^{83}Rb AND ^{137}Cs METABOLISM IN PERSONS AFFECTED BY MUSCLE DISEASE

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^{83}Rb AND ^{137}Cs METABOLISM IN PERSONS AFFECTED BY MUSCLE DISEASE

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ABSTRACT: Since normal muscle tissue can incorporate rubidium and cesium ions, a double tracer of the gamma-ray emitting radionuclides ^{83}Rb + ^{137}Cs was administered orally to the following 38 persons:

- 9 male control subjects, ages 4 to 80;
- 5 female control subjects, ages 14 to 52;
- 7 female genetic carriers of Duchenne muscular dystrophy, ages 14 to 50;
- 8 boys with Duchenne dystrophy, ages 5 to 19; and
- 9 additional subjects, ages 12 to 61, who were affected by different forms of muscular dystrophy or by other muscle disease.

Radioactivity in the blood, in excreta, and in the total body was determined by gamma-ray counting. The retention of ^{83}Rb measured in the body for about 6 months after administration and that of ^{137}Cs for about 12 months after administration was found to be a function of age and sex in healthy persons. Retention of ^{83}Rb and especially ^{137}Cs by subjects with advanced muscle disease was generally much lower than in control subjects of corresponding age and sex. The degree of difference appeared to depend upon the severity of the disease. Biological retention of ^{137}Cs was greater than ^{83}Rb in subjects without muscle disease, but there was a reversal of this pattern in 4 boys severely affected and 2 boys moderately affected with Duchenne dystrophy and in a 19-year old girl severely affected with infantile muscular atrophy. Two 5-year old boys slightly affected with Duchenne dystrophy exhibited retention patterns similar to those of two 4-year old boys without muscle disease. All persons in this series exhibiting a 3 term exponential equation for ^{137}Cs retention having a term of intermediate biological half-time which represented more than 1/2 of the total were also moderately or severely affected with Duchenne muscular dystrophy or with infantile muscular atrophy. Whereas the term of longest biological half-time represented only about 1% to 12% of the total retention of ^{137}Cs in severely affected Duchenne boys, the longest-lived exponential term in healthy persons accounted for about 1/2 or more of the total retention. There appeared to be no definitive difference between female genetic carriers of Duchenne dystrophy and age-matched female controls in either the form of the retention equations or in the biological half-time of Rb or Cs.

Comparison of the ^{83}Rb and ^{137}Cs activity in blood, urine, and the total-body at common times after administration showed that although kidney clearance of both Rb and Cs from the plasma was similar in diseased and healthy subjects of corresponding age and sex, the fraction of retained total-body ^{83}Rb and ^{137}Cs circulating in the plasma was significantly greater in diseased subjects. Partitioning of Rb and Cs between red cells and plasma was similar for all subjects.

These findings of distinctive retention patterns, increased excretion, but normal kidney function, and normal erythrocyte-to-plasma ratios in diseased persons are consistent with the concept that a cellular defect, resulting in altered membrane permeability in some cells, may account for the enhanced elimination of Rb and Cs in persons with muscular dystrophy.

INTRODUCTION

Preliminary studies⁽¹⁻⁴⁾ of the metabolism of environmental ^{137}Cs and ^{40}K indicated that persons with advanced muscle disease exhibit significantly decreased biological half-times for cesium as compared to healthy individuals of corresponding age and sex. A subsequent investigation was made⁽⁵⁾ in which 4 boys, aged 13 to 19 years, afflicted with Duchenne muscular dystrophy, and 1 healthy man were each given a double tracer of $^{83}\text{Rb} + ^{137}\text{Cs}$. This study confirmed the earlier results for environmental cesium and revealed that in the subjects with advanced muscular dystrophy the biological half-time of rubidium appeared also to be decreased, but not as dramatically as that of cesium. Whereas in the healthy adult, cesium was retained more tenaciously than rubidium, the reverse was observed in the dystrophic boys. Comparison of the ^{83}Rb and ^{137}Cs retention, excretion, concentration in the blood, and kidney clearance showed some similarities as well as some important differences between the normal and the dystrophic subjects. A critical limitation was the lack of suitable control subjects for the teen-aged dystrophy patients. Because of this limitation, it could not be clearly determined from that investigation whether contrasting data for the dystrophics as compared to the adult subject were entirely attributable to the disease or, at least in part, to the difference in age.

As a consequence, other similar studies were undertaken which included healthy and diseased subjects of both sexes and of various ages. The objectives were to establish the pertinent metabolic parameters for cesium and rubidium as a function of age for control subjects, to correlate differences between control and dystrophic subjects in cesium and rubidium metabolism with degree of disease severity, to compare Duchenne dystrophy with other dystrophic and non-dystrophic muscle diseases, and to search for

possible differences in data of female controls and female genetic carriers^(6,7) of Duchenne dystrophy.

METHODS

Fasting subjects (Tables 1, 2, and 3) were given orally a few ml of sterile saline solution containing about 6 μCi ^{83}Rb and 1 μCi ^{137}Cs . Control subjects less than 18 years of age received only half as much of each radio-nuclide. Urine was collected for 2 days following the administration of radioactivity. Feces were not collected, as it had been established previously that the urine accounted for about 85% of the total excretion of potassium and cesium^(2,5,8-11) and about 80% of the total excretion of rubidium^(5,12,13) by both control subjects and dystrophics. Correction for fecal excretion was made for those subjects that reported defecation during the 2 day period of urine collection.

Urine was collected continuously except for brief vacation periods from the 4 dystrophic boys LS, KS, DH, and CM as initially reported in reference 5 (and also included in Table 2) for about 4 months after the administration of radioactivity. Fecal collections were also made for at least a one week period beginning 1 to 2 weeks after administration. Total collections of urine and feces were made by the control subject CWM as initially reported in reference 5 (and also included in Table 1) during the first 3 months after administration; virtually total collections were made during the next 3 months; and intermittent collections were made for an additional 3 months.

Samples of whole blood were withdrawn from the antecubital vein at 1 and 2 days following radionuclide ingestion. At the completion of centrifugation of the sample, which began within a few minutes to tens of minutes after blood drawing, the separated plasma was removed with a transfer pipette

TABLE 1. SUBJECTS WITHOUT MUSCLE DISEASE GIVEN ^{83}Rb AND ^{137}Cs

Subject	Age (yr)	Weight (kg)	Height (cm)	Body Potassium (g)	Remarks
MALES					
DA	4	19.1	111	40	
JM	4	18.0	106	39	
WM	10	31.8	140	70	
JS	14	50.3	170	110	
KM	19	66.4	183	141	
GA	25	69.6	180	155	
CWM ⁺	37	79.7	178	151	
SG	53	73.5	164	121	
DB	80	73.0	171	106	
FEMALES					
JL	14	50.2	154	84	Presumed control*
SB	18	68.5	173	93	
SAS	28	66.5	171	104	
BS	39	71.4	167	101	
MR	52	60.2	157	93	
VG	14	83.8	161	116	Presumed carrier**
CL	18	55.5	161	88	Presumed carrier**
GG	35	57.8	157	81	Duchenne carrier
BL	39	54.8	157	83	Duchenne carrier
SS	46	63.3	165	79	Duchenne carrier
FJ	47	56.6	166	91	Duchenne carrier***
EP	50	58.5	162	80	Duchenne carrier

⁺ Initially reported in reference 5.

* Sister of Duchenne dystrophic, but having consistently normal CPK (creatine phosphokinase).^(6,7)

** Sister of Duchenne dystrophic, and having significantly elevated CPK.^(6,7)

*** Mother of 2 dystrophic sons; other dystrophic boys in family.

TABLE 2. SUBJECTS WITH MUSCLE DISEASE GIVEN ^{83}Rb AND ^{137}Cs

Subject	Age (yr)	Weight (kg)	Height (cm)	Body Potassium (g)	Disease
MALES					
KB	5	18.0	96	36	Duchenne dystrophy*
RG	5	21.0	108	34	Duchenne dystrophy*
TM	7	20.6	111	29	Duchenne Dystrophy**
MP	8	19.0	124	23	Duchenne dystrophy**
CM ⁺	13	37.9	155	29	Duchenne dystrophy***
DH ⁺	14	68.8	138	37	Duchenne dystrophy***
KS ⁺	16	19.8	148	21	Duchenne dystrophy***
LS ⁺	19	47.3	162	35	Duchenne dystrophy***
JC	34	50.0	170	73	Duchenne dystrophy§**
RA	12	37.2	150	85	Myotonic dystrophy*
LP	26	86.5	183	123	Limb girdle dystrophy*
RB	30	66.8	186	133	FSH dystrophy*
WS	44	76.0	178	75	FSH dystrophy**
BD	61	56.6	165	90	Amyotrophic Lateral Sclerosis**
FEMALES					
AG	29	58.8	171	63	Limb girdle dystrophy**
BA	37	66.6	169	70	Myotonic dystrophy**
PB	19	14.0	51	11	Infantile Muscular atrophy***

+ Initially reported in reference 5.

