

The Metabolism of ^{137}Cs Inhaled as $^{137}\text{CsCl}$ by the Beagle Dog* (33699)

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(Introduced by R. O. McClellan)

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As part of a long-term program to investigate the effects of inhaled radioactive fission products, the normal whole-body retention, tissue distribution and excretion patterns of inhaled ^{137}Cs have been reported for the rat by Stara and Thomas (1) and Lie (2) and for the guinea pig by Stara (3). A report of a similar experiment in which purebred beagle dogs were given a single, short inhalation exposure to a CsCl aerosol contaminated with ^{137}Cs and then were observed for periods up to 1 year postexposure to determine the biological behavior of inhaled ^{137}Cs is presented in this paper.

Methods and Materials. The 25 dogs used in this experiment (12 male, 13 female) were purebred beagles ranging in age from 17 to approximately 72 months at time of exposure. For confinement acclimation, all dogs were placed in stainless steel metabolism cages 2–4 weeks prior to exposure. Initially, these dogs were fed Wayne dog food (Allied Mills Inc.) moistened with water; however, during this experiment, food mixing equipment became available and the diet of the entire dog colony was changed to a standard mixture of Wayne dog food, raw ground beef, water and a vitamin–mineral supplement. Water was supplied *ad libitum*.

Two or three dogs were exposed on a given day. Before exposure, each dog was given 60 mg of phenobarbital orally and an intravenous injection of 0.25 mg/lb of triflupromazine hydrochloride (Vetame, E. R. Squibb and Sons). Each dog was given a single, 10-min inhalation exposure in an apparatus described previously by Boecker *et al.* (4) that permitted “nose-only” exposure and measurement, by plethysmography, of

the total volume of air inspired during exposure. The aerosol was generated from a 1% CsCl solution contaminated with ^{137}Cs . Average air concentrations of ^{137}Cs ranged from 2.6 to 8.9 $\mu\text{Ci/liter}$. Some dogs were exposed to an aerosol with an activity median aerodynamic diameter (AMAD) of 1.6 μ and others to an AMAD of 2.0 μ ; σ_g was always 1.8.

The body burden of ^{137}Cs was determined immediately after exposure and at selected intervals thereafter by whole-body counting using a NaI system initially and a $\approx 4\pi$ liquid scintillation system later when lower activity levels were present. All dogs were housed individually in metabolism cages between exposure and sacrifice with daily collections of excreta samples. Sacrifices were performed serially from 0 to 366 days postexposure by maximal blood withdrawal from a heart puncture performed under pentobarbital sodium anesthesia. The ^{137}Cs content of urine, feces, and tissue samples was measured by gamma counting in a liquid scintillation well detector.

Results. A. Deposition. Initial body burdens determined by whole-body counting immediately after exposure ranged from 20 to 130 μCi . The percentage deposition in the total body was calculated by dividing the initial body burden by the amount of ^{137}Cs inspired during exposure which was the product of the total inspired air volume times the average exposure air concentration of ^{137}Cs . The mean total deposition was 77% (SD = 12%) with similar results for both the 1.6 μ and 2.0 μ AMAD aerosols.

B. Whole-body retention. The whole-body retention of inhaled ^{137}Cs was examined for each dog by visually fitting smooth curves to the whole-body counting data. An arithmetic mean retention curve for the 11 dogs followed 128 days or more postexposure is presented in Fig. 1. This curve was construct-

* Research performed under Contract AT(29-2)-1013 between the U. S. Atomic Energy Commission and the Lovelace Foundation for Medical Education and Research.

