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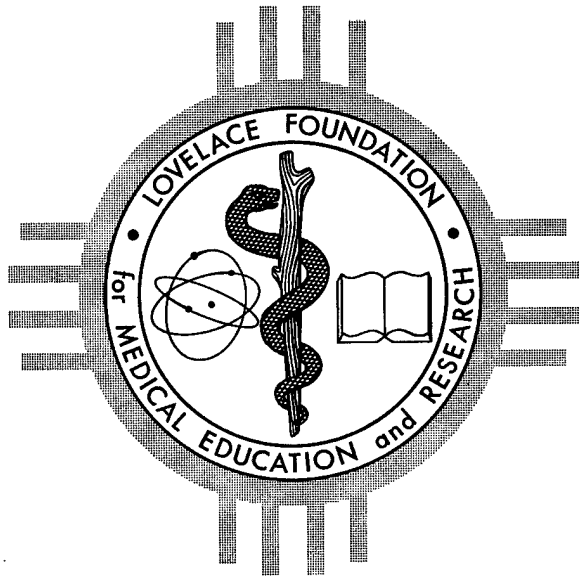

Albuquerque, New Mexico

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THE TISSUE DISTRIBUTION AND EXCRETION OF CESIUM-137 FOLLOWING INHALATION

PRELIMINARY DATA FOR RATS

by

J. F. STARA AND R. G. THOMAS

April 1963

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THE TISSUE DISTRIBUTION AND EXCRETION OF CESIUM-137 FOLLOWING INHALATION - PRELIMINARY DATA FOR RATS

by
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ABSTRACT

Data were obtained for the distribution-excretion pattern of cesium in rats over a period of 102 days following inhalation exposure. Three groups of 20 rats each were exposed to aerosols generated from solutions of "carrier-free", 1 and 8 per cent cesium chloride which contained cesium-137 as a tracer. Urine and feces of all rats were collected daily until sacrifice, and the time-tissue distribution patterns were determined after death. All measurements were made by gamma counting with sodium iodide crystals.

Cesium chloride, being extremely soluble, was absorbed rapidly from the lungs and the digestive tract and the amount initially deposited in lung was reduced to less than 1 per cent during the first post-exposure day. The initial deposition in the lung was dependent on the aerosol particle size which was varied by the addition of the cesium chloride "carrier"; more lung deposition occurred with the smallest particle sizes. After the first day, the skeletal muscle and skin contained the largest amounts of this fission product but several organs such as lung and kidney had approximately the same concentrations. Because of lack of significant amounts of radioactivity at the later sacrifice times, no definite decision could be made regarding the choice of one "critical" organ for greatest radiation effect.

Total excretion of Cs^{137} displayed an early rapid phase followed by two successively slower phases, presumably the entire pattern being fit by an exponential function. These three phases, obtained from the whole body retention curve, can be resolved into half-lives of approximately .6, 7.0 and 18.7 days.

The importance of interspecies comparison in obtaining parameters for estimating hazards to man is discussed, using cesium metabolism as an example.

ACKNOWLEDGMENTS

The particle size analysis and many suggestions of Dr. T. T. Mercer, the technical assistance of Miss Toni Pagano, and the Laboratory Staff of the Section of Radiobiology at the Lovelace Foundation are gratefully acknowledged.

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INTRODUCTION

Studies of cesium metabolism have been reported in the literature by several investigators who used different routes of administration in a variety of animal species. Scott, et al. (1) administered Cs^{134} and Cs^{135} to rats by the oral and intramuscular (IM) routes and found no significant difference in the tissue distribution patterns. Hamilton (2) reported no difference in distribution of Cs^{135} after oral and intraperitoneal (IP) administrations, and established the muscle as the organ of principal localization, with a retention half-life (T 1/2) of 15 days. Hood and Comar (3) obtained the tissue distribution of Cs^{137} in several animal species, including the rat, using both oral and IM routes. They found that muscle accumulated the largest concentration of cesium. Woodward, Richmond and Langham (4) administered Cs^{134} to rats IP and reported retention components (T 1/2) of 1.5, 7.0 and 14 days. Ballou and Thompson (5, 6) attempted to determine if a certain fraction of deposited Cs^{137} is retained longer than suggested by the previous shorter studies. Their results confirm that muscle becomes the largest depot of cesium, the residence time being represented by biological half-lives of 8 and 16 days in muscle as well as in all other tissues. Richmond (7), in his excellent thesis, used oral and IP routes for Cs^{134} administration and obtained a tri-exponential disappearance curve with exponential components having biological half-lives of 0.8, 6.8 and 13.5 and 1.5, 7.0 and 14.0 days respectively. He suggested a relationship between the retention time of this isotope and the animal body surface area, and supported this hypothesis by demonstrating the retention curve in several species including man. Most recently, Nisiwaki, et al. (8) administered Cs^{137} to rats subcutaneously, and in their report, divided all organs into two groups according to the more rapid or slower cesium uptake pattern. Among organs that reached their maximum concentration by one hour after injection were heart, lung, liver, kidney, gastrointestinal (GI) tract and spleen; muscle, bone, testes

