Morphology of the Accessory (Pharyngeal) Adenohypophysis and Its Relationship with the Pharyngeal Tonsil in the Human Fetus

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The pharyngeal pituitary was examined in human fetuses during weeks 16 to 32 of development by light microscopy with routine and histochemical treatment of slices. All the fetuses examined possessed a pharyngeal pituitary, which develops from the epithelium of the upper pharyngeal wall, just like the main pituitary. Rathke's pouch becomes transformed into a cord and grows towards the midbrain forming the hypophysis cerebri, while some cells at the base of the cord remain in the integumentary epithelium of the pharynx and give rise to the pharyngeal pituitary. This organ represents a group of long epithelial cords under the integumentary epithelium within the connective tissue of the pharyngeal mucosa. The cords contain light and dark cells with signs of a secretory cycle. The pituitary cords grow into the lymphoid tissue of the pharyngeal tonsil. The integumentary epithelium does not contain protective structures at the site of origin of the pharyngeal pituitary.

Key Words: *pharyngeal pituitary; development; human fetus*

The accessory pituitary is usually disregarded in studies of the histophysiology of development of the hypophysis cerebri [2,4]. Some authorities [3], however, claim that the pharyngeal tonsil should be classed not only among the organs of immunogenesis, but also in the endocrine system, as it contains hormonal substances which directly influence tissues in the organism [1]. When tadpoles eat tonsillar tissue autohydrolysate, their melanophores constrict and body growth is sharply accelerated. Some adults have been reported to possess a pharyngeal pituitary, which was revealed at autopsy. It is thought to be the source of nasopharyngeal tumors. Some reports [9] describe cell accumulations in this area in adults which are similar to cells of the anterior lobe of the pituitary. Secretion of adrenocorticotropic hormone, prolactin, thyroid hormone, and growth hormone is detected in the region of the pharyngeal tonsil in some adults [8]. Electron microscopy shows cells with granules of four types [6]. Pathological processes have been described in the nasopharynx where its adenocytes become the source of tumor growth [5,10].

Hence, the nasopharynx is a complex and little-studied organ from the viewpoint of its development, function, and morphology. During a study of the development of all organs of the human fetal immune system, including the lymphoid ring, we came across a group of specific epithelial cells in the nasopharynx which belonged to the pharyngeal pituitary, and carried out a special morphological study of this site.

Our purpose was to find out whether the pharyngeal pituitary is an independent organ or a part of the pharyngeal tonsil; to determine how often the pharyngeal pituitary occurs in man; and to examine the development and structure of the pha-

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ryngeal pituitary and its relationships with the lymphoid tissue of the tonsil in the human fetus.

MATERIALS AND METHODS

The nasopharynx of 12 human fetuses of the 16th to 32nd weeks of development was examined. After the pituitary cell mass with the adjacent tissue had been carefully detached, it was fixed in Carnoy's fluid, passed through absolute ethyl alcohol and benzene, and embedded in paraffin. Serial 5-7 μ slices were stained with hematoxylin-eosin and with Schiff's reagent after Dominici-Kedrovskii, which permits the detection of chromaffin and chromophobic cells of the pituitary. In addition, these slices were impregnated with a solution of silver nitrate as described previously [7].

RESULTS

A pharyngeal pituitary was found in all the fetuses examined. In 16-week fetuses its primordium lies directly under the integumentary epithelium of the upper wall of the pharynx along the midline from the nasal septum and presents as an accumulation of epithelial cells lying in the mesenchyma. As the nasopharynx grows, the cords of the pituitary epitheliocytes stretch out parallel to the surface of the integumentary epithelium. By week 32 the cords in the connective tissue of the mucosa located parallel to the epithelial lining spread far from the site of their origin; upon reaching the lymphoid tissue of the pharyngeal tonsil, they grow into it. Figure 1, *a*, shows a cross section of an adenocyte cord, in which two types of cells, dark and light, are distinguished. Such cells are also to be found in the integumentary epithelium of the nasopharynx near the origin of the adenohypophysis (Fig. 1, *b*). Dark cells of the cords contain large granules. In some cells there is an accumulation of granules, in others a degranulation, and in still others the cytoplasm is free of granules (Fig. 1, *c*). Evidently, a secretory cycle is already taking place in the pharyngeal pituitary of the fetus.

