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RADIATION RESEARCH 19, 643–654 (1963)

I. Cesium-137 Metabolism in Man[1]

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INTRODUCTION

The study of the metabolism and distribution of cesium-137 is of particular interest at present because it is a biologically important fission product present in radioactive fallout. Animal experiments have shows species differences in the excretion patterns of parenterally and orally administered Cs^{137}. For example, in rats and rabbits the primary route of excretion is via the kidney, whereas in cows and sheep most of the cesium is excreted in the feces (*1–3*). In sheep, 50% to 80% of orally ingested Cs^{137} was found to be absorbed (*3*). Tissue distribution studies in animals have shown that the largest concentration of cesium per gram of wet tissue is found in muscle (*1–3*).

Previous investigations of cesium in man have been primarily concerned with the measurement of the levels of fallout-produced Cs^{137} in various population groups (*4*). Recently, with the development of total-body counters, it has also been possible to measure the biological half-life of Cs^{137} in man (*5, 6*). The results obtained with these measurements are discussed in Part II of this presentation. This report describes a study of the excretion and distribution of Cs^{137} man, after both oral and intravenous administration of tracer doses of this isotope. Attempts to increase the excretion rate of Cs^{137} by various chemical agents are also described.

MATERIALS AND METHODS

The urinary and fecal excretion of Cs^{137} was determined in nine patients with neoplastic disease and in two patients with pulmonary diseases. These patients

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TABLE I

PATIENTS IN WHOM Cs^{137} EXCRETION AND ENHANCEMENT STUDIES WERE PERFORMED

Patient	*Age*	*Sex*	*Diagnosis*	*Route of administration*	*Study*	
					Type	*Days*
1	46	M	Hodgkin's disease	Intravenous	Excretion	160
2	57	M	Carcinoma of lung	Intravenous	Excretion	60
3	63	F	Carcinoma of colon	Intravenous	Excretion	21
4	45	M	Hodgkin's disease	Intravenous	Excretion Enhancement	42
5	50	M	Chronic pulmonary disease	Oral	Excretion	9
6	57	M	Chronic tuberculosis, inactive	Oral	Excretion	27
7	48	F	Carcinoma of colon with metastases to spine	Oral	Excretion	15
8	59	M	Carcinoma of lung	Oral	Excretion	19
9	55	F	Carcinoma of breast	Oral	Excretion	27
10	53	F	Carcinoma of breast	Oral	Excretion Enhancement	39
11	64	M	Multiple myeloma	Oral	Excretion Enhancement	35

had good nutrition and normal kidney function, and their gastrointestinal tract was not involved in disease (Table I). A single tracer dose of 10 to 50 μc of carrier-free Cs^{137} as chloride was injected intravenously to four patients and administered orally to seven. Blood samples were drawn at frequent intervals on the day of Cs^{137} administration, daily for the following 10 days, and periodically thereafter during the study. The total 24-hour excretion was collected for the duration of the excretion studies, which ranged from 9 to 160 days. In four of these patients, agents which might increase the excretion of cesium were administered at time intervals ranging from 10 to 31 days after the intravenous or oral administration of Cs^{137} (Table II). Normal saline was infused intravenously, and hydrodiuril, ammonium chloride, corticosteroids, the resin kayexalate, and ϵ-aminocaproic acid were administered orally. The tissue distribution of Cs^{137} was studied in four other patients who had expired at various time intervals after administration of the tracer (Table III).

Dose standards for intravenously administered tracers were prepared by quantitatively transferring an equivalent dose from the same syringe and needle into a volumetric flask and diluting with saline to an appropriate volume. Standards for oral doses were prepared by pipetting an equivalent dose into a volumetric flask and diluting in the same manner as above. Aliquots of the standard, whole

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TABLE II

Cs^{137} ENHANCEMENT STUDIES

Patient	Start of treatment after Cs^{137} doses (days)[a]	Enhancing agent	Dose/day	Duration of treatment (days)
4	13	Infusion of physiologic saline	500 ml	2
4	24	Hydrodiuril	50 mg	3
	31	Ammonium chloride	9 gm[b]	5
10	26	Prednisone	40 mg	14
11	10	Kayexalate	16 gm	5
	21	ε-Aminocaproic acid	24 gm	11

[a] A single tracer dose of $Cs^{137}Cl$ was given orally on the first day of the study.
[b] Three grams given three times per day.

