On the Secretion of Thermothyrin A in the Finnish Steam-Bath

In 1943 in a comprehensive monograph in German, which was also published in 1949 as an English translation, MANSFELD[1] has shown the existence of two thyroxin-antagonistic principles of the thyroid gland, which retard the oxidation phenomena in mammalian tissue. MANSFELD calls these hormones thermothyrin *A* and *B*. The former is always secreted into the blood independent of the season on occasions when the mammal enters a hot environment, where a danger of overheating threatens. Thermothyrin *B*, on the other hand, is found continuously in the blood in the summer, the warm season, in spite of slight changes in the temperature.

MANSFELD's investigations have attracted very little attention. Since in our laboratory the physiology of temperature regulation in animals has been under continuous investigation, one of the authors, SUOMALAINEN, has also directed study to the thermothyrins. With careful repetition of MANSFELD's methods of chemical isolation and physiological determination, the existence in various experimental animals of factors with a similar physiological effect has been demonstrated in this laboratory. In the blood of different experimental animals kept in warmth a factor has been found which retards metabolic activity (thermothyrin *A*). In the summer, on the other hand, a factor with similar effect (thermothyrin *B*) is found continuously in the blood of various mammals. These investigations will be discussed in detail elsewhere.

The temperature regulation of man is put to a severe test in the hot bath. In Finland the steam-bath is a national custom. It was therefore interesting to investigate the extent to which the steam-bath causes the secretion of thermothyrin A into human blood.

A good Finnish bath is dry and its temperature is high. In this kind of steam-bath the skin endures a temperature of even 80–90°C. In the heat the body temperature begins slowly to rise. This shows that the temperature regulation of the body is not sufficient to prevent over-heating despite the profuse sweating.

In the experiments reported here the experimental subjects spent the day at their normal work. The blood samples from which the thermothyrins were determined were taken from each subject at about 12 o'clock and again at about 6 p. m., this time immediately after a hot dry Finnish bath. The temperature of the bath after the production of heat was 70–85°C, measured with a dry thermometer at about 20 cm above the sitting bench. The experimental subjects were in the heat at 75°C for 15–20 minutes; thus their temperature regulation was put to a severe test.

From each blood sample thermothyrin A and B were determined separately. The thermothyrin crystals obtained were dissolved in water (1·5 ml). 0·5 ml of the aqueous solution was injected subcutaneously into the thigh of a white mouse. The metabolism of the experimental mouse was determined using a modification of the Haldane and Kendeigh method immediately before injection and 5, 10, 15, 20, and 25 hours after the injection. In the experiments on metabolism the amount of carbon dioxide and water excreted by the mouse during 2 hours was determined. From these the amount of oxygen consumed was obtained by calculation. Only male mice were used in the experiments, in order to prevent possible disturbances in metabolism due to the sexual cycle, which would affect the determinations. In order to avoid any sources of error possibly caused by the diurnal rhythm, the experiments were always performed at the same time of day. If the injection contained thermothyrins, metabolic activity was greatly reduced and gradually restored again during the series of experiments.

Since the blood samples were taken in the early winter, thermothyrin *B* was no longer present in the samples. However, a strong thermothyrin *A* reaction was obtained from the blood of all the subjects who had been in the steam-bath. The results of the experiments will in due course be published elsewhere, when experiments on the further fate of the thermothyrin secreted into the blood have been completed. Thus the Finnish steam-bath and apparently also other hot baths cause the secretion of thermothyrin *A* into the blood of the bather. The hormone apparently has a temporarily decreasing effect on metabolism in man also. It is thus a contributing factor in the control of over-heating.

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Zusammenfassung

Das finnische Hitzebad, die sogenannte Sauna, verursacht eine Sekretion von Thermothyrin *A* in das Blut des Badenden. Das Hormon wirkt offenbar auch beim Menschen vorübergehend herabsetzend auf den Stoffwechsel ein und trägt dadurch seinerseits zur Verhütung einer Überhitzung bei.

[1] G. MANSFELD, *Die Hormone der Schilddrüse und ihre Wirkungen* (Benno Schwabe, Basel 1943); *The thyroid hormones and their action* (Frederick Muller, London, 1949).

Effect of Methyl- and Propylthiouracil on Ovarian Function

The effect of thiouracil derivatives on the ovary has been investigated by several authors. In the experiments of MACKENZIE and MACKENZIE[1] sulfapyridin had no effect on the oestrus of rats. WILLIAMS and his co-workers[2] found, that the weight of the ovaries decreased after thiouracil administration, but no histological changes were observed. THYSSEN[3] stated that thiourea has no effect on weight or histological structure of the ovary and uterus. On the other hand, PAWIK[4] observed the cessation of oestrus in mice treated with thiouracil. KOPF, MEYER and LOESER[5] reported that thiouracil administration is followed in rats by a decrease of the number of the follicles and marked luteinization.

