a self-defensive struggle. The result,

even though a part of the brain is asleep and the muscles paralyzed,

is the same as that produced by the interception of the terrifying

sound of the gun, or of the sight of the dangerous reptile,

since the stimulation of the motor mechanism is prevented.

By both the positive and the negative evidence we are forced

to believe that the emotions are primitive instinctive reactions

which represent ancestral acts; and that they therefore utilize

the complicated motor mechanism which has been developed by the forces

of evolution as that best adapted to fit the individual for his

struggle with his environment or for procreation.

The mechanism by which the motor acts are performed and the mechanism

by which the emotions are expressed are one and the same.

These acts in their infinite complexity are suggested by association--

phylogenetic association. When our progenitors came in contact

with any exciting element in their environment, action ensued then

and there. There was much action--little restraint or emotion.

Civilized man is really in auto-captivity. He is subjected

to innumerable stimulations, but custom and convention frequently

prevent physical action. When these stimulations are sufficiently

strong but no action ensues, the reaction constitutes an emotion.

A phylogenetic fight is anger; a phylogenetic flight is fear;

a phylogenetic copulation is sexual love, and so one finds in this

conception an underlying principle which may be the key to an

understanding of the emotions and of certain diseases.

PAIN, LAUGHTER, AND CRYING[\*]

[\*] Address delivered before the John Ashhurst, Jr.. Surgical Society

of the University of Pennsylvania, May 3, 1912.

PAIN

Pain, like other phenomena, was probably evolved for a particular purpose--

surely for the good of the individual; like fear and worry,

it frequently is injurious. What then may be its purpose?

We postulate that pain is one of the phenomena which result

from a stimulation to motor action. When a barefoot boy steps

on a sharp stone it is important that the injuring contact be

released as quickly as possible; and therefore physical injury pain

results and impels the required action. Anemia of the soft parts

at the points of pressure results from prolonged sitting or lying

in one position, and as a result pain compels a muscular action

that shifts the damaging pressure--this is the pain of anemia;

when the rays of the blazing sun shine directly upon the retina,

pain immediately causes a protective muscular action--the lid is closed,

the head turns away--this is light pain; when standing too close

to a blazing fire the excessive heat causes a pain which results

in the protective muscular action of moving away--this is heat pain;

when the urinary bladder is acutely overdistended the resultant

pain induces voluntary as well as involuntary muscular contraction--

this is evacuation pain; associated with defecation is a characteristic

warning pain, and an active pain which induces the required

muscular action--this, like the pain accompanying micturition,

is an evacuation pain; in obstruction of the urinary passages

and of the large and the small intestine the pain is exaggerated,

as is the accompanying muscular contraction--this is a pathologic

evacuation pain; when the fetus reaches full term and labor is

to begin, it is heralded by pain which is associated with rhythmic

contractions of the uterine muscle; later, many other muscles

take part in the birth and pain is associated with all these

muscular contractions--these are labor pains; when a foreign body,

be it ever so small, falls upon the conjunctiva or cornea there

results what is perhaps the acutest pain known, and quick and active

muscular action follows--this is special contact pain. Special pain

receptors are placed in certain parts of the nose, the pharynx,

and the larynx, the stimulation of which causes special motor acts,

such as sneezing, hawking, coughing. Curiously vague pains are

associated with the protective motor act of vomiting and with the sexual

motor acts--these may be termed nausea pains and pleasure pains.

We now see, therefore, that against the injurious physical contacts

of environment, against heat and cold, against damaging sunlight,

against local anemia when resting or sleeping, the body is protected

by virtue of the muscular action which results from pain.

Then, too, for the emptying of the pregnant uterus, for the evacuation

of the intestine and of the urinary bladder as normal acts,

and for the overcoming of obstructions in these tracts,

pain compels the required muscular actions, For passing gall-stones

and urinary calculi, urgent motor stimuli are awakened by pain.

For each of these diversified pains the consequent muscular action

is specific in type, distribution, and intensity. This statement

is so commonplace that we are apt to miss the significance and

the wonder of it. It is probable that every nerve-ending in the skin

and every type of stimulation represents a separate motor pattern,

the adequate stimulation of which causes always the same response.

Let us pass on to the discussion of another and perhaps even

more interesting type of pain, that associated with infection.

Not all kinds of infection are painful; and in those infections

that may be associated with pain there is pain only when certain

regions of the body are involved. Among the infections that are not

associated with pain are scarlet fever, typhoid fever, measles, malaria,

whooping-cough, typhus fever, and syphilis in its early stages.

The infections that are usually, though not always, associated with

pain are the pyogenic infections. The pyogenic infections

and the exanthemata constitute the great majority of infections

and are the basis of the discussion which follows.

I will state one of my principal conclusions first, \_i.

e\_., that the only types of infection that are associated with pain

are those in which the infection may be spread by muscular action

or those in which the fixation of parts by continued muscular

rigidity is an advantage; and, further, as a striking corollary,

that the type of infection that may cause muscular action when it

attacks one region of the body may cause no such action when it

attacks another region.

The primary, and perhaps the most striking, difference between

the painless exanthemata and the painful pyogenic infections is that

in the case of the exanthemata the protective response of the body

is a chemical one,--the formation of antibodies in the blood,

which usually produce permanent immunity,--while the response to the

pyogenic infections is largely phagocytic. In the pyogenic infections,

in order to protect the remainder of the body, which, of course,

enjoys no immunity, every possible barrier against the spread

of the infection is thrown about the local point of infection.

How are these barriers formed? First, lymph is poured out, then the part

is fixed by the continuous contraction of the neighboring muscles

and by the inhibition of those muscles that, in the course of their

ordinary function, would by their contractions spread the infection.

Wherever there is protective muscular rigidity there is also pain.

On the other hand, in pyogenic infections in the substance

of the liver, in the substance of the kidney, within the brain,

in the retroperitoneal space, in the lobes of the lung, in the chambers

of the heart and in the blood-vessels of the chest and the abdomen,

in all locations in which muscular contractions can in no way assist

in localizing the disease, pyogenic infections produce no muscular

rigidity and no pain. Apparently, therefore, only those infections are

painful which are associated with a protective muscular contraction.

This explains why tuberculosis of the hip is painful, while tuberculosis

of the lung is painless.

There is a third type of pain which modifies muscular action

in a curious way. We have already stated that local pain serves

an adaptive purpose. In this light let us now consider headache.

Headache is one of the commonest initiatory symptoms of the

various infections, especially of those infections which are

accompanied by no local pain and by no local muscular action.

In peritonitis, cholecystitis, pleurisy, arthritis, appendicitis,

salpingitis, child-birth, in obstructions of the intestinal

and the genito-urinary tract, in short, in those acute processes

in which the local symptoms are powerful enough to govern

the individual as a whole,--to make him lie down and keep quiet,

refuse food and possibly reject what is already in the stomach,--

in all these conditions there is rarely a headache, but in the diseases

in which local pain is absent, such as the exanthemata, typhoid fever,

and auto-intoxication, which have no dominating local disturbances

to act as policemen to put the individual to bed and to make him

refuse food that he may be in the most favorable position to combat

the oncoming disease, in such cases in which these masterful and

beneficent local influences are absent we postulate that headache

has been evolved to perform this important service.

On the hypothesis that it is good for the individual who is acutely

stricken by a disease or who is poisoned by autointoxication to rest

and fast, and that the muscular system obeys the imperial command

of pain, and in view of the fact that the brain is not only in constant

touch with the conditions of every part of the body but that it

is also the controlling organ of the body, one would expect that in

these diseases the major pain whose purpose it is to govern general

muscular action would be located in the head and there we find it.

How curious and yet how intelligible is the fact that, though a

headache may be induced by even a slight auto-intoxication,

an abscess may exist within the brain without causing pain.

When an obliterative endarteritis is threatening a leg with

anemic gangrene, or when one lies too long in the same position on

a hard bed, there is threatening injury from local anemia, and as a

result there is acute pain, but when the obliterative endarteritis

threatens anemia of the brain, or when an embolism or thrombosis has

produced anemia of the brain, there may be no accompanying pain.

The probable explanation of the pain which results in the first instance

and the lack of pain in the second is that in the former muscular action

constitutes a self-protective response, but in the other it does not.

Diseases and injuries of the brain are notoriously difficult

to diagnosticate. This may well be because it has always been so well

protected by the skull that there have been evolved within it few

tell-tale self-protective responses, so that in the presence of injury

and disease within itself the brain remains remarkably silent.

It should occasion no surprise that there are in the brain no receptors,

the mechanical stimulation of which can cause pain, because its bony

covering has always prevented the adaptive implantation within it

of contact pain receptors. Dr. Frazier tells me that in the course

of his operations on the brains of unanesthetized patients

he is able to explore the entire brain freely and without pain.

From my own experience I am able to confirm Dr. Frazier's observation.

In addition, the two-stage operation for the excision of the Gasserian

ganglion provides an observation of extraordinary interest.

If at the first seance the ganglion is exposed, but is not disturbed

except by the iodoform gauze packing, then on the following

day the gauze may be removed, the ganglion picked up, and its

branches and root excised without anesthesia and without pain.

The same statement and explanation may be made regarding the distribution

of pain receptors for physical contact within the parenchyma of the liver,

the gall-bladder, the abdominal viscera, the spleen, the heart,

the lungs, the retroperitoneal tissue, the deep tissue of the back,

the vertebrae, and in certain portions of the spinal cord.

Just what is the distribution of the receptors for heat and for cold

I am unable to state, but this much we do know, that without

anesthesia the intestines may be cauterized freely without the least

pain resulting, and in animals the cauterization of the brain causes

no demonstrable change in the circulatory or respiratory reactions.

It is probable therefore that the distribution of the pain receptors

for physical contact and for heat are limited to those parts of the body

that have been exposed to injurious contacts with environment.

Of special significance is the pain which is due to cold,

which increases muscular tone and produces shivering. The general

increase in muscular tone produces an interesting postural phenomenon:

the limbs are flexed and the body bent forward, a position which probably

is due to the fact that the flexors are stronger than the extensors.

As muscular action is always accompanied by heat production,

the purpose of the muscular contraction and the shivering

is quite certainly caused by cold to assist in the maintenance

of the normal body temperature.

We have now discussed many of the causes of pain and in each instance

we have found an associated muscular action which apparently

serves some adaptive purpose (Figs. 24 and 25). If we assume

that pain exists for the purpose of stimulating muscular reactions,

we may well inquire what part of the nervous are is the site of

the sensation of pain--the nerve-endings, the trunk, or the brain?

Does pain result from physical contact with the nerve-endings, with

the physical act of transmitting an impression along the nerve trunk,

or with the process within the brain-cells by which energy is released

to cause a motor act?

It seems most probable that the site of the pain is in the brain-cells.

If this be so, then what is the physical process by which the

phenomena of pain are produced? The one hypothesis that can be

tested experimentally is that pain is a phenomenon resulting from

the rapid discharge of energy in the brain-cells. If this be true,

then if every pain receptor of the body were equally stimulated

in such a manner that

{illust. caption = FIG. 25.--FEAR AND AGONY. "Amid this dread

exuberance of woe ran naked spirits wing'd with horrid fear."--

Dante's "Inferno," Canto XXIV, lines 89, 90. all the stimuli

reached the brain-cells simultaneously, the cells would find

themselves in equilibrium and no motor act would be performed.

But if all the pain receptors of the body but one were equally stimulated,

and this one stimu-lated harder than the rest, then the latter

would gain possession of the final common path, the sensation

of pain would be felt, and a muscular contraction would result.

It is well known that when a greater pain is thrown into

competition with a lesser one, the lesser is completely submerged.

In this manner the school-boy initiates the novice into the mystery

of the painless plucking of hair. The simultaneous, but severe

application of the boot to the blindfolded victim takes complete

and exclusive possession of the final common path and the hair

is painlessly plucked through the triumph of the boot stimulus over

the hair stimulus in the struggle for the possession of the final

common path. Another argument in favor of this hypothesis that

pain is an accompaniment of the release of energy in the brain-

cells is found in the fact that painless stimuli received through

the special senses may completely submerge the painful stimuli

of physical injury; for although the stimuli to motor action,

which are received through the senses of sight, hearing, and smell,

cause even more powerful motor action than those caused by

physical contact stimuli, yet they are not accompanied by pain.

Examples of this triumph of stimulation of the special senses over

contact stimulation are frequently seen in persons obsessed by anger

or fear, and to a less degree in those obsessed by sexual emotion.

In the fury of battle the soldier may not perceive his wound until

the emotional excitation is wearing away, when the sensation

of warm blood on the skin may first attract his attention.

Religious fanatics are said to feel no pain when they subject themselves

to self-injury. Now, since both psychic and mechanical stimuli cause motor

action by the excitation ofprecisely the same mechanism in the brain,

and since the more rapid release of energy from psychic stimuli

submerges the physical stimuli and prevents pain, it would seem

that pain must be a phenomenon which is associated with the process

of releasing energy by the brain-cells. Were physical injury inflicted

in a quiescent state equal to that inflicted in the emotional state,

great pain and intense muscular action would be experienced.

Now the emotions are as purely motor excitants as is pain.

The dynamic result is the same the principal difference being the greater

suddenness and the absolute specificity of the pain stimuli as compared

with the more complex and less peremptory stimuli of the emotions.

A further evidence that pain is a product of the release of brain-cell

energy is the probability that if one could pierce the skin at

many points on a limb in such a manner that antagonistic points

only were equally and simultaneously stimulated, then an equilibrium

in the governing brain- cells would be established and neither

pain nor motion would follow. An absolute test of this assumption

cannot be made but it is supported by the obtainable evidence.

We will now turn to a new viewpoint, a practical as well as a

fascinating one, which can best be illustrated by two case histories:

A man, seventy-eight years old, whose chief complaint was obstinate

constipation, was admitted to the medical ward of the Lakeside Hospital

several years ago. The abdomen was but slightly distended;

there was no fever, no increased leukocytosis, no muscular rigidity,

and but slight general tenderness. He claimed to have lost in weight

and strength during the several months previous to his admission.

A tentative diagnosis of malignant tumor of the large intestine was made,

but free movements weresecured rather easily, and we abandoned

the idea of an exploratory operation. The patient gradually failed

and died without a definite diagnosis having been made by either

the medical or the surgical service. At autopsy there was found

a wide-spread peritonitis arising from a perforated appendix.

A child, several years old, was taken ill with some indefinite disease.

A number of the ablest medical and surgical consultants of a leading

medical center thoroughly and repeatedly investigated the case.

Although they could make no definite diagnosis they all

agreed that the trouble surely could not be appendicitis

because there was neither muscular rigidity nor tenderness.

The autopsy showed a gangrenous appendix and general peritonitis.

How can these apparently anomalous cases be explained?

These two cases are illustrations of the same principle that underlies

the freedom from pain which results from the use of narcotics

and anesthetics, the same principle that explains the fact that

cholecystitis may occur in the aged without any other local symptoms

than the presence of a mass and perhaps very slight tenderness;

and that accounts in general for the lack of well-expressed disease

phenomena in senility and in infancy. The reason why the aged,

the very young, and the subjects of general paresis show but few

symptoms of disease is that in senility the brain is deteriorated,

while in infancy the brain is so undeveloped that the mechanism

of association is inactive, hence pain and tenderness,

which are among the oldest of the associations, are wanting.

Senility and infancy are by nature normally narcotized.

The senile are passing through the twilight into the night;

while infants are traversing through the dawn into the day.

Hence it is that the diagnosis of injury and disease in the extremes

oflife is beset by especial difficulties, since the entire body

is as silent as are the brain, the pericardium, the mediastinum,

and other symptomless areas. For the same reason, when a patient

who is seriously ill with a painful disease turns upon the physician

a glowing eye and an eager face, and remarks how comfortable he feels,

then the end is near. This is a brilliant and fateful clinical mirage.

When one reflects on the vast amount of evidence as to the origin

and the purpose of pain, he is forced to conclude that pain is

a phenomenon of motor stimulation, and that its principal role is

the protection of the individual against the gross and the microscopic

enemies in his environment. The benefits of pain are especially

manifested in the urgent muscular actions by means of which the body

moves away from physical injury; obstructions of the hollow

viscera are overcome; rest is compelled in the acute infections--

the infected points are held rigidly quiet, the muscles of the abdomen

are fixed, and harmful peristalsis is arrested in peritonitis;

while there is absolutely no pain in the diseases or injuries

which affect those regions of the body in which in the course

of evolution no pain receptors were placed, or in those diseases

in which muscular inhibition or contraction is of no help.

In a biologic sense pain is closely associated with the emotional stimuli,

for both pain and the emotions incite motor activity for the good

of the individual. The frequent occurrence of post-operative and

post- traumatic pain is accounted for by the fact that the operation

or the injury has lowered the threshold of the brain- cells to trauma;

the brain and not the local sensitive field is the site of the pain.

I have found that, by blockingthe field of operation with

local anesthesia, post-operative pain is diminished; that is,

since the local anesthesia prevents the strong stimuli of the

trauma from reaching the brain, its threshold is not lowered.

There is a close resemblance between the phenomena of pain habit,

of education, of physical training, of love and of hate. In education,

in pain habit, in all emotional relations, a low brain- cell threshold

is established which facilitates the reception of specific stimuli;

all these processes are motor acts, or are symbolic of motor acts,

and we may be trained to perceive misfortune and pain as readily as we

are trained to perceive mathematical formulae or moral precepts.

In each and every case, readiness of perception depends, as it seems to me,

upon a modified state of the brain-cells, their threshold especially,

the final degree of perception possible in any individual being perhaps

based on the type of potential molecules of which the brain is built.

We must believe also that every impression is permanent, as only thus

could an individual animal or a man be fitted by his own experience

for life's battles. LAUGHTER AND CRYING What is laughter?

What is its probable origin, its distribution, and its purpose?

Laughter is an involuntary rhythmic contraction of certain

respiratory muscles, usually accompanied by certain vocal sounds.

