ACTA STEREOL 1985; 4/1: 67–76
ORIGINAL SCIENTIFIC PAPER

FOLLICULAR, PARAFOLLICULAR AND MAST CELLS IN MOUSE THYROID GLAND AFTER ANTITHYROID DRUG APPLICATION

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ABSTRACT

Fortyeight male mice BALB/c strain were divided in 6 groups with 8 animals in each. The experimental groups with 4 animals were given 1,2% $NaClO_4$ in the drinking water for 2,4,8,16,32 or 64 days respectively. The following stereological variables have been estimated at objective magnification x63: volume density of follicular cells, colloid, parafolicullar cells, mast cells and other interstitium; absolute (total) volumes, absolute numbers and average volumes of follicular, parafollicular and mast cells. Average tangent diameters of parafollicular and mast cell nuclei were measured using an ocular micrometer. The absolute volumes, expressed as a ratio of the experimental to the control values, shows a similar increase for all three cell lines between the 4^{th} and 32^{nd} day. After this time the volume ratio for mast cells shows a further sharp increase, for follicular cells a moderate increase, and for parafollicular cells a decrease. The volume increase in all three cell lines is a result of their hyperplasia and not of hypertrophy. An initiating role should be ascribed to the mast cells because their reaction occurs at the earliest time and is in average the most expressed.

Key words: mast cells, mouse, parafollicular cells, sodium perchlorate, thyroid gland

INTRODUCTION

The aim of this investigation was a quantitative analysis of the microscopic image of the mouse thyroid gland after sodium perchlorate ($NaClO_4$) application, with special emphasis on the relationship between follicular, parafollicular and mast cells. Our previous study showed hypertrophy and hyperplasia of the follicular cells in these conditions (Pajer, Kališnik 1983). In addition, Melander et al. (1972) showed that TSH administration in rodents increased the number of intrathyroid mast cells and promoted the release of biogenic amines from such cells, suggesting that at least a part of the changes induced by TSH in the thyroid gland was mediated by TSH-induced mast cells degranulation. On the other hand, Wuttke et al. (1971) described an increase in nuclear size of parafollicular cells after perchlorate application, which was interpreted as an indirect effect of TSH on the parafollicular cells through influence on interstial tissue.

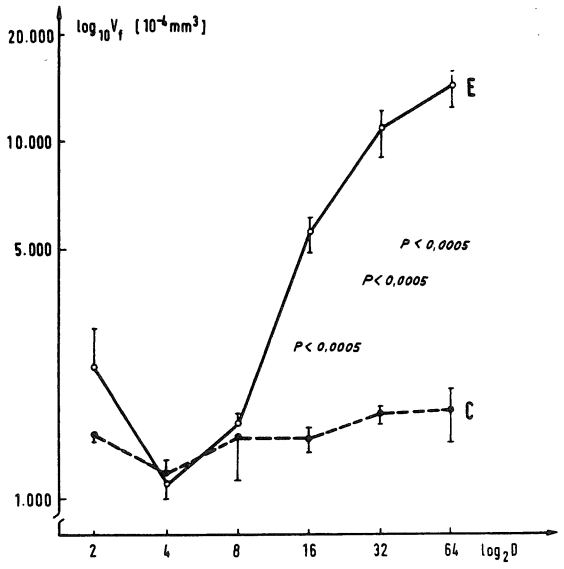
MATERIALS AND METHODS

In this experiment 48 male mice BALB/c strain, 6 weeks old, were divided into 6 groups with 8 animals in each. The experimental groups with 4 animals were given 1,2% $NaClO_4$ in the drinking water for 2,4,8,16,32 and 64 days respectively. All the experimental groups had corresponding controls with 4 animals, drinking tap water without perchlorate. The thyroid glands were fixed in Bouin's solution, cut into 6 μm step serial sections, the interval of the steps being 60 μm. One series was stained with toluidine blue at pH 4 and PAS, the second series according to Fernandez-Pasqual and toluidine blue. The first series was used for counting of the mast cells, the second for the parafollicular cells, taking into account all slices. In the first series the volume density of the epithelium, colloid, mast cells and interstitium was stereologically estimated by point counting at an objective magnification of x63. Then, the numerical density of the mast cells was estimated using our procedure (Pajer, Kališnik 1984). In addition, the absolute volume of the thy-

