

## **Stability of Radiothyroxine Plasma Disappearance Curve Despite Catharsis and Unblocked Thyroidal Uptake of Radioiodide**

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*Plasma radioactivity was measured over 21 days after an intravenous injection of 50  $\mu$ Ci of  $^{125}\text{I-T}$ , in eight normal men. No thyroid-blocking medication was given. Four subjects (castor oil group) received 30 ml of castor oil on each of Days 13, 14, and 15, while the other four subjects (control group) were studied without medication. After a 5-day equilibration period, plasma  $^{125}\text{I-T}$ , was measured on Days 5–13 in order to calculate the disappearance curve for each subject and to derive the mean for each experimental group. The curves were then extrapolated to Day 21. Measured radioactivity did not depart significantly from the extrapolated line, either during the castor oil period (Days 14, 15, and 16) or during the recovery period (Days 17, 19, and 21). The castor oil, therefore, had no observable effect on the clearance of plasma radioactivity. None of the subjects had a late increase in plasma radioactivity to suggest recirculation of radioiodide or buildup of iodoproteins. In normal subjects, radiothyroxine plasma levels up to 21 days are not significantly affected by short-term catharsis or by failure to block thyroidal radioiodide uptake.*

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In clinical and research studies involving long-term assessment of radiothyroxine disappearance rates, it is customary to block thyroidal uptake of the radioiodide resulting from hormonal metabolism. This blockage is usually desirable, as it protects the thyroid gland against unnecessary irradiation. It also prevents contamination of the peripheral radiothyroxine pool by new radiothyroxine made by the thyroid gland from the radioiodide split off from the original radiothyroxine dose. Most commonly, stable iodine is used to block thyroidal uptake and prevent this "recirculation." While this blocking dose probably has no significant effect on the peripheral disappearance of radiothyroxine (1), iodine certainly has other profound effects on thyroidal economy which may interfere with the experiment or study planned. In such a case, blocking medication must be omitted.

The relative importance of the gastrointestinal thyroxine cycle on overall thyroxine behavior in man remains an open question. Hiss and Dowling (2)

showed that, in cases of severe malabsorption syndrome, thyroxine disappearance is significantly accelerated. Little is known, however, about the possible role of diarrhea, such as occurs after short-term catharsis (e.g., in preparation for x-ray studies) or after an incidental infectious or drug-induced enteritis. Since thyroxine disappearance studies take a number of days, such intervening episodes in hospitalized patients are not rare.

The present study was undertaken to determine whether either short-term catharsis or unblocked uptake of metabolic radioiodide significantly affects the usual radiothyroxine disappearance curve.

### **METHODS**

Eight normal young men, college students over

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the age of 21, served as subjects. The nature of the experiment, including the fact that radioactive thyroid hormone and castor oil would be administered, was described in detail and informed written consent was obtained.

Subjects were given a single intravenous dose of 50  $\mu$ Ci of  $^{125}$ I-thyroxine. Blood was collected for measurement of plasma radioactivity at Day 1 (in the control subjects) and at Days 5, 7, 9, 12, 13, 14, 15, 17, 19, and 21. Four subjects (the "castor oil" group) were given 30 ml of castor oil immediately after blood collection on Days 13, 14, and 15. These subjects reported a brief brisk diarrhea several hours after each dose of castor oil. These episodes of diarrhea might be expected to affect blood samples obtained on the following day, that is, those of Days 14, 15, and 16.

Blood plasma was separated, pipetted into well counter tubes, and counted in comparison with dose-solution standards using an automatic gamma spectrometer. Plasma concentrations were expressed as percent of injected dose per liter of plasma. Subsequently, these percentages were converted to logarithms, and linear regression curves were calculated for Days 5–13 and for Days 13–21 for each of the eight individual subjects. Similar analyses were performed for the average values for the four subjects in each experimental group. From the regression lines for Days 5–13, plasma values were extrapolated for Days 14, 15, 16, 17, 19, and 21 for each subject and for the average of each experimental group. Possible statistical significance of differences between predicted and observed blood values, and between the individual regression lines, was assessed by Student's t-test.

RESULTS

Figure 1 displays thyroxine disappearance curves for the averaged data from the two experimental groups. The calculated regression lines are indicated as solid lines over the time region upon which they are calculated (Days 5–13) and as dotted lines over the time regions where they are extrapolated. Table 1 shows the differences between observed and predicted values for each individual subject and for the averaged data of each experimental group during the later observational periods. Table 2 shows the daily fractional losses of  $^{125}$ I-T<sub>4</sub>, calculated from the individual regression lines for the data from Days 5–13 and 14–21, respectively. None of these individual differences nor any of the combinations tested approached statistical significance.

