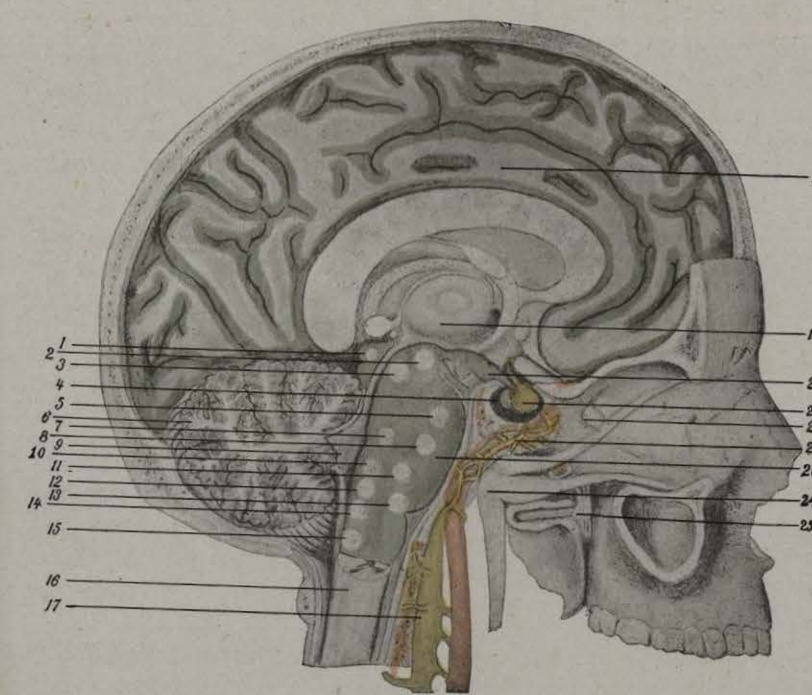
ground for the previously-mentioned postulate that the posterior pituitary is a chief center from which arise excito-motor impulses now thought to originate in the bulb.

The relationship that exists between the cranial nerves and the posterior pituitary body now becomes apparent. Not only does it seem as if the motor properties either *in toto* or in part owed their functional impulses to this body, but those which regulate its functional blood-supply also. Again, as *all* organs require functional impulses and blood, and inasmuch as these impulses and the blood must be incited and governed, *all* organs must be functionally dominated by the posterior pituitary body. Indeed, all the data that I have presented in this work tend to show that *the posterior pituitary body is a dominant center of the organism; it influences the functional activity of all organs, through the intermediary of the subsidiary centers located in the bulb and spinal cord.* The scope of these functions is defined in the sixteenth chapter.

The anatomical relations of the posterior pituitary are shown in the annexed plate which portrays the relationship between this organ, the floor of the third ventricle, the medulla, the pons, and the cord—all of which are continuous.

THE POSTERIOR PITUITARY AS THE SENSORIUM COMMUNE.

From all the data submitted and the normal functional association embodied in reflex phenomena manifested through various nerves—the vagus, for example—motor-efferent phenomena are the normal sequences of sensory-afferent impressions, and the two are necessarily linked. The pons Varolii, or at least its *gray ganglionic substance,* is now thought to originate motor impulses that are independent of mental processes and to be the seat of *instinctive* acts. "It is, indeed, to the pons," says Professor Duval, "that, in a general way, we appear authorized to ascribe the most important rôle in great emotional expressions: laughing, weeping, the cry of pain; in a word, involuntary manifestations. It is in this sense that the term *sensorium commune* applied to the pons should be understood. Indeed, if, as was done by Vulpian, the *corpora striata,* the *optic thalami,* the *tubercula quadrigemina,* and the *cerebellum* are



THE POSTERIOR PITUITARY BODY AS GENERAL CENTER OF THE NERVOUS SYSTEM. *[Sajous.]*

Showing Continuation from the Posterior Pituitary Body, of the Infundibulum, the Floor of the Third Ventricle, the Medulla Oblongata, and the Cord.

