LABOR AND DIURNAL RHYTHM OF MITOTIC ACTIVITY OF THE CELLS OF THE INTERALVEOLAR SEPTA OF THE LUNGS IN HYPOPHYSECTOMIZED RATS

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Several investigations [4,13] have shown that hypophysectomy, leading to exclusion of the somatotropic hormone from the hormonal regulation of the body, differs in its action on the level of mitotic activity in the various organs and tissues. For instance, L. D. Liozner and co-workers [4,5] showed that processes of physiological regeneration (cell proliferation) take place without difficulty after hypophysectomy in the epithelium of the cornea, tongue, esophagus, and the crypts of Lieberkühn in the small intestine. Meanwhile in the liver, the lateral orbital gland, and the kidney of hypophysectomized animals, the level of mitotic activity was considerably depressed.

Recent experimental investigations [7,9,10,12,13] have demonstrated the existence of a third group of organs and tissues (the epidermis, the cells of the sebaceous glands, the superficial cells of the gastric mucous membrane), in which cell proliferation is stimulated by hypophysectomy.

The object of the present investigation was to determine the effect of hypophysectomy on the mitotic activity and its diurnal rhythm in the cells of the interalveolar septa of the lungs in mammals, because the collection of factual data of this type may help to some extent to determine the range of action of the somatotropic hormone on the physiological regeneration of different organs.

EXPERIMENTAL METHOD

Hypophysectomy was performed on male rats weighing 170-240 g by Smith's method modified by Gasanov[3]. On the 19th day after the operation, 4-6 experimental and 8 control animals were sacrificed at each of the following times: 4 A.M., 7 A.M., 10 A.M., 6 P.M., and 10 P.M. The main group of experimental rats consisted of animals in which no remains of the pituitary were found in the region of the sella turcica at autopsy and the testes of which showed severe atrophy. The experimental conditions were described fully in an earlier paper [5].

The lungs of the rats were fixed in 10% formalin,and in sections 7 μ thick the mitoses were counted in 4000 cells of the interalveolar septa, excluding the blood cells from these counts. The numerical results were analyzed statistically by the Fisher–Student method.

EXPERIMENTAL RESULTS

As in the author's earlier special investigations [6] to study the dynamics of mitotic activity in the lung parenchyma of rats during the 24-h period, a diurnal rhythm of division was also observed in the control animals of this series of experiments in the cells of the interalveolar septa (see figure).

The maximal number of mitoses with mean values of the mitotic coefficient (MC) of 1.10 and 1.38‰, respectively, occurred at 7 and 10 A.M., and the minimal number in the evening and at night (6 and 10 P.M., 4 A.M.), when the values of the MC were 0.6, 0.37, and 0.46‰, respectively. It may thus be concluded from this repetition of the main features of the earlier results that the diurnal variations in proliferation of the cells of the interalveolar septa in rats' lungs is a regular phenomenon and that the most intensive cell division takes place during the morning (7-10 A.M.).

Meanwhile a comparatively low mean diurnal MC (0.78‰) was observed in the lung cells of the animals of this series of experiments by comparison with the mean MC for the 24-h period (1.6‰) characteristic of the lungs of rats investigated previously [6]. These differences may evidently be attributed to variations in the experimental conditions: in the first case,the animals were at a biological station and received many vitamins (fresh food), while

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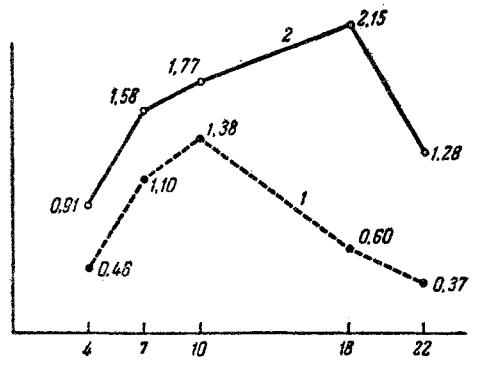

Curves showing changes in mitotic activity of interalveolar septal cells of the lungs of normal (1) and hypophysectomized (2) rats during the 24-h period. Along the axis of ordinates – mitotic coefficient (in ‰), along the axis of abscissas – time of day.

during the present investigation the rats were kept in the vivarium of the Institute. The results of these experiments are in agreement with data in the literature [9], showing that in the morning (11 A.M.) the MC in the lung cells of rats may vary from 0.4 to 1.8‰, with a mean value of 1.1‰.

In all the hypophysectomized rats, irrespective of the time of day, mitoses were found in the lung cells. The general course of the curve reflecting the changes in mitotic activity in the lungs of the experimental animals during the 24-h period was the same as in the case of the control rats (see figure).

At 6 P.M. a high MC (2.15‰) was found in the lungs of the hypophysectomized rats, and this was slightly modified by the diurnal rhythm of mitotic activity characteristic of the lungs of the normal animals. At the same time the aggregated indices of cell proliferation at certain times of day (7 and 10 A.M., 6 P.M.) were higher than during the evening and night (10 P.M., 4 A.M.) as in the control rats. These differences were statistically significant ($P = 0.0164$), and consequently, after hypophysectomy the diurnal rhythm of cell division in the lung persisted although its character was changed.

The mean indices of proliferation (MC) in hypophysectomized rats were higher at all the times investigated than in the control group of animals (see figure). This was due to the higher level of the mean diurnal MC of the experimental rats (0.78‰ in the control, 1.53‰ in the experimental animals). These differences are statistically significant ($P = 0.004$).

The results showed that diurnal changes in mitotic activity take place in the cell of the interalveolar septa of rats' lungs, just as in the epithelium of the cornea, tongue, and esophagus, and the cells of the crypts of Lieberkühn in the small intestine [4,5] after hypophysectomy, although they differ somewhat in character.

The increase in the mean diurnal MC in the lungs of the hypophysectomized rats was evidently not an accidental phenomenon, because stimulation of proliferation in the absence of the pituitary is also observed in the superficial cells of the gastric epithelium [7], the epidermis [13], and the cells of the sebaceous glands [12].

Hence, after hypophysectomy, not only may proliferation of the cells of an organ be inhibited or remain at its previous level, but it may also be stimulated.

We know from the literature [11] that, after subtotal hypophysectomy, marked atrophy of the adrenals and sex glands take place and the thyroid activity is depressed. Meanwhile, in investigations [1] of the hormonal regulation of cell division, it has been found that adrenalin and cortisone are powerful antimitotic agents. In this connection, we can share the views of those investigators [13] who consider that hypophysectomy, leading to atrophy of the adrenals, depresses the level of the hormones secreted by these glands into the blood of the hypophysectomized animals and the "release" of the cells of the organs from their "inhibitory" influence. This suggestion, however, requires further experimental verification.

In the author's view the possibility is not ruled out that disturbances may take place not only in the mitotic cycle of the cell or its individual periods (S, g, g_2), but also in the duration of mitosis itself in the organs, which may lead to changes in the mitotic activity of the cells after hypophysectomy.

Special investigations are required to determine the details of the mechanism of stimulation of cell division in organs, and in particular in the lungs, after hypophysectomy.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of the first issue of this year.
