which endowed the "interstitial organ" of the ovary with *active* rôle. Such being the case, and the interstitial gland corresponding, as observed by Mulon, Wallach, and myself, with the adrenal cortex, we are brought to realize that *the secondary sex characteristics are attributable, in the female, to the ovarian interstitial cells, which correspond morphologically and chemically with those of the adrenal cortex.*

On the other hand, the foregoing analysis tends to show that *the interstitial cells of the female are not the same structures as the interstitial (Leydig) cells in the male; the Leydig cells, connected functionally as they are with the sperm-cells, correspond with the Graafian follicles and their corpora lutea, as secreting structures.*

On the whole, however, and in keeping with conclusion 1 submitted in respect to the testicles: *There is no true internal secretion of the ovaries, the products of the Graafian follicles and their corpora lutea and of the interstitial stroma-cells being derived mainly from adrenal rests in those cells.*

Here, however, the physiological rôle of the testicular products cannot be reproduced, for if, as in the male, the products of the adrenal rests were absorbed when not secreted through sexual congress, masturbation, etc., the male characteristics would assert themselves in the female through the accumulation of the secretion of her interstitial cells. Hence, *to provide against the loss of female characteristics through accumulation of the secretion of the inerstitial glands in the body at large, the products of the ovarian adrenal rests are eliminated periodically,* i.e., *during the menstrual cycle.*

It is because of this fact, as we have seen, that the loss of the testicular glands causes in the male the appearance of female characteristics, while in the female the accumulation through tumors, etc., of adrenal cells, causes the development of male characteristics.

Finally, when pregnancy occurs, all the dynamism which the adrenal rests provide through the influence of their secretion, acting mainly as catalyzer, on oxidation, become necessary for the development of the new being, lactation, etc., and the menstrual cycle ceases.

CHAPTER X.

THE POSTERIOR PITUITARY AS A GENERAL NERVE-CENTER AND AS CO-CENTER OF THE ANTERIOR PITUITARY IN SUSTAINING LIFE.

THE IDENTITY OF THE LOWER BRAIN.

In the earlier editions of this work I urged that certain centers in the medulla oblongata were probably but subsidiary centers which received nervous impulses from the pituitary body by way of the tuber cinereum and other basal structures. I held, moreover, that "inhibition" as obtained by physiologists represented a pathological phenomenon in that it was caused by excessive constriction of the cardiac arterioles provoked by vasoconstrictors contained in the nerve stimulated, the vagus.

As is well known, it was the work of the brothers Weber (1845) which first suggested that the heart could be "inhibited" by stimulation of a definite region in the medulla. Their experiments differed from those we have reviewed in that the tissues of the base of the brain were traversed by the current, thus exciting structures in which we have seen sympathetic and other nerves pass from the pituitary to the bulb. One pole having been placed in the nasal cavity of a frog and the other on the spinal cord over the fourth or fifth vertebra, the heart's action momentarily ceased, then gradually resumed its normal activity. Approximation of the poles upon the cerebral hemispheres and stimulation of the cord produced no effect upon the heart. "Not until the medulla oblongata between the corpora quadrigemina and the lower end of the calamus scriptorius was stimulated," says William T. Porter, "did the arrest take place. Cutting away the spinal cord and the remainder of the brain did not alter the result." The level of fibers from structures below the brain is also suggested by the effects of experimental injury of the bulbar area which Flourens termed *le nœud vital.*

Galen had already noticed that death ensued when a certain spot in the floor of the fourth ventricle close to that which is now known as the center of the vagus was injured. But Legallois and Flourens have added much to our knowledge of its physiological relations, and the spot in question, as we have seen, is still considered as the respiratory center. "The results of various investigations show, however," says Reichert,[1] "that Flourens's area, as well as certain other parts of the medulla oblongata that have been looked upon by others as being respiratory centers, are not such, but are largely or wholly collections of nerve-fibers which arise chiefly in the roots of the vagal, spinal accessory, glosso-pharyngeal, and trigeminal nerves, and which, therefore, are probably nerve-paths to and from the respiratory center. Moreover, excitation of the *'nœud vital' does not excite respiratory movements,* but simply increases the tonicity of the diaphragm; nor is the destruction of the area always followed by a cessation of respiration. While the precise location of the center is still in doubt, there is abundant evidence to justify the belief in its existence in the lower portion of the spinal bulb." That we are again dealing with the aggregate of centers to which the pituitary body projects its fibers suggests itself. Flourens located his "vital knot" in an area five millimeters wide *between* the nuclei of the vagus and spinal accessory nerves—again in the *lower end of the calamus scriptorius: i.e.,* a region comprised in the area to which the Weber brothers applied one electrode, the other being in the nose, when cardiac arrest or inhibition was first observed by them.

