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THE GROSS RETENTION AND METABOLISM OF TRITIUM OXIDE IN THE MOUSE

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THE GROSS RETENTION AND METABOLISM OF TRITIUM OXIDE IN THE MOUSE

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January 23, 1951

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ABSTRACT

Tritium oxide was injected daily into white mice for 13 days. The animals were sacrificed at intervals during and after the injection period and the body water and total tissue compounds analyzed for tritium. The initial biological half-life for tritium oxide in body water was about 1.1 days, for tissue-bound tritium about 3 days. Thirty-two days after the final injection 90 per cent of the tritium in the animal was in the bound state and being lost with a half-life of approximately 30 days.

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THE GROSS RETENTION AND METABOLISM OF TRITIUM OXIDE IN THE MOUSE

INTRODUCTION

This document reports the preliminary results of a program designed to evaluate the radiation hazard involved in the handling of tritium. Information has been obtained on the extent to which tritium administered as the oxide is retained by mice both in body water and incorporated into tissue compounds.

METHODS

Thirty-one mature CF-1 mice, 18 males and 13 females, were used in the experiment. The animals were not of uniform weight (see Table 1) but showed no trend toward increase in weight during the course of the experiment. They were housed in individual cages and kept in a hood during the course of the investigation. Cages were 800 ml pyrex beakers fitted with four-mesh hardware cloth floors raised above the bottom of the beaker. Water and Purina dog chow were available ad. lib.

Tritium oxide was administered in an 0.86 per cent saline solution containing 190 μc tritium per ml. One-half ml of this solution was injected intraperitoneally daily for 13 consecutive days.

Animals were sacrificed by decapitation at intervals during and following the injection period, the last animals being killed 32 days after the final injection. Animals sacrificed during the injection period were killed 24 hours after the last previous injection.

Entire carcasses were ground with 100 ml of benzene in a Waring Blendor. Body water was obtained by distilling the benzene suspension into an overflow receiver which returned the supernatant benzene to the distilling flask but collected the water which separated as the bottom layer. Distillation was continued until no further increase was obtained in the volume of water collected. Water recovered by this procedure averaged 63.3 per cent of the total weight of the mouse. This body water sample was analyzed for tritium content.

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Benzene was removed from the carcass residue by distillation. The water-free residue was mixed with CuO and burned in a 19 mm i. d. Vycor combustion tube, 75 cm long, filled with CuO for a distance of about 40 cm exclusive of sample. The sample with admixed CuO occupied a length of about 20 cm. Temperature during burning was maintained at 750°C. by means of a stationary electric furnace around the "permanent" tube filling and a smaller movable furnace which was advanced slowly over the sample. Because of the large amount of material burned it was necessary to replace a considerable portion of the "permanent" filling after each combustion. Control experiments indicated complete removal of tritium from the sample by this procedure.

The water evolved in the combustion was collected in a double trap cooled with solid CO_2. This sample was analyzed as a measure of the tritium incorporated into tissue compounds.

Tritium analyses were performed by the method of Thorburn (1) which involves conversion of the water to acetylene and measurement of its activity with a vibrating reed electrometer.

RESULTS AND DISCUSSION

All data pertinent to the experiment are summarized in Tables 1 and 2. The mouse designated "control" received no injections and was processed in apparatus previously employed for the active mice. It served, therefore, as a control on the possibility of cross contamination due to incomplete recovery of activity from the apparatus.

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TABLE I

RETENTION OF TRITIUM IN THE MOUSE DURING THE INJECTION PERIOD

Mouse No.	Sex	Day Killed	Wt. (g) When Killed	Tritium in Body Water (μc)	Bound Tritium (μc)	Total Tritium (μc)	Per cent of Tritium Bound
Control	M	0	-	< 0.04	< 0.06	< 0.10	-
1	M	1	36.1	51	1.8	52.8	3.4
2	F	1	30.4	73	3.0	76.0	3.9
3	M	2	30.9	50	3.0	53.0	5.7
4	F	2	28.4	82	6.5	88.5	7.3
5	M	3	32.0	84	6.7	90.7	7.4
6	F	3	34.4	110	8.3	118	7.0
7	M	6	30.6	140	13	153	8.5
8	F	6	26.5	72	7.3	79.3	9.2
9	M	8	29.5	96	8.2	104	7.9
10	F	9	25.9	170	11	181	6.1
11	M	10	30.6	150	15	165	9.1

