

CELL DIVISION IN THE THYROID AND PARATHYROID  
GLANDS, SMALL INTESTINE, AND CORNEA  
AFTER ADMINISTRATION OF ADRENALIN TO RATS  
RECEIVING METHYLTHIOURACIL

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The effect of adrenalin on cell division was studied in the epithelium and stroma of the thyroid gland and the epithelium of the parathyroid gland, the small intestine, and cornea of rats in the presence of a deficiency of thyroid hormones (administration of methylthiouracil). Inhibition of cell division in the parathyroid but no effect of the hormone on cell division in the small intestine were found. Inhibition of mitosis in the corneal epithelium under these conditions was delayed by comparison with normal animals. Injection of adrenalin led to a sharp increase in the number of mitoses in the epithelium and stroma of the thyroid gland.

The opinion has been expressed that interaction between hormones of the adrenal medulla and thyroid hormones is closely connected with their action on the physiological functions of the organism [7-9, 12]. These hormones play an important role in the regulation of cell division in the body [1, 5-7].

In the present investigation the effect of adrenalin on cell division was studied in the epithelium and stroma of the thyroid, and the epithelium of the parathyroid gland, small intestine, and cornea of rats while thyroid function was modified with methylthiouracil (MTU).

#### EXPERIMENTAL METHOD

Male albino rats weighing  $162 \pm 16$  g were used in the experiments. The controls were 10 animals (group 1), of which 5 were sacrificed at the beginning and 5 at the end of the experiment. MTU was given to 30 animals for 5 days as a 0.1% solution in milk in a dose of 7-10 mg/100 g body weight daily. Of these rats, 15 received adrenalin by intraperitoneal injection in a dose of  $2 \mu$  g/g body weight. Five animals of this group were sacrificed 50 min after injection of the hormone (group 4), 5 1 h 50 min after injection (group 5) and another 5 after 2 h 35 min (group 6). Of the remaining 15 animals receiving MTU, 5 received injections of the equivalent volume of physiological saline and were sacrificed 50 min later (group 3), and 10 received MTU only (group 2), of which 5 were sacrificed at the beginning and 5 at the end of the experiment.

The mitotic index (in promille) was calculated in the organs, and the height of the follicular cells in the thyroid was measured with a screw-operated ocular micrometer.

#### EXPERIMENTAL RESULTS

Administration of MTU to the rats led to the development of a typical goitrogenic reaction of the thyroid. In the corneal epithelium of rabbits receiving MTU, a decrease in the mitotic index (MI) to 22-24% of normal was observed 50 min and 1 h 50 min after injection of adrenalin. At 50 min after injection, a sharp decrease in the percentage of prophases and metaphases and an increase in the percentage of anaphases and telophases were found (Fig. 1). After 1 h 50 min the percentage of the first two phases of mitosis increased sharply. Mitoses disappeared completely 2 h 35 min after injection of adrenalin (Table 1).

A tendency for the MI to increase compared with the control was observed in the epithelium of the small intestine of animals receiving MTU for 5 days. An increase in MI of the epithelium of the small intestine is characteristic of the early stages of action of MTU [2, 4, 6]. In the animals of the remaining

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TABLE 1. Mitotic Index (in ‰) in Epithelium and Stroma of Thyroid, and in Epithelium of Parathyroid Gland, Small Intestine, and Cornea After Injection of Adrenalin into Rats receiving MTU