roid gland was determined stereologically in order to calculate the absolute (total) number and volume of the mast cells. Finally the average volume of the mast cells was calculated. In the second series at the same magnification and using same methods the absolute (total) volume, the absolute (total) number and the average volume of the parafollicular cells was estimated. At an objective magnification of x100 the average tangent diameters of the parafollicular and mast cell nuclei was measured using an ocular micrometer. Student's t-test was used for the statistical analysis.

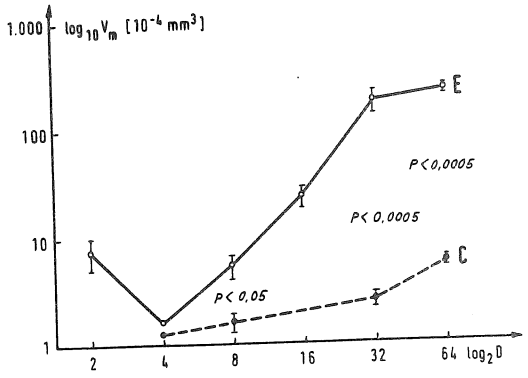
RESULTS

After the initial decrease of the absolute volume of the follicular cells on the fourth day a steady and sharp increase is obvious in the experimental group by the end of this experiment (Graph 1).

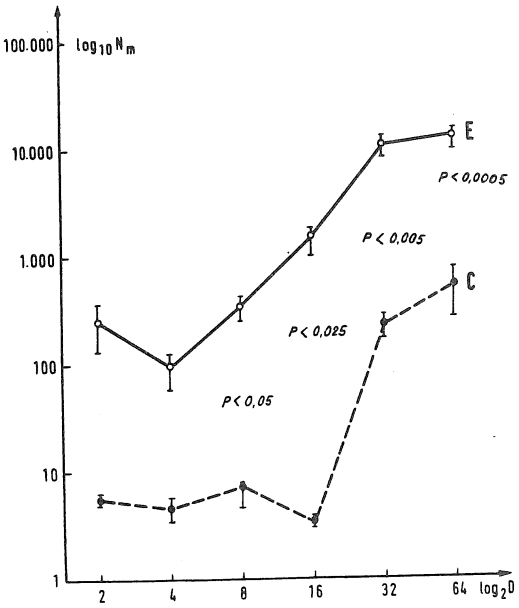


Graph 1. The absolute (total) volume of the follicular cells during 64 days' duration of the experimental (E) and control (C) group. The average and one standard error for each term. The significances of differences are indicated by notation of the corresponding risk levels (P) for rejection of the null hypothesis.

Similar trends are shown in the absolute volume (Graph 2) and absolute number of mast cells in the experimental groups (Graph 3).

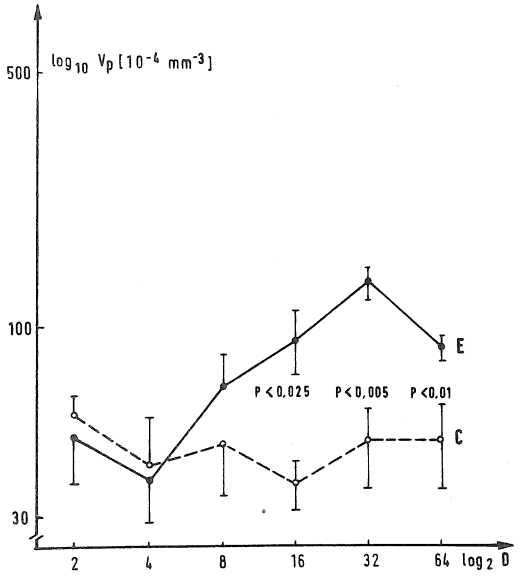


Graph 2. The absolute (total) volume of the mast cells during 64 days.