* Slightly affected.

** Moderately affected, ambulatory.

*** Severely affected, confined to a wheelchair.

§ An atypical case, possibly Becker's benign form of Duchenne dystrophy.

¶ Patient died before sufficient counting times had accumulated for an accurate evaluation of body potassium content.

TABLE 3. RELATIONSHIPS AMONG SUBJECTS GIVEN ^{83}Rb AND ^{137}Cs

Relationships	
<u>Controls</u>	
EP	Mother of dystrophic MP; aunt (maternal) of BL
SS	Mother of control JS and dystrophics KS and LS
BL	Mother of controls JL and CL and one dystrophic son
GG	Mother of control VG, dystrophic RG, and 2 other dystrophic sons
KM	Brother of control WM and dystrophic CM
JM	Brother of dystrophic TM
<u>Dystrophics</u>	
BA	Mother of dystrophic RA; adopted mother of control DA

and placed in a 10 ml capacity vial; the boundary layer between cells and plasma was discarded; and the separated red cells were similarly transferred to a separate vial using a fresh pipette. Blood samples from the 1 control subject and the 4 dystrophic boys reported in reference 5 were taken on a somewhat different schedule (at 4, 9, 16, 24, and 31 days after administration for control subject CWM, at 8 and 16 days for dystrophics LS and KS, and at 21 and 32 days for dystrophics DH and CM). No blood samples could be obtained from subject PB.

The content of ^{83}Rb , ^{137}Cs , and naturally occurring ^{40}K in the subjects, in blood samples, and in excreta was determined by gamma-ray spectroscopy. Total-body retention was measured inside a low background room constructed of 12 inch thick steel plate, with two 8 x 4 inch NaI(Tl) crystals suspended about 60 cm above an isoresponse surface upon which the subject reclined.^(5,14) Radioactivity in excreta samples was also measured inside the low background

chamber using a single 8 x 4 inch NaI(Tl) crystal. Blood samples were similarly assayed using Knothole,⁽¹⁵⁾ a side-well NaI(Tl) crystal. Net counting rates at 0.53 MeV (^{83}Rb), 0.66 MeV (^{137}Cs) and 1.46 MeV (^{40}K) were each corrected for contributions from the other gamma-ray emitters in the spectra and were compared with net counting rates of ingestion duplicates or other standards prepared in phantoms appropriate for blood, excreta, or human counting. The total-body counter was calibrated for each subject via the individual determinations of ^{83}Rb and ^{137}Cs in his excreta. Spectra recorded for all subjects prior to radionuclide administration indicated that their fallout ^{137}Cs content was insignificant in comparison with their subsequent retention of ingested ^{137}Cs , and that their corrected net counting rates at 0.53 MeV were negligible. Therefore, no subsequent correction for fallout ^{137}Cs was made except for the measurement at about 1 year after administration.

RESULTS AND DISCUSSION

Total-body retention.

Results of total-body counting are shown in Figures 1-38. As observed for the adult control subject initially reported in reference 5, the ultimate biological retention of cesium was greater than rubidium in all of the subjects without muscle disease (Table 1). However, rubidium was retained better than cesium in the 2 boys TM (Figure 24) and MP (Figure 25) who were moderately affected with Duchenne dystrophy. Their retention pattern was similar to that exhibited by the 4 boys CM, DH, KS, and LS, (Figures 26-29) initially reported in reference 5, who were severely affected with Duchenne dystrophy. This is in contrast to the retention of the 5-year old subjects KB (Figure 22) and RG, (Figure 23) only slightly affected with Duchenne dystrophy, who

both showed retention patterns similar to the control subjects DA (Figure 1) and JM (Figure 2) of similar age. Adult subject JC (Figure 30), moderately affected with an atypical form of Duchenne dystrophy, retained cesium better than rubidium. Subjects with other types of dystrophic muscle disease (RA, LP, RB, WS, AG, and BA, Figures 31-34, 36-37) also exhibited a higher retention of cesium than rubidium, as did BD (Figure 35), an adult subject moderately affected with amyotrophic lateral sclerosis, a neurogenic atrophy of muscle. Subject PB (Figure 38), a victim of infantile muscle atrophy, not only showed the reversal in relative cesium and rubidium retention characteristic of advanced muscular dystrophy, but had the highest elimination rate for ^{137}Cs of any subject which we have studied, including infants. ^(2,8)

A variety of equations can describe the retention data for each subject (Figures 1-38). We have elected to represent the retention of ^{83}Rb and ^{137}Cs by our subjects as sums of exponentials. Equations were determined by the method of least squares. The number of exponential terms in each equation was chosen so as to give the lowest value of the calculated error variance = $\sum_{i=1}^n (Y_o - Y_c)^2 / \text{DF}$, where Y_o = observed retention, Y_c = retention calculated from the equation, and DF = degrees of freedom = number of measurements minus twice the number of exponential terms, since each exponential term has 2 parameters, a coefficient and a half-time. Equations other than those shown in Figures 1-38 may represent the retention measurements at least as well. The interested reader is encouraged to use these data to produce his own version of the retention equations and to subject them to his own interpretations.

Tables 4 and 5 summarize the retention data as described by the equations shown in Figures 1-38. The relative component size (f) and biological

TABLE 4. RELATIVE COMPONENT SIZES (f) AND BIOLOGICAL HALF-TIMES ($T_{1/2}$) OF RETENTION EQUATIONS FOR ^{83}Rb DETERMINED FOR THE 38 SUBJECTS IN THIS STUDY. ALSO SHOWN IS THE EQUIVALENT BIOLOGICAL HALF-TIME (T_Q) FOR EACH SUBJECT. (SEE FIGURES 1-38).

Subject	Short Component		Intermediate Component		Long Component		T_Q , days
	f	$T_{1/2}$, days	f	$T_{1/2}$, days	f	$T_{1/2}$, days	
DA	0.071	8.6			0.929	24.0	22.9
JM	0.036	1.8			0.964	23.8	23.0
WM	0.156	9.5			0.844	33.0	29.3
JS	0.054	3.7			0.946	41.5	39.5
KM	0.038	2.9			0.962	51.0	49.2
GA					1.00	42.8	42.8
CWM	0.035	3.8			0.965	59.2	57.3
SG	0.049	4.4			0.951	33.3	31.9
DB					1.00	36.9	36.9
JL					1.00	37.5	37.5
SB					1.00	46.8	46.8
SAS					1.00	46.8	46.8
BS					1.00	53.7	53.7
MR	0.017	1.8			0.983	40.1	39.4
VG	0.070	8.5			0.930	44.4	41.9
CL	0.055	2.8			0.945	46.1	43.7
GG	0.034	2.1			0.960	43.6	41.9
BL	0.048	1.9			0.952	32.4	30.9
SS	0.081	3.6			0.919	35.0	32.5
FJ					1.00	39.2	39.2
EP					1.00	39.8	39.8
KB ¹					1.00	28.4	28.4
RG ¹	0.155	7.0			0.845	24.7	22.0
TM ²	0.057	6.2			0.943	19.6	18.8
MP ²	0.235	9.0			0.765	25.2	21.4
CM ³			0.933	26.8	0.067	63.6	29.3
DH ³			0.961	24.5	0.039	97.2	27.3
KS ³	0.158	4.3	0.786	22.1	0.056	82.9	22.7
LS ³	0.153	2.1	0.824	20.9	0.023	79.6	19.4
JC ²	0.027	1.3			0.973	49.5	48.2
RA ¹	0.115	16.3			0.885	38.3	35.8
LP ¹	0.034	14.4			0.966	44.4	43.4
RB ¹	0.023	2.8			0.977	34.7	34.0
WS ²	0.058	5.0			0.942	38.9	36.9
BD ²					1.00	29.2	29.2
AG ²	0.042	1.9			0.958	29.6	28.4
BA ²					1.00	37.5	37.5
PB ³					1.00	17.5	17.5

Disability:

¹ = slight

² = moderate, ambulatory

³ = severe, confined to a wheelchair

TABLE 5. RELATIVE COMPONENT SIZES (f) AND BIOLOGICAL HALF-TIMES ($T_{1/2}$) OF RETENTION EQUATIONS FOR ^{137}Cs DETERMINED FOR THE 38 SUBJECTS IN THIS STUDY. ALSO SHOWN IS THE EQUIVALENT BIOLOGICAL HALF-TIME (T_Q) FOR EACH SUBJECT. (SEE FIGURES 1-38).