Group of animals	Thyroid epithelium	Thyroid stroma	Parathyroid gland	Intestine	Cornea
$M \pm \sigma$					
1-st	$0,900 \pm 0,672$	$0,425 \pm 0,283$	$0,390 \pm 0,311$	$26,4 \pm 4,6$	$8,73 \pm 2,05$
2-nd	$4,635 \pm 6,371$ $P_1=0,013$	$0,473 \pm 0,621$	$1,114 \pm 0,910$ $P_1=0,024$	$29,8 \pm 7,9$	$7,21 \pm 3,08$
3-rd	$6,642 \pm 6,410$ $P_1=0,015$	$0,655 \pm 0,731$	$0,732 \pm 0,281$ $P_1=0,006$	$25,9 \pm 2,4$	$6,84 \pm 2,66$
4-th	$5,382 \pm 3,510$ $P_1=0,010$	$0,176 \pm 0,250$ $P_2=0,303$	$0,000$	$23,9 \pm 4,6$ $P_2=0,120$	$1,62 \pm 1,49$ $P_1 \rightarrow \infty$ $P_2=0,005$ $P_3=0,010$
5-th	$37,717 \pm 23,700$ $P_1=0,044$ $P_2=0,009$ $P_3=0,024$ $P_4=0,011$	$2,135 \pm 0,670$ $P_1 \rightarrow \infty$ $P_2=0,002$ $P_3=0,027$ $P_4 \rightarrow \infty$	$0,000$	$27,5 \pm 2,9$	$1,79 \pm 3,09$ $P_1=0,003$ $P_2=0,018$ $P_3=0,027$
6-th	$11,507 \pm 7,890$ $P_1=0,010$ $P_2=0,014$	$0,685 \pm 0,480$ $P_5=0,004$	$0,000$	$24,8 \pm 3,9$	$0,01 \pm 0,01$ $P_1 \rightarrow \infty$ $P_2 \rightarrow \infty$ $P_3 \rightarrow \infty$ $P_4=0,047$ $P_5=0,048$

Note. Numbers attached to P (1, 2, etc) denote degree of significance of result relative to data for group designated by same number in table.

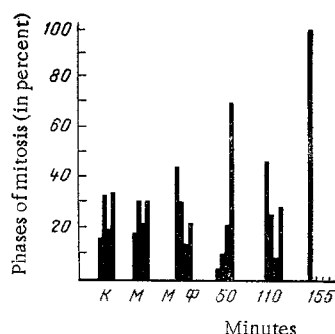


Fig. 1. Percentage of individual phases of mitosis in epithelial cells after injection of adrenalin into rats receiving MTU. Successive columns denote pro-, meta-, ana-, and telophases; C control; M administration of MTU; M+P administration of MTU and physiological saline; numbers denote time of action of adrenalin.

groups, MI in the small intestine remained essentially unchanged, although the insignificant decrease in MI 50 min after injection of adrenalin into rats receiving MTU should be noted.

Administration of MTU to rats increases mitotic activity in the thyroid epithelium. Injection of physiological saline into such animals did not change MI of the thyroid epithelium. Injection of adrenalin, however, led after 1 h 50 min to a sharp increase in MI (by 8.1 times compared with the action of MTU). No significant variations in the percentages of individual phases of mitosis were observed. The MI fell 2 h 35 min after injection. Similar results for changes in MI of connective-tissue cells of the thyroid stroma were obtained after injection of adrenalin into rats receiving MTU.

In the parathyroid epithelium the value of MI increased about three times after administration of MTU, as regularly occurs at this stage of action of MTU [6]. After injection of adrenalin, inhibition of mitoses took place in the parathyroid epithelium (Table 1).

Measurement of the height of the follicular cells of the thyroid showed that it was increased by 16% 1 h 50 min after injection of adrenalin compared with the height of the cells in rats receiving only MTU. By the end of the experiment the hypertrophy of the follicular cells was decreased.

It has previously been shown that the first 4-6 h of action of MTU in rats are characterized by the development of temporary hyperthyroidism [3, 4, 6]. The results of the present investigation show that under these conditions inhibition of mitoses in the corneal epithelium by adrenalin takes place later than in control animals [1]. Cell division was sharply stimulated in the thyroid epithelium and stroma 1 h 50 min after the beginning of the experiment, whereas in the thyroid of the control animals adrenalin produced no significant changes in MI. The reaction of cell division to adrenalin in the parathyroid gland and small intestine was similar to that in the control animals receiving adrenalin (personal observation).

The results are evidence of absence of universality in the inhibitory action of adrenalin on cell division and of dependence of this action on thyroid function. The fact that under these experimental conditions adrenalin stimulated the transition from phase  $G_2$  into mitosis by cells in the epithelium and stroma of the thyroid is interesting for it is evidence of the existence of a considerable reserve pool of cells in that organ in the  $G_2$  phase, and according to our experimental results the number of these cells, even in the actively proliferating thyroid gland, is 6-9 times greater than the pool of dividing cells. The potentiating action of adrenalin on activity of thyrotropic hormone has been described in the literature [11]. It may be postulated that the increase in MI in the thyroid gland is connected with potentiation of the thyrotropic response of the gland by adrenalin, as is demonstrated by results showing an increase in the height of the follicular cells of the gland under these experimental conditions.

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