and brain reached their maxima more slowly. In all of the above experiments, the cesium was administered as the chloride (CsCl). Several other investigators examined certain aspects of Cs^{137} behavior in the body, and in general, obtained similar results (9-19). Cohn, et al. (20, 21) exposed experimental animals to mixed fission products using the inhalation route but the uncertainty in the amount of contribution of individual isotopes to the body burden limits the applicability of their results in the study of cesium as a single isotope. Recently an extensive study of cesium metabolism in goats, pigs, and hens has been made by Ekman (22).

This experimental series was designed to furnish quantitative data from the exposure of rats to aerosols containing Cs^{137} and to compare the resulting distribution and excretion patterns with those obtained by other routes of administration. By adding this information to the present knowledge, more representative values for retention and excretion can be obtained for use in radiation hazards evaluation and control.

METHODS

Three groups of 20 Holtzman strain rats, evenly divided by sex, weighing 150 $\pm$ 25 grams, and approximately 7-8 weeks old, were exposed to aerosols generated from solutions containing carrier-free*, 1 per cent, and 8 per cent cesium chloride (CsCl) solution with Cs^{137} as a tracer. The radioactive solution was obtained from Oak Ridge National Laboratory as a CsCl in HCl solution (.03 normal acid) with a concentration of approximately 5.46 mc/ml.

Prior to exposure, animals were given IP injections of pentobarbital sodium (22 mg/kg) and chlorpromazine hydrochloride (12 mg/kg). Each rat was placed into a plastic baby bottle which had been altered to permit "clean" nose-only exposure (23, 24). (The base of the bottle had been cut away allowing the animal to be inserted head first and the end of the nipple was snipped away also, allowing the rat's nose to barely protrude into the atmosphere.) Twenty rats per experiment were treated in this manner and placed into a 25 liter "pickle jar" glass exposure chamber. This entire exposure procedure has been described in detail previously (24). The aerosol was introduced to the chamber from a Dautrebande D_{30}-type generator (25).

* Carrier-free, in this case, is defined by the Oak Ridge National Laboratory Isotopes Branch as a solution to which no stable cesium was added during separation of the radioactive isotope.

The concentration of Cs^{137} in the chamber air was determined from aerosol samples collected on Millipore filters, type AA. These filters were strategically placed among the baby bottles and one-minute samples taken at intervals throughout the exposures. Two of the exposures (SA, SB groups) were of 30 minute duration, one (SC group - 8% carrier) of 45 minutes. Simultaneously, samples for particle size analysis were collected directly on electron microscope grids using a small electrostatic precipitator (26). These samples were later shadowed with chromium at 30° and electron micrographs of the deposited particles were obtained at a magnification of 12,000 times. Subsequent enlargement to approximately 35,000 times was used for measurement of particle diameters (27).

Following exposure, animals were removed from the chamber and their heads washed with a 1:7 solution of Radiacwash (Atomlab Products Co., Long Island, New York) in order to remove topically deposited isotope from the skin and hair of the head. The rats were wiped dry, placed individually into plastic bags, and whole body counted in a 3 x 5 inch NaI well crystal in order to establish the initial body burden. They were then paired and placed into metabolism cages for daily determination of the amount of isotope in urine and feces. These metabolism setups consisted of a plastic tray (directly below the entire cage) which was beveled toward a funnel shaped snout in the center. Feces were collected on a wire cloth screen which fit near the top of the tray; cotton was placed in the snout opening to stop any food or feces particles from entering the urine container sitting below. These setups are larger but similar in principle to those described by Tuttle and Baxter (28). Four rats from each experiment were whole body counted each day, utilizing the same NaI well counters. This enables determination of the retention kinetics and allows a simple comparison between the animals exposed to the three different CsCl aerosol concentrations.

Two rats were sacrificed shortly following exposure and removal from the chamber, and two were sacrificed at 1, 2, 4, 8, 16, 32, 64, 90, and 102 days thereafter. Selection of animal pairs and sacrifice times were done randomly. Sacrifices were performed by maximal blood withdrawal from the heart under ether anesthesia. The blood was counted directly to determine its Cs^{137} content; the animals were dissected into 30 different tissues (whole organs or a significant sample thereof) for similar determinations.