Subject	Short Component		Intermediate Component		Long Component		T_Q , days
	f	$T_{1/2}$, days	f	$T_{1/2}$, days	f	$T_{1/2}$, days	
DA	0.155	1.7	0.399	16.2	0.446	29.9	20.1
JM	0.234	1.1	0.159	10.4	0.607	29.2	19.6
WM	0.158	1.7	0.146	15.5	0.696	43.9	33.1
JS	0.238	4.4			0.762	73.6	57.1
KM	0.149	2.1			0.851	90.4	77.2
GA	0.091	0.9			0.909	91.7	83.4
CWM	0.076	1.5			0.924	140.0	129.5
SG	0.191	3.8			0.809	81.5	66.7
DB	0.117	2.4			0.883	79.7	70.7
JL	0.120	1.5	0.178	10.1	0.702	75.4	54.9
SB	0.159	3.8			0.841	70.8	60.1
SAS	0.104	4.9			0.896	119.7	107.8
BS	0.166	0.5	0.053	15.3	0.781	101.5	80.2
MR	0.031	0.6	0.136	9.0	0.833	86.9	73.6
VG	0.127	1.2	0.115	16.7	0.758	82.0	64.2
CL	0.223	3.7			0.777	72.2	56.9
GG	0.102	1.0	0.124	11.1	0.774	75.4	59.8
BL	0.196	2.4			0.804	69.5	56.3
SS	0.143	1.7	0.163	9.7	0.694	58.7	42.6
FJ	0.076	1.0	0.099	13.8	0.825	86.1	72.5
EP	0.134	1.3	0.049	18.8	0.817	97.5	80.8
KB ¹	0.135	1.8	0.226	18.7	0.639	34.3	26.4
RG ¹	0.094	1.9	0.237	15.6	0.669	29.1	23.3
TM ²	0.207	1.6	0.657	14.9	0.136	27.2	13.8
MP ²	0.242	1.6	0.512	12.9	0.246	25.3	13.2
CM ³	0.047	1.0	0.896	16.9	0.057	42.3	17.6
DH ³	0.139	4.4	0.742	18.9	0.119	41.0	19.5
KS ³	0.353	3.7	0.570	17.4	0.077	38.9	14.2
LS ³	0.233	3.7	0.757	16.2	0.010	68.6	13.8
JC ²	0.166	2.3			0.834	71.2	59.8
RA ¹	0.213	3.1			0.787	51.7	41.3
LP ¹	0.143	1.6	0.065	10.4	0.792	97.2	77.9
RB ¹	0.102	1.3	0.043	27.5	0.855	90.8	78.9
WS ²	0.195	2.6	0.233	17.4	0.572	67.3	43.1
BD ²	0.247	4.6			0.753	70.2	54.0
AG ²	0.254	4.0			0.746	47.5	36.5
BA ²	0.230	3.8			0.770	68.6	53.7
PB ³	0.214	2.7	0.786	9.8			8.3

Disability:

1 = slight

2 = moderate, ambulatory

3 = severe, confined to a wheelchair

half-time ($T_{1/2}$) are given for each exponential term in each equation. Also tabulated for each equation is the equivalent biological half-time (T_Q) which is defined^(2,5) as the average of all the component half-times in a retention equation each weighted by its relative component size.

It appears that the subjects with an intermediate term in their ^{137}Cs retention equation which represented 1/2 or more of the total retention (Table 5) were those who were moderately or severely affected with Duchenne dystrophy or infantile muscular atrophy. Those with about 1/4 of their total ^{137}Cs represented by an intermediate component were the slightly affected boys with Duchenne dystrophy (KB and RG) plus the adult who was moderately affected with FSH dystrophy (WS). There appeared to be no definitive difference between female genetic carriers of Duchenne dystrophy and age matched female controls in either the number of exponential terms in the ^{137}Cs retention equation or the relative size of the intermediate component. In addition, the average equivalent biological half-time for ^{137}Cs of the carriers was not significantly different from that of the controls ($P > 0.2$). About 1 year after administration a number of our carriers and controls were re-measured in an attempt to detect a longer term exponential in their ^{137}Cs retention equations than had been determined from the data collected during the first half year. At about the same time, several age-matched subjects of corresponding sex who had not been given a ^{137}Cs tracer were also total-body counted to indicate the magnitude of the ^{137}Cs from fallout in our experimental subjects. An appropriate correction to the measured body content of ^{137}Cs was made therefrom for the 1 year values. In no case was there evidence of an exponential term of longer biological half-time than the longest-term exponential derived from the retention data measured over the

first half-year after radionuclide administration. This was true whether the corrected 1-year data points or the data points uncorrected for the contribution from fallout ^{137}Cs were considered. In fact, the residual ^{137}Cs body content almost exactly matched within a few percent and, in some cases, was even slightly less than the value predicted from the ^{137}Cs retention equation for each subject (Table 6).

Only the 4 subjects severely affected with Duchenne dystrophy exhibited an intermediate component in their ^{83}Rb retention equations. Subjects CM and DH appeared to have an undetectable short term component. The average equivalent biological half-time (T_Q) for ^{83}Rb in these 4 subjects of 24.7 days agrees closely with the 27.2 day average for ^{86}Rb in 7 Japanese subjects afflicted by Duchenne dystrophy which was reported by Nagai et al.⁽¹⁶⁾ Among our other subjects, many seemed to show a ^{83}Rb retention equation with only a single exponential (Table 4). Where 2 exponential terms were required to describe the retention, the component size of the shortest-lived term was characteristically quite small with a few exceptions. No definitive difference in the number of exponential terms in their ^{83}Rb retention equations were apparent between genetic carriers of Duchenne dystrophy and age-matched female controls. However, there was a slight suggestion of a possible difference ($0.10 > P > 0.05$) between the 38.6 day average equivalent biological half-time (T_Q) of carriers and the 44.8 day average T_Q of the controls. Nevertheless, we do not believe that our studies have thus far provided any usable method of distinguishing female genetic carriers from non-carriers of Duchenne dystrophy with radiotracer techniques.

Unique among the retention functions for ^{83}Rb displayed in Table 4 was the small, long-term component of the 4 boys severely affected with Duchenne dystrophy. Autopsy samples⁽¹⁷⁾ were obtained from subject CM at

TABLE 6. MEASURED BODY ^{137}Cs CONTENT AT ABOUT 1 YEAR FOLLOWING
INGESTION COMPARED WITH THAT PREDICTED BY THE ^{137}Cs
RETENTION EQUATION BASED ON DATA FOR THE FIRST HALF
YEAR

<u>Subject</u>	<u>Days after Ingestion</u>	<u>Measured Body ^{137}Cs*</u>	<u>Predicted Body ^{137}Cs</u>	<u>$\left[\frac{\text{Measured}}{\text{Predicted}} \right]$</u>
JS	418	1.57 %	1.49 %	1.054
GA	409	4.54	4.12	1.102
CWM	372	14.9	14.7	1.014
SG	365	4.02	3.62	1.110
DB	364	3.98	3.72	1.070
JL	375	2.26	2.24	1.009
SB	364	2.61	2.38	1.097
SAS	360	11.2	11.1	1.009
BS	415	4.32	4.59	0.941
MR	415	2.89	3.04	0.951
VG	413	2.11	2.31	0.913
CL	375	2.27	2.12	1.071
GG	413	1.34	1.74	0.770
BL	415	1.13	1.28	0.883
SS	418	0.48	0.50	0.960
EP	416	3.43	4.24	0.809
Average				0.985

*In excess of the small amount of fallout ^{137}Cs estimated from total body
counting at the same time of control subjects matched by sex and age.