Adenocytes in the pharyngeal pituitary are assembled in groups and, as in the pituitary, are surrounded by numerous wide capillaries (Fig. 1, *d*). Secretory granules are seen both in the vascular lumen and along the gaps between cells. The origin of the pharyngeal pituitary is a question of interest. The hypophysis cerebri develops very early in the human embryo, when its length is only 4 mm, from the pharyngeal pouch (Rathke's pouch) epithelium on the upper wall of the pharynx [2,4]. In a 17-mm embryo Rathke's pouch is obliterated near the lumen of the pharynx and becomes transformed into an epitheliocyte cord opening from the integumentary epithelium of the roof of the pharynx. Tracing the embryogenesis of the pituitary through the early stages of development, scientists have disregarded an essential aspect which shows up on microphotographs. When the cord becomes detached (establishment of the pituitart), some epitheliocytes at its base do not break away from the pharyngeal epithelium and are not released by the integumentary epithelium but remain within it. These remaining cells become the source of growth and subsequent differentiation of the pharyngeal pituitary. Here the remaining epithelial cells grow and differentiate in the nasopharynx according to the glandular type, just as in the pituitary, but far away from it. The nasopharyngeal integumentary epithelium is strictly differentiated at the site of the nasopharynx, where hypophyseal cells begin to grow. Figure 1, *d* shows that this site generally has an extensive cavity above which the ciliated epithelium comes to an end, being replaced by a simple squamous or cuboidal epithelium without cilia. Such epithelium often contains adenocyte granules. Hence, the nasopharyngeal mucosa is commonly devoid of protective devices such as cilia and mucosal cells at the site of the pharyngeal pituitary outgrowth.

Close to the time of birth, intimate topographic relationships are established between the pharyngeal pituitary and pharyngeal tonsil. The pituitary adenocyte cords are surrounded by lymphoid tissue, and postcapillary venules intrinsic to the tonsillar lymphoid tissue lie alongside the large blood vessels of the pituitary.

Hence, an adenohypophysis in the nasopharyngeal region was found in all the fetuses examined. It develops as a separate organ independent of the tonsil. During embryogenesis the pharyngeal tonsil is formed from the mesenchyma and then becomes transformed into reticular tissue populated by lymphocytes; the pharyngeal pituitary, like the pituitary, develops from the epithelium of Rathke's pouch in the upper wall of the future nasopharynx. As the pituitary develops, when Rathke's pouch grows up toward the midbrain, some of the cells at the base of the epithelial cord become detached and are left in the epithelium. The remaining cells grow there or many form cords in the nasopharynx. The cords spread far from their point of origin under the integumentary epithelium. The pharyngeal pituitary cells start to produce secretion in the embryonal