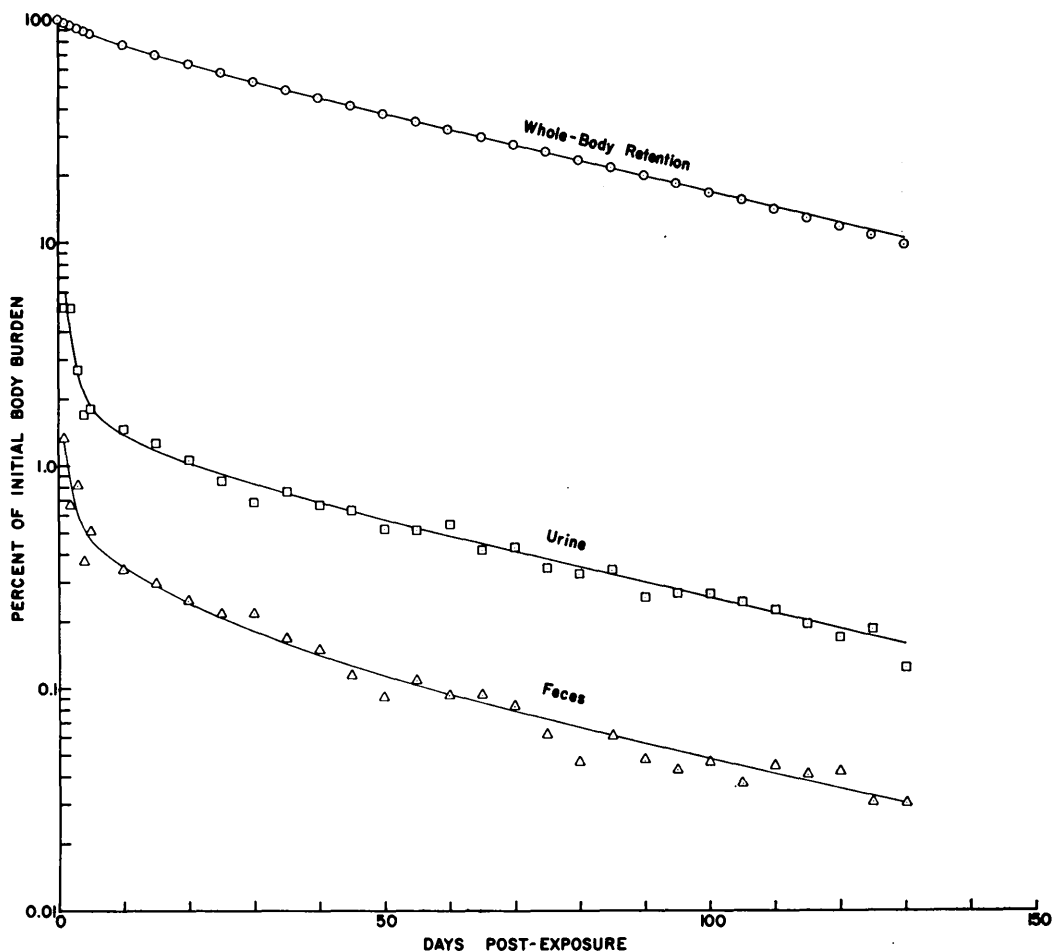


FIG. 1. Mean whole-body retention and excretion in the urine and feces of ^{137}Cs for 11 beagle dogs exposed to $^{137}\text{CsCl}$ by inhalation. The mean values for the first 5 days postexposure and every fifth day thereafter are shown.

ed from mean values of points taken from each dog's curve daily for the first 5 days postexposure and every fifth day thereafter. The equation of this curve was determined by the graphical subtraction technique to be:

$$R_t = 14e^{-.11t} + 86e^{-.016t}$$

where R_t is the whole-body retention at time t expressed as a percentage of the initial body burden. The two exponents represent effective half-lives (T) of 6.2 and 43 days. Because of the long physical half-life (T_p) of ^{137}Cs , the biological half-lives (T_b) are essentially equal to the values of T observed during these 1-year experiments.

Shortly after 100 days postexposure, the

experimental points fell away from the smooth curve in a downward direction indicating an increased rate of ^{137}Cs excretion. This result can be studied more closely by examination of the individual curves in Fig. 2 for two of eight dogs that were sacrificed at 256 or 366 days postexposure. Dog A-7 was one of two dogs that had no change in its retention curve. In contrast, the whole-body retention pattern for Dog A-17 showed a decided shift that began about the time of the colony-wide diet change mentioned earlier. A comparison of the broken line (a straight line extension of the rate prevailing just before the shift) with the solid line drawn through