Regarding the diverging data and the fact that the mechanism of the action of these drugs has not yet been examined, the problem seemed worth further investigations. First of all the effect of thiouracil on the *normal oestrus cycle* of rats was examined. The vaginal smears of two groups of rats each consisting of 15 animals were observed for one month. (Young rats weighing about 200 g were selected.) From both groups 10 rats with a

[1] J. B. MACKENZIE and C. G. MACKENZIE, Endocrin. *32*, 185 (1943).

[2] R. H. WILLIAMS, A. R. WEINGLASS, G. W. BISSEL, and J. B. PETERS, Endocrin. *34*, 317 (1944).

[3] J. THYSSEN, Acta Pharm. Tox. *3*, Suppl. 2 (1945).

[4] W. PAWIK, Przeg. Lek. *4*, 23 (1948).

[5] R. KOPF, A. LOESER, and G. MEYER, Klin. Wschr. *26*, 202 (1948).

regular cycle were separated. In the first group each animal was given 0·10 g methylthiouracil per 1000 g body weight daily per os. In the other group the same dose of propylthiouracil was administered. Treatment was continued for two months and vaginal smears were observed daily.

Table I
(Methylthiouracil)

Animal No.	Number of oestrus-days	
	Preceding treatment	During thiouracil administration
1	8	3
2	8	2
3	8	3
4	10	2
5	7	1
6	10	3
7	7	0
8	8	4
9	7	1
10	7	2
11	10	3
Average:	8·2	2·2

The results are shown in table I and II. As may be seen, the number of oestrus-days has been markedly reduced in both groups. The differences are statistically significant. It must be noted that even after eight weeks treatment oestrus was not inhibited completely.

Table II
(Propylthiouracil)

Animal No.	Number of oestrus-days	
	Preceding treatment	During thiouracil administration
1	10	4
2	7	1
3	7	2
4	7	0
5	7	2
6	7	2
7	9	1
8	9	4
9	8	0
10	8	3
11	10	5
Average:	8·1	2·2

The histological picture of the ovaries was characteristic. They revealed an increased luteinization and a great decrease in the number and size of the follicles; ovaries of some animals were made up of corpora lutea only (fig.). The thyroid of the animals shows the well-known picture resulting from thiouracil treatment[1].

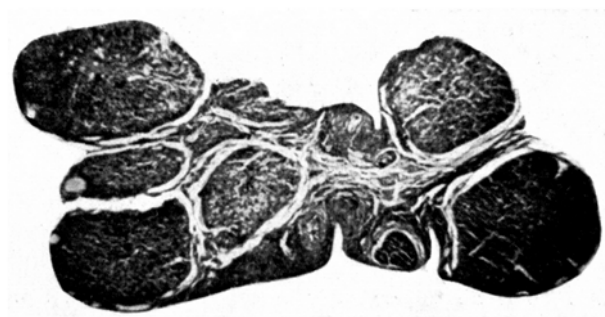
The same experiment was carried out on *thyroidectomized animals*. The average oestrus-days during one month in 13 normal rats was 8·0. After removal of the thyroid gland the oestrus-days averaged 6·7. As may be seen from table III practically no oestrus was observed after the administration of thiouracil in the thyroidectomized rats, while that of the controls remained unchanged.

[1] I. Doniach and E. P. Sharpey-Schafer, J. Endocrin. *5*, 131 (1947).

Table III

Animal No.	Number of oestrus-days		
	Preceding treatment	After thyroidectomy alone	After operation during thiouracil
1	7	7	0
2	8	2	0
3	9	6	0
4	8	6	1
5	10	6	0
6	8	9	0
7	7	8	0
8	7	7	0
9	8	7	0
10	9	9	0
Average:	8·0	6·7	0·1

The average oestrus-days of thyroidectomized untreated controls was during the same period 7·2.



The ovaries exhibited the same histological changes as found in thiouracil-treated normal rats.

Apparently, thiouracil inhibits oestrus and stimulates luteinization. These effects are even more conspicuous in thyroidectomized animals. Variation in thyroid function may account for the diverging data of various authors.

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Zusammenfassung

Durch Methyl- und Propylthiourazilbehandlung wird der Östrus von normalen jungen Rattenweibchen reduziert, der von schilddrüsenlosen Tieren aber aufgehoben. Das histologische Bild der Ovarien zeigte in beiden Gruppen eine starke Luteinisierung und Verminderung der Follikelzahl.

Der Einfluß von Serumfaktor und Herzmuskelextrakt (Recosen) auf die Tätigkeit des «Venenherzens» (*Chiroptera*)

Im Zusammenhang mit Untersuchungen über die Wirkung der natürlichen Reize auf die isolierte Flughautvene der Fledermäuse und Flederhunde (*Chiroptera*)