1, Corpora Quadrigemina. 2, Motor Oculi. 3, Patheticus. 4, Posterior Pituitary Body. 5, Motor Branch of Fifth. 6, Cerebellum. 7, Abducens. 8, Trigeminus. 9, Fourth Ventricle. 10, Glosso-pharyngeus. 11, Facial. 12, Pneumogastric [Vagus]. 13, Auditory. 14, Hypoglossal. 15, Spinal Accessory. 16, Spinal Cord. 17, Superior Cervical Ganglion. 18, Left Hemisphere. 19, Third Ventricle. 20, Infundibulum. 21, Anterior Pituitary Body. 22, Optic Nerve. 23, Carotid Plexus. 24, Casserian Ganglion. 25, Spheno-palatine Ganglion. 26, Pons Varolii.

successively removed, the animal still shows, by characteristic agitations and *plaintive* cries, the pain it experiences when submitted to strong external excitations: *i.e.,* when its leg is squeezed with pincers or a bare nerve is excited. If the pons itself and the upper part of the medulla are now destroyed, the animal at once ceases to respond by similar cries and agitations." . . . "An animal that has lost its pons has therefore lost *a center for the perception of sensitive impressions.*" The gray ganglionic substance of the pons is, we have seen, a part of the central gray matter which begins in the posterior pituitary body: a fact which suggests that the latter may be the seat of functions now ascribed to this part of the pons.

Indeed, these instinctive involuntary acts are dominant in the entire phylogenetic scale even in vertebrates devoid of skull or brain: the amphioxus, for example, down to which Andriezen traced the structures which ultimately become the pituitary bodies. It is difficult to conceive of an *inciting* and *governing* efferent impulse from the posterior pituitary without an afferent impulse conveying to it the needs of the organ to be incited to activity and governed. Duval refers to weeping, for instance; tears, we have seen, are brought on by increased circulation and stimulation of the cellular elements of the lacrymal glands; what is this but functional activity enhanced by impulses to the posterior pituitary—if my previous conclusions are at all warranted?

True, we are dealing primarily with a mental phenomenon, but this only proves that afferent impulses may reach the posterior pituitary from the cortex of the hemispheres as they can from any organ. Nor is the act an instinctive one; but this fact also affords supporting testimony, since it tends to show that the organ is not only influenced by impressions of a purely reflex kind, or connected merely with organic life, but also by the highest form of nervous action: *i.e.,* mentality. What better evidence can we have of this than the violent cardiac action; the trembling; the involuntary excretion of urine, of fæces, of sweat; or even the sudden arrest of the heart, all of which phenomena may attend intense fear, and all due to loss of control *by the posterior pituitary,* under the violence of the mental impulses over . . . muscular tissue: cardiac, skeletal, cystic, intestinal, and sudorific? To this list I may add loss of control over all vasoconstrictors, since we have relaxation of the larger internal vascular trunks, central engorgement, in virtue of the principle—"vessels supplied with a muscular coat and capillaries are mutually antagonistic in contraction and dilation"—submitted in the earlier chapters and the mechanism of which we can now understand. Both antagonistic conditions are expressed in another symptom of fear: *i.e.*, intense pallor, the lividity of Asiatic cholera and, indeed, of the moribund. Truly instinctive, however, is the sudden cry or scream brought on by unexpected pain: evidently the result of an impulse to the posterior pituitary, since we again have a series of muscular actions of the chest, glottis, etc., which are necessary for the cry. Laughing, sneezing, coughing, and other kindred acts are all manifestations of motor activity; and so is vomiting the result of afferent and efferent vagal impulses, again with muscular structures as the mechanical factors and the posterior pituitary as inciting and governing organ.

And a striking proof of this is furnished by the fact that these manifestations of activity not only prevail in a frog deprived of its hemispheres, but that, if the animal is kept alive and in good health, signs suggestive of intelligence appear. "For days or even weeks after the operation," says Professor Foster, "there may be no signs whatever of the working of any volition; but, after the lapse of months, movements, previously absent, of such a character as to suggest that they ought to be called voluntary, may make their appearance. . . . Even in their most complete development such movements do not negate the view that the frog, in the absence of the cerebral hemispheres, is wanting in what we ordinarily call a 'will.'" Nor need they, for these so-called involuntary, instinctive acts are dominant even in vertebrates devoid of skull or brain: the amphioxus, for example, down to which Andriezen traced the structures which ultimately become the pituitary bodies.

