Of course, this applies to both pituitary bodies, but I have shown that the anterior lobe could originate motor impulses in the partition separating it from the posterior lobe, and transmit them via the latter, the basal tissues, the bulb, the cord, the sympathetic chain and finally the splanchnic nerve to the adrenals. That the investigations of Andriezen, though sustained by the previously recorded results of removal of the pituitary by Vassale and Sacchi,[5a] should have borne but little fruit, so far, is probably accounted for by his statement that "variations in weight bring it under the Darwinian law of panmixia; if so, the indication being, what study of lower vertebrates shows, namely: that it has probably passed the acme of its activity and in man is functioning less vigorously."

I must express the belief, however, that, when man is in question, cessation of natural selection may not always mean that an organ has become useless, but instead that it has reached the acme of perfection. Loss of functional vigor may denote, in this connection, what it denotes in the human hand as compared to that of the gorilla: *i.e.,* gain in functional precision and delicacy.

In the embryo, the posterior pituitary body opens directly *into* the third ventricle through the infundibulum. If during uterine existence "the whole life-achievement of myriads of generations of living things" is represented, the phylogenetic history of this organ should show traces of its ultimate functions. Andriezen found that in the amphioxus its analogue is represented by "a subneural glandular organ, a duct lined by ciliated epithelium which affords a communication between the buccal and neural cavities, and a group of nerve-cells around and at the back of the upper opening where the duct widens into the ventricular cavity." We have here the main primitive structures of the pituitary in man.

Referring to Andriezen's investigations, Berkley[6] says: "He has farther shown that particles of carmine, suspended in the water surrounding the animals, will be taken up with the water *passing through the infundibular duct* and carried by ciliary action *into the ventricle,* and thence into the *central*

[5a] Vassale and Sacchi: Rev. Sper. di Fren., p. 83, 1894.
[6] Berkley: Brain, Winter, 1894.

canal of the cord; finally the particles of carmine may be traced right up to the free end of the canal, where the spinal cord opens into the exterior by the blastopore; therefore it is made manifest that the infundibular duct carries a stream of oxygen-bearing water for the nutrition of the tissues and the carrying off of their effete products." Alluding to personal studies to which I will presently refer, Berkley then adds: "It is quite curious to find essentially the same structures preserved in as high a vertebrate as the dog, and descending to so low a zoological order as amphioxus, though, as Müller remarks, the pituitary is practically the same *from myxine to man.*" Yet in man the infundibular orifice is *closed,* and the posterior pituitary, during its evolution, must, therefore, have assumed some function other than that possessed by the organ during the earlier phases of its career and of which the earlier forms should also show traces.

We have seen that oxygenation of the blood, the highest development of the function carried out by the water-vascular system in the amphioxus, belongs to the domain of the anterior pituitary. The remaining inference afforded by the phylogenetic history of the organ, therefore, is, in my opinion, that *the group of nerve cells* around and behind the upper opening *which in Amphioxus and Amocœtes forms the threshold of the oxygen-bearing water system is the prospective adrenal center in the human pituitary,* which center, we have seen, is also concerned with oxygenation.

I must state that I consider this perfect concordance between the functions of the anterior and posterior pituitaries as I have conceived them and those found throughout the entire evolutional scale of zoological forms as far back as the amphioxus by Andriezen as very strong evidence that my views are sound.

HISTOLOGY OF THE POSTERIOR PITUITARY BODY.

What is the physiological relationship between the two lobes? Déjerine[7] states that vertical and horizontal sections of both organs show that they are absolutely distinct and sepa-

