MASTER

CESIUM, RUBIDIUM, AND POTASSIUM METABOLISM STUDIES OF MUSCLE SEEKING RADIONUCLIDES

Radiobiology Division of the Department of Anatomy
University of Utah, College of Medicine
Salt Lake City, Utah 84112

December 1968

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*from
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Studies of Muscle Seeking Radionuclides

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RETENTION OF INGESTED ^{83}Rb AND ^{137}Cs
BY FOUR PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

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Abstract. Since normal muscle tissue can incorporate rubidium and cesium ions, a double tracer of ^{83}Rb plus ^{137}Cs was administered orally to 4 boys (aged 13-19 years) afflicted with Duchenne muscular dystrophy. The double tracer was also given to 1 healthy man. Total-body retention was determined from 0 to 250 days after administration. Blood samples and excreta were also analysed for radioactivity. About 80% of the excreted Rb and nearly 90% of the excreted Cs was in the urine for each of these 5 subjects. Equivalent biological half-times for Rb and Cs, respectively, were 57 and 130 days in the healthy adult, but averaged only 25 and 16 days in the dystrophic boys. The enhanced elimination of Rb and especially Cs by the dystrophics was mainly because their blood contained an elevated fraction of the retained body burden. Kidney clearance of both Rb and Cs from the blood plasma was in the order of 10 liters per day for all 5 subjects. These data are consistent with the concept that a cellular defect, resulting in altered membrane permeability, may account for the short half-times of Rb and Cs in patients with muscular dystrophy.

INTRODUCTION

Previous studies^(1,2) have shown that patients with advanced muscular dystrophy exhibit abnormally short equivalent biological half-times** for ^{137}Cs : ten boys afflicted with Duchenne dystrophy had equivalent biological half-times averaging 22% of the normal value for their age (4 to 18 years). These studies were based on the measurement of body burdens and excretion rates utilizing environmental ^{137}Cs from fallout. Since the equivalent biological half-time is a weighted average of all the component half-times of a multi-exponential retention function, the single value computed for

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**Equivalent biological half-time = $0.693 \frac{\text{body content}}{\text{excretion rate}}$

each subject using this technique neither indicated the number of components in his retention equation nor their relative magnitude. On the other hand, retention measurements following a single intake of ^{137}Cs can show the number and size of components in a multi-exponential retention function as well as their individual half-times. Comparison of these parameters with corresponding ones for normal individuals might yield additional information about the way in which dystrophy affects the metabolism of cesium and other muscle-seeking alkali metals.

MATERIALS AND METHODS

^{83}Rb is a suitable nuclide for studying the long-term metabolism of rubidium. Its 83 day physical half-period is significantly longer than the more commonly used isotope, 19 day ^{86}Rb . Since its decay is by electron capture,⁽³⁾ the resulting radiation dose per administered unit activity is relatively low. ^{83}Rb for use in this study was produced at Oak Ridge by the proton bombardment of isotopically enriched ^{84}Sr and the subsequent chemical separation of Rb.

During June 1967, ten ml of sterile saline solution containing 6 μCi ^{83}Rb and 0.8 μCi ^{137}Cs were administered orally to each of four boys severely disabled with Duchenne muscular dystrophy and confined to wheelchairs and to one healthy adult male control subject as shown in Table 1. Urine was collected from the boys continuously (except for brief vacation periods) for about 4 months after the administration of radioactivity. Fecal collections were also made for at least a one week period beginning 1-2 weeks after administration. Total excreta collections were made by the control subject during the first three months; virtually total collections during the next 3 months; and intermittent collections during the remainder of the experiment.

Table 1. Subjects given ^{83}Rb and ^{137}Cs .

<u>Subject</u>	<u>Age (yr)</u>	<u>Weight (kg)</u>	<u>Height (cm)</u>
LS*	19	47.3	162
KS*	16	19.8	148
DH	14	68.8	138
CM	13	37.9	155
CWM (control)	37	79.7	178

*LS and KS were brothers.

Total-body retention of the administered $^{83}\text{Rb} + ^{137}\text{Cs}$ was measured inside a low background room constructed of 12 inch thick steel plate, using a total-body counter with two 8 x 4 inch NaI(Tl) crystals suspended about 60 cm above an isoresponse surface upon which the subject reclined (Figure 1). Data were recorded by a 400 channel pulse-height analyser. Severe contractions in the dystrophic boys resulted in non-standard body configurations. Therefore, to minimize positioning errors, at every subsequent count each boy's position was made to conform with the position shown in his photograph taken in the positioner at the initial count. Radioactivity in excreta samples was also measured inside the low background chamber using an 8 x 4 inch NaI(Tl) crystal. Blood samples obtained from all of the subjects and a semen sample obtained from the adult control subject were similarly assayed for ^{83}Rb and ^{137}Cs using Knothole,⁽⁴⁾ a side-well NaI crystal. Net counting rates at 0.53 MeV (^{83}Rb) and 0.66 MeV (^{137}Cs) were corrected for contributions from other gamma-ray emitters and were compared with net counting rates of ingestion duplicates prepared in appropriate phantoms. Calculations were done on a Control Data Corporation (CDC) Model 405 computer. The total-body counter was calibrated for each subject via his individual excreta measurements.

RESULTS AND DISCUSSION

Total-body retention.

Results of total-body counting are shown in Tables 2-6 and in Figures 2-6. Values obtained on the day before administration (-1) indicated that fallout ^{137}Cs content of the boys was low (< 1 nCi) and that the corrected net counting rates at 0.53 MeV of the pre-administration spectra of all subjects were negligible. The fallout ^{137}Cs content of control subject CWM was about 10 nCi but was only about 1% of the administered ^{137}Cs activity. Therefore, no subsequent correction for fallout ^{137}Cs content was made for any of the subjects. Most striking is the observation that whereas the administered ^{137}Cs was retained more tenaciously than ^{86}Rb by the control subject, the reverse was true for the dystrophic patients. The retention of both elements was considerably lower in the dystrophics than in the control subject, and this difference was especially pronounced for ^{137}Cs .

A variety of retention equations can describe the data shown in each of Figures 2-6. We have elected to represent the retention of Rb and Cs by our subjects as sums of exponentials. Equations were fitted to the data with the aid of a CDC 405 computer and a Univac 1108 computer. The equation which gave a reasonable fit with the fewest number of exponentials was selected from the series generated for each set of data. Equations other than the ones given in Figures 2-6 may represent the measured points at least as well. The interested reader is encouraged to use the data given in Tables 2-6 to produce his own version of the retention equations and to subject them to his own interpretations.

Tables 7 and 8 summarize the retention data as described by the equations obtained. Again, it is obvious that although there were

Table 2. Measured total-body biological retention
in dystrophic subject LS.

DAYS AFTER ADMINISTRATION	PERCENT OF INGESTED ACTIVITY	
	<u>^{83}Rb</u>	<u>^{137}Cs</u>
-1	0.005%	0.02%
0	100.0%	100.0%
1	92.2	91.4
2	84.1	82.2
3	81.5	82.7
4	78.4	73.6
5	76.4	72.6
7	66.3	60.6
8	67.0	60.8
9	63.9	56.4
10	62.1	53.9
11	58.6	51.5
14	46.5	44.2
16	52.2	41.6
18	47.8	34.2
26	38.0	25.7
33	32.9	21.3
40	25.7	15.4
47	21.9	11.8
63	14.8	6.71
77	9.31	3.65
99	5.35	1.74
124	2.44	0.674
152	1.14	0.354
187	0.600	0.140
222	0.347	0.076
250	0.280	0.100

Table 3. Measured total-body biological retention
in dystrophic subject KS.

