UPTAKE OF RADIOACTIVE IODINE BY CELLS OF THE FOLLICULAR AND INTERFOLLICULAR EPITHELIUM OF THE THYROID GLAND

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Three components are now usually distinguished in the parenchyma of the thyroid gland [3]: 1) the thyroid parenchyma proper, consisting of follicular and interfollicular thyrocytes, a derivative of the prechordal plate; 2) epithelium of ultimobranchial genesis; 3) the parafollicular cells (C cells), arising from neuroblasts, migrating in early embryonic life from the newly formed neural tube, into the mucuous membrane of the pharyngeal pouch, and incorporated together with the ultimobranchial bodies in the anlage of the thyroid gland [9, 10].

The thyrocytes, as the main component of the thyroid parenchyma, are distinguished by the specific property of assimilating iodine and converting it into organic compounds. Consequently, the chief criterion of functional activity of the thyroid parenchyma proper is the intensity of uptake of radioactive iodine by the thyroid gland [6, 7]. In the thyroid parenchyma the epithelium lining the follicles — the adenomeres of the thyroid gland — can be distinguished from the interfollicular epithelium, which is responsible for the formation of new follicles and, consequently, for proliferation of the parenchyma. In the wall of the formed follicles, follicular buds arise from time to time, and as they grow, they serve as the source of the interfollicular epithelium, which later differentiates into new follicles of the gland [1, 2].

The parafollicular cells, which have become incorporated into the thyroid gland, are located not only in the interfollicular spaces, but also frequently in the wall of the follicles, where they lie between the bases of neighboring thyrocytes. Because of their superficial similarity, some workers have classed the C cells together with the follicular buds under the same, highly unsatisfactory, and unjustified name "pale cells," and they have thus identified the follicular buds with the parafollicular cells [8, 11]. However, since they are neuroendocrine cells of neural origin, the parafollicular cells cannot assimilate iodine, whereas this is the specific property of the thyrocytes.

For the reasons given above, in order to study the nature of the follicular buds, the investigation described below was undertaken in order to establish whether they are able to assimilate iodine.

EXPERIMENTAL METHOD

Male albino rats weighing 150-180 g were used. To stimulate the appearance of follicular buds the experimental animals were given a preliminary single intraperitoneal injection of 1 μCi of ^{131}I, for previous investigations showed that this dose of the isotope stimulates follicular bud formation [5]. The experimental animals were autopsied 3, 6, 9, 12, 24, 48, and 96 h after the injection. Autoradiographs were prepared with liquid type R photographic emulsion [4] and sections 5 μ thick were stained with Mayer's hematoxylin and eosin. The number of tracks (after deduction of the background) above the cytoplasm of the different cells of the thyroid parenchyma proper of the gland was counted in the sections by scanning along the object and with the aid of a special ocular grid, in a square with a side of 3 μ. In the follicles that did not assimilate ^{131}I, i.e., in adenomeres of the gland not accumuting the iodine isotope at that moment, no counting was done. Follicles with maximal uptake of iodine likewise were not counted, for it was impossible to count the number of tracks above their thyrocytes and colloid. The results of scanning of three sections and in three animals at each time of sacrifice were analyzed. The total number of cells discovered during

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TABLE 1. Intensity of Uptake of ^{131}I (number of tracks) by Cells of Thyroid Parenchyma Proper in Thyroid Gland of Albino Rats at Various Times after Injection of 1 μCi of Isotope (M ± m)

Period of investigation, h	Ordinary thyrocytes	Follicular buds	Thyrocytes of follicular islets	Thyrocytes of microfollicles
3	3,9±0,4	0,6±0,2	0,3±0,1	1,2±0,4
6	4,6±0,4	1,0±0,3	0,8±0,2	3,1±0,2
9	26,8±2,2	1,8±0,4	3,6±0,3	8,2±1,2
12	22,7±1,2	2,6±0,4	3,7±0,3	11,5±0,9
24	58,6±2,6	2,7±0,4	5,9±0,5	18,3±1,3
48	70,2±4,4	2,5±0,5	2,3±0,5	25,6±3,1
96	6,3±0,9	1,9±0,4	0,9±0,2	7,1±0,1

examination of the sections were grouped depending on the number of tracks and the types of the cells, and the results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

As Table 1 shows, thyrocytes of follicles of the gland formed in the usual manner accumulated most of the isotope. The maximum of accumulation usually occurs 24 h after injection of the indicator dose of ^{131}I, but in the present experiments the maximum occurred 48 h after the injection, when there were 70.2 ± 4.4 tracks. This was perhaps the result of superposition of the radiation of the radioactive iodide which accumulated in the cells and radiation of iodinated thyroid hormone, which had already begun to be secreted from the follicles into the blood stream and lymphatic circulation.