A list of these 30 tissues and the methods used for anti-contamination dissections have been described previously (29).

RESULTS

When the tissue distribution data following each of the three experiments (tracer level, 1%, and 8% CsCl) were compared, they appeared as though derived from the same population. This was tested by doing a two-way analysis of variance to indicate any significant differences among the three exposure regimes, for any one tissue cesium content at any one sacrifice time. From this analysis it was determined that the amount of cesium carrier did not significantly alter tissue retention kinetics, except in the decreased amount of isotope initially deposited in the lung. This difference disappeared very shortly after exposure and thereafter all data could be treated as deriving from the same sample population. Therefore, the values to follow are presented and discussed as pooled averages from all three experimental studies.

The initial Cs^{137} deposition in the lung (as just mentioned) did appear to bear some relationship to the amount of "carrier" cesium in the aerosol, presumably due in part to the resulting difference in the size of the deposited particles. Other factors may be the length of exposure time and the rate of lung clearance during the 20 minutes between the end of exposure and the time of sacrifice. Also, the particle shadows in the electron micrographs indicated that the particles were collected as droplets of CsCl solution, rather than dry crystals. In general, the degree of dryness attained by the particles at the time of collection increased with increasing concentration of CsCl in the generator, therefore increasing the density of the droplets. Measurements were made of both the apparent particle diameter and the length of the particle shadow. From these measurements it was possible to calculate the diameter that the CsCl particle would have had upon reaching complete dryness. It was assumed that the logarithms of the particle diameters were normally distributed, and the count median diameter and geometric standard deviation* were calculated for each sample. The results of these calculations, as well as the initial deposition in the lungs, are shown in Table 1. The values for

* The geometric standard deviation is equal to a ratio of the diameter which is equal to or greater than the diameters of 84.1 per cent of the particles to the count median diameter.

TABLE I

Rat Groups	Approximate CsCl Concentration in the Generator	Exposure Time	Count Median Diameter	Geometric Standard Deviation	Median Initial Whole Body Burden	Initial Lung Deposition ***
SA	0% *	30 min	.023 μ	1.94	0.13 μc	10.25 (9.53 - 10.97)
SB	1%	30 min	.028 μ	2.08	0.17 μc	8.31 (7.70 - 8.92)
SC	8%	45 min	.1 μ **	1.91	0.17 μc	2.48 (1.64 - 3.32)

* No carrier added to stock solution.

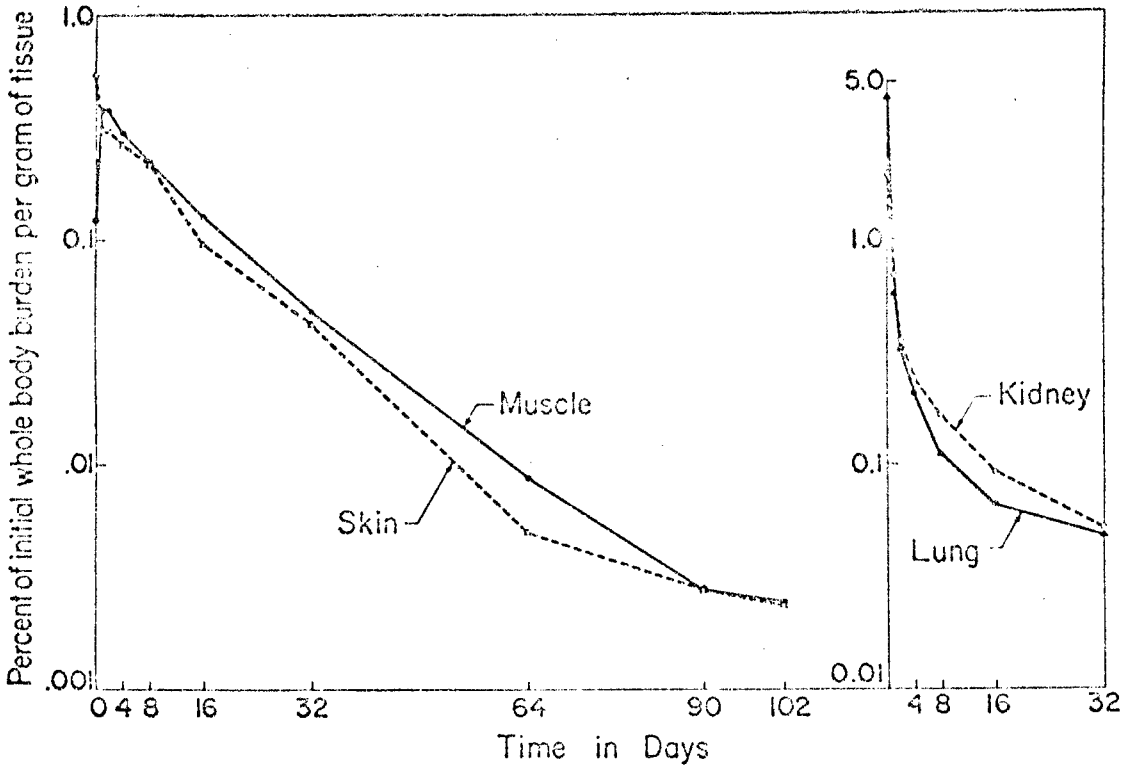
** Estimated from distribution obtained with 10 per cent solution in the generator. The median diameter is assumed to be proportional to the cube root of the concentration.