An interesting relationship seems to me to exist between these two sets of experimental results. Indeed, the area to which the pituitary body sends its fibers thus becomes the source of antagonistic effects involving the same structures: *i.e.,* the Weber brothers caused arrest of the heart by causing undue constriction of its coronaries and ischæmia of the myocardium, while the lesion produced in the manner previously described, when sufficiently severe, blocked by Flourens in the same area, the flow of impulses to and from the heart. Flourens's *nœud*

[1] Reichert: *Loc. cit.*

vital, therefore, is no more the respiratory center than the area traversed by the current can be called an "inhibitory" area. We are simply dealing with the results of two morbid factors: overstimulation (Weber) and interruption (Flourens) of physiological—and therefore functional—impulses transmitted *through* the medulla and the cord.

In the fifth chapter reference was made to the fact that the posterior pituitary lobe alone, as shown by Howell, contained an active principle. This lobe, the "infundibular," has long been termed the "neural" portion of the whole organ, and appears to me to present anatomical features that further suggest a direct connection between it and the cerebro-spinal centers. Hence the use of the words "physiological impulses transmitted *through* the medulla and the cord." The question becomes all the more worthy of a searching inquiry, inasmuch as a casual examination of the mutual relations, anatomical and physiological, of the cerebral structures traversed by the current in the experiment of the Weber brothers suffices to show that the elements thus submitted to excessive stimulation coincide with those which would normally fall under the influence of the posterior pituitary body.

The physiological characteristics of the parts influenced by the current must first be ascertained. In the frog, the distance between the nose and the medulla being very short, a current would implicate all elements in its direct path, considering the character of the structures traversed. In this animal, the lizard, etc., the nasal nervous terminals, the tissues about the floor of the median ventricle and the habenula, appear to me as the paths that would be involved. In man the distance between the olfactory area or the nasal subdivisions of the fifth pair and the medulla is also relatively limited, and the intervening structures are of such a nature as to also allow the current to pass uninterruptedly in a straight path. But the floor of the median or third ventricle, which in its anterior portion overlies the base of the skull and is very thin, becomes what appears to be the inevitable path of free conduction, owing to this proximity of the olfactory bulb and the trigeminal nasal terminals to the medullary centers. Of special interest here, however, is the fact that in man (and to a great extent in the frog) the first structure reached by the current after the nasal structures would be the infundibular portion of the third ventricle: *i.e.,* that connected with the posterior pituitary lobe. Again, and very suggestive, is the fact that these structures and all those falling in the line of the current form part of what Professor Foster terms "in point of origin the oldest part of the brain" and "the central gray matter" which "seems to serve chiefly as a bed for the development of the nuclei of the cranial nerves." Indeed, we might repeat that, as stated by Reichert,[2] "one center has been located in the rabbit in the *tuber cinereum,* which has been named a polypnœic center because, when excited, the respirations are rendered extremely frequent." . . . "Another area has been located in the optic thalamus, in the floor of the third ventricle; this center," says the author, "is believed to be excited by impulses carried by the nerves of sight and hearing, and when irritated causes an acceleration of the respiratory rate."

The more dorsal portion of the current would strike a no less important physiological region. "Next to the central gray matter," says Professor Foster, "and more or less associated with it, comes what is called the tegmental region, of which the reticular formation coming into prominence in the bulb and continued on to the subthalamic region forms, as it were, the core. Belonging to the tegmental system are numerous masses of gray matter from the conspicuous optic thalamus and the red nucleus in front to the several nuclei of the bulb behind. This complex tegmental system, which may, perhaps, be regarded as a more or less continuous column of gray matter, comparable to the gray matter of the spinal cord, serves as a sort of *backbone to the rest of the central nervous system.*"

The morbid effects of the current become normal consequences when we consider that the structures traversed by it include those that even emotions will disturb. Referring to the posterior portion of the pons, that adjoining the tissues that form the fourth ventricle and which represents the downward continuation of the tegmentum, Professor Duval says: "It is, indeed, to the pons that we seem to be authorized to

[2] Reichert: *Loc. cit.*

attribute the most important rôle in the greater emotional expressions, laughing and weeping, cries of pain: in a word, involuntary manifestations." That the structures such as those penetrated by the current should be suddenly jarred and forcibly thrown into vibratory conditions entirely foreign to their normal vibratory rhythm is manifest. That such jarring, especially when the current follows axially a direction opposite to that of a physiological stream of impulses, should so pervert its normal influence upon the organs to which these impulses are normally distributed—heart, lungs, stomach, etc.—as to temporarily or permanently arrest their functions is not only logical, but in accord with the known effects of electricity upon the more highly developed structures.

