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The Nature of the so-called Herring Bodies

A study of normal human neurohypophyses

By

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With 21 Figures

In 1908 *Herring* described peculiar globular structures in the neurohypophysis which he explained as homogeneous products of epithelial cells. *Tello* (1912) believed them to be products of nerve fiber degeneration. The application of special histological methods permitted *Scharrer* and *Scharrer* (1954) and *Bargmann* (1954) to recognize these elements as an accumulation of neurosecretory substance. In their opinion these bodies represent thickenings of the nerve fibers of the hypothalamo-hypophysial tract in which the neurosecretory substance is stored.

Despite various contributions of the past half century, the knowledge of the morphology of the hypothalamo-hypophysial system is still incomplete. The pituicytes which where described by *Bucy* (1930) have been regarded by some investigators as the source of neurosecretion; other investigators classify the pituicytes as supporting glial elements identical with those found in the rest of the central nervous system (*Vasquez-Lopez,* 1942; *Hild,* 1954). The morphology of the release mechanism of the neurosecretory substance has never been fully investigated.

Many of the problems have been clarified by the combined effort of the different related disciplines mainly under the application of experimental conditions. The present study is limited to a morphological analysis based on normal human material.

Material and Methods

The present investigation has utilized about 150 normal human neurohypophyses obtained on routine post-mortem examination. In 48 cases the pituitary and infundibulum were cut sagitally in the midline, one block was routinely imbedded in paraffin and stained with chrome-hematoxylin-phloxin (CHP) and aldehyde-fuchsin (AF); the other block was cut on the freezing microtome and impregnated with variants of the silver carbonate technique of *del Rio Hortega.* For

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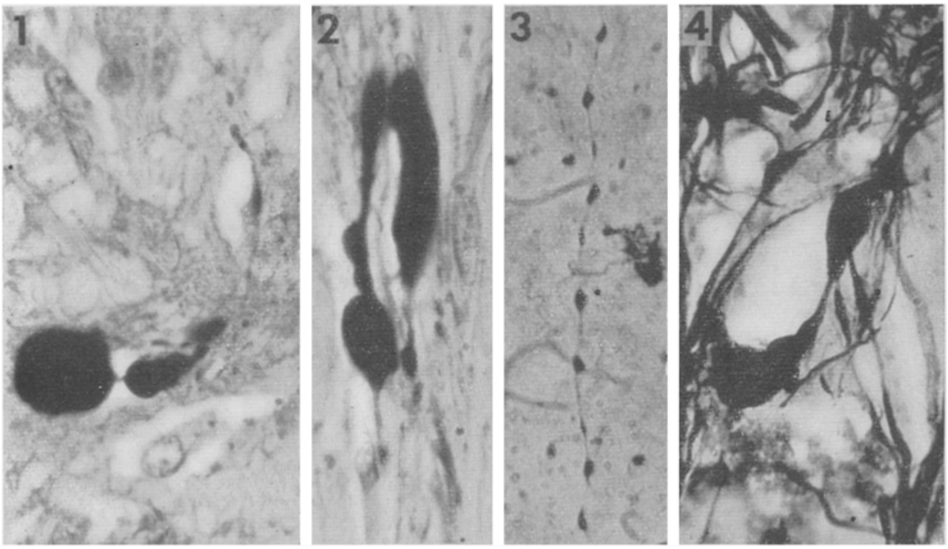
the examination of the remaining 100 neurohypophyses only the silver carbonate technique was employed. All illustrations are photomicrographs which had not been retouched.

Description of the Material

In the sections stained with CHP and AF the presence of neurosecretory material was established. The structures which were found *Gomori*-positive were also visualized with silver impregnation. The advantage of employing the silver carbonate technique lies in the distinct impregnation of both neural and non-neural structures.



Figs. 1 and 2.

Nerve fibers with pearl-like swellings. Chrome-hematoxylin-phloxin. Zeiss Neofluar 100 ×.

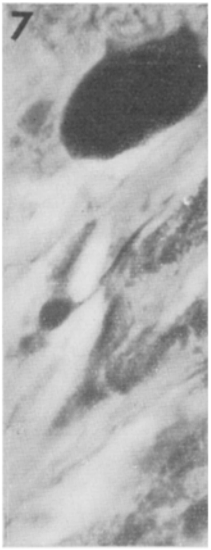
Fig. 3.

Nerve fiber with droplets of the neurosecretory material. Silver carbonate. Zeiss Neofluar 100 ×.