*** Mean per cent of initial body burden and the ranges. Animals for the determination of initial lung deposition were sacrificed within 20 minutes post-exposure.

the 8% solution were estimated from a previous experiment using a 10% solution of cesium chloride which yielded a calculated mass median diameter of 0.39 μ. A sample taken during that run with a Casella cascade impactor gave a mass median diameter of $\frac{0.52}{\sqrt{\rho}}$ μ and a geometric standard deviation of 1.86. At the time of collection, the particle density, ρ, is unknown but it is necessarily less than 4.0 (the density of the dry crystal), so that the two results would appear to be in reasonable agreement.

Animals used for the determination of the initial lung deposition were sacrificed within 20 minutes after the completion of an exposure. The data of Table 1 show a definite trend for an increased lung deposition with decrease in count median diameter. It would be rather meaningless however, to attempt quantitating the relationship between these two variables on the basis of only two rats per point. In general, the mass median diameter is a much more meaningful parameter for comparison with fraction of the aerosol deposited in the lung, and this will be done much more extensively in future studies.

The distribution of Cs^{137} in certain tissues is presented in Figure 1 in terms of mean per cent of initial body burden per gram wet weight. Muscle, skin, lungs and kidneys are demonstrated as the representative organs according to faster or slower "turn-over" rate. The data have been normalized to an animal weight of 200 grams to correct for the isotope dilution effect due to growth throughout the experiment. This manner of normalization assumes a direct ratio of organ weight to body weight over the range covered here, an assumption that holds quite well. The plots in Figure 1 indicate a single exponential decrease in muscle and skin cesium concentration after the first day or two and show these two organs to treat the isotope in approximately the same quantitative manner. Kidney and lung handle cesium in quite a different manner from muscle and skin, but very similar to each other. These organs are initially (< 1 day) quite high in cesium concentration but lose it very rapidly, whereas an organ like muscle builds up its reservoir over the first day, presumably in part from material passing from lung to blood. The rapid loss of cesium from lung can be observed in Figure 1 and the amount remaining at 24 hours is approximately 0.5% of the initial body burden. Thus the radiation dose under these experimental conditions would be attributed mostly to the long term kinetics rather than these very early distribution patterns. It should be pointed out here, and it will be stressed



Cesium[137] Organ Concentrations in Rats Following Inhalation
(Data are normalized to a constant rat weight)

FIGURE 1

later, that beyond 32 days the content of most organs was too low to permit a significant analysis.

Data presented in Table 2 were calculated as mean percentages of sacrifice body burden per organ. The skeletal muscle and the bone were assumed to be 46% and 6.4% of the total body weight respectively, in order to express the data as obtained from representative samples in terms of total organ content (30, 31). Although these assumptions lead to what are presented as extremely accurate calculations, it should be recognized that anything over one or two significant figures is subject to question. The results demonstrate that the skeletal muscle was the largest depot of cesium and at 16 days, when the body burden had decreased to 20% of the initial value, almost 65% of the remaining isotope was located in this organ. Skin was the organ with second highest deposition, accounting for approximately 20% of the body burden at each time of sacrifice. At 65 days, practically all detectable activity was located in muscle and skin and beyond 32 days, the content of most organs was too low to permit a significant analysis. These data again indicate that the tracer was rapidly translocated from the lungs to most other tissues shortly after exposure with some organs such as muscle, bone and testes reaching their highest absolute level as late as 24 hours post-exposure.