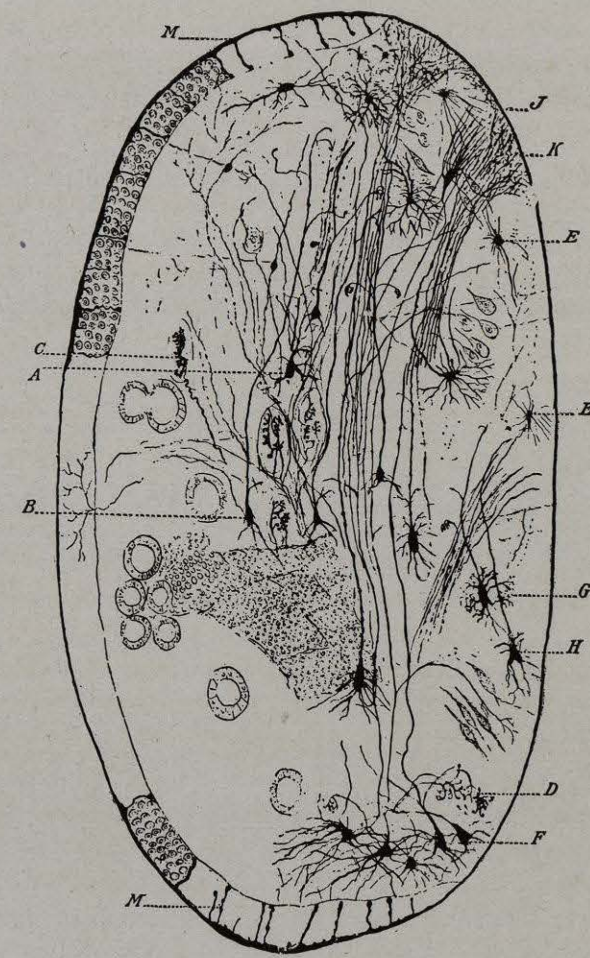
[7] Déjerine: "Anatomie des Centres Nerveux," vol. i, 1895.

rated by a fibrous lamina; and, furthermore, that "the posterior lobe alone is connected with the infundibulum." . . . "It is developed from the brain" and "is a dependence of the middle ventricle." The anterior lobe is only connected with the cerebral structures through vessels which, according to Berkley,[8] "directly pass into it from the *substance* of the infundibulum." The blood-supply of the posterior lobe is also derived from the same source, but it is less rich, though sufficiently so to satisfy the needs of an active function. Indeed, the organs differ mainly in the character and wealth of their nerve-supply—much to the advantage of the posterior lobe, however. The development of the anterior lobe from the ectoderm of the primary oral cavity, instead of, as in the case of the posterior lobe, from the embryonic brain, accounts for what anatomical dissimilarities prevail.

The histological characteristics of the posterior lobe also suggest that it is the seat of some nervous function of a high order. This is well illustrated by the exhaustive study by H. J. Berkley[9] after an examination of some two thousand five hundred slides. A summary of such a work hardly does it justice; I must therefore refer the reader to the original paper for details other than those that I will presently submit.

The outer layer of the organ was found by Luschka and Müller to be composed of gray matter similar to that found over the infundibulum. Berkley refers to this layer as composed of slightly irregular *ependymal* cells three or four deep, through which rather thick ball-tipped filaments penetrate to the second anatomical subdivision of the lobe. This outer coating of cells does not extend around the entire lobe, however, but covers only its free, or posterior, surface. Its anterior portion, that nearest the partition between the two lobes, has no such covering, so that its elements appear to be in contact with the partition itself or to be only separated from it by its capsule. The second subdivision of the posterior organ occupies, judging from Berkley's drawings, about one-third of its mass, and recalls, as to structure, that of the anterior lobe.

[8] Berkley: Brain, Winter, 1894.
[9] *Ibid.*



VERTICAL SECTION OF THE POSTERIOR PITUITARY BODY. [Berkley.]

Somewhat diagrammatic to indicate various types of cells.
Its normal size is that of a small pea.

[*Brain.*]