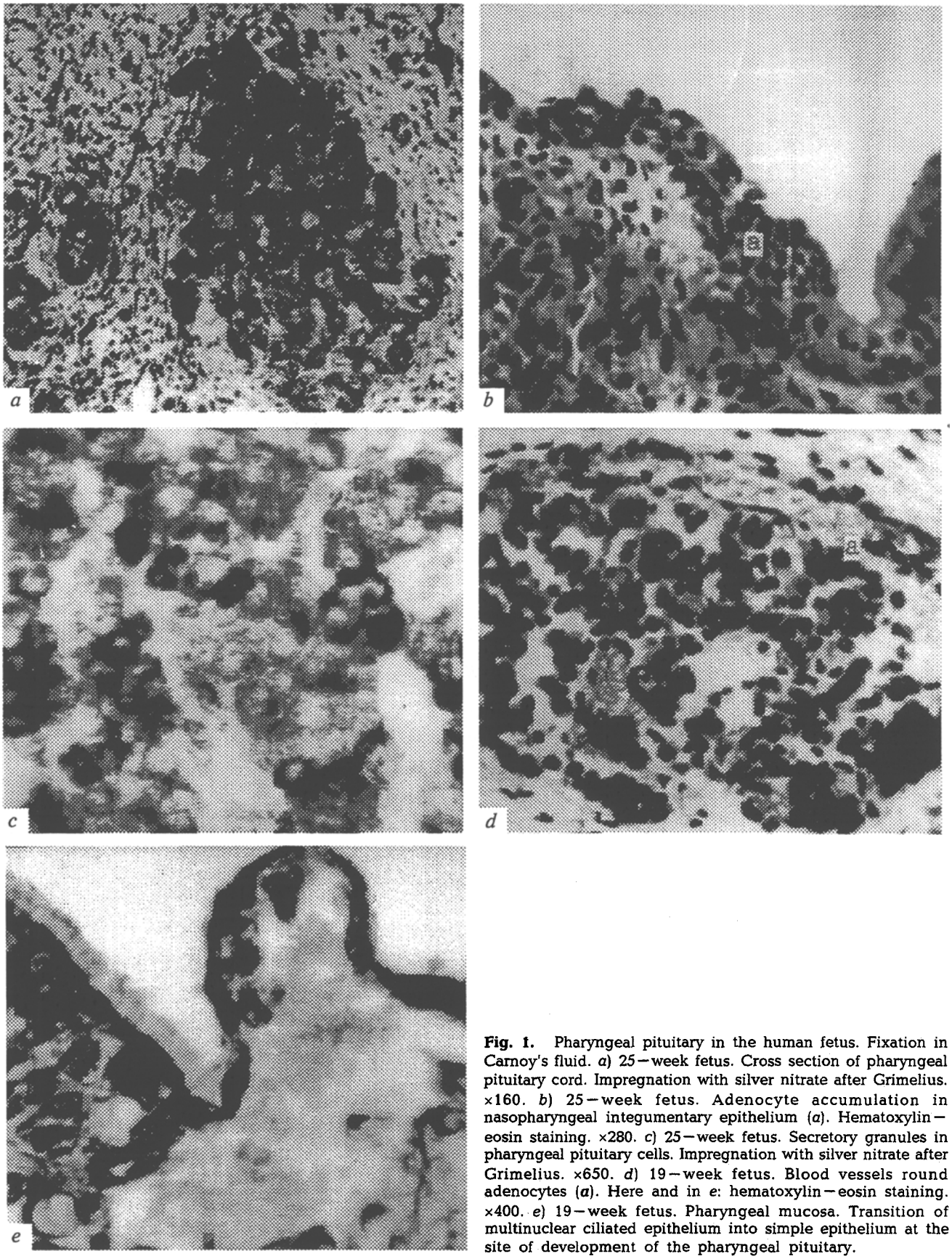

Fig. 1. Pharyngeal pituitary in the human fetus. Fixation in Carnoy's fluid. *a*) 25-week fetus. Cross section of pharyngeal pituitary cord. Impregnation with silver nitrate after Grimelius. ×160. *b*) 25-week fetus. Adenocyte accumulation in nasopharyngeal integumentary epithelium (*a*). Hematoxylin-eosin staining. ×280. *c*) 25-week fetus. Secretory granules in pharyngeal pituitary cells. Impregnation with silver nitrate after Grimelius. ×650. *d*) 19-week fetus. Blood vessels round adenocytes (*a*). Here and in *e*: hematoxylin-eosin staining. ×400. *e*) 19-week fetus. Pharyngeal mucosa. Transition of multinuclear ciliated epithelium into simple epithelium at the site of development of the pharyngeal pituitary.

period. Close territorial relationships between the nasopharyngeal pituitary and pharyngeal tonsil are established during this period, too. We do not believe there is justification for saying that the pharyngeal tonsil possesses endocrine functions, because the hormonal effects of extracts of the pharyngeal tonsil reported by some authorities can be explained by the fact that the extracts were derived from tonsillar tissue and pharyngeal pituitary adenocytes. The part of the nasopharyngeal mucosa with the pharyngeal adenohypophysis deserves the serious attention of endocrinologists and surgeons performing operations in this area. Evidently, there is merit to the previous reports of Western scientists that this area devoid of protective structures in the epithelium is very often prone to disease.

REFERENCES

1. T. N. Aspisov, *On the Intrasecretory Function of the Pharyngeal Tonsil* [in Russian], Author's Synopsis of Thesis of Cand. Biol. Sci., Moscow (1946).
2. E. P. Volodina, *Probl. Endokrinol.*, № 1, 16-20 (1966).
3. M. B. Kochurova, *Proc. Research Institute of Physiology* [in Russian], Vol. 1, Stalingrad (1934), p. 258.
4. L. I. Falin, *An Atlas of Human Embryology* [in Russian], Moscow (1976).
5. B. Corehblum, F. Le Blanc, and M. Weitenabl, *JAMA,* **243**, № 14, 1456-1457 (1980).
6. C. B. Gohsales, G. F. Valdes, and D. R. Ciocca, *Acta Anat. (Basel)*, **97**, № 2, 224-231 (1977).
7. L. Grimelius, *Acta Soc. Med. Uppsala,* **73**, 232 (1968).
8. U. Hachmeister, *Endocrinologie,* **51**, № 3-4, 145-169 (1967).
9. B. Romeis, in: *Handbuch der Mikroscopischen Anatomie der Menschen* (Ed. W. von Molendorf), Vol. 6, Part 3, Berlin (1940), p. 3.
10. F. Weber and Y. Mori, *Helv. Paediatr. Acta,* **31**, № 3, 261-270 (1977).