EFFECT OF HYPOPHYSECTOMY AND GROWTH HORMONE ON DURATION OF MITOSIS IN THE ESOPHAGEAL EPITHELIUM OF RATS*

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The effect of hypophysectomy and growth hormone on the duration of mitosis in the rat esophageal epithelium was studied with the aid of demecolcine. In the absence of the pituitary the duration of mitosis is increased, while if growth hormone is administered to these animals it is reduced, but not to its initial level. Injection of growth hormone into intact animals does not affect the duration of mitosis.

There is now considerable factual evidence of variation in the duration of mitosis. The duration of mitosis has been shown to change during the 24-h period [4, 6, 7]. Changes have also been discovered in its duration during regeneration of the tail epidermis in tadpoles [5] and after administration of L-thyroxine to these animals or after a change in their temperature [9].

The role of pituitary hormones and, in particular, of growth hormone in the regulation of the duration of mitosis has not been studied. The writer has previously shown that in the absence of the pituitary, the period of DNA synthesis in the esophageal epithelium of rats is lengthened. After administration of growth hormone to these animals the duration of the S-period was completely restored. Administration of growth hormone to intact rats reduced the period of DNA synthesis still more [1].

In this connection it was important to study the effect of hypophysectomy and growth hormone on the duration of mitosis in the esophageal epithelium of rats. No information on the duration of mitosis in this tissue has yet been published in the literature.

EXPERIMENTAL METHOD

Male rats (56) with a mean weight of 150 g were divided into 4 groups with 12-16 animals in each group: 1) intact rats; 2) hypophysectomized rats; 3) hypophysectomized rats receiving growth hormone (somatotrophic hormone, STH); 4) intact rats receiving STH only. The method of hypophysectomy and the scheme of administration of growth hormone were described in the previous paper [1]. The duration of mitosis was determined with the use of demecolcine. For this purpose each group was further divided into 2 subgroups with 6-8 rats in each: the animals of one subgroup received demecolcine, the other acted as the control.

The animals were used in the experiment 24 h after the last injection of STH. Demecolcine (2.5 mg/kg body weight) was injected intraperitoneally at 6.30 A.M. The animals of the experimental sub-

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group were sacrificed 3 h later. The control animals of each group were sacrificed at hourly intervals in batches of 1 or 2 during the period of action of demecolcine in order to obtain mean values of the mitotic index (MI). MI was calculated for 3000 cells of the stratum basale of the esophageal epithelium. The duration of mitosis was calculated by the formula

$$t_M = \frac{MI \times A}{MI_{col}},$$

where A is the time of action of the demecolcine.

EXPERIMENTAL RESULTS

The value of MI in the esophageal epithelium of intact rats was $11.94^0/_{00}$. This figure is in agreement with the results obtained by Liozner et al. [3] and Dobrokhotov and Kurdyumova [2]. The index of colchicine mitoses (C-mitoses) was $56.6^0/_{00}$, and the duration of mitosis 38 min. According to the literature [10], the duration of mitosis in the esophageal epithelium of mice is 42 min.

After hypophysectomy the mitotic index fell to $6.0^0/_{00}$ ($P = 0.001$). This is in agreement with the results obtained by Liozner et al. [3] at the same time in hypophysectomized rats. The index of C-mitoses also fell sharply, to $16.6^0/_{00}$ ($P \leq 0.001$). Comparison of the results obtained in the intact and hypophysectomized rats shows that MI for the intact animals was twice as high as for the hypophysectomized rats ($P = 0.001$), while the index of C-mitoses was 3 times higher ($P \leq 0.001$), indicating an increase in the duration of mitosis after hypophysectomy. In fact, the duration of mitosis in the esophageal epithelium of the hypophysectomized rats was 65 min, i.e., it was increased by 27 min.

Injection of STH into the hypophysectomized rats gave the following results: MI was $5.8^0/_{00}$ and was almost identical to the value of MI obtained in the group of hypophysectomized animals ($6.0^0/_{00}$), while the index of C-mitoses showed a significant increase over that of the hypophysectomized rats ($21.5^0/_{00}$, $P = 0.02$). This was evidence of the shortening of mitosis to 48 min in the esophageal epithelium of hypophysectomized rats under the influence of STH.

After administration of STH to intact animals no significant changes were observed: MI was $13.2^0/_{00}$ and the index of C-motoses $59.0^0/_{00}$. The duration of mitosis was only slightly changed, to 41 min.

In no case were late phases of mitosis observed. This shows that no "jumps" took place and that all mitoses were blocked in metaphase.

The results of this investigation thus show that hypophysectomy lengthened mitosis in the esophageal epithelium of the rats from 38 to 65 min. Administration of STH to the hypophysectomized rats shortened the duration of mitosis to 48 min, but the characteristic values for intact rats were not thereby attained. A complete normalizing effect is evidently dependent on the presence of other pituitary trophic hormones. These results indicate that the duration of mitosis, at least in the esophageal epithelium of rats, is regulated by pituitary hormones, notably by growth hormone. The increase in the duration of mitosis in hypophysectomized rats and its decrease after administration of STH can be considered to be connected with the general retardation of RNA and protein synthesis in hypophysectomized rats and its restoration by administration of STH. This retardation, in turn, delays the synthesis of proteins required by the cell for mitosis.

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