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Received February 15, 1960. P.S.E.B.M., 1960, v103.

Peripheral Metabolism of Thyroxine and Triiodothyronine in Iodine Deficient Rat.*† (25697)

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In the iodine deficient rat, iodide trapping activity and rate of hormonal secretion by thyroid are markedly enhanced(1). Morphologic and metabolic aspects of the gland indicate extreme activity while there is insufficient output of hormones. The present experiments were therefore undertaken to determine whether the iodine deficient state influences peripheral disposition of thyroidal hormones, more particularly, rate of disappearance from serum of radiothyroxin (T4*) and radiotriiodothyronine (T3*), their space of distribution and quantity of hormone degraded daily.

Materials and methods. In each experiment, 14 male rats were divided into 2 groups of 7 each. One group was placed on iodine deficient diet‡ and distilled water for 5 weeks; the control group received tap water and pellet diet containing 43 μg of KI/100 g of diet. Then, all rats were injected subcutaneously with 50 mg of propylthiouracil (PTU) in 0.5 ml of saline and 15 minutes later *via* tail vein with about 20 μc of radiohormone.§. They were bled from tail vein at 6 and 12 hours and every 12 hours thereafter until autopsy, at which time they were exsanguinated. For T4*, period of observation lasted 72 hours, and for T3* 48 hours. Urines and feces were collected for each 24 hour period. At autopsy, thyroids were removed, cleaned of adventitial tissue, and weighed on torsion balance to the nearest 0.1 mg. Radioactivity in thyroids, urine, feces and whole carcass (minus blood and thyroids) was counted. A measured aliquot of serum from each bleeding was counted for total and Somogyi precipitable radioactivity. Half-lives of radiohormones were determined by inspection of the disappearance curves, constructed on semi-log paper plotting serum radioactivity against time in hours. Space of distribution was calculated from total radioactivity injected, divided by counts/min/ml of serum at zero time, the latter figure obtained by extrapolating the straight line of disappearance curve to the ordinate axis. Chromatograms were made from extracts of each bleeding and from each 24 hour urine collection. One ml of serum from each animal of a group was pooled for each bleeding. Pooled sera and a mixture of mono-iodotyrosine, diiodotyrosine, triiodothyronine and thyroxine were prepared for chromatography as previously described(1), using butanol-acetic and water-collidine-ammonia systems. NaI solution was run separately in the same chromatocab at the same time. Spots were developed with sulfanilic diazonium chloride and palladium chloride for iodide ion. The chromatogram was divided into 1 cm wide strips and each strip counted. The spots were then removed and counted. Urines for each 24 hours were handled in the same fashion. Serum I^{127} determinations were done on samples taken from rats at autopsy.‖

Results. Disappearance of radioactivity from serum of rats given PTU and T4* was linear over 72 hours. The half life of hormone was approximately 18 hours in both iodine deficient and control groups of animals. In Fig.

* This work was supported by grant of U.S.P.H.S.

† Reprint No. 240 of Dept. of Pathology, Univ. of Pittsburgh School of Med.

‡ Nutritional Biochemicals Corp., Cleveland, O.

§ Radiothyroxine and radiotriiodothyronine were supplied by Abbott Labs., Oak Ridge, Tenn.

‖ Performed in laboratory of Dr. J. Sugarman, Pittsburgh, Pa.

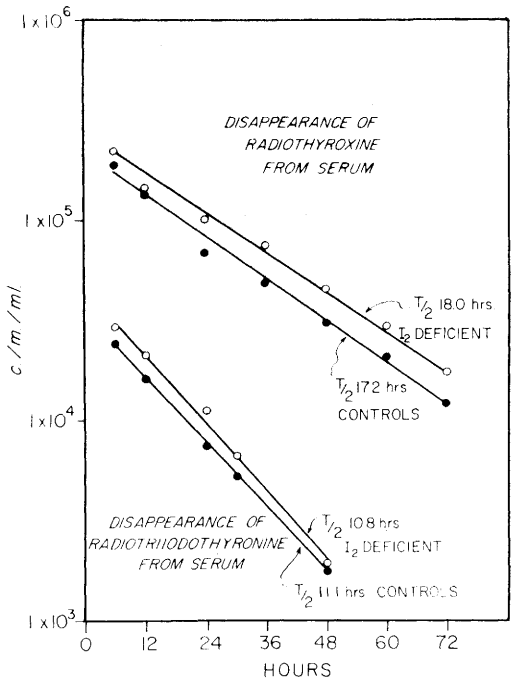

FIG. 1. Disappearance curve of radiothyroxine and radiotriiodothyronine from the serum of iodine-deficient and control rats.

1, curves were constructed from averages of each group, representing protein bound I^{131}/ml of serum. Within 6 hours of intravenous injection, 70-75% of circulating I^{131} was precipitable. The precipitable I^{131} remained at this level 48 hours, then gradually dropped to 65% at 72 hours. By chromatography, T4* and I^{131} iodide were found, most radioactivity being in the T4* spot.

