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IODINE METABOLISM IN THE THYROID GLAND IN CHRONIC URANIUM POISONING

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Metabolism of radioactive and stable iodine in the thyroid gland and blood of rats with chronic uranium poisoning was studied for 21 days after administration of ^{131}I. In uranium poisoning the number of iodide-transport loci in the gland and the size of the intrathyroid iodine pool are reduced and the concentration of stable iodine in the thyroid tissue is lowered. The compensatory reaction of the gland takes the form of an increase in its mass and in the rate of thyroid metabolism.

KEY WORDS: *Thyroid gland; uranium; iodine.*

When it enters the body, uranium disturbs thyroid function [1, 3-5]. However, the mechanisms of this effect have not been explained.

In this investigation the kinetics of metabolism of radioactive and stable iodine in the thyroid tissue and blood was studied at widely spaced time intervals during chronic uranium poisoning.

EXPERIMENTAL METHOD

Experiments were carried out on 80 Wistar rats weighing 170-220 g. The animals were given drinking water containing 0.05% (group 1) and 0.5% (group 2) uranium nitrate for 2 months. The experiments with the animals of group 1 were carried out in September and October, and those with group 2 in November and December 1974-1975. A single dose of 20 μCi

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TABLE 1. Effect of Uranium Nitrate on ^{131}I Metabolism in Thyroid Gland (activity of ^{131}I/mg/sec) and Blood (activity of ^{131}I/μl/sec); M±m

Group of animals	Days aft. admin. of ^{131}I	Thyroid gland				Blood			
		PBI		iodide		PBI		iodide	
		control	exptl.	control	exptl.	control	exptl.	control	exptl.
1	1	8206±1359	6222±376	56,4±14,3	30,2±3,4	0,52±0,097	1,7±0,4	0,30±0,08	0,36±0,11
	3	7789±607	6189±1690	17,7±2,9	17,9±3,3	0,43±0,13	1,8±0,06	0,04±0,006	0,047±0,009
	7	4819±1092	2614±187	17,7±1,5	13,4±2,8	0,32±0,07	0,5±0,11	0,06±0,004	0,035±0,007
2	1	1886±273	1474±242	22,7±4,8	3,3±0,6	0,15±0,09	0,135±0,03	0,05±0,015	0,045±0,007
	3	1499±119	919±311	8,7±0,6	13,5±2,1	0,10±0,03	0,26±0,07	0,013±0,004	0,05±0,01
	7	669±37	665±208	6,3±1,6	6,9±1,3	0,15±0,01	0,123±0,01	0,05±0,005	0,03±0,004
	10	541±31,5	400±157	3,9±2,2	1,24±0,8	0,033±0,004	0,04±0,009	0,018±0,006	Background
	14	178±41	126±29	1,16±0,1	1,23±0,3	0,06±0,01	0,06±0,01	Background	"
	17	106±41	80±21	1,05±0,3	0,8±0,09	Background	0,02±0,002	"	"
	21	42±12	39±4,7	0,12±0,07	0,6±0,17	"	0,013±0,002	"	"

per rat (group 1) or 6 μCi per rat (group 2) of ^{131}I was given (part of the gland from the animals of group 1 was used to determine ^{131}I metabolism in phospholipids, for which a larger dose of ^{131}I was required). The rats were killed on the first, third, seventh, 10th, 14th, 17th, and 21st days after injection of ^{131}I (four or five animals at each time). Protein-bound iodine (PBI) was determined in the thyroid gland and blood [4]. The stable iodine concentration in the thyroid and blood was determined by a neutron-activation method [2] on an analyzer with a Ge(Li) crystal.

