FUNCTIONAL ROLE OF THE ASKANAZY CELLS OF THE THYROID

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Histochemical investigation of human thyroid glands revealed high succinate dehydrogenase, α-glycerophosphate dehydrogenase, and monoamine oxidase activity in the Askanazy cells. Investigation of the biogenic monoamines in these cells revealed yellow fluorescence of a granular character characteristic of 5-hydroxytryptamine (serotonin). The demonstration of an independent function of the Askanazy cells, linked with the accumulation of the biogenic monoamine, is evidence that they exist in the thyroid gland as an independent cell type playing an active part in the regulation of thyroid function. Askanazy cells would be better described as B-cells, from the first letter of the words "biogenic monoamines."

In 1898 Askanazy [13] described large, strongly eosinophilic cells with granular cytoplasm in the thyroid gland of an elderly woman with thyrotoxicosis. Later, many writers described these cells incorrectly as Hürthle's cells, although Hürthle himself [20] had in fact described parafollicular cells in the thyroid gland of puppies. Until recently Askanazy cells have been interpreted as a variety of follicular cells in which degenerative changes indicative of severe disturbances of intracellular metabolism have taken place [1, 2, 19]. Detailed histochemical studies of the Askanazy cells showed that they have very high enzyme activity [7-9, 11].

Because of the definite similarity between certain histochemical properties of the Askanazy cells and cells of the so-called APUD-system [21], which produce polypeptide hormones and can actively accumulate the precursors of the biogenic monoamines and oxidize them to the monoamines themselves, it has been suggested that the Askanazy cells belong to the same system [8, 10]. Considering that the actual functional role of the Askanazy cells remains unknown, and in view of the earlier hypothesis, investigations were carried out to study the biogenic monoamines in these cells in adenomas, carcinomas, Hashimoto's goiter, and thyrotoxic goiter [3-6].

However, it was not established whether biogenic monoamines are found in Askanazy cells in the normal thyroid gland, and the investigation described below was carried out to study this problem.

EXPERIMENTAL METHOD

The test material consisted of human thyroid glands removed on account of diffuse and nodular goiter, Hashimoto's goiter, adenomas, and carcinomas of the thyroid gland. Altogether 73 glands were studied. In addition, in 33 cases normal regions of the thyroid taken at a distance from the neoplasms and not affected by the tumor were studied.

Besides the ordinary histological investigation a histochemical study was made of the enzymes succinate dehydrogenase, α-glycerophosphate dehydrogenase, and monoamine oxidase. The first two enzymes were studied in order to identify the Askanazy cells [7, 10], the third as directly related to monoamine metabolism. The biogenic monoamines were studied by Eränkö's method [17] in the modification of Sakharova and Sakharov [9].

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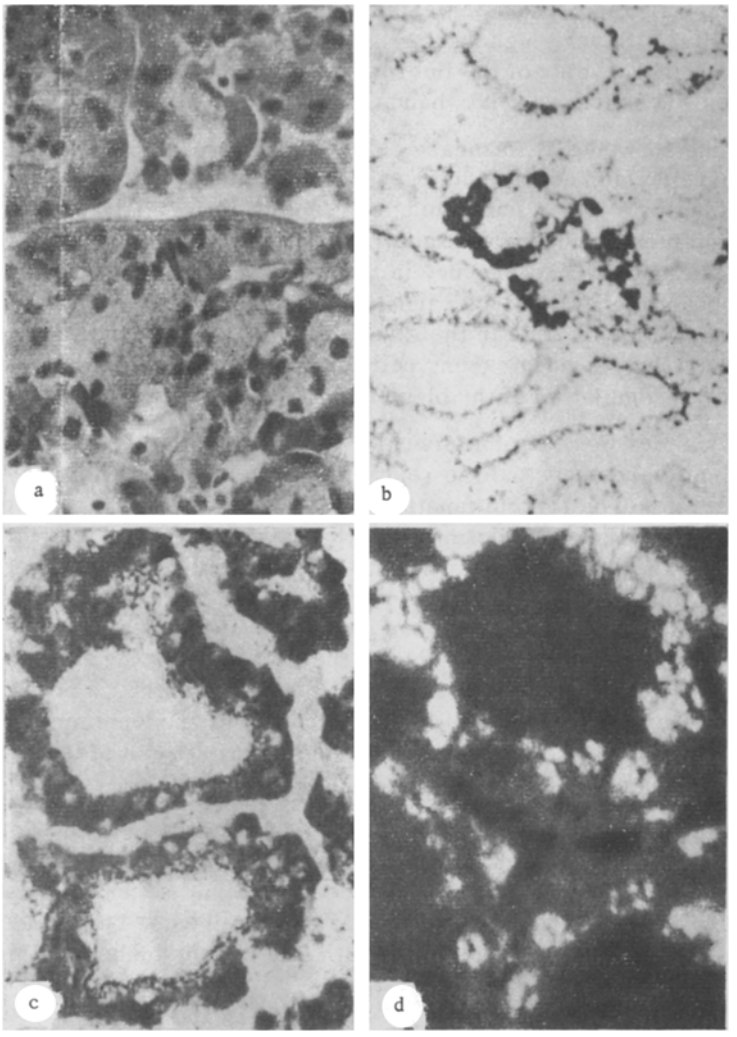