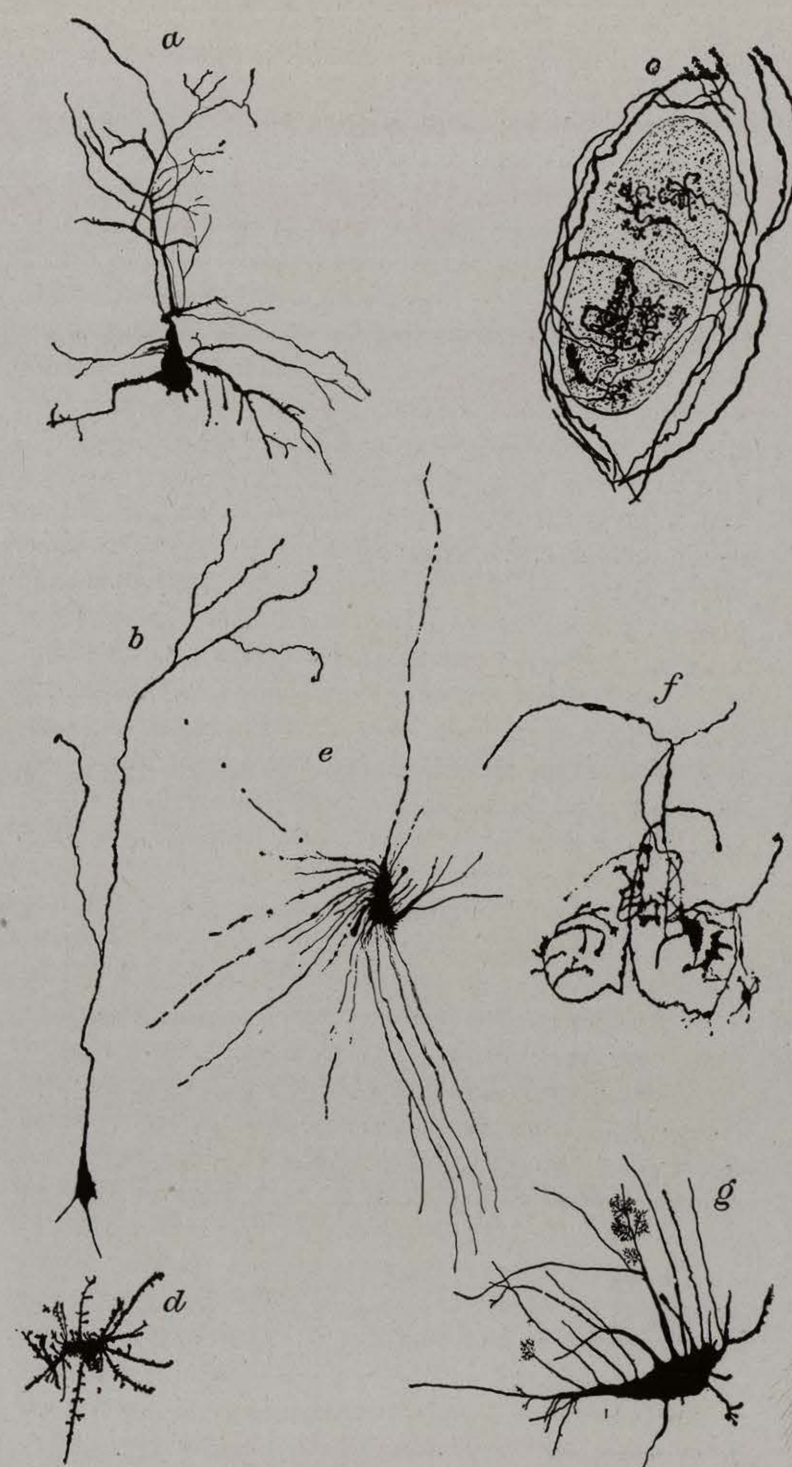
Again do we find the closed glands, or alveoli, including the colloid substance. Again are the glandular elements supported by connective-tissue trabeculæ permeated with capillaries, though the caliber of the larger vessels is somewhat smaller. Yet—a feature which seems to me important—the colloid alveoli are always most numerous near the outer edge of the ependymal cells, that portion farthest away from the interlobular partition, while the space between these structures and the partition is occupied by cellular elements of an entirely different kind.

The third portion may be said to occupy nearly two-thirds of the entire lobe: a perfect maze of nervous elements, some of which have not so far been found elsewhere in the organism. Yet connective-tissue partitions carrying blood-vessels are discernible throughout this entire area: a feature which suggests that an orderly subdivision exists. Its nervous elements vary greatly in form, but they may be divided into three general classes: 1. Cells that give off protoplasmic extensions, neuraxons, etc., that are not sufficiently long to reach the upper, anterior region of the lobe: *i.e.*, the infundibular region. 2. Cells the extensions of which reach this region. 3. Cells that are found mainly or only in this portion of the organ.