Tables 3, 4 and 5 show the same data expressed as a percentage of the initial body burden per organ (Table 3) and per gram of tissue (Table 4) and as percentage of the sacrifice body burden per gram of tissue (Table 5). Again, the lack of significant activity in most organs beyond a 32 day sacrifice time is evident. Perhaps the most interesting data are those expressed on a per gram basis in Tables 4 and 5. Although there are few significant values available beyond 32 days, most tissues for which there are data at that time have quite comparable concentrations to those found in muscle and skin. Also, it will be noted in Figure 1 that the curves for lung and kidney are indicating a smaller slope than for muscle and skin at that time. The point being made is that there are not enough significant tissue data available in these experiments to yield a clear-cut choice of a "critical" organ for radiation damage. Obviously it is the very large size of the sample which renders the muscle and skin to be the only organs containing measurable radioactivity at the later times.

TABLE 2

DISTRIBUTION OF Cs^{137} IN ORGANS OF RATS FOLLOWING INHALATION

Values Expressed as Mean Percentage and Standard Deviation of Sacrifice Body Burden

ORGAN \ DAY	0	1	2	4	8	16	32	64	90	102
Muscle**	11.0±2.8*	44.4±4.0	51.2±3.0	51.3±5.7	60.3±6.7	64.3±7.4	62.5±4.3	62.6±18.0	57.9±14.1	56.8±11.4
Skin	19.0±9.0	16.4±3.8	18.2±.54	18.9±.83	20.8±5.5	15.2±6.4	18.4±1.2	23.2±9.8	25.8±3.5	22.0±8.5
G.I. Tract & Contents	15.3±4.4	14.6±2.9	12.1±1.1	9.1±1.4	7.0±.64	7.1±1.2	8.4±2.4	3.8±2.5	–	–
Bone**	1.6±.54	4.7±.28	5.3±.22	5.3±1.0	4.2±.59	5.1±.69	5.1±1.0	–	–	–
Male U.G. System	.59±.15	2.8±.43	2.4±.51	2.2±.22	2.3±.18	2.4±.16	2.8±.86	–	–	–
Liver	3.8±.86	7.5±1.4	4.7±.95	3.4±.34	2.8±.20	3.1±.39	2.8±.15	–	–	–
Kidney	3.2±.86	1.7±.24	.97±.80	.81±.54	.88±.16	.86±.16	1.2±.56	–	–	–
Lungs	7.0±4.0+	.78±.10	.75±.34	.67±.12	.63±.12	.58±.14	.74±.10	–	–	–
Brain	.82±1.1	.67±.27	.82±.26	.65±.28	.64±.13	.64±.21	.62±.40	–	–	–
Heart	.88±.29	.52±.12	.39±.083	.28±.031	.29±.0071	.40±.094	–	–	–	–
Spleen	.28±.063	.38±.071	.29±.077	.20±.089	.25±.077	.43±.077	–	–	–	–
Blood	.55±.062	.49±.060	.77±.077	.58±.14	.50±.065	.58±.087	–	–	–	–

*Mean and standard deviation of 6 animals. $\left(\bar{x} = \frac{\Sigma x}{n},\ \sigma = \pm\sqrt{\frac{\Sigma x^2 - \Sigma x(\bar{x})}{n-1}}\right)$

**Muscle and bone calculated on basis of 45.5% and 6.41% of body weight.

+Statistically significant difference between groups (see Table 1); mean used for sake of uniformity.

TABLE 3

DISTRIBUTION OF Cs^{137} IN ORGANS OF RATS FOLLOWING INHALATION

Values Expressed as Mean Percentage and Standard Deviation of Initial Body Burden

ORGAN \ DAY	0	1	2	4	8	16	32	64	90	102
Muscle**	11.3±2.0*	34.5±3.6	34.4±2.45	28.1±2.6	20.4±1.2	11.3±1.3	4.4±.200	.80±.098	.29±.031	.20±.073
Skin	17.4±6.0	11.9±3.6	11.2±2.44	10.6±.71	6.1±2.3	2.8±1.3	1.6±.140	.30±.110	.13±.042	.089±.034
G.I. Tract & Contents	15.3±3.4	10.6±2.4	7.7±1.0	11.7±1.1	2.3±.17	1.2±.26	.66±.260	–	–	–
Bone**	1.8±.56	3.5±.71	3.5±.36	2.8±.70	1.6±.36	.64±.024	.49±.140	–	–	–
Male U.G. System	.56±.15	2.0±.58	1.5±.30	1.5±.053	.88±.09	.42±.083	.23±.089	–	–	–
Liver	3.8±.26	5.7±1.4	3.1±.64	1.8±.34	.95±.12	.53±.089	.20±.054	–	–	–
Kidney	3.2±.79	1.2±.22	.64±.19	.43±.12	.29±.055	.15±.031	.094±.040	–	–	–
Lungs	7.0±3.7+	.59±.11	.49±.21	.36±.09	.21±.044	.099±.024	.063±.010	–	–	–
Brain	.79±1.0	.51±.22	.54±.16	.34±.17	.22±.054	.12±.050	.051±.030	–	–	–
Heart	.89±.28	.39±.10	.26±.05	.15±.031	.099±.0031	.075±.020	–	–	–	–
Spleen	.28±.08	.29±.063	.19±.05	.10±.044	.087±.030	.069±.0054	–	–	–	–
Blood	.55±.062	.49±.065	.51±.05	.31±.10	.18±.022	.097±.026	–	–	–	–