Fig. 4. Swelling of nerve fibers caused by accumulation of neurosecretory material. Silver carbonate. Zeiss Neofluar 100 ×.

Fig. 1 and 2 show nerve fibers of the hypothalamo-hypophysial tract from the lower part of the infundibulum; these nerve fibers show pearl-like swellings and large end-structures which are *Gomori*-positive and represent the accumulation of the neurosecretory substance. The impregnation with silver carbonate distinctly shows the neurosecretory substance which may appear in the nerve fibers as tiny droplets (Fig. 3) or as marked thickenings (Fig. 4). Fig. 5 shows distinct globular end-structures or so-called *Herring* bodies filled with *Gomori*-positive substance.

The so-called *Herring* bodies are round or oval in shape and may vary greatly in size. They are closely related to nerve fibers, some of them are large and appear homogeneously impregnated with silver carbonate (Fig. 6);



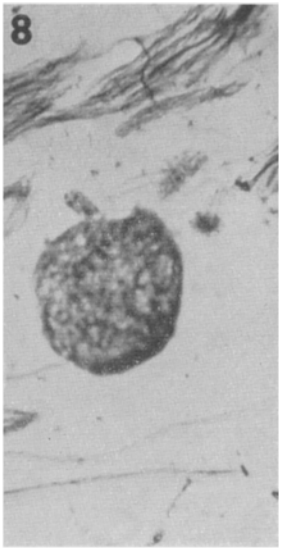
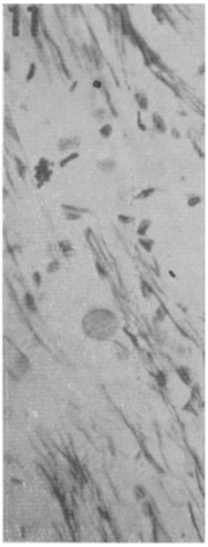


Fig. 5. Neurosecretory end-bulbs. Aldehyde-fuchsin. Zeiss Neofluar 100 ×.

Fig. 6. Neurosecretory end-bulbs. Silver carbonate. Zeiss Neofluar 100 ×.

Fig. 7.
Large and small neurosecretory end-bulbs. Chrome-hematoxylin-phloxin. Zeiss Neofluar 100 ×.

Fig. 8. Globar body filled with small granules. Note the mesh-like ground structure. Silver carbonate. Zeiss Neofluar 100 ×.



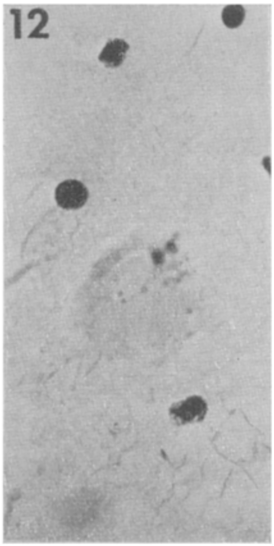


Fig. 9. Very pale end-bulb ("ghost body"). Silver carbonate. Zeiss Neofluar 100 ×.

Fig. 10. "Ghost body" filled with granules. Silver carbonate. Zeiss Neofluar 100 ×.

Fig. 11. "Ghost body" among the fibers of the hypothalamo-hypophyseal tract. Silver carbonate. Zeiss Neofluar 40 ×.

Fig. 12. "Ghost body". Silver carbonate. Zeiss Neofluar 100 ×.

others are very small (Fig. 7). Numerous bodies are found in which the nerve fibers which connect them are hard to identify; these elements are filled with granules and have a mesh-like ground structure (Fig. 8). There are also pale bodies which are *Gomori*-negative but display with the silver carbonate impregnation all the characteristics of neurosecretory bulbs except that they are not deeply impregnated and often have no granules (Fig. 9). These are the ghost bodies which display many different forms. Some of them make a distinct connection with nerve fibers and contain sparse gra-