That the posterior pituitary is a *discerning* organ, and one, at that, capable of simultaneously subserving many functions, seems very probable. Totally independent of the brain, *though its servant when need be*, it appears to me as the undoubted seat of the many centers—*i.e.*, for cardiac action, respiration, vasomotor action, sneezing, coughing, etc.—that have been located in the medulla oblongata. True, local disease or traumatism point to the "bulbar" areas concerned as "centers." But if the bulb is given the rôle which I believe it to fulfill, —*i.e.*, that of a secondary or rather subsidiary *consociating* organ,—it will become apparent that any lesion capable of blocking the multitude of afferent and efferent impulses that traverse it at all times and which represent the aggregate of the organisms inciting and governing energy must necessarily compromise life or the functions of an organ to which the blocked nerves are distributed.

I have expressed the belief that there are but two general subdivisions of the nervous system, and that both of these have the posterior pituitary body as their general center. This view has not only been sustained by the analysis of the functions of the various organs, but it seems to me fully to coincide with established facts.

As Regards Efferent (Motor) Impulses.—It has been experimentally determined that all fibers that originate from roots in the *anterior* portion of the cord are *efferent: i.e.*, transmit motor impulses from the cord to the periphery. Section of these fibers causes: in muscles, paralysis; in glands, cessation of secretion; in vessels, dilation.

Interpreted from my standpoint, these morbid phenomena are accounted for as follows: As the *active* functional state of any organ is brought on, we have seen, by strictodilation of its arterioles, *i.e.*, constriction of their vasa vasorum (that attending the *passive* functional state), section of the nerve transmitting the constrictive impulses brings on the opposite of active function,—*i.e.*, paralysis,—or, if distributed to a gland, arrest of secretion. Although the same impulses serve to *incite* and *govern* the cellular activity of the organ, paralysis, muscular or glandular, is not due to the loss of these two functional attributes, since section of vagal efferent nerves, which only incite and govern the active functional state beyond tonic contraction, does not cause paralysis. The immediate cause of the latter is slowing of the blood-stream: *i.e.*, reduction of the supply of oxidizing substance. The cellular elements lose their mechanical energy and can no longer be incited to action and governed. The mechanical energy being due to the adrenoxidase present, it is traceable through the adrenal system to the *anterior pituitary body*, while the inciting and governing influence, being of cerebro-spinal origin through the anterior root severed, is traceable to the *posterior pituitary body*. That it is of central origin is shown by the fact that removal of the pituitary is followed by general vasodilation.

Control experiments are represented by the well-known facts that stimulation of an anterior root causes vasoconstriction and increased functional activity, and, if sufficiently strong, convulsive movements of muscles. The latter, as we have repeatedly seen, are due to excessive oxidation of the muscular elements—complemental testimony to the effect that inadequate oxidation is a primary source of paralysis or at least of functional inhibition.

I have previously shown that the bulbar vasomotor center and the cranial nerves that possessed motor properties occupied the same medullary region: the *upper*. As general motor nerves possess vasomotor properties, the reason for this is obvious. Again, we have seen that the cranial nerves which acquire motor properties by anastomosis were grouped in the *lower* portion of the medulla. The entire organ thus becomes a conductor for general motor impulses, whether transmitted by the cord (as indicated by the general vasodilation incident upon medullary section) or by cranial nerves.

Although this aggregate of motor areas in the medulla represents but radiating paths from a common center, the posterior pituitary lobe, present conceptions as to their distribution—whether to the extremities, the thorax, the cranial nerves, etc.—or their anatomical relations with the hemispheres—the cerebellum, etc.—are in no way modified. All we need to bear in mind, and as will be shown later, the sympathetic system is not an autonomous system of nerves, and that it is a subdivision of the general motor system originating, like all motor nerves, from the cord, while its impulses emanate from the pituitary.

Summarized, these facts—which will be supplemented by evidence in the second volume—suggest that, *while the medulla oblongata is an important consociating organ, its centers receive impulses from, and are controlled and co-ordinated by, the posterior pituitary body.*

Unlike the anterior lobe, which governs and sustains oxidation and metabolism through the adrenals, however, the posterior lobe is not necessary to life, since it is but a co-ordinating structure.

As Regards Afferent (Sensory) Impulses.—It has likewise been experimentally ascertained that all fibers that originate from roots in the posterior portion of the cord are *afferent: i.e.,* transmit sensory impulses from the periphery toward the cord. Section of these roots is followed by loss of sensation.

