

BROMINE METABOLISM IN THE THYROID GLAND OF GUINEA PIGS DURING
EXPERIMENTAL HYPERTHYROIDISM AND IN RATS FED ON
METHYLTHIOURACIL

I. N. Verkhovskaia and L. M. Tsofina

From the Institute of Biological Physics (Director — Corresponding Member of the AMN SSSR G. M. Frank)
of the Academy of Sciences of the USSR, Moscow

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The study of the bromine metabolism of the thyroid gland in normal conditions and in various functional states is of considerable theoretical and practical interest. In this connection we carried out two series of experiments: in the first we studied the influence of experimental hyperthyroidism on the content of radiobromine in the thyroid gland of animals, and in the second, we studied the influence of methylthiouracil (MTU) on the appearance of injected bromine, labeled with Br^{82} , in the thyroid gland of animals. Further, in both series we studied the distribution of radiobromine between the protein and nonprotein fractions isolated from the tissue of the thyroid gland.

It was shown by a number of workers [1, 8, 9] that the bromine content of the thyroid gland is usually higher than in other tissues and, what is particularly important, higher than in the blood passing through the gland. As our own findings [2] showed, in thyrotoxicosis in man the bromine content of the thyroid gland rises considerably. On the other hand, E. N. Emel'ianova and Iu. B. Skebel'skaia [7] showed that during relatively brief administration of bromine to animals, hypertrophy and hyperplasia of the thyroid glands are observed.

1. The Influence of Experimental Hyperthyroidism on the Radiobromine Content of the Thyroid Gland in Guinea Pigs

The experimental method was as follows. Hyperthyroidism was produced in guinea pigs by injecting them with thyrotrophic hormone*. The hormone was dissolved in physiological saline and injected subcutaneously into the experimental guinea pigs for a period of five to seven days in a dose of 22.5-72.5 mg. The last dose of the hormone was injected simultaneously with a solution of sodium bromide, labeled with Br^{82} , 16-18 hours before decapitation of the experimental and control animals. The control animals were injected with radiobromine alone. Next the activity of the tissues was measured and the relative activity calculated (the activity of the blood was taken as 1). The results obtained are shown in Table 1.

From Table 1 it is seen that the experimental thyrotoxicosis in guinea pigs a considerable increase takes place in the weight of the thyroid gland. So far as the relative activity of the thyroid gland tissues is concerned, in hyperthyroidism it was considerably higher (1.79 ± 0.15) than in controls (1.32 ± 0.08). In other tissues which we investigated, no change in the relative activity of the bromine was observed in hyperthyroidism as compared with normal.

It was important to explain how experimental hyperthyroidism affects the appearance of Br^{82} in the protein fraction of the thyroid gland tissue. For this purpose the thyroid gland tissue was ground up in a mortar and the

* We take this opportunity to thank N. M. Rudenko for preparing the thyrotrophic hormone for us.

TABLE 1

Distribution of Bromides Labeled With Br⁸² in Certain Organs and Tissues of Guinea Pigs in Normal Conditions and in Experimental Hyperthyroidism

Number of animals investigated in four experiments	Control 12	Hyperthyroidism 12	Difference
Weight of thyroid glands in mg	35,6±1,61	73,8±2,22	38,2±2,74
Name of organs and tissues	Relative activity		
Blood	1	1	0
Thyroid gland.	1,32±0,08	1,79±0,15	0,47±0,17
Pituitary	0,68±0,063	0,68±0,079	0,00±0,10
Nerves	0,66±0,026	0,67±0,038	0,01±0,05
Cerebral hemispheres . .	0,25±0,008	0,27±0,017	0,02±0,02
Midbrain	0,29±0,011	0,31±0,010	0,02±0,01
Cerebellum	0,29±0,012	0,31±0,012	0,02±0,01
Medulla	0,33±0,011	0,34±0,011	0,01±0,01
Spinal cord	0,38±0,038	0,36±0,017	0,02±0,04
Adrenals	0,34±0,01	0,41±0,05	0,07±0,05

TABLE 2

Content of Br⁸² in the Protein and Nonprotein Fraction of the Thyroid Gland Tissue of Guinea Pigs in Normal Conditions and in Hyperthyroidism