TABLE III

Cs^{137} TISSUE DISTRIBUTION STUDIES

Patient	Age	Sex	Diagnosis	Days after intravenous injection of Cs^{137}
1	46	M	Hodgkin's disease	165
12	55	M	Carcinoma of lung	3
13	66	M	Malignant lymphoma	10
14	66	F	Hodgkin's disease	16
15	61	F	Carcinoma of uterus	3

blood, serum, urine, and feces were pipetted directly into counting tubes. Samples of the tissues obtained at autopsy were wet-weighed and placed in counting tubes. The radioassays were performed in a well-type NaI crystal scintillation counter. A single-channel pulse-height analyzer permitted counting at the cesium photopeak. Dose standards were counted at the time the samples were radioassayed. The data are expressed in per cent of the administered dose. For the calculations of the amount of Cs^{137} in whole blood and plasma, the volume of whole blood was assumed to be 5 liters, and of plasma 3 liters.

RESULTS

Excretion Studies

Intravenous Administration. The concentration of Cs^{137} in plasma and in whole blood in a representative study (patient 3) immediately after intravenous injec-

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Study	
Type	Days
Excretion	160
Excretion	60
Excretion	21
Excretion	42
Enhancement	
Excretion	9
Excretion	27
Excretion	15
Excretion	19
Excretion	27
Excretion	39
Enhancement	
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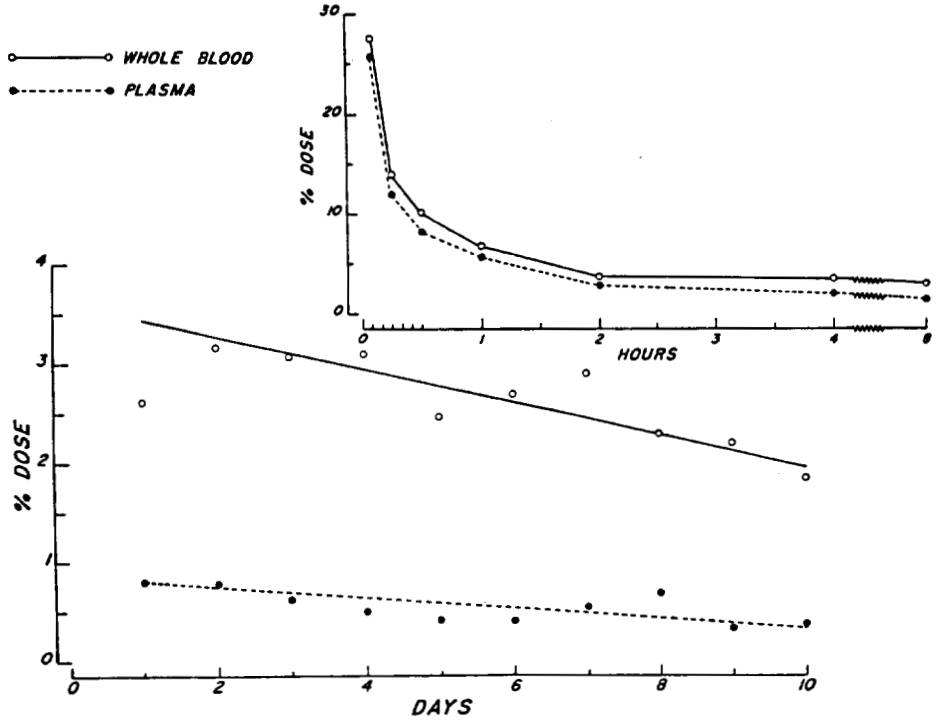

FIG. 1. A single tracer dose of $Cs^{137}Cl$ was injected intravenously. The concentration of Cs^{137} in whole blood and in plasma was determined on the first day of the study at frequent time intervals (see insert) and daily thereafter.

tion is shown in Fig. 1. At 5 minutes after injection of the isotope, the amounts of Cs^{137} in whole blood and in plasma were about equal, 27% and 26%, respectively. These levels decreased in a similar manner over the first 2 hours. The amount of Cs^{137} in whole blood at 2 hours (3.5%) remained the same for several days and then gradually declined to 2% at 10 days. In contrast, the Cs^{137} plasma level continued to decrease from the 2-hour level of 3% to 0.8% at 24 hours and stayed at approximately the same range for the next 10 days.