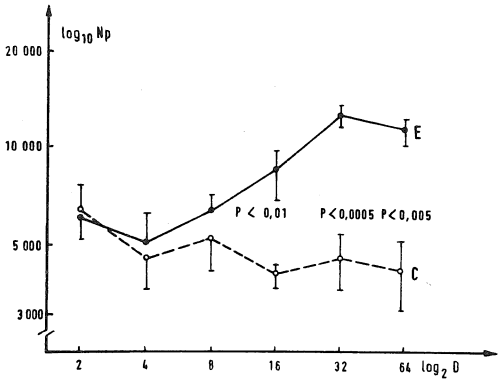
Graph 3. The absolute (total) number of the mast cells in the thyroid gland during 64 days.

A slight increase in the absolute volume of the mast cells in the control groups toward the end of the observation is indicated. But, a considerable increase in the absolute number of the mast cells in the control group is obvious, especially between 16 and 64 days. The average volume of the mast cells between the experimental and control group is not significantly different; in both groups it is significantly smaller on the 64th day in comparison with the 2nd day ($P < 0,05$). The average diameter of the mast cell nuclei in the experimental groups is 4,7 μm, though in the controls it is 4.1 μm, this difference not being significant. The absolute volume and number of the parafollicular cells in the experimental group increases by 32nd day, showing a decrease afterwards (Graph 4 and 5).



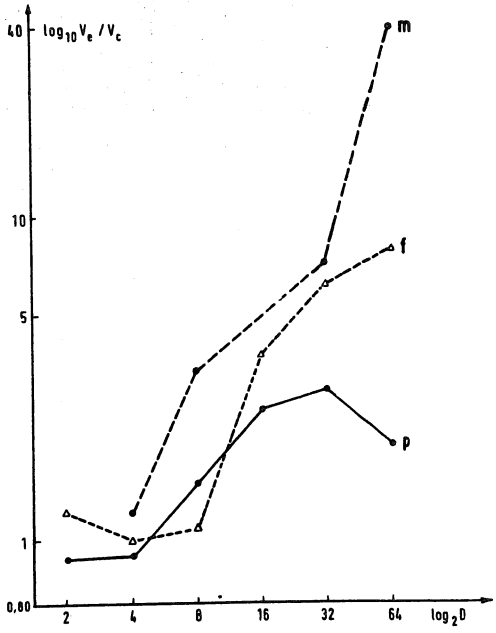
Graph 4. The absolute (total) volume of the parafollicular cells during 64 days.

The average volume of the parafollicular cells shows insignificant oscillations in both groups during the experiment. The average diameter of the parafollicular cell nuclei in the experimental groups is 6.2 μm and 6.1 μm in the control groups.

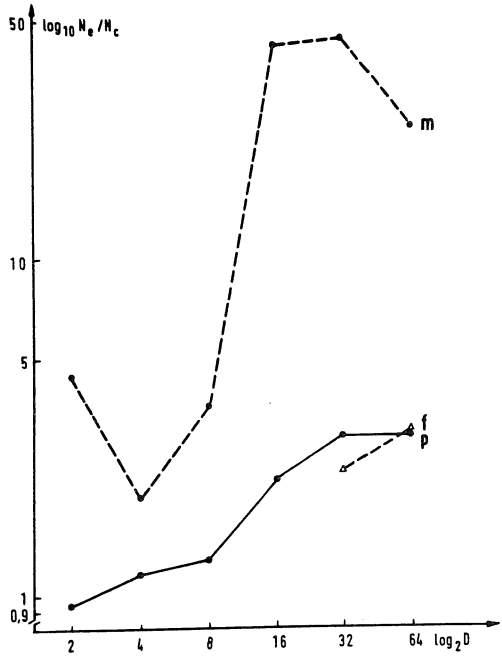


Graph 5. The absolute (total) number of the parafollicular cells in the thyroid gland during 64 days.