Interpreted from my standpoint, sensory impressions are similarly transmitted from all parts of the organism, and the one general sensory system supplies the needs of all. The nature of the impulse being governed by the specific cellular characteristics of the peripheral structures which receive the impressions, whether related to a special sense, general sensibility, variations of functional activity, etc., they all reach the posterior pituitary. That such is the case is suggested by the fact that, while frogs deprived of the hemispheres exhibit typical signs of continued co-ordination and sensation, removal of the bulb then causes them no longer to show these signs. This does not exclude the functions of subsidiary centers,—*i.e.,* reflex centers, ganglia, etc.,—which probably serve as accumulators of energy, and act in lieu of the posterior pituitary body unless the peripheral stimulation exceed their potential as to the efferent energy actively used. The law of generalization of Pflüger,—*i.e.,* propagation of (reflex) impulses to the medulla under excessive excitation,—which, according to my view, applies to the posterior pituitary, typifies the maximum effect produced under such conditions, and further demonstrates the connection between the periphery and the latter organ.

Control experiments are represented by the familiar results of stimulation of the dorsal roots, which causes augmentation of reflex activities and of conscious sensations. The reflex inhibition of functional activity of certain organs I have ascribed to excessive stimulation: in accord, therefore, with foregoing facts. This affords the complementary concordance required to place my conception of the functions involved on a solid foundation.

All these data suggest a postulate, the importance of which must be emphasized: *i.e.*, the identity of the posterior pituitary body as the center upon which all emotions, shock, etc., react, and as the organ which initiates the phenomena that attend the impressions thus produced.

That this organ is directly or indirectly connected with the cerebrum in all phenomena pertaining to intelligence, reason, and will, precisely as its motor functions—other than the purely automatic ones—may be dominated by these higher manifestations of nervous activity, need hardly be emphasized. "Sensory" in its broad sense, from my viewpoint, and refers to impressions received by all end-organs endowed with sensation, as previously stated. Whether these first reach the eye, the ear, the cutaneous surface, the gustatory papillæ, the olfactory area, etc., or be due to traumatism, surgical procedures, an abnormal mental state, such as attends fear, grief, or other emotions, etc., we are always dealing with molecular jarring of the posterior pituitary body: harmless when slight, pathogenic when sufficiently intense, but fatal when a certain limit is reached. Precisely as the current passed through the region by the Weber brothers inhibited the heart, so can fright, intense pleasure, or shock prove fatal by inhibiting the heart, but primarily by *jarring the posterior pituitary body*—or, speaking more correctly, by inducing excessive molecular vibration of its elements.

The maximum effect of shock thus becomes an arrest of nervous impulses through which function is sustained *via* the cerebro-spinal axis. This may well be illustrated by the description given by Professor Stewart of the "various phenomena which are grouped together under the name of shock" as exemplified by section of the cord. "When the spinal cord of a dog is divided,—*e.g.*, in the dorsal region,—all power—all vitality, one might almost say—seems to be forever gone from the portion of the body below the level of the section. The legs hang limp and useless. Pinching or tickling them calls forth no reflex movements. The vasomotor tone is destroyed, and the vessels gorged with blood. The urine accumulates,

overfills the paralyzed bladder, and continually dribbles away from it. The sphincter of the anus has lost its tone, and the fæces escape involuntarily." I hardly need to emphasize the fact that we have here a summary of all the phenomena which attend loss of functional activity: of those, at least, I ascribe to the posterior pituitary body.

But this experimental section of the cord was also chosen as an example of the wonderful resources of nature when life's functions are to be preserved. "If we were to continue our observations only for a short time, a few hours or days," continues the author, "we should be apt to appraise at a very low value the functions of that part of the cord which still remains in connection with the paralyzed extremities. But these symptoms are essentially temporary. They are the results of shock; they are not true 'deficiency' phenomena. And if we wait for a time, we shall find that this torpor of the lower dorsal and lumbar cord is far from giving a true picture of its normal state; that, cut off, as it is, from the influence of the brain, it is still endowed with marvelous powers. If we wait long enough, we shall see that, although voluntary motion never returns, reflex movements of the hind-limbs, complex and co-ordinated to a high degree, are readily induced. Vasomotor tone comes back. The functions of defecation and micturition are normally performed. Erection of the penis and ejaculation of the semen take place in a dog. A man with complete paralysis below the loins and destitute of all sensation in the paralyzed region has been known to become a father (Brachet). Pregnancy carried on to labor at full term has been observed in a bitch whose cord was completely divided above the lumbar enlargement."