*Mean and standard deviation of 6 animals. $\left(\bar{x} = \frac{\Sigma x}{n}, \sigma = \pm\sqrt{\frac{\Sigma x^2 - \Sigma x(\bar{x})}{n-1}}\right)$

**Muscle and bone calculated on basis of 45.5% and 6.41% of body weight.

+Statistically significant difference between groups (see Table 1); mean used for sake of uniformity.

TABLE 4

DISTRIBUTION OF Cs^{137} IN ORGANS OF RATS FOLLOWING INHALATION

Values Expressed as Mean Percentage and Standard Deviation of Initial Body Burden Per Gram of Tissue*

DAY / ORGAN	0	1	2	4	8	16	32	64	90	102
Muscle+	.12±.028**	.38±.055	.37±.044	.30±.044	.22±.024	.13±.020	.048±.0063	.0088±.0045	.0038±.0017	.0025±.0004
Skin	.54±.19	.30±.19	.30±.024	.26±.0031	.21±.080	.095±.048	.042±.0051	.0050±.0020	.0028±.00098	.0024±.00051
G.I. Tract & Contents	.50±.14	.41±.25	.27±.10	.18±.071	.11±.024	.057±.020	.031±.012	.015±.009	–	–
Bone+	.13±.014	.28±.044	.27±.031	.22±.055	.12±.031	.068±.014	.037±.010	–	–	–
Male U. G. System	.18±.058	.25±.078	.28±.034	.29±.031	.15±.024	.065±.010	.039±.016	–	–	–
Liver	.41±.084	.56±.13	.30±.054	.18±.045	.098±.014	.060±.014	.023±.0077	–	–	–
Kidney	1.9±.44	.69±.12	.35±.077	.24±.055	.16±.026	.092±.020	.052±.026	–	–	–
Lungs	4.2±2.9++	.57±.44	.32±.040	.21±.054	.11±.024	.066±.031	.049±.010	–	–	–
Brain	.36±.44	.22±.089	.24±.020	.19±.071	.11±.014	.073±.034	.045±.029	–	–	–
Heart	1.0±.25	.49±.20	.34±.095	.21±.034	.13±.044	.11±.044	–	–	–	–
Spleen	.46±.18	.53±.12	.35±.078	.20±.092	.14±.055	.13±.040	–	–	–	–
Blood	.069±.038	.091±.037	.065±.014	.046±.020	.034±.0022	.012±.0044	–	–	–	–

*Data were corrected to normalized rat weight.

**Mean and standard deviation of 6 animals.

+Muscle and bone calculated on basis of 45.5% and 6.41% of body weight.

++Statistically significant difference between groups (see Table 1); mean used for sake of uniformity.

TABLE 5

DISTRIBUTION OF Cs^{137} IN ORGANS OF RATS FOLLOWING INHALATION

Values Expressed as Mean Percentage and Standard Deviation of Sacrifice Body Burden Per Gram of Tissue*

ORGAN \ DAY	0	1	2	4	8	16	32	64	90	102
Muscle+	.12±.035**	.49±.042	.56±.035	.57±.063	.66±.077	.71±.077	.69±.044	.69±.20	.64±.15	.62±.12
Skin	.53±.24	.43±.28	.43±.017	.46±.013	.60±.21	.40±.12	.49±.050	.76±.30	.76±.069	.70±.24
G.I. Tract & Contents	.49±.17	.56±.084	.44±.089	.34±.10	.34±.045	.33±.077	.40±.11	.34±.22	–	–
Bone+	.13±.044	.36±.071	.41±.044	.41±.071	.37±.067	.40±.056	.49±.080	–	–	–
Male U.G. System	.19±.064	.33±.063	.44±.038	.50±.080	.47±.060	.36±.028	.47±.13	–	–	–
Liver	.41±.089	.74±.15	.59±.27	.33±.077	.30±.045	.35±.031	.33±.045	–	–	–
Kidney	1.9±.48	.92±.14	.53±.27	.46±.084	.50±.071	.51±.11	.72±.28	–	–	–
Lung	4.2±1.7++	.53±.077	.48±.055	.39±.071	.34±.062	.39±.14	.58±.063	–	–	–
Brain	.37±.46	.27±.083	.37±.084	.32±.062	.33±.057	.40±.0071	.55±.36	–	–	–
Heart	1.1±.25	.64±.11	.52±.13	.37±.071	.36±.031	.60±.16	–	–	–	–
Spleen	.45±.12	.69±.13	.53±.10	.37±.17	.19±.037	.39±.024	–	–	–	–
Blood	.071±.044	.10±.025	.095±.014	.084±.025	.068±.022	.080±.017	–	–	–	–

*Data were corrected to normalized rat weight.