The follicular buds also accumulated radioactive iodine, although with lower intensity than thyrocytes of the follicular epithelium. Accumulation in cells of the follicular buds reached a maximum 24 h after the injection, but it was only 2.7 ± 0.4 tracks. Accumulation of radioactive iodine then began to decline.

Thyrocytes of the interfollicular islets accumulated radioactive iodine more intensively than the follicular buds. Accumulation in them reached a maximum also 24 h after the injection (9.5 ± 0.5 tracks), after which uptake diminished, and after 96 h it had fallen to 0.9 ± 0.2 track. However, when cells of the interfollicular islets began to differentiate into microfollicles, the ability of their thyrocytes to assimilate iodine increased again and at the maximum of accumulation, which occurred 48 h after the injection, there were close to 25.6 ± 3.1 tracks.

The results show that cells of the follicular buds assimilate iodine, and they confirm the fact that these cells have the specific property of thyrocytes, although with rather lower intensity. The cause of this decreased intensity is not clear. If it is recalled that organic conversion of iodine in the thyroid gland takes place in the lumen of the follicles at the boundary with the apical membrane of the thyrocytes [6], and that cells of the follicular bud lose their contact with the lumen of the follicle, they evidently no longer find the conditions for organic conversion of iodine, so that iodine is retained in their cytoplasm in a very reduced amount. As the synthesis of thyroglobulin in the cells of the interfollicular islets increases in intensity, which determines the beginning of differentiation of the microfollicles, assimilation of iodine by their thyrocytes once more increases gradually.

Cells of the follicular buds, which give rise to the interfollicular epithelium of the thyroid gland, are thus not parafollicular neuroendocrine cells, but thyrocytes, which preserve the specific properties of typical thyrocytes, but which lose contact with the lumen of the follicle.

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CHARACTERISTICS OF PHOSPHODIESTERASE OF CYCLIC NUCLEOTIDES AND CALMODULIN IN THE MUCOSA OF THE RABBIT SMALL INTESTINE

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Cyclic nucleotides play a decisive role in the development of certain acute intestinal infections. However, mechanisms of action of intestinal toxins have been studied chiefly on enzyme and membrane preparations of tissues such as the brain, heart, and erythrocytes [13]. This is because the enzymes of cyclic nucleotide metabolism have been well studied in those tissues but practically not at all in the intestinal mucosa. The difficulties of isolating these enzymes from the mucosa, the absence of sufficiently accessible, simple, and reproducible methods of purifying the mucosal membranes, the small quantities of this tissue available, and various other technical difficulties have led to the result that the cyclase system of the mucosal cells has been studied much less thoroughly than in other tissues. Cyclic nucleotide metabolism is closely bound up with the Ca^{++} concentration in the cell. Cyclic AMP increases the passive permeability of the outer cytoplasmic membrane of the cell for Ca^{++} [12] and accelerates active Ca^{++} transport by the intracellular cisterns of the endoplasmic reticulum [4]. In turn, Ca^{++} activates cyclic AMP synthesis [1, 6] and the hydrolysis of this nucleotide [3, 5, 10]. All these effects of Ca^{++} are mediated through its binding with a special regulator protein, namely calmodulin [1, 3, 5, 6, 10].

In the present investigation, the action of Ca^{++} on phosphodiesterase (PDE) of cyclic nucleotides was studied and the properties of calmodulin determined in a preparation of mucosa of the rabbit jejunum and ileum.

EXPERIMENTAL METHOD

After decapitation of a rabbit weighing 1 kg the corresponding parts of the small intestine were quickly removed and washed with physiological saline, after which the mucosa was curetted and homogenized for 3 min in a Potter's homogenizer in 50-100 ml of a cold solution of 20 mM Tris-HCl and 1 mM EDTA, pH 7.4, at 4°C. The homogenate was filtered through three layers of gauze and centrifuged at 4000g for 15 min. The residue was discarded and the supernatant used for isolation of PDE and calmodulin.

Dry ammonium sulfate was added to the supernatant up to 60% saturation, mixed for 1 h, and the mixture was then centrifuged at 10,000g for 20 min. The supernatant obtained after centrifugation was used to obtain the Ca-dependent protein regulator, and the residue, which contained PDE, was dissolved in the minimal volume of a solution containing: 10 mM Tris-HCl,

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