It is a motor act of the respiratory apparatus primarily, although if

intense it may involve not only the extraordinary muscles of respiration,

but most of the muscles of the body. There are many degrees

of laughter, from the mere brightening of the eyes, a fleeting smile,

tittering andgiggling, to hysteric and convulsive laughter.

Under certain circumstances, laughter may be so intense and

so long continued that it leads to considerable exhaustion.

The formation of tears is sometimes associated with laughter.

When integrated with laughter, the nervous system can perform

no other function. Crying is closely associated with laughter,

and in children especially laughter and crying are readily interchanged.

We postulate that laughter and weeping serve a useful purpose.

According to Darwin, only man and monkeys laugh (Fig. 26);

other animals exhibit certain types of facial expression accompanying

various emotions, but laughter in the sense in which that word

is commonly used is probably an attribute of the primates only,

although it is probable that many animals find substitutes for laughter.

The proneness of man to laughter is modified by age, sex, training,

mental state, health, and by many other factors. Healthy, happy children

are especially prone to laughter, while disease, strong emotions,

fatigue, and age diminish laughter. Women laugh more than do men.

The healthy, happy maturing young woman perhaps laughs most, especially

when she is slightly embarrassed. What causes laughter? Good news,

high spirits, tickling, hearing and seeing others laugh; droll stories;

flashes of wit; passages of humor; averted injury; threatened breach

of the conventions; and numerous other causes might be added.

It is obvious that laughter may be produced by diverse influences,

many of which are so unlike each other that it would at first sight

seem improbable that a single general principle underlies all.

Before presenting a hypothesis which harmonizes most of the facts,

and which mayoffer an explanation of the origin and purpose of laughter,

let us return for a moment to some previous considerations--

that man is essentially a motor being; that all his responses to

the physical forces of his environment are motor; {illust. caption

= FIG. 26.--LAUGHING CHIMPANZEE. "Mike," the clever chimpanzee

in the London Zoo, evidently enjoys a joke as well as any one else.

(Photo by Underwood and Underwood, N. Y.)}

that thoughts and words even are symbolic of motor acts;

that in the emotions of fear, of anger, and of sexual love

the whole body is integrated for acts which are not performed.

These integrations stimulate the brain-cells, the ductless glands,

and other parts, and the energizing secretions, among which are epinephrin,

thyroid and hypophyseal secretions, are thrown into the blood-stream,

while that most available fuel, glycogen, is also mobilized in the blood.

This body-wide preparation for action may be designated kinetic reaction.

The fact that emotion is more injurious to the body than is

muscular action is well known, the difference being probably caused

by the fact that when there is action the above-mentioned products

of stimulation are consumed, while in stimulation without action

they are not consumed and must be eliminated as waste products.

Now these activating substances and the fuel glycogen may be consumed

by any muscular action as well as by the particular muscular action

for which the integration and consequent stimulation were made;

that is, if one were provoked to such anger that he felt impelled

to attack the object of his anger, one of three things might happen:

First, he might perform no physical act but give expression to

the emotion of anger; second, he might engage in a physical struggle

and completely satisfy his anger; third, he might immediately engage

in violent gymnastic exercises and thus consume all the motor-producing

elements mobilized by the anger and thus clarify his body.

In these premises we find our explanation of the origin and purpose

of laughter and crying, for since they consist almost wholly

of muscular exertion, they serve precisely such clarifying purposes

as would be served by the gymnastic exercises of an angry man.

As it seems to me, the muscular action of laughter clears the system

of the energizing substances which have been mobilized in various

parts of the body for the performance of other actions (Figs. 27

to 29). If this be true, the first question that presents itself is,

Why is the respiratory system utilized for such a clarifying purpose?

Why do we not laugh with our feet and hands as well?

Were laughter expressed with the hands, the monkey might fall

from the tree and, if by the feet, man might fall to the ground.

He would at least be ataxic. In fact, laughter has the great

advantage of utilizing a group of powerful muscles which can be

readily spared without seriously interfering with the maintenance

of posture. Laughter, however, is only one form of muscular action

which may consume the fuel thrown into the blood by excitation.

That these products of excitation are often consumed by other motor

acts than laughter is frequently seen in public meetings when

the stamping of feet and the clapping of hands in applause gives

relief to the excitation (Fig. 30). Why the noise of laughter?

In order that the products of excitation may be quickly and

completely consumed, the powerful group of expiratory muscles must

have some resistance against which they can exert themselves strongly

and at the same time provide for adequate respiratory exchange.

The intermittent closure of the epiglottis serves this purpose admirably,

just as the horizontal bars afford the resistance against which muscles

may be exercised. The facial muscles are not in use for other purposes,

hence their contractions will consume a little of the fuel.

An audience excited by the words of an impassioned speaker undergoes

a body-wide stimulation for action, all of which may be eliminated

by laughter or by applause (Fig. 31).

Let us test this hypothesis by some practical examples.

The first is an incident that accidentally occurred in our laboratory

during experiments on fear which were performed as follows:

A keen, snappy fox terrier was completely muzzled by winding a broad strip

of adhesive plaster around his jaw so as to include all but the nostrils.

When this aggressive little terrier and the rabbit found themselves

in close quarters each animal became completely governed by instinct;

the rabbit crouched in fear, while the terrier, with all the ancestral

assurance of seizing his prey, rushed, upon the rabbit, his muzzle

always glancing off and his attack ending in awkward failure.

This experiment was repeated many times and each time provoked

the serious-minded scientific visitors who witnessed it

to laughter. Why? Because the spectacle of a savage little terrier

rushing upon an innocent rabbit as if to mangle it integrated

the body of the onlooker with a strong desire to exert muscular

action to prevent the cruelty. This integration caused a conversion

of the potential energy in the brain-cells into kinetic energy,

and there resulted a discharge into the blood-stream of activating

internal secretions for the purpose of producing muscular action.

Instantly and unexpectedly the danger passed and the preparation

for muscular action intended for use in the protection of the rabbit

was not needed. This fuel was consumed by the neutral muscular

action of laughter, which thus afforded relief.

A common example of the same nature is that encountered on the street

when a pedestrian slips on a banana peel and, just as he is

about to tumble, recovers his equilibrium. The onlookers secure

relief from the integration to run to his rescue by laughing.

On the other hand, should the same pedestrian fall and fracture

his skull the motor integration of the onlookers would be consumed

by rendering physical assistance--hence there would be no laughter.

In children almost any unexpected phenomenon, such as a sudden "booing"

from behind a door, is attended by laughter, and in like manner

the kinetic reaction produced by the innumerable threats of danger

which are suddenly averted, a breach of the conventions, a sudden

relief from acute nervous tension; a surprise--indeed, any excitant

to which there is no predetermined method of giving a physical response--

may be neutralized by the excitation of the mechanism of laughter.

In the same way the laughter excited by jokes may be explained.

An analysis of a joke shows that it is composed of two parts--

the first, in which is presented a subject that acts as a stimulus

to action, and the second, in which the story turns suddenly

so that the stimulus to action is unexpectedly withdrawn.

The subject matter of the joke affects each hearer according

to the type of stimuli that commonly excites that individual.

Hence it is that a joke may convulse one person while it bores another,

and so there are jokes of the classes, bankers' jokes, politicians' jokes,

the jokes of professional men, of the plebeian, of the artist, etc.

If the joke fails, the integration products of the excitation may

be used in physical resentment (Fig. 32).

Another type of laughter is that associated with the ticklish points

of certain parts of the body, the soles of the feet and certain

parts of the trunk and of the abdomen. The excitation of the

ticklish receptors, like pain, compels self-defensive motor acts.

This response is of phylogenetic origin, and may be awakened only

by stimuli which are too light to be painful. In this connection

it is of interest to note that a superficial, insect-like contact

with the skin rarely provokes laughter, and that the tickling

of the nasal, oral, and pulmonary tracts does not produce laughter.

The ticklish points that cause laughter are rather deeply placed,

and a certain type of physical contact is required to constitute

an adequate stimulus. That is, the contact must arouse a phylogenetic

association with a physical struggle or with physical exertion.

In the foot, the adequate stimuli for laughter are such contacts

as resemble or suggest piercing by stones or rough objects.. The

intention of the one who tickles must be known; if his intention

be playful, laughter results, whereas if injury be intended,

then an effort toward escape or defense is excited, but no laughter.

If deep tickling of the ribs is known to be malicious, it will excite

physical resentment and not laughter. Self-tickling rarely causes

laughter for the reason that auto-tickling can cause only a known

degree of stimulation, so that there results no excessive integration

which requires relief by the neutral muscular activity of laughter.

In fact, one never sees purposeful acts and laughter associated.

According to its severity, an isolated stimulus causes either

an action or laughter. The ticklish points in our bodies were

probably developed as a means of defense against serious attacks

and of escape from injurious contacts.

Anger, fear, and grief are also strong excitants and, therefore,

are stimuli to motor activity. It is obvious that whatever the excitant

the physico-chemical action of the brain and the ductless glands

cannot be reversed--the effect of the stimulus cannot be recalled,

therefore either a purposeful muscular act or a neutralizing act

must be performed or else the liberated energy must smoulder

in the various parts of the body.

It is on this hypothesis that the origin and the purpose of laughter

and crying may be understood. Even a superficial analysis of the

phenomena of both laughter and crying show them to be without any

external motor purpose; the respiratory mechanism is intermittently

stimulated and inhibited; and the shoulder and arm muscles, indeed,

many muscles of the trunk and the extremities are, as far as any

external design is concerned, purposelessly contracted and released

until the kinetic energy mobilized by excitation is utilized.

During this time the facial expression gives the index to

the mental state.

Crying, like laughter, is always preceded by a stimulation

to some motor action which may or may not be performed

(Figs. 33 and 34). If a mother is anxiously watching the course

of a serious illness of her child and if, in caring for it, she is

stimulated to the utmost to perform motor acts, she will continue

in a state of motor tenseness until the child recovers or dies.

If relief is sudden, as in the crisis of pneumonia, and the mother

is not exhausted, she will easily laugh if tired, she may cry.

If death occurs, the stimulus to motor acts is suddenly

withdrawn and she then cries aloud, and performs many motor

acts as a result of the intense stimulation to motor activity

which is no longer needed in the physical care of her child.

With this clue we can find the explanation of many phenomena. We can

understand why laughter and crying are so frequently interchangeable;

why they often blend and why either gives a sense of relief;

we can understand why either laughter or crying can come only

when the issue that causes the integration is determined; we can

understand the extraordinary tendency to laughter that discloses

the unspoken sentiments of love; we can understand the tears

of the woman when she receives a proposal of marriage from the man

she loves; we can understand why any averted circumstance,

such as a threatened breach of the conventions, which would have led

to embarrassment or humiliation, leads to a tendency to laughter;

and why the recital of heroic deeds by association leads to tears,

On the other hand, under the domination of acute diseases,

of acute fear, or of great exhaustion, there is usually neither

laughter nor crying because the nervous system is under the control

of a dominating influence as a result of which the body is so

exhausted that the excess of energy which alone can produce laughing

or crying is lacking.

A remarkable study of the modification of laughter and crying by disease

is found in that most interesting of diseases--exophthalmic goiter.

In this disease there is a low threshold to all stimuli.

That the very motor mechanism of which we have been speaking

is involved, is shown by an enormous increase in its activity.

There is also an increase in the size of certain at least of the

activating glands--the thyroid and the adrenals are enlarged and overactive

and the glycogen-producing function of the liver is stimulated.

The most striking phenomenon of this disease, however, is the remarkable

lowering of the brain thresholds to stimuli. In other words,

in Graves' disease the nervous system and the activating glands--

the entire motor mechanism--are in an exalted state of activity.

If this be true, then these patients should exhibit behavior

precisely contrary to that of those suffering from acute infection,

that is, they should be constantly clearing their systems of

these superabundant energizing materials by crying or laughing,

and this is precisely what happens--the flood-gates of tears are open

much of the time in Graves' disease--a disease of the emotions.

We have already interpreted pain as a phenomenon of motor activity.

When pain does not lead to muscular activity it therefore frequently

leads to crying or to moaning, just as tickling, which is equally

an incentive to motor activity, results in laughter if it does

not find full expression in action.

From the foregoing we infer that pain, the intense motor response

to tickling, and emotional excitation are all primitive biologic

reactions for the good of the individual, and that all have

their origin in the operation of the great laws of evolution.

If to this inference we add the physiologic dictum that the nervous

system always acts as a whole, and that it can respond to but one

stimulus at a time, we can easily understand that while diverse

causes may integrate the nervous system for a specific action,

if the cause be suddenly removed, then the result of the

integration of the nervous system may be, not a specific action,

but an undesigned muscular action, such as crying or laughter.

Hence it is that laughter and crying may be evoked by diverse

exciting causes. The intensity of the laughter or of the crying

depends upon the intensity of the stimulus and the dynamic state

of the individual.

The linking together of these apparently widely separated phenomena

by the simple law of the discharge of energy by association perhaps

explains the association of an abnormal tendency to tears with an

abnormally low threshold for pain (Fig. 36). In the neurasthenic,

tears and pain are produced with abnormal facility. Hence it is that,

if a patient about to undergo a surgical operation is in a state of fear

and dread before the operation, the threshold to all stimuli is lowered,

and this lowered threshold will continue throughout the operation,

even under inhalation anesthesia, because the stimulus produced by

cutting sensitive tissue is transmitted to the brain just as readily

as if the patient were not anesthetized. In like manner, the brain

may be sensitized by the administration of large doses of thyroid

extract prior to operation, the threshold to injury in such a case

continuing to be low to traumatic stimuli even under anesthesia.

Under the sensitizing influences of thyroid extract or of Graves'

disease the effect of an injury, of an operation, or of emotional

excitation is heightened. The extent to which the threshold to pain

or to any other excitant is affected by Graves' disease is illustrated

by the almost fatal reaction which I once saw result from the mere

pricking with a hypodermic needle of a patient with this disease.

As the result of a visit from a friend, the pulse-rate of a victim of this

disease may increase twenty beats and his temperature rise markedly.

I have seen the mere suggestion of an operation produce collapse.

As the brain is thus remarkably sensitized in Graves' disease, we find

that in these patients laughter, crying, emotional disturbances,

and surgical shock are produced with remarkable facility.

I hope that even this admittedly crude and imperfect consideration

of this subject will suggest the possibility of establishing

a practical viewpoint as to the origin and purpose of pain,

of tickling, and of such expressions of emotion as laughter and crying,

and that it may help us to understand their significance in health

and in disease.

THE RELATION BETWEEN THE PHYSICAL STATE OF THE BRAIN-CELLS AND

BRAIN FUNCTIONS--EXPERIMENTAL AND CLINICAL[\*]

[\*] Address before The American Philosophical Society, April 18, 1913.

The brain in all animals (including man) is but the clearing-house

for reactions to environment, for animals are essentially motor

or neuromotor mechanisms, composed of many parts, it is true,

but integrated by the nervous system. Throughout the phylogenetic history

of the race the stimuli of environment have driven this mechanism,

whose seat of power--the battery--is the brain.

Since all normal life depends upon the response of the brain

to the daily stimuli, we should expect in health, as well

as in disease, to find modifications of the functions and the

physical state of the component parts of this central battery--

the brain-cells. Although we must believe, then, that every

reaction to stimuli, however slight, produces a corresponding

change in the brain-cells, yet there are certain normal, that is,

non-diseased, conditions which produce especially striking changes.

The cell changes due to the emotions, for example, are so similar,

and in extreme conditions approach so closely to the changes produced

by disease, that it is impossible to say where the normal ceases

and the abnormal begins.

In view of the similarity of brain-cell changes it is not strange

that in the clinic as well as in daily life, we are confronted

constantly by outward manifestations which are so nearly

identical that the true underlying cause of the condition in

any individual case is too often overlooked or misunderstood.

In our laboratory experiments and in our clinical observations

we have found that exhaustion produced by intense emotion,

prolonged physical exertion, insomnia, intense fear, certain toxemias,

hemorrhage, and the condition commonly denominated surgical shock,

produce similar outward manifestations and identical brain-cell changes.

It is, therefore, the purpose of this paper to present the definite

results of laboratory researches which show certain relations

between alterations in brain functions and physical changes

in the brain-cells.

Fear.--Our experiments have shown that the brain-cell changes due

to fear may be divided into two stages: First, that of hyperchromatism--

stimulation; second, that of hypochromatism--exhaustion (Figs. 5 and

13). Hyperchromatism was shown only in the presence of the activating

stimuli or within a very short time after they had been received.

This state gradually changed until the period of maximum exhaustion

was reached--about six hours later. Then a process of reconstruction

began and continued until the normal state was again reached.

Fatigue.--Fatigue from overexertion produced in the brain-cells

like changes to those produced by fear, these changes being

proportional to the amount of exertion (Fig. 4). In the extreme

stage of exhaustion from this cause we found that the total

quantity of Nissl substance was enormously reduced.

When the exertion was too greatly prolonged, it took weeks or

months for the cells to be restored to their normal condition.

We have proved, therefore, that in exhaustion resulting from emotion

or from physical work a certain number of the brain-cells are

permanently lost. This is the probable explanation of the fact

that an athlete or a race-horse trained to the point of highest

efficiency can reach his maximum record but once in his life.

Under certain conditions, however, it is possible that, though some

chromatin is forever lost, the remainder may be so remarkably developed

that for a time at least it will compensate for that which is gone.

Hemorrhage.--The loss of blood from any cause, if sufficient to reduce

the blood-pressure, will occasion a change in the brain-cells, provided

that the period of hypotension lasts for more than five minutes.

This time limit is a safeguard against permanent injury

from the temporary hypotension which causes one to faint.

If the hemorrhage be long continued and the blood-pressure be low,

there will be a permanent loss of some of the brain-cells. This

explains why an individual who has suffered from a prolonged

hemorrhage will never again be restored to his original powers.