**Mean and standard deviation of 6 animals.

+Muscle and bone calculated on basis of 45.5% and 6.41% of body weight.

++Statistically significant difference between groups (see Table 1); mean used for sake of uniformity.

The whole body retention curve for Cs^{137} and the cumulative urinary and fecal excretion, both plotted as percentages of the initial body burden, are presented in Figure 2. The retention curve has been divided into three exponential components for adequate description (7, 3) and their fit was computed by the least squares method. Each point, up to 64 days post-exposure, represents the average of 12 animals and thereafter, the number decreases until subsequent to the 90th day there are only 2 animals remaining. Fifty per cent of the inhaled Cs^{137} was eliminated within 4 days and only 1 per cent remained at 65 days. The long retention component indicates a somewhat larger biological half-life than previously reported (18.7 days compared to 16 days or less). However, these differences may well not be significant due to the small number of animals available for whole body counting at the later times. Also, it is possible that the long half-lived reservoir in skin, presumably not due to contamination, may serve to extend the whole body retention curve. If the main reservoir were muscle, as noted by most previous authors, then certainly the whole body data here would more closely fit those of other studies.

Figure 2 also presents data obtained on the daily excretion of Cs^{137} as per cent of initial whole body burden. These are cumulative data and show that most of the cesium has been excreted by 20 days post-exposure, a fact which is also reflected in the whole body retention curve of Figure 2. The urine to feces ratio of cesium content is about 3.5:1, 79% of the total excreted appearing in the urine by 102 days. This is another indication of the extreme solubility of CsCl.

An attempt was also made to resolve the retention exponential curves for several organs of interest into their half-life components in the same manner as for the whole body in Figure 2. The retention data of tissues tested were analyzed on the assumption that two or three components would provide the best fitting and most meaningful line. Table 6 shows these equation parameters for muscle and skin as well as whole body and indicates that their long components have slightly greater half-life than previously reported. All other tissues tested exhibited comparable components of $(T\ 1/2)c$ = 13-17 days and $(T\ 1/2)b$ = 6-8 days half-life. The third component of .5-2 days half-life could be obtained from the retention kinetics of most tissues. The absence of this early component in muscle, bone and testes is due to the

Retention of Cs^{137} in Rats Following Inhalation

(Values represent the mean and the range)

Excretion Pattern of Cs^{137} in Rats Following Inhalation

(Graphs represent cumulative urinary and fecal excretions)

