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Effect of Altered Thyroid States on Chromium Uptake in Rat Blood

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Abnormal thyroid states, hypothyroidism and hyperthyroidism, alter metabolic processes such as protein synthesis (RAWSON et al. 1969). The effects of hypo- and hyperthyroidism on metal and mineral metabolism have been reported by several investigators (AIKAWA 1960, HUMPHRAY and HEATON 1972, JONES et al. 1966, KOVTUNYAK and TSAPOK 1971, KOVTUNYAK et al. 1972). These effects may be due to changes in protein levels or some other effect of thyroxine on the body.

A change in the uptake, transportation, or rate of removal of a metal in the body could significantly affect metabolic processes. These effects could lead to toxicity resulting from either excessive or deficient amounts of the metal. This paper reports an investigation of the retention of trivalent ^{51}Cr in the blood of rats having experimentally altered thyroid states.

MATERIALS and METHODS

Fifty four male Sprague-Dawley descendent rats weighing 180-200 g were used. They were randomly assigned to individual cages and were given free access to food and water. The rats were randomly divided into three groups, hyperthyroid, euthyroid, and hypothyroid, with 18 rats per group. The hyperthyroid group received intraperitoneal injections of 20 µg of L-thyroxine sodium pentahydrate (T4) per 0.5 ml (MANN 1975), and the hypothyroid group received intraperitoneal injections of 2 mg of propylthiouracil per 0.5 ml (MANN 1975). The euthyroid group received 0.5 ml of normal saline. Injections were performed daily for 15 days to establish the desired thyroid state.

On day 16, ^{51}Cr in the form of trivalent chromium chloride was intraperitoneally injected into all rats. The chromium concentration was such that 1 ml gave 21.5 µCi of ^{51}Cr and 5 µg of chromium as chromium chloride. The volume given was adjusted for the weight of each rat to give 10 µg of chromium/kg. A standard was prepared from the solution so that the total activity injected into each rat could be calculated.

All rats were allotted at random to a sacrifice time so that six rats from each treatment group were sacrificed 12, 24, or 96 hr after ^{51}Cr administration. Drug treatments were continued

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daily until sacrifice time, since it was known (GALTON 1975) that the thyroxine blood level rapidly decreases during the 24-hr period following administration.

At the time of sacrifice, the rats were anesthetized and blood was obtained by cardiac puncture in Vacutainers containing heparin. Approximately 3 ml was placed in pre-weighed counting tubes. Blood weights were obtained and the tubes were counted in a well type NaI(Tl) crystal.

RESULTS and DISCUSSION

The activities of the standard and blood were used to calculate the percentage of the total activity administered per gram in the blood of each rat. The means and standard errors of these values are shown in Table 1.

TABLE 1

Means and standard errors of percentage of activity injected per gram of blood.

Time (hr)	Hypothyroid	Euthyroid	Hyperthyroid
12	0.075 ± 0.006	0.047 ± 0.003	0.051 ± 0.008
24	0.050 ± 0.007	0.027 ± 0.004	0.029 ± 0.002
96	0.013 ± 0.001	0.004 ± 0.000	0.003 ± 0.001

No transformation was needed to obtain homogeneity of variance by the Foster-Burr test. A two-way analysis of variance (ANDERSON and MCLEAN 1974) was run to test for treatment and time of sacrifice effects. This analysis showed significant ($P < 0.05$) treatment and time of sacrifice effects but no significant treatment by time interaction. Therefore it was possible to pool across times to analyze for treatment effect and to pool across treatments to analyze for time effect. A Newman-Keuls range test (ANDERSON and MCLEAN 1974) was run to determine where the differences occurred. These results are shown in Table 2.

Blood from the hypothyroid rats had an enhanced ability to accumulate ^{51}Cr (Table 2). It accumulated 60% more chromium than that of the control rats at 12 hr, 85% more at 24 hr, and 225% more at 96 hr. No significant difference appeared between hyperthyroid and euthyroid rats.

TABLE 2

Newman-Keuls multiple comparisons.

A. Comparison of the treatment means pooled across times	S*	T	P
B. Comparison of the time means pooled across treatments	96*	24	12

*Designations represent the drug treatment (S = saline, control; T = L-thyroxine, hyperthyroid; P = propylthiouracil, hypothyroid); and the time intervals after ^{51}Cr injection at which the rats were sacrificed (12, 24, and 96 hr). They are arranged in order of increasing magnitude from left to right. Those underlined are not different ($P > 0.05$).

The percentage values versus time for the hypothyroid and euthyroid treatments were plotted, and the areas under the curves between 12 hr and 96 hr were measured. The area for the hypothyroid treatment was 129% greater than that for the control. These areas are proportional to the chromium content on a per gram basis within the time period studied. No data are available on the total blood volumes of the two groups, and so a calculation of the total blood content cannot be made.

The ^{51}Cr levels decreased with time in all treatment groups as seen in Table 2. The ^{51}Cr remaining in the blood at 96 hr was 17, 9, and 6% of the 12-hr amount for the hypothyroid, euthyroid, and hyperthyroid treatments, respectively. Thus, between 12 and 96 hr the rate of elimination of ^{51}Cr from the blood of hypothyroid rats was about two times that of the controls.

The reason for the differences in uptake and retention seen is not known. It may be due to differences in binding in the blood itself as a result of the treatments or to some other effect of thyroxine. At any rate, the differences found are large and should be considered when the toxicity of trivalent chromium is evaluated.

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