<u>DAYS AFTER</u> <u>ADMINISTRATION</u>	<u>PERCENT OF INGESTED ACTIVITY</u>	
	<u>^{83}Rb</u>	<u>^{137}Cs</u>
-1	(-)0.002%	0.02%
0	100.0%	100.0%
1	97.4	90.1
2	96.0	87.5
3	81.6	80.6
4	82.6	75.3
5	79.9	74.2
7	68.7	61.3
8	69.7	62.3
9	68.2	59.9
10	63.2	53.6
11	62.4	52.6
14	49.0	41.4
16	56.0	43.9
18	47.7	35.6
26	38.0	26.8
33	33.2	21.6
40	26.4	15.3
47	23.4	12.4
63	15.7	7.66
77	10.3	4.44
99	5.97	2.06
124	3.37	0.936
152	2.03	0.595
187	1.28	0.210
222	0.977	0.100
250	0.668	0.137

Table 4. Measured total-body biological retention
in dystrophic subject DH.

<u>DAYS AFTER</u> <u>ADMINISTRATION</u>	<u>PERCENT OF INGESTED ACTIVITY</u>	
	<u>⁸³Rb</u>	<u>¹³⁷Cs</u>
-1	0.002%	0.06%
0	100.0%	100.0%
1	99.2	95.7
2	87.7	89.4
3	86.6	81.7
4	88.3	84.3
6	80.9	73.7
8	78.3	70.2
11	66.8	63.5
14	61.2	55.2
17	62.5	48.7
20	54.4	43.8
22	58.8	40.8
23	55.0	41.4
25	52.6	38.7
30	47.6	34.4
38	39.1	25.7
46	32.8	19.4
53	25.6	15.6
62	21.6	12.8
76	14.8	8.01
102	8.16	3.87
123	4.88	1.97
151	2.66	1.21
186	1.53	0.584
221	0.974	0.313
251	0.798	0.130

Table 5. Measured total-body biological retention in dystrophic subject CM.

DAYS AFTER ADMINISTRATION	PERCENT OF INGESTED ACTIVITY	
	<u>⁸³Rb</u>	<u>¹³⁷Cs</u>
-1	(-)0.006%	(-)0.02%
0	100.0%	100.0%
1	97.1	96.5
2	87.5	88.3
3	89.1	82.6
4	88.9	82.3
6	84.3	73.7
8	81.3	68.6
11	76.1	62.7
17	75.2	48.8
20	61.3	42.5
22	56.9	36.0
23	49.6	34.9
25	54.9	32.2
30	44.4	27.4
38	41.7	22.7
46	36.4	16.0
53	30.1	13.3
62	25.5	9.80
76	17.1	5.91
99	9.49	2.87
123	4.87	1.04
151	2.38	0.529
186	1.42	0.376
251	0.811	0.088

Table 6. Measured total-body biological retention
in control subject CWM.

<u>DAYS AFTER ADMINISTRATION</u>	<u>PERCENT OF INGESTED ACTIVITY</u>	
	<u>^{83}Rb</u>	<u>^{137}Cs</u>
-1	(-)0.006%	1.3%
0	100.0%	100.0%
1	98.1	96.0
2	97.1	94.5
3	95.5	92.8
4	93.7	91.8
5	90.6	91.0
6	89.0	90.2
7	88.4	89.7
10	85.4	87.9
13	83.4	86.6
17	80.0	84.7
20	76.9	83.1
22	75.4	82.3
26	72.2	80.7
28	70.3	79.8
33	65.0	77.4
41	58.7	73.0
49	54.4	68.4
56	51.8	69.1
65	46.3	66.3
79	39.2	61.5
101	32.1	55.1
125	23.4	47.6
153	17.8	43.2
188	10.7	35.1
224	6.49	30.5
252	4.80	26.6

Table 7. Components in the retention equations of four dystrophic boys and one healthy adult given ^{86}Rb orally. ^{86}Rb data for a healthy Japanese man (NY)⁽⁵⁾ and 3 Los Alamos men⁽⁷⁾ are also tabulated for comparison.

SUBJECT	Rapid Component		Intermediate Component		Long Component		Equiv. Biol.
	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	$T_{1/2}(\text{d})$
LS	15.3	2.1	82.4	20.9	2.3	79.6	19.4
KS	15.8	4.3	78.6	22.1	5.6	82.9	22.7
DH	----	---	96.1	24.5	3.9	97.2	27.3
CM	----	---	93.3	26.8	6.7	63.6	29.3
Average for dystrophics							24.7
CWM	3.5	3.8	----	----	96.5	59.2	57.
NY ⁽⁵⁾	6.9	6.5	----	----	93.1	53.2	50
3 men ⁽⁷⁾	10.0	4.0	----	----	90.0	95.0	86.

Table 8. Components in the retention equations of four dystrophic boys and one healthy adult given ^{137}Cs orally. ^{137}Cs data for a healthy Japanese man (NY)⁽⁵⁾ and ^{134}Cs and ^{137}Cs data for 4 Los Alamos men⁽⁷⁾ are also tabulated for comparison.

SUBJECT	Rapid Component		Intermediate Component		Long Component		Equiv. Biol.
	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	$T_{1/2}(\text{d})$
LS	23.3	3.7	75.7	16.2	1.0	68.6	13.8
KS	35.3	3.7	57.0	17.4	7.7	38.9	14.2
DH	13.9	4.4	74.2	18.9	11.9	40.9	19.5
CM	4.7	0.95	89.6	16.9	5.7	42.2	17.6
Average for dystrophics							16.3
CWM	7.6	1.5	----	----	92.4	140.0	130
NY ⁽⁵⁾	8.0	0.9	----	----	92.0	71.5	66
4 men ⁽⁷⁾	16.0	3.0	----	----	84.0	144.0	121

differences among the dystrophic boys, their retention of Rb and Cs was very much different from that of the adult control subject. The calculated equivalent biological half-times (average of all the component half-times in a retention equation each weighted by its relative component size) are shown in the last column of Tables 7 and 8. The average equivalent biological half-time for ^{137}Cs in the boys (16.3 days) agrees quite well with the 13.9 day average previously measured in 10 dystrophic boys using dietary environmental ^{137}Cs from fallout.⁽²⁾ Three of these 4 subjects were also included in the earlier study, and although they were almost 2 years older at the time the second study was begun, their equivalent biological half-times were only slightly longer (Table 9). The value

Table 9. Comparison of equivalent biological half-times using environmental and administered ^{137}Cs .

SUBJECT	EQUIVALENT BIOLOGICAL HALF-TIME	
	<u>Environmental Cs⁽²⁾</u>	<u>Administered Cs</u>
CM	11 $\pm$ 6 days	17.6 days
KS	12 $\pm$ 7	14.2
LS	12 $\pm$ 7	13.8
CWM	144 $\pm$ 7	130

obtained in this study for the adult control subject of 130 days compares reasonably well both with the average measured previously of 105 ± 25 days for adult men and with the average of 144 ± 7 days for this same individual based on total body counting and 19 excreta collections made over a 3 year period.⁽²⁾

The average equivalent biological half-time for ^{86}Rb in these 4 dystrophic boys of 24.7 days agrees closely with the 27.2 day value for

^{86}Rb in 7 Japanese subjects afflicted with Duchenne muscular dystrophy studied by Nagai et al. ^(a)

Ratios of equivalent biological half-times ($^{137}\text{Cs}/^{86}\text{Rb}$) were 0.66 (0.60 to 0.71) for the dystrophic boys but 2.27 for adult subject CWM. The average ^{86}Rb equivalent half-time for the boys (24.7 days) was 43% of the 57.3 day value for adult subject CWM while the average ^{137}Cs equivalent half-time for the boys (16.3 days) was only 13% of the 130 day value for CWM. Equivalent biological half-times for ^{137}Cs in the 4 boys were between 15% and 25% of the equivalent half-times for normal boys of the same age. ^(a)

In adult men about 90% of the ingested cesium tracer is associated with a long-term component, ^(7,8) (Table 8) and, presumably, somewhat similar partitioning may exist for normal adolescent boys. However, for the dystrophic boys, only 1 to 12% of the ingested cesium was associated with a long-term component (Table 8). In addition, the half-times of these longest-term components (39 to 69 days) were less than the equivalent biological half-times for normal boys aged 13 to 19 years of 70 to 95 days, ^(a) which are, by definition, shorter than their longest-term components. Our data suggest that in these 4 dystrophic boys, ^{137}Cs did not appear to be retained within "normal" cesium-bearing tissue in significant amounts long after intake.

