# THE CELLULAR ELEMENTS OF THE HUMAN NEUROHYPOPHYSIS

A STUDY WITH SILVER-CARBONATE

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#### THIRTY-ONE FIGURES

The cellular elements of the neurohypophysis were investigated by Retzius (1894) who recognized their neuroepithelial nature. Bucy ('30, '32) separated these cells from other types of glia and called them pituicytes. Romeis ('40) distinguished several varieties of pituicytes and emphasized the technical difficulties encountered in the study of neurohypophyseal structures. However, the development of the silver-carbonate method of del Rio Hortega permits a much more detailed analysis than was possible with the older silver techniques and early variants of this observer.

## MATERIAL AND METHODS

Human pituitary glands were used for this study. The ages of the patients ranged from 3 to 74 years. Because of the structural similarity between the neurohypophysis and the infundibulum the latter was also examined. The material was fixed in brom-formalin, cut vertically on a freezing microtome at  $15 \mu$  and impregnated with silver-carbonate.

#### HISTOLOGIC EXAMINATION

In the infundibulum and the neurohypophysis there are 4 different types of pituicytes:

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1. Bipolar cells with oval or elongated bodies. These elements show several variations. There are oval, bipolar cells with coarse pigmentation of the polar, triangular areas and more delicate granules in the central part of the cytoplasm (fig. 1 "A") and other oval elements which are almost homogeneously black due to the presence of abundant coarse granules (fig. 1 "B" and "C"). Spindle-shaped cells with one long, slender and one thick process (fig. 2), oval bipolar cells with homogeneously impregnated body and no granlues (fig. 3), and deeply impregnated, oval, bipolar pituicytes with one thick, long, slightly wavy and one filamentous process (fig. 4) are present. Certain very large bipolar pituicytes are demonstrable; these have oval, deeply impregnated bodies with one powerful and one delicate polar process (fig. 5). Large bipolar elements occur with numerous fine granules in the central part of the cytoplasm, but none in the triangular polar area. Such elements have two long, slender processes, although only one of these processes is visible in the reproduced photomicrograph (fig. 6). In the neurohypophysis, the infundibulum and the supraoptic, paraventricular and infundibular nuclei, there are cells with large, oval bodies filled with coarse granules but without definite processes. The nature of these cells is not quite clear; possibly they are pituicytes (figs. 7 and 8).

2. "Astrocyte-like" pituicytes are represented by two varieties with small, darkly impregnated bodies and two or more long processes. Some have a small, nearly round cell body and two polar processes (fig. 9 "A"); others are multipolar and have spider-like processes (figs. 9 "B," 10 and 11).

3. The triangular pituicyte is an easily differentiable type of cell. It has a triangular body with round or oval nucleus and long, distinct polar processes. There is a moderate amount of pigment and a delicate fibrillary structure in the cytoplasm (fig. 12). These cells are interconnected by a delicate basilar fiber and form either long chains (fig. 13) or an irregular network through which the cells are possibly connected with other types of pituicytes (fig. 14). In the border area between the radix infundibuli and the hypothalamus there are both pituicytes and astrocytes. In figure 15 "A" there is a large, approximately oval pituicyte with very numerous granules in the cytoplasm but with no visible processes. The pituicyte at "B" has a slender body filled with numerous coarse, black granules and two polar processes; the fiber at "x" belongs to another cell. The pituicyte at "C" has a pyriform body, delicate granules in the cytoplasm and a round, eccentric nucleus. The cell at "D" is an astrocyte.

Some of the pituicytes are connected with blood vessels. Figure 16 shows a unipolar cell with a large, oval cell body and one long process which splits to form a dense perivascular network.

4. The glomerular pituicyte is an entirely different type of cell, which has not been described previously. The processes of these cells form complicated glomerular or basket structures. Several varieties can be distinguished:

(a) Pituicytes are present with large, round bodies and one short, thick process, which forms a dense irregular bundle (fig. 17). Some of these are unipolar pituicytes with an elongated body and one short process which terminates with a distinct fiber basket (fig. 18), others are bipolar pituicytes with an oval, darkly impregnated body having one delicate and one thick process which ends with a large basket-like glomerulus (figs. 19 and 20).

(b) Elongated unipolar pituicytes occur which have very coarse, dark granules in the cytoplasm and a thick process which ends with an elongated bundle of coarse loops and fibers (fig. 21).

(c) Unipolar pituicytes were seen with small oval bodies and a long process of increasing caliber, which forms a very large, deeply impregnated glomerulus (fig. 22).

(d) From an oval cell (fig. 23 "x") arise twin glomeruli of "skein type" distinctly interconnected by fibers; they represent a part of a glomerular chain (fig. 23). These "skeins" have a very complicated structure (fig. 24); the body of the

pituicyte is partly obscured (x), a bundle of long fibers ends with a large glomerulus of basket type (y); an apparently recurrent fiber from glomerulus (y) ends with a small glomerulus (z). A twin glomerulus (zz) is connected with the glomerular system by a distinct bundle of fibers. Pituicytes of this type form long chains with interconnected glomeruli. Figure 25 shows such a formation which has five glomeruli. These glomerular chains are connected with vessels.

Between the fibers of the hypothalamo-hypophyseal tract there are numerous round or pear shaped bodies of either homogeneous or slightly reticular or granular appearance which are connected with the nerve fibers of the tract. In some, the neurofibrils of a single nerve fiber enter the body (fig. 26); others are connected with two thin nerve fibers (fig. 27). Occasionally a nerve fiber bifurcates and ends in a twin body (fig. 28) or interconnected triple body (fig. 29). A similar body with a thick fiber of undetermined origin is represented in figure 30. These elements are definitely connected with the nerve fibers of the hypothalamo-hypophyseal tract (fig. 31).