Drugs.--According to their effect upon the brain-cells, drugs

may be divided into three classes: First, those that stimulate

the brain-cells to increased activity, as strychnin (Fig. 37);

second, those that chemically destroy the brain-cells, as alcohol

and iodoform (Figs. 38 and 39); third, those that suspend the functions

of the cells without damaging them, as nitrous oxid, ether, morphin.

Our experiments have shown that the brain-cell changes induced

by drugs of the first class are precisely the same as the cycle

of changes produced by the emotions and by physical activity.

We have found that strychnin, according to the dosage, causes convulsions

ending in exhaustion and death; excitation followed by lassitude;

stimulation without notable after-results; or

{illust. caption = A, Section of Cerebellum of Normal Dog. C, Section of

Cerebellum of Dog after Repeated Doses of Strychnin. FIG. 37.--

BRAIN-CELLS SHOWING STAGE OF HYPERCHROMATISM FOLLOWED BY CHROMATOLYSIS

RESULTING FROM THE CONTINUATION OF THE STIMULUS. (Camera lucida

drawings.)increased mental tone; while the brain-cells accurately

display these physiologic alterations in proportional hyperchromatism

in the active stages, and proportional chromatolysis in the stages

of reaction. The biologic and therapeutic application of this fact

is as obvious as it is important.

In our experiments, alcohol in large and repeated dosage caused

marked morphologic changes in the brain-cells which went as far

even as the destruction of some of the cells (Fig. 39). Ether,

on the other hand, even after five hours of administration,

produced no observable destructive changes in the brain-cells.

The effect of iodoform was peculiarly interesting, as it was the only

drug that produced a rise of temperature. Its observed effect upon

the brain-cells was that of wide-spread destruction.

Infections.--In every observation regarding the effect of pyogenic

infections on dogs and on man we found that they caused definite

and demonstrable lesions in certain cells of the nervous system,

the most marked changes being in the cortex and the cerebellum

(Fig. 40). For example, in fatal infections resulting from

bowel obstruction, in peritonitis, and in osteomyelitis, the real

lesion is in the brain-cells. We may, therefore, reasonably conclude

that the lassitude, the diminished mental power, the excitability,

irritability, restlessness, delirium, and unconsciousness which may

be associated with acute infections, are due to physical changes

in the brain-cells.

Graves' Disease.--In Graves' disease the brain-cells show marked

changes which are apparently the same as those produced by overwork,

by the emotions, and by strychnin. In the postmortem examination

of one advanced case it was found that a large number of brain-cells

were disintegrated beyond the power of recuperation, even had

the patient lived. This is undoubtedly the reason why a severe case

of exophthalmic goiter sustains a permanent loss of brain power.

Insomnia.--The brains of rabbits which had been kept awake for one

hundred hours showed precisely the same changes as those shown

in physical fatigue, strychnin poisoning, and exhaustion from

emotional stimulation. Eight hours of continuous sleep restored

all the cells except those that had been completely exhausted.

This will explain the permanent ill effect of long-continued insomnia;

that is, long-continued insomnia permanently destroys a part

of the brain-cells just as do too great physical exertion,

certain drugs, emotional strain, exophthalmic goiter, and hemorrhage.

We found, however, that if, instead of natural sleep, the rabbits

were placed for the same number of hours under nitrous oxid anesthesia,

not only did the brain-cells recover from the physical deterioration,

but that 90 per cent. of them became hyperchromatic.

This gives us a possible clue to the actual chemical effect of sleep.

For since nitrous oxid owes its anesthetic effect to its influence

upon oxidation, we may infer that sleep also retards the oxidation

of the cell contents. If this be true, then it is probable

that inhalation anesthetics exert their peculiar influence upon

that portion of the brain through which sleep itself is produced.

If nitrous oxid anesthesia and sleep are chemically identical, then we

have a further clue to one of the primary mechanisms of life itself;

and as a practical corollary one might be able to produce artificial

sleep which would closely resemble normal sleep, but which would

have this advantage, that by using an anesthetic which interferes with

oxidation the brain-cells might be reconstructed after physical fatigue,

after emotional strain, or after the depression of disease.

In the case of the rabbit in which nitrous oxid was substituted

for sleep, the appearance of the brain-cells resembled that in

but one other group experimentally examined--the brain-cells

of hibernating woodchucks.

Insanity.--Our researches have shown that in the course of a fatal

disease and in fatal exhaustion, however produced, death does not

ensue until there is marked disorganization of the brain tissue.

In the progress of disease or exhaustion one may see in different

patients every outward manifestation of mental deterioration,

manifestations which, in a person who does not show any other sign of

physical disease, mark him as insane. Take, for example, the progressive

mental state of a brilliant scholar suffering from typhoid fever.

On the first day of the gradual onset of the disease he would

notice that his mental power was below its maximum efficiency;

on the second he would notice a further deterioration, and so

the mental effect of his disease would progress until he would

find it impossible to express a thought or to make a deduction.

No one can be philanthropic with jaundice; no one suffering

from Graves' disease can be generous; no mental process is possible

in the course of the acute infectious diseases. Just prior to death

from any cause every one is in a mental state which, if it could

be continued, would cause that individual to be judged insane.

If the delirium that occurs in the course of certain diseases

should be continued, the patient would be judged insane.

In severe cases of Graves' disease the patient is insane.

Individuals under overwhelming emotion may be temporarily insane.

Every clinician has seen great numbers of cases in which insanity

is a phase of a disease, of an injury, or of an emotion.

The stage of excitation in anesthesia is insanity.

The only difference between what is conventionally called insanity

and the fleeting insanity of the sick and the injured is that of time.

We may conclude, therefore, what must be the brain-picture of the person

who is permanently insane. This \_a priori\_ reasoning is all that

is possible, since the study of the brain in the insane has thus far

been confined to the brains of those who have died of some disease.

And it is impossible to say which changes have been produced by the

fatal disease, and which by the condition which produced the insanity.

The only logical way by which to investigate the physical basis

of insanity would be to make use of the very rare opportunities

of studying the brains of insane persons who have died in accidents.

Our experiments have proved conclusively that whether we call a person

fatigued or diseased, the brain-cells undergo physical deterioration,

accompanied by loss of mental power (Figs. 40 to 43). Even to the minutest

detail we can show a direct relationship between the physical state

of the brain-cells and the mental power of the individual, that is,

the physical power of a person goes \_pari passu\_ with his mental power.

Indeed, it is impossible to conceive how any mental action,

however subtle, can occur without a corresponding change in the

brain-cells. It is possible now to measure only the evidences of

the effects on the brain-cells of gross and violent mental activity.

At some future time it will doubtless be possible so to refine

the technic of brain-cell examinations that more subtle changes

may be measured. Nevertheless, with the means at our disposal

we have shown already that in all the conditions which we

have studied the cells of the cortex show the greatest changes,

and that loss of the higher mental functions invariably accompanies

the cell deterioration.

A MECHANISTIC VIEW OF PSYCHOLOGY[\*]

[\*] Address delivered before Sigma Xi, Case School

of Science, Cleveland, Ohio, May 27, 1913, and published

in \_Science\_, August 29, 1913.

Traditional religion, traditional medicine, and traditional psychology

have insisted upon the existence in man of a triune nature.

Three "ologies" have been developed for the study of each nature

as a separate entity--body, soul, and spirit--physiology, psychology,

theology; physician, psychologist, priest. To the great minds

of each class, from the days of Aristotle and Hippocrates on,

there have come glimmerings of the truth that the phenomena

studied under these divisions were interrelated. Always, however,

the conflict between votaries of these sciences has been sharp,

and the boundary lines between them have been constantly changing.

Since the great discoveries of Darwin, the zoologist, biologist,

and physiologist have joined hands, but still the soul-body-spirit

chaos has remained. The physician has endeavored to fight the gross

maladies which have been the result of disordered conduct;

the psychologist has reasoned and experimented to find the laws

governing conduct; and the priest has endeavored by appeals to an

unknown god to reform conduct.

The great impulse to a deeper and keener study of man's relation,

not only to man, but to the whole animal creation, which was given

by Darwin, has opened the way to the study of man on a different basis.

Psychologists, physicians, and priests are now joining hands as never

before in the great world-wide movement for the betterment of man.

The new science of sociology is combining the functions of all three,

for priest, physician, and psychologist have come to see that man

is in large measure the product of his environment.

My thesis to-night, however, will go beyond this common agreement,

for I shall maintain, not that man is in \_\*large measure\_ the product

of his environment, but that environment has been the actual CREATOR

of man; that the old division between body, soul, and spirit

is non-existent; that man is a unified mechanism responding in every

part to the adequate stimuli given it from without by the environment

of the present and from within by the environment of the past,

the record of which is stored in part in cells throughout

the mechanism, but especially in its central battery--the brain.

I postulate further that the human body mechanism is equipped, first,

for such conflict with environment as will tend to the preservation

of the individual; and, second, for the propagation of the species,

both of these functions when most efficiently carried out tending

to the upbuilding and perfection of the race.

Through the long ages of evolution the human mechanism has been

slowly developed by the constant changes and growth of its parts

which have resulted from its continual adaptation to its environment.

In some animals the protection from too rough contact with

surroundings was secured by the development of an outside armor;

in others noxious secretions served the purposes of defense,

but such devices as these were not suitable for the higher animals

nor for the diverse and important functions of the human race.

The safety of the higher animals and of man had to be preserved

by some mechanism by means of which they could become adapted

to a much wider and more complex environment, the dominance over

which alone gives them their right to be called "superior beings."

The mechanism by the progressive development of which living

beings have been able to react more and more effectually to their

environment is the central nervous system, which is seen in one

of its simplest forms in motor plants, such as the sensitive

plant and the Venus fly-trap, and in its highest development only

in the sanest, healthiest, happiest, and most useful men.

The essential function of the nervous system was primarily to secure

some form of motor activity, first as a means of securing food,

and later as a means of escaping from enemies and to promote procreation.

Activities for the preservation of the individual and of the species

were and are the only purposes for which the body energy is expended.

The central nervous system hag accordingly been developed for the purpose

of securing such motor activities as will best adapt the individuals

of a species for their self-preservative conflict with environment.

It is easy to appreciate that the simplest expressions of nerve response--

the reflexes--are motor in character, but it is difficult to understand

how such intangible reactions as love, hate, poetic fancy, or moral

inhibition can be also the result of the adaptation to environment

of a distinctively motor mechanism. We expect, however, to prove

that so-called "psychic" states as well as the reflexes are products

of adaptation; that they occur automatically in response to adequate

stimuli in the environment; that, like the reflexes, they are

expressions of motor activity, which, although intangible and unseen,

in turn incite to activity the units of the motor mechanism of the body;

and finally, that any "psychic" condition results in a definite depletion

of the potential energy in the brain-cells which is proportionate

to the muscular exertion of which it is the representative.

That this nerve mechanism may effectively carry out its

twofold function, first, of self-adaptation to meet adequately

the increasingly complicated stimuli of environment; and second,

of adapting the motor mechanism to respond adequately to its demands,

there have been implanted in the body numerous nerve ceptors--

some for the transmission of stimuli harmful to the mechanism--

nociceptors some of a beneficial character--beneceptors; and still

others more highly specialized, which partake of the nature of both

bene- and nociceptors--the distance ceptors, or special senses.

A convincing proof that environment has been the creator

of man is seen in the absolute adaptation of the nociceptors

as manifested in their specific response to adequate stimuli,

and in their presence in only those parts of the body which throughout

the history of the race have been most exposed to harmful contacts.

We find they are most numerous in the face, the neck, the abdomen,

the hands, and the feet; while in the back they are few in number,

and within the bony cavities they are lacking.

Instances of the specific responses made by the nociceptors might be

multiplied indefinitely. Sneezing, for example, is a specific response

made by the motor mechanism to stimulation of nociceptors in the nose,

while stimulation of the larynx does not produce a sneeze, but a cough;

stimulation of the nociceptors of the stomach does not produce cough,

but vomiting; stimulation of the nociceptors of the intestine

does not produce vomiting, but increased peristaltic action.

There are no nociceptors misplaced; none wasted; none that do not

make an adequate response to adequate stimulation.

Another most significant proof that the environment of the past

has been the creator of the man of to-day is seen in the fact

that man has added to his environment certain factors to which

adaptation has not as yet been made. For example, heat is

a stimulus which has existed since the days of prehistoric man,

while the \_x\_-ray is a discovery of to-day; to heat, the nociceptors

produce an adequate response; to the \_x\_-ray there is no response.

There was no weapon in the prehistoric ages which could move at

the speed of a bullet from the modern rifle, therefore, while slow

penetration of the tissues produces great pain and muscular response,

there is no response to the swiftly moving bullet.

The response to contact stimuli then depends always on the presence

of nociceptors in the affected part of the body and to the type

of the contact. Powerful response is made to crushing injury by

environmental forces; to such injuring contacts as resemble the impacts

of fighting; to such tearing injuries as resemble those made by teeth

and claws (Fig. 9). On the other hand, the sharp division of tissue

by cutting produces no adaptive response; indeed, one might imagine

that the body could be cut to pieces by a superlatively sharp knife

applied at tremendous speed without material adaptive response.

These examples indicate how the history of the phylogenetic experiences

of the human race may be learned by a study of the position

and the action of the nociceptors, just as truly as the study

of the arrangement and variations in the strata of the earth's

crust discloses to us geologic history.

These adaptive responses to stimuli are the result of the action

of the brain-cells, which are thus continually played upon by

the stimuli of environment. The energy stored in the brain-cells

in turn activates the various organs and parts of the body.

If the environmental impacts are repeated with such frequency that

the brain-cells have no time for restoration between them, the energy

of the cells becomes exhausted and a condition of shock results.

Every action of the body may thus be analyzed into a stimulation

of ceptors, a consequent discharge of brain-cell energy,

and a final adaptive activation of the appropriate part.

Walking, running, and their modifications constitute an adaptation

of wonderful perfection, for, as Sherrington has shown,

the adaptation of locomotion consists of a series of reflexes--

ceptors in the joints, in the limb, and in the foot being stimulated

by variations in pressure.

As we have shown, the bene- and nociceptors orientate man to all

forms of physical contact--the former GUIDE HIM TO the acquisition

of food and to sexual contact; the latter DIRECT HIM FROM contacts

of a harmful nature. The distance ceptors, on the other hand,

adapt man to his distant environment by means of communication

through unseen forces--ethereal vibrations produce sight; air waves

produce sound; microscopic particles of matter produce smell.

The advantage of the distance ceptors is that they allow time

for orientation, and because of this great advantage the majority

of man's actions are responses to their adequate stimuli.

As Sherrington has stated, the greater part of the brain has been

developed by means of stimuli received through the special senses,

especially through the light ceptors, the optic nerves.

We have just stated that by means of the distance ceptors animals

and man orientate themselves to their distant environment.

As a result of the stimulation of the special senses chase and escape

are effected, fight is conducted, food is secured, and mates are found.

It is obvious, therefore, that the distance ceptors are the primary

cause of continuous and exhausting expenditures of energy.

On the other hand, stimuli applied to contact ceptors lead to short,

quick discharges of nervous energy. The child puts his hand

in the fire and there is an immediate and complete response

to the injuring contact; he sees a pot of jam on the pantry shelf

and a long train of continued activities are set in motion,

leading to the acquisition of the desired object.

The contact ceptors do not at all promote the expenditure of energy

in the chase or in fight, in the search for food or for mates.

Since the distance ceptors control these activities, one would expect to

find that they control also those organs whose function is the production

of energizing internal secretions. Over these organs--the thyroid,

the adrenals, the hypophysis--the contact ceptors have no control.

Prolonged laboratory experimentation seems to prove this postulate.

According to our observations, no amount of physical trauma inflicted upon

animals will cause hyperthyroidism or increased adrenalin in the blood,

while fear and rage do produce hyperthyroidism and increased adrenalin

(Fig. 44) (Cannon). This is a statement of far-reaching importance

and is the key to an explanation of many chronic diseases--

diseases which are associated with the intense stimulation of

the distance ceptors in human relations.

Stimuli of the contact ceptors differ from stimuli of the distance

ceptors in still another important particular. The adequacy of stimuli

of the contact ceptors depends upon their number and intensity,

while the adequacy of the stimuli of the distance ceptors depends

upon the EXPERIENCE of the species and of the individual.

That is, according to phylogeny and ontogeny this or that sound,

this or that smell, this or that sight, through association

recapitulates the experience of the species and of the individual--

awakens the phylogenetic and ontogenetic memory. In other words, sights,

sounds, and odors are symbols which awaken phylogenetic association.

If a species has become adapted to make a specific response to a

certain object, then that response will occur automatically in an

individual of that species when he hears, sees, or smells that object.

Suppose, for example, that the shadow of a hawk were to fall

simultaneously on the eyes of a bird, a rabbit, a cow, and a boy.

That shadow would at once activate the rabbit and the bird to an

endeavor to escape, each in a specific manner according to its

phylogenetic adaptation; the cow would be indifferent and neutral;

while the boy, according to his personal experience or ontogeny,

might remain neutral, might watch the flight of the hawk with interest

or might try to shoot it.

Each phylogenetic and each ontogenetic experience by an indirect

method develops its own mechanism of adaptation in the brain;

and the brain threshold is raised or lowered to stimuli by

the strength and frequency of repetition of the experience.

Thus through the innumerable symbols supplied by environment the distance

ceptors drive this or that animal according to the type of brain

pattern and the particular state of threshold which has been developed

in that animal by its phylogenetic and ontogenetic experiences.

The brain pattern depends upon his phylogeny, the state of threshold

upon his ontogeny. Each BRAIN PATTERN is created by some particular

element in the environment to which an adaptation has been made

for the good of the species. The \_\*state of threshold\_ depends

upon the effect made upon the individual by his personal contacts

with that particular element in his environment. The presence

of that element produces in the individual an associative recall

of the adaptation of his species--that is, the brain pattern developed

by his phylogeny becomes energized to make a specific response.