Fig. 1. Askazany cells (B-cells) in the human thyroid gland. a) B-cells of large size with granular cytoplasm (hematoxylin-eosin, 500 ×); b) high succinate dehydrogenase activity in the B-cells and low-activity in the follicular (A-cells, 120 ×); c) high succinate dehydrogenase activity in the B-cells lining the follicles (500 ×); d) specific (yellow) fluorescence in the B-cells (500 ×).

EXPERIMENTAL RESULTS

Askanazy cells were found in 44 of 106 cases. In addition, two adenomas and three papillary carcinomas were identified as Askanazy cell tumors.

The Askanazy cells had a characteristic appearance: large size, clear outlines, absence of polarity. Their cytoplasm was filled with eosinophilic granules and their nuclei were round (Fig. 1a).

By their degree of enzyme activity the Askanazy cells differed sharply from follicular cells and could be clearly distinguished from them (Fig. 1b). In tests for succinate dehydrogenase and α-glycerophosphate dehydrogenase, deposits of diformazan consisting of tiny granules completely filled the cell cytoplasm, and often because of the large number of granules they joined together to give a diffuse staining of the cytoplasm (Fig. 1c). Monoamine oxidase activity in the Askanazy cells also was high.

In the tests for the biogenic monoamines a yellow fluorescence, as a rule granular in character, was found in the Askanazy cells. The specific yellow fluorescence was localized in the cyotplasm chiefly around the nucleus. The intensity of the fluorescence varied, for sometimes the cell contained single granules but more frequently the fluorescence was homogeneous in character on account of fusion of the granules into a

general mass (Fig. 1d). Specific fluorescence was absent in the nuclei. In the adenomas and carcinomas arising from Askanazy cells, with very high enzyme activity, biogenic monoamines also were found in most of the tumor cells. The character of the fluorescence in the tumors clearly outlined the corresponding histological structures: follicles, papillae, bands.

The investigation thus showed that Askanazy cells, not only in pathologically changed areas, but also in normal areas of the thyroid gland contained biogenic monoamines as well as high activity of oxido-reductases. Spectroscopic analysis [16, 18] and the use of inhibitors [12] have shown that the yellow fluorescence in tests for biogenic monoamines is characteristic of 5-hydroxytryptamine (serotonin). These observations suggest that the yellow fluorescence in the Akanazy cells is produced by serotonin, although the presence of other monoamines of this type cannot be ruled out. The presence of a biogenic monoamine (serotonin) and also of monoamine oxidase in the Askanazy cells are evidence against the widely held view that these cells are degenerating, spent, or dying cells,and for the view that the function of the Askanazy cells is connected with the accumulation of the biogenic monoamine, serotonin.

In the study of the complex mechanisms of neuro-humoral regulation of the physiological functions of the body very little attention has been paid to relations between serotonin and thyroid gland activity. The inhibitory action of serotonin on thyroid function has been established experimentally by a few workers. For instance, serotonin lowered the assimilation of I^{131} by the thyroid gland [23]. It has also been shown that this monoamine inhibits the deiodination of thyroid hormones at the level of cell metabolism [14]. Administration of serotonin inhibits thyroid function whereas administration of its antagonists activates thyroid function. The prolonged action of serotonin can actually lead to a decrease in size of the follicles [15]. Considering the (admittedly not very extensive) data in the literature on the effect of serotonin on thyroid function and the present writers' own observations showing the presence of a powerful and evidently highly reactive independent cell system connected with the function of this biogenic monoamine in this endocrine organ, it is reasonable to suppose that the serotonin of the Askanazy cells of the thyroid gland plays an important role in the regulation of its functions.

Bearing in mind the tendency to name endocrine cells by the letters of the Roman alphabet and considering that the parafollicular cells, which synthesize calcitonin, are called for this reason C cells and that the follicular cells are sometimes known as the A cells, it would seem reasonable to call the Askanazy cells B-cells from the first letter of the words "biogenic monoamines." Three independent types of cells can thus be distinguished in the human thyroid gland, with different histochemical properties, morphology, and functions: the A, B, and C cells.

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