Immediately apparent in Table 7 is the small, long-term component of the dystrophic boys' retention equation for ^{86}Rb . Autopsy samples were obtained from subject (CM) 300 days after the administration of radioactivity and from subject (KS) 333 days after administration, considerably after total-body ^{86}Rb or ^{137}Cs was no longer detectable. No ^{137}Cs could be detected in any of the tissues, and no ^{86}Rb could be found except in bone.

The biological concentration of ^{83}Rb in cortical bone was 2.6×10^{-6} dose/g for CM and 1.5×10^{-6} dose/g for KS. The respective concentrations in samples containing both cortical and trabecular bone were 3.6 and 2.0 times lower. Perhaps the small, long-lived component in the retention equation of ^{83}Rb for dystrophic boys is associated with the deposition of activity in the skeleton. Thomas and Thomas⁽⁹⁾ have reported a small, long-lived component in the multi-exponential retention equation for ^{137}Cs in rats attributed to skeletal retention.

Half times for Cs are considerably longer in adults than in children and adolescents.^(2,10,11) This may also be true of Rb. Therefore, a man 37 years of age is certainly not an appropriate control for a group of teen-aged dystrophic boys. We hope to obtain ^{83}Rb and ^{137}Cs retention data in a few non-affected male siblings of corresponding age in order to determine whether age or the disease state is associated with the greater retention of Rb relative to Cs and to establish the Rb half-time in non-dystrophic boys. The number of components in the ^{137}Cs retention equation of normal boys, their half-times, and the percentage that each represents would be also of great interest.

^{83}Rb and ^{137}Cs in urine and feces.

No great differences were seen in the partitioning of either ^{83}Rb or ^{137}Cs between urine and feces by the 4 dystrophic boys and the control subject (Table 10). For each of the boys, the ^{83}Rb or ^{137}Cs activity excreted in the urine was totaled for the coincident time period during which the fecal collections were made. In all cases, the time of beginning was considered to be the last time that the bladder or bowel was emptied

Table 10. Urinary fraction (Urine/Total) of ^{83}Rb and ^{137}Cs excretion.

<u>Subject</u>	<u>Urine/Total Excretion</u>	
	<u>^{83}Rb</u>	<u>^{137}Cs</u>
LS	0.84	0.81
KS	0.90	0.93
DH	0.72	0.85
CM	<u>0.79</u>	<u>0.88</u>
Average	0.81	0.87
CWM	0.77	0.88
Ref. 10		0.85
Ref. 11		0.80
Ref. 12		0.86
Ref. 13	0.77	
Ref. 5	0.68	

prior to the start of the collection period. Subject (KS) defecated infrequently, and only a single fecal sample was obtained during this study. Therefore his fecal elimination of ^{83}Rb and ^{137}Cs may have been abnormally low during this period. The collection period for control subject CWM included the entire first three months after administration. His calculated (urine/total) values for any sufficiently long subdivision of the 3 month period or for subsequent periods of collection were very similar to the 3 month averages. Agreement of the urinary fraction of Cs excretion with that reported in other studies^(10,11,12) is excellent, as is the agreement of the urinary fraction of Rb excretion with the data of Ray, Threefoot, and Burch.⁽¹³⁾ Agreement of our data with that of Yamagata et al.⁽⁵⁾ for subjects on Japanese diets is not as good however (see Table 10).

^{83}Rb and ^{137}Cs in blood and semen.

Venous blood samples, which were carefully separated into plasma and erythrocyte fractions, showed that the relative partitioning of total blood activity between the erythrocytes and plasma was similar in our 5 subjects (Table 11).

Table 11. Relative concentration (percent administered activity of ^{83}Rb and ^{137}Cs per gram) in erythrocytes and blood plasma.

<u>Subject</u>	<u>No. of Samples</u>	<u>Erythrocyte concentration Plasma concentration</u>	
		<u>$^{83}\text{Rb}^*$</u>	<u>$^{137}\text{Cs}^*$</u>
LS	2	24.4 ± 1.7	6.6 ± 1.6
KS	2	25.4 ± 1.6	7.4 ± 0.6
DH	2	23.4 ± 2.5	7.7 ± 2.5
CM	2	28.6 ± 4.2	6.8 ± 1.1
Average (dystrophics)		25.4 ± 2.2	7.2 ± 0.5
CWM	5	21.3 ± 2.3	9.3 ± 3.5

*Average and experimental standard deviation

The concentration of ^{83}Rb and ^{137}Cs in a subject's plasma was compared with the urinary excretion rate at the time of blood withdrawal. Clearances of activity from the plasma by the kidney could then be calculated (Table 12). No great differences between the control subject and the dystrophic boys were evident. Therefore, three additional comparisons were made. Table 13 shows the results obtained by dividing each subject's kidney clearance in liters per day by (a) his weight, or by (b) his body surface area, in an attempt to adjust the data in Table 12 for the relative sizes of the individual subjects.

Table 12. Kidney clearance of ^{83}Rb and ^{137}Cs from the plasma (Liters Plasma/Day).

<u>Subject</u>	<u>^{83}Rb (Liters/Day)</u>	<u>^{137}Cs (Liters/Day)</u>	<u>Rb/Cs</u>
LS	9.0	11.9	0.76
KS	5.8	8.1	0.72
DH	6.9	10.8	0.64
CM	<u>6.8</u>	<u>8.6</u>	<u>0.79</u>
Average (dys.)	7.1	9.8	0.73
CWM	10.1	9.6	1.05

Table 13. Kidney clearance of ^{83}Rb and ^{137}Cs from the plasma adjusted for body mass (kg) and for body surface area (m^2).

<u>Subject</u>	<u>Body* Surface Area (m^2)</u>	<u>^{83}Rb</u>		<u>^{137}Cs</u>	
		<u>Liters/Day</u> kg	<u>Liters/Day</u> m^2	<u>Liters/Day</u> kg	<u>Liters/Day</u> m^2
LS	1.42	0.19	6.34	0.25	8.38
KS	0.86	0.29	6.74	0.41	9.42
DH	1.62	0.10	4.26	0.16	6.67
CM	1.24	<u>0.18</u>	<u>5.48</u>	<u>0.23</u>	<u>6.94</u>
Average (dys.)		0.19	5.70	0.26	7.85
CWM	1.94	0.13	5.21	0.12	4.95

*Body surface area calculated from the formula of Brody et al. ⁽¹⁴⁾:
 $A = 0.024 (W^{0.53}) (H^{0.40})$ where A = body surface area in m^2 , W = weight in kg, H = height in cm.