And we can also doubtless better understand why respiration still continues very much as usual after removal of the brain above the medulla, and why, indeed, all nervous manifestations other than ideation can persist after such mutilation. While there is no *"nœud vital,"* or ganglion of life, in the sense given these words by Flourens,—*i.e.,* in the spot of the medulla where injury arrests respiration,—and the area so injured is not "the mysterious seat of the unknown principle of life," there is, nevertheless, in this location, not a *locus minus resistentiæ,* but an aggregation of nervous paths from all directions, which an injury can functionally impair or destroy, according to the quantity of tissue involved and the kind of lesion produced. Flourens doubtless caused death; but in looking for death in his experimental animals he doubtless did not treat the *"nœud vital"* with the gentleness of a dove. Death ensued—the result of conditions similar to those produced by the Weber brothers with electricity in the sense that molecular disturbance was produced. Yet the Weber brothers only jarred the naso-bulbar structures, and produced temporary inhibition of cardiac action; being more diffuse, the current spread over greater bulbar surface and did less injury. Flourens's puncture, on the contrary, produced an organic lesion, capable not only of destroying the tissues involved, but also of annulling, by the circumferential compression of the neighboring elements caused, the functions over which the latter preside. Even the process of repair, which at once begins under such conditions, may lead to a fatal issue, the infiltration throttling, as it were, the paths *to* and *from* organs through which life is sustained. When we consider the small relative size of the fourth ventricle, and the fact that the so-called "vital knot" is located in an area which may be computed only by a few millimeters; when we furthermore recognize that such an injury would thus include the vagal, spinal accessory, glossopharyngeal, and hypoglossal within its radius of morbid influence, death as an injury to the spot becomes a normal consequence. The heart and the entire respiratory system—to refer only to those directly concerned with life's processes—are the mechanisms first functionally arrested.

And yet while obstruction of these few square millimeters of bulbar elements will rapidly destroy life, it is possible, says Professor Foster, in the case of some animals "to remove the cerebral hemispheres and to keep the animal not only alive, but *in good health* for a long time—days, weeks, or even months after the operation!"

There must prevail in this connection, however, another contradictory interpretation of experimental phenomena. Indeed, how can we reconcile the presence of motor *centers* in the cerebral cortex with the ability of an animal from which both hemispheres have been removed to execute the motions ascribed to these areas? That an animal deprived of its hemispheres will do this is graphically shown in the following lines of Professor Foster's: "We may, perhaps, broadly describe the behavior of a frog from which the cerebral hemispheres only have been removed by saying that such an animal, though exhibiting no spontaneous movements, can by the application of appropriate stimuli be induced to perform all, or nearly all, the movements which an entire frog is capable of executing. It can be made to swim, to leap, and to crawl. Left to itself, it assumes what may be called the natural posture of a frog, with the forelimbs erect, and the hindlimbs flexed, so that the line of the body makes an angle with the surface on which it is resting. When placed on its back, it immediately regains its natural posture. When placed on a board, it does not fall from the board when the latter is tilted up so as to displace the animal's center of gravity; it

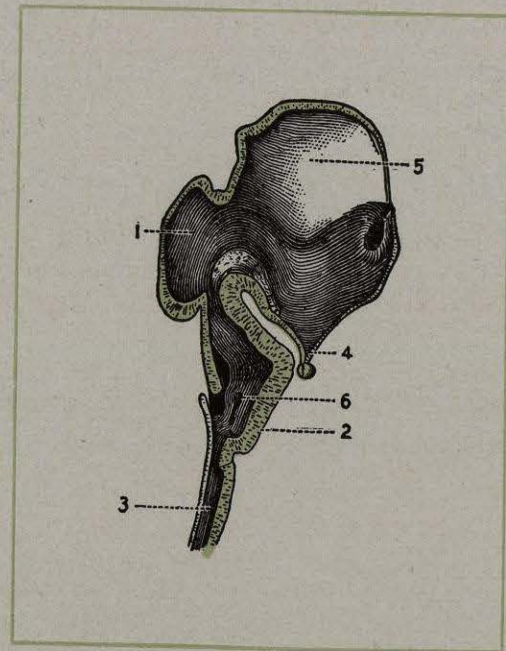
crawls up the board until it gains a new position in which its center of gravity is restored to its proper place. Its movements are exactly those of an entire frog except that they need an external stimulus to call them forth." It is quite clear that all motor phenomena are carried out, notwithstanding the absence of parts of the brain which have been undeniably shown by experiments in animals, pathological conditions of the human hemispheres, etc., capable of inciting them. The familiar convulsive movements in various parts of the body trunk, leg, arm, etc., when certain motor areas are stimulated would mean nothing to us if the use of electricity for this purpose were the basis of this doctrine, but *lesions* in these areas have unquestionably proven that they do preside over motor functions, not only in a general way, but in the sense implied by "cerebral localization." How account for the self-evident discrepancy which the entire absence of these structures indicates in present conceptions of the processes involved?