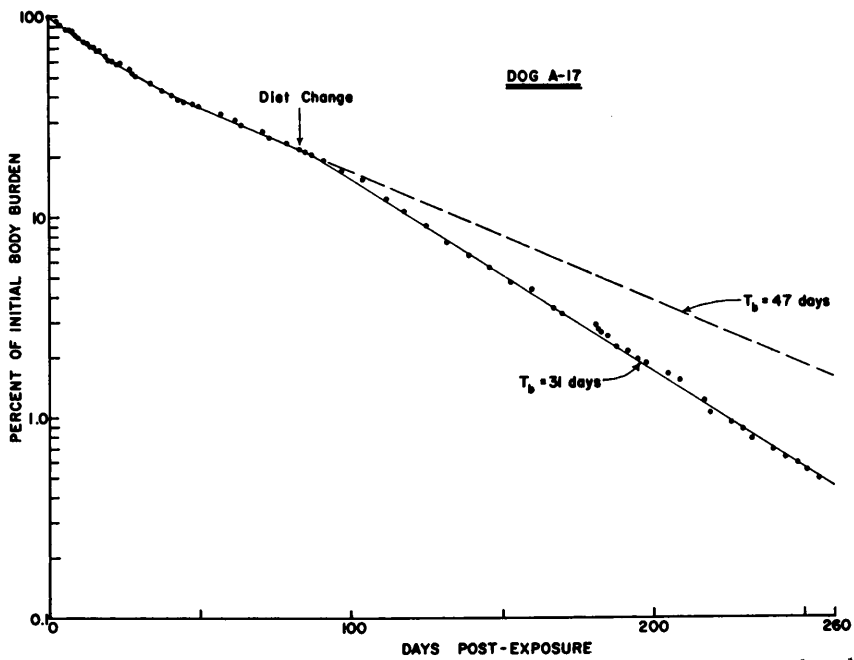
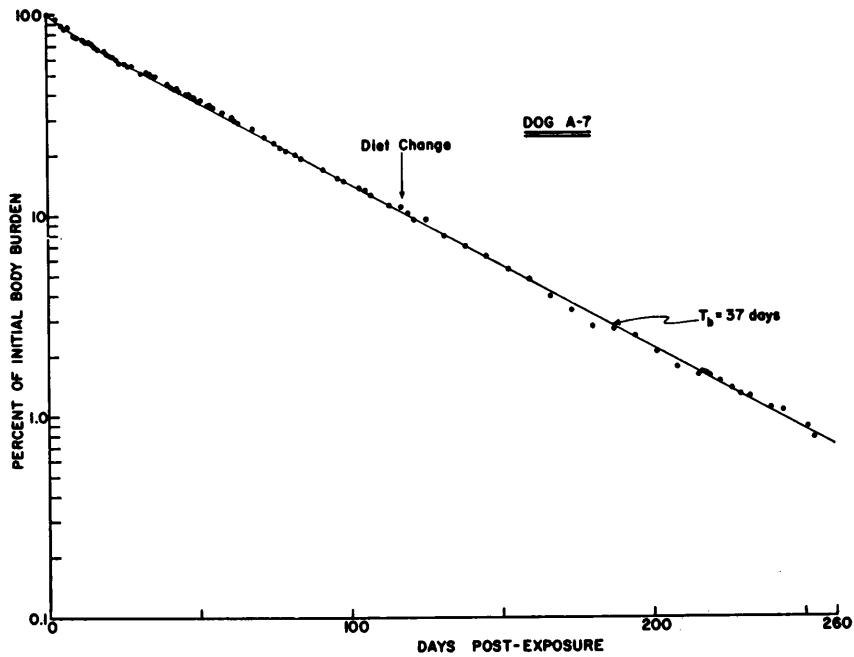


FIG. 2. Individual curves of ^{137}Cs whole-body retention for two beagle dogs exposed to $^{137}\text{CsCl}$ by inhalation. A colony-wide diet change occurred at the time indicated by the arrow.

the actual data points indicates the mean T_b for these eight dogs was 42 days prior to the shift and 36 days afterwards.

C. Excretion. Individual values for ^{137}Cs excretion in urine and feces for 11 dogs kept at least 128 days postexposure have been averaged and presented in Fig. 1 for the first 5 days postexposure and every fifth day thereafter. The rate of ^{137}Cs excretion in the urine and feces was highest during the first 3 days postexposure and decreased throughout the observation period. After the early clearance phase, the excretion of ^{137}Cs in the urine and feces closely paralleled the whole-body retention. All three curves in Fig. 1 have a long-term component with a biological half-life of 43 days. From 10 to 130 days postexposure, the urinary values corresponded to the excretion of from 1 to 2% of the existing body burden per day while corresponding values for the feces ranged from 0.2 to 0.4%. The ratio of ^{137}Cs excretion in the urine to that in the feces (U/F) usually fell in the range of 3–7.