300 days after the administration of $^{83}\text{Rb} + ^{137}\text{Cs}$ and from subject KS at 333 days following administration, after ^{83}Rb and ^{137}Cs were no longer detectable by total-body counting. No ^{137}Cs could be detected in any of the tissues, and no ^{83}Rb could be found except in bone. The biological concentration of ^{83}Rb in cortical bone was 2.6×10^{-6} of the administered ^{83}Rb per gram for CM and $1.5 \times 10^{-6}/\text{g}$ 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-term component in the retention equation of ^{83}Rb for boys severely affected with Duchenne dystrophy is associated with the deposition of activity in the skeleton. Thomas and Thomas⁽¹⁸⁾ reported a small, long-term component in the multiexponential retention equation for ^{137}Cs in rats attributable to skeletal deposition. Our data (Table 6) do not show a corresponding effect on ^{137}Cs retention in humans at as much as 1 year following administration.

Figures 39 and 40 exhibit the relationship between the age of the male and female subjects and their equivalent biological half-times (T_Q) for ^{137}Cs . Open symbols represent data for the subjects listed in Tables 1 and 2, while solid symbols represent data obtained using fallout ^{137}Cs * taken from Reference 2. Where the T_Q for an individual subject was determined in this study and in the earlier study, both values are shown with a line connecting the two symbols. For most of the subjects with a T_Q determination from both studies, the two values agree fairly well. One exception is female subject AG (Figures 36 and 40) whose T_Q appeared to decrease significantly during the nearly 5 years separating the two measurements at ages 25 and 29 years. Her disability increased significantly during

$$*T_Q = 0.693 \left(\frac{\text{body content of } ^{137}\text{Cs}}{\text{daily excretion of } ^{137}\text{Cs}} \right)$$

the interval, possibly accounting for the change in measured T_Q . Another even more striking exception is male subject RB (Figures 33 and 39) whose disability had not increased noticeably during the nearly 5 years between determinations at ages 25 and 30 years. We had previously discussed^(2,4) the possibility that since an incomplete excreta collection could result in an erroneously long calculated T_Q using fallout ^{137}Cs , the unexpectedly high value for subject RB may have been in error; however, a second measurement which had been made 3 months after the first yielded an almost identical T_Q , which could have also been in error if the excreta collection was consistently incomplete.

Except for those minimally affected, subjects with muscle disease appeared to have significantly shorter values of $^{137}\text{Cs } T_Q$ than that of the control subjects of corresponding age and sex. The degree of T_Q shortening appeared to be roughly correlated with the degree of disability.

Figures 41 and 42 exhibit the relationship between the age of the male and female subjects and their equivalent biological half-times (T_Q) for ^{83}Rb . Severely or moderately affected subjects with Duchenne dystrophy appeared to have a shortened T_Q as compared to non-affected boys of corresponding age. Female subjects with muscle disease also may have had a shorter T_Q for ^{83}Rb than their age-matched controls.

Figures 43 and 44 show the relationship for males and females of the ratio ($\text{Cs } T_Q / \text{Rb } T_Q$) and the age of the subjects. For very young control subjects and for the boys only slightly affected with Duchenne dystrophy, this ratio approximated unity. With increasing age of control subjects, the ratio increased to an adult value of about 2.05 for males and about 1.75 for females. Males moderately or severely affected with muscular dystrophy appeared to have a ($\text{Cs } T_Q / \text{Rb } T_Q$) ratio which was markedly less than

their age matched controls, as did the female subject severely affected with muscle disease. There was no significant difference in the ($Cs T_Q/Rb T_Q$) ratio in genetic carriers of Duchenne dystrophy and age-matched female controls.

^{83}Rb and ^{137}Cs in Blood and Excreta.

The concentration (% of ingested activity per gram) of both ^{83}Rb and ^{137}Cs was much greater in the erythrocyte fraction of blood than in the plasma fraction for all subjects. Moreover, the ratio of (erythrocyte concentration/plasma concentration) increased by a factor of about 1 1/2 times between 1 day and 2 days after ingestion from values of about 12 at 1 day to 18 at 2 days for ^{83}Rb and from values of about 3.5 at 1 day to 5.5 at 2 days for ^{137}Cs . In the case of ^{83}Rb , the observed increase in the ratio was principally due to an increase averaging about 27% of the ^{83}Rb concentration in erythrocytes, while the plasma concentration decreased by an average of 11%. For ^{137}Cs , the observed increase in the ratio resulted from an increase averaging only about 15% of the ^{137}Cs concentration in erythrocytes, with an average decrease in plasma concentration of 27%. Between 1 and 2 days after administration, therefore, the ^{137}Cs concentration in plasma decreased much more abruptly than did the ^{83}Rb concentration in plasma, but the ^{83}Rb concentration in erythrocytes increased more rapidly than did the ^{137}Cs concentration in erythrocytes, although the overall ratio of (erythrocyte concentration/plasma concentration) increased by a factor of about 1 1/2 times for both elements (1.43 for ^{83}Rb and 1.58 for ^{137}Cs).

Corresponding ratios for the 5 subjects from whom blood samples were taken at other than on days 1 and 2 also indicated that there was an increase in erythrocyte as compared to plasma concentration for both ^{83}Rb and

^{137}Cs as a function of time. For control subject CWM, studied most intensively, the (erythrocyte/plasma) concentration ratios for ^{83}Rb were 18.3 at 4 days, 19.5 at 9 days, 23.7 at 16 days, 22.0 at 24 days, and 22.9 at 31 days. His ratio at between 1 and 2 days, linearly extrapolated from the measured values, was about 17.9, in good agreement with the average $\pm$ S.D. for the subjects measured at 1 and 2 days of 15.0 ± 1.6 . His ratios for ^{137}Cs were 7.3 at 4 days, 7.9 at 9 days, 11.8 at 16 days, 6.3 at 24 days, and 14.0 at 31 days, linearly extrapolated to 7.0 at between 1 and 2 days, in fair agreement with the average $\pm$ S.D. of the other subjects of 4.4 ± 0.8 . Data for the 4 dystrophic boys for whom (erythrocyte/plasma) concentration ratios were determined only twice at other than 1 and 2 days after administration suggested that extrapolated values for ^{83}Rb at between 1 and 2 days were about 15.0 for CM, 15.0 for DH, 22.5 for KS and 21.0 for LS. For ^{137}Cs , the extrapolated values were about 5.0 for CM, 5.0 for DH, 6.0 for KS and 3.5 for LS. Table 7 summarizes these data and indicates that the (erythrocyte concentration/plasma concentration) ratios were somewhat similar in all subjects for ^{137}Cs as well as for ^{83}Rb at comparable times after radionuclide intake.

The concentration of ^{83}Rb and ^{137}Cs in each subject's plasma was compared with the urinary excretion rate at the time of blood withdrawal. Clearance of radioactivity from the plasma by the kidney was calculated as liters of plasma cleared by urinary excretion per day = $(\mu\text{Ci excreted/day}) \div (\mu\text{Ci/liter of plasma})$. Kidney clearance of ^{83}Rb and ^{137}Cs (Table 8) appeared to be about 3.8 to 20.3 liters per day and 5.7 to 21.9 liters per day, respectively, with no clear-cut differences between subjects with muscle disease and those without muscle disease. Therefore, three additional comparisons were made in an attempt to adjust the kidney clearance data for the relative

TABLE 7. GEOMETRIC MEANS OF THE (ERYTHROCYTE CONCENTRATION/
PLASMA CONCENTRATION) RATIOS FOR 1 DAY AND 2 DAYS
AFTER THE ADMINISTRATION OF ^{83}Rb AND ^{137}Cs .