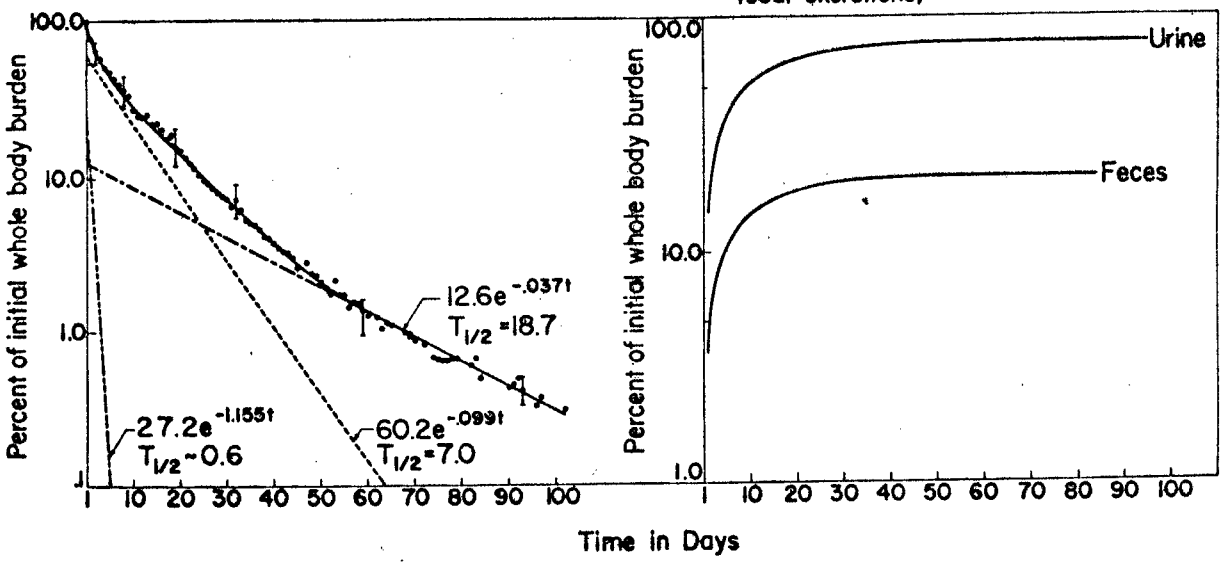


FIGURE 2

TABLE 6

Cesium^{137} Retention in the Whole Body, Muscle and Skin of Rats

	$Q = Q_o (ae^{-\lambda_1 t} + be^{-\lambda_2 t} + ce^{-\lambda_3 t})$*								
	a	λ_1	$(T_{1/2})_a$	b	λ_2	$(T_{1/2})_b$	c	λ_3	$(T_{1/2})_c$
Whole body	.272	1.155	~.6	.600	.0990	7.0	.128	.0370	18.75
Muscle**	-	-	-	.750	.0845	8.2	.250	.0357	19.5
Total muscle mass***	-	-	-	.813	.0845	8.2	.187	.0346	20.0
Skin	-	-	-	.840	.0866	8.0	.160	.0315	22.0

*Retention equation symbols:

$Q = Cs^{137}$ whole body or organ burden at time t (in days)

$Q_o = Q$ at $t = 0$ (extrapolated from the retention curve)

a, b, c = intercepts of components

$\lambda_1, \lambda_2, \lambda_3$ = rate constants, where $\lambda = \frac{.693}{T_{1/2}}$

$T_{1/2}$ = biological half-life in days

**Sample of muscle from femoral region

***Total muscle mass calculation based on 45.5% of body weight

aforementioned slower build-up of the tracer in these organs.

DISCUSSION

Although the long components for muscle and skin were estimated in Table 6 to be 19.5 and 22 days respectively, the significance of these values is uncertain since the amount of activity in both samples was less than 0.2 per cent of the initial body burden at 90 days. Also, it should be re-emphasized that the cesium concentration in tissues such as lung, brain, and kidney may be as high as these two larger organs at the later times where significant data are lacking. This fact, plus the ever-present question of the relative radiosensitivity of different organs, definitely lends these experiments to be classified "preliminary" as far as predicting a most likely site for radiation insult. However, the data do show a similarity to other studies with regard to the kinetics of distribution and excretion of cesium in the rat, as reviewed in the Introduction. Cesium chloride is so soluble in body fluids that only minor differences, if any, appear to exist between various routes of administration to the rat. In fact this is one of the few cases where the inhalation route is so very much like parenteral injection in the body's manner of the handling of a material. In many cases, even though water solubility would predict a similar metabolism regardless of route of entry, the distribution and excretion pattern following inhalation may be quite different than after other modes of entry to the body.

One point of great importance regarding species differences in the handling of a given material should be re-emphasized here. It has been pointed out concretely by Richmond, et al. at the Los Alamos Scientific Laboratory that a great range in half-lives exists in the kinetics of cesium metabolism, depending upon the size of the animal (33, 7). They report a long component half-life in man to be greater than 100 days, whereas their results from rats agree with those reported herein. Thus, all precautions should be employed in extrapolating similar findings from one species to another, eg. rodents to man, even though data obtained within one species may be extremely uniform and quantitatively sound. This points up the importance of using as many species as feasible, particularly whenever applied experimentation is being carried out. It is interesting that the National Committee on Radiological Protection in 1953 listed the

biological half-life of cesium as 17 days, based upon rodent data, and in 1959 this had been changed upward by a factor of 8, based upon data obtained on humans (36, 37).

SUMMARY

1) Three groups of rats have been exposed to aerosols generated from solutions containing approximately zero, 1, and 8 per cent cesium chloride, using Cs^{137} as a tracer.

2) A larger initial deposition in the lung occurred with the lower salt concentration, but all deposited material entered the circulation very rapidly.

3) Because of this extreme solubility in body fluids, the tissue distribution data from all three exposure regimes could be combined as if derived from one population.

4) Muscle and skin were the largest reservoirs of cesium chloride but on a concentration basis kidney, brain, and perhaps other soft tissues could be equally important in radiation damage. However, significant data are lacking in these organs at the later time (beyond 32 days) due to depletion of radioactivity beyond significant detection limits.

5) The lack of a good choice of "critical" organ and the differences in cesium metabolism between species is stressed.

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