The plasma volume for control subject CWM was calculated by the formula given on p. 66 of Ref. 15 which relates plasma volume to body weight for normal males. Lacking specific data for dystrophics and because Moore et al. ⁽¹⁵⁾ imply that plasma fractions are not greatly affected by wasting diseases, plasma volumes for the dystrophic boys were also calculated by this formula. These plasma volumes were used with data of Table 12 to

estimate the equivalent number of times per day that the activity in the total plasma was cleared by the kidney. Results of these calculations are shown in Table 14.

Table 14. Kidney clearance of ^{83}Rb and ^{137}Cs from the plasma.

Subject	Estimated Plasma Volume (Liters)*	Plasma Volumes Cleared Per Day	
		^{83}Rb	^{137}Cs
LS	2.416	3.7	4.9
KS	1.550	3.7	5.2
DH	3.092	2.2	3.5
CM	2.120	3.2	4.1
Average (dystrophics)		3.2	4.4
CWM	3.435	2.9	2.8

*Plasma volumes estimated from the formula of Moore *et al.* (15):
 $PV = 927 + 31.47 W$, where PV = plasma volume in ml and W = body weight in kg. This formula may underestimate plasma volumes in dystrophic patients with very little subcutaneous adipose tissue such as LS, KS, and CM.

Nowhere in Tables 12-14 are the differences between the control and dystrophics in kidney clearance rates large enough to entirely account for the observed differences in total body retention, especially of ^{137}Cs . Tables 13 and 14 indicate that adjusted kidney clearance rates in the dystrophic boys may have been somewhat higher than in the adult control subject. Ratios of these rates (boys/control) were about 1.1 to 1.5 for ^{83}Rb and about 1.6 to 2.2 for ^{137}Cs , whereas the rates of elimination by the boys were greater than the control by 2.3 times for ^{83}Rb and 8.0 times for ^{137}Cs (Tables 7 and 8). Therefore, all of the difference in retention between dystrophics and normals cannot be accounted for by a difference in kidney clearance rates. The fraction of excreted radioactivity in the urine for both ^{83}Rb and ^{137}Cs was similar for the

dystrophics and the control subject in our study (Table 10). Normal kidney function, relative to body surface area, in patients with Duchenne dystrophy has been shown by inulin and para-aminohippurate clearance studies.⁽¹⁶⁾ Thus it appears unlikely that the enhanced elimination rates for ^{83}Rb and ^{137}Cs by patients with Duchenne dystrophy was a consequence of altered renal function.

Plasma levels of ^{83}Rb and especially ^{137}Cs relative to the body burden were correspondingly higher in dystrophics (Table 15).

Table 15. Comparison of plasma and total-body concentrations of ^{83}Rb and ^{137}Cs .

<u>Subject</u>	<u>Number of Measurements</u>	<u>Plasma Concentration</u> <u>Body Concentration</u> $\times 10^{-2}$ *	
		<u>^{83}Rb</u>	<u>^{137}Cs</u>
LS	2	17.1 ± 1.1	21.8 ± 4.8
KS	2	10.2 ± 0.7	12.8 ± 1.4
DH	2	17.6 ± 2.5	16.8 ± 1.8
CM	2	12.7 ± 3.7	16.8 ± 0.1
Average (dystrophics)		14.4 ± 3.6	17.1 ± 3.7
CWM (control)	5	6.5 ± 0.7	4.9 ± 2.3
Dystrophics/control		2.2	3.5

*Average $\pm$ Experimental Standard Deviation

These findings tend to give support to the possibility that the anomalous retention observed in dystrophics is due to a defect resulting in abnormal membrane permeability in some cells. Erythrocytes appear to be relatively unimpaired in their ability to concentrate Rb or Cs (Table 11).

A comparison of ^{83}Rb and ^{137}Cs concentration in erythrocytes with the concentration in the total body on the same day (Table 16) showed

Table 16. Comparison of total-body and erythrocyte ^{83}Rb and ^{137}Cs concentration.

<u>Subject</u>	<u>Number of Measurements</u>	<u>Body Concentration</u>	
		<u>Erythrocyte Concentration</u>	
		<u>^{83}Rb*</u>	<u>^{137}Cs*</u>
LS	2	0.241 ± 0.001	0.709 ± 0.014
KS	2	0.388 ± 0.054	1.07 ± 0.028
DH	2	0.244 ± 0.011	0.803 ± 0.184
CM	2	0.284 ± 0.042	0.855 ± 0.148
Average (dystrophics)		0.289 ± 0.068	0.867 ± 0.154
CWM	5	0.728 ± 0.029	2.71 ± 0.75

*Average $\pm$ Experimental Standard Deviation

that, in dystrophics, the total body concentrated ^{83}Rb only about 29% as well as erythrocytes, while, in our control, the total body concentrated ^{83}Rb about 73% as well as erythrocytes. For ^{137}Cs , the (total body/erythrocyte) ratios were almost 90% for the dystrophics but about 270% for the control. There was about a factor of 3 discrepancy for each nuclide between the ratios for the dystrophics and the control. Based on the measurement of stable rubidium in blood and excreta, data of Wood⁽¹⁷⁾ allow the concentration ratio of (total body/erythrocytes) to be calculated for subject (DH) and for subject (CWM). Stable Rb values give 0.233 for (DH) and 0.704 for (CWM), in good agreement with the values reported in Table 16 of 0.244 and 0.728, respectively. It appears that the radioactive ^{83}Rb was truly a tracer for stable Rb in the total-body and erythrocytes of these 2 subjects.

A composite 9.2 g semen sample was obtained from the control subject spanning the period 19 to 21 days after tracer administration. Concentration of activity in the semen was about 6.0 and 1.6 times the concentration

in blood plasma during this same period for ^{83}Rb and ^{137}Cs , respectively, while the semen concentration was 0.27 and 0.29 that of the erythrocytes. This was probably because the cell fraction of semen is intermediate between plasma and erythrocytes. The cells in semen probably concentrated ^{83}Rb and ^{137}Cs in about the same relative proportions as did erythrocytes.

Comparison of potassium with rubidium and cesium.

The total potassium content of each subject and of each excreta sample were obtained via the 1.46 MeV gamma-ray associated with the radioactive decay of the natural emitter ^{40}K . These data were used to calculate the equivalent biological half-time for the subjects in our study (Table 17).

Table 17. Measured equivalent biological half-times for potassium compared with those for rubidium (see Table 7) and cesium (see Table 8). Also shown are K and Cs values of two healthy boys KO and JN (aged 13 and 17 years) for comparison. ^(2,18)

Subject	Body K Content (g)	Potassium Concentration (gK/kg body)	Equivalent Biological Half-Time (days)		
			K	Rb	Cs
LS	35	0.74	13.4	19.4	13.8
KS	21	1.06	8.0	22.7	14.2
DH	37	0.54	13.4	27.3	19.5
CM	29	0.77	16.5	29.3	17.6
Average (dystrophics)		0.78	12.8	24.7	16.3
KO	86	2.09	20	----	77
JN	169	2.32	33	----	88
Average (normal boys)		2.20	26		82
CWM	151	1.89	34	57	130

Note that for control subject CWM, the rubidium half-time was nearly twice, and the cesium half-time was nearly 4 times as long as that for potassium. For the dystrophic boys, the rubidium half-time was similarly about twice

as long as the potassium half-time, but the cesium half-time was almost equal to that for potassium. Corresponding values of the ratio of cesium half-time and potassium half-time of about 3.7 and 1.7, respectively, were observed in 13 normal men and 3 normal children aged 5 to 9 years, (10) while the average ratio for the two healthy teen aged boys shown in Table 17 was about 3.2, which is intermediate between these values for men and young children.

These data suggest that advanced muscular dystrophy may cause body cells to lose (to a large extent) their ability to distinguish between potassium and cesium atoms.

