PLASMA AND THYROID LEVELS OF PROTEIN-BOUND IODINE IN PROGENY OF HYPOTHYROID RATS

L. M. Gol'ber and A. G. Khomasuridze

UDC 616.152.15+616.441-008.921.5]-02:616.441-008.64-056.716-092.9

Thyroidectomy performed on female rats causes initial activation followed by inhibition of thyroid function in the progeny.

* * *

Depression of thyroid function in the mother is known to have a marked influence not only on general physical development [2, 4, 17], but also on the state of the thyroid gland of the progeny [3, 4, 9]. No attempts have hitherto been made, however, to assess the reactivity of the thyroid in the progeny of hypothyroid animals at various stages of postnatal life.

The object of the present investigation was to examine this problem by assessing the initial state of the thyroid in rats born from thyroidectomized females and also the response of this gland to a specific stimulant: the thyrotropic hormone of the pituitary (PTH).

EXPERIMENTAL METHOD

Experiments were carried out on Wistar rats. The progeny of 32 control females numbered 300 young rats, and that of 72 thyroidectomized females numbered 357. The methods and times of the operation were as described previously [6]. Thyroid function was estimated by determination of protein-bound iodine (PBI) in the plasma and in the gland itself [5,7]. The experimental and control animals were divided into 7 age groups: 1, 2, 3, and 10 days, 1 and 4 months, and 1.5 years. Each group contained not less than 15 control and experimental rats. Experiments with PTH loading were carried out on animals aged 1 and 4 months and also 1.5 years. At each of these times 10 control and 10 experimental rats were investigated. PTH was injected intraperitoneally twice daily into the animals aged 1 month in a dose of 15 i.u. for 5 days, and into the animals aged 4 months and 1.5 years in a dose of 25 i.u. using the same scheme. Plasma and thyroid gland tissue were taken for investigation 5 h after the last injection of the hormone.

EXPERIMENTAL RESULTS

The results given in Table 1 show that during the first days of postnatal development the PBI concentration in the plasma of the control rats rose rapidly, but by the age of 10 days it had begun to fall again. This decrease continued during the subsequent periods, so that the value of this index reached a minimum at the age of 1.5 years.

The age dynamics of the PBI concentration in the experimental rats was similar to that in the controls, but the absolute value of the index for experimental rats aged 1 day was appreciably higher than in the control ($P < 0.03$), although at the age of 1 month and, in particular, of 4 months, on the contrary it was lower ($P < 0.01$ and 0.0001 respectively).

Administration of PTH was accompanied by a marked increase in the plasma PBI level of all animals. However, in the experimental rats aged 4 months and 1.5 years this increase was significantly less ($P < 0.0001$) in both absolute and relative terms than in the controls.

The PBI concentration in the thyroid gland (Table 2) of the control animals reached a maximum at the age of 1 day. Later (until 4 months inclusive) this index fell gradually, but by the age of 1.5 years the PBI level in the gland was significantly ($P < 0.0001$) higher than at the preceding age period. The PBI concentration

Laboratory of Pathophysiology, Institute of Experimental Endocrinology and Hormone Chemistry, Academy of Medical Sciences of the USSR, Moscow (Presented by Academician N. A. Yudaev, Academy of Medical Sciences of the USSR.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 67, No. 7, pp. 51-53, July, 1969. Original article submitted October 24, 1968.

TABLE 1. PBI Concentration (in μg%) in Plasma of Rats Born from Thyroidectomized and Normal Females

Age	Group	Before PTH loading		After PTH loading		Difference	
		M±t	P	M±t	P	Absolute	P
1 day	Control	2.2±0.4	<0.02	–	–	–	–
	Experiment	3.9±0.48					
2 days	Control	4.9±0.64	>0.1	–	–	–	–
	Experiment	6.4±0.26		–	–	–	–
3 "	Control	5.6±0.26	>0.1	–	–	–	–
	Experiment	7.2±0.19		–	–	–	–
10 "	Control	2.9±0.3	>0.1	–	–	–	–
	Experiment	3.45±0.1		–	–	–	–
1 month	Control	1.99±0.07	<0.01	4.53±0.27	>0.6	2.54	<0.04
	Experiment	1.75±0.06		4.19±0.1		2.44	<0.0001
4 months	Control	1.74±0.09	<0.0001	4.58±0.07	<0.0001	2.84	<0.0001
	Experiment	1.33±0.04		2.64±0.14		1.31	<0.004
1.5 years	Control	0.79±0.23	>0.4	2.8±0.13	<0.0001	2.01	<0.02
	Experiment	0.34±0.05		0.9±0.07		0.56	<0.0001

TABLE 2. PBI (in μg/mg) Concentration in Thyroid of Rats Born from Thyroidectomized and Normal Females

Age	Group	Before PTH loading		After PTH loading		Difference	
		M±t	P	M±t	P	Absolute	P
1 day	Control	5.28±0.1	<0.0001	–	–	–	–
	Experiment	7.53±0.07		–	–	–	–
2 days	Control	3.7±0.09	<0.0001	–	–	–	–
	Experiment	4.9±0.09		–	–	–	–
3 "	Control	2.2±0.09	<0.0001	–	–	–	–
	Experiment	3.02±0.05		–	–	–	–
10 "	Control	1.2±0.1	<0.0001	–	–	–	–
	Experiment	1.88±0.09		–	–	–	–
1 month	Control	1.14±0.07	>0.1	2.46±0.12	<0.003	1.32	<0.0001
	Experiment	0.99±0.08		1.98±0.07		0.99	<0.0001
4 months	Control	1.19±0.06	<0.04	2.88±0.1	<0.0001	1.69	<0.0001
	Experiment	0.99±0.07		1.63±0.08		0.64	<0.0001
1.5 years	Control	1.8±0.08	<0.0001	3.55±0.11	<0.0001	1.75	<0.0001
	Experiment	1.24±0.07		2.24±0.1		1.00	<0.0001

in the gland of the experimental animals during the first 10 days of postnatal life was significantly higher ($P< 0.0001$) than in the control rats, but later it was lower, and the significance of the difference between the control and experimental animals increased progressively.