The intensity of the response depends upon the state of threshold--

that is, upon the associative recall of the individual's

own experience--his ontogeny.

If the full history of the species and of the individual

could be known in every detail, then every detail of that

individual's conduct in health and disease could be predicted.

Reaction to environment is the basis of conduct, of moral standards,

of manners and conventions, of work and play, of love and hate,

of protection and murder, of governing and being governed, in fact,

of all the reactions between human beings--of the entire web of life.

To quote Sherrington once more: "Environment drives the brain,

the brain drives the various organs of the body."

By what means are these adaptations made? What is the mechanism through

which adequate responses are made to the stimuli received by the ceptors?

We postulate that in the brain there are innumerable patterns

each the mechanism for the performance of a single kind of action,

and that the brain-cells supply the energy--electric or otherwise--

by which the act is performed; that the energy stored in the brain-cells

is in some unknown manner released by the force which activates

the brain pattern; and that through an unknown property of these brain

patterns each stimulus causes such a change that the next stimulus

of the same kind passes with greater facility.

Each separate motor action presumably has its own mechanism--

brain pattern--which is activated by but one ceptor and by

that ceptor only when physical force of a certain intensity

and rate of motion is applied. This is true both of the visible

contacts affecting the nociceptors and of the invisible contacts

by those intangible forces which affect the distance ceptors.

For example, each variation in speed of the light-producing

waves of ether causes a specific reaction in the brain.

For one speed of ether waves the reaction is the perception

of the color blue; for another, yellow; for another, violet.

Changes in the speed of air waves meet with specific response

in the brain patterns tuned to receive impressions through the

aural nerves, and so we distinguish differences in sound pitch.

If we can realize the infinite delicacy of the mechanisms adapted

to these infinitesimal variations in the speed and intensity of

invisible and intangible stimuli, it will not be difficult to conceive

the variations of brain patterns which render possible the specific

responses to the coarser contacts of visible environment.

Each brain pattern is adapted for but one type of motion,

and so the specific stimuli of the innumerable ceptors play

each upon its own brain pattern only. In addition, each brain

pattern can react to stimuli applied only within certain limits.

Too bright a light blinds; too loud a sound deafens. No mechanism

is adapted for waves of light above or below a certain rate of speed,

although this range varies in different individuals and in different

species according to the training of the individual and the need

of the species.

We have already referred to the fact that there is no receptive

mechanism adapted to the stimuli from the \_x\_-ray, from the

high-speed bullet, from electricity. So, too, there are innumerable

forces in nature which can excite in man no adaptive response,

since there exist in man no brain patterns tuned to their waves,

as in the case of certain ethereal and radioactive forces.

On this mechanistic basis the emotions may be explained as activations

of the entire motor mechanism for fighting, for escaping, for copulating.

The sight of an enemy stimulates in the brain those patterns formed

by the previous experiences of the individual with that enemy, and also

the experiences of the race whenever an enemy had to be met and overcome.

Each of these many brain patterns in turn activates that part of

the body through which lies the path of its own adaptive response--

those parts including the special energizing or activating organs.

Laboratory experiments show that in an animal driven strongly

by emotion the following changes may be seen: (1) A mobilization

of the energy-giving compound in the brain-cells, evidenced by a

primary increase of the Nissl substance and a later disappearance

of this substance and the deterioration of the cells (Figs. 5 and 13);

(2) increased output of adrenalin (Cannon), of thyroid secretion,

of glycogen, and an increase of the power of oxidation in the muscles;

(3) accelerated circulation and respiration with increased

body temperature; (4) altered metabolism. All these are adaptations

to increase the motor efficiency of the mechanism. In addition,

we find an inhibition of the functions of every organ and tissue that

consumes energy, but does not contribute directly to motor efficiency.

The mouth becomes dry; the gastric and pancreatic secretions are

lessened or are completely inhibited; peristaltic action stops.

The obvious purpose of all these activations and inhibitions is

to mass every atom of energy upon the muscles that are conducting

the defense or attack.

So strong is the influence of phylogenetic experience that though

an enemy to-day may not be met by actual physical attack,

yet the decks are cleared for action, as it were, and the weapons

made ready, the body as a result being shaken and exhausted.

The type of emotion is plainly declared by the activation

of the muscles which would be used if the appropriate physical

action were consummated. In anger the teeth are set, the fists

are clenched, the posture is rigid; in fear the muscles collapse,

the joints tremble, and the running mechanism is activated

for flight; in sexual excitement the mimicry is as obvious.

The emotions, then, are the preparations for phylogenetic activities.

If the activities are consummated, the fuel--glycogen--and the activating

secretions from the thyroid, the adrenals, the hypophysis are consumed.

In the activation without action, these products must be eliminated

as waste products and so a heavy strain is put upon the organs

of elimination. It is obvious that the body under emotion might be

clarified by active muscular exercise, but the subject of the emotion

is so strongly integrated thereby that it is difficult for him

to engage in diverting, clarifying exertion. The person in anger

does not want to be saved from the ill effects of his own emotion;

he wants only to fight; the person in fear wants only to escape;

the person under sexual excitement wants only possession.

All the lesser emotions--worry, jealousy, envy, grief, disappointment,

expectation--all these influence the body in this manner, the consequences

depending upon the intensity of the emotion and its protraction.

Chronic emotional stimulation, therefore, may fatigue or exhaust

the brain and may cause cardiovascular disease, indigestion, Graves'

disease, diabetes, and insanity even.

The effect of the emotions upon the body mechanism may be compared

to that produced upon the mechanism of an automobile if its engines

are kept running at full speed while the machine is stationary.

The whole machine will be shaken and weakened, the batteries and weakest

parts being the first to become impaired and destroyed, the length

of usefulness of the automobile being correspondingly limited.

We have shown that the effects upon the body mechanism of the action

of the various ceptors is in relation to the response made by the brain

to the stimuli received. What is this power of response on the part

of the brain but CONSCIOUSNESS? If this is so, then consciousness

itself is a reaction to environment, and its intensity must vary

with the state of the brain and with the environmental stimuli.

If the brain-cells are in the state of highest efficiency, if their

energy has not been drawn upon, then consciousness is at its height;

if the brain is fatigued, that is, if the energy stored in the cells

has been exhausted to any degree, then the intensity of consciousness

is diminished. So degrees of consciousness vary from the height

maintained by cells in full vigor through the stages of fatigue

to sleep, to the deeper unconsciousness secured by the administration

of inhalation anesthetics, to that complete unconsciousness

of the environment which is secured by blocking the advent to

the brain of all impressions from both distance and contact ceptors,

by the use of both local and inhalation anesthetics--the state

of anoci-association (Fig. 14).

Animals and man may be so exhausted as to be only semi-conscious.

While a brain perfectly refreshed by a long sleep cannot immediately

sleep again, the exhausted brain and the refreshed brain when subjected

to equal stimuli will rise to unequal heights of consciousness.

The nature of the physical basis of consciousness has been

sought in experiments on rabbits which were kept awake from

one hundred to one hundred and nine hours. At the end of this

time they were in a state of extreme exhaustion and seemed

semi-conscious. If the wakefulness had been further prolonged,

this state of semi-consciousness would have steadily changed

until it culminated in the permanent unconsciousness of death.

An examination of the brain-cells of these animals showed physical

changes identical with those produced by exhaustion from other causes,

such as prolonged physical exertion or emotional strain (Figs. 45

and 46). After one hundred hours of wakefulness the rabbits were

allowed a long period of sleep. All the brain-cells were restored

except those that had been in a state of complete exhaustion.

A single seance of sleep served to restore some of the cells,

but those which had undergone extreme changes required prolonged rest.

These experiments give us a definite physical basis for explaining

the cost to the body mechanism of maintaining the conscious state.

We have stated that the brain-cell changes produced by prolonged

consciousness are identical with those produced by physical exertion

and by emotional strain. Rest, then, and especially sleep,

is needed to restore the physical state of the brain-cells which

have been impaired, and as the brain-cells constitute the central

battery of the body mechanism, their restoration is essential

for the maintenance of normal vitality.

In ordinary parlance, by consciousness we mean the activity

of that part of the brain in which associative memory resides,

but while associative memory is suspended the activities of the brain

as a whole are by no means suspended; the respiratory and circulatory

centers are active, as are those centers which maintain muscular tone.

This is shown by the muscular response to external stimuli made

by the normal person in sleep; by the occasional activation of motor

patterns which may break through into consciousness causing dreams;

and finally by the responses of the motor mechanism made to the injuring

stimuli of an operation on a patient under inhalation anesthesia only.

Direct proof of the mechanistic action of many of life's phenomena

is lacking, but the proof is definite and final of the part

that the brain-cells play in maintaining consciousness;

of the fact that the degree of consciousness and mental

efficiency depends upon the physical state of the brain-cells;

and finally that efficiency may be restored by sleep,

provided that exhaustion of the cells has not progressed too far.

In this greatest phenomenon of life, then, the mechanistic theory

is in harmony with the facts.

Perhaps no more convincing proof of our thesis that the body is

a mechanism developed and adapted to its purposes by environment

can be secured than by a study of that most constant manifestation

of consciousness--pain.

Like the other phenomena of life, pain was undoubtedly evolved

for a particular purpose--surely for the good of the individual.

Like fear and worry, it frequently is injurious. What then may

be its purpose?

We postulate that pain is a result of contact ceptor stimulation

for the purpose of securing protective muscular activity.

This postulate applies to all kinds of pain, whatever their cause--

whether physical injury, pyogenic infection, the obstruction

of hollow viscera, childbirth, etc.

All forms of pain are associated with muscular action, and as in every

other stimulation of the ceptors, each kind of pain is specific

to the causative stimuli. The child puts his hand in the fire;

physical injury pain results, and the appropriate muscular

response is elicited. If pressure is prolonged on some parts

of the body, anemia of the parts may result, with a corresponding

discomfort or pain, requiring muscular action for relief.

When the rays of the sun strike directly upon the retina, light pain

causes an immediate protective action, so too in the evacuation

of the intestine and the urinary bladder as normal acts, and in

overcoming obstruction of these tracts, discomfort or pain compel

the required muscular actions. This view of pain as a stimulation

to motor action explains why only certain types of infection are

associated with pain; namely, those types in which the infection

may be spread by muscular action or those in which the fixation

of parts by continued muscular rigidity is an advantage.

As a further remarkable proof of the marvelous adaptation

of the body mechanism to meet varying environmental conditions,

we find that just as nociceptors have been implanted in only those

parts of the body which have been subject to nocuous contacts,

so a type of infection which causes muscular action in one part

of the body may cause none when it attacks another.

This postulate gives us the key to the pain-muscular phenomena

of peritonitis, pleurisy, cystitis, cholecystitis, etc., as well as to

the pain-muscular phenomena in obstructions of the hollow viscera.

If pain is a part of a muscular response and occurs only

as a result of contact ceptor stimulation by physical injury,

infection, anemia, or obstruction, we may well inquire which part

of the nerve mechanism is the site of the phenomenon of pain.

Is it the nerve-ending, the nerve-trunk, or the brain? That is,

is pain associated with the physical contact with the nerve-ending,

or with the physical act of transmission along the nerve-trunk,

or with the change of brain-cell substance by means of which

the motor-producing energy is released?

We postulate that the pain is associated with the discharge of energy

from the brain-cells. If this be true, then if every nociceptor in

the body were equally stimulated in such a manner that all the stimuli

should reach the brain-cells simultaneously, then the cells would

find themselves in equilibrium and no motor act would be performed.

But if all the pain nerve ceptors but one were equally stimulated,

and this one more strongly stimulated than the rest, then this

one would gain possession of the final common path--would cause

a muscular action and the sensation of pain.

It is well known that when a greater pain or stimulus is thrown

into competition with a lesser one, the lesser is submerged.

Of this fact the school-boy makes use when he initiates

the novice into the mystery of the painless pulling of hair.

The simultaneous but severe application of the boot to the blindfolded

victim takes complete but exclusive possession of the final common

path and the hair is painlessly plucked as a result of the triumph

of the boot stimulus over the pull on the hair in the struggle

for the final common path.

Persons who have survived a sudden, complete exposure to superheated steam,

or whose bodies have been enwrapped in flame, testify that they

have felt no pain. As this absence of pain may be due to the fact

that the emotion of fear gained the final common path, to the exclusion

of all other stimuli, we are trying by experimentation to discover

the effects of simultaneous painful stimulation of all parts of the body.

The data already in hand, and the experiments now in progress,

in which anesthetized animals are subjected to powerful stimuli

applied to certain parts of the body only, or simultaneously to

all parts of the body, lead us to believe that in the former case

the brain-cells become stimulated or hyperchromatic, while in the latter

case no brain-cell changes occur. We believe that our experiments

will prove that an equal and simultaneous stimulation of all parts

of the body leaves the brain-cells in a state of equilibrium.

Our theory of pain will then be well sustained, not only by common

observation, but by experimental proof, and so the mechanistic view

will be found in complete harmony with another important reaction.

We have stated that when a number of contact stimuli act simultaneously,

the strongest stimulus will gain possession of the final common path--

the path of action. When, however, stimuli of the distance ceptors

compete with stimuli of the contact ceptors, the contact-ceptor

stimuli often secure the common path, not because they are stronger

or more important, but because they are immediate and urgent.

In many instances, however, the distance-ceptor stimuli are strong,

have the advantage of a lowered threshold, and therefore compete

successfully with the immediate and present stimuli of the

contact ceptors. In such cases we have the interesting phenomenon

of physical injury without resultant pain or muscular response.

The distance-ceptor stimuli which may thus triumph over even powerful

contact-ceptor stimuli are those causing strong emotions--as great

anger in fighting; great fear in a battle; intense sexual excitement.

Dr. Livingstone has testified to his complete unconsciousness

to pain during his struggle with a lion; although he was torn

by teeth and claws, his fear overcame all other impressions.

By frequently repeated stimulation the Dervish secures a low

threshold to the emotions caused by the thought of God or the devil,

and his emotional excitement is increased by the presence of others

under the same stimulation; emotion, therefore, secures the final

common path and he is unconscious of pain when he lashes, cuts,

and bruises his body. The phenomena of hysteria may be explained

on this basis, as may the unconsciousness of passing events

in a person in the midst of a great and overwhelming grief.

By constant practice the student may secure the final common path for

such impressions as are derived from the stimuli offered by the subject

of his study, and so he will be oblivious of his surroundings.

Concentration is but another name for a final common path secured

by the repetition and summation of certain stimuli.

If our premises are sustained, then we can recognize in man no will,

no ego, no possibility for spontaneous action, for every action must

be a response to the stimuli of contact or distance ceptors, or to their

recall through associative memory. Memory is awakened by symbols which

represent any of the objects or forces associated with the act recalled.

Spoken and written words, pictures, sounds, may stimulate the brain

patterns formed by previous stimulation of the distance ceptors;

while touch, pain, temperature, pressure, may recall previous

contact-ceptor stimuli. Memory depends in part upon the adequacy

of the symbol, and in part upon the state of the threshold.

If one has ever been attacked by a snake, the threshold to any

symbol which could recall that attack would be low; the later

recall of anything associated with the bite or its results would

produce in memory a recapitulation of the whole scene, while even

harmless snakes would thereafter be greeted with a shudder.

On the other hand, in a child the threshold is low to the desire

for the possession of any new and strange object; in a child,

therefore, to whom a snake is merely an unusual and fascinating object,

there is aroused only curiosity and the desire for the possession

of a new plaything.

If we are to attribute to man the possession of a governing

attribute not possessed by other parts of the animal creation,

where are we to draw the boundary line, and say "here the ego--

the will--the reason--emerges"? What attribute, after all, has man

which in its ultimate analysis is not possessed by the lowest

animals or by the vegetable creation, even? From the ameba,

on through all the stages of animal existence, every action is

but a response to an adequate stimulus; and as a result of adequate

stimuli each step has been taken toward the higher and more

intricate mechanisms which play the higher and more intricate parts

in the great scheme of nature.

The Venus fly-trap responds to as delicate a stimulus as do

any of the contact ceptors of animals, and the motor activity

resulting from the stimulus is as complex. To an insect-like touch

the plant responds; to a rough contact there is no response; that is,

the motor mechanism of the plant has become attuned to only such

stimuli as simulate the contact of those insects which form its diet.

It catches flies, eats and digests them, and ejects the refuse

(Fig. 47). The ameba does no less. The frog does no more,

excepting that in its place in creation a few more reactions are

required for its sustenance and for the propagation of its species.

Man does no more, excepting that in man's manifold relations

there are innumerable stimuli, for meeting which adequately,

innumerable mechanisms have been evolved. The motor mechanism

of the fly-trap is perfectly adapted to its purpose.

The motor mechanism of man is adapted to its manifold uses,

and as new environmental influences surround him, we must believe

that new adaptations of the mechanism will be evolved to meet

the new conditions.

Is not this conception of man's activities infinitely more wonderful,

and infinitely more comprehensible than is the conception that his

activities may be accounted for by the existence of an unknown,

unimaginable, and intangible force called "mind" or "soul"?

We have already shown how the nerve mechanism is so well adapted

to the innumerable stimuli of environment that it can accurately

transmit and distinguish between the infinite variations of speed

in the ether waves producing light, and the air waves producing sound.

Each rate of vibration energizes only the mechanism which has

been attuned to it. With marvelous accuracy the light and sound

waves gain access to the nerve tissue and are finally interpreted

in terms of motor responses, each by the brain pattern attuned

to that particular speed and intensity. So stimuli and resultant

actions multiplied by the total number of the motor patterns

in the brain of man give us the sum total of his life's activities--

they constitute his life.

As in evolutionary history the permanence of an adaptation of the body

mechanism depends upon its value in the preservation of the life

of the individual and upon its power to increase the value of

the individual to the race, so the importance and truth of these

postulates and theories may well be judged on the same basis.