Experiment No.	Radiobromine injected (μC/kg)	Bromine injected (mg/kg)	Material (thyroid glands)	nonprotein fractions (fissions, min)	Activity			Total activity of 100 mg of tissue	
					%	protein fractions (fission/min.)	%	fissions, min.	%
1	2	3	4	5	6	7	8	9	10
38	16,36	2,4	Control	332	5,9	5280	94,1	5612	
				346	6,4	5020	93,6	5366	
			Average		6,15			5490	100
			Hyperthyroidism (thyrotropic hormone injection)	500	7,4	6840	92,6	7340	
				355	5,1	6650	94,9	7005	
				342	5,7	5730	94,3	6088	
			Average		6,07			6811	124
38 a	16,36	2,4	Hyperthyroidism (thyrotropic hormone + NaBr injected)	255	4,0	6180	96,0	6435	
				145	2,5	5640	97,5	5785	
			Average		3,25			6110	111
37	12,2	1,86	Control (glands from 3 guinea pigs)	532	19,9	2132	80,1	2664	100
			Hyperthyroidism (thyrotropic hormone injected) (glands from 3 guinea pigs)	382	12,3	2713	87,7	3095	116

TABLE 3

The Influence of Methylthiouracil on the Appearance of Bromine (Br^{82}) and Iodine (I^{131}) in the Thyroid Gland of Rats

Experiment No.	№ 10 ¹ 30/I—8/II 1952	№ 20 ¹ 4/III—14/III 1952	№ 67 ^{1,2} 14/VI—24/VI 1955	№ 85 24/XII—2/I 1956	№ 87 10/I—1/II 1956	№ 76 17/IX—1/X 1955
Br^{82} injected ($\mu\text{C}/\text{kg}$)	14,7	3,45	16,36	19,6	30	0,1 $\mu\text{C}/\text{kg}$ ¹³¹
Bromine injection (mg/kg)	0,54	0,46	0,54	3,0	6,16	0 (without vehicle)
Duration of experiment (in days)	10	10	10	10	20	10
Number of animals (n)	Control 10 Experiment 10	Control 10 Experiment 5	Control 5 Experiment 5	Control 6 Experiment 6	Control 5 Experiment 6	Control 3 Experiment 3
MTU given (mg)	0	300	0	300	0	300
Weight of thyroid glands (in mg) As a % of control	16,6 ± 1,4 61,3 ± 3,6 15,2 ± 1,0 49,0 ± 4,1 359	1,51 ± 0,10	1,12 ± 0,12	1,66 ± 0,031	1,26 ± 0,06	1,95 ± 0,15
Relative activity of the thyroid glands As a % of control	1,21 ± 0,08	1,75 ± 0,19	1,62 ± 0,16	1,57 ± 0,15	0,88 ± 0,05	0,86 ± 0,04
	145	108	148	143	227	5,9
						Activity of 100 mg of thyroid gland tissue (in fissions, min)
						4130 ± 420

* Prof. I. A. Eskin and E. B. Pavlova took part in experiments Nos. 10 and 20.

proteins were precipitated with 10% trichloroacetic acid in the cold. The protein precipitate was next washed 4-5 times with trichloroacetic acid with the addition of inactive sodium bromide, after which it was dissolved in weak alkali. The solutions containing the protein and nonprotein fractions were transferred to disks and evaporated to dryness and their activity was measured. The results obtained, calculated per 100 mg dry gland tissue, are shown in Table 2.

It may be seen from Table 2 that the total bromine content of the thyroid gland in guinea pigs is increased in hyperthyroidism as compared with normal (columns 9 and 10). The preliminary administration of bromine slightly reduces this effect. It may also be seen (column 6) that in hyperthyroidism there is a tendency towards reduction of the quantity of radiobromine entering the protein fraction of the thyroid gland tissue. As was to be expected, the preliminary administration of bromine considerably reduces the quantity of radiobromine entering the protein fraction of the thyroid gland tissue as compared with normal.

2. The Influence of Methylthiouracil on the Appearance of Radiobromine in the Thyroid Gland

The experimental method was as follows. Experimental rats received methylthiouracil in addition to their diet for a period of 10-20 days. The total amount of methylthiouracil taken by each animal differed in the different experiments - 30, 300 and 600 mg. Later on both experimental and control animals were given subcutaneous injections of sodium bromide solution, labeled with Br^{82} , after which, 15-18 hours later, they were decapitated. Next the activity of the blood and the thyroid glands was measured and, taking the activity of the blood as unity, the relative activity of the thyroid gland tissue was calculated. The conditions for the performance of the experiments, as well as the results obtained, are shown in Table 3.