Under the influence of PTH, all animals showed a definite increase in PBI concentration in the thyroid glands, although the magnitude of this increase was smaller in the experimental rats than in the controls at all periods of the investigation.

The ability of the rat thyroid to synthesize thyroxine and tri-iodothyronine is known to develop later in ontogenesis than the preceding stages of thyroid hormone synthesis [18,19]. The relative hypothyroidism of the fetus (aggravated by the low permeability of the placenta to maternal thyroid hormones [1,13] and also by the deiodizing ability of the fetal liver which increases toward the end of pregnancy [8]) may activate the thyroid function of the fetal pituitary, which matures much sooner in onotogenesis than the thyroid [4, 11,16]. As a result, hypertrophy of the thyroid must develop in the fetuses toward the end of pregnancy and iodine metabolism in the gland must be activated. This is what in fact takes place [4,10]. This mechanism probably lies at the basis of the high PBI concentration discovered in the thyroids of the newborn rats. On

the first days of postnatal life, when the hormone-forming function of the glands has completely developed, increased secretion of thyroxine and tri-iodothyronine into the blood stream must take place, and this was evidently reflected in the increase in the PBI level in the plasma and its decrease in the gland.

Naturally, in the absence of maternal hormones, the thyrotropic function of the fetus is "de-inhibited" to a greater degree, and the thyroid function, judging from the PBI concentration in the gland and the plasma, must be increased in the early stages of postnatal development of the progeny of hypothyroid rats. Similar results have been obtained by other investigators [2,4,9,14]. However, this increase in function, as the present results show, leads to definite consequences. Signs of exhaustion of the thyroid gland were observed in the experimental rats aged 1 and 4 months and 1.5 years. The PBI level in the plasma and thyroid glands of these animals was lower than in the control animals of the corresponding age. Signs of exhaustion of thyroid function in the progeny of the hypothyroid rats were seen particularly clearly in the experiments with PTH loading, in which the increase in PBI concentration both in the plasma and in the thyroid gland itself was lower in these animals than in the controls.

The fact that in the present experiments PTH led to an increase in the PBI concentration in the thyroid gland was probably due to the method of its administration. After repeated injection of PTH, not only the stages of proteolysis of thyroglobulin and of secretion of the thyroid hormones are in fact activated, but also the preceding stages of their biosynthesis [12,15], and this could lead to raising of the PBI level in the gland.

LITERATURE CITED

1. I. A. Arshavskii, Z. F. Surovtseva, and M. G. Nemets, in: Tissue-Blood Barriers [in Russian], Moscow (1961), p. 293.
2. L. I. Gromov and G. I. Plakutina, in: Establishment of Endocrine Functions in Ontogenesis [in Russian], Moscow (1964), p. 137.
3. L. A. Lisenkova, in: Endocrine Diseases in Children [in Russian], Moscow (1964), p. 73.
4. M. S. Mitskevich, Glands of Internal Secretion in the Embryonic Development of Birds and Mammals [in Russian], Moscow (1957), pp. 66, 172.
5. G. S. Stepanov, Lab. Delo, No. 10, 594 (1965).
6. A. G. Khomasuridze, in: Current Problems in Obstetrics and Gynecology [in Russian], Part I, Moscow (1967), p. 127.
7. S. B. Barker, M. Y. Humphrey, and H. Soley, J. Clin. Invest., 30, 55 (1951).
8. V. A. Galton, Endocrinology, 82, 282 (1968).
9. J. P. Geloso, in: Proceedings of the 2nd International Congress of Endocrinologists, Part II, London (1965), p. 764.
10. A. Gorbman and H. M. Evans, Endocrinology, 32, 113 (1943).
11. A. R. Hall and H. W. Kaan, Anat. Rec., 84, 221 (1942).
12. N. S. Halmi, B. N. Spirtos, E. N. Bogdanove, et al., Endocrinology, 52, 19 (1953).
13. E. Knobil and J. B. Josimovich, Ann. N. Y. Acad. Sci., 75, 895 (1959).
14. L. Lampe, L. Kerter, F. Peter, et al., Acta Physiol. Acad. Sci. Hung., 20, 11 (1961).
15. W. L. Money, J. E. Rall, and R. W. Rawson, J. Clin. Endocrinol., 12, 1495 (1952).
16. T. Noumura, Jap. J. Zool., 12, 301 (1959).
17. T. E. Prout, Am. J. Obstet. Gynec., 96, 148 (1966).
18. J. B. Trunnell and P. Wade, J. Clin. Endocrinol., 15, 107 (1955).
19. H. E. Van Heyningen, Endocrinology, 69, 720 (1961).