The fundamental instincts of all living matter are self-preservation

and the propagation of the species. The instinct for self-preservation

causes a plant to turn away from cold and damaging winds toward

the life-giving sun; the inert mussel to withdraw within its shell;

the insect to take flight; the animal to fight or to flee; and man

to procure food that he may oppose starvation, to shelter himself

and to provide clothes that he may avoid the dangers of excessive

cold and heat, to combat death from disease by seeking medical aid,

to avoid destruction by man or brute by fight or by flight.

The instinct to propagate the species leads brute man by crude methods,

and cultured man by methods more refined, to put out of his way sex

rivals so that his own life may be continued through offspring.

The life of the species is further assured by the protective

action exercised over the young by the adults of the species.

As soon as the youngest offspring is able successfully to carry on his

own struggle with environment there is no longer need for the parent,

and the parent enters therefore the stage of disintegration.

The average length of life in any species is the sum of the years

of immaturity, plus the years of female fertility, plus the adolescent

years of the offspring.

The stimuli resulting from these two dominant instincts are now

so overpowering as compared with all other environmental stimuli

that the mere possession of adequate knowledge of the damaging effects

of certain actions as compared with the saving effects of others will

(other things being equal) lead the individual to choose the right,--

the self- and species-preservative course of action, instead of the wrong,--

the self- and species-destructive course of action.

The dissemination of the knowledge of the far-reaching

deleterious effects of protracted emotional strain, of overwork,

and of worry will automatically raise man's threshold to

the damaging activating stimuli causing the strong emotions,

and will cause him to avoid dangerous strains of every kind.

The individual thus protected will therefore rise to a plane

of poise and efficiency far above that of his uncontrolled fellows,

and by so much will his efficiency, health, and happiness be augmented.

A full acceptance of this theory cannot fail to produce in those

in whose charge rests the welfare of the young, an overwhelming

desire to surround children with those environmental stimuli only

which will tend to their highest ultimate welfare.

Such is the stimulating force of tradition that many who

have been educated under the tenets of traditional beliefs

will oppose these hypotheses--even violently, it may be.

So they have opposed them; so they opposed Darwin; so they

have opposed all new and apparently revolutionary doctrines.

Yet these persons themselves are by their very actions proving

the efficiency of the vital principles which we have enunciated.

What is the whole social welfare movement but a recognition

on the part of municipalities, educational boards, and religious

organizations of the fact that the future welfare of the race

depends upon the administration to the young of forceful

uplifting environmental stimuli?

There are now, as there were in Darwin's day, many who feel that man

is degraded from his high estate by the conception that he is not

a reasoning, willing being, the result of a special creation.

But one may wonder indeed what conception of the origin of man can

be more wonderful or more inspiring than the belief that he has

been slowly evolved through the ages, and that all creatures

have had a part in his development; that each form of life has

contributed and is contributing still to his present welfare

and to his future advancement.

Recapitulation

Psychology,--the science of the human soul and its relations,--

under the mechanistic theory of life, must receive a new definition.

It becomes a science of man's activities as determined by the

environmental stimuli of his phylogeny and of his ontogeny.

On this basis we postulate that throughout the history of the race nothing

has been lost, but that every experience of the race and of the individual

has been retained for the guidance of the individual and of the race;

that for the accomplishment of this end there has been evolved through

the ages a nerve mechanism of such infinite delicacy and precision

that in some unknown manner it can register permanently within

itself every impression received in the phylogenetic and ontogenetic

experience of the individual; that each of these nerve mechanisms

or brain patterns has its own connection with the external world,

and that each is attuned to receive impressions of but one kind,

as in the apparatus of wireless telegraphy each instrument can

receive and interpret waves of a certain rate of intensity only;

that thought, will, ego, personality, perception, imagination,

reason, emotion, choice, memory, are to be interpreted in terms

of these brain patterns; that these so-called phenomena of human

life depend upon the stimuli which can secure the final common path,

this in turn having been determined by the frequency and the strength

of the environmental stimuli of the past and of the present.

Finally, as for life's origin and life's ultimate end,

we are content to say that they are unknown, perhaps unknowable.

We know only that living matter, like lifeless matter, has its own

place in the cosmic processes; that the gigantic forces which operated

to produce a world upon which life could exist, as a logical sequence,

when the time was ripe, evolved life; and finally that these cosmic

forces are still active, though none can tell what worlds and what

races may be the result of their coming activities.

A MECHANISTIC THEORY OF DISEASE[\*]

[\*] Oration in Surgery. Delivered at the 147th Annual Meeting of the

Medical Society of New Jersey, at Spring Lake, N. J., June 11, 1913.

In this address the paragraphs which were taken from the preceding

paper, "A Mechanistic View of Psychology," have been omitted,

those portions only being republished in which the premises have

been applied in a discussion of certain medical problems rather

than of psychological problems.

The human body is an elaborate mechanism equipped first for such

conflict with environment as will tend to the preservation

of the individual, and second for the propagation of the species,

both of these functions, when most efficiently carried out,

tending to the upbuilding and perfection of the race.

From the date of Harvey's discovery of the circulation of the blood,

to the present day, the human body has been constantly compared

to a machine, but the time for analogy and comparison is past.

I postulate that the body is itself a mechanism responding in every

part to the adequate stimuli given it from without by the environment

of the present and from within by the environment of the past,

the memory of which is stored in the central battery of the mechanism--

the brain.

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If the full history of the species and of the individual

could be known in every detail, then every detail of that

individual's conduct in health and disease could be predicted.

Reaction to environment is the basis of conduct, of moral standards,

of manners and conventions, of work and play, of love and hate,

of protection and murder, of governing and being governed, in fact,

of all the reactions between human beings--of the entire web of life.

As Sherrington has stated, "Environment drives the brain, the brain

drives the various organs of the body," and here we believe we find

the key to a mechanistic interpretation of all body processes.

On this basis we may see that the activities of life depend upon

the ability of the parts of the body mechanism to respond adequately

to adequate stimulation. This postulate applies not only to stimuli

from visible forces, but to those received by the invasion of

the micro-bodies which cause pyogenic or non-pyogenic infections.

In the case of dangerous assaults by visible or invisible enemies,

the brain, through the nerves and all parts of the motor mechanism,

meets the attack by attempts at adaptation. Recovery, invalidism,

and death depend upon the degree of success with which the attacking

or invading enemies are met. Questions regarding disease become,

therefore, questions in adaptation, and it is possible that,

when studied in the light of this conception, the key to many hitherto

unsolved physical problems may be found.

Perhaps no more convincing proof of our thesis may be secured

than by a study of that ever-present phenomenon--pain. In whatever

part of the body and by whatever apparent cause pain is produced,

we find that it is invariably a stimulation to motor activity--

whose ultimate object is protection. Thus by the muscular action

resulting from pain we are protected against heat and cold;

against too powerful light; against local anemia caused by prolonged

pressure upon any portion of the body. So, too, pain of greater

or less intensity compels the required emptying of the pregnant

uterus and the evacuation of the intestine and the urinary bladder.

It should be noted that in every instance the muscular activity

resulting from pain is specific in its type, its distribution,

and its intensity, this specificity being true not only of pain

which is the result of external stimulation, but also of the pain

associated with certain types of infection.

Pain, however, is not the only symptom of the invasion of

the body by pyogenic or parasitic organisms. Fever, invariably,

and chills, often, accompany the course of the infections.

Can these phenomena also be explained as adaptations of the motor

mechanism for the good of the individual?

As the phenomena of chills and fever are most strikingly exhibited

in malaria, let us study the course of events in that disease.

It is known that the malarial parasite develops in the red

blood-corpuscles, and that the chills and fever appear when

the cycle of parasitic development is complete and the adults

are ready to escape from the corpuscles of the blood plasma.

Bass, of New Orleans, has proved that the favorable temperature

for the growth of the malarial organism is 98'0, and that at 102'0

the adult organisms will be killed, though the latter temperature

is not fatal to the spores. The adult life of the malarial

parasite begins after its escape into the blood plasma, and it is

there that the organism is most susceptible to high temperature.

We must infer, therefore, that the fever is an adaptation on the part

of the host for despatching the enemy.

What, then, may be the protective part played by the chill?

A chill is made up of intermittent contractions of all the external

muscles of the body. This activity results in an increase

of the body heat and in an anemia of the superficial parts

of the body, so that less heat can be lost by radiation.

By this means, therefore, the external portions of the body contribute

measurably to the production of the beneficent and saving fever.

It must be remembered that this power of adaptation is not peculiar

to man alone, but that it is a quality shared by all living creatures.

While the human body has been adapting itself for self-protection

by producing a febrile reaction whereby to kill the invading organisms,

the invaders on their side have been adapting themselves for a life

struggle within the body of the host. In these mortal conflicts

between invaders and host, therefore, the issue is often in doubt,

and sometimes one and sometimes the other will emerge victorious.

We must believe that a similar adaptive response exists in all

parasitic infections--the cycles varying according to the stages in

the development of the invaders. If the bacteria develop continuously,

the fever is constant instead of intermittent, since the adequate

stimulus is constantly present.

Bacteriology has taught us that both heat and cold are fatal

to pathogenic infections; for this reason either of the apparently

contradictory methods of treatment may help, \_i. e\_., either hot

or cold applications. It should be borne in mind, however, that we have

to deal not only with the adult organisms, but with the spores also.

The application of cold may keep the spores from developing,

while heat may promote their development, and the course of the disease

may vary, therefore, according to our choice of treatment.

From this viewpoint, we can understand the intermittent temperature

in a patient who is convalescing from an extreme infection,

as peritonitis, pylephlebitis, multiple abscess of the liver, etc.

In these conditions there may occur days of normal temperature,

followed by an abrupt rise which will last for several days--

this in turn succeeded by another remittance. This cycle may be

repeated several times, and on our hypothesis we may believe it

is caused by the successive development to maturity of spores

of varying ages.

If these premises are sound, the wisdom of reducing the temperature

in case of infection may well be questioned.

On this mechanistic basis the emotions also may be explained

as activations of the entire motor mechanism for fighting,

for escaping, for copulating.

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The emotions, then, are the preparation for phylogenetic activities

(Fig. 48). If the activities were consummated, the fuel--glycogen--

and the activating secretions from the thyroid, the adrenals,

the hypophysis, would be consumed. In the activation without

action these products must be eliminated as waste products

and so a heavy strain is put upon the organs of elimination.

It is obvious that the body under emotion might be clarified

by active muscular exercise, but the subject of the emotion is so

strongly integrated thereby that it is difficult for him to engage

in diverting, clarifying exertion.

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So, as we have indicated already, certain deleterious effects are

produced when the body mechanism is activated without resultant action.

For example, the output of adrenalin is increased, and, as a consequence,

arteriosclerosis and cardiovascular disease may occur in persons

who have been subjected to prolonged emotional strain, since it

has been proved that the prolonged administration of adrenalin

will cause these conditions. We have stated that the emotions cause

increased output of glycogen. Glycogen is a step toward diabetes,

and therefore this disease, too, is prone to appear in persons

under emotional strain. It is most common in those races which

are especially emotional in character, so we are not surprised

to find it especially prevalent among Jews. So common is this

particular result of prolonged emotion that some one has said,

"When the stocks go down in New York, diabetes goes up."

Nephritis, also, may result from emotional stress, because of the strain

put upon the kidneys by the unconsumed activating substances.

The increased heart action and the presence of these activating

secretions may cause myocarditis and heart degeneration.

Claudication also may result from the impaired circulation.

The emotions may cause an inhibition of the digestive secretions

and of intestinal peristalsis. This means that the digestive processes

are arrested, that putrefaction and autointoxication will result,

and that still further strain will thus be put upon the organs

of elimination. Who has not observed in himself and in others when under

the influence of fear, anger, jealousy, or grief that the digestive

processes and general well-being are rapidly and materially altered;

while as tranquillity, peace, and happiness return the physical

state improves accordingly?

Dentists testify that as a result of continued strong emotion the character

of the saliva changes, pyorrhea develops, and the teeth decay rapidly.

Every one knows that strong emotion may cause the hair to fall

out and to become prematurely gray.

As to the most important organ of all--the brain--every one is

conscious of its impaired efficiency under emotional strain,

and laboratory researches show that the deficiency is accounted

for by actual cell deterioration; so the individual who day by day

is under heavy emotional strain finds himself losing strength slowly--

especially do his friends note it. By summation of stimuli

his threshold becomes lowered until stimuli, which under normal

conditions would be of no effect, produce undue responses.

"The grasshopper becomes a burden," and prolonged rest and change

of environmental conditions are necessary for restoration.

If in a long emotional strain the brain is beaten down;

if the number of "low-efficiency" cells increases, the driving

power of the brain is correspondingly lessened and therefore

the various organs of the body may escape through the very

inefficiency of the brain to produce in them forced activity.

On the other hand, if the brain remains vigorous, the kidneys

may take the strain and break down; if the kidneys do not break,

the blood-vessels may harden; if the blood-vessels are not affected,

the thyroid may become hyperplastic and produce Graves' disease;

if the thyroid escapes, diabetes may develop; while if the iron

constitution of the mechanism can successfully bear the strain

in all its parts, then the individual will break his competitors,

and their mechanisms will suffer in the struggle.

This whole train of deleterious results of body activation without

action may be best observed and studied in that most emotional

of diseases--exophthalmic goiter. In this disease the constantly

stimulated distance ceptors dispossess the contact ceptors from

the common path, and drive the motor mechanism to its own destruction,

and the patient has the appearance of a person in great terror,

or of a runner approaching the end of a Marathon race (Figs. 16

and 48 to 54).

Exophthalmic goiter may result from long emotional or mental stress

in those cases in which the thyroid takes the brunt of the strain upon

the mechanism. As adrenalin increases blood-pressure, so thyroid

secretion increases brain activity, and increased brain activity

in turn causes an increased activation of the motor mechanism

as a whole.

We know that a deficiency or lack of thyroid secretion will inhibit

sexual emotion and conception, will produce stupidity and inertia;

will diminish vitality. On the other hand, excessive thyroid secretion

drives the entire mechanism at top speed; the emotions are intensified;

the skin becomes soft and moist, the eyes are brilliant and staring;

the limbs tremble; the heart pounds loudly and its pulsations often

are visible; the respiration is rapid; the stimulation of the fear

mechanism causes the eyes to protrude (Fig. 16); the temperature

mounts at every slight provoca-tion and may reach the incredible

height of 110'0 even. In time, the entire organism is destroyed--

literally consumed--by the concentration of dynamic energy.

It is interesting to note that in these patients emotion gains complete

possession of the final common path; they are wild and delirious--

but they never have pain.

All the diseases caused by excessive motor activity may be called

kinetic diseases. Against the conditions in life which produce

them man reacts in various ways. He intro-

{illust. caption = FIG. 51.--CROSS-COUNTRY RACE. Winner of six-mile

cross-country race showing typical expression of exhaustion.

(Copyright by Underwood and Underwood, N. Y.) duces restful variety

into his life by hunting and fishing; by playing golf and tennis;

by horseback riding; by cultivating hobbies which effectually.

turn the current of his thoughts{illust. caption = FIG. 52.--{A B

and C} from the consuming stress and strain of his business

or professional life. These diversions are all rational

attempts to relieve tension by self-preservative reactions.

For the same reason man attempts to relieve the strain of

contention with his fellow-man by unions, trusts, corporations.

In spite of all efforts, however, many constitutions are

still broken daily in the fierce conflicts of competition.

We know how often the overdriven individual endeavors to minimize

the activities of his motor mechanism by the use of agents which diminish

brain activity, such as alcohol, tobacco, and various narcotics.

Occasionally also, some person, who can find no respite from his own

relentless energies, seeks relief in oblivion by suicide.

Most fortunately, two fundamental instincts--self-preservation and

the propagation of the species--act powerfully to prevent

this last fatal result, and instead the harassed individual

seeks from others the aid which is lacking within himself.

He may turn to the priest who seeks and often secures the final

common path for faith in an over-ruling Providence, a faith which in

many incontrovertible instances has proved sufficient in very truth

to move mountains of lesser stimuli; or he turns to a physician,

who too often treats the final outcome of the hyperactivity only.

The physician who accepts the theory of the kinetic diseases,

however, will not only repair as far as he may the lesions caused

by the disordered and forced activities, but will, by compelling and

forceful suggestion, secure the final common path for right conduct,

that is, for a self- and species-preservative course of action

as opposed to wrong conduct-a self- and species-destructive

course of action.

By forcefully imparting to his patient the knowledge of the far-reaching

effects of protracted emotional strain, of overwork, and of worry,

the physician will automatically raise his threshold to the damaging

activating stimuli which have produced the evil results.

Even though some parts of his organism may have been permanently disabled,

a patient thus protected may yet rise to a plane of poise and

efficiency far above that of his uncontrolled fellows.

In extreme cases it does not seem unreasonable to believe that the

uncontrolled patient might be rescued by the same principle which has

proved effective in saving patients from the emotional and traumatic strain

of surgical operations--the principle of anoci-association. That is,

by disconnecting one or more of the activating organs from the brain,

the motor mechanism might be saved from its self-destruction.

Under this hypothesis, that man in disease, as in health,

is the product of his phylogeny as well as of ontogeny, the sphere

of the physician's activities takes on new aspects of far-reaching

and inspiring significance. Prognosis will become definite in proportion

to the physician's knowledge not only of the ontogenetic history of

the individual patient, but also of the phylogenetic history of the race.

As that knowledge increases, as he appreciates more and more keenly

the significance of environment in its effect upon individual development,

in so far will the physician be in a position to contribute mightily

to the welfare of the race.

THE KINETIC SYSTEM[\*]

[\*] Address delivered before the New York State Medical Society, April 28,

1914, to which has been added a further note regarding studies

of hydrogen ion concentration in the blood.

In this paper I formulate a theory which I hope will harmonize a large

number of clinical and experimental data, supply an interpretation

of certain diseases, and show by what means many diverse causes

produce the same end effects.

Even should the theory prove ultimately to be true, it will in the mean

time doubtless be subjected to many alterations. The specialized

laboratory worker will, at first, fail to see the broader clinical view,

and the trained clinician may hesitate to accept the laboratory findings.

