24-HOUR PERIODICITY OF MITOTIC DIVISION IN THE THYROID AND PARATHYROID GLANDS OF RATS AND MICE

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The study of the 24-hour periodicity of mitosis in organs and tissues has a direct bearing on the discovery of the principles governing cell division in the body and its regulation. The 24-hour periodicity of mitosis has now been established for most mammalian organs. However, in the glands of internal secretion, the changes in the number of mitoses throughout the 24-hour period have not been adequately investigated.

Details of the 24-hour periodicity of mitosis in the thyroid gland of rats have been published [9-11], but not only do they not agree, but in some cases they are directly contradictory. In some cases [9], for example, the number of mitoses was found to be minimal at 8 a.m., and maximal at 11 p.m. Other authors [10, 11] report that the number of mitoses in the thyroid cells is maximal at 7 a.m. and minimal at 10 p.m. In the investigations cited above, the time intervals between the counting were long (8-12 h) so that no clear idea could be obtained of the dynamics of the changes in the mitotic index throughout the 24-hour period.

No figures for the 24-hour periodicity of mitosis in the parathyroid gland could be found in the literature.

The object of the present investigation was to study the changes in the number of mitoses throughout the 24-hour period in the epithelium and the connective tissue stroma of the thyroid and the epithelium of the parathyroid gland in rats and mice.

EXPERIMENTAL METHOD

Male albino rats with a mean weight of 100 g and male hybrid C57B1 × CBA mice with a mean weight of 20 g were used in the experiment. The animals were kept on a natural diet and fed once daily at 9.30 a.m. and thereafter were sacrificed at 3-hourly intervals during the next 24-hour period. At each time the glands of 5 rats and 7 mice were investigated. The thyroids of the rats were fixed in Zenker-formol and the glands of the mice in Bouin's fluid. Serial sections were cut to a thickness of 5-6 μ and stained with hematoxylin-eosin.

The mitotic index of the thyroid epithelium was calculated as a percentage of the total number of thyroid cells, based on an examination of an average of 20,000-30,000 cells in each case. The mitotic index of the connective tissue cells of the thyroid stroma was calculated as a percentage of the total number of thyroid cells, and the number of mitoses in the parathyroid epithelium as a percentage of the total number of cells in the organ (7,000-10,000 cells in each case).

EXPERIMENTAL RESULTS

It is clear from the figure that the mitotic index of the thyroid epithelium of the rats and mice varied throughout the 24-hour period. The number of mitoses in the thyroid epithelium of the rats reached a minimum at 9 p.m. (0.005%). By midnight it had increased to more than 10 times its previous level, with a mean value of 0.052% ($P < 0.05$). By 6 a.m. the mitotic index had fallen to 0.009% ($P < 0.05$), after which it increased to 0.026% at 9 a.m. and 0.027% at noon (by comparison with the values at 6 a.m. P was less than 0.1 and 0.05 respectively). At 3 p.m. and 6 p.m. the number of mitoses in the thyroid epithelium again showed a decrease to 0.006 and 0.010% (compared with the figures for noon, P was less than 0.05 and 0.1 respectively). The mean mitotic activity in the thyroid epithelium of the rats for the 24-hour period was 0.020%.

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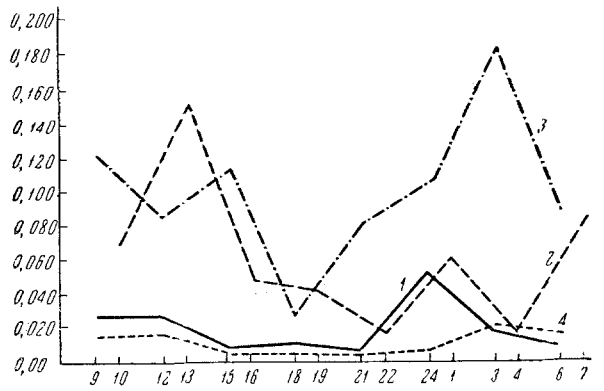

Changes in mitotic index in the epithelium and stroma of the thyroid and epithelium of the parathyroid gland. 1) Thyroid epithelium of rats; 2) thyroid epithelium of mice; 3) parathyroid epithelium of rats; 4) thyroid stroma of rats. Along the axis of ordinates) Mitotic index (in %), along the axis of abscissas) time of day.