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TABLE 2

RETENTION OF TRITIUM IN THE MOUSE FOLLOWING THE INJECTION PERIOD

Mouse No.	Sex	Day Killed	Wt. (g) When Killed	Tritium in Body Water (μc)	Bound Tritium (μc)	Total Tritium (μc)	Per cent of Tritium Bound
12	M	13	34.9	150	16	166	9.6
13	F	13	28.0	140	13	153	8.5
14	M	14	36.0	62	7.6	69.6	11
15	F	14	30.0	83	10	93	11
16	M	15	39.1	40	7.5	47.5	16
17	F	15	28.8	28	4.7	32.7	14
18	M	17	32.1	15	4.4	19.4	23
19	F	17	29.1	19	4.8	23.8	20
20	M	20	30.2	3.5	1.7	5.2	33
21	F	20	33.5	2.9	2.8	5.7	49
22	M	22	34.2	1.9	1.9	3.8	50
23	F	23	27.4	0.38	1.3	1.68	77
24	M	24	33.0	0.34	1.3	1.64	79
25	F	27	--	0.88	1.3	2.18	60
26	M	28	36.1	0.30	0.76	1.06	72
27	M	31	36.6	0.36	2.1	2.46	85
28	F	34	21.6	0.17	0.54	0.71	76
29	M	37	--	0.11	0.66	0.77	86
30	M	44	36.4	0.07	0.44	0.51	86
31	M	44	38.0	0.10	0.84	0.94	89

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The data are graphically represented in Figure 1; the curves represent tritium content of body water and bound tritium content as a function of time. Points along the curves are rather scattered, but no more so than one might anticipate considering the fact the points are derived from different individuals of varying weights. The curves are, in any case, sufficiently well defined to show clearly that incorporation of tritium into tissues occurs to a significant extent and to indicate that this bound tritium is replaced at a much slower rate than is the tritium of the body water.

The slope of the body water curve following the last injection indicates a biological half-life for body water in the mouse of approximately 1.1 days. As the tritium activity in the body water decreases, the percentage which is derived from tissue bound tritium will increase and the slope of the body water curve will eventually represent the rate at which this bound tritium is being lost from the tissues. The observed biological half-life in the body water fraction at the end of the present experiment was about 10-15 days. This figure is very uncertain because of the small number of points in this region of the curve and the low level of activity in the samples.

More accurate information on the biological half-life of tissue bound tritium can be obtained from the bound tritium curve (Figure 1). The major fraction of this bound tritium was lost with a half-life of about 3 days. The slope of the latter portion of the curve, however, would indicate that approximately 10 per cent of this bound tritium is being replaced with a half-life of around 30 days. Again the exact figure is very uncertain because of the small number and considerable scatter of points.

Of the total tritium remaining in the mouse 24 hours after the first injection, about 3.6 per cent was present in the tissue bound state. The total percentage bound increased to about nine per cent at the end of the 13 day injection period, and at the conclusion of the experiment was about 90 per cent of the remaining activity. From the radiation hazard