Our viewpoint has been gained from a consideration of both lines

of evidence on rather a large scale.

The responsibility for the kinetic theory is assumed by myself,

while the responsibility for the experimental data is shared fully

by my associates, Dr. J. B. Austin, Dr. F. W. Hitchings, Dr. H. G. Sloan,

and Dr. M. L. Menten.[t]

[t] From H. K. Cushing Laboratory of Experimental Medicine,

Western Reserve University, Cleveland.

Introduction

The self-preservation of man and kindred animals is effected

through mechanisms which transform latent energy into kinetic energy

to accomplish adaptive ends. Man appropriates from environment

the energy he requires in the form of crude food which is refined

by the digestive system; oxygen is taken to the blood and carbon

dioxid is taken from the blood by the respiratory system;

to and from the myriads of working cells of the body, food and oxygen

and waste are carried by the circulatory system; the body is cleared

of waste by the urinary system; procreation is accomplished through

the genital system; but none of these systems was evolved primarily

for the purpose of transforming potential energy into kinetic energy

for specific ends. Each system transforms such amounts of potential

into kinetic energy as are required to perform its specific work;

but no one of them transforms latent into kinetic energy for the purposes

of escaping, fighting, pursuing, nor for combating infection.

The stomach, the kidneys, the lungs, the heart strike no physical

blow-their role is to do certain work to the end that the blow may

be struck by another system evolved for that purpose. I propose

to offer evidence that there is in the body a system evolved primarily

for the transformation of latent energy into motion and into heat.

This system I propose to designate "The Kinetic System."

The kinetic system does not directly circulate the blood,

nor does it exchange oxygen and carbon dioxid; nor does it perform

the functions of digestion, urinary elimination, and procreation;

but though the kinetic system does not directly perform these functions,

it does play indirectly an important role in each, just as the kinetic

system itself is aided indirectly by the other systems.

The principal organs which comprise the kinetic system are

the brain, the thyroid, the adrenals, the liver, and the muscles.

The brain is the great central battery which drives the body;

the thyroid governs the conditions favoring tissue oxidation;

the adrenals govern immediate oxidation processes; the liver fabricates

and stores glycogen; and the muscles are the great converters

of latent energy into heat and motion.

Adrenalin alone, thyroid extract alone, brain activity alone,

and muscular activity alone are capable of causing the body temperature

to rise above the normal. The functional activity of no other gland

of the body alone, and the secretion of no other gland alone, can cause

a comparable rise in body temperature--that is, neither increased

functional activity nor any active principle derived from the kidney,

the liver, the stomach, the pancreas, the hypophysis, the parathyroids,

the spleen, the intestines, the thymus, the lymphatic glands,

or the bones can, \_per se\_, cause a rise in the general body

temperature comparable to the rise that may be caused by the activity

of the brain or the muscles, or by the injection of adrenalin

or thyroid extract. Then, too, when the brain, the thyroid,

the adrenals, the liver, or the muscles are eliminated, the power

of the body to convert latent into kinetic energy is impaired or lost.

I shall offer evidence tending to show that an excess of either

internal or external environmental stimuli may modify one or more

organs of the kinetic system, and that this modification may cause

certain diseases. For example, alterations in the efficiency

of the cerebral link may yield neurasthenia, mania, dementia;

of the thyroid link, Graves' disease, myxedema; of the adrenal link,

Addison's disease, cardiovascular disease.

This introduction may serve to give the line of our argument.

We shall now consider briefly certain salient facts which relate to

the conversion of latent into kinetic energy as an adaptive reaction.

The experimental data are so many that they will later be published

in a monograph.

The amount of latent energy which may be converted into kinetic

energy for adaptive ends varies in different species, in individuals

of the same species, in the same individual in different seasons;

in the life cycle of growth, reproduction and decay;

in the waking and sleeping hours; in disease and in activity.

We shall here consider briefly the reasons for some of those variations

and the mechanisms which make them possible.

Biologic Consideration of the Adaptive Variation in Amounts

of Energy Stored in Various Animals

Energy is appropriated from the physical forces of nature

that constitute the environment. This energy is stored in

the body in quantities in excess of the needs of the moment.

In some animals this excess storage is greater than in other animals.

Those animals whose self-preservation is dependent on purely

mechanical or chemical means of defense--such animals as crustaceans,

porcupines, skunks or cobras--have a relatively small amount

of convertible (adaptive) energy stored in their bodies.

On the contrary, the more an animal is dependent on its muscular

activity for self-preservation, the more surplus available

(adaptive) energy there is stored in its body. It may be true that all

animals have approximately an equal amount per kilo of chemical energy--

but certainly they have not an equal amount stored in a form

which is available for immediate conversion for adaptive ends.

Adaptive Variation in the Rate of Energy Discharge

What chance for survival would a skunk have without odor; a cobra

without venom; a turtle without carapace; or a porcupine shorn

of its barbs, in an environment of powerful and hostile carnivora?

And yet in such an hostile environment many unprotected animals

survive by their muscular power of flight alone. It is evident that

the provision for the storage of "adaptive" energy is not the only

evolved characteristic which relates to the energy of the body.

The more the self-preservation of the animal depends on motor activity,

the greater is the range of variation in the rate of discharge of energy.

The rate of energy discharge is especially high in animals evolved

along the line of hunter and hunted, such as the carnivora and

the herbivora of the great plains.

Influences That Cause Variation in the Rate of Output of Energy

in the Individual

Not only is there a variation in the rate of output of energy among

various species of animals, but one finds also variations in the rate

of output of energy among individuals of the same species.

If our thesis that men and animals are mechanisms responding to

environmental stimuli be correct, and further, if the speed of energy

output be due to changes in the activating organs as a result of

adaptive stimulation, then we should expect to find physical changes

in the activating glands during the cycles of increased activation.

What are the facts? We know that most animals have breeding

seasons evolved as adaptations to the food supply and weather.

Hence there is in most animals a mating season in advance of

the season of maximum food supply so that the young may appear at

the period when food is most abundant. In the springtime most birds

and mammals mate, and in the springtime at least one of the great

activating glands is enlarged--the thyroid in man and in animals shows

seasonal enlargement. The effect of the increased activity is seen

in the song, the courting, the fighting, in the quickened pulse,

and in a slightly raised temperature. Even more activation

than that connected with the season is seen in the physical state

of mating, when the thyroid is known to enlarge materially,

though this increased activity, as we shall show later, is probably

no greater than the increased activity of other activating glands.

In the mating season the kinetic activity is speeded up; in short,

there exists a state--a fleeting state--of mild Graves' disease.

In the early stages of Graves' disease, before the destructive phenomena

are felt, the kinetic speed is high, and life is on a sensuous edge.

Not only is there a seasonal rhythm to the rate of flow of energy,

but there is a diurnal variation--the ebb is at night,

and the full tide in the daytime. This observation is verified

by the experiments which show that certain organs in the kinetic

chain are histologically exhausted, the depleted cells being

for the most part restored by sleep.

We have seen that there are variations in speed in different species,

and that in the same species speed varies with the season of the year

and with the time of day. In addition there are variations also in

the rate of discharge of energy in the various cycles of the life

of the individual. The young are evolved at high speed for growth,

so that as soon as possible they may attain to their own power

of self-defense; they must adapt themselves to innumerable bacteria,

to food, and to all the elements in their external environment.

Against their gross enemies the young are measurably protected

by their parents; but the parents--except to a limited extent in

the case of man--are unable to assist in the protection of the young

against infectious disease.

The cycle of greatest kinetic energy for physiologic ends is the period

of reproduction. In the female especially there is a cycle of increased

activity just prior to her development into the procreative state.

During this time secondary sexual characters are developed--

the pelvis expands, the ovaries and the uterus grow rapidly,

the mammary glands develop. Again in this period of increasing

speed in the expenditure of energy we find the thyroid,

the adrenals, and the hypophysis also in rapid growth.

Without the normal development of the ovary, the thyroid,

and the hypophysis, neither the male nor the female can develop

the secondary sexual characters, nor do they develop sexual desire

nor show seasonal cycles of activity, nor can they procreate.

The secondary sexual characters--sexual desire, fertility--may be

developed at will, for example, by feeding thyroid products from

alien species to the individual deprived of the thyroid.

At the close of the child-bearing period there is a permanent

diminution of the speed of energy discharge, for energy is no

longer needed as it was for the self-preservation of the offspring

before adolescence, and for the propagation of the species

during the procreative period. Unless other factors intervene,

this reduction in speed is progressive until senescent death.

The diminished size of the thyroid of the aged bears testimony

to the part the activating organs bear in the general decline.

We have now referred to variations in the rate of discharge of

energy in different species; in individuals of the same species;

in cycles in the same individual--such as the seasons of food supply,

the periods of wakefulness and of sleep, the procreative period,

and we have spoken of those variations caused artificially

by thyroid feeding, thus far having confined our discussion

to the conversion for adaptive purposes of latent into kinetic

energy in muscular and in procreative action. We shall now consider

the conversion of latent into kinetic energy in the production of

heat,[\*] and endeavor to answer the questions which arise at once:

Is there one mechanism for the conversion of latent energy into heat

and another mechanism for its conversion into muscular action?

What is the adaptive advantage of fever in infection?

[\*] We use the terms "heat" and "muscular action" in the popular sense,

though physicists use them to designate one and the same kind of energy.

The Purpose and the Mechanism of Heat Production in Infections

Vaughan has shown that the presence in the body of any alien protein

causes an increased production of heat, and that there is no difference

between the production of fever by foreign proteins and by infections.

Before the day of the hypodermic needle and of experimental medicine,

the foreign proteins found in the body outside the alimentary tract

were brought in by invading microorganisms. Such organisms interfered

with and destroyed the host. The body, therefore, was forced

to evolve a means of protection against these hostile organisms.

The increased metabolism and fever in infection might operate

as a protection in two ways--the increased fever, by interfering

with bacterial growth, and the increased metabolism, by breaking up

the bacteria. Bacteriologists have taught us that bacteria grow best

at the normal temperature of the body, hence fever must interfere

with bacterial growth. With each rise of one degree centigrade

the chemical activity of the body is increased 10 per cent.

In acute infections there is aversion to food and frequently there

is vomiting. In fever, then, we have diminished intake of energy,

but an increased output of energy--hence the available potential

energy in the body is rapidly consumed. This may be an adaptation

for the purpose of breaking up the foreign protein molecules

composing the bacteria. Thus the body may be purified by a chemical

combustion so furious that frequently the host itself is destroyed.

The problems of immunity are not considered here.

As to the mechanism which produces fever, we postulate that it

is the same mechanism as that which produces muscular activity.

Muscular activity is produced by the conversion of latent energy

into motion, and fever is produced largely in the muscles by

the conversion of latent energy into heat. We should, therefore,

find similar changes in the brain, the adrenals, the thyroid,

and the liver, whatever may be the purpose of the conversion of energy--

whether for running, for fighting, for the expression of emotion,

or for combating infection.

We shall first present experimental and clinical evidence which tends

to show what part is played by the brain in the production of both

muscular and febrile action, and later we shall discuss the parts

played by the adrenals, the thyroid, and the liver. Histologic Changes

in the Brain-cells in Relation to the Maintenance of Consciousness

and to the Production of the Emotions, Muscular Activity, and Fever

We have studied the brain-cells in human cases of fever,

and in animals after prolonged insomnia; after the injection

of the toxins of gonococci, of streptococci, of staphylococci,

and of colon, tetanus, diphtheria, and typhoid bacilli; and after

the injection of foreign proteins, of indol and skatol, of leucin,

and of peptones. We have studied the brains of animals which had been

activated in varying degrees up to the point of complete exhaustion

by running, by fighting, by rage and fear, by physical injury,

and by the injection of strychnin (Figs. 2, 4, 5, and 37). We have

studied the brains of salmon at the mouth of the Columbia River

and at its headwater (Fig. 55); the brains of electric fish,

the storage batteries of which had been partially discharged,

and of those the batteries of which had been completely discharged;

the brains of woodchucks in hibernation and after fighting;

the brains of humans who had died from anemia resulting from hemorrhage,

from acidosis, from eclampsia, from cancer and from other chronic diseases

(Figs. 40 to 43, 56, 74, and 75). We have studied also the brains

of animals after the excision of the adrenals, of the pancreas,

and of the liver (Figs. 57 and 60).

In every instance the loss of vitality--that is, the loss

of the normal power to convert potential into kinetic energy--

was accompanied by physical changes in the brain-cells (Figs. 45

and 46). The converse was also true, that is, the brain-cells

of animals with normal vital power showed no histologic changes.

The changes in the brain-cells were identical whatever the cause.

The crucial question then becomes: Are these constant changes in

the brain-cells the result of work done by the brain-cells in running,

in fighting, in emotion, in fever? In other words, does the brain

perform a definite role in the conversion of latent energy into

fever or into muscular action; or are the brain-cell changes caused

by the chemical products of metabolism? Happily, this crucial

question was definitely answered by the following experiment:

The circulations of two dogs were crossed in such a manner that the

circulation of the head of one dog was anastomosed with the circulation

of the body of another dog, and vice versa. A cord encircled the neck

of each so firmly that the anastomosing circulation was blocked

(Fig. 58). If the brain-cell changes were due to metabolic products,

then when the body of dog "A" was injured, the brain of dog "A"

would be normal and the brain of dog "B" would show changes.

Our experiments showed brain-cell changes in the brain of the dog

injured and no changes in the brain of the uninjured dog.

The injection of adrenalin causes striking brain-cell changes:

first, a hyperchromatism, then a chromatolysis. Now if adrenalin

caused these changes merely as a metabolic phenomenon and not as a

"work" phenomenon, then the injection of adrenalin into the carotid

artery of a crossed circulation dog would cause no change in its

circulation and its respiration, since the brain thus injected

is in exclusive vascular connection with the body of another dog.

In our experiment the blood-pressures of both dogs were recorded

on a drum when adrenalin was injected into the common carotid.

The adrenalin caused a rise in blood-pressure, an increase

in the force of cardiac contraction, increase in respiration,

and a characteristic adrenalin rise in the blood-pressure of both dogs.

The rise was seen first in the dog whose brain alone received adrenalin

and about a minute later in the dog whose body alone received adrenalin

(Fig. 59). Histologic examinations of the brains of both dogs

showed marked hyperchromatism in the brain receiving adrenalin,

while the brain receiving no adrenalin showed no change.

Here is a clear-cut observation on the action of adrenalin

on the brain, for both the functional and the histologic

tests showed that adrenalin causes increased brain action.

The significance of this affinity of the brain for adrenalin begins

to be seen when I call attention to the following striking facts:

1. Adrenalin alone causes hyperchromatism followed by chromatolysis,

and in overdosage causes the destruction of some brain-cells.

2. When both adrenal glands are excised and no other factor

is introduced, the Nissl substance progressively disappears from

the brain-cells until death. This far-reaching point will be taken

up later (Fig. 60).

Here our purpose is to discuss the cause of the brain-cell changes.

We have seen that in crossed brain and body circulation trauma

causes changes in the cells of the brain which is disconnected

from the traumatized body by its circulation, but which is

connected with the traumatized body by the nervous system.

We have seen that adrenalin causes activation of the body connected

with its brain by the nervous system, and histologic changes in

the brain acted on directly by the adrenalin, but we found no notable

brain-cell changes in the other brain through which the products

of metabolism have circulated.

In the foregoing we find direct evidence that the products of

metabolism are not the principal cause of the brain-cell changes.

We shall now present evidence to show that for the most part

the brain-cell changes are "work" changes. What work? We postulate

that it is the work by which the energy stored in the brain-cells is

converted into electricity or some other form of transmissible energy

which then activates certain glands and muscles, thus converting latent

energy into beat and motion. It has chanced that certain other studies

have given an analogous and convincing proof of this postulate.

In the electric fish a part of the muscular mechanism is replaced

by a specialized structure for storing and discharging electricity.

We found "work" changes in the brain-cells of electric fish

after all their electricity had been rapidly discharged

(Fig. 61). We found further that electric fish could not discharge

their electricity when under anesthesia, and clinically we

know that under deep morphin narcosis, and under anesthesia,

the production both of heat and of muscular action is hindered.

The action of morphin in lessening fever production is probably

the result of its depressing influence on the brain-cells, because

of which a diminished amount of their potential energy is converted

into electricity and a diminished electric discharge from the brain

to the muscles should diminish heat production proportionally.

We found by experiment that under deep morphinization brain-cell

changes due to toxins could be largely prevented (Fig. 62);

in human patients deep morphinization diminishes the production

of muscular action and of fever and conserves life when it is

threatened by acute infections. The contribution of the brain-cells

to the production of heat is either the result of the direct

conversion of their stored energy into heat, or of the conversion

of their latent energy into electricity or a similar force,

which in turn causes certain glands and muscles to convert latent

energy into heat.

A further support to the postulate that the brain-cells contribute

to the production of fever by sending impulses to the muscles

is found in the effect of muscular exertion, or of other forms of

motor stimulation, in the presence of a fever-producing infection.

Under such circumstances muscular exertion causes additional fever,

and causes also added but identical changes in the brain-cells. Thyroid

extract and iodin have the same effect as muscular exertion and infection

in the production of fever and the production of brain-cell changes.

All this evidence is a strong argument in favor of the theory that

certain constituents of the brain-cells are consumed in the work

performed by the brain in the production of fever.

That the stimulation of the brain-cells without gross activity

of the skeletal muscles and without infection can produce heat

is shown as follows:

(\_a\_) Fever is produced when animals are subjected to fear without

any consequent exertion of the skeletal muscles.

(\_b\_) The temperature of the anxious friends of patients will rise

while they await the outcome of an operation (Fig. 63).

(\_c\_) The temperature and pulse of patients will rise as a result

of the mere anticipation of a surgical operation (Fig. 64).

(\_d\_) There are innumerable clinical observations as to the effect

of emotional excitation on the temperature of patients.