CONCLUSIONS

Total-body retention data for Rb and Cs in healthy teen-aged boys are needed before final conclusions about the retention curves observed in dystrophic boys can be drawn. Of special interest will be the relative retention of these two elements by normal boys, since there was a reversal in dystrophics compared with a number of healthy adults.

The enhanced elimination rate for Rb and especially Cs in dystrophic patients appears to be associated with elevated plasma levels of these elements relative to body content and is not accounted for only by increased kidney clearance rates. The observed differences between dystrophics and non-dystrophics may result from failure of some cells in dystrophics to incorporate or retain these alkali metal ions as well as the cells of normal subjects.

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Figure 1. Photograph of the human total-body counter showing the two 8 x 4 inch NaI(Tl) crystals suspended above an isoresponse surface upon which the subject is positioned for counting. The subject (SM) shown here is a healthy 8 year old girl 133 cm tall weighing 26 kg.

Figure 2. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in dystrophic subject LS.

Figure 3. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in dystrophic subject KS.

Figure 4. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in dystrophic subject DH.

Figure 5. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in dystrophic subject CM.

Figure 6. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in control subject CWM.

POTASSIUM CONCENTRATIONS AND TISSUE WEIGHTS IN
THREE PATIENTS DYING WITH DUCHENNE
MUSCULAR DYSTROPHY

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Abstract: Following the death of 3 severely disabled dystrophic boys (aged 14-17 years and weighing 40-50 lbs.) selected tissues were weighed wet and evaluated for potassium content. Organ weights were abnormally small except for the brain which was normal. Although skeletal muscle contains 84 g of potassium in standard man, it contained only about 2-6 g of potassium in each of these dystrophic boys. Dystrophic skeletal muscle was white in color with many of the muscle cells being replaced by fat and fibrous connective tissue. Its potassium concentration was extremely low, averaging only about 1/4 of the normal 3 g/kg for healthy skeletal muscle. In contrast, dystrophic G.I. tract (which contains smooth muscle) and dystrophic heart muscle had concentrations which were normal for these tissues. Normal concentrations were also found in adipose tissue, skin, brain, lungs, kidneys, pancreas and testes. Concentration in the liver was low in 1 patient; but normal in the other 2. However, potassium concentration in the spleen and in samples of skeleton (bone + marrow) were below normal range in the 3 patients. These combined results indicate that the observed reduction of total body potassium in patients with advanced Duchenne muscular dystrophy is principally a result of decreased potassium in the remaining skeletal muscle.

INTRODUCTION

Patients with advanced muscular dystrophy have markedly reduced concentrations of total body potassium.⁽¹⁻⁵⁾ Is this primarily due to (a) loss of muscle mass, (b) reduction of potassium concentration in muscle, or (c) reduced potassium concentration in other tissues? As will be shown, the effect is primarily due to (a) and (b), at least for the Duchenne type of dystrophy.

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MATERIALS AND METHODS

Tissue samples were obtained at autopsy from 3 dystrophic patients who had died suddenly as a result of acute respiratory insufficiency incident to their disease. All were severely disabled and wasted. Height was estimated with a flexible steel tape bent to conform to the abnormal curvature of the spine (scoliosis) and to the inability to straighten the hip and knee joints (contractures). Body weight was estimated from previous weighings taken several months prior to death, and from the appearances of the bodies at autopsy. It is unfortunate that a suitable scales for measuring body weight was unavailable in the autopsy room, but we believe that true weights at death were within the limits given in Table 1.

Table 1. Patients included in this study. True heights and weights are believed to be within the limits shown.

<u>Subject</u>	<u>Age (yr.)</u>	<u>Height (cm)</u>	<u>Weight at death (kg)</u>	<u>years in wheelchair</u>
CM	14	155 $\pm$ 5	23 $\pm$ 3	4
JM	15	135 $\pm$ 5	23 $\pm$ 3	7
KS	17	148 $\pm$ 5	19 $\pm$ 1	9

Samples were weighed while fresh, put in plastic bags, and inserted in #2 cans (8 cm diameter by 11 cm height) for non-destructive potassium analysis by counting the 1.46 MeV γ -rays from ^{40}K , a naturally radioactive potassium isotope. Samples were placed for counting between two 8 inch by 4 inch NaI(Tl) scintillation crystals with their faces 10 cm apart. These detectors were operated within a low-background room constructed of 12 inch thick steel plate. The summed output of the 2 crystals was

recorded by a 400 channel pulse-height analyzer. The net counting rate for each sample in the photopeak band for ^{40}K (1.35 - 1.57 MeV) was corrected for the effect of sample size on γ -ray self absorption, and was then compared to the net counting rate of a canned potassium standard. Counting periods for samples (and backgrounds) were 30-1000 minutes each, depending on the potassium content of the sample.

The visceral samples were rather complete, but only fractions of the total muscle, adipose tissue, skeleton and skin were obtained. Autopsies were finished within 6-12 hours following death.

RESULTS AND DISCUSSION

Potassium concentrations measured in the dystrophic boys (Table 2) are compared with Tipton's values for standard man (based on the analysis of 150 adult victims of accidental death within the U.S.A.).⁽⁶⁾ Eighty percent of this non-dystrophic population had concentrations between the tabulated 10% and 90% values, which we will regard as the normal range.

Concentrations in most of the dystrophic tissues fell within normal range, but there were important exceptions. Most striking was the extremely low potassium concentration in skeletal muscle. This was expected because of the progressive destruction of skeletal muscle cells and their partial replacement by fat and fibrous connective tissue as the disease advances.⁽⁷⁾

In addition, concentrations for all 3 patients were below the normal range in the spleens and in samples of skeleton (vertebral bodies plus proximal and distal ends of femurs*). Liver concentration was low for

*Potassium concentration for the skeleton of standard man is based on the assay of rib samples.⁽⁶⁾ It is unknown whether this might account for some of the difference.

Table 2. Potassium concentrations (g/kg $\pm$ statistical counting error) in tissues from 3 boys with Duchenne dystrophy compared with values for standard man.⁽⁶⁾

<u>Tissue</u>	Dystrophic Boy C.M.	Dystrophic Boy J.M.	Dystrophic Boy K.S.	<u>Median</u>	<u>Standard Man</u> <u>10% value</u>	<u>90% value</u>
Muscle (calf + thigh)	1.07 $\pm$ 0.19	0.88 $\pm$ 0.37	0.46 $\pm$ 0.21	3.00	2.11	- 4.29
Calf muscle	-----	1.18 $\pm$ 0.26	0.38 $\pm$ 0.16	3.00	2.11	- 4.29
Thigh muscle	-----	0.65 $\pm$ 0.19	0.52 $\pm$ 0.13	3.00	2.11	- 4.29
Adipose	0.49 $\pm$ 0.16	0.35 $\pm$ 0.06	-----	0.32	0.14	- 0.90
Skeleton	0.75 $\pm$ 0.04	0.56 $\pm$ 0.04	0.53 $\pm$ 0.04	1.50	1.00	- 1.90
Skin	-----	0.62 $\pm$ 0.19	0.64 $\pm$ 0.10	0.86	0.47	- 1.18
Liver	2.67 $\pm$ 0.11	2.36 $\pm$ 0.09	1.39 $\pm$ 0.10	2.50	1.72	- 3.61
Brain	2.92 $\pm$ 0.11	3.16 $\pm$ 0.19	2.94 $\pm$ 0.11	3.00	2.07	- 4.07
G.I. Tract	1.70 $\pm$ 0.16	1.98 $\pm$ 0.09	1.87 $\pm$ 0.07	1.25	0.61	- 2.08
Lungs	1.33 $\pm$ 0.23	2.34 $\pm$ 0.11	1.88 $\pm$ 0.18	1.90	-----	-----
Heart	2.36 $\pm$ 0.50	2.38 $\pm$ 0.55	2.52 $\pm$ 0.66	2.40	1.80	- 3.43
Kidneys	1.82 $\pm$ 0.24	2.46 $\pm$ 0.16	2.04 $\pm$ 0.28	1.90	1.29	- 2.52
Spleen	2.06 $\pm$ 0.21	1.56 $\pm$ 0.29	1.87 $\pm$ 0.37	3.11	2.22	- 4.61
Pancreas	1.93 $\pm$ 0.43	2.10 $\pm$ 0.50	2.05 $\pm$ 0.59	2.30	1.11	- 3.50
Testes*	-----	2.02 $\pm$ 0.33	2.02 $\pm$ 0.33	2.00	1.20	- 2.83

*Testes from J.M. and K.S. combined into a single sample.