It was necessary to inject PTU to obtain a straight line disappearance curve of serum I^{131}. In other experiments without PTU, recycling of I^{131} was sufficiently rapid, especially in iodine deficient rats, that an exponential decay curve was not observed. The efficacy of PTU was demonstrated by thyroidal uptake of I^{131} in iodine deficient rats after 3 days of 0.25% of the radioactive dose given or 50-100 times less than uptake in deficient rats without PTU. It is also to be noted that the iodine deficient thyroid concentrated about 5 X more I^{131} than its control.

The space of distribution of T4* was similar in both experimental and control rats, being 76 ml or 17.3% of body weight and 84 ml or 18.4% of body weight for the 2 groups respectively. PBI^{127} levels in iodine deficient and control groups averaged 2.7 μ and 4.0% respectively (Table II).

From above data of turnover rate, space of distribution and I^{127} level, quantity of thyroxine degraded daily was calculated, assuming that 4/5 of the PBI^{127} was thyroxine. The iodine deficient group of rats degraded daily much less thyroxine than did their controls.

Both renal and fecal excretion of I^{131} were less in deficient rats than in controls, despite the fact that the thyroid was excluded from the metabolic pool. These differences in excretion and retention between control and experimental rats were not statistically significant because of wide spread of values from animal to animal.

Results similar to those just recorded for T4* were obtained in iodine deficient and control rats following administration of PTU and T3*. The half life was between 10.5 to 11 hours for the 2 groups of animals (Fig. 1). The curves represent averages of protein bound radioactivity/ml of serum. Within 6 hours of intravenous injection of T3*, only 50-60% of circulating radioactivity was protein bound, and this was T3* by chromatography. At 48 hours, PBI^{131} decreased between 10-20% of circulating radioactivity.

Space of distribution was of the same dimension for both deficient and control groups (Table II). PBI^{127} averaged 1.5μ% in experimental rats compared with 2.2μ% in controls. If one estimated circulating T3 to be 1/5 of total circulating PBI^{127}, then again the quantity of T3 degraded daily would be less in deficient rats than in controls (Table II).

Discussion. In the iodine deficient state, despite markedly augmented activity of the thyroid and the accelerated cycling of iodine compounds, peripheral metabolism of T4* and T3* remained unaffected. Turnover rates or half lives observed in iodine deficient groups were of the same order as for controls and as was found by others(2-6). Nor was there an alteration of space of distribution resulting from iodine deficiency. There was, however, a diminution in quantity of hormone degraded daily in the deficient group, simply because of inedaquate secretion of thyroid hormones. In short, the iodine deficient rat had less thy-

TABLE I. Excretion, Retention and Thyroidal Uptake of I^{131} in Iodine Deficient Rats Following Injection of PTU and T4* or T3*.

Animal	Body wt, g	Thyroid wt, mg	Thyroid wt, % of body wt	Thyroid uptake, % of dose	Urine excretion, % of dose	Fecal excretion, % of dose
T4* + PTU						
I_2 deficient	436	*29.2 ± .70**	*6.7 ± .4*	*.25 ± .027*	16.0 ± 1.17	35.4 ± 5.3
Controls	455	18.1 ± 1.21	4.0 ± .15	.03 ± .007	22.9 ± 3.2	47.8 ± 2.6
T3* + PTU						
I_2 deficient	468	*30.1 ± 3.45*	*6.4 ± .55*	*.34 ± .06*	28.9 ± 1.5	46.5 ± 7.1
Controls	420	19.2 ± 1.01	4.6 ± .34	.07 ± .008	40.0 ± 4.5	35.5 ± 4.7

* ± stand. error of mean.

Italicized figures are significantly different from controls at 1% level or less.

TABLE II. Half-Life, Space of Distribution and Daily Degradation of Thyroidal Hormones in Iodine-Deficient and Control Rats.

Animal	Half-life hours	Daily turnover rate	Space of distribution, ml	Serum I^{127}, μ%	Daily degradation,* μ
T4* + PTU					
I_2 deficient	18.6	.89	76	2.7	1.46
Controls	18.2	.91	84	4.0	2.44
T3* + PTU					
I_2 deficient	10.3	1.65	300	1.5	1.49
Controls	11.0	1.50	389	2.2	2.57

* Assuming $\frac{4}{5}$ of serum PBI^{127} is T4 and $\frac{1}{5}$ is T3.

roidal hormone than its control, but metabolised whatever was available at the same rate as the control.

Summary. The peripheral metabolism of radiothyroxine (T4*) and radiotriiodothyronine (T3*) was studied in iodine deficient and control rats. The half-life and space of distribution of these hormones were similar in the 2 groups of animals. The quantity of hormone degraded daily, however, was less in iodine deficient than in its control rat because less was produced.

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Received February 15, 1960. P.S.E.B.M., 1960, v103.

Lipid Synthesis by Ascites Tumor Cells.* (25698)

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We have shown(1) that palmitic acid is readily absorbed by Ehrlich mouse ascites tumor cells *in vitro,* especially when presented as the albumin complex. Moreover, an average of about 40% of the absorbed palmitic acid was oxidized to CO_2 per hour under these conditions. However, it was not ascertained

* These studies were supported by contract between Atomic Energy Commission and Univ. of California.