16040 P

Effects of Radiotoxic Dosages of I^{131} upon Thyroid and Contiguous Tissues in Mice.*

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It seems remarkable that despite the extensive use of radioactive iodine in experimental and clinical studies no information has appeared in the literature concerning the radiation dosage from which injury may be expected in the thyroid gland. Such information seems implied in the use of I^{131} for the destructive irradiation of human thyroid carcinoma, but even here knowledge of a possible differential in radiation-sensitivity between normal and neoplastic thyroid tissue is greatly to be desired.

In an exploratory study, 36 inbred mice (A and C_{57} strains), 2 to 5 months old, and of both sexes, have been given "tracer" quantities of I^{131} in the form of NaI in neutral aqueous solution by subcutaneous injection. Mice were fed purina laboratory chow and kept at a constant temperature of $72° \pm 1°$F. Radiation dosages ranged from 100 to 1000 microcuries. Calculation of dosage was made from standardizations on a Geiger counter which, in a survey by the National Bureau of Standards in June, 1947, compared favorably in sensitivity to I^{131} with instruments at most other institutions. Mice were sacrificed 2, 3, 24, or 120 days after injection. Thyroids and surrounding tissues were serially sectioned.

Table I provides an approximate summary of the observations made.

A striking early effect of the localized radiation was a periglandular edema which separated the thyroid from surrounding structures and extended even into neighboring muscle. The edematous connective tissue was extensively infiltrated by lymphocytes, polymorphonuclear leucocytes, and some mast cells. Pycnosis of areas of tracheal epithelium was common. In animals killed on the second day following injection of 300 microcuries (20-23 millicuries I^{131} per kg) there was little effect beyond this. In the animal killed 2 days after receiving 53 mc per kg the thyroid appeared as an eosinophilic mass, amorphous in medullary parts, but with recognizable surviving follicles in the peripheral parts of the gland. Cells with still stainable nuclei either were pycnotic or else showed signs of activity (hypertrophy, exhaustion of colloid). In all instances surviving thyroid tissue was in the isthmus or the cranial apex of the gland where, presumably, self-radiation would have been minimal.

On the third day after injection thyroid destruction varied from minimal with lower dosages to complete with the 50 mc per kg dose. Parathyroid involvement paralleled these changes. Furthermore, dosages above 20 mc per kg produced pycnosis of nuclei of neurilemma and sheath cells in the recurrent laryngeal nerve, in those sections most intimately associated with the thyroid.

After a 24 day exposure to I^{131} radiation even the low dose (3-5 mc per kg) produced extensive destruction, and a medium dose (18-22 mc per kg) produced complete thyroidal destruction. At this time fibrosis had replaced the amorphous mixtures of epithelial debris and leucocytes with a somewhat edematous type of fibrous tissue. No normal parathyroid tissue remained.

At the 120 day interval the thyroid consisted of a shrunken fibrous band, the edema and leucocytic reaction having disappeared. In animals having received the low dose of I^{131} most glandular tissue had disappeared but a few surviving small follicles were imbedded in the fibrous tissue, and seemed to be secreting actively, and possibly serving as a reservoir for regeneration.

* This investigation has been aided by a grant from the Jane Coffin Childs Memorial Fund for Medical Research.

TABLE I.
Summary of Results.

Exposure to I^{131}, days	No. of mice	Dose, millicuries per kg	Approx. % thyroid destruction	Approx. % parathyroid destruction
2	2	20-23	0	0
2	1	53	90	75
3	6	3-5	10	0
3	4	17-18	75	25
3	4	30-35	80-90	75
3	3	50-55	100	95
24	8	3-5	25-50	10
24	4	18-22	100	50
120	4	3-4	90	100

Summary. Dosages of I^{131} from 3 to 50 millicuries per kilogram were given to young mice on a normal diet. Higher dosages produced complete thyroidal destruction within a few days. Lower dosages permitted survival of some thyroidal epithelium in the isthmus and cranial apex of the thyroid for as long as 120 days after injection, but resulted in loss of the parathyroids. Lesions were noted in the tracheal epithelium with all dosages, and in the recurrent laryngeal nerve with higher dosages.

16041 P

Thiouracil and Conversion of Carotene to Vitamin A Measured by Liver Storage in the Rat.*

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In a recent report, Canadell and Valdecasas[1] fed rats, which previously were on a vitamin A-free diet with thiouracil administered in the drinking water, 60 γ of carotene per week. The administered carotene was unable to relieve the ocular symptoms produced by a vitamin A deficiency. However, these symptoms were alleviated if small amounts of thyroid powder were administered with the carotene or vitamin A was fed to the thiouracil-treated animals. Their interpretation of this phenomenon was that it involved an inhibition of carotenase.

If this is true, then the feeding of carotene to vitamin A deficient-animals previously treated with thiouracil should produce little or no vitamin A in the liver. Therefore, this experiment was attempted, and a preliminary report of the results obtained is presented.

Twenty-six rats were placed on a vitamin A-low diet when they were 10 days old. When they reached a body weight of 43 g, they were divided into 2 groups. One group was continued on the same diet for 4 weeks while the second group received a similar diet to which 0.25% of thiouracil had been added. All rats were continued for an additional 2 weeks on identical diets except that they were made vitamin A-free by replacing the commercial casein with vitamin A-free test casein

* Aided by a grant from the Nutrition Foundation.

1 Canadell, J. M., and Voldecasas, F. G., *Experientia,* 1947, **3**, 35.