Potassium concentrations below the 10% value for standard man are shown in boldface numerals.

patient K.S. but normal for the other two boys. Microscopic examination revealed central lobular necrosis in the liver cells from KS, but a normal appearance of the liver cells from CM and JM.

The finding of apparently normal concentrations of potassium in the G.I. tract and in the heart was somewhat unexpected in view of the known changes in smooth and cardiac muscle in patients with Duchenne dystrophy⁽⁷⁾.

Tissue weights were measured except where an approximate sign (~) indicates that the weight was estimated (Tables 4-6). Total skeletal muscle was grossly estimated to be about 3 times the muscle sample taken from both legs. Total adipose tissue, exclusive of that within the muscle, skin, and bone marrow, was estimated to be about 5 times the fat sample which was dissected. Shafts of the long bones were markedly reduced in diameter. Consequently the skeletal weight was estimated at 2/3 that of a reference human of the same height. The skeleton (bone plus marrow) of a reference human was assumed proportional to the 3rd power of height and taken as 10 kg for a 174 cm tall standard man.⁽⁶⁾ Skin weight was assumed proportional to body surface area, as calculated by the formula of Brody et al⁽⁶⁾: $A = 0.024 (W^{0.53}) (H^{0.40})$ where A = body surface area in square meters, W = weight in kg, and H = height in cm. Skin was normalized to the 4.9 kg of dermis plus epidermis in standard man whose body surface is 1.8 square meters.⁽⁶⁾

Observed potassium concentrations in the dystrophics were tabulated when available (Tables 4-6). When not available (indicated by asterisk*)

values for standard man were substituted except that a potassium concentration of 1 g/kg was assumed for the residual.

Potassium content was computed as the product of tissue weight and potassium concentration. The summed potassium content from the totaled tissues agreed closely with that measured by total body counting the subjects several months prior to death. The close agreement may be a consequence of the fact that the terminal wasting largely involved the loss of tissues which had low potassium concentrations, such as fat and dystrophic muscle.

Whereas skeletal muscle contains 60% of the total body potassium in standard man, it only contained an estimated 10-20% of body potassium in these dystrophics. The reduced content of potassium in dystrophic skeletal muscle is the combined consequence of reduced muscle mass and a very low potassium concentration in the remaining diseased muscle. The dystrophic muscle was white in color and was composed of surviving muscle cells with a large admixture of fat and fibrous connective tissue. Because of the intimate mixture of these 3 components, it was not possible in this analysis to determine whether the potassium concentration in surviving muscle cells was abnormally low, or whether the low concentration in the composite samples of skeletal muscle was due to the low concentration in its fatty and connective tissue components.

CONCLUSION

These results apply to teenage boys dying with advanced Duchenne muscular dystrophy. Different results might or might not occur in patients disabled with other types of muscular wasting.^(?) Certainly, different effects should be expected in patients whose dystrophy is less advanced.

Table 3. Tissue Composition - Standard Man

Tissue	Weight (g)	Potassium	
		Concentration (g/kg)	Content (g)
Muscle (skeletal)	28000	3.00	84
Adipose	12500	0.32	4.0
Skeleton	10000	1.50	15
Skin	4900	0.86	4.2
Liver	1800	2.50	4.5
Brain	1400	3.00	4.2
G.I. Tract	1200	1.25	1.5
Lungs (2)	1000	1.90	1.9
Heart	350	2.40	0.84
Kidneys (2)	310	1.90	0.59
Spleen	180	3.11	0.56
Pancreas	100	2.30	0.23
Testes (2)	60	2.00	0.12
Residual	8200	2.24§	18.36
Total Body	70000	2.00	140

§Calculated from total body values minus values for the tissues listed. The true potassium concentration in the residual probably averages closer to 1 g/kg because the residual is composed largely of connective tissue, non-trapped blood, and intestinal contents--all of which have low concentrations of potassium.

Table 4. Tissue Composition - Dystrophic C.M.

Tissue	Weight (g)	Potassium	
		Concentration (g/kg)	Content (g)
Muscle (skeletal)	~4000	1.07	4.280
Adipose	~1000	0.49	0.490
Skeleton	~4700	0.75	3.525
Skin	~2600	0.86*	2.236
Liver	650	2.67	1.736
Brain	1350	2.92	3.942
G.I. Tract	920	1.70	1.564
Lungs (2)	300	1.33	0.399
Heart	175	2.36	0.413
Kidneys (2)	220	1.82	0.400
Spleen	140	2.06	0.288
Pancreas	60	1.92	0.115
Testes (2)	~30	2.00*	0.060
Residual	~6855	1.00*	6.855
Total Body (autopsy 8 Apr 68)	~23000	1.14	26.3
Total Body (count 19 Feb 68)	29300	1.00	29.4

*Assumed concentrations (see Table 3).

Table 5. Tissue Composition - Dystrophic J.M.

<u>Tissue</u>	<u>Weight</u> <u>(g)</u>	<u>Potassium</u>	
		<u>Concentration</u> <u>(g/kg)</u>	<u>Content</u> <u>(g)</u>
Muscle (skeletal)	~6000	0.88	5.280
Adipose	~2000	0.35	0.700
Skeleton	~3100	0.56	1.736
Skin	~2400	0.62	1.488
Liver	530	2.36	1.251
Brain	1320	3.16	4.171
G.I. Tract	550	1.98	1.089
Lungs (2)	290	2.34	0.679
Heart	160	2.38	0.381
Kidneys (2)	205	2.46	0.504
Spleen	100	1.56	0.156
Pancreas	45	2.10	0.094
Testes (2)	35	2.02	0.070
Residual	~6265	1.00*	6.265
Total Body (autopsy 15 Apr 68)	~23000	1.04	23.9
Total Body (count 31 Jul 67)	36400	0.70	25.4

Table 6. Tissue Composition - Dystrophic K.S.

<u>Tissue</u>	<u>Weight</u> <u>(g)</u>	<u>Potassium</u>	
		<u>Concentration</u> <u>(g/kg)</u>	<u>Content</u> <u>(g)</u>
Muscle (skeletal)	~5000	0.46	2.300
Adipose	~1000	0.32*	0.320
Skeleton	~4100	0.53	2.173
Skin	~2300	0.64	1.472
Liver	550	1.39	0.764
Brain	1400	2.94	4.116
G.I. Tract	750	1.87	1.402
Lungs (2)	360	1.88	0.677
Heart	150	2.52	0.378
Kidneys (2)	150	2.04	0.306
Spleen	55	1.87	0.103
Pancreas	25	2.05	0.051
Testes (2)	28	2.02	0.057
Residual	~3132	1.00*	3.132
Total Body (autopsy 10 May 68)	~19000	0.91	17.3
Total Body (count 20 Jan 68)	19400	1.08	21.0

*Assumed concentrations (see Table 3).

