THE INFLUENCE OF RADIOACTIVE IODINE UPON THE NONSTIMULATED AND STIMULATED THYROID GLAND

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Radioactive iodine, I^{131}, is used on an ever increasing scale, not only as a diagnostic, but also as a therapeutic preparation which permits bloodless radiostrumectomy in cases of thyrotoxicosis.

Any rational and effective clinical application of I^{131}, however, must be based on a precise and detailed analysis of the pathological changes which develop in the tissues exposed to radiation after administration of therapeutic as well as of diagnostic doses.

The doses of I^{131} used for diagnostic purposes have to a great extent been established empirically. In view of the possibility that the ionizing radiation produced by the breakdown of the I^{131} atoms accumulated in the thyroid gland exerts a toxic effect, the question arises whether exposure of the thyroid cells to this dose is indifferent and consequently safe.

There are reports in the literature according to which indicator doses of I^{131} of about 1-25 μC change the functional state of the thyroid parenchyma, producing a state of excitation and causing a number of structural changes in the cytoplasm and karyoplasm of the thyroid cell [11,15].

In our previous investigations [8,9] we were able to establish that an indicator dose of 1 μC I^{131} causes appreciable changes in the state of the biological colloids in the thyroid parenchyma of white rats, a fact which becomes above all manifest in changes in the isoelectric point and also in changes in the adsorption capacity in the first four days after the injection of the isotope into the animal body. The changes which take place in the biological colloids of the thyroid parenchyma under the influence of internal ionizing radiation arrive in waves as established in the studies of I. A. Pigalev [10] and P. D. Gorizontov [3,4]: the first wave of changes can be observed in the period between six and 48 hours and the second wave of changes in the period between 96 and 144 hours after a single injection of the isotope in question. These findings concern the thyroid gland of animals in a state of relative functional rest. In clinical practice, however, I^{131} is as a rule applied in cases of thyroid diseases which are accompanied by an increased functional activity. In this context it must be emphasized that L. A. Kashchenko [7] established in 1955 that the destructive effect of radiation becomes much more manifest if the thyroid gland is in a state of increased functional activity. On the other hand, I^{131} itself causes, as we said above, a certain functional stimulation of the thyroid parenchyma.

It was the aim of the present paper to study those changes in the biological colloids of the thyroid cells which develop as a result of exposure of the stimulated thyroid gland to the action of ionizing radiation produced by injection of an indicator dose of I^{131}.

METHOD

The experiments were carried out on two groups of male white rats weighing 180-200 g. The increased functional activity of the thyroid gland was induced by ingestion of 6-methylthiouracil [1,2,5,6]. One group of animals received the latter preparation for 25 days, after which they were given a single intraperitoneal injection of μC I^{131}. Then the injections of 6-methylthiouracil were discontinued and the changes in the colloidal system

of the thyroid parenchyma were investigated in the period of restitution after the influence of the thyrostatic agent had been discontinued.

Another group of animals were given 6-methylthiouracil with the food for 20 days; then the animals received a single injection of 1 μC I^{131}. In this group the administration of the thyrostatic agent was continued and consequently our investigation revealed the changes in the colloid system of the thyroid parenchyma which take place under the influence of internal ionizing radiation emitted by 1 μC I^{131} in both the stimulated and nonstimulated thyroid gland respectively. The animals in both groups were sacrificed 3,6,9,12,24,48,96,144 and 192 hours after the injection of I^{131}. The intensity of the adsorption process in the thyroid parenchyma was established by the method of D. N. Nasonov and V. Ya. Aleksandrov; the isoelectric point of the biological colloids in the follicular cells was established by staining reactions in buffer solution of different pH according to the method described by A. Pishinger and G. Roskin.

TABLE 1. Influence of 1 μC I^{131} on the Changes in the Biological Colloids of the Thyroid Parenchyma during the Period of Restitution after Administration of 6-Methylthiouracil Continued for 25 Days