EXPERIMENTAL RESULTS AND DISCUSSION

The results are given in Table 1. Accumulation of ^{131}I in the gland reached a maximum 24 h after its injection. However, its distribution in the tissue and metabolic rate varied in different parts of the gland because of functional heterogeneity of the follicles. The sources of iodine for the gland were active transport and passive diffusion of the ion from the blood and also the breakdown of unstable tyrosine derivatives. The effect of uranium on these various mechanisms differed: With a decrease in active transport the contribution of iodide through processes of intrathyroid decomposition of PBI-131 increased [5]. The ratio between the total thyroid iodide and its concentration in 0.1 ml serum is an index of the acceptor loci of the gland [6]. This index was much lower in the experimental rats (21.9 in group 1 compared with 32.1 in the control; 7.1 in group 2 compared with 43 in the control) on the first day after injection of ^{131}I, indicating that uranium blocked the iodide transport loci of the gland. A previous investigation [5] showed that in acute uranium poisoning the rate of PBI-131 metabolism in the thyroid tissue is greatly altered: In the interval from 15 to 240 min activity of PBI-131 in the experimental series was increased by 15 times compared with only 3.8 times in the control. A higher rate of PBI-131 metabolism also was observed in chronic uranium poisoning. In the rats of group 1 the PBI-131 level in the gland by the seventh day was reduced by 1.7 times in the control and by 2.3 times in the experimental series; the blood PBI-131 concentration was reduced by 1.6 and 3.4 times respectively, and the blood iodide-131 level was reduced by five and 10 times respectively. The rate and extent of the liberation of PBI-131 from the gland determined the kinetics of PBI-131 metabolism in the blood. The intensity of secretion of the hormonal components of the gland (the ratio between the blood PBI-131 and the thyroid gland PBI-131) in the experimental rats was almost four times higher than in the control and its level remained stable throughout the experiments. This explains the higher percentage of the total radioactivity of the blood in the form of radioactivity of PBI-131 in the experimental series (82.5-96.2-94.3%) than in the control (63.5-91.4-82.0%) on the first, third, and seventh days. The general pattern of metabolism of radioactive iodine in the animals of group 2 was qualitatively indistinguishable from that in the rats of group 1: At all time intervals the PBI-131 content in the gland was higher in the control than in the experimental series, whereas the PBI-131 concentration in the blood was higher in the experimental than in the control series on the third, 10th, 17th, and 21st days. The blood PBI-131/gland PBI-131 ratio also was higher in the experimental than in the control series. The results partly explain changes in thyroid function in uranium poisoning. These changes are the result of reduced uptake of iodide by the gland, reduced conversion to organic iodine compounds, increased decomposition of unstable tyrosine derivatives, and increased liberation of PBI-131 into the blood stream.

Determination of the concentrations of stable iodine in the thyroid and blood in some cases also gives additional information on the hormonal status of the organism compared with

the radioiodine tests, for if the level of secretion of the hormones into the blood remains constant, the contribution of PBI-131 to the total volume of secretion can vary within wide limits, which are determined by the size of the intrathyroid iodine pool. A decrease in its size leads to an increase in the contribution of PBI-131, although the total volume of secretion of hormonal components into the blood is unchanged. The results of investigation of stable iodine metabolism in the thyroid and blood confirmed the inequality of changes in PBI-131 and PBI-127 in uranium poisoning. In the animals of group 1, for instance, the stable iodine concentration in the gland was 0.61±0.067 mg/g in the control and 0.40±0.069 mg/g in the experimental series ($P<0.05$). The total iodine content in the gland was the same in both control and experimental series (0.108±0.02 and 0.107±0.038 mg respectively) as the result of an increase in the weight of the gland in the experimental rats (26.9±4.8 mg compared with 17.0±1.67 mg in the control). The blood PBI-127 concentration in the control (3.4±0.48 μg/100 ml) and experimental series (4.1±1.14 μg/100 ml) was similar ($P>0.05$) but the PBI-131 concentration differed considerably, the difference being significant ($P<0.05$) on the first and third days.

In chronic uranium poisoning the number of iodide-transport loci in the gland is thus reduced, the rate of metabolism of ^{131}I in the rapidly metabolized iodine compartment is increased, and the concentration of stable iodine in the thyroid tissue is lowered. The compensatory reaction of the gland is manifested as an increase in its mass and an increase in the rate of thyroid metabolism.

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