Most of the intravenously injected cesium was excreted in urine, whereas the fecal cesium excretion contributed only minimally to the total excretion. The excretion curves of patients 1 and 2 who were studied for 160 and 60 days, respectively, are very similar (Fig. 2). The urinary cesium excretion of patient 2 was slightly lower and the fecal excretion was slightly higher than in patient 1, resulting in a similar total excretion for both patients over a 60-day period. The excretion patterns of patients 3 and 4 who were studied for 21 and 11 days, respectively, were similar. Patient 3 excreted 16% of the dose in urine and 4% in stool in the first 11

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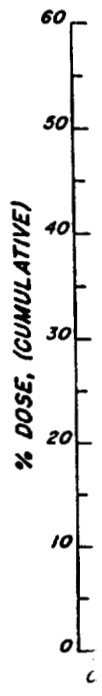

FIG. 2.
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days, and patient 4 excreted 27% in urine and 2% in stool in the same period of time.

Cs^{137} Body Retention (Intravenous Administration). The amount of cesium remaining in the body was calculated from the total excretion data for patients 1 and 2 (Fig. 3). Each point represents the retention at consecutive 10-day intervals after the intravenous injection of Cs^{137}. Approximately 50% of the dose was present in the body of patient 1 at 50 days, and of patient 2 at 60 days.

Oral Doses. The amount and distribution of Cs^{137} in whole blood and in plasma after the oral administration of Cs^{137} were comparable to those found after the intravenous dose (Fig. 4). In patient 6, the amounts of Cs^{137} in whole blood and in plasma were equal at 1 hour, and at 4 hours there was less in plasma than in whole blood. From 4 to 96 hours, the Cs^{137} level remained relatively constant in whole blood but continued to decrease in plasma. A 4:1 ratio of blood to plasma was reached in 24 hours. In patient 5, the amount of cesium in plasma was already less than in whole blood at 1 hour, and, although both continued to decrease, the

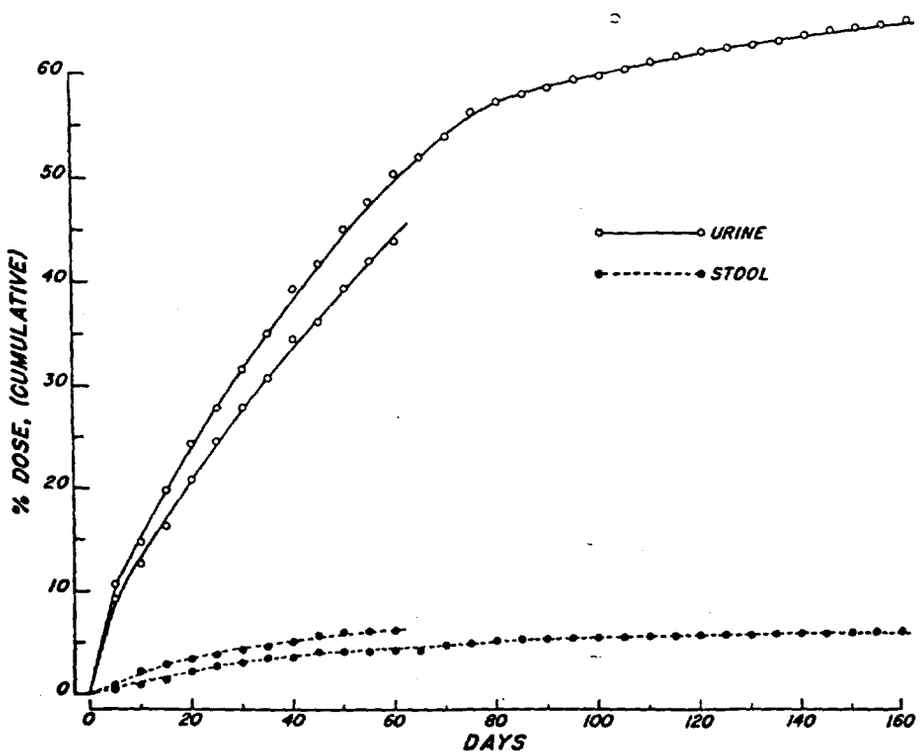

FIG. 2. Urinary and fecal Cs^{137} excretions of patients 1 and 2 after a single intravenous injection of $Cs^{137}Cl$. Patient 1—160-day study; patient 2—60-day study.