Subject	(^{83}Rb) E/P*	(^{137}Cs) E/P*
DA	13.7	3.8
JM	15.0	4.5
WM	14.2	4.2
JS	15.7	4.8
KM	15.0	4.3
GA	19.3	6.1
CWM	17.9**	7.0**
SG	14.9	5.3
DB	17.7	5.7
JL	15.2	4.3
SB	12.4	4.1
SAS	13.8	4.6
BS	13.5	3.9
MR	13.4	3.9
VG	15.6	4.5
CL	15.3	3.8
GG	15.5	4.5
BL	15.3	4.4
SS	14.6	4.9
FJ	15.8	4.9
EP	15.4	4.6
KB	12.7	3.5
RG	14.6	4.0
TM	13.8	3.6
MP	15.3	4.3
CM	15.0**	5.0**
DH	15.0**	5.0**
KS	22.5**	6.0**
LS	21.0**	3.5**
JC	15.1	4.3
RA	13.9	3.8
LP	17.8	5.1
RB	19.0	7.0
WS	14.2	4.1
BD	14.6	3.8
AG	12.8	3.5
BA	14.9	4.1

*E/P = (erythrocyte concentration/plasma concentration)

**extrapolated value

sizes of the individual subjects. Table 8 shows the results of dividing each subject's kidney clearance in liters per day by (a) his body mass in kg, or (b) his calculated body surface area in square meters. Table 8 also lists values calculated for the equivalent number of times per day that the activity in the total plasma was cleared by the kidney = plasma volumes cleared per day = (liters of plasma cleared per day) ÷ (calculated plasma volume of the subject). Body surface areas were obtained from the formula of Brody et al.⁽¹⁹⁾ $A = 0.024 (W^{0.53}) (H^{0.40})$ where A = body surface area in m², W = body mass in kg, H = height in cm. Plasma volumes for normal males and for normal females were calculated from the formulas given by Moore et al.⁽²⁰⁾

$$PV \text{ (males)} = 927 + 31.47 W \quad \text{and}$$

$$PV \text{ (females)} = 849 + 25.86 W \quad \text{where}$$

PV = plasma volume in ml and W = body mass in kg.

Lacking specific data for dystrophics or persons with other muscle disorders and because Moore et al.⁽²⁰⁾ imply that plasma fractions are not greatly affected by wasting diseases, plasma volumes for other than normal subjects were also calculated by these formulas. In none of the comparisons shown in Table 8 was there a clear-cut difference between dystrophic boys and their age-matched controls; between dystrophic adults and their sex and age-matched controls; or between female genetic carriers for Duchenne dystrophy and their age-matched female controls.

Normal kidney function, relative to body surface area, in patients with Duchenne muscular dystrophy, has also been shown by inulin and para-aminohippurate clearance studies.⁽⁷⁾ Thus, it appears unlikely that the

TABLE 8. KIDNEY CLEARANCE OF ^{83}Rb AND ^{137}Cs FROM THE PLASMA: LITERS OF PLASMA CLEARED PER DAY, LITERS OF PLASMA CLEARED PER DAY PER KG BODY MASS, LITERS OF PLASMA CLEARED PER DAY PER SQUARE METER BODY SURFACE AREA, AND NUMBER OF PLASMA VOLUMES CLEARED PER DAY.

Subject	$^{83}\text{Rb}^*$				$^{137}\text{Cs}^*$			
	l/day	$\frac{\text{l/day}}{\text{kg}}$	$\frac{\text{l/day}}{\text{m}^2}$	plasma vol. day	l/day	$\frac{\text{l/day}}{\text{kg}}$	$\frac{\text{l/day}}{\text{m}^2}$	plasma vol. day
DA	4.1	0.21	5.39	2.7	6.6	0.35	8.68	4.3
JM	7.1	0.39	9.86	4.8	13.8	0.77	19.17	9.2
WM	6.5	0.20	6.02	3.4	12.9	0.41	11.94	6.7
JS	9.5	0.19	6.33	3.8	12.8	0.25	8.53	5.1
KM	7.8	0.12	4.38	2.6	10.0	0.15	5.62	3.3
GA	12.4	0.18	6.81	4.0	14.0	0.20	7.69	4.5
CWM	10.1	0.13	5.21	2.9	9.6	0.12	4.95	2.8
SG	16.7	0.23	9.28	5.2	14.2	0.19	7.89	4.4
DB	16.2	0.22	8.90	5.0	14.7	0.20	8.08	4.6
JL	6.5	0.13	4.55	3.0	10.6	0.21	7.41	4.9
SB	5.5	0.08	3.11	2.1	6.6	0.10	3.73	2.5
SAS	6.4	0.10	3.68	2.5	6.7	0.10	3.85	2.6
BS	14.0	0.20	7.82	5.2	19.9	0.28	11.12	7.4
MR	10.1	0.17	6.35	4.2	8.2	0.14	5.16	3.4
VG	19.0	0.23	9.90	6.3	16.3	0.19	8.49	5.4
CL	8.3	0.15	5.39	3.6	10.1	0.18	6.56	4.4
GG	9.2	0.16	5.90	3.9	11.2	0.19	7.18	4.8
BL	8.7	0.16	5.76	3.8	9.0	0.16	5.96	4.0
SS	10.4	0.16	6.23	4.7	15.8	0.25	9.46	7.1
FJ	10.5	0.19	6.65	4.5	8.6	0.15	5.44	3.7
EP	8.6	0.15	5.41	3.6	8.6	0.15	5.41	3.6
KB	3.8	0.21	5.51	2.5	5.7	0.32	8.26	3.8
RG	10.8	0.51	13.85	6.8	10.4	0.50	13.33	6.5
TM	7.0	0.34	8.97	4.4	13.4	0.65	17.18	8.5
MP	6.5	0.34	8.23	4.3	10.3	0.54	13.04	6.8
CM	6.8	0.18	5.48	3.2	8.6	0.23	6.94	4.1
DH	6.9	0.10	4.26	2.2	10.8	0.16	6.67	3.5
KS	5.8	0.29	6.74	3.7	8.1	0.41	9.42	5.2
LS	9.0	0.19	6.34	3.7	11.9	0.25	8.38	4.9
JC	5.9	0.12	3.96	2.4	7.2	0.14	4.83	2.9
RA	7.1	0.19	5.87	3.4	9.8	0.26	8.10	4.7
LP	8.9	0.10	4.34	2.4	11.6	0.13	5.66	3.2
RB	20.3	0.30	11.28	6.7	14.2	0.21	7.89	4.7
WS	14.7	0.19	7.78	4.4	21.9	0.29	11.59	6.6
BD	7.1	0.13	4.52	2.6	9.3	0.16	5.92	3.4
AG	7.8	0.13	4.79	3.3	17.6	0.30	10.80	7.4
BA	5.3	0.08	3.06	2.1	6.2	0.09	3.58	2.4

*l/day = liters of plasma cleared per day

enhanced elimination rates and resulting shortened biological half-times for ^{83}Rb and ^{137}Cs in patients with Duchenne dystrophy and other muscle diseases is a consequence of altered renal function. Rather than the kidney clearing a larger fraction of the circulating ^{83}Rb and ^{137}Cs in the dystrophic, a fraction similar to that in the normal subject is cleared by the kidney, but the plasma levels relative to total-body content are higher in the dystrophic, producing an increased fractional excretion. Table 9 demonstrates this difference. It shows the relationship between ^{83}Rb and ^{137}Cs circulating in the plasma at 1 and 2 days after administration and the measured total-body retention of ^{83}Rb and ^{137}Cs at corresponding times. Similar data were also calculated for the 5 subjects from whom blood samples were taken at other than 1 and 2 days after administration. Values for day 1 and day 2 were obtained by linear extrapolation and were in each case similar to but somewhat greater than the values calculated directly for other times. The percent of retained ^{83}Rb or ^{137}Cs circulating in plasma declined with time for these 5 subjects as well as for those subjects from whom blood was obtained on days 1 and 2.

The difference in percent of retained ^{137}Cs in the circulating plasma between boys affected with Duchenne dystrophy (group V in Table 9) and their age matched controls (group I in Table 9) was found to be very highly significant ($P < 0.001$). The same was found for ^{83}Rb between these 2 groups ($P < 0.001$). Again, there was no significant difference between female genetic carriers of Duchenne dystrophy (group IV in Table 9) and their age-matched female controls (group III in Table 9) for either ^{83}Rb or ^{137}Cs ($P > 0.20$). No significant differences for either ^{83}Rb or ^{137}Cs could be found between adult male controls (group II) and adult female controls (group III).