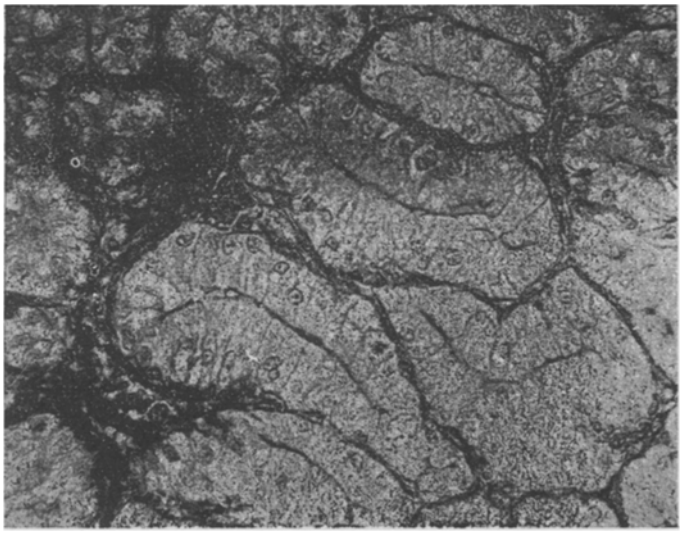
Time of experiments, hr	Average wt. of gland, mg		Intensity of neutral red adsorption, %	I^{131} uptake, %	Av. follicular cell ht., μ	Isoelectric point (pH)	
	wet wt.	dry wt.				follicular cell cytoplasm	follicular cell karyoplasm
Control animals	13,52	3,20	100,0	—	7,4	3,60	3,50
During 25-day feeding of 6-methylthiouracil	34,80	7,24	51,2	—	15,76	3,10	2,90
3 hours after I^{131} injection	35,20	8,00	59,2	15,68	13,38	3,26	3,20
6 " " " "	36,40	7,50	81,5	16,37	15,61	3,10	3,00
9 " " " "	36,00	5,83	97,0	18,81	18,40	3,37	3,20
12 " " " "	37,90	11,63	60,5	21,79	12,42	3,73	3,69
24 " " " "	41,60	11,22	56,5	9,85	14,36	3,93	3,82
48 " " " "	36,20	9,25	52,2	1,90	13,64	4,03	3,82
96 " " " "	40,00	8,90	54,4	0,95	12,66	3,93	3,82
144 " " " "	32,10	8,34	46,7	0,70	10,32	3,93	3,77
192 " " " "	31,00	8,00	49,7	0,20	9,44	3,72	3,62

TABLE 2. Influence of 1 μC I^{131} on the Changes in the Biological Colloids of the Thyroid Parenchyma in a State of Excitation Caused by Continued Administration of 6-Methylthiouracil

Time of experiments, hr	Av. wt. of gland, mg		Intensity of neutral red adsorption, %	Av. follicular cell ht. μ	Isoelectric point (pH)	
	wet wt.	dry wt.			follicular cell cytoplasm	follicular cell karyoplasm
Control	8,95	2,63	100,0	6,47	3,55	3,45
During the 20-day feeding of 6-methylthiouracil	45,20	10,52	70,0	16,58	3,20	3,10
3 hours after I^{131} injection	39,90	8,28	90,3	17,29	3,20	3,10
6 " " " "	51,80	11,27	81,0	17,62	3,20	3,10
9 " " " "	36,20	4,89	133,2	17,61	3,10	2,86
12 " " " "	33,40	6,67	130,0	17,33	3,10	2,86
24 " " " "	42,60	8,94	75,2	16,58	3,84	3,66
48 " " " "	40,90	9,63	59,3	19,20	3,84	3,66
96 " " " "	41,10	7,62	110,0	17 41	3,84	3,75
144 " " " "	23,70	6,71	89,0	15,80	—	—
192 " " " "	43,90	7,71	84,9	14,45	3,93	3,84

RESULTS

The results of the two series of experiments, given in Tables 1 and 2, I^{131} show that the internal ionizing radiation produced by an indicator dose of I^{131} intensifies the processes of stimulation of the thyroid parenchyma caused by 6-methylthiouracil to considerable degree. These swellings of the thyroid cells become more marked, a fact which is reflected in an increase of the average relative wet weight of the thyroid gland and the average height of the cells of the thyroid epithelium, as well as in the increased intensity of adsorption of neutral red compared with the adsorption found after 20-25 days' exposure to the action of thyrostatic substances, and finally in the stronger shift of the isoelectric pooint in the karyoplasm and cytoplasm of the follicular cells toward the acid side. The changes in the colloid systems of the thyroid cells enumerated above are much more marked if the exposure of the thyroid parenchyma to 6-methylthiouracil is continued (see Table 2).



Follicles in the central part of the thyroid gland of a rat treated with 6-methylthiouracil 48 hours after injection of 1 μC I^{131}. Azan stain; photomicrograph; magnification 400 ×.

Study of the structural changes in the thyroid gland of the experimental animals revealed that exposure of both the stimulated and the nonstimulated thyroid gland to internal ionizing radiation in a dose of 1 μC I^{131} leads to degenerative changes in the thyroid epithelium, changes which become manifest in the marked vacuolization of the cytoplasm, polymorphism of the nuclei, karyorrhexis and pycnosis(see figure). If the administration of 6-methylthiouracil is continued, the degenerative changes in the thyroid gland are much more marked.

SUMMARY

Administration of a single 1 μC I^{131} dose to albino male rats provokes considerable changes in their thyroid glands and marked alterations in the physico-chemical composition of the cytoplasm and karyoplasm of the thyroid epithelium. In the first 2 days this is manifested in the dislocation of the isoelectric point of the above cellular components toward increased acidity, in the intensified neutral red sorption, in the increased mean height of follicular cells and the mean relative crude weight of the gland.

The aforementioned changes proved more pronounced in the thyroid gland previously activated by the action of 6-methylthiouracil. With the continuing 6-methylthiouracil action on the thyroid gland after radioiodine injection, the thyroid parenchyma becomes a scene of the following pathological changes: marked polymorphism of the follicular epithelium cells, large perinuclear vacuolization, a rise in the number of nuclear pycnoses and karyorrhexis and, here and there, desquamation into the follicular cavity. Thus, radioiodine affects both the unstimulated and stimulated thyroid; in the latter case the effect is considerably intensified even by small doses of radioiodine.

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