It may be seen from Table 3 that the administration of MTU causes a considerable increase in the weight of the thyroid glands compared with controls. It may also be seen that in five of the six experiments a statistically significant increase was observed in the activity of the thyroid gland tissue of the experimental animals as compared with the controls, which proves the accumulation of Br^{82} in this tissue. It should be pointed out that the largest accumulation of Br^{82} was observed in experiment No. 87, i.e. after the largest dose of MTU.

TABLE 4

Influence of Methylthiouracil (MTU) on the Content of Br^{82} and I^{131} in the Protein and Nonprotein Fractions of the Thyroid Gland Tissue of Rats

Experiment No.	Thyroid gland tissue	Number of animals	MTU administered (in mg)	Br ⁸² injected (in μ C/kg)	¹³¹ I injected (in mg/kg)	Bromine injected (in mg/kg)	Iodine injected (in mg/kg)	Activity				Total activity in fissions, min
								of the pro- tein fraction		of the nonpro- tein fraction		
								fissions, min	in %	fissions, min	in %	
1	2	3	4	5	6	7	8	9	10	11	12	13
85	Control	6	0	19,62	—	3	—	264	7,6	3 190	92,4	3 454
	Experiment	6	300	19,62	—	3	—	83	1,8	4 650	98,2	4 733
87	Control	6	0	30,6	—	2	—	45	1,2	3 659	98,8	3 704
	Experiment	5	600	30,6	—	2	—	77	0,6	11 863	99,4	11 940
76	Control	3	0	—	0,39	—	0	22 311	93,1	1 654	6,9	23 965
	Experiment	3	300	—	0,39	—	0	2 658	82,6	558	17,4	3 216

Although the action of MTU on the iodine metabolism of the thyroid gland has often been investigated [4, 5, 6], we carried out experiments with radioiodine in order to compare the action of MTU on the appearance of bromine (Br^{82}) and iodine (I^{131}) in the thyroid gland under identical conditions. The results of this experiment (No. 76) are shown at the end of Table 3. It may be seen from these that the administration of MTU causes a very considerable fall in the content of radioiodine in the thyroid gland - down to 5.9% as compared with the normal value of 100.

By comparing the results obtained with bromine and iodine (see the bottom line in Table 3), it may be seen that the influence of MTU on the content of bromine and iodine in the thyroid gland (after an identical interval of time) is opposite — the content of Br^{82} is increased 1.5-2.0 times, whereas the content of I^{131} is sharply reduced — by 17 (!) times.

We also studied the influence of MTU on the distribution of bromine between the protein and nonprotein fractions of the thyroid gland tissue. For this purpose the thyroid gland tissues of experimental and control rats containing Br^{82} (experiments Nos. 85 and 87), after measurement of their activity, were scraped from the glass disk and fractionated. The same course was adopted with the thyroid gland tissues of rats receiving I^{131} (experiment No. 76). Fractionation was done by the method described above, with the exception that the weighted samples were taken from air-dried rather than fresh gland tissue. The results obtained on the activity of the fractions, expressed as the number of fissions per minute and as a percentage, are shown in Table 4.

From Table 4 (column 10) it may be seen that in experimental rats taking MTU in the diet, the percentage content of radiobromine in the protein fraction of the thyroid gland tissues, never very high, is still further reduced (1.8% instead of 7.6% and 0.6% instead of 1.2%). As may be seen from column 13, the total content of radiobromine in the thyroid gland of rats receiving MTU in the diet increases. It may be seen that the percentage content of radioiodine in the protein fraction of the thyroid gland tissue of the experimental animals is also reduced (82.6% instead of 93.1%). It should be particularly emphasized that the absolute radioiodine content of the thyroid gland tissue of the experimental rats is sharply reduced — in samples of equal weight an activity of 3216 fissions/min instead of 23,965 fissions/min is observed.

SUMMARY

A significant increase in the weight of the thyroid glands and of the bromine content was noted in experimental hyperthyroidism of guinea pigs. The relative quantity of the protein-combined bromine does not change. Preliminary administration of bromine greatly decreases the entrance of bromine into the protein fraction of the thyroid gland tissue.

The percentage of bromine in the protein fraction of the thyroid gland tissue is considerably diminished in rats fed methylthiouracil; whereas the total amount of bromine entering the thyroid gland of experimental animals rises.

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