Effect of Hypophysectomy on the Intrathyroidal Metabolism of I^{131}. (18724)

A. Albert and Nona Lorenz.

From the Endocrinology Laboratory, Mayo Clinic, Rochester, Minn.

Morton *et al.*(1) reported that hypophysectomy induced a qualitative defect in the treatment of iodine by the thyroid in that the conversion of iodine to thyroxine was definitely limited or almost inhibited. However, it would appear more likely from other work on the pituitary-thyroid system that the defect induced by hypophysectomy would be quantitative rather than qualitative. If the latter were true, then a longer time interval would be needed to manifest the existence of a slow rate of conversion of diiodotyrosine to thyroxine in hypophysectomized rats than in normal rats. Also improved methods of analysis would be needed to detect any small differences in the proportions of thyroidal diiodotyrosine and thyroxine at varying intervals in normal and hypophysectomized rats. Consequently, the experiments of Morton *et al.* were repeated with two modifications: (1) observations were extended over a longer time interval, and (2) methods of analysis which we believe represent advances over those used by Morton *et al.* were employed.

Material and methods. Weanling Sprague-Dawley male rats were used after they had been maintained for 2 weeks on an iodine deficient diet under conditions described previously(2). On the sixth day after hypophysectomy, the hypophysectomized and the control rats were injected with a tracer dose of 10 μc of radioiodine. Groups of animals were killed at 3, 6, 24, 48, 72, 96 and 144 hours after the injection of the tracer dose. The thyroids were removed, and the radiation was determined in a gamma ray counter and expressed as per cent of dose by counting simultaneously an aliquot of the administered dose. Each thyroid was then homogenized in a few ml of 10% trichloracetic acid in an all-glass homogenizer. The homogenate was then centrifuged, and the supernatant liquid was transferred to a 15 ml centrifuge tube. The precipitate was then washed twice with 5 ml of trichloracetic acid. After centrifugation, the supernatant solutions were combined and the radiation in the acid-soluble and acid-insoluble fractions was determined. The percentage of radioactivity in each fraction was then computed by dividing the radioactivity in each fraction by the sum of the activity of the two fractions. The acid-insoluble fraction consists of protein-bound I^{131} and any free thyroxine that may be present. The acid-soluble fraction contains, among other things, inorganic iodide and any free diiodotyrosine that may be present. The protein-bound or acid-insoluble fraction was emulsified in 10 ml of water in a 15 ml centrifuge tube, and 1% sodium hydroxide was added until the pH of the emulsion was just alkaline to phenolphthalein. One ml of 2 N sodium hydroxide solution was then added, and the tube was placed in an incubator at 95°C for 8 hours. After cooling, the solution was neutralized with trichloracetic acid. To each hydrolyzed sample was added sufficient saturated sodium chloride solution to make a 1% solution, 0.1 ml of human albumin solution (Cutter Laboratories) and 1 mg each of sodium iodide, diiodotyrosine and thyroxine as carriers. The procedure for obtaining and computing the acid-soluble and acid-insoluble fractions as described previously was repeated.

The efficiency of this method, both before and after hydrolysis of thyroid tissue, was determined by performing recovery experiments with radioactive iodide, radioactive diiodotyrosine and radioactive thyroxine. Ninety-three per cent of the radiothyroxine added to thyroid homogenate was recovered in the acid-insoluble fraction, and 96 and 91% respectively of iodide and diiodotyrosine were recovered in the acid-soluble fraction. Ninety-two per cent of radiothyroxine added after hydrolysis was recovered in the acid-

1. Morton, M. E., Perlman, I., Anderson, Evelyn, and Chaikoff, I. L., *Endocrinology*, 1942, v30, 495.

2. Randall, R. V., Lorenz, Nona, and Albert, A., *Endocrinology*, 1951, v48, 339.

TABLE I. Effect of Hypophysectomy on Intrathyroidal Metabolism of I^{131}.

	Hr after injection						
	3	6	24	48	72	96	144
Total I^{131} % uptake							
Normal	53.65 (7)*	60.96 (2)	55.07 (2)	77.27 (6)	59.39 (2)	52.98 (2)	44.08 (7)
H†	4.29 (8)	9.06 (3)	25.99 (3)	29.76 (9)	28.82 (4)	33.59 (4)	18.66 (5)
% acid-insoluble							
Normal	96.95 (4)	94.43 (4)	95.67 (2)	95.25 (2)	97.58 (2)	95.75 (2)	
H	82.55 (8)	90.82 (8)	93.77 (3)	94.79 (4)	97.51 (4)	95.29 (4)	
% acid-soluble							
Normal	3.06 (4)	5.58 (4)	4.34 (2)	4.75 (2)	2.42 (2)	4.25 (2)	
H	17.46 (8)	9.18 (8)	6.23 (3)	5.21 (4)	2.50 (4)	4.71 (4)	
After hydrolysis % acid-insoluble							
Normal	16.80 (9)	20.93 (4)	38.34 (1)	43.49 (6)	42.51 (2)	45.99 (2)	52.71 (7)
H	15.74 (13)	10.98 (8)	9.87 (3)	22.44 (8)	15.14 (4)	17.49 (4)	25.04 (4)
% acid-soluble							
Normal	83.20 (9)	79.08 (4)	61.66 (1)	56.51 (6)	57.49 (2)	54.02 (2)	47.29 (7)
H	84.26 (13)	89.01 (8)	90.13 (3)	77.57 (8)	84.86 (4)	82.51 (4)	74.96 (4)

* Numbers in parentheses are numbers of animals.
† H = hypophysectomized.

insoluble fraction, and 97 and 90% of iodide and diiodotyrosine respectively added after hydrolysis were recovered in the acid-soluble fraction.

Results. The results are shown in Table I, which gives average values for each group of rats and, in parentheses, the number of animals on which each mean value is based. It is evident from this table that, while substantially all of the I^{131} became protein-bound within a day in the hypophysectomized animals, the rate and extent of the protein-binding was somewhat slower than in normal animals. The most significant observation was in the behavior of the acid-soluble and acid-insoluble components after hydrolysis of the protein-bound I^{131}. In the normal animals, there was a progressive increase in the acid-insoluble fraction until more than half of the radioiodine was in the form of thyroxine. In the hypophysectomized animals, there was a much smaller increment in the thyroxine fraction after 144 hours. Concomitantly, the acid-soluble fraction in normal animals decreased rapidly over the period of 144 hours, whereas in hypophysectomized animals, there was a smaller decrease.

Discussion. The present results indicate that hypophysectomy induces a quantitative rather than a qualitative defect in the intrathyroidal metabolism of I^{131}. In hypophysectomized rats the proportion of acid-soluble I^{131}, assumed to be the precursor of thyroxine, decreases slightly over a period of 144 hours but the slope* of this decrease (0.092% per hour $\pm$ 0.026) is significantly different from zero. This would indicate that hypophysectomized animals are capable of converting iodide into thyroxine but at a rate which is only a fraction that of normal animals.

Summary. Hypophysectomy reduced but did not abolish the over-all conversion of I^{131} into labeled thyroxine.

* The curves were analyzed by Dr. Joseph Berkson, to whom we are indebted.

Received April 24, 1951. P.S.E.B.M, 1951, v77.