The ratio of the absolute volumes between the experimental and control groups for all three cell lines is presented in graph 6. The trends are congruent by the 32nd day, but afterwards the mast cell ratio shows a further sharp increase, the follicular cells ratio a moderate increase and the parafollicular cells ratio a decrease. The ratios of the absolute numbers between the experimental and control groups of the same cell lines show the highest increase for the mast cells and moderate increases for the follicular and parafollicular cells (Graph 7). In an earlier similar study it was shown that the absolute number of the follicular cells rises constantly during the first two months (Pajer, Kališnik 1981). Since no counting of the follicular cells has been performed in the present study, we have used the above mentioned data for construction of graph 7.



Graph 6. The ratio between the absolute volumes of mast cells (m), follicular cells (f) and parafolicular cells (p) between the experimental (V_e) and control (V_c) groups.



Graph 7. The ratio between the absolute numbers of all three cell lines presented as in graph 6, between the experimental (N_e) and control (N_c) groups.

DISCUSSION

The blockade of the iodine pump in the follicular cells seems to be incomplete but sufficient to increase greatly TSH blood concentration (Pajer et al.,1983). The effect on the follicular cells is well described qualitatively and quantitatively (Pajer et al.,1981). It is known from the earlier experiments, that follicular cell stuctural and functional responses occur very rapidly after perchlorate administration, even after 2 hours (Poredoš, 1979).

Several publications have implicated mast cells in the regulation of the activity of the thyroid gland. Thus, in mice, TSH was shown to greatly increase the number of intrathyroid mast cells and to promote the release of the metachromatic material and biogenic amines of these cells (Nunez, Gershon 1973). Biogenic amines including serotonin have been found to act on follicular cells to increase their rate of endocytosis of colloid and the release of ^{131}I into the blood (Bianco, 1983). Serotonin, moreover, stimulates the organification of iodine and the formation of iodothyronines, as well as adenyl cyclase activity (Maayan, 1971). In addition, histamine and/or serotonin stimulate thyroid blood flow and/or permeability under the influence of TSH (Melander et al., 1975). Since the intrathyroid mast cells significantly increase in absolute volume and number even before the follicular cells, they seem to play an important role in the compensatory activation of thyroid epithelial cells to chronical application of an antithyroid substance. We have no explanation for the sharp increase in the absolute number of the mast cells in the control group between days 16 and 32. We intend to control these data in the further experiments.

Calcitonin secreted by the parafollicular cells influence calcium homeostasis, parathormone secreted by parathyroid glands playing a known major role. It is well known that elevated blood calcium concentration is a specific stimulus for the release of calcitonin from the parafollicular cells.

But the results of research into the influence of the hypophysis on the parafollicular cells are partly contradictory (cf. Kališnik 1981 for references).

Aliapoulios and Munson (1965) found no difference in the total thyroid content of calcitonin between controls and rats fed propylthiouracil for 10 days. On the other hand Peng et al. (1978) described parafollicular cell hyperplasia and increased calcitonin level in rats several months after the cessation of 0.05% propylthiouracil in drinking water when serum TSH had returned to normal; according to them continous excess TSH stimulation was not essential for hypercalcitoninism. In our experiment in mice, however, with 1.2% $NaClO_4$ we observed in the parafollicular cells a significant increase of the absolute volume after 16 days and of the absolute number after 8 days. This discrepancy could be the effect of different antithyroid substances and their dose.

Our findings show a certain congruence in the growth reactivity of all three cell lines in the thyroid gland, at least by the end of the first month. An initiating role should be ascribed to the mast cells because their growth reaction occurs at the earliest time and is on average the most expressed.

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Received: 1984-09-14
Accepted: 1984-10-18