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CESIUM AND RUBIDIUM STUDIES IN MICE

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Abstract. Total-body retention of ^{137}Cs or ^{134}Cs administered by gastric gavage to female C-57 B1 mice was greater in older animals. Equivalent biological half-times for cesium were 2.2 days in 68 day-old mice, 2.6 days in 121 day-old mice, 2.8 days in 152 day-old mice, and 3.6 days in one year old mice. In one 85 day old mouse, the equivalent biological half-time for similarly administered ^{83}Rb was 2.9 days but it was 3.3 days in 5 mice 121 days of age. Pregnancy decreased the excretion rate of both ^{83}Rb and ^{134}Cs in one animal that conceived and delivered a litter of young following double-tracer administration. Concentration of ^{83}Rb in liver exceeded that in the muscle of 2 mice sacrificed one and ten days after administration. Skeletal ^{83}Rb concentration was 66% and 76% that of muscle ^{83}Rb concentration in these two animals.

INTRODUCTION

The metabolism of the alkali metal elements cesium and potassium has been studied⁽¹⁻⁶⁾ in the human as a function of age, sex, disease state and in pregnancy utilizing fallout ^{137}Cs and natural ^{40}K , a component of normally occurring potassium (0.011%).⁽⁷⁾ Rubidium, another alkali metal element, is intermediate in atomic number between cesium and potassium. Retention of rubidium has been studied in several species using the 19 day rubidium isotope, ^{86}Rb , as a tracer;⁽⁸⁻¹²⁾ however, its relatively short physical half-period precludes long-term metabolic studies following a single intake. Eighty-three day ^{83}Rb is a much more suitable nuclide for studying rubidium metabolism because its longer physical half-period and its mode of radioactive decay by electron capture results in a lower radiation dose per administered unit activity than the β -emitter, ^{86}Rb . These considerations make ^{83}Rb the radioisotope of choice for evaluating rubidium metabolism in man.

The experiment reported herein was designed as a pilot study for a

later Rb + Cs tracer investigation in humans*. The following information was sought:

- (a) to verify the lack of chemical toxicity of our ^{83}Rb , ^{134}Cs and ^{137}Cs stock solutions;
- (b) to compare the relative retention of orally-administered Rb and Cs in mice;
- (c) to establish the general pattern of ^{83}Rb concentration in various tissues of the mouse;
- (d) to verify an effect of age at administration on the Cs half-time in mice;
- (e) to find whether pregnancy in the mouse will markedly alter the rate of Cs elimination and/or Rb elimination.

MATERIALS AND METHODS

Female C-57 B1 mice of various ages were given, via gastric gavage, 0.5 ml of distilled water containing 0.2 μCi ^{83}Rb ; or 0.4 μCi ^{137}Cs ; or 0.2 μCi ^{83}Rb + 0.4 μCi ^{134}Cs . All of the animals were housed 2 to a cage, and one of each pair was ear-marked for accurate identification. Only mice given the same type of tracer were put together. The room in which the cages were kept was maintained at a controlled temperature of 70° F. Water and food were available ad libitum.

Three mice 85 days old received the Rb tracer. One of them was sacrificed at 1 day, while another was sacrificed at 10 days after

*See preceeding article, "Retention of ingested ^{83}Rb and ^{137}Cs by four patients with Duchenne muscular dystrophy", in this report.

administration. The ^{83}Rb content of tissue samples from these animals was determined by gamma-ray spectroscopy using Knothole,⁽¹³⁾ a side-well NaI(Tl) detector connected to a 400 channel pulse-height analyser. Three mice 68 days old and three mice about 368 days of age received the ^{137}Cs tracer. Six mice 121 days old received the $^{83}\text{Rb} + ^{134}\text{Cs}$. Seven days later, a male C-57 Bl mouse was placed in each of 2 of the 3 cages containing the $^{83}\text{Rb} + ^{134}\text{Cs}$ animals, thus exposing 4 of the 6 females to the possibility of pregnancy. The males were removed from the cages after two days' occupancy. At 152 days of age, i.e. 31 days after the original tracer, three of the double-tracer mice were also given ^{137}Cs . At that time their original ^{83}Rb and ^{134}Cs body burdens had decreased to less than 1% of the initial value.

Immediately following administration of the tracer and at frequent intervals thereafter, the retention of radioactivity by each mouse was determined by total-body counting. During counting, the animal was held in a lucite cylinder 4.3 cm in diameter and 9.0 cm long which was supported on a lucite platform between two 8 x 4 inch NaI(Tl) crystals with their faces spaced 10 cm apart. These detectors were operated within a low background chamber constructed of 6 inch thick steel plate.⁽¹⁴⁾ Data were recorded by a 400 channel pulse-height analyser. Ampoules containing a duplicate of the administered tracer in 10 ml of solution were also counted on each mouse-counting day. The ampoules were placed in a lucite mouse phantom 0.8 cm thick which rested on the platform between the crystals. Based on data given in Reference 15, the gamma-ray self absorption of 10 ml of solution in an ampoule plus the mouse phantom was calculated to be similar to that produced by the body of a mouse. Correction for the contribution to the counting rate in the primary photopeak by other emitters

was made for each spectrum recorded, by the method of simultaneous equations.⁽¹⁶⁾ The ratio of the corrected net counting rate in the photo-peak of interest in the mouse spectrum to the ampoule spectrum, when normalized to the ratio obtained immediately after administration, yielded the fractional retention in the mouse. In each case, serial counting was continued until the body burden had decreased to less than 1% of the administered activity.

RESULTS AND DISCUSSION

The measured total-body retention values obtained are shown in Figures 1-3 for the mice given ^{137}Cs ; in Figure 4 for the long-term ^{83}Rb mouse; in Figures 5-9 for 5 mice given $^{83}\text{Rb} + ^{134}\text{Cs}$ (3 of these double tracer mice were later given ^{137}Cs , see Figure 2); in Figure 10 for the $^{83}\text{Rb} + ^{134}\text{Cs}$ mouse which delivered a litter of young; and in Figure 11 for the baby mice. Figures 1-9 also exhibit equations which were fitted to each of these sets of experimental data. We have elected to represent the retention of Rb and Cs in these mice by multi-exponential functions. Equations other than those given may also fit the data at least as well; the interested reader is encouraged to produce his own version and to subject the equations thus derived to his own interpretations. Tables of retention values will be furnished for this purpose upon request.

Summaries of the retention equations shown in Figures 1-9 are given in Tables 1-6. The equivalent biological half time for each animal was calculated as an average of all the half-times in the individual retention equation each weighted by its relative component size. The equivalent biological half-time for cesium increased from 2.2 days in 68 day old mice

to 2.6 days in 121 day old mice to 2.8 days in 152 day old mice to 3.6 days in mice about one year of age. Although the measured half-times for mouse M13 following ^{134}Cs administration when 121 days old and following ^{137}Cs administration when 152 days old were similar, with the second being slightly shorter than the first, a clear-cut age effect could be seen in the other two animals given a Cs tracer at these two different ages. The effect of age on the equivalent biological half time for cesium in mice appears to be similar to this effect in humans. The younger animals had shorter half-times. A corresponding age effect on Cs metabolism has been reported by Matsusaka et al. ⁽¹⁷⁾ using intraperitoneal injections into CRF male mice and by Miller et al. ⁽¹⁸⁾ using intravenous injections into female mice.