A rise of a degree or more is a common result of a visit from

a tactless friend. There is a traditional Sunday increase

of temperature in hospital wards. Now the visitor does not bring

and administer more infection to the patient to cause this rise,

and the rise of temperature occurs even if the patient does

not make the least muscular exertion as a result of the visit.

I once observed an average increase of one and one-eighth degrees

of temperature in a ward of fifteen children as a result of a Fourth

of July celebration.

Is the contribution of the brain to the production of heat due

to the conversion of latent energy directly into heat, or does

the brain produce heat principally by converting its latent energy

into electricity or some similar form of transmissible energy which,

through nerve connections, stimulates other organs and tissues,

which in turn convert their stores of latent energy into heat?

According to Starling, when the connection between the brain

and the muscles of an animal is severed by curare, by anesthetics,

by the division of the cord and nerves, then the heat-producing power

of the animal so modified is on a level with that of cold-blooded animals.

With cold the temperature falls, with heat it rises. Such an animal

has no more control over the conversion of latent energy into heat

than it has over the conversion of latent energy into motion.

Electric stimulation done over a period of time causes brain-cell changes,

and electric stimulation of the muscles causes a rise in temperature.

Summary of Brain-cell Studies

In our crossed circulation experiments we found that neither waste

products nor metabolic poisons could be considered the principal

cause of the brain-cell changes. We found that in the production

both of muscular action and of fever there were brain-cell changes

which showed a quantita-tive relation to the temperature changes

or to the muscular work done. We observed that under deep

morphinization the febrile response or the muscular work done was

either diminished or eliminated and that the brain-cell changes were

correspondingly diminished or eliminated. We found also that brain-cell

changes and muscular work followed electric stimulation alone.

I conclude, therefore, that the brain-cell changes are work changes.

We shall next consider other organs of the kinetic system in their

relation to muscular activity, to emotion, to consciousness,

to sleep, to hibernation, and to heat production.

The Adrenals

In our extensive study of the brain in its relation to the production

of energy and the consequent exhaustion caused by fear and rage;

by the injection of foreign proteins, of bacterial toxins,

and of strychnin; by anaphylaxis; by the injection of thyroid extract,

of adrenalin, and of morphin, we found that, with the exception

of morphin, each of these agents produced identical changes in

the brain-cells. As we believed that the adrenals were intimately

associated with the brain in its activities, we concluded that

the adrenals also must have been affected by each of these agents.

To prove this relation, we administered the above-mentioned

stimuli to animals and studied their effects upon the adrenals

by functional, histologic, and surgical methods, the functional

tests being made by Cannon's method.

Functional Study of the Adrenals.--Our method of applying

the Cannon test for adrenalin was as follows: (\_a\_) The blood

of the animals was tested before the application of the stimulus.

If this test was negative, then (\_b\_) the stimulus was applied

and the blood again tested. If this second test was negative,

a small amount of adrenalin was added. If a positive reaction

was then given, the negative result was accepted as conclusive.

(\_c\_) If the control test was negative, then the stimulus was given.

If the blood after stimulation gave a positive result for adrenalin,

a second test of the same animal's blood was made twenty-five minutes

or more later. If the second test was negative, then the positive

result of the first test was accepted as conclusive.

We have recorded 66 clear-cut experiments on dogs, which show that

after fear and rage, after anaphylaxis, after injections of indol

and skatol, of leucin and creatin, of the toxins of diphtheria and

colon bacilli, of streptococci and staphylococci, of foreign proteins,

and of strychnin, the Cannon test for adrenalin was positive.

The test was negative after trauma under anesthesia, and after

intravenous injections of thyroid extract, of thyroglobin,

and of the juices of various organs injected into the same animal from

which the organs were taken. Placental extract gave a positive test.

The test was sometimes positive after electric stimulation

of the splanchnic nerves. On the other hand, if the nerve supply

to the adrenals had been previously divided, or if the adrenals

had been previously excised, then the Cannon test was negative

after the administration of each of the foregoing adequate stimuli.

Blood taken directly from the adrenal vein gave a positive result,

but under deep morphinization the blood from the adrenal vein

was negative, and under deep morphinization the foregoing adequate

stimuli were negative.

In brief, the agencies that in our brain-cell studies were found to

cause hyperchromatism followed by chromatolysis gave positive results

in the Cannon test for adrenalin (Fig. 62). The one agent which was

found to protect the brain against changes in the Nissl substance--

morphin--gave a negative result in the Cannon test for adrenalin.

After excision of the adrenals, or after division of their nerve supply,

all Cannon tests for adrenalin were negative.

Histologic Study of the Adrenals.--Histologic studies of the adrenals

after the application of the adequate stimuli which gave positive

results to the Cannon test for adrenalin are now in progress,

and thus far the histologic studies corroborate the functional tests.

In hibernating woodchucks, the cells of the adrenal cortex were found

to be vacuolated and shrunken. In one hundred hours of insomnia,

in surgical shock, in strong fear, in exhaustion from fighting,

after peptone injections, in acute infections, the adrenals undergo

histologic changes characteristic of exhaustion (Figs. 66 to 67).

We have shown that brain and adrenal activity go hand in hand,

that is, that the adrenal secretion activates the brain, and that

the brain activates the adrenals. The fundamental question which now

arises is this: Are the brain and the adrenals interdependent?

A positive answer may be given to this question, for the evidence

of the dependence of the brain upon the adrenals is as clear as is

the evidence of the dependence of the adrenals upon the brain.

(1) After excision of the adrenals, the brain-cells undergo

continuous histologic and functional deterioration until death.

During this time the brain progressively loses its power

to respond to stimuli and there is also a progressive loss

of muscular power and a diminution of body temperature.

(2) {illust. caption = FIG. 66.In our crossed circulation experiments

we found that adrenalin alone could cause increased brain activity,

while histologically we know that adrenalin alone causes an increase

of the Nissl substance. An animal, both of whose adrenals

had been excised, showed no hyperchromatism in the brain-cells

after the injection of strychnin, toxins, foreign proteins, etc.

(3) When the adrenal nerve supply is divided (Cannon-Elliott), then

there is no increased adrenal activity in response to adequate stimuli.

From these studies we are forced to conclude not only that the brain

and adrenals are interdependent, but that the brain is actually

more dependent upon the adrenals than the adrenals upon the brain,

since the brain deteriorates progressively to death without the adrenals,

while the adrenal whose connection with the brain has been broken

by the division of its nerve supply will still produce sufficient

adrenalin to support life.

From the strong affinity of the brain-cells for adrenalin which was

manifested in our experiments we may strongly suspect that the Nissl

substance is a volatile, extremely unstable combination of certain

elements of the brain-cells and adrenalin, because the adrenals alone

do not take the Nissl stain and the brain deprived of adrenalin

also does not take Nissl stain. The consumption of the Nissl

substance in the brain-cells is lessened or prevented by morphin,

as is the output of adrenalin; and the consumption of the Nissl

substance is also lessened or prevented by nitrous oxid.

But morphin does not prevent the action of adrenalin injected

into the circulation, hence the control of morphin over energy

expenditure is exerted directly on the brain-cells. Apparently morphin

and nitrous oxid both act through this interference with oxidation

in the brain. We, therefore, conclude that within a certain range

of acidity of the blood adrenalin can unite with the brain-cells

only through the mediation of oxygen, and that the combination

of adrenalin, oxygen, and certain brain-cell constituents

causes the electric discharge that produces heat and motion.

In this interrelation of the brain and the adrenals we have what is,

perhaps, the master key to the automatic action of the body.

Through the special senses environmental stimuli reach the brain

and cause it to liberate energy, which in turn activates certain

other organs and tissues, among which are the adrenals. The increased

output of adrenalin activates the brain to still greater activity,

as a result of which again the entire sympathetic nervous system

is further activated, as is manifested by increased heart action,

more rapid respiration, raised blood-pressure, increased output

of glycogen, increased power of the muscles to metabolize glucose, etc.

If this conclusion be well founded, we should find corroborative evidence

in histologic changes in that great storehouse of potential energy,

the liver, as a result of the application of each of the adequate

stimuli which produced brain-cell and adrenal changes.

The Liver

Prolonged insomnia, prolonged physical exertion, infections, injections of

toxins and of strychnin, rage and fear, physical injury under anesthesia,

in fact, all the adequate stimuli which affected the brain and

the adrenals, produced constant and identical histologic changes

in the liver--the cells stained poorly, the cytoplasm was vacuolated,

the nuclei were crenated, the cell membranes were irregular, the most

marked changes occurring in the cells of the periphery of the lobules

(Figs. 69 and 70). In prolonged insomnia the striking changes

in the liver were repaired by one seance of sleep.

Are the histologic changes in the liver cells due to metabolism or toxic

products, or are they "work" changes incident to the conversion of latent

into kinetic energy? Are the brain, adrenals, and liver interdependent?

The following facts establish the answers to these queries:

(1) The duration of life after excision of the liver is about

the same as after adrenalectomy--approximately eighteen hours.

(2) The amount of glycogen in the liver was diminished in all the

experiments showing brain-adrenal activity; and when the histologic

changes were repaired, the normal amount of glycogen was again found.

(3) In crossed circulation experiments changes were found in the liver

of the animal whose brain received the stimulus.

From these premises we must consider that the brain, the adrenals,

and the liver are mutually dependent on one another for the conversion

of latent into kinetic energy. Each is a vital organ, each equally vital.

It may be said that excision of the brain may apparently cause death

in less time than excision of the liver or adrenals, but this statement

must be modified by our definition of death. If all the brain

of an animal be removed by decapitation, its body may live on for at

least eleven hours if its circulation be maintained by transfusion.

An animal may live for weeks or months after excision of the cerebral

hemispheres and the cerebellum, while an overtransfused animal may

live many hours, days even, after the destruction of the medulla.

It is possible even that the brain actually is a less vital organ

than either the adrenals or the liver.

In our research to discover whether any other organs should be

included with the brain, the adrenals, and the liver in this mutually

interdependent relation, we hit upon an experiment which throws

light upon this problem.

Groups of rabbits were gently kept awake for one hundred hours

by relays of students, an experiment which steadily withdrew

energy but caused not the slightest physical or emotional injury

to any of them; no drug, toxin, or other agent was given to them;

they were given sufficient food and drink. In brief, the internal

and external environments of these animals were kept otherwise normal

excepting for the gentle stimuli which insured continued wakefulness.

This protracted insomnia gradually exhausted the animals completely,

some to the point of death even. Some of the survivors were killed

immediately after the expiration of one hundred hours of wakefulness,

others after varying intervals.

Histologic studies were made of every tissue and organ in the body.

Three organs, the brain, the adrenals, and the liver, and these three only,

showed histologic changes. In these three organs the histologic changes

were marked, and were almost wholly repaired by one seance of sleep.

In each instance these histologic changes were identical with

those seen after physical exertion, emotions, toxins, etc.[\*] It

would appear, then, that these three organs take the stress of life--

the brain is the "battery," the adrenals the "oxydizer," and the liver

the "gasoline tank." This clear-cut insomnia experiment corresponds

precisely with our other brain-adrenal observations.

[\*] Further studies have given evidence that the elimination of the acids

resulting from energy-transformation as well as the conversion

of energy stored in the kinetic organs causes histologic changes

in the liver, the adrenals, and possibly in the brain.

With these three kinetic organs we may surely associate also the

"furnace," the muscles, in which the energy provided by the brain,

adrenals, and liver, plus oxygen, is fabricated into heat and motion.

Benedict, in his monumental work on metabolism, has demonstrated

that in the normal state, at least, variations in the heart-beat

parallel variations in metabolism. He and others have shown also that

all the energy of the body, whether evidenced by heat or by motion,

is produced in the muscles. In the muscles, then, we find the fourth

vital link in the kinetic chain. The muscles move the body,

circulate the blood, effect respiration, and govern the body temperature.

They are the passive servants of the brain-adrenal-liver syndrome.

Neither the brain, the adrenals, the liver, nor the muscles, however,

nor all of these together, have the power to change the rate of

the expenditure of energy; to make possible the increased expenditure

in adolescence, in pregnancy, in courting, and mating, in infections.

No one of these organs, nor all of them together, can act as a

pace-maker or sensitizer. The brain acts immediately in response

to the stimuli of the moment; the adrenals respond instantly

to the fickle brain and the effects of their actions are fleeting;

the liver contains fuel only and cannot activate, and the muscles

in turn act as the great furnace in which the final transformation

into available energy is made. The Thyroid

Another organ--the thyroid--has the special power of governing

the RATE OF DISCHARGE of energy; in other words, the thyroid is the

pace-maker. Unfortunately, the thyroid cannot be studied to advantage

either functionally or histologically, for there is as yet no available

test for thyroid secretion in the blood as there is for adrenalin,

and thyroid activity is not attended by striking histologic changes.

Therefore the only laboratory studies which have been satisfactory

thus far are those by which the iodin content of the thyroid

has been established. Iodin is stored in the colloid lacunae

of the thyroid and, in combination with certain proteins,

is the active agent of the thyroid.

Beebe has shown that electric stimulation of the nerve supply of

the thyroid diminishes the amount of iodin which it contains, and it

is known that in the hyperactive thyroid in Graves' disease the iodin

content is diminished. The meagerness of laboratory studies, however,

is amply compensated by the observations which the surgeon has been

able to make on a vast scale--observations which are as definite

as are the results of laboratory experiments.

The brain-cells and the adrenals are securely, concealed from

the eye of the clinician, hence the changes produced in them

by different causes escape his notice, but the thyroid has always

been closely scrutinized by him. The clinician knows that every

one of the above-mentioned causes of increased brain-cell, adrenal,

liver and muscle activity may cause an increase in the activity

of both the normal or the enlarged thyroid; and lie knows only too

well that in a given case of exophthalmic goiter the same stimuli

which excite the brain, the adrenals, the liver, and the muscles

to increased activity will also aggravate this disease.

The function of the thyroid in the kinetic chain is best evidenced,

however, by its role in the production of fever. Fever results

from the administration of thyroid extract alone in large doses.

In the hyperactivity of the thyroid in exophthalmic goiter one sees

a marked tendency to fever, in severe cases there is daily fever.

In fact, in Graves' disease we find displayed to an extraordinary

degree an exaggeration of the whole action of the kinetic mechanism.

We have stated that in acute Graves' disease there is a tendency

to the production of spontaneous fever, and that there is a magnified

diurnal variation in temperature which is due to an increased output

of energy in even the normal reaction producing consciousness. In Graves'

disease there is, therefore, a state of intensified consciousness, which is

associated with low brain thresholds to all stimuli--both to stimuli

that cause muscular action and to stimuli that cause fever. The intensity

of the kinetic discharge is seen in the constant fine tremor.

It is evident that the thresholds of the brain have been sensitized.

In this hypersensitization we find the following strong evidence as to

the identity of the various mechanisms for the production of fever.

In the state of superlative sensitization which is seen in Graves'

disease we find that the stimuli that produce muscular movement,

the stimuli that produce emotional phenomena, and the stimuli that

produce fever are as nearly as can be ascertained equally effective.

Clinical evidence regarding this point is abundant, for in

patients with Graves' disease we find that the three types

of conversion of energy resulting from emotional stimulation,

from infection stimulation, and from nociceptor stimulation

(pain), are, as nearly as can be judged, equally exaggerated.

In the acute cases of Graves' disease the explosive conversion

of latent energy into heat and motion is unexcelled by any other

known normal or pathologic phenomenon. Excessive thyroid secretion,

as in thyrotoxicosis from functioning adenomata, and excessive

thyroid feeding, cause all the phenomena of Graves' disease except

the exophthalmos and the emotional facies (Figs. 15 and 23).

The ligation of arteries, the division of its nerve supply,

or the excision of part of the gland, may reverse the foregoing picture

and restore the normal condition. The patient notes the effect

on the second day and often within a week is relatively quiescent.

On the contrary, if there is thyroid deficiency there results

the opposite state, a reptilian sluggishness.

At will, then, through diminished, normal, or excessive administration

of thyroid secretion, we may produce an adynamic, a normal,

or an excessively dynamic state. By the thyroid influence,

the brain thresholds are lowered and life becomes exquisite;

without its influence the brain becomes a globe of relatively

inert substance. Excessive doses of iodin alone cause

most of the symptoms of Graves' disease. As we have stated,

the active constituent of the thyroid is iodin in a special

protein combination which is stored in the colloidal spaces.

Hence one would not expect to find changes in the cells of the thyroid

gland as a result of increased activity unless it be prolonged.

We have thus far considered the normal roles played by the brain,

the adrenals the liver, the muscles, and the thyroid in transforming

latent into kinetic energy in the form of heat and motion as an

adaptive response to environmental stimuli.

The argument may be strengthened, however, by the discussion of

the effect of the impairment of any of these links in the kinetic

chain upon the conversion of latent into kinetic energy.

Effect Upon the Output of Energy of Impaired or Lost Function

of Each of the Several Links in the Kinetic Chain

(1) \_The Brain\_.--In cerebral softening we may find all the organs

of the body comparatively healthy excepting the brain.

As the brain is physically impaired it cannot normally stimulate

other organs to the conversion of latent energy into heat or

into motion, but, on the contrary, in these cases we find feeble

muscular and intellectual power. I believe also that in patients

with cerebral softening, infections such as pneumonia show a lower

temperature range than in patients whose brains are normal.

(2) \_The Adrenals\_.--In such destructive lesions of the adrenals

as Addison's disease one of the cardinal symptoms is a subnormal

temperature and impaired muscular power. Animals upon whom double

adrenalectomy has been performed show a striking fall in temperature,

muscular weakness,--after adrenalectomy the animal may not be able

to stand even,--and progressive chromatolysis.

(3) \_The Liver\_.--When the function of the liver is impaired

by tumors, cirrhosis, or degeneration of the liver itself,

then the entire energy of the body is correspondingly diminished.