D. Tissues. The ^{137}Cs concentration in samples of skeletal muscle (taken from the deep muscles of the thigh) diaphragm, kidneys, and mandibular salivary glands were slightly higher than the whole-body average whereas values for lung, skin, femur, fat, and blood were somewhat lower. The remaining tissues including liver, spleen, gastrointestinal tract, heart, pancreas, thyroid, and adrenals had ^{137}Cs concentrations approximately equal to the mean whole-body values.

A plot for several of the tissues (Fig. 3) shows that the ranking of the ^{137}Cs concentrations in these tissues, when compared with that in the total body, remained quite constant throughout the duration of this 1-year experiment. The general shapes of these curves are distorted due to the change in rate of whole-body retention in the middle of the experiment. Even though the ^{137}Cs was administered by inhalation, the lung quickly became one of the tissues to exhibit a low concentration of ^{137}Cs . The much lower concentration of ^{137}Cs is bone compared with soft

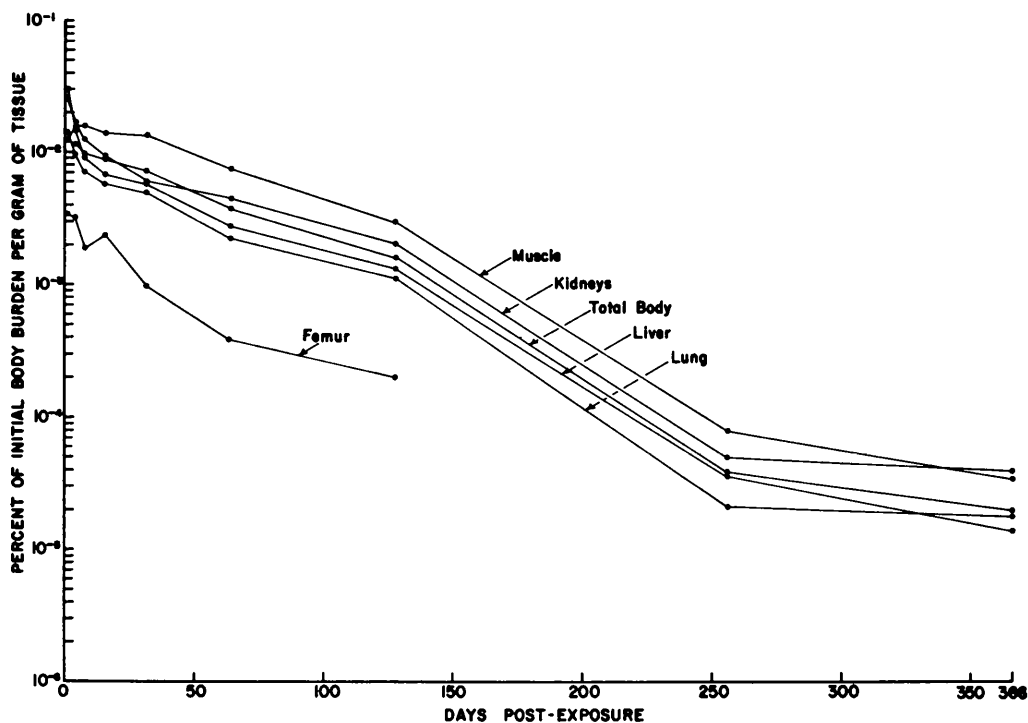


FIG. 3. Mean concentration of ^{137}Cs in various tissues of beagle dogs as a function of time after a single inhalation exposure to $^{137}\text{CsCl}$. Each point is the mean of 1, 2, 3, or 5 values.

tissues is also apparent from this graph.

Discussion. The deposition data indicate that a large percentage (about 80%) of the inhaled material was deposited within the dogs initially. The variability seen among dogs in the percentage deposition is typical of results which have been observed in this laboratory in several other experiments.

Following an inhalation exposure, a rapid reduction in body burden is usually seen during the first few days (perhaps a 50–75% loss) corresponding to clearance via the gastrointestinal tract of inhaled material that was initially deposited in the upper respiratory tract. Such was not the case for these dogs where less than 25% of the initial body burden was cleared early, and then most of it in the urine, with the remainder being associated with the long-term retention phase. Presumably some ^{137}Cs was cleared from the upper respiratory tract and ingested but, because of its solubility in body fluids, was reabsorbed during its passage through the gastrointestinal tract.