TABLE 9. PERCENT OF RETAINED ^{83}Rb AND ^{137}Cs THAT WAS CIRCULATING IN PLASMA AT 1 AND 2 DAYS AFTER ADMINISTRATION. MEASURED PLASMA CONCENTRATIONS WERE MULTIPLIED BY PLASMA VOLUMES CALCULATED FROM REFERENCE 20 TO OBTAIN TOTAL NUCLIDE IN PLASMA, WHICH WAS THEN EXPRESSED AS A PERCENT OF THE OBSERVED BODY CONTENT AT THE CORRESPONDING TIME.

Group	Subject	Age	^{83}Rb		^{137}Cs	
			day 1	day 2	day 1	day 2
(I)	DA	4	0.246 %	0.259 %	0.408 %	0.390 %
	JM	4	0.248	0.224	0.457	0.285
	WM	10	0.210	0.224	0.359	0.271
	JS	14	0.156	0.132	0.251	0.193
	KM	19	0.138	0.130	0.287	0.192
(II)	GA	25	0.219	0.207	0.408	0.338
	CWM	37	0.325*	0.320*	0.395*	0.377*
	SG	53	0.323	0.291	0.557	0.413
	DB	80	0.377	0.310	0.608	0.411
(III)	JL	14	0.267	0.248	0.484	0.359
	SB	18	0.378	0.385	0.635	0.551
	SAS	28	0.297	0.297	0.496	0.393
	BS	39	0.344	0.296	0.802	0.580
	MR	52	0.308	0.327	0.609	0.521
(IV)	VG	14	0.130	0.130	0.261	0.172
	CL	18	0.325	0.279	0.671	0.468
	GG	35	0.319	0.284	0.618	0.410
	BL	39	0.321	0.282	0.663	0.414
	SS	46	0.384	0.305	0.571	0.403
	FJ	47	0.279	0.292	0.482	0.389
	EP	50	0.354	0.302	0.679	0.485
(V)	KB	5	0.644	0.614	0.934	0.830
	RG	5	0.571	0.396	0.780	0.587
	TM	7	0.664	0.605	0.836	0.742
	MP	8	0.712	0.683	1.061	0.779
	CM	13	1.280*	1.260*	1.120*	1.110*
	DH	14	1.090*	1.075*	0.980*	0.970*
	KS	16	0.910*	0.900*	1.190*	1.180*
	LS	19	1.000*	0.990*	1.390*	1.370*
(VI)	JC	34	0.534	0.474	0.952	0.732
	RA	12	0.367	0.389	0.729	0.593
	LP	26	0.406	0.348	0.740	0.609
	RB	30	0.246	0.214	0.314	0.238
	WS	44	0.621	0.479	0.908	0.681
	BD	61	0.380	0.332	0.629	0.552
	AG	29	0.450	0.413	0.707	0.601
	BA	37	0.542	0.395	0.850	0.673

*extrapolated value

Differences for both ^{83}Rb and ^{137}Cs were very highly significant ($P < 0.001$) between moderately affected adults (5 subjects in group VI) and adult controls (groups II and III).

CONCLUSIONS

Total-body retention of ingested ^{83}Rb and ^{137}Cs is dependent upon sex, age, and degree of disability produced by muscle disease. Decreased retention by diseased persons is not a result of altered renal function, but appears to be a consequence of an elevated fraction of total-body ^{83}Rb and ^{137}Cs in circulating plasma. These observations are consistent with the concept that a cellular defect, resulting in altered membrane permeability, may account for the increased relative excretion of Rb and Cs by persons with muscular dystrophy. If this increased excretion were due mainly to the observed decrease in potassium-containing tissue in these persons, it seems probable that Rb and Cs elimination would be affected similarly, and a reversal of their relative retentions in diseased as compared to healthy subjects would not be expected. It has not been clearly determined whether the observed increase in circulating ^{83}Rb and ^{137}Cs is because of a decreased entry of these ions into cells, an altered ratio of entry into various kinds of cells, or an increased rate of release from cells into which they have been incorporated, relative to that in healthy persons. We presently favor the last of these 3 possibilities because: (a) less than 2% of the residual body burden of Rb and Cs is still circulating in plasma at 1 and 2 days after administration (Table 9), even in the most severely affected subjects, and declines thereafter; (b) uptake of ^{83}Rb and ^{137}Cs by blood cells from the plasma is similar in diseased and healthy persons (Table 7); and (c) autopsy samples from diseased subject PB, who died 33 days after $^{83}\text{Rb} + ^{137}\text{Cs}$

administration, indicated that formalin-fixed tissues, such as muscle, bone, viscera, and brain had incorporated ^{83}Rb and ^{137}Cs . We found 0.7% and 0.7%, respectively, of the residual ^{83}Rb and ^{137}Cs body content in 43 g of muscle tissue and 41.5% and 62.6%, respectively, of the residual body content in 1310 g of brain; muscle concentration was nearly 8 times and 30 times, respectively, that of the average body concentration, while brain concentration was 4.4 times and 6.7 times, respectively, that of average body concentration.

Boys severely affected with Duchenne dystrophy exhibit a relatively large component of intermediate biological half-time in their retention equations for ^{83}Rb and ^{137}Cs and only a relatively small component of long half-time. This is in contrast to the relatively large long-term component and small or undetectable intermediate component in the retention equations for healthy persons. Most of the long-term component may in fact represent retention by functional tissue, large in healthy persons, small in dystrophics, while much of the large intermediate component of dystrophics may represent retention by diseased muscle: the relative sizes of the long and the intermediate components of persons with muscular dystrophy might indicate the ratio of functional to diseased muscle tissue.

The reversal in ultimate relative retention of ^{83}Rb and ^{137}Cs compared to age-matched controls which was observed in boys moderately or severely affected with Duchenne dystrophy is not unique to their disease, since a girl severely affected with infantile muscular atrophy also exhibited a similar retention pattern. Young boys only slightly affected with Duchenne dystrophy do not show this reversal in ^{83}Rb and ^{137}Cs retention. Their pattern corresponds to that in healthy boys of similar age.

We have not been able to find any significant differences in cesium, rubidium, or potassium⁽²¹⁾ metabolism between female genetic carriers of Duchenne muscular dystrophy and their age-matched female controls.

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Days After Administration	Percent Biological Retention ^{83}Rb	Percent Biological Retention ^{137}Cs
0	100	100
1	98.1	94.2
2	95.3	84.7
6	79.7	68.1
13	67.2	54.1
27	43.7	36.4
55	18.2	16.9
90	6.35	6.30
118	2.95	3.11
153	1.11	1.31
181	0.54	0.67
209	0.13	0.35

Figure 1. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 4-year old male control subject DA.

Days After Administration	Percent Biological Retention	
	^{83}Rb	^{137}Cs
0	100	100
1	97.0	83.5
2	92.5	77.0
5	83.7	66.9
12	67.1	52.7
19	54.7	43.3
26	45.0	35.5
40	30.5	24.3
68	12.8	12.0
96	6.17	6.12
124	2.61	3.10
159	0.97	1.39
194	0.33	0.63

Figure 2. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 4-year old male control subject JM.

Days After Administration	Percent Biological Retention	
	^{83}Rb	^{137}Cs
0	100	100
1	97.5	87.8
2	96.2	84.8
5	87.9	75.7
12	74.5	66.6
19	62.3	57.6
26	50.0	47.7
40	37.4	37.6
72	18.9	21.6
107	9.44	12.8
124	5.92	9.27
161	2.83	5.51
193	1.51	3.43

Figure 3. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 10-year old male control subject WM.

Days After Administration	Percent Biological Retention ^{83}Rb	Percent Biological Retention ^{137}Cs
0	100	100
1	95.7	88.9
2	95.1	87.4
5	90.9	82.6
12	78.4	74.6
19	68.4	66.7
26	59.8	60.3
40	48.2	52.7
71	29.7	39.2
96	19.0	30.3
129	10.9	21.9
161	6.75	16.7
196	3.37	12.1
(418)		(1.57)

Figure 4. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 14-year old male control subject JS.

Days After Administration	Percent Biological Retention	
	^{83}Rb	^{137}Cs
0	100	100
1	97.9	94.0
2	97.0	90.4
5	89.6	85.5
12	82.2	81.7
19	74.2	75.1
26	67.2	70.3
40	56.1	62.1
72	37.0	49.0
107	23.2	37.7
124	17.6	32.5
161	10.8	24.9

Figure 5. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 19-year old male control subject KM.