## DISCUSSION AND SUMMARY

Review of literature shows that there is no consensus regarding the nature of the pituicytes. Retzius (1894) believed that the elements are regressive forms of glia, even though with the Golgi method he demonstrated multipolar elements with radiating process and bi- and unipolar cells. Herring ('08) also considered the neurohypophyseal cells to be glia which formed a dense network; he described oval bodies filled with colloid-like substance. However, the nature of these elements remained obscure. Stumpf ('11) described "glial cells with plasmatic processes" in the posterior lobe. Such cells formed a syncytium and he thought them to be astrocytes. He also found pigmented cells which were not glial in nature, basophilic cells and colloidal cysts. Tello ('12) spoke of "neuroglial cells" and also described small, round and oval bodies connected with nerve fibers which he called "bolas de degeneration." He considered them to be identical with "Herring bodies."

Bucy ('30, '32) introduced the name "pituicytes" and emphasized the independent character of these cells. According to Bucy the pituicytes "vary greatly in size and shape. The nuclei are small, but may be round, oval or even elongated and flattened. . . The cytoplasm has no constant shape and in these preparations (Penfield-Hortega) is always finely granular. It is supplied with a varying number of long and short processes." He found that the pituicytes are often uni- or bipolar and their processes are much longer than those of glial cells. Bucy concluded that pituicytes may be a special type of glia.

Romeis ('40) recognized four types of pituicytes: reticulopituicytes, micropituicytes, fibropituicytes and adenopituicytes. Reticulopituicytes are glial elements rich in cytoplasm that form a delicate reticulum. Romeis believed that they represent a fundamental form from which all other forms of pituicytes are derived. Micropituicytes are elements smaller than the reticular type; they are irregular in shape and have numerous plasmatic processes, some of which end on vessels. These elements Romeis considered as unquestionably glia. Fibropituicytes are elements which "freed themselves from reticulum''; they are larger than the micropituicytes and some of them have long plasmatic and others fibrillary processes. There are multi-, bi- and unipolar elements; the processes of some of them end on vessels. Adenopituicytes are cells which resemble glandular cells in appearance. Romeis also stated that there are glial fibers in the posterior lobe but did not trace them to any cells. Berkley (1894, 1895) is the only author who regarded the cells of the posterior lobe of the pituitary as neurons. This view has never been confirmed.

As can be seen from this brief review of the literature, the nature of the pituicytes is still in doubt. This is not surprising in view of the limited knowledge of these elements. Our findings indicate that there are at least four different types. Type 1: Spindle- or oval-shaped pituicytes (figs. 1 and 2) form whorls in the posterior lobe and are arranged in parallel formations in the infundibulum; these elements are characterized by abundant granules. Bipolar cells of various size with homogeneously impregnated cytoplasm (figs. 3 and 4) occur; there are also some very large bipolar cells (fig. 5). Another variety is represented by very large bipolar cells with numerous delicate granules in the cytoplasm and with long processes (fig. 6). A somewhat different type is oval in shape and contains numerous granules but lacks definite processes. The nature of the latter variety is not clear since they are also present in the nuclei of the hypothalamo-hypophyseal system; possibly they are pituicytes (figs. 7 and 8).

Type 2: These pituicytes resemble astrocytes but exhibit morphologic variations; they have been previously described by Retzius and Bucy (figs. 9-11).

Type 3: Triangular-shaped cells are present which are, in some respects, similar to the reticulopituicytes of Romeis in that they form complicated reticular structures; however, these cells have fibrillary processes and not the plasmatic processes which, according to Romeis, characterize reticulopituicytes. They are present throughout the posterior lobe and infundibulum and are connected with other pituicytes. We found no evidence to support the view of Romeis that these elements represent an early form of pituicytes from which other types are derived.

Type 4: Pituicytes with glomerular structures formed from the processes of round, oval, elongated uni- or bipolar cells can be demonstrated. The glomeruli resemble wire baskets or skeins, some are almost homogeneously black; there are also double, triple or multiple glomerular formations arranged in long chains.

The nature of the structures known as "Herring bodies" is still in doubt. Herring ('08) considered them to be a product of "epithelial cells," Tello ('12) as degenerated nerve fibers, Gersh and de Lawder Tarr ('35) as artifacts and Bargmann ('54) as neurosecretory bulbs. Our findings suggest that they are an integral cellular part of the posterior lobe of the pituitary and apparently have important functions.

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- 1 and 2 Bipolar pituicytes with granular cytoplasm.
- 3 and 4 Bipolar pituicytes with homogeneously impregnated bodies.
- 5 Large, bipolar, homogeneously impregnated pituicyte.
- 6 Large, bipolar pituicyte with fine granules in cytoplasm.
- 7 and 8 Oval pituicytes with granular cytoplasm.



- 9-11 Different types of pituicytes, which resemble astrocytes.
- 12 A single triangular pituicyte.
- 13 A chain of triangular pituicytes.
- 14 A reticular network formed by triangular pituicytes.



- 15 Cells from radix infundibuli. A-C, different pituicytes. D, an astrocyte. x, a pituicyte fiber.
- 16 A pituicyte with a fiber forming a perivascular structure.



#### EXPLANATION OF FIGURES

17-22 Different types of pituicytes forming glomeruli.



- 23 A twin glomerulus arising from the pituicyte at "x."
- 24 An interconnected glomerular system. From the pituicyte "x" a fiber arises which ends with a glomerulus "y"; recurrent fibers from this glomerulus form the glomeruli "z" and "zz."
- 25 A glomerular chain formation.



### EXPLANATION OF FIGURES

26-31 Elements in the neurohypophysis connected with the nerve fibers of the hypothalamo-hypophyseal tract.