How can the return of functions—so far unexplained by physiologists—be accounted for? The foregoing data suggest that the pituitary should be the organ "shocked" by the operation. Moreover, removal of this organ, except after its gradual destruction by disease, produces identical effects. Indeed, the resumption by the lower and dorsal cord of its normal functions would not occur if the path from the pituitary to the adrenals had also been severed. As Goltz and Ewald have shown, animals deprived of their cord from the bulb down cannot keep warm, and even die of cold; but Ott found that this did not happen when the section was made below the fifth dorsal. As this is immediately below the region where the pituitaro-adrenal nerves leave the cord to enter the sympathetic chain and thence pass on to the adrenals, these results find their ready explanation: As soon as the posterior pituitary had recovered from the shock, it resumed its influence on the adrenals, the secretion of which, as previously shown, endows the hæmoglobin with its oxygenizing constituent. Metabolism—the life process—being resumed in the severed segment of the spinal cord, its normal functions returned.

It seems extraordinary to connect the adrenals—as I did in 1903 in the present work—with fright, anger, traumatic shock, etc.; and yet the recent experimental work of Cannon and de la Paz,[63] in the Harvard laboratories of physiology, has demonstrated that under the influence of such emotions in the cat the inferior vena cava contains an excess of secretion. Cannon and Hoskins[63a] also state in this connection: "The similarity between surgical shock and the condition of an animal after removal of the adrenal glands suggests that possibly in surgical shock the injury to large nerve trunks may discharge the adrenal glands to such a degree that they are unable to continue their normal functioning."

If to all this be added the fact that the manner in which violent emotions, fright, trauma, shock, etc., provoke various diseases, exophthalmic goiter, railway spine, and concussion, for instance, it seems probable that *the posterior pituitary body, as the most highly organized aggregate of somatic nerve-centers, is the organ upon which all shocks—physical,* i.e., *cerebral or traumatic—react.*

Illustrative also of the rôle of shock, physical and mental, in the production of disease is acromegaly. Fully 20 per cent. of these cases are due to some form of accident, often falls upon the head. Its syndrome, better than any other disease, shows, from my viewpoint, the relationship between the pituitary and the body at large. Hence its presence at the end of the present chapter.

[63] Cannon and de la Paz: American Journal of Physiology, April 1, 1911.
[63a] Cannon and Hoskins: *Ibid.*, April and December, 1911.

ACROMEGALY: PIERRE MARIE'S DISEASE, AND GIGANTISM.

The first question that imposes itself in this connection is whether the pathogenesis of this disease of the pituitary body must be based upon the prevailing belief that this organ is a secreting gland or, as I believe, upon its identity as a coordinating center which includes, among its functions, that of governing the secretory activity of the adrenals and thyroid apparatus.

I have already urged that the prevailing opinion that the pituitary is a secreting gland has so far remained unproven, while every item of evidence brought in favor of this view can be shown to be questionable as such. The main argument in its favor is that extracts of its posterior lobe can produce vasomotor phenomena; but this fact loses its value in the presence of Wiesel's[64] demonstration that this lobe is rich in chromaffin substance, *i.e.*, in adrenal principle. That under these conditions its extracts should give rise to the same phenomena as the latter is plain. To enumerate these phenomena is to rehearse all those that were credited to the secretion of the adrenals in the second chapter by the many investigators cited therein. Thus, Mairet and Bosc[65] found in 1896 that subcutaneous injections of pituitary extract caused a rise of temperature which lasted a couple of hours. An intravenous dose produced marked myosis, slowing of the respiration, powerful cardiac beats, and hyperthermia as main signs, the animals recovering, however. Schäfer and Vincent[66] then found that pituitary substance raised the blood-pressure, and that this substance when applied to mucous membrane caused blanching, as is the case when a solution of adrenalin is applied. They also noted that in small mammals it caused, in toxic doses, paralytic symptoms which *they* also consider analogous to those caused by adrenal extracts. According to Jas. Barr,[67] pituitary extract actively produces arteriosclerosis, and it is also known to produce glycosuria. Finally, Hallion and Carrion, studying its therapeutic action, found that pituitary extracts "always produced their effects by

[64] Wiesel: International Clinics, vol. ii, 15th series, 1905.
[65] Mairet and Bosc: Arch. de physiol., p. 600, 1896.
[66] Schäfer and Vincent: Jour. of Physiol., vol. xxv, p. 87, 1899.
[67] Barr: Lancet, Nov. 13, 1899.