<u>Days After Administration</u>	<u>Percent Biological Retention</u>	
	<u>⁸³Rb</u>	<u>¹³⁷Cs</u>
0	100	100
1	97.0	93.2
2	96.8	92.0
14	82.0	81.0
25	69.4	75.5
53	43.8	60.8
89	25.2	46.5
117	16.1	37.4
151	8.83	29.1
180	4.98	23.0
208	2.92	19.1
(409)		(4.54)

Figure 6. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 25-year old male control subject GA.

Days After Administration	Percent Biological Retention ⁸³ Rb	Percent Biological Retention ¹³⁷ Cs
0	100	100
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
(372)		(14.9)

Figure 7. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 37-year old male control subject CWM.

<u>Days After Administration</u>	<u>Percent Biological Retention</u> <u>⁸³Rb</u>	<u>¹³⁷Cs</u>
0	100	100
1	96.9	94.4
2	93.6	89.3
6	87.5	85.6
13	73.2	74.6
24	58.7	67.2
52	30.9	51.4
87	15.5	38.7
115	8.78	30.1
150	4.26	22.3
178	2.30	17.7
210	0.99	13.8
(365)		(4.02)

Figure 8. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 53-year old male control subject SG.

Days After Administration	Percent Biological Retention	
	^{83}Rb	^{137}Cs
0	100	100
1	97.8	95.3
2	94.8	90.7
6	88.1	87.8
13	76.9	78.5
24	63.3	72.0
52	38.3	55.6
87	20.5	41.7
115	12.3	32.6
150	5.94	24.0
178	3.40	18.8
206	1.95	14.6
(364)		(3.98)

Figure 9. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 80-year old male control subject DB.

<u>Days After Administration</u>	<u>Percent Biological Retention</u>	
	<u>⁸³Rb</u>	<u>¹³⁷Cs</u>
0	100	100
1	98.3	96.6
2	96.2	87.9
6	88.1	78.2
13	77.6	69.5
27	63.4	61.8
57	35.9	41.4
90	19.5	30.8
118	11.3	23.5
153	6.13	17.5
181	3.42	13.3
209	1.84	10.2
(375)		(2.26)

Figure 10. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 14-year old female control subject JL.

Days After Administration	Percent Biological Retention	
	^{83}Rb	^{137}Cs
0	100	100
1	98.5	95.4
2	97.3	90.8
7	90.9	84.9
14	81.7	72.9
25	71.9	66.4
53	47.4	50.3
88	27.3	35.7
116	17.0	26.4
151	10.3	18.8
179	6.83	14.6
207	4.73	11.3
(364)		(2.61)

Figure 11. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 18-year old female control subject SB.

<u>Days After Administration</u>	<u>Percent Biological Retention</u> <u>⁸³Rb</u>	<u>¹³⁷Cs</u>
0	100	100
1	98.0	96.6
2	96.8	95.2
7	92.1	93.2
16	77.4	79.4
26	69.8	77.3
54	44.9	65.4
89	28.8	53.6
117	18.5	45.1
152	10.8	37.7
180	6.76	31.4
208	3.99	26.9
(360)		(11.2)

Figure 12. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 28-year old female control subject SAS.

<u>Days After Administration</u>	<u>Percent Biological Retention</u> <u>⁸³Rb</u>	<u>¹³⁷Cs</u>
0	100	100
1	95.4	84.9
2	95.0	83.8
5	92.1	79.7
11	85.9	75.6
18	82.6	74.8
25	74.5	65.7
39	63.9	59.4
67	45.5	49.1
95	30.9	41.5
127	19.7	33.2
157	12.6	26.7
193	7.36	20.7
(415)		(4.32)

Figure 13. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 39-year old female control subject BS.

Days After Administration	Percent Biological Retention ^{83}Rb	Percent Biological Retention ^{137}Cs
0	100	100
1	98.9	95.7
2	95.4	92.9
5	89.5	87.8
11	82.3	83.5
18	72.3	76.0
25	63.8	69.8
39	50.2	61.7
67	31.7	48.7
95	19.9	39.5
123	11.7	30.7
157	6.55	23.8
193	3.49	17.9
(415)		(2.89)

Figure 14. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 52-year old female control subject MR.

Days After Administration	Percent Biological Retention	
	^{83}Rb	^{137}Cs
0	100	100
1	97.5	92.1
2	94.1	89.1
5	87.8	81.2
12	80.5	77.1
19	70.4	69.8
26	63.9	64.0
40	50.4	54.9
68	32.6	44.0
96	20.4	33.9
124	13.3	26.2
159	8.03	19.8
194	4.54	14.8
(413)		(2.11)

Figure 15. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 14-year old female subject VG, presumed to be a genetic carrier of Duchenne dystrophy.

Days After Administration	Percent Biological Retention ^{83}Rb	Percent Biological Retention ^{137}Cs
0	100	100
1	97.4	97.1
2	92.2	87.9
6	86.1	79.7
13	77.3	71.4
27	64.3	63.4
57	39.5	44.6
90	24.4	34.4
118	16.6	27.8
153	9.46	17.8
181	5.64	12.4
209	3.34	9.30
(375)		(2.27)

Figure 16. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 18-year old female subject CL, presumed to be a genetic carrier of Duchenne dystrophy.

<u>Days After Administration</u>	<u>Percent Biological Retention</u> <u>⁸³Rb</u>	<u>¹³⁷Cs</u>
0	100	100
1	97.1	92.8
2	95.8	89.6
5	87.2	82.8
12	77.1	75.3
19	69.4	68.7
26	61.7	62.0
40	51.0	53.0
68	33.8	42.0
96	21.6	32.8
124	13.3	23.9
159	7.68	18.0
194	4.35	13.1
(413)		(1.34)

Figure 17. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 35-year old female subject GG, a genetic carrier of Duchenne dystrophy.

Days After Administration	Percent Biological Retention	
	^{83}Rb	^{137}Cs
0	100	100
1	98.4	94.1
2	93.5	90.4
5	84.6	81.0
11	73.5	74.7
19	62.9	66.2
26	54.5	61.4
40	41.0	52.7
68	23.2	40.9
96	12.8	31.9
124	7.13	24.1
159	3.22	16.6
194	1.50	11.2
(415)		(1.13)

Figure 18. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 39-year old female subject BL, a genetic carrier of Duchenne dystrophy.

<u>Days After Administration</u>	<u>Percent Biological Retention</u> <u>^{83}Rb</u>	<u>^{137}Cs</u>
0	100	100
1	96.6	87.2
2	93.6	84.3
5	86.6	78.4
12	73.7	68.2
19	62.3	59.2
26	53.5	51.9
40	40.5	43.1
71	23.6	29.7
96	14.1	22.8
129	7.22	14.8
161	3.98	10.9
196	1.77	6.67
(418)		(0.48)

Figure 19. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 46-year old female subject SS, a genetic carrier of Duchenne dystrophy.

Days After Administration	Percent Biological Retention	
	^{83}Rb	^{137}Cs
0	100	100
1	97.4	93.7
2	95.5	92.8
5	90.5	86.9
12	78.8	80.3
19	71.3	74.6
26	63.5	68.7
40	50.0	60.0
68	30.5	47.1
96	19.2	38.6
124	11.6	30.4
157	6.26	23.1
194	2.96	17.3

Figure 20. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 47-year old female subject FJ, a genetic carrier of Duchenne dystrophy.

Days After Administration	Percent Biological Retention ^{83}Rb	Percent Biological Retention ^{137}Cs
0	100	100
1	96.3	91.0
2	94.7	89.9
5	89.5	84.2
11	80.5	79.7
18	71.0	73.9
25	65.6	70.2
39	52.9	63.2
67	33.3	50.0
95	19.5	40.9
123	12.6	34.0
158	6.53	26.9
193	3.21	20.7
(416)		(3.43)

Figure 21. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 50-year old female subject EP, a genetic carrier of Duchenne dystrophy.

<u>Days After Administration</u>	<u>Percent Biological Retention</u> <u>⁸³Rb</u>	<u>¹³⁷Cs</u>
0	100	100
1	97.0	92.5
2	95.5	87.6
6	87.6	76.5
13	72.1	61.7
27	53.1	45.1
55	26.7	24.9
90	11.6	11.1
118	5.98	6.28
155	2.32	2.85
181	1.16	1.68
209	0.53	0.96

Figure 22. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 5-year old male subject KB, slightly affected with Duchenne dystrophy.