The time at which the shift appeared in the whole-body retention curves for some of the dogs was close to the time when the diet for the entire dog colony was changed. Because others have shown that an increase in dietary potassium can enhance ^{137}Cs excretion (5, 6), the potassium levels in the old and new diets were examined and found to be similar, 0.68 and 0.73%, respectively. Since equal quantities of both diets were fed, there was not a significant difference in dietary potassium. Weight gains (4% in one dog and 12–31% in the other seven during the first 120 days after the diet change) and improved coats indicated that the dogs' general states of health were improved following the diet change and this probably contributed to the observed changes in ^{137}Cs excretory rate.

The values of T_B obtained from whole-body counting can be compared with those reported by others following intravenous injection. Richmond (7) observed four beagles for a year and obtained data whose mean values could be fitted with a three-component exponential equation whose long-term component had a $T_B = 43$ days. Norris *et al.* (8)

reported an age effect on the whole-body retention of ^{137}Cs . In fifteen 5-month old dogs the mean T_B was 16 days (range = 12–23 days) whereas in twenty-seven 13-month old dogs, the mean T_B was 20 days (range = 15–26 days) and in 10 dogs that were 4–5 years old at injection, the mean T_B was 37 days (range = 26–50 days). Most of the dogs used in the present experiment were between 17 and 34 months of age and had values of T_B that fell in between the values reported by Norris *et al.* for 13 month old and 4–5 year old beagles.

The tissue concentration data presented in Fig. 3 show that after the first few days postexposure, the relationships of ^{137}Cs concentrations in the various tissues remained quite constant, indicating that the biological half-life seen for the whole-body also applies to the individual tissues. In other ^{137}Cs inhalation experiments involving rats and guinea pigs (1–3) the ranking of ^{137}Cs tissue concentrations was approximately the same as reported here. Lie (2) noted that although muscle had a slightly higher ^{137}Cs concentration, most of the other tissues had concentrations that were within a factor of two of that in muscle.

Similar rankings of ^{137}Cs concentrations in various tissues have been reported by Ballou and Thompson (9) for rats given single intraperitoneal injections of ^{137}Cs , Furchner *et al.* (10) for dogs and mice exposed by chronic ingestion of ^{137}Cs , and by Norris *et al.* (11) for a beagle dog given ^{137}Cs intravenously. Because the present data obtained with beagle dogs exposed to $^{137}\text{CsCl}$ by inhalation are in good agreement with data obtained for other routes of administration, one can conclude that the route of administration is not a critical factor in the resulting tissue distribution pattern. Since ^{137}Cs is so soluble in body fluids, inhaled ^{137}Cs passes rapidly from the lungs to the other organs where higher ^{137}Cs concentrations are maintained.

Summary. Results are presented for a group of beagle dogs given single, short inhalation exposures to a CsCl aerosol contaminated with ^{137}Cs . The mean biological half-

life derived from the long-term component of whole-body retention was 42 days before, and 36 days after, a colony-wide diet change. For times greater than about 10 days post exposure, approximately constant percentages of the body burden were excreted each day in the urine and feces. The U/F ratio normally fell between 3 and 7. Highest tissue concentrations of ^{137}Cs were observed in skeletal muscle, mandibular salivary glands, and kidneys while the lowest were in lung, skin, fat, and bone. These results indicate that since ^{137}Cs is very soluble in body fluids, the route of administration has very little effect on its subsequent distribution and excretion.

The author is indebted to personnel from the Aerosol Physics Department for producing and characterizing the aerosols and to personnel from the Veterinary Medicine Department for animal care and collection of excreta samples. Invaluable technical assistance was given by Frizelle L. A. Riley, M. A. Glora, L. S. Gomez, M. Gonzales, S. R. Wright, E. J. Salas, and Patricia S. Mewhinney. Critical reviews and helpful suggestions regarding the

manuscript were provided by Dr. R. O. McClellan, F. C. Rupprecht, and several other members of the staff.

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Received Sept. 11, 1968. P.S.E.B.M., 1969, Vol. 130.