HISTOLOGICAL AND ENZYMOLOGICAL CHARACTERISTICS OF THYROID C-CELLS

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A comparative histochemical investigation was made of the thyroid C-cells of various species of animals. In their histochemical characteristics they differ from follicular cells in their high nonspecific esterase activity and their moderate activity of α-glycerophosphate and succinate dehydrogenases. Irrespective of their number and arrangement, the C-cells share identical histochemical properties in animals of different species.

In addition to the follicular epithelium, so-called parafollicular cells are found in the thyroid gland.

The more articles are written about these cells, the more names are suggested for their identification: parafollicular cells, pale cells, macrothyrocytes, mitochondria-rich, interstitial, or argyrophilic cells, and so on. Not until it had been shown that these cells secrete calcitonin [7, 9] – a hormone regulating the blood calcium level – was it suggested by Pearse [13] that they be called C-cells, so that their name would reflect their function.

In their histochemical properties these cells differ from follicular cells in their relatively high α-glycerophosphate dehydrogenase and esterase activity [8, 9, 13]. However, no complete description of the histochemical properties of the C-cells has yet been published, so that many of the problems connected with the study of the structure of the normal thyroid gland and its changes under pathological conditions is thus rendered more difficult.

It was accordingly decided to investigate a wide spectrum of histochemical properties of the thyroid C-cells of different animals.

EXPERIMENTAL METHOD

The test material consisted of thyroid glands from 30 animals: 8 puppies, 6 pigs, 6 cows, 5 sheep, and 5 calves.

Besides the ordinary histological examination, a histochemical study was made of the oxido-reductases concerned with the function of the Krebs' cycle (succinate, malate, and isocitrate dehydrogenases), with glycolysis (lactate dehydrogenase), fatty acid metabolism (α-glycerophosphate dehydrogenase), the pentose cycle (glucose-6-phosphate and 6-phosphogluconate dehydrogenases), amino acid synthesis (glutamate dehydrogenase), electron transport (NAD and NADP diaphorases), and monoamine metabolism (monoamine oxidase). These enzymes were demonstrated by the methods described in Pearse's textbook [6] with slight modifications as regards the concentration of certain reagents and the incubation time [3].

Hydrolytic enzymes (nonspecific acid and alkaline phosphatases [12]), specific phosphatases (adenosinetriphosphatase, 5-nucleotidase [17], and glucose-6-phosphatase [4]), and nonspecific esterase [12] also were investigated.

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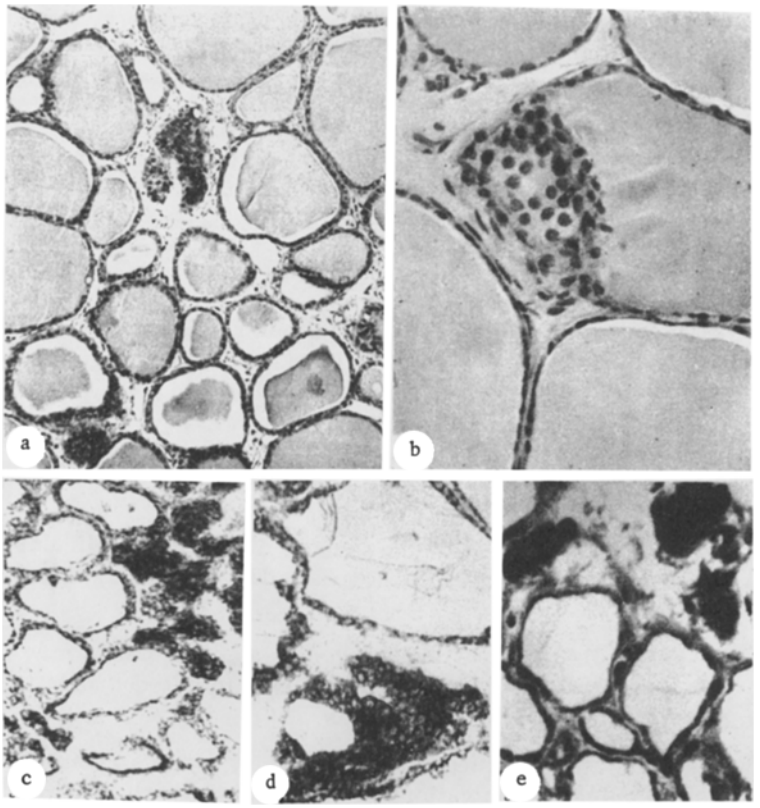