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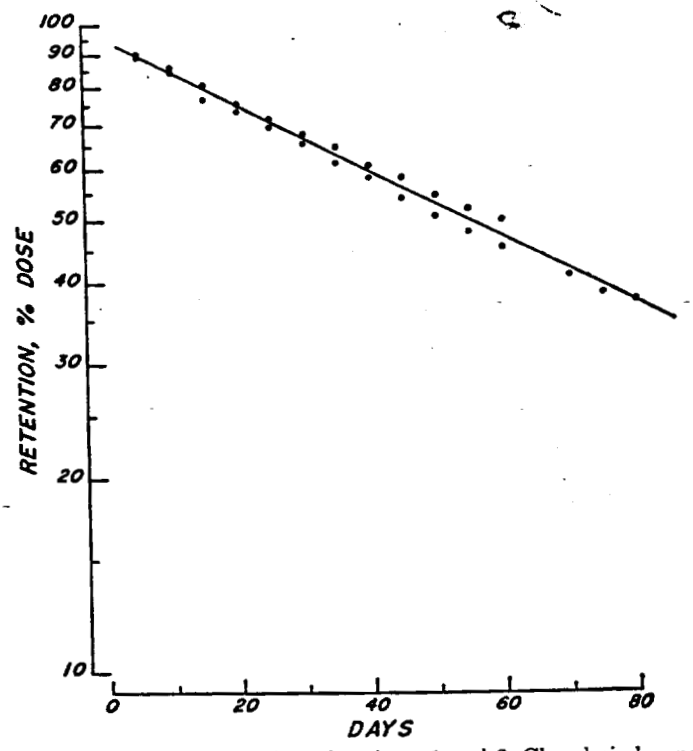

FIG. 3. Cesium-137 whole-body retention of patients 1 and 2. Closed circles, patient 1; open circles, patient 2. A single tracer of $Cs^{137}Cl$ was given intravenously on the first day of the study. The body retention was determined from the excretion data.

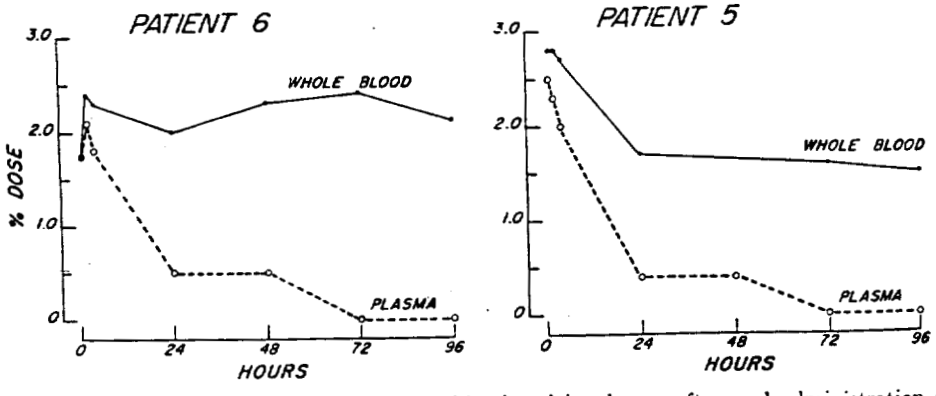

FIG. 4. Cesium-137 concentration in whole blood and in plasma after oral administration of $Cs^{137}Cl$ (patients 5 and 6).

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TABLE IV

EXCRETION OF THE TRACER Cs^{137} AFTER ORAL ADMINISTRATION

Patient	*Cumulative excretion for 7 days (% of Administered Dose)*		
	Urine	*Stool*	*Total*
5	7.6	1.8	9.4
6	5.0	2.0	7.0
7	15.7	1.6	17.3
8	12.4	2.1	14.5
9	11.1	1.5	12.6
10	14.5	2.0	16.5
11	7.0	1.8	8.8

plasma levels decreased at a faster rate. At 24 hours the amount of cesium in whole blood was 1.7% of the administered dose, and 0.4% in the plasma.