The *first class* includes flask-like cells with knot-tipped fibers that recall those of the anterior lobe (Fig. *A*, Plate I, and Fig. *a*, Plate II). These bodies are widely distributed, but their multitude of ramifications end freely among neighboring structures. Similar, though smaller, cells (Fig. *B*, Plate I, and Fig. *b*, Plate II) are found chiefly in the center, and have processes that extend upward a considerable distance and there often terminate in a brush-like figure. In this class may be included peculiar oval bodies (Fig. *C*, Plate I, and Fig. *c*, Plate II), mainly found in the center of the organ, that recall closed follicles. They give off axis-cylinders that coil about them irregularly, and fibers which terminate either in irregular figures resembling combs with knob-tipped teeth or in cat-o'-nine-tail-like tufts. Neuroglia cells, especially those of the mossy kind, are shown in Fig. *d*, Plate II, while spider-cells (Fig. *E*, Plate I, and Fig. *e*, Plate II) are mainly found where the nerve-cells are very numerous: *i.e.*, the anterior third of the lobe. The spider-cells, however, which only differ from those found in the cerebral tissues by their larger size in proportion to the length of their tentacles, outnumber the other cells as the upper infundibular region of the lobe is reached.

The cells included in the *second class* are all, as stated, distinguished by one or more protoplasmic extensions, which insinuate themselves between all the elements intervening between their starting-point and the infundibular area referred to, where they break up into figures. The lowermost of these, the ganglion-cells shown in Fig. *F*, Plate I, and Fig. *f*, Plate II, exemplify this type very well, since their extensions traverse the entire organ in an upward direction and end in the upper infundibular area. Higher up in the organ large pyramidal and oval cells are found (Fig. *G*, Plate I; Fig. *g*, Plate II, and *g*, Plate III), the terminal subdivisions of which break up into exceedingly fine feathery filaments. The only axis-cylinder of this cell, after distributing a few branches to neighboring elements, continues upward and subdivides, when near the upper margin of the infundibular region, into a complex net-work which entwines the alveoli found there. A third type, characterized by short dendrites and many hair-like processes (Fig. *H*, Plate I, and Fig. *h*, Plate III), is found throughout the entire nervous area and also gives off one long dendrite, which extends a long distance upward and forward; this extension may possibly reach the infundibular region or its neighborhood. Coming from every direction, these long dendrites seem, at any rate, to point all toward this one region. The other dendrites are short and distinguished by the presence of more or less numerous hairy processes, while some of the terminal ramifications are ball-tipped—suggesting a possible identity as collectors of energy, which, transformed in the body of the cell, are directed upward by the long dendrites.

In the infundibular region of the lobe—*i.e.*, the cellular elements of the *third class*—the final ramifications of the long dendrites form an extremely complex aggregation of tufted figures, wavy threads, and feathery protoplasmic ramifications. In the midst of this maze of nervous elements certain cells are to be found, the like of which Berkley has not been able to detect in any part of the central or peripheral nervous system.



VARIOUS TYPES OF CELLS IN THE POSTERIOR PITUITARY BODY. *[Berkley.]*

[*Brain.*]

They are small and round, and give off strong dendrites, which appear knotted or covered with thorns, giving them a "prickly appearance" (Fig. *J*, Plate I, and Fig. *j*, Plate III). Another variety found in abundance in this region is a small cell with a rich, apical tuft of fine, wavy processes. They are also distributed in the midst of a net-work of varicose nerve-fibers (Fig. *K*, Plate I, and Fig. *k*, Plate III) in the upper and near the anterior border of the lobe "along the space formerly occupied by the infundibular duct." As already stated, the spider-cell is to be found in great abundance in this locality, which, added to the other two varieties of cell, gives us three main cellular elements as representatives of the class of cells found mainly or only in the upper infundibular region of the organ.

As already stated, I do not regard it as a secreting structure. The view that it produces an internal secretion is merely assumed. Howell found that, while an extract of the anterior lobe produced no effect, an extract of the posterior lobe caused a rise of the blood-pressure. Since then, also, considerable use of such extracts has been made in therapeutics. But the facts that these effects correspond admittedly with those of adrenal extract, that they give the adrenal reaction, and that the presence in the organ of chromaffin cells has been established suggest that we are not dealing with a secretion. In fact, in practically all animals, excepting the cat and dog, there is no connection with the third ventricle above.