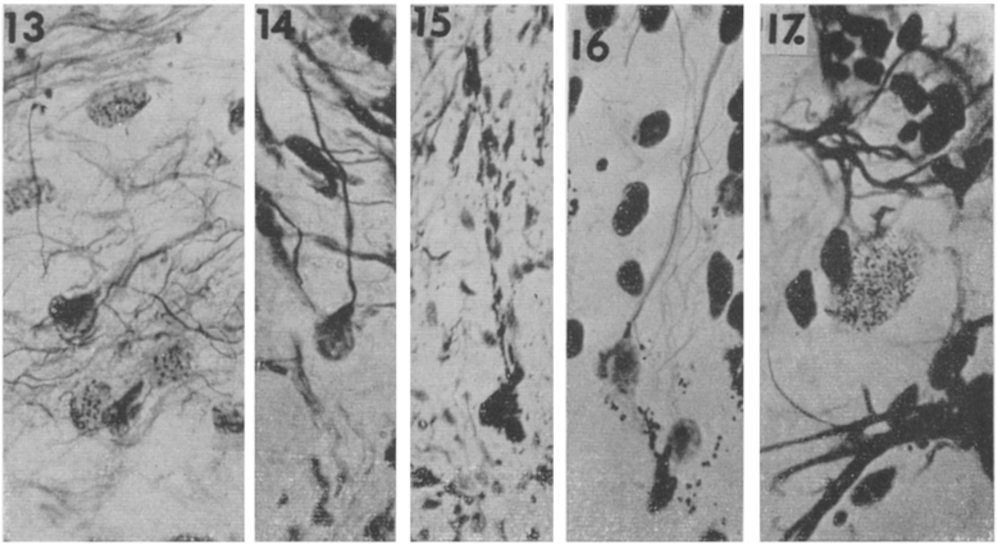


Fig. 13. Pituicytes and nervous network. Silver carbonate. Zeiss Neofluar 100 ×.

Fig. 14. Pituicyte with nerve fiber ending in its protoplasm. Silver carbonate. Zeiss Neofluar 100 ×.

Fig. 15. Pituicyte connected with a nerve fiber. The nerve fiber is carrying droplets of neurosecretory substance. Silver carbonate. Zeiss Neofluar 100 ×.

Fig. 16. Pituicyte with droplets partly filling the protoplasm. Note the distinct connection between the nerve fiber and pituicyte, and the peri-pituicytic nervous network. Silver carbonate. Zeiss Neofluar 100 ×.

Fig. 17. Pituicyte with markedly enlarged body filled with droplets. Silver carbonate. Zeiss Neofluar 100 ×.

nules (Fig. 10), others are pale and appear homogeneously impregnated (Fig. 11). It was also possible to distinguish very few extremely pale bodies which have small round nucleus-like structure located eccentrically (Fig. 12).

All the described forms represent neurosecretory bulbs either filled with the substance or the remaining skeleton structure which previously contained the neurosecretory substance.

The process of formation and the growing of the neurosecretory globules can be observed on pituicytes which are surrounded by very elaborate nervous structures (Fig. 13). Some of the nerve fibers terminate around, or in the bodies of the pituicytes (Fig. 14). These nerve fibers carry the neurosecretory substance and it can be observed how a nerve fiber filled with neurosecretory droplets connects with a pituicyte (Fig. 15). Eventually the granules are deposited in the protoplasm of the pituicyte (Fig. 16). The pituicytes freshly filled with neurosecretory droplets can be identified as cellular elements (Fig. 17), until the accumulation of the neurosecretory substance is so dense that the cellular characteristics become indistinct (Fig. 18 and 19) and finally are completely lost (Fig. 20). Another variety

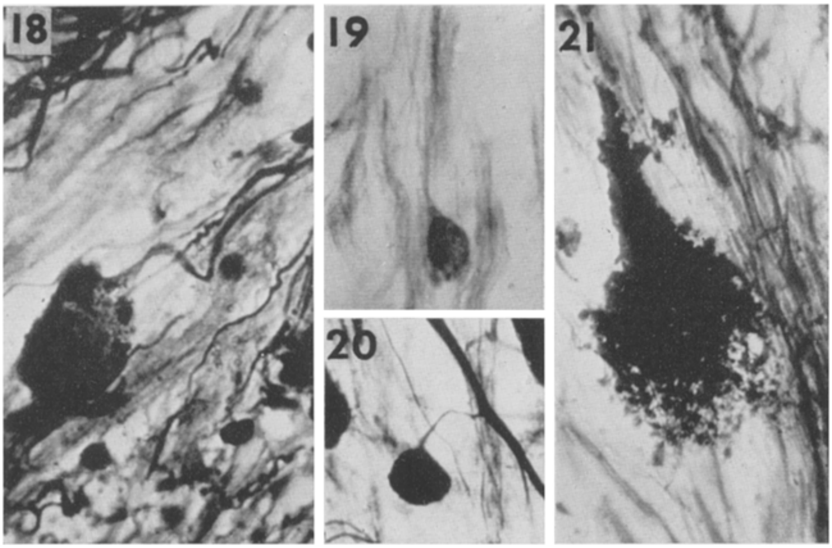


Fig. 18. Pituicyte densely filled with droplets. The cellular characteristics are indistinct. Silver carbonate. Zeiss Neofluar 100 ×.