Fig. 1. Localization, morphology, and histochemical properties of thyroid C-cells: a) clearly demarcated islet of C-cells lying between follicles (hematoxylin-eosin, 180×); b) C-cells, large in size with pale cytoplasm (hematoxylin-eosin, 350×); c) α-glycerophosphate dehydrogenase: activity of enzyme is moderate in C-cells but low in follicular cells (nitro-BT, 180×); d) succinate dehydrogenase: activity of enzyme is moderate in C-cells but low in follicular cells (nitro-BT, 350×); e) nonspecific esterase: activity of enzyme is high in C-cells but low or moderate in follicular cells (fast blue BB, 250×).

EXPERIMENTAL RESULTS

The C-cells are usually arranged in groups throughout the thyroid gland to form islets between the follicles. They are more common close to the parathyroid gland (Fig. 1a). Sometimes they can be seen in the wall of a follicle next to the basement membrane, but separated from the colloid by follicular cells. They are numerous in puppies and calves, and their localization is predominantly parafollicular. Morphologically they have the appearance of large (larger than follicular cells), pale, slightly eosinophilic cells with a round nucleus and often with a double nucleolus (Fib. 1b).

The investigation showed that the C-cells, regardless of their number, arrangement, and species-specificity, possess identical histochemical properties, with only certain quantitative variations, so that their general histochemical characteristics can be described.

The α-glycerophosphate dehydrogenase activity in the follicular cells is uniform in the different areas and varies only from very low to low. Activity of this enzyme in the C-cells is higher than in the follicular cells and was assessed as moderate (Fig. 1c). It reached high in individual calves and puppies.

Staining for succinate dehydrogenase revealed low activity of this enzyme in most follicular cells. In the C-cells small regular diformazan granules were found at the sites of the enzyme in quantities indicating moderate succinate dehydrogenase activity (Fig. 1d).

Histochemical tests for the remaining oxido-reductases showed no appreciable difference in activity between the C-cells and follicular cells. Both C-cells and follicular cells possess the same moderate activity of malate, glutamate, lactate, and glucose-6-phosphate dehydrogenases and monoamine oxidase.

Only a very small quantity of reaction product was formed at the sites of 6-phosphogluconate dehydrogenase, indicating low activity of this enzyme. Tests for NAD and NADP diaphorases in the C-cells revealed regular diformazan granules in amounts indicating high activity of these enzymes. Alkaline phosphatase gave a negative reaction in the follicular cells, and single granules of reaction product were visible only in individual cells in areas of proliferation. Weak alkaline phosphatase activity was detected in the C-cells mainly of cows.

Nonspecific esterase activity was moderate in most follicular cells, while in the C-cells the reaction product completely filled the cytoplasm as tiny granules. Because of their large numbers, some of these granules merged so as to give the cell a diffusely stained appearance (Fig. 1e). C-cells differ from follicular cells in their high level of nonspecific esterase activity.

Activity of acid phosphatase, adenosinetriphosphatase, 5-nucleotidase, and glucose-6-phosphatase was equally low in both C-cells and follicular cells.

Hence, by their histochemical characteristics the C-cells differ from follicular cells in their high nonspecific esterase activity and moderate α-glycerophosphate dehydrogenase and succinate dehydrogenase activity.

The term mitochondria-rich cells was previously given by some authors to the C-cells [9, 11]. However, it was subsequently shown that they are not particularly rich in mitochondria [5, 14], thus accounting for their only moderate activity of certain oxido-reductases.

In the thyroid gland it is in fact the Ashkinazy cells [10, 15] which are rich in mitochondria. This agrees with the results of histochemical investigations of the Ashkinazy cells, in which activity of all the above-mentioned oxido-reductases is very high [2, 3, 16].

Consequently, the C-cells differ from the Ashkinazy cells in their comparatively low oxido-reductase activity. It is important to emphasize this point, because the different histochemical properties of the C-cells and Ashkinazy cells, together with other features (morphological appearance, location in the thyroid gland), indicate that these cells are independent cell groups.

This investigation also showed that the C-cells, irrespective of their number and location, possess identical histochemical properties in animals of different species. There is therefore every reason to suppose that in man the C-cells will possess the same histochemical properties as in the group of mammals investigated.

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