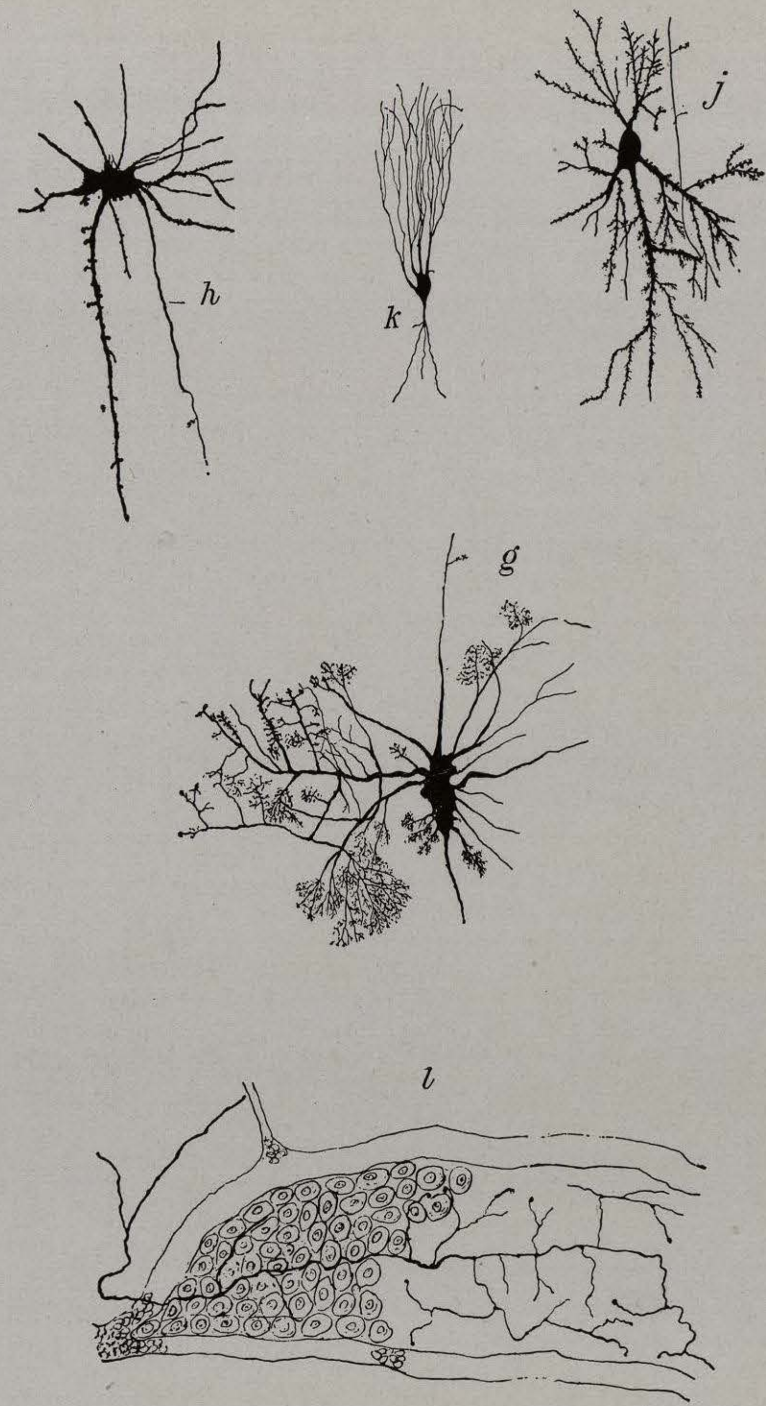
On the other hand, there is, we have seen, good ground for the belief that, as I pointed out in 1903, the posterior lobe is a general nerve-center, and that, through its nervous connection with the adrenals, it governs, besides, general oxygenation. That this view is gaining ground is shown by the recent statement of Lewin, of Berlin,[10] that "the majority hold that the hypophysis is a ductless gland that has an influence over the nervous system or has something to do with the red blood-corpuscles."