A suggestion of an age effect on Rb metabolism can be found in Tables 5 and 6, although data for only one younger (85 days of age) mouse are available. A corresponding age effect on ^{86}Rb metabolism in mice is reported in Reference 12. Of particular interest in Figures 4 and 5-9 and in Tables 5 and 6 is the small, long-term component in the ^{83}Rb retention equation. This can also be seen in Figure 10. Other investigators ⁽¹⁹⁾ have reported a small long-term component in the retention equation for ^{137}Cs of the rat which they found to be associated with Cs deposition in the skeleton. This component for ^{83}Rb in the mouse may also be due to retention of activity by bone.

Data in Table 7 indicate that muscle is not necessarily the tissue of highest Rb concentration in the mammal. Iinuma et al. ⁽¹¹⁾ reported significant ^{86}Rb concentration in liver and other organs relative to its concentration in muscle tissue. Since a mouse has more grams of muscle than liver, bone, or kidney, the largest fraction of a retained Rb body burden is

Table 1. ^{137}Cs retention in 68 day old female mice.

Animal	First Component		Second Component		Third Component		Equivalent biological half-time (days)
	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	
M21	50.7	1.16	47.1	3.55	2.2	8.12	2.439
M25	65.7	1.41	33.8	3.87	0.5	11.04	2.290
M26	56.9	1.01	42.9	3.25	0.2	13.33	1.996
Average	57.8	1.19	41.2	3.56	1.0	10.83	2.2

Table 2. ^{134}Cs retention in 121 day old female mice.

Animal	First Component		Second Component		Third Component		Equivalent biological half-time (days)
	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	
M11	32.7	0.715	41.9	2.342	25.4	5.212	2.534
M12	36.9	0.654	30.9	2.166	32.2	5.212	2.589
M13	32.0	0.846	34.8	2.318	33.2	4.987	2.733
M14	33.1	1.033	27.5	1.920	39.4	4.748	2.741
M15	34.0	0.714	28.5	2.153	37.5	4.652	2.601
Average	33.7	0.792	32.7	2.180	33.5	4.962	2.6

Table 3. ^{137}Cs retention in 152 day old female mice.

Animal	First Component		Second Component		Third Component		Equivalent biological half-time (days)
	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	
M11	45.7	0.797	26.6	3.22	27.7	5.37	2.708
M12	31.3	0.693	40.9	2.90	27.8	5.92	3.049
M13	30.0	0.680	50.3	2.78	19.7	5.42	2.632
Average	35.6	0.723	39.3	2.97	25.1	5.57	2.8

Table 4. ^{137}Cs retention in 368 day old female mice.

Animal	First Component		Second Component		Third Component		Equivalent biological half-time (days)
	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	
M22	28.8	0.996	58.2	4.47	13.0	7.51	3.866
M23	41.5	0.680	49.1	4.23	9.4	6.66	2.984
M24	34.2	1.500	18.9	4.05	46.9	5.73	3.967
Average	34.8	1.060	42.1	4.25	23.1	6.63	3.6

Table 5. ^{83}Rb retention in 121 day old female mice.

Animal	First Component		Second Component		Equivalent biological half-time (days)
	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	
M11	99.3	3.136	0.7	21.66	3.266
M12	99.3	3.151	0.7	11.77	3.211
M13	99.3	3.270	0.7	7.58	3.300
M14	99.2	3.239	0.8	13.15	3.318
M15	99.5	3.180	0.5	21.73	3.273
Average	99.3	3.195	0.7	15.18	3.3

Table 6. ^{83}Rb retention in an 85 day old female mouse.

Animal	First Component		Second Component		Third Component		Equivalent biological half-time (days)
	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	%	$T_{1/2}(\text{d})$	
M02	88.50	2.46	11.34	5.33	0.16	48.47	2.859

Table 7. Relative concentration of ^{83}Rb in tissues of the mouse.

Tissue	Percent of residual body burden per gram	
	Mouse M03 (1 day after Administration)	Mouse M01 (10 days after Administration)
Liver	5.35	8.66
Muscle	4.99	6.64
Bone	3.28	5.05
Kidney	2.54	5.76
Erythrocytes	2.44	
Brain	0.61	
Blood Plasma	0.28	

probably found in muscle. However, the concentration in both liver and skeleton in these two animals may be of some significance. More detailed studies of Rb distribution are needed before data in Table 7 can be adequately evaluated.

Although the counting data for mouse M16 was probably unreliable beginning about 55 days after administration (Fig. 10), there appears to be a small, relatively long-lived component in ^{83}Rb retention and perhaps even in ^{134}Cs retention. As in the other double-tracer mice, M16 initially retained ^{83}Rb better than ^{134}Cs . At about 2 weeks after administration, the retention of ^{134}Cs exceeded that of ^{83}Rb . This relative retention pattern was also observed in the other double tracer mice that were followed for about one month after administration. Another reversal in relative retention was observed in M16 at about $1\frac{1}{2}$ months burden time. Subsequently, the ^{83}Rb retention exceeded that of ^{134}Cs .

Approximately 10 days after administration, a change occurred in the slopes of both the ^{83}Rb and the ^{134}Cs retention curves for M16. A similar alteration was not evident in the curves for any of the other animals. This unique change occurred only in the mouse which delivered a litter of young

and occurred during the pregnancy (between about 2 and 12 days' gestation). An alteration of the elimination rate for both Rb and Cs therefore seems to have been associated with this pregnancy, but the effect was a decrease in the excretion rate rather than an increase as has been observed in the human.^(1,4) The slopes of the Rb and Cs retention curves for M16 appeared to increase at about 20 days after administration, approaching their pre-pregnancy values.

The young mice produced by M16 were found to contain ^{83}Rb and ^{134}Cs at birth (Figure 11). During the suckling period, activity of both nuclides initially increased; then a decrease in ^{83}Rb and ^{134}Cs content of the 7 young mice became evident. It appears that following birth, about a one week delay exists in the beginning of significant Rb and Cs excretion by the newborn mouse. This effect was also observed by Matsusaka and Inaba⁽²⁰⁾ in mice given ^{137}Cs or ^{86}Rb at birth and then suckled by their non-radioactive mother. A similar effect has been reported for newborn rats given ^{134}Cs ⁽²¹⁾.

CONCLUSIONS

No evidence of chemical toxicity was observed in any mouse given ^{83}Rb , ^{137}Cs , or ^{134}Cs from our stock solutions by gastric gavage. An effect of age on Cs metabolism in mice is similar to that observed in humans, and an analogous effect seems also to exist for Rb. Although the greatest fraction of retained Rb is probably in muscle, significant concentration can occur in liver, bone, kidney, and possibly in other tissues. Pregnancy appears to have an effect on both Rb and Cs elimination rates in the mouse opposite to the increase in Cs elimination rates observed in the pregnant human.

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Figure 1. ^{137}Cs retention in 68 day old female mice.

Figure 2. ^{137}Cs retention in 152 day old female mice.

Figure 3. ^{137}Cs retention in 368 day old female mice.

Figure 4. ^{83}Rb retention in an 85 day old female mouse.

Figure 5. ^{83}Rb and ^{134}Cs retention in 121 day old female mouse M11.

Figure 6. ^{83}Rb and ^{134}Cs retention in 121 day old female mouse M12.

Figure 7. ^{83}Rb and ^{134}Cs retention in 121 day old female mouse M13.

Figure 8. ^{83}Rb and ^{134}Cs retention in 121 day old mouse M14.

Figure 9. ⁸³Rb and ¹³⁴Cs retention in 121 day old female mouse M15.

Figure 10. ^{83}Rb and ^{134}Cs retention in a 121 day old female mouse that conceived and delivered a litter of young 27 days after radio-nuclide administration.

Figure 11. ^{83}Rb and ^{134}Cs retention in the young mice delivered by mouse M16 (see Figure 10).