Days After Administration	Percent Biological Retention	
	^{83}Rb	^{137}Cs
0	100	100
1	96.2	93.0
2	92.1	89.7
5	81.6	80.4
12	67.0	67.6
19	52.4	55.2
26	41.5	43.4
40	26.9	28.7
68	12.9	14.4
96	5.60	7.13
124	2.46	3.29
159	0.97	1.47
194	0.37	0.68

Figure 23. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 5-year old male subject RG, slightly affected with Duchenne dystrophy.

<u>Days After Administration</u>	<u>Percent Biological Retention ^{83}Rb</u>	<u>Retention ^{137}Cs</u>
0	100	100
1	97.0	85.8
2	92.2	80.7
5	82.5	67.4
12	63.3	49.6
19	48.2	36.5
26	37.1	26.3
40	22.8	14.8
68	8.63	5.19
96	3.19	1.94
124	1.17	0.72
159	0.34	0.25
194	0.10	0.11

Figure 24. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 7-year old male subject TM, moderately affected with Duchenne dystrophy.

Days After Administration	Percent Biological Retention	
	⁸³ Rb	¹³⁷ Cs
0	100	100
1	97.5	84.9
2	91.3	78.4
5	83.4	64.2
11	65.6	48.2
18	52.2	35.1
25	42.2	25.5
39	27.3	14.8
67	12.5	5.46
95	5.70	2.16
123	2.53	0.90
158	0.98	0.33
193	0.38	0.13

Figure 25. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 8-year old male subject MP, moderately affected with Duchenne dystrophy.

Days After Administration	Percent Biological Retention	
	⁸³ Rb	¹³⁷ Cs
0	100	100
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	0.53
186	1.42	0.38
251	0.81	0.09

Figure 26. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 13-year old male subject CM, severely affected with Duchenne dystrophy.

Days After Administration	Percent Biological Retention	
	⁸³ Rb	¹³⁷ Cs
0	100	100
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	0.58
221	0.97	0.31
251	0.80	0.13

Figure 27. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 14-year old male subject DH, severely affected with Duchenne dystrophy.

Days After Administration	Percent Biological Retention	
	⁸³ Rb	¹³⁷ Cs

0	100	100
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	53.9
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	0.94
152	2.03	0.60
187	1.28	0.21
222	0.98	0.10
250	0.67	0.14

Figure 28. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 16-year old male subject KS, severely affected with Duchenne dystrophy.

<u>Days After Administration</u>	<u>Percent Biological Retention</u> <u>⁸³Rb</u>	<u>¹³⁷Cs</u>
0	100	100
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	0.67
152	1.14	0.35
187	0.60	0.14
222	0.35	0.08
250	0.28	0.10

Figure 29. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 19-year old male subject LS, severely affected with Duchenne dystrophy.

Days After Administration	Percent Biological Retention	
	⁸³ Rb	¹³⁷ Cs
0	100	100
1	97.8	92.8
2	95.4	89.2
7	86.8	80.7
14	77.9	72.7
25	69.6	65.6
53	47.6	50.1
88	29.4	35.5
116	19.2	26.6
151	11.7	18.9
179	8.02	14.7
207	5.35	11.2

Figure 30. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 34-year old male subject JC, moderately affected with Duchenne dystrophy.

Days After Administration	Percent Biological Retention	
	^{83}Rb	^{137}Cs
0	100	100
1	98.5	95.9
2	96.0	88.1
6	86.3	76.7
13	77.0	67.8
27	58.5	56.7
55	31.7	37.3
90	17.3	22.9
118	10.7	15.8
153	5.97	10.2
181	3.34	6.96
209	1.93	4.84

Figure 31. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 12-year old male subject RA, slightly affected with myotonic dystrophy.

Days After Administration	Percent Biological Retention	
	⁸³ Rb	¹³⁷ Cs
0	100	100
1	98.2	93.8
2	95.3	87.4
6	90.2	81.4
13	82.8	75.0
27	64.5	66.0
55	41.1	53.7
90	23.4	40.5
118	15.6	34.1
153	9.14	27.0
181	5.75	22.0
209	3.71	17.7

Figure 32. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 26-year old male subject LP, slightly affected with limb-girdle dystrophy.

Days After Administration	Percent Biological Retention ⁸³ Rb	Percent Biological Retention ¹³⁷ Cs
0	100	100
1	97.6	94.7
2	93.8	91.9
6	84.4	85.0
12	77.1	81.1
23	63.4	74.6
51	36.1	59.0
86	17.5	43.5
114	10.3	35.7
149	5.12	27.3
177	2.62	22.2
205	1.33	18.0

Figure 33. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 30-year old male subject RB, slightly affected with fascioscapulohumeral (FSH) dystrophy.

<u>Days After Administration</u>	<u>Percent Biological Retention</u> <u>^{83}Rb</u>	<u>Retention</u> <u>^{137}Cs</u>
0	100	100
1	97.0	93.9
2	93.5	87.4
6	87.6	76.2
12	77.9	64.9
26	60.4	52.7
54	36.5	35.5
89	19.0	23.1
117	11.6	17.2
152	6.26	12.2
180	3.58	8.77
208	2.32	6.71

Figure 34. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 44-year old male subject WS, moderately affected with fascioscapulohumeral (FSH) dystrophy.

Days After Administration	Percent Biological Retention	
	⁸³ Rb	¹³⁷ Cs
0	100	100
1	95.5	97.0
2	92.3	91.7
6	84.3	80.6
13	69.3	67.6
27	51.9	57.3
55	28.4	44.2
90	12.4	31.2
118	6.48	23.2
153	2.71	16.5
181	1.26	12.7

Figure 35. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 61-year old male subject BD, moderately affected with amyotrophic lateral sclerosis.

Days After Administration	Percent Biological Retention ^{83}Rb	Percent Biological Retention ^{137}Cs
0	100	100
1	97.7	96.8
2	95.0	89.4
6	83.4	76.6
13	70.6	64.5
27	50.9	50.4
55	27.8	33.4
90	12.8	20.1
118	6.47	13.5
153	2.66	7.99
181	1.28	5.25
209	0.52	3.60

Figure 36. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 29-year old female subject AG, moderately affected with limb-girdle dystrophy.

Days After Administration	Percent Biological Retention	
	⁸³ Rb	¹³⁷ Cs
0	100	100
1	98.8	95.6
2	95.9	89.6
6	90.4	80.6
13	79.5	69.8
27	61.6	59.5
55	36.7	43.8
90	19.6	31.5
118	11.4	23.7
155	5.86	14.8
181	3.33	12.8
209	1.90	9.59

Figure 37. Measured total-body biological retention of ⁸³Rb and ¹³⁷Cs in 37-year old female subject BA, moderately affected with myotonic dystrophy.

Days After Administration	Percent Biological Retention	
	^{83}Rb	^{137}Cs
0	100	100
1	97.2	89.9
2	92.3	81.1
6	76.0	54.3
15	53.0	27.2
26	35.6	12.5

Figure 38. Measured total-body biological retention of ^{83}Rb and ^{137}Cs in 19-year old female subject PB, severely affected with infantile muscular atrophy (died 33 days after radionuclide administration).

Figure 39. Equivalent biological half-time (T_Q) for ^{137}Cs in male subjects as a function of age. Solid symbols represent measurements made using fallout ^{137}Cs ^(2,4) while open symbols represent measurements for the subjects listed in Tables 1 and 2 following ^{137}Cs administration.

Figure 40. Equivalent biological half-time (T_Q) for ^{137}Cs in female subjects as a function of age. Solid symbols represent measurements made using fallout ^{137}Cs ^(2,4) while open symbols represent measurements for the subjects listed in Tables 1 and 2 following ^{137}Cs administration.

Figure 41. Equivalent biological half-time (T_Q) for ^{83}Rb as a function of age in male subjects following ^{83}Rb administration.

Figure 42. Equivalent biological half-time (T_0) for ^{83}Rb as a function of age in female subjects following ^{83}Rb administration.

Figure. 43. Ratio of the T_0 for ^{137}Cs to the T_0 for ^{83}Rb in male subjects as a function of age.

Figure 44. Ratio of the T_Q for ^{137}Cs to the T_Q for ^{83}Rb in female subjects as a function of age.