The minimal mitotic activity in the thyroid epithelium of the mice was found at 10 p.m. (0.017%). By 1 a.m. the number of mitoses increased to 0.063%, i.e., by approximately 4 times ($P < 0.05$), but by 4 a.m. it decreased to 0.019% ($P < 0.05$). At 7 a.m. the mitotic index had increased to 0.083% ($P < 0.01$), at 10 a.m. it was not significantly changed from its level at the previous time (0.068%) but by 1 p.m. it had increased sharply to 0.152% ($P < 0.02$). At 4 p.m. the mitotic index again showed a sharp decrease to 0.050% ($P < 0.01$), and even fewer mitoses were seen in the gland at 7 p.m. (0.041%). The mean mitotic index in the thyroid epithelium of the mice for the 24-hour period was 0.062%.

The lowest level of mitotic activity in the connective-tissue cells of the thyroid stroma of the rats was observed at 9 p.m. (0.003%). By 3 a.m. it had increased to 0.021% ($P < 0.01$) and remained at a comparatively high level until noon. At 6 and 9 a.m. and at noon the mitotic index of the connective-tissue cells of the thyroid stroma differed significantly ($P < 0.05$) from the index at 3, 6, and 9 p.m. The mean mitotic activity in the thyroid stroma of the rats for the 24-hour period was 0.009%.

In the parathyroid gland the minimal mitotic index was observed at 6 p.m. (0.027%). At 9 p.m. the mitotic index was higher, although the difference was not statistically significant; it became significant at the next time of investigation (midnight) when its value was 0.108% ($P < 0.05$). At 3 a.m. the number of mitoses reached its maximum – 0.185% (compared with the figures at 6 and 9 p.m., P was less than 0.01 and 0.05 respectively, and compared with the figure at midnight, less than 0.05). The mitotic index at 6 and 9 a.m., noon, and 3 p.m. was significantly higher than 6 p.m. ($P < 0.05$). The mean mitotic index in the parathyroid epithelium of the rats for the 24-hour period was 0.106%.

Hence, in the epithelium of the thyroid and parathyroid glands and in the stroma of the thyroid, a clearly defined 24-hour periodicity was observed in the number of mitoses. However, the curves showing the changes in the mitotic index in the investigated tissues during the 24-hour period were different in character. Whereas the curves for the thyroid epithelium had two maxima, the curves for the thyroid stroma and the parathyroid epithelium had only one. In previous analyses of the 24-hour rhythm of mitosis [2, 7, 8], the question of the organ-specificity of the rhythm has repeatedly been raised. On the basis of the results showing differences in the 24-hour periodicity of mitoses in the epithelial and connective-tissue cells of the thyroid and in the epithelium of the parathyroid glands, the existence not only of organ-specificity, but also of tissue-specificity may be assumed in the changes in the number of mitoses throughout the 24-hour period.

In most mammalian organs (the liver, kidneys, intestine, cornea, etc.) the maximum of the number of mitoses occurs in the morning and the minimum in the evening [2, 4]. In the thyroid epithelium one of the two maxima of the number of mitoses occurs at night and the other during the day. In the thyroid stroma and the parathyroid epithelium the maximum of mitotic activity also takes place at night. Investigations of the 24-hour rhythm of mitotic activity in the adrenal cortex of rats and mice, by counting the number of mitoses per standard area of section, revealed a maximum of the number of mitoses during the evening [1, 10, 11]. When the mitotic index was determined at intervals during the 24-hour period in the adrenal cortex in the zona glomerulosa, zona fasciculata, and zona reticularis separately, it was found that the maximum of the number of mitoses in the zona glomerulosa occurred at 10 p.m., and the maximum in the zona fasciculata and zona reticularis at 1 p.m. [3]. The maximum of the number of mitoses in the zona glomerulosa of the adrenal cortex in rats occurs at 9 p.m., while in the various layers of the zona fasciculata two maxima are found in the number of mitoses – at 1 a.m. and at noon [5]. In the zona glomerulosa of the adrenal cortex in rats the mitotic activity of the cells is maximal at 6 a.m. and 9 p.m., while in the zona fasciculata it is maximal at noon [6].

It may thus be concluded from data in the literature and personal observations that in the endocrine organs, or at least in the thyroid and parathyroid glands and the adrenal cortex, the character of the 24-hour rhythm of mitosis differs from its rhythm in nonendocrine organs. The main differences are that in the endocrine glands the maximum, or one of the two maxima in the number of mitoses is observed during the evening or night.

The existence of two maxima in the curve of the 24-hour rhythm of mitosis in the thyroid gland, reflecting an increase in the mitotic index during the day and at night, evidently cannot serve as evidence to support the view that mechanisms such as the influence of photoperiodicity and the motor activity of the animals, usually invoked to explain the 24-hour rhythm of mitosis, can be applied universally.

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