The 7-day cumulative urinary and fecal Cs^{137} excretions of seven patients who received the tracer orally showed that the total Cs^{137} excretions varied from patient to patient (Table IV). The fecal Cs^{137} excretion was low in all cases and ranged from 1.5% to 2.1% of the administered dose. In each of these patients the urinary Cs^{137} excretion was two and one-half to ten times as high as the fecal Cs^{137} excretion.

The cumulative Cs^{137} excretions over different time intervals after the intravenous and oral administrations of the tracer are compared in Fig. 5. These data show that the urinary and fecal Cs^{137} excretions after oral administration were

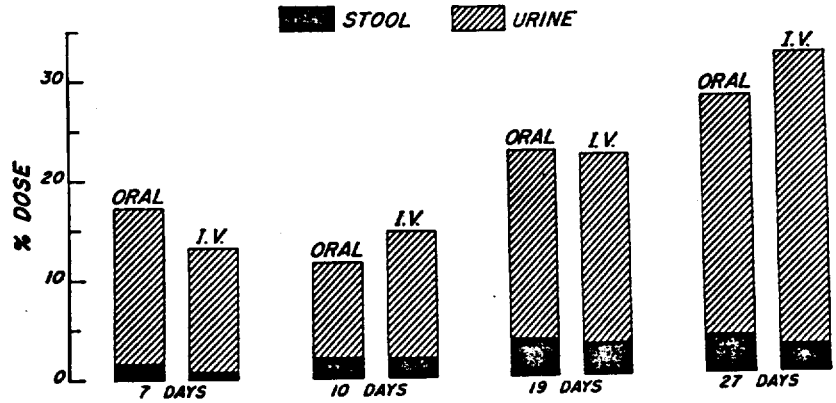

FIG. 5. Cumulative excretion of $Cs^{137}Cl$ after oral and intravenous administration of a single tracer dose given on the first day of the respective studies.

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similar to those after intravenous injection. The main pathway of excretion was via the kidney subsequent to the Cs^{137} entry into the body by either route.

Enhancement Studies

Infusions of 500 ml of physiologic saline given on the thirteenth and fourteenth days after the administration of Cs^{137} were ineffective in increasing the urinary or fecal cesium excretion in patient 4 (Table II). Similarly, the administration of 50 mg of hydrochlorothiazide given orally on three consecutive days (days 24 to 26 of study) and of 9 gm of ammonium chloride given daily for 5 days (days 31 to 35 of study) was of no avail in enhancing the Cs^{137} excretion. The administration of 40 mg of prednisone per day given for 14 days (days 26 to 39 after injection of Cs^{137}) was also ineffective in raising the urinary Cs^{137} excretion. A potassium ion-exchange resin, kayexalate, (16 gm/day), given orally from the tenth to the fifteenth day and ϵ-aminocaproic acid (24 gm/day) given orally for 11 days starting on the twenty-first day after the ingestion of Cs^{137} were ineffective in increasing the urinary or fecal Cs^{137} excretion in patient 10.

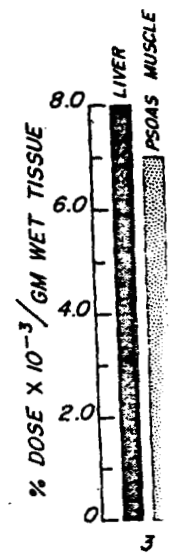
Tissue Distribution Studies

Cesium-137 tissue distribution studies were performed on five patients described in Table III.

