EFFECT OF THYROID AND METHYLTHIOURACIL ON BASAL METABOLISM AND MORPHOLOGY OF THE THYROID GLAND IN C3H AND C57BL MICE

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In mice of line C3H highly susceptible to cancer, the height of the follicular epithelium of the thyroid gland is less than in mice of line C57BL with low susceptibility to cancer. Administration of methylthiouracil caused a sharp decrease in weight of C3H mice and thyroxin produced the same effect on C57BL mice. No differences were found in the basal metabolism of mice of these two lines.

The role of the thyroid in the genesis of spontaneous mammary gland cancer in mice of highly susceptible lines has not been adequately studied. Besides results showing that the blood thyroxin level in mice of cancer-susceptible line C3H is higher than in mice of the insusceptible line C57BL [13], there are also data indicating a decrease in the rate of thyroxin secretion in mice of line A compared with C57BL mice [9].

Romanov [5], working in the author's laboratory, showed that the number of thyrotropic cells in the pituitary of line C3H mice is less than in C57BL mice.

However, without a direct study of the morphology or physiology of the thyroid, it cannot be concluded from these results whether the decrease in the number of thyrotropic cells is connected with increased thyroid function, as if by a feedback mechanism, or whether the decrease in the number of thyrotropic cells is connected with disturbance of hypothalamic function.

In the present investigation, an attempt was made to establish the presence or absence of differences in the basal metabolism and morphological structure of the thyroid in mice of lines C3H and C57BL, susceptible and insusceptible to cancer, respectively.

EXPERIMENTAL METHOD

Experiments were carried out on female C3H and C57BL mice weighing initially 23-24 g. The mice of each line were divided into four series with 40 animals in each series. The animals of series I and II of both lines received thyroid with their food in doses of 0.1 and 8 mg daily, respectively. The animals of series III received 10 mg methylthiouracil daily. The mice of series IV acted as control.

The experiment lasted 9 months. The weight and basal metabolism of the mice of all series were determined from time to time. The basal metabolism was measured in a specially designed 6-chamber apparatus [6] working on the principle of Szent–Györgyi's apparatus [16].

At the end of the experiment, all the mice were sacrificed by decapitation. The thyroid was removed from six mice of each control series and three of each experimental series for histological investigation.

EXPERIMENTAL RESULTS

As the results given in Table 1 show, the height of the follicular epithelium in the C3H mice was less than in the C57BL mice. The difference in height of the follicular epithelium of C3H and C57BL mice is statistically significant ($P < 0.001$).

The decreased height of the follicular epithelium, together with the diminished number of thyrotropic cells in the pituitary of C3H mice [5], suggests that the depressed thyroid function was due to disturbances of hypothalamic activity. It also follows from the results given in Table 1 that the dimensions of the follicles in the thyroid of C3H mice are greater than in C57BL mice.

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TABLE 1. Effect of Thyroid and Methylthiouracil on Histological Structure of the Thyroid Gland and Basal Metabolism and Weight of C3H and C57BL Mice

Line of mice	Series	Height of follicular epithelium (in μ)	Diameter of follicles (in μ)	Basal metabolism (in %)	Body weight (in g)	
					initial	at end of experiment
C57BL	Control	7,6±0,3	36±2,9	100±1,9	23	28
»	Thyroid, 0.1 mg	6,3±0,8	48±4,1	111±6,3	23	28
»	" 8 mg	4,9±0,5	46±1,5	204±27,0	24	22
»	Methylthiouracil, 10 mg	12,2±0,8	30±6,5	106±4,6	23	25
C3H	Control	5,9±0,2	47±4,7	102±2,2	23	27
»	Thyroid, 0.1 mg	4,3±0,3	61±2,5	112±5,7	24	26
»	" 8 mg	4,0±0,3	72±4,0	164±6,5	23	27
»	Methylthiouracil, 10 mg	11,2±1,0	32±5,6	110±6,0	24	22

Corresponding to the lower height of the follicular epithelium of the C3H mice, methylthiouracil, which disturbs thyroxin synthesis, caused a greater decrease in weight of these mice. Conversely, thyroxin was more toxic and caused a greater loss of weight in the mice of line C57BL (Table 1).

No difference was found in the character of the histological changes in the thyroids of mice of the two lines following administration of thyroid and methylthiouracil. No differences likewise were discovered in the basal metabolism of the two lines. Such a difference might have been predicted on the animals' behavior. The C3H mice were quiet and made few movements, while the C57BL mice were very active and gave well developed defensive reactions.

The absence of difference in the basal metabolic rate of the investigated lines of mice could be explained on the assumption that oxidative phosphorylation was disturbed in the C3H mice although the normal level of oxidative processes was preserved. In this case the reduced mobility of the mice of this line, the weakening of their immunologic responses [4,12], and the decrease in their resistance to carcinogenic hydrocarbons [8] must also be attributed, as well as to other causes, to a disturbance of the formation of high-energy bonds.

After administration of methylthouracil in a dose of 10 mg daily, the basal metabolism of the mice of both lines was not only not reduced, but actually was slightly increased (Table 1).

The basal metabolism also was not reduced in the animals receiving methylthiouracil for long periods in doses of 2 and 30 mg.

Signs of hypothyroidism, expressed mainly as a decrease in the number of thyrotropic cells in the central zone of the adenohypophysis [5] and a decrease in height of the follicular epithelium of the thyroid, and also as a modified reaction to thyroid extract and methylthiouracil, observed in the C3H mice provide a somewhat different interpretation of the pathogenesis of spontaneous mammary gland carcinoma in mice of line C3H.

Experimental hypothyroidism [15] and also the hypothyroidism of domestic animals associated with an inadequate intake of iodine into the body [7] are known to be accompanied by delay or absence of ovulation as a result of the inadequate production of luteinizing hormone. It is also known that the administration of iodine preparations or of thyroid to such animals stimulates the production of luteinizing hormone and accelerates the ripening of Graafian follicles and ovulation [3,7,10,11].

In the light of the facts described above, hormonal disturbances in the activity of the pituitary and ovaries observed in C3H mice [4,2,5,14] may be associated with the hypothyroid state of these mice. The more prolonged excretion of follicle-stimulating hormone found in mice of a line susceptible to cancer than in mice of insusceptible lines [1] may in fact be connected with the reduced production of luteinizing hormone in hypothyroidism. Prolonged excretion of follicle-stimulating hormone leads to an increased duration of estrus [2,14] and, consequently, to increased estrogenization of the mammary gland, creating favorable conditions for neoplastic development in them.

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