This diminution of energy is evidenced by muscular and mental weakness,

by diminished response and by gradual loss of efficiency which finally

reaches the state of asthenia.

(4) \_The Muscles\_.--It has been observed clinically that if the muscles

are impaired by long disuse, or by a disease such as myasthenia gravis,

then the range of production of both heat and motion is below normal.

This is in agreement with the experimental findings that anesthetics,

curare, or any break in the muscle-brain connection causes diminished

muscular and heat production.

(5) \_The Thyroid\_.--In myxedema one of the cardinal symptoms

is a persistently subnormal temperature and, though prone

to infection, subjects of myxedema show but feeble febrile response

and readily succumb. This clinical observation is strikingly

confirmed by laboratory observations; normal rabbits subjected

to fear showed a rise in temperature of from one to three degrees,

while two rabbits whose thyroids had been previously removed and who

had then been subjected to fright showed much less febrile response.

Myxedema subjects show a loss of physical and mental energy

which is proportional to the lack of thyroid. Deficiency in any

of the organs of the kinetic chain causes alike loss of heat,

loss of muscular and emotional action, of mental power, and of the power

of combating infections--the negative evidence thus strongly supports

the positive. By accumulating all the evidence we believe we

are justified in associating the brain, the adrenals, the thyroid,

the muscles, and the liver as vital links in the kinetic chain.

Other organs play a role undoubtedly, though a minor one.

Studies in Hydrogen Ion Concentration in Activation of the Kinetic System

Having established the identity of some, at least, of the organs

which constitute the kinetic chain, we endeavored to secure still

further evidence regarding the energy-transforming function of these

organs by making studies of the H-ion concentration of the blood,

as one would expect, \_prima facie\_, that the normal reaction would

be altered by kinetic activation.[\*]

[\*] The H-ion observations were made in my laboratory by Dr. M. L. Menten.

H-ion concentration tests were made after the application

of the adequate stimuli by which the function of the kinetic

organs had been determined, and we studied also the effect upon

the acidity of the blood of strychnin convulsions after destruction

of the medulla; of deep narcotization with morphin before anesthesia;

of deep narcotization with morphin after the H-ion concentration

had already been increased by fear, by anger, by exertion,

by injury under anesthesia, or by anesthesia alone.

The complete data of these experiments will be later reported in

a monograph; here it is sufficient to state that anger, fear, injury,

muscular exertion, inhalation anesthesia, strychnin, alcohol, in fact,

all the stimuli which we had already found to produce histologic

changes in the brain, the adrenals, and the liver-excepting

bacterial toxins--caused increased H-ion concentration.

Of striking significance is the fact that morphin alone caused

no change in the H-ion concentration, while if administered before

the application of a stimulus which by itself produced increased

H-ion concentration, the action of that stimulus was neutralized

or postponed. If, however, morphin was administered after increased

acidity had been produced by any stimulus, or by inhalation anesthesia,

then the time required for the restoration of the normal alkalinity

was much prolonged, and in some instances the power of acid

neutralization was permanently lost.

After excision of the liver, the normal H-ion concentration

was maintained for periods varying from one to several hours,

after which the concentration (acidity) began to increase as

the vitality of the animal began to decline, the concentration

(acidity) increasing rapidly until death. After excision of

the adrenals the blood remained normal for from four to six hours,

when the H-ion concentration increased rather suddenly,

the increase being synchronous with the incidence of the phenomena

which immediately preceded death.

In none of these cases was it determined whether the increased

H-ion concentration was due to other causes of death or whether

death was due to the increased acidity.

It is also significant that after the application of each of

the adequate stimuli which increased the H-ion concentration

of the blood in other parts of the body the blood from the adrenal

vein showed a slight diminution in acidity, as, in most instances,

did the blood from the hepatic vein also.

In fact, the H-ion concentration of the blood in the adrenal vein

was less than in the blood of any other part of the circulation.

Kinetic Diseases

If our conclusions are sound, then in the kinetic system we find

an explanation of many diseases, and having found the explanation,

we may find new methods of combating them.

When the kinetic system is driven at an overwhelming rate of speed,--

as by severe physical injury, by intense emotional excitation,

by perforation of the intestines, by the pointing of an abscess

into new territory, by the sudden onset of an infectious disease,

by an overdose of strychnin, by a Marathon race, by a grilling fight,

by foreign proteins, by anaphylaxis,--the result of these acute

overwhelming activations of the kinetic system is clinically

designated shock, and according to the cause is called traumatic shock,

toxic shock, anaphylactic shock, drug shock, etc.

The essential pathology of shock is identical whatever the cause.

If, however, instead of an intense overwhelming activation,

the kinetic system is continuously or intermittently overstimulated

through a considerable period of time, as long as each of the links

in the kinetic chain takes the strain equally the result will be

excessive energy conversion, excessive work done; but usually,

under stress, some one link in the chain is unable to take the strain

and then the evenly balanced work of the several organs of the kinetic

system is disturbed. If the brain cannot endure the strain,

then neurasthenia, nerve exhaustion, or even insanity follows.

If the thyroid cannot endure the strain, it undergoes hyperplasia,

which in turn may result in a colloid goiter or in exophthalmic goiter.

If the adrenals cannot endure the strain, cardiovascular disease

may develop. If the liver cannot take the strain, then death from

acute acidosis may follow, or if the neutralizing effect of the liver

is only partially lost, then the acidity may cause Bright's disease.

Overactivation of the kinetic system may cause glycosuria and diabetes.

Identical physical and functional changes in the organs of

the kinetic system may result from intense continued stimulation

from any of the following causes: Excessive physical labor,

athletic exercise, worry or anxiety, intestinal autointoxication,

chronic infections, such as oral sepsis, tonsillitis, and adenoids;

chronic appendicitis, chronic cholecystitis, colitis, and skin infections;

the excessive intake of protein food (foreign protein reaction);

emotional strain, pregnancy, stress of business or professional life--

all of which are known to be activators of the kinetic system.

From the foregoing statements we are able to understand

the muscular weakness following fever; we can understand why

the senile have neither muscular power nor strong febrile reaction;

why long-continued infections produce pathologic changes in the organs

constituting the kinetic chain; why the same pathologic changes

result from various forms of activation of the kinetic system.

In this hypothesis we find a reason why cardiovascular disease may

be caused by chronic infection, by auto-intoxication, by overwork,

or by emotional excitation. We now see that the reason why we find

so much difficulty in differentiating the numerous acute infections

from each other is because they play upon the same kinetic chain.

Our postulate harmonizes the pathologic democracy of the kinetic organs,

for it explains not only why, in many diseases, the pathologic

changes in these organs are identical, but why the same changes

are seen as the result of emotional strain and overwork.

We can thus understand how either emotional strain or acute or chronic

infection may cause either exophthalmic goiter or cardiovascular disease;

how chronic intestinal stasis with the resultant absorption of

toxins may cause cardiovascular disease, neurasthenia, or goiter.

Here is found an explanation of the phenomena of shock, whether the

shock be the result of toxins, of infection, of foreign proteins,

of anaphylaxis, of psychic stimuli, or of a surgical operation

with its combination of both psychic and traumatic elements.

This conception of the kinetic system has stood a crucial test by making

possible the shockless operation. It has offered a plausible explanation

of the cause and the treatment of Graves' disease. Will the kinetic

theory stand also the clinical test of controlling that protean

disease bred in the midst of the stress of our present-day life?

Present-day life, in which one must ever have one hand on the sword and

the other on the throttle, is a constant stimulus of the kinetic system.

The force of these kinetic stimuli may be lessened at the cerebral

link by intelligent control--a protective control is empirically

attained by many of the most successful men. The force of the kinetic

stimuli may be broken at the thyroid link by dividing the nerve supply,

reducing the blood supply, or by partial excision; or if the adrenals

feel the strain, the stimulating force may be broken by dividing

their nerve supply, reducing the blood supply, or by partial excision.

No theory is worth more than its yield in practice, but already we

have the shockless operation, the surgical treatment of Graves'

disease, and the control of shock and of the acute infections

by overwhelming morphinization (Figs. 62, 72, and 73).

Conclusions

To become adapted to their environment animals are transformers of energy.

This adaptation to environment is made by means of a system of organs

evolved for the purpose of converting potential energy into heat

and motion. The principal organs and tissues of this system are

the brain, the adrenals, the thyroid, the muscles, and the liver.

Each is a vital link, each plays its particular role, and one cannot

compensate for the other. A change in any link of the kinetic

chain modifies proportionately the entire kinetic system which is

no stronger than its weakest link.

In this conception we find a possible explanation of many diseases

one which may point the way to new and more effective therapeutic

measures than those now at our command.

ALKALESCENCE, ACIDITY, ANESTHESIA--A THEORY OF ANESTHESIA[\*]

[\*] Paper delivered before the Virginia Medical Association,

Washington, D. C., October 29, 1914.

Alkalis and bases compose the greater part of the food of man

and animals, the blood in both man and animals under normal conditions

being slightly alkaline or rather potentially alkaline; that is,

although in circulating blood the concentration of the OH-ions--

upon which the degree of alkalinity depends--is but little more

than in distilled water, yet blood has the power of neutralizing

a considerable amount of acid (Starling, Wells). At the time of death,

whatever its cause, the concentration of H-ions in the blood increases,--

the concentration of H-ions being a measure of acidity,--that is,

the potential or actual alkalinity decreases and the blood becomes

actually neutral or acid.

To determine what conditions tend to diminish the normal alkalinity

of the blood, many observations were made for me in my laboratory

by Dr. M. L. Menten to determine by electric measurements

the H-ion concentration of the blood under certain pathologic

and physiologic conditions.

As a result of these researches we are able to state that the H-ion

concentration of the blood--its acidity--is increased by excessive

muscular activity; excessive emotional excitation; surgical shock;

in the late stages of infection; by asphyxia; by strychnin convulsions;

by inhalation anesthetics; after excision of the pancreas, and in the late

stages of life after excision of the liver and excision of the adrenals.

Morphin and decapitation cause no change in the H-ion concentration.

Ether, nitrous oxid, and alcohol produce an increased acidity

of the blood which is proportional to the depth of anesthesia.

Many of the cases studied were near death, as would be expected,

since it is well known that a certain degree of acidity is

incompatible with life.

Since alkalis and bases preponderate in ingested food;

since alkalinity of the blood is diminished by bodily activity;

and since at the point of death the blood is always acid, we may

infer that some mechanism or mechanisms of the body were evolved

for the purpose of changing bases into acids that thus energy

might be liberated.

These observations lead naturally to the question, May not

acidity of itself be the actual final cause of death?

We believe that it may be so from the facts that--(1)

The intravenous injection of certain acids causes death quickly,

but that convulsions do not occur, since the voluntary muscles

lose their power of contraction; and (2) the intravenous injection

of acids causes extensive histologic changes in the brain,

the adrenals, and the liver which resemble the changes invariably

caused by activation of the kinetic system (Figs. 74 and 75). In view

of these facts may we not find that anesthesia and many instances

of unconsciousness are merely phenomena of acidity?

As has been stated already, we have found that the H-ion concentration

of the blood--its acidity--is increased by alcohol, by ether,

and by nitrous oxid. In addition our tests have shown that under

ether the increase of the H-ion concentration--acidity--is more

gradual than under nitrous oxid, an observation which accords well

with the fact that nitrous oxid more quickly induces anesthesia

than does ether.

Further striking testimony in favor of the hypothesis that

the production of acidity by inhalation anesthetics is the method

by which anesthesia itself is produced is found in the fact

that although lethal doses of acid cause muscular paralysis,

yet this paralysis may be mitigated by adrenalin--which is alkaline.

This observation may explain in part the remarkable success of

the method of resuscitation devised by me, in which animals "killed"

by anesthetics and asphyxia are revived by the use of adrenalin.

In animals under inhalation anesthesia Williams found that no

nerve-current could be detected by the Einthoven string galvanometer,

a fact which might be explained by postulating that nerve-currents

can flow from the brain to the muscles and glands only when there

is a difference of potential. Any variation from the normal

alkalinity of the body must change the difference in potential.

Since the nerve-currents in animals under anesthesia are not demonstrable

by any apparatus at our command, and since anesthesia produces acidity,

then we may infer that acidity reduces the difference in potential.

As long as there is life, a galvanometer of sufficient delicacy

would perforce detect, a nerve-current until the acidity increased

to such a point as to reduce the difference in potential to zero--

the point of death. If at this point a suitable alkali--

adrenalin solution--can be introduced quickly enough, the vital difference

in potential may be restored and the life processes will be renewed.

Bearing especially on this point is the fact that if adrenalin

in sufficient quantities be administered simultaneously with an acid,

it will not only prevent the fall in blood-pressure usually

caused by the acid, but will also prevent the histologic changes

in the brain, adrenals, and liver which are usually caused by

the intravenous injection of acids.

This hypothesis regarding the cause of anesthesia and unconsciousness

explains and harmonizes many facts. It explains how asphyxia,

overwhelming emotion, and excessive muscular exertion, by causing acidity,

may produce unconsciousness. It explains the acidosis which results

from starvation, from uremia, from diabetes, from Bright's disease,

and supplies a reason for the use of intravenous infusions of sodium

bicarbonate to overcome the coma of diabetes and uremia (Fig. 76).

It may explain the quick death from chloroform and nitrous oxid;

and may perhaps show why unconsciousness is so commonly the immediate

precursor of death.

One of the most noticeable immediate effects of the administration

of an inhalation anesthetic is a marked increase in the rapidity

and force of the respiration. The respiratory center has evidently

been evolved to act with an increase of vigor which is proportional--

within certain limits--to the increase in the H-ion concentration,

whereas the centers governing the voluntary muscles are inhibited.

In this antithetic reaction of the higher cortical centers and the lower

centers in the medulla to acidity we find a remarkable adaptation

which prevents the animal from killing itself by the further increase

in acidity which would be produced by muscular activity. That is,

as the acidity produced by muscular action increases and threatens life,

the respiratory action, by which carbon dioxid is eliminated and

oxygen supplied, is increased, while the driving power of the brain,

which produces acidity, is diminished or even inhibited entirely;

that is, the state of unconsciousness or anesthesia is reached.

We conclude first that, without this life-saving regulation,

animals under stress would inevitably commit suicide; and, second,

that it is probable that the remarkable phenomenon of anesthesia--

the coincident existence of unconsciousness and life--is due to this

antithetic action of the cortex and the medulla.

In the human, as in the animal, the degree of acidity parallels

the depth of inhalation anesthesia.

Within a few seconds after beginning nitrous oxid anesthesia the acidity

of the blood is increased. This rapid acidulation is synchronous

with almost instantaneous unconsciousness and increased respiration.

If the oxygen in the inhaled mixture be increased, a decrease in

acidity is again synchronous with lighter anesthesia and a decrease

in the respiratory rate.

If these premises be sound, we are justified in asserting that the state

of anesthesia is due to an induced acidity of the blood. If the acidity

is slight, then the anesthesia is slight and the force of the nerve

impulses is lessened, but the patient is still conscious of them.

As the acidity increases associative memory is lost, and the patient

is said to be unconscious: the centers governing the voluntary muscles

are not inhibited, however, and cutting the skin causes movements.

If the acidity is further increased, there is loss of muscular tone

and even the strong contact ceptor stimuli of a surgical operation

do not cause any muscular response, and, finally, the acidity may be

increased to the point at which the respiratory and circulatory centers

can no longer respond by increased effort, and anesthetic death--

that is, ACID death--follows.

Certain clinical phenomena are clarified by this theory and serve

to substantiate it. For example, it is well known that inhalation

anesthesia precipitates the impending acidosis which results

from starvation, from extreme Graves' disease, from great exhaustion,

from surgical shock, and from hemorrhage, and which is present

when death from any cause is imminent.

We see, therefore, that anesthesia is made possible, first, by the fact

that inhalation anesthetics cause acidity, and, second, by the antithetic

adaptation of the higher centers in the brain and of the centers

governing respiration and circulation.

In deep contrast to the action of inhalation anesthetics is that

of narcotics. Deep narcotization with morphin and scopolamin is

induced slowly; the respiratory and pulse-rate are progressively lessened--

and there is no acidity.

By our researches we have established in what consists the generic

difference between inhalation anesthetics and narcotics.

In our experiments no increase in the H-ion concentration was produced

by morphin or by scopolamin, no matter how deep the narcotization.

In animals already narcotized by morphin the production of acid by any

of the acid-producing stimuli was delayed or prevented. On the other hand,

in animals in which an acidity had already been produced by ether,

by shock, by anger, or by fear, the later administration of morphin

delayed or inhibited entirely the neutralization of the acidity.

In other words, morphin interferes with the normal mechanism by

which acidity is neutralized possibly because its inhibiting action

on the respiratory center is sufficient to overcome the stimulating

action of acidity on that center, for, as we have stated,

the neutralization of acidity is in large measure accomplished

by the increased respiration induced by the acidity itself.

SUMMARY

Acidity inhibits the functions of the cerebral cortex,

but stimulates those of the medulla. This antithetic reaction

to the stimulus of increased H-ion concentration is an adaptation

to prevent animals from committing suicide by over-activity,

for the mechanism for the initiation and control of the

transformation of energy is in the higher centers of the brain,

while an essential part of the mechanism for the neutralization

of acidity--the centers governing circulation and respiration--

is in the medulla. This explains many clinical phenomena--

why excessive acidity causes paralysis, why there is great thirst

after inhalation anesthesia, after excessive muscular activity,

excessive emotion--after all those activities which we have found

to be acid-producing, for water, like air, neutralizes acids.

The excessive use of alcohol, anesthetics, excessive work,

intense emotion, all produce lesions of the kidney and of the liver.

The explanation is found in the fact that all these stimuli

increase the acidity of the blood. and that, if long continued,

the neutralizing mechanism must be broken down and so the end-products

of metabolism are insufficiently prepared for elimination.

In view of these considerations we may well conclude that the maintenance

of the normal potential alkalinity of the blood is to be estimated

as the keystone of the foundation of life itself.

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