The tissue distribution of Cs^{137} at 3, 10, 16, and 165 days after the administration of the dose is presented in Fig. 6. At 3 days the level of Cs^{137} in per cent of dose per gram of wet tissue was highest in liver (8×10^{-3}). The concentration of both spleen and psoas muscle was slightly lower (7×10^{-3}). The concentration of Cs^{137} was still lower in the following organs, in decreasing order: pancreas, heart muscle, skeletal muscle, rib, adrenals, and lung. The concentration in lung was the lowest of all the tissues analyzed (3×10^{-3}). The tissues of two patients obtained 10 and 16 days after Cs^{137} administration had a concentration about one-half those of the 3-day study. Here again, the concentration in liver and skeletal muscle was highest (3×10^{-3}), with that of spleen, heart muscle, kidney, and lung being similar and slightly lower than that of liver and skeletal muscle. Pancreas showed a concentration of 2×10^{-3}, and rib and adrenals were 1.5×10^{-3}, one-half that of liver. In patient 1, 165 days after Cs^{137} administration all tissues showed a much lower concentration of Cs^{137}. Liver and kidney contained 2×10^{-4}, and the other tissues contained about 1×10^{-4} of the injected dose.

DISCUSSION

Cesium, like potassium, disappears rapidly from the blood stream when injected intravenously. The ratio of whole blood to plasma was 4:1 at 24 hours, and this difference was maintained for several days. Cesium may exchange for potassium in erythrocytes or may be taken up by a similar mechanism as potassium.



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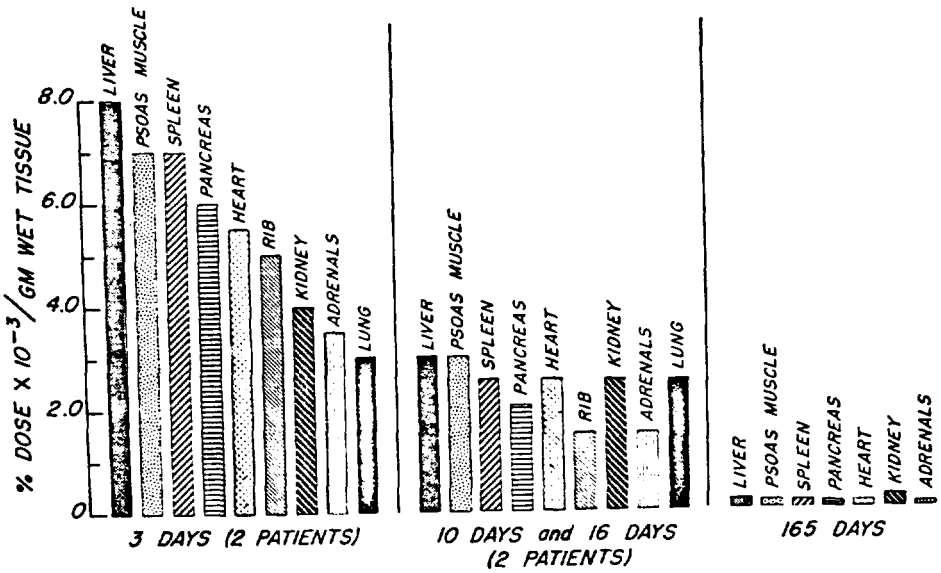

FIG. 6. A single tracer dose of $Cs^{137}Cl$ was injected intravenously to five patients. Tissue samples were obtained at autopsy in two patients 3 days after the injection of the tracer. In one patient each, the samples were obtained at 10, 16, and 165 days after the injection of the tracer.

Relman (7) has shown that cesium accumulates preferentially to potassium in muscle tissue, and the same may be true for red blood cells. The rapid and almost complete absorption of orally administered cesium is indicated by the fact that 2% to 3% of the dose is present within 1 hour in whole blood, and a fairly constant level is reached in whole blood in less than 24 hours, similar to the results obtained after the intravenous injection. The cesium accumulation in red blood cells and in other tissues does not seem to be due to passive diffusion between plasma and cells, but the cellular uptake may take place against a concentration gradient. For instance, a 20-fold differential exists between tissues and plasma concentration 3 days after the administration of Cs^{137}.

The results of Cs^{137} excretion studies in man are in good agreement with previously reported findings in animals (*1–3*), the main pathway of excretion being via the kidney. However, the urinary–fecal Cs^{137} excretion ratio of 10:1 in man is considerably higher than in animals. For instance, this ratio was reported to be 3:1 in mice (*8*). Since the soft-tissue concentration decreases with time, the low but continuous urinary Cs^{137} excretion in man is most likely due to a slow release of cesium from cells into the extracellular space and excretion via the kidneys. Some of the loss of cesium from the tissues might be due to exchange with potassium.

