THE BIOLOGICAL ROLE OF URANIUM IN THE MAMMALIAN BODY

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Uranium is known to be present in nearly all human tissues and organs, and according to Hoffmann[5], the thyroid gland is the depot for uranium compounds.

In a previous communication [2] we showed that the action of uranium nitrate in our experiments could be compared with the action of certain thyroid gland inhibitors: thiourea, thiouracil, etc., which block the follicular cells of the thyroid gland and thereby inhibit the hormone-producing function. Hence it may be concluded that this element bears some relationship to the function of the thyroid gland. In order to study this problem, we undertook a series of experimental investigations on white rats and rabbits.

EXPERIMENTAL METHOD

Experiments were carried out on 67 experimental and 20 control rats of both sexes, aged $2^1/_2$-3 months; 40 rats received 0.05 mg of uranium (uranyl) nitrate per 100 g body weight in milk daily for 7 months, and the remaining 27 animals received 0.01 mg/100 g body weight in the form of subcutaneous injections. Each rat received on the average of 10 mg of uranium in milk or 2 mg by subcutaneous injection. The rats were weighed every 2 weeks. The average initial weight of the rats was 122 g, and the average final weight 200 g. After 7 months the rats were sacrificed for the purpose of histological examination of their organs – the thyroid gland, the hypophysis, the adrenals and the spleen.

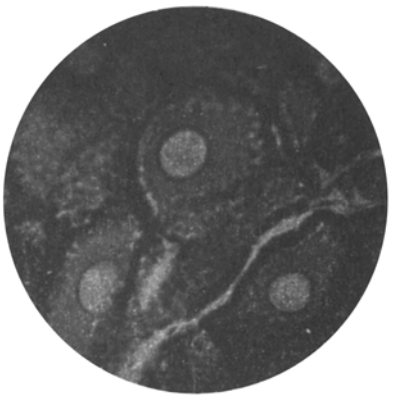

Fig. 1. The thyroid gland of a rabbit after receiving uranium nitrate for 1 month. The colloid is thick and highly vacuolated. Many interfollicular cells. Ocular 10×, objective 40×.

Experiments were also performed on rabbits. Ten rabbits were used initially for an investigation of the normal functional state of the thyroid gland by means of administration of radioactive iodine (I^{131}) to the animals in a dose of 1.5 μC to each animal. One month later, the same rabbits were given subcutaneous injections of 0.1 mg uranyl per kg body weight in 1 ml distilled water daily for 30 days. At the end of the course of injections the rabbits were again given the same dose of I^{131} as before (1.5 μC) in order to ascertain any possible changes in the functional activity of the gland. Six rabbits were used as controls and received no treatment.

The activity of the thyroid gland in absorption of I^{131} was measured as γ-irradiation by means of a pickup and a

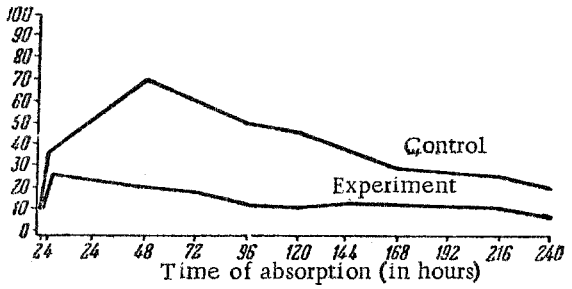

Fig. 2. 10-day absorption curves of radioactive iodine by the thyroid gland of normal rabbits (upper curve) and of the same rabbits after receiving uranium nitrate (lower curve). Vertical axis — absorption of I^{131} as % of total activity of dose injected.

"B" apparatus 2, 4 and 24 hours after administration of the I^{131}, and thereafter once a day for 10 days. The activity of absorption of I^{131} by the gland was expressed as a percentage of the total activity of the dose administered.

EXPERIMENTAL RESULTS

No difference was found between the growth of the experimental and control rats. The average weight of the control rats at the end of the experiment was 190 g, and the average weight of the experimental rats was 200 g. In contrast to the use of large doses (2.5%) of uranyl in the food [3], the above doses evidently had no marked effect on growth. At the same time it must be pointed out that a considerable number of the experimental rats died (32 and 37%). The mortality was especially high in the last 3 months of the experiment. At necropsy the majority of the animals showed foci of suppuration in the lungs, and in some animals there were lesions of the cervical lymphatic glands. The glands were greatly enlarged and pus was present inside them.

No death of the control animals was observed. From the above it may be deduced that the cause of death of the animals was slow poisoning with uranyl.

Significant histological changes were found in the thyroid gland of the experimental rats. In the majority of cases the follicles were small, the epithelium cubical, and the colloid thick and highly vacuolated. The number of cells of the interfollicular epithelium was far in excess of normal. In the adrenals a considerable thickening of the cortex was observed without visible destruction of the cortical and medullary substance. No appreciable abnormalities were found in the hypophysis and spleen.

The rabbits were incomparably more sensitive to uranyl than the rats. According to Haven and Hodge [4], the mean lethal dose for subcutaneous injection to rabbits is 0.7 mg/kg body weight, and accordingly we used one seventh of the lethal dose. The subcutaneous injection of 0.1 mg/kg body weight of uranyl daily for 30 days caused no outwardly visible pathological signs, but on the 20th day of the experiment a considerable quantity of albumin appeared in the urine of the rabbits. If it is remembered that in the course of the month each rabbit received 6 mg of uranyl, the toxicity of this element will be obvious.

Histological examination showed that the number of basophilic cells in the hypophysis was increased. The sinuses of the spleen were engorged with blood and dilated. The morphological changes in the thyroid gland were the most demonstrative: the follicles were small and the epithelium cubical. Occasionally large follicles were encountered with Sanderson's cushions* The colloid was thick and highly vacuolated (Fig. 1). A large number of interfollicular cells was observed.

The results of the investigation of absorption of I^{131} by the thyroid gland are shown in Fig. 2. The upper curve indicates the mean absorptive power of the gland in normal rabbits, the lower — the mean absorptive power of the gland in the same rabbits after treatment with uranyl. The variations between the values obtained in individual rabbits were insignificant. Comparison of these curves showed convincingly that uranyl, even in very small doses, has a depressing effect on the function of the thyroid gland. The peak I^{131} absorption in the experimental series is far lower than that in the controls, and is displaced to the left. This suggests a significant fall in the absorptive power of the gland. Whereas the maximum absorption of I^{131} in the control series shows over 70% of the total activity of the dose injected, the maximum absorption in the experimental series is about 25%, i.e., slightly more than one third. It is also interesting that the lower curve is of a character which greatly resembles the curve of myxedema as shown in the paper by N. A. Gabelova [1].

It may thus be concluded from the foregoing that uranyl, when given to rabbits even in small doses, causes great changes in both the structure and the function of the thyroid gland or, in other words, uranyl behaves like certain strongly acting inhibitors towards the thyroid gland.

* Name not verified.

SUMMARY

Uranium nitrate injected subcutaneously into rabbits in the dose of 0.1 mg/kg of body weight for a period of 30 days causes a considerable depression of the ability of the thyroid gland to include radioiodine administered to the animal. The gland is enlarged and the changes in the parenchyma histologically resemble those seen in goiter.

A similar histological picture was observed in rats; the latter are much less sensitive to uranium salts than rabbits. Thus, uranium nitrate (uranyl) is a natural powerful inhibitor of the thyroid gland, and may be one of its natural goiterogenic factors.

LITERATURE CITED

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* Original Russian pagination. See C. B. Translation.