THYROID FUNCTION IN HEAT STROKE

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The development of heat stroke in rats during exposure to a high ambient temperature (45° C) is accompanied by reduced accumulation of I^{131} in the thyroid gland, a reduced content of PBI-I^{131} and thyroxine in the peripheral blood plasma, and a reduced rate of disappearance of intravenously injected NaI^{131} from the blood stream. The relative content of mono- and, in particular, diiodotyrosines and also, to a lesser extent, of iodothyronines is reduced in trypsin digests of the thyroid gland.

KEY WORDS: thyroid gland; heat stroke; hormone biosynthesis.

Depression of thyroid function during prolonged exposure to a moderately increased (27-34° C) ambient temperature can now be regarded as firmly established [2, 9, 11, 12, 14]. However, data on the action of a higher (40-45° C) temperature, leading to the rapid development of heat stroke, are highly contradictory [1, 5, 6-8, 10, 13].

Considering the importance of the study of thyroid function in order to elucidate the mechanism of development of heat stroke, the investigation described below was carried out.

EXPERIMENTAL METHOD

Experiments were carried out on 97 noninbred male albino rats weighing 180-220 g. The animals were exposed to a high ambient temperature (45°C, relative humidity 30%) in a special hot chamber until they developed heat stroke. The onset of heat stroke was judged from the spread-out position of the body, the absence of reflexes to changes in posture and to nociceptive stimulation, although the corneal reflex remained clearly marked.

It was shown by means of NaI^{131} (Table 1) that the development of heat stroke is accompanied by a sharp fall in I^{131} incorporation into the thyroid gland tissue. The percentage accumulation of I^{131} by the thyroid gland in vivo also was significantly reduced in heat stroke ($P < 0.01$).

The protein-bound iodine (PBI-I^{131} level) in the peripheral blood plasma of the hyperthermic animals was lower than in the control ($P < 0.05$); this, it is generally considered, is evidence of a decrease in the concentration of thyroid hormones in the blood stream. Direct determination of the thyroxine concentration in the peripheral blood plasma by the competitive binding method [15] in fact showed a clear decrease in this parameter in the experimental animals ($P < 0.001$).

The results of these experiments thus show that thyroid function in rats is sharply inhibited during the development of heat stroke.

To obtain a more detailed estimate of the process of hormone formation in the gland a radiochromatographic analysis was made of trypsin digests of the thyroid gland in a butanol–ethanol–ammonia (5 : 1 : 2) system [3]. The results are given in Table 2. They indicate a relative decrease in the concentration of diiodotyrosine and a tendency for the iodothyronine to be reduced in the thyroid gland of rats during the development of heat stroke. The relative content of free I^{131} in the thyroid gland of the experimental animals was higher than in the control. After determination of the relative percentages of iodine-containing frac-

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TABLE 1. Indices of Thyroid Gland Activity in Rats with Heat Stroke (M ± m)

Experimental conditions	Radioactivity of plasma (counts/min/0.1 ml)	Radioactivity of thyroid gland (counts/min/mg)	Percent accumulation of I^{131} by thyroid gland	% PBI-I^{131}		Thyroxine (in μg/100 ml blood plasma)
				in blood plasma	in thyroid gland	
Control (n=12)	407±18	7439±430	14,4±0,9	9,3±0,7	84,8±5,8	6,48±0,53
Heat stroke (n=12)	485,9±21*	4716±291*	10,5±0,8*	7,1±0,45*	81,3±6,2	3,58±0,4*

Legend in Tables 1 and 2. Control and experimental rats were sacrificed at equal time intervals after injection of NaI^{131}.
*Here and in Table 2, $P < 0.05$ compared with the control.

TABLE 2. Percentage Content of Fractions in Digest of Thyroid Gland (M ± m)

Parameter studied	Control (n = 13)		Heat stroke (n = 15)	
	content in percent	% of injected dose	content in percent	% of injected dose
Free I^{131}	11,2±0,8	1,59	15,3±1,3*	1,61
Monoiodotyrosine	44,7±1,8	6,35	47,4±2,3	4,98
Diiodotyrosine	33,5±1,4	5,04	30,0±1,0*	3,15
Triiodotyrosine + thyroxine	8,6±0,7	1,22	7,3±0,5	0,77

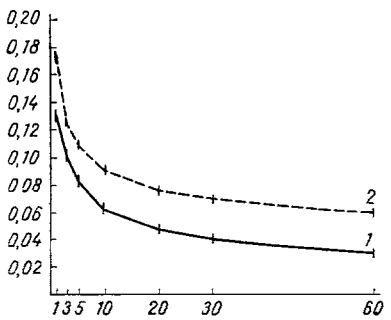

Fig. 1. Dynamics of disappearance of intravenously injected NaI^{131} (2 μCi) from the blood stream. Abscissa, time after injection (in min); ordinate, percent of injected dose of NaI^{131} in 1 ml blood. 1) Control, 2) heat stroke.

tions and the total accumulation of I^{131} in the thyroid gland, their relative content was determined depending on the injected dose of NaI^{131}, thus providing a more accurate estimate of hormone production in the gland. The results indicate a decrease in the formation of mono- and, in particular, of diiodotyrosine, as well as a decrease in the content of thyroxine + triiodothyronine in the gland during heat stroke. The development of heat stroke can be considered to be accompanied by a disturbance of the activity of the enzyme systems for synthesis of thyroid hormones. Meanwhile, the process of accumulation of free I^{131} by the thyroid gland was not significantly affected under these circumstances. Consequently, the decrease in the incorporation of I^{131} into the thyroid gland in heat stroke (Table 1) was probably connected with damage to the enzyme systems responsible for the synthesis of thyroid hormones, in particular, for its first two stages – iodotyrosine synthesis – and not with a disturbance of the mechanism of selective uptake of I^{131}.

Considering data in the literature on the mechanisms of control over thyroid gland function [11-14], it can be postulated that the action of heat stroke is an indirect one through the higher hypothalamic centers of regulation of the pituitary–thyroid system. Since the most sensitive link in the chain of thyroid hormone synthesis in heat stroke is the enzyme systems connected with the iodination of tyrosine, the possibility cannot be ruled out that in addition to proteolysis of thyroglobulin, an important point of application of the action of pituitary thyrotropin may also be the first stages of thyroid hormone biosynthesis.

It is important to note that besides the marked decrease in the plasma – PBI-I^{131} level in heat stroke, the total radioactivity of the plasma in the experimental rats exceeded the control figures (Table 1). This fact could be explained by acceleration of the absorption of intraperitoneally injected I^{131}. However, the rate of utilization of intravenously injected I^{131} (Fig. 1) proved to be lower in the experimental animals than in the control. For instance, whereas in the control animals the radioactivity of the blood fell by 50% 9 min

after injection of the preparation, in rats in a state of heat stroke it did so after 12.5 min. The total decrease in radioactivity of the blood 1 h after injection of NaI^{131} also was significantly greater in the control animals than in the experimental animals. It can be concluded from these results that the higher levels of radioactivity of the peripheral blood plasma at the moment of development of heat stroke were attributable mainly to a slowing of the rate of I^{131} utilization, as a result of depression of thyroid function. The hemoconcentration usually observed in experimental animals at this period of the investigation [4], with a resulting smaller volume of distribution of the injected NaI^{131}, may also have an important role to play.

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