And, yet, what is the connecting structure between the posterior pituitary body and the parts to which, under such conditions, its energy would be supplied? Berkley believes—erroneously we have seen—that none of the nervous elements

[10] Lewin: quoted by Archibald Church, Journal Am. Med. Assoc., July 10, 1909.

of the infundibular lobe itself pass beyond its limits into the infundibulum. His histological work shows that, while "all the axis-cylinder processes and the long dendrites have a general tendency upward and forward, both dendrites and neuraxons branching as they proceed onward, all traces of the dendrites of the inferior and median cells of the lobe are lost some little distance below the superior edge." After an allusion to the vessels and fibrillated tissues that connect the infundibulum with the posterior lobe, he says: "The whole arrangement of the structures of the infundibulum" is "here altered." Then, referring to both lobes, *i.e.,* the hypophysis, he remarks: "Elsewhere it shows no break in the described arrangement, the line of differentiation between hypophysis and infundibulum being sharply drawn, a layer of coarse connective-tissue bundles being placed between and separating the glandular and other structures of the pituitary from the tissues of the infundibulum." While the neural lobe is autonomous, Ramon y Cajal, Andriezen, Gentès and others have conclusively shown, as previously stated, that nerve-fibers passed from this lobe and the *pars intermedia* to the tuber cinereum and beyond.

Notwithstanding this striking autonomy of the organ, there are several features in its histological make-up that suggest an additional connecting-link between it and the infundibular structures. Berkley refers to the "outer lamina of slightly irregular ependymal cells (Fig. *M,* Plate I) three or four deep, arranged after the manner of the *cuticular epithelium.*" This lamina, which older anatomists considered as a continuation of the ventricular gray substance, only covers, we have seen, the free portion of the posterior lobe and is not continuous with the infundibular ependyma. Again, "there are seen, extending from the thin capsule surrounding it" (here Berkley alludes to the *capsule* that surrounds the entire posterior lobe), "numbers of rather thick varicose threads, all unbranched, and invariably ending, when their terminations can be discovered, in a ball-shaped figure, at a definite line in the substance of the body, usually at the *inward* ending of the first layer of epithelial cells, at the line of separation from the more centrally situated elements. These knobby threads," he says, "strongly resemble the ependymal glia-cells of embryonic life, and possibly may be related to them; but, as their



VARIOUS TYPES OF CELLS IN THE ANTERIOR AND POSTERIOR PITUITARY BODIES. [Berkley.]

Figs. h, j, k, and g: Cells in the Posterior Pituitary Body. Fig. l: Portion of Glandular Elements of the Anterior Pituitary Body.

[Brain.]

basal end is shrouded in a blackened aggregation of cellular masses, their histological origin must remain a matter of some uncertainty."

If, with these histological data before us, we examine Plate I, a suggestive fact asserts itself: *i.e.*, that the lamina of ependymal cells referred to forms a skull-cap-like covering for the posterior two-thirds of the posterior lobe. The glandular alveoli of the latter, with their colloid substance, are, therefore, in the best possible position for the reception of any nervous impulse that the ependymal cells may be able to transmit outwardly. This is emphasized in Plate I, which shows that this layer exactly covers the entire surface of the posterior region without reaching beyond its limits. The posterior surface of the posterior lobe thus seems to be held in the grasp, as it were, of its ependymal covering, which in turn contains the nervous, "rather thick, varicose threads." This suggests that the capsule may not be the insignificant structure it is now thought to be. Even the fragmentary data we have concerning it tend to indicate that it plays an important rôle in the functions of the organ.

Mere protective structures are usually detached without much difficulty from the underlying tissues. Berkley states, referring to the posterior body: "This lobe is so strongly adherent to the dura that it pulls out of the rest of the pituitary body in removing this with the brain, unless the membrane is dissected with it from the base of the skull." Since the capsule is the part of the lobe so strongly connected with the dura, it must as firmly adhere to the layer of ependymal cells beneath; otherwise efforts at removal would tear it away from the latter. This firm hold of the capsule on the cellular layer is fully accounted for by the thin, fibrous partitions the former sends through the latter, but this in itself suggests an intimate relationship between capsule and cellular layer, especially since the "blackened aggregation of cellular masses," referred to by Berkley, which form the basal extremities of the nervous "threads," all terminate in what appears to be, in his drawings, thickenings in the capsule proper. That such a relationship between the capsule and the nervous elements must exist is further shown by his reference, in the descriptive text of the