Fig. 19. Neurosecretory end-bulb. Chrome-hematoxylin-phloxin. Zeiss Neofluar 100 ×.

Fig. 20. Neurosecretory end-bulb. Silver carbonate. Zeiss Neofluar 100 ×.

Fig. 21. Giant end-structure filled with droplets. Silver carbonate. Zeiss Neofluar 100 ×.

of globule is represented by a pear-shaped formation with no obvious relationship to pituicytes (Fig. 21). These bodies are usually very large and are connected with a nerve fiber which is filled with droplets.

Discussion

In the present investigation the neurosecretory material was impregnated with silver carbonate. The argentophile droplets found along the nerve fibers and in the end-globules, were identified as neurosecretory material, after sections from the same neurohypophyses stained with CHP and AF were used as indicators.

The investigations of *Scharrer* and *Scharrer, Bargmann* and others have shown that the *Gomori*-positive substance in the hypothalamus and neurohypophysis gives an equivalent picture of the neurosecretory material.

In earlier investigations (*Liss*, 1956) a definite relationship between the cellular elements of the neurohypophysis and the so-called *Herring* bodies was suggested. The pituicytes are highly modified glial elements and several different types of pituicytes can be differentiated. These types are so distinct in character that they are individually capable of forming neoplasms (*Liss*). The pituicytes are imbedded in a complex nervous structure and the nerve fibers terminate around and in the protoplasm of the pituicytes. Some of the nerve fibers of the hypothalamo-hypophysial tract which connect with pituicytes carry droplets of the neurosecretory substance.

Eventually the droplets of neurosecretory material are deposited in the protoplasm of the pituicytes. The accumulation of the neurosecretory material in the pituicytes causes enlargement of the cell body and displacement of the nucleus until the cells become completely filled and lose their cellular characteristics. The present studies indicate that the so-called *Herring* bodies represent pituicytes filled with neurosecretory substance.

Another type of globule is formed by the accumulation of *Gomori*-positive droplets which is dense in the center and sparse at the periphery and is connected by a nerve fiber filled with neurosecretory substance. This type may represent a mode of storage of the neurosecretory substance without utilization of the pituicytes and will not be discussed in this paper.

As previously stated, *Gomori*-positive end-globules lose completely their cellular characteristics. In silver impregnated material there were pale bodies which otherwise had all the characteristics of the end-globules but contained a nucleus, and in the comparative sections were *Gomori*-negative. The presence of these ghost bodies, which have cellular characteristics but contain no neurosecretory substance, may be explained as enlarged nerve-connected pituicytes from which the neurosecretory substance has been released.

Rennels and *Drager* (1955) observed the close relationship between neurosecretory material and pituicytes. According to these authors, "the neurosecretory material is applied to the external surface of the pituicytes". These authors have also observed nerve endings imbedded in the pituicytes, but believe them to be the result of enlargement of the pituicytes without enlargement of a pericellular nervous network. In our previous studies the different types of nervous end-structures have been outlined, and the nerve endings which are instrumental in deposition of the neurosecretory substance in the pituicytes may be any of the following three types: 1. free nerve endings; 2. bud-like end formations; 3. brush-like endings.

Since different types of the peri-pituicytic nervous network appear unrelated to the transportation of the neurosecretory substance, they may well represent the regulatory and release mechanism connected both with the hypothalamo-hypophysial tract and sympathetic perivascular network.

The present investigation represents further evidence that the pituicytes play a vital active role in the process of storage and release of neurosecretory substances.

Summary

The neurosecretory end-globules or the so-called *Herring* bodies have been investigated with silver carbonate and *Gomori* techniques and the relationship between these end-globules and pituicytes has been discussed.

Zusammenfassung

Die neurosekretorischen Endkörper oder die sogenannten *Herring*-Körper wurden mit der Silbercarbonat-Methode und der *Gomori*-Technik untersucht. Die Zusammenhänge zwischen diesen Endkörpern und den Pituicyten wurden besprochen.

Résumé

Les corpuscules terminaux neurosécrétoires ou les soi-disant corps de *Herring* ont été examinés avec la méthode au carbonate d'argent et la technique de *Gomori.* Les relations entre ces corpuscules terminaux et les pituicytes furent discutées.

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