DISCUSSION

Radiothyroxine is rapidly distributed to the liver in relatively large quantities, where it is then conju-

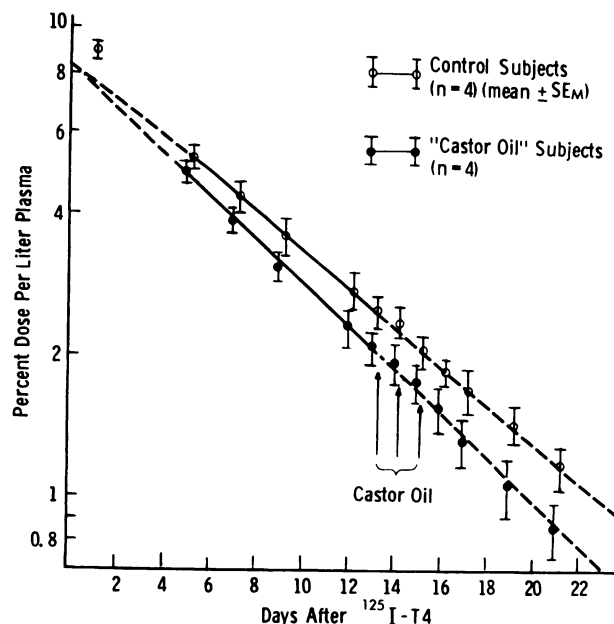


FIG. 1. Thyroxine disappearance curves (semilog) for averaged values of both experimental groups. Solid lines represent regression lines calculated for Days 5–13; dotted lines are extrapolations.

TABLE 1. DIFFERENCES BETWEEN OBSERVED RADIOTHYROXINE PLASMA LEVELS AND LEVELS PREDICTED BY EXTRAPOLATION FROM DAYS 5–13

Subject	Mean differences in plasma radiothyroxine levels*	
	Days 14–16 (castor oil period)	Days 17–21 (postcontrol period)
<b>Castor oil group:</b>		
1	0.03	–0.03
2	0.15	0.05
3	0.12	–0.04
4	0.00	–0.07
Pooled data	0.08	–0.02
<b>Control group:</b>		
5	0.01	–0.19
6	–0.19	–0.01
7	0.13	0.15
8	0.11	–0.07
Pooled data	0.01	0.01

\* Data expressed as percent injected dose per liter of plasma.

gated and secreted in the bile. Although little is known directly about the fate of this conjugated thyroxine in the small bowel, it is believed to be broken down ultimately by intestinal bacteria, with partial reabsorption of the labeled thyroxine. Fecal radioactivity after radiothyroxine administration is thought to be in the form of unaltered thyroxine, excreted

TABLE 2. FRACTIONAL LOSS OF  $^{125}\text{I-T}_4$  PER DAY, CALCULATED FROM LEAST-SQUARES FIT OF INDIVIDUAL DATA

	Castor oil group				Control group			
	1	2	3	4	5	6	7	8
Days 5-13	0.112	0.103	0.111	0.089	0.097	0.084	0.095	0.082
Days 13-21	0.103	0.098	0.116	0.090	0.097	0.083	0.097	0.084
Difference	+0.009	+0.005	-0.005	-0.001	0.000	+0.001	-0.002	-0.002
Mean difference		+0.002				-0.001		
t (paired samples)		0.67				0.88		
p		Not significant				Not significant		

from the bile (3). For the present study, castor oil was chosen to induce catharsis, as castor oil has its primary action in the small bowel (4). A significant portion of thyroxine resident in the small bowel, it was believed, might be washed out by this intermittent catharsis. The present study shows clearly that the diarrhea produced by three doses of castor oil did not significantly alter the long-term metabolism of the radiothyroxine dose given. The slight (statistically insignificant) transient rises in radiothyroxine levels noted after catharsis may be due to transient decreases in plasma volume.

Stable iodine is customarily administered to subjects undergoing thyroxine distribution studies. Under these circumstances, normal subjects display a monoexponential decay pattern after a 1-4-day period for equilibration (5-9). In the present study, 5 days were allowed in order to remove any question of an individual subject's showing delayed equilibration.

In the unblocked thyroid gland, a fraction of the radioiodide resulting from radiothyroxine breakdown will be "recirculated" and ultimately rereleased into the circulation as new radiothyroxine. In normal individuals, whose turnover of the thyroidal iodine pool is slow, this release initially constitutes only an insignificant fraction of the total circulating radiothyroxine. However, as the concentration of the injected radiothyroxine progressively decreases, the continued release of this new fraction ultimately might become important. Were that to occur, there would be a clear-cut relative increase in plasma radiothyroxine levels with passage of time. Such a phenomenon was not observed, since the measured radiothyroxine values were almost precisely those predicted through the 21 days studied.

The stability of the radiothyroxine disappearance curve also shows that, in man, possible late release of tissue-bound radiothyroxine [the NEI of Oppenheimer, Surks, and Schwartz (10)] does not statis-

tically affect late radiothyroxine metabolism. Preliminary studies under way in this laboratory confirm the presence, but in low proportion, of labeled iodoproteins in the sera of normal subjects at late times after radiothyroxine administration. This study supports the descriptive accuracy of a monoexponential disappearance curve even during periods of mild bowel dysfunction or when, for good reasons, uptake of radioiodide by the thyroid has not been blocked.

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