EFFECT OF URANIUM NITRATE ON MORPHOLOGY AND FUNCTION OF THE RABBIT THYROID GLAND

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Uranium nitrate not only depresses thyroid function but also leads to the formation of thyroid autoantibodies. The picture of colloid goiter was detected in the thyroid, with the development of solitary adenomas of parenchymatous structure. The widely spread, radioactive, and highly toxic element uranium has been detected in very small quantities in all tissues of the body. According to Hoffman [7], the thyroid, in particular, acts as a uranium depot. Uranium compounds are known to inhibit thyroid function [3, 4].

Because uranium is being used on an increasing scale, with a consequent increase in the number of persons coming into contact with it, and because of the lack of information on the character of its action on the thyroid gland, it was decided to investigate the effect of uranium on iodine metabolism in the thyroid and also, having regard to its well-marked chelating activity and toxicity, to study whether uranium can induce the formation of thyroid autoanibodies.

EXPERIMENTAL METHOD

Experiments were carried out on 12 rabbits, 4 of which were controls. Uranium nitrate was injected subcutaneously in a dose of 0.025 mg/kg body weight daily for 5 days. The total dose per animal was 0.28-0.33 mg. The animals were sacrificed 41-45 days after the last injection of uranium. Thyroid function was assessed on the basis of the accumulation of I^{131} in the gland after 2, 4, and 24 h, the content of protein-bound iodine (PBI^{131}), the degree of conversion of inorganic into organic iodine, and the thyroxine test using thyroxine-I^{131}. The thyroxine test was used on all animals throughout the experiment, while the other radioiodine diagnostic tests were carried out on the control animals before the experiment began and on the experimental animals before sacrifice.

Antibodies against the thyroid gland were detected by the passive hemagglutination test (PHT) [6]. Antigen was obtained by Alekseeva's method [1]. Histological sections for morphological investigation were made from the removed thyroid glands.

EXPERIMENTAL RESULTS

Results showing the effect of uranium nitrate on the thyroid function are given in Table 1. They show inhibition of both the inorganic and organic phases of iodine metabolism. Inhibition of the inorganic phase is reflected by the values of I^{131} accumulation in the gland, changes in which were particularly marked 4 and 24 h after injection of an indicator dose of I^{131}. The degree of conversion of inorganic iodine into organic was reduced, and this was reflected in the PBI values and the thyroxine test.

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TABLE 1. Effect of Uranium Nitrate on Thyroid Function

	Number of animals	Accumulation of I^{131} after 2, 4, and 24 h (in percent)	PBI (in %)	Degree of conversion (in %)	Thyroxine test
Control	4	7,9; 10,8; 18,2	0,14±0,035	46,6±2,65	1,6 ±0,005
Expt. (before sacrifice)	8	4,0; 2,3; 2,6	0,031±0,014	26,0±2,83	2,03±0,39
P			<0,01	<0,001	<0,001

TABLE 2. Dynamics of Titer of Autoantibodies after Administration of Uranium Nitrate

Serial No.	Number of animals	Weight before experiment	Weight before sacrifice	Dose of uranium given	Passive hemagglutination test: days of investigation (administr. of U ended on Dec. 14) 12/21	12/23	12/26	12/29	1/5	1/12	1/19	1/26	1/28
Control	4	2 350	2 400										
		3 000	3 050										
		2 500	2 470										
		2 750	2 700										
1	1	2 500	2 670	0,31	1:64	1:64	1:64	1:64	1:64	1:128	1:128	1:256	
2	1	2 750	2 720	0,33				1:64	1:64	1:128	1:128	1:32	
3	1	2 450	2 640	0,32		1:32	1:64	1:64	1:64	1:128	1:64	1:32	
4	1	2 600	2 350	0,28			1:64	1:128	1:128	1:128		1:256	1:512
5	1	2 300	2 510	0,31			1:16	1:16	1:128	1:64	1:32	1:16	
6	1	2 500	2 740	0,33		1:128	1:128	1:128	1:128	1,256	1:256	1:256	1:256
7	1	2 300	2 300	0,28	1:16	1:16	1:32	1:32	1:128	1:128	1:64	1:32	1:32
8	1	2 900	2 540	0,31	1:64	1:64	1:64	1:128	1:256	1:256	1:256	1:256	1:128

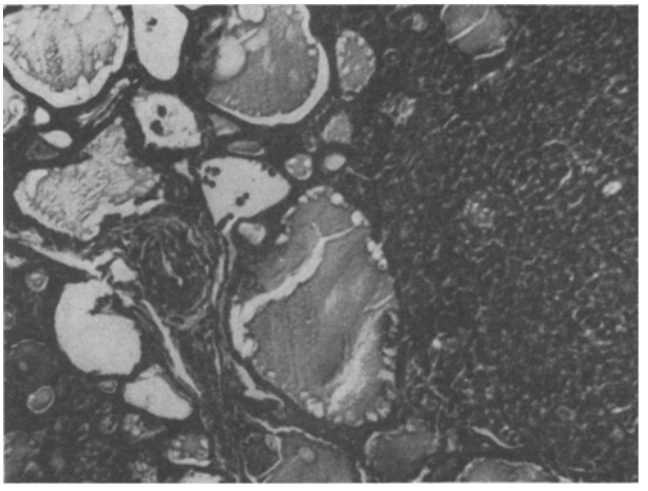

Fig. 1. Adenoma of rabbit thyroid. Hematoxylin-eosin, 240×.

The protein-bound iodine (PBI), representing the content of thyroid hormones circulating in the blood, was reduced from 0.14 to 0.031%, while the results of the thyroxine test, reflecting the transporting power of the serum proteins, showed an increase from 1.6 to 2.03 as the result of a decrease in the concentration of endogenous thyroxine.

The results of investigation of changes in the titer of thyroid autoantibodies are given in Table 2. They show that on the 7th day after the last injection of uranium, 3 rabbits possessed autoantibodies in low titers. Subsequently the PHT was positive in a titer of 1 : 512 in one animal, and in the rest in titers of between 1 : 128 and 1 : 256. A temporary increase in the titer of antibodies to 1 : 128-1 : 256 was observed in 5 animals on the 3rd week of the experiment, after which the titers began to decrease. In 3 rabbits (Nos. 1, 4, and 6) there was a progressive rise in the antibody titer until the end of the experiment.

In 3 animals (Nos. 1, 2, and 4) the PHT was positive with kidney antigen, and in 2 animals (Nos. 1 and 6) with rabbit liver antigen in titers of 1:64.

A picture of colloid goiter, characterized by small and medium-sized follicles, was detected in the thyroid glands. In 3 animals (Nos. 4, 6, and 8) adenomas of parenchymatous structure were found in the thyroid gland tissues (Fig. 1).

Besides inhibition of thyroid function, uranium nitrate thus also induces the formation of adenomas in the thyroid gland and of autoantibodies against it. This last effect is probably due to the radiation-chemical properties of uranium [2, 5].

The appearance of antibodies against other organs than the thyroid gland can probably be explained by the kinetics of distribution of uranium in the body and by its direct action on them.*

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