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It is also possible that the excretion of cesium in man represents a release of cesium from tissues due to cell catabolism. Mraz *et al.* (*9*) suggest that cesium is released from tissues only as a result of catabolism. The fecal excretion might in part be due to excretion via the biliary system into the intestine, since the concentration of cesium is very high in the liver. Hood and Comar (*1*) found that the Cs^{137} level in the liver of rats decreased fairly rapidly with time, and Nelson *et al.* (*10*) reported similar results in mice.

The tissue distribution studies in man reported here reveal that the concentration decreased with time and that the distribution of cesium in soft tissues was uniform by 10 days. Nelson showed in autoradiographic studies in mice that the uptake in liver and spleen was not so high as in muscle and cartilage and that the concentration decreased at a much faster rate (*10*). The tissue analyses in man, however, indicate a fairly uniform concentration in soft tissues at 10 days. The relatively high Cs^{137} concentration in the rib was unexpected in view of the uniform soft-tissue distribution of this isotope. However, no attempt was made to remove the bone marrow from the rib samples, and therefore the concentration in rib may indicate either bone uptake or uptake of cesium in the blood-forming cells of the bone marrow. Further investigations are necessary to verify these observations. The complete absorption of orally administered Cs^{137} in man suggests that the tissue distribution after this route of administration would be similar to that after the intravenous dose. This is also suggested by the work of others in animals (*3*).

The biological half-life of Cs^{137} in man assumes importance in view of the fact that the tissues are exposed to both γ- and β-radiation. Cs^{137} is a β-emitter, but its daughter Ba^{137m} decays by γ-emission to stable Ba^{137} (*11*). Recent studies in dogs exposed to Cs^{137} have shown that in most cases the contribution of the β-radiation to the tissue exposure is considerably greater than that of the γ-radiation (*12*). In the patients studied, 50% of the intravenously administered Cs^{137} was excreted in urine and stool in time ranging from 50 to 60 days. These data are in agreement with the body retention determined by whole-body counting of five other patients who received Cs^{137} intravenously and/or orally. (See Part II of this presentation.)

Enhancement studied in man reported here and elsewhere and those carried out in animals underscore the difficulty in removing Cs^{137} from the body once the radioisotope is deposited in the tissues. Mraz *et al.* (*9, 13*) have shown that an increase of potassium in the diet increases the excretion of acutely administered Cs^{134} in rats and sheep. Richmond and Furchner (*14*) using Cs^{137} confirmed these results in rats. Wasserman and Comar (*15*) found in studies of chronic ingestion of Cs^{137} that the retention of cesium did not appreciably decrease when the dietary potassium intake was increased, and that a 9-fold increase in dietary potassium resulted in only a 2-fold decrease in cesium concentration in muscle. Similar results

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were reported for man (*16*). Increasing the potassium intake had no significant long-term effect on the excretion of chronically ingested Cs^{137}. It has been suggested that stable cesium might be effective in washing out Cs^{137} from tissues, but recent studies in rats indicate that orally administered cesium chloride does not enhance Cs^{137} excretion, and the toxic effects, in fact, reduce the normal excretion rate (*17*). These reports suggest that further studies with potassium in man under carefully controlled conditions seem to be indicated. Different doses of orally administered diamox were shown to enhance the excretion of Cs^{137} in rats (*18*). To date, the use of catabolic agents which cause a release of tissue potassium and of ion-exchange resins was ineffective in our hands.

SUMMARY

1. The main pathway of Cs^{137} excretion in man after either intravenous or oral administration is via the kidney; the ratio of urinary to fecal excretion is approximately 10:1.

2. Orally administered Cs^{137} is rapidly and almost completely absorbed. The metabolism of the radioisotope was shown to be similar after either intravenous or oral administration.

3. Cs^{137} disappears very rapidly from plasma and is taken up by red blood cells.

4. The biological half-life of cesium in man, determined by analyses of excreta of 2 patients, was found to be 50 and 60 days, respectively. These values are similar to the biological half-lives obtained by long-term whole-body counting studies.

5. The tissue distribution of Cs^{137} in man decreases with time, and the concentration is fairly uniform in the soft tissues by 10 days.

6. Attempts to enhance the excretion rate of Cs^{137} with diuretics, corticosteroids, and ion-exchange resins were unsuccessful.

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