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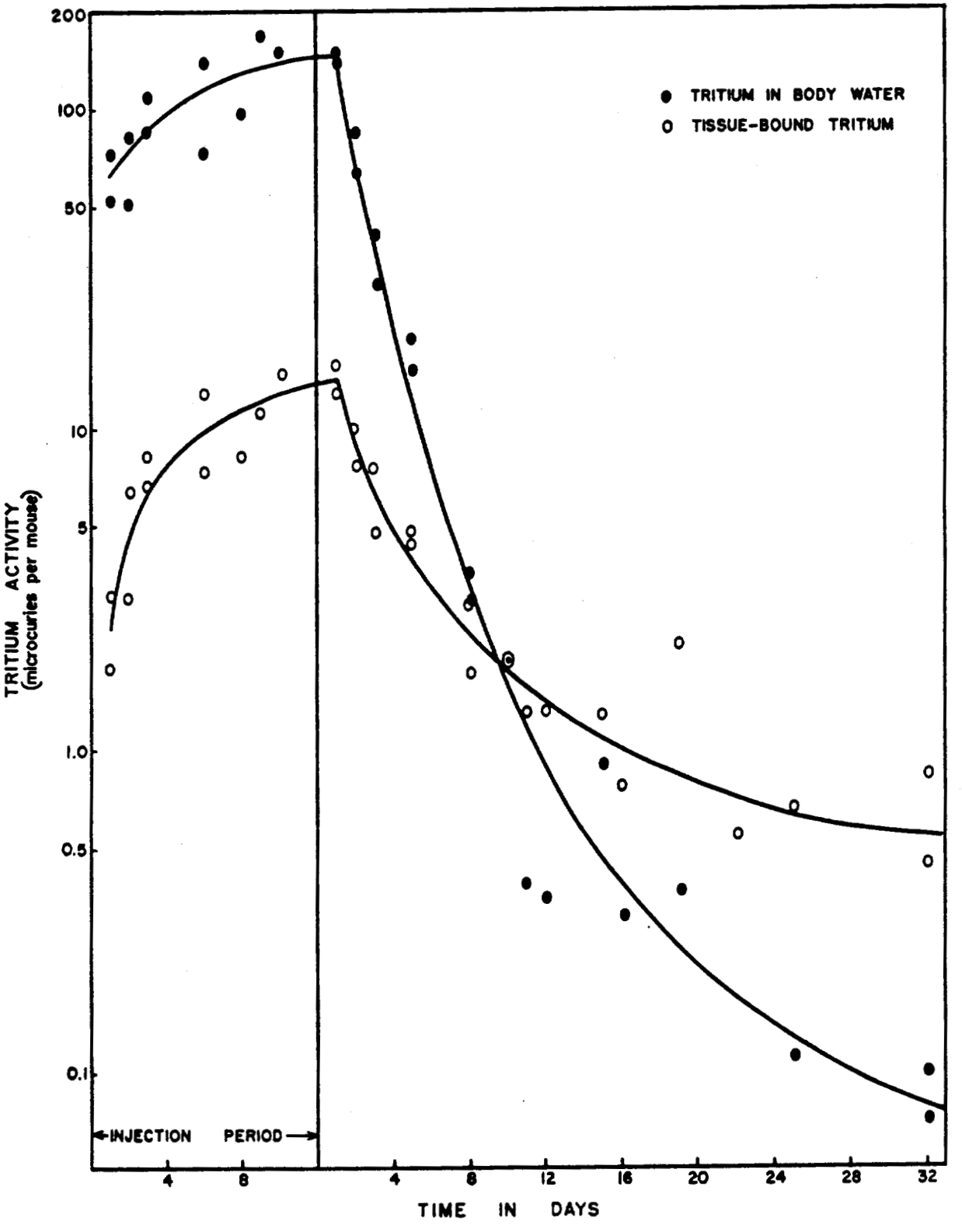

FIGURE 1. RETENTION BY MICE OF TRITIUM ADMINISTERED AS THE OXIDE

standpoint, the presence of even a small fraction of tightly bound tritium is of great significance, especially for the case of chronic exposures. Not only will the total exposure be increased as a result of such binding, but also the estimation of total tritium in a human at any given time will be considerably complicated since all practical routine methods for body tritium estimation (urine analysis, breath analysis, blood analysis, etc) measure only the tritium in body water. In the present experiment, the total radiation received by a mouse from the end of the injection period until total excretion of the tritium is 50 per cent higher when calculated from the sum of the areas under the body water and bound tritium curves than when calculated from the observed 1.1 day half-life of the body water.

The presence of significant quantities of bound tritium also suggests the possible existance of a critical organ other than total body water for chronic exposures. It would be extremely rash, however, to attempt to extrapolate the results of the present preliminary experiment to the point of drawing any conclusions regarding human tritium metabolism. Additional experiments are in progress with mice and rats at higher tritium levels which will permit the extension of the data of the present experiment to cover a much longer period of time and, in the case of the rats, to permit the determination of tritium in individual organs and tissues.

SUMMARY

Thirty-one mice were injected intraperitoneally with tritium oxide. Animals were sacrificed at intervals during and following the injection period. Tritium was determined in body water and in water produced by combustion of the dry animal. The initial biological half-life for tritium in body water was about 1.1 days lengthening to 10-15 days, 32 days after the last injection. Tissue bound tritium was lost with a half-life of about 3 days for the bulk of the activity with about 10 per cent exhibiting an apparent half-life of about 30 days. At the conclusion of the experiment, 32 days after the last injection, 90 per cent of the tritium remaining in the animal was present in the bound state.

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ACKNOWLEDGEMENTS

Tritium analyses were performed by Rosemary B. Holm and Bernice S. Vreeland of the Analytical Group. Audrey Pixley assisted in the distillation and burning of the mice.

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