We are brought nearer to a solution when the removal of cerebral tissues—those to which I have referred as jarred by the electric current passed by the Weber brothers between the nose and the bulb—is continued downward until the cord only is left. "Very marked is the contrast," says Professor Foster, "between the behavior of such a frog which, though deprived of its cerebral hemispheres, still retains the other parts of the brain, and that of a frog which possesses a spinal cord only. The latter when placed on its back makes no attempt to regain its normal posture; in fact, it may be said to have completely lost its normal posture, for even when placed on its belly it does not stand with its forefeet erect, as does the other animal, but lies flat on the ground. When thrown into water, instead of swimming it sinks like a lump of lead. . . . When a board on which it is placed is inclined sufficiently to displace its center of gravity it makes no effort to regain its balance, but falls off the board like a lifeless mass." Such a frog moves its limbs irregularly, but one has but to witness such motions to at once conclude that they are aimless, mere random expressions of the inherent power to contract possessed by all muscular tissues, and which even persist some time after death, especially in the case of the heart-muscle. Very marked is the contrast, indeed, between this animal and one still endowed with the tissues of the base of the brain. "Pigeons, for instance, have been kept alive for five or six weeks," says the same author, "after complete removal of the cerebral hemisphere with the exception of portions of the crura and corpora striata immediately surrounding the optic thalami." . . . "In warm-blooded animals, as in the more lowly cold-blooded frog, the parts of the brain *below or behind* the cerebral hemispheres constitute a nervous machinery by which *all the bodily movements* are carried out."[3]

That this mechanism is located below the hemispheres in man has also been illustrated by many cases reported, among which may be cited the famous crow-bar case, in which, "by a premature explosion of gunpowder, an iron bar three and a half feet long, one and a quarter inches in diameter, and weighing thirteen and a quarter pounds, was shot completely through a man's head, and perforated his brain. This man walked up a flight of stairs after the accident, and gave his account of how it happened. Although his life was naturally despaired of for some time, he *developed no paralysis;* nor did marked impairment of his intellectual faculties follow convalescence. Eventually he recovered his health. Twelve years elapsed before his death, during which time he was a laborer on a farm."[4] This pointedly suggests that while the cerebral hemispheres from the lowly frog to the highest mammal can only awaken motion through volition, *i.e.*, voluntary movements, *the base of the brain—the pituitary body as we will see—can automatically govern motion through the intermediary of spinal gray matter.*

A remark which in this connection is of particular interest to us is that of Professor Duval, when, referring to the meaning of bulbar functions, according to modern conceptions, he says: "For the physiologist, the medulla extends above the limits of the vertebral column into the cranium and *about up to* the sella turcica." *I* would say *into* the sella turcica, for it seems clear to me that *the posterior pituitary lobe presents*

[3] The italics are my own.
[4] A. B. Ranney: "Lectures on Nervous Diseases."



MEDIAN AND VERTICAL SECTION OF A THREE MONTHS' EMBRYO. *[Dejerine.]*

1, Aqueduct of Sylvius. 2, Medulla Oblongata. 3, Central Canal. 4, Infundibulum and Pituitary Bodies [the latter have been added to the original]. 5, Optic Thalamus. 6, Fourth Ventricle.

the functional characteristic that would fulfill the requirements of the complemental processes that the functions of the hemispheres demand.

The annexed colored plate, which represents a median and vertical section of the encephalon and bulb of a three months' embryo, distinctly indicates the direct continuation of the cord up to the posterior or infundibular pituitary lobe. The tract connected with the posterior pituitary is colored bluish gray. The pituitary has been added to the infundibular extremity of the original illustration. The relations of the structures which ultimately become the corpora quadrigemina by meeting the posterior part of the third ventricle are well shown.

That my views in this connection are based on a solid foundation is further sustained by the painstaking investigations of Andriezen,[5] who traced a direct connection between the pituitary and the medullary and other more anterior structures through the various phylogenetic stages of vertebrates. The following statements and the table appended are quoted from his paper: "A survey and investigation based on all classes of vertebrates show that the hypophysis occupies the position and relationship to the other structures which may be condensed in the following table:—

"RELATION OF PITUITARY TO OTHER NERVE-CENTERS AND HEAD-STRUCTURES IN ORDER FROM BEFORE BACK."

Nerve-center.	Olfactory center.	Posterior lobe of pituitary.	The bulbo-spinal centers.
Nerves.	Olfactory nerves.	Hypophyseal nerves.	Bulbo-spinal nerves.
Distribution.	Epithelium of nasal sac.	Pituitary duct gland (anterior lobe).	Buccal, etc., and general subcutaneous.
Body-region.	Pre-oral (prostomial).	Oral.	Post-oral (branchial, etc.) and general body."

[5] Andriezen: British Medical Journal, Jan. 13, 1894.