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U.S. ENVIRONMENTAL PROTECTION AGENCY
Environmental Monitoring and Support Laboratory
Las Vegas, Nevada 89114

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by

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ABSTRACT

Groups of lactating cows and goats were used to examine americium-241 metabolism in dairy animals. Following either single oral or intravenous nuclide doses, samples of milk, urine, blood and feces were taken over a 168-hour collection period and the americium concentrations were determined by gamma counting. Gastrointestinal uptake of americium by both cows and goats was estimated to be 0.014 percent of the respective oral doses. The cumulative percentage of oral dose transported to milk and urine was 4.4×10^{-4} and 1.1×10^{-3} respectively for cows and 4.4×10^{-3} and 1.2×10^{-3} respectively for goats. The relatively high americium concentrations noted in caprine milk following the oral doses are discussed. Plasma concentrations of americium decreased rapidly following all intravenous injections. The average percentage of injected americium transferred to milk, urine and feces was 3, 6 and 2 percent respectively for cows and 2, 4 and 2 percent respectively for goats. In both intravenously dosed groups, approximately 30 percent of all americium released from the body was found in the urine during the first 24 hours after injection. All animals were sacrificed 8 to 9 days after dosing. Bovine bone retained the greatest fraction of the administered dose followed by the liver. However, liver retained the greatest amount of americium in the goats following both oral and intravenous doses. Comparisons are presented between americium-241 and plutonium-238 transport in dairy cows.

INTRODUCTION

Bovine and, to a somewhat lesser extent, caprine metabolism of ingested americium is of considerable importance for an analysis of exposure pathways to human populations. Milk and milk products form a direct link in man's food supply and a significant percentage of beef comes from cows and bulls discarded from dairy herds. Results on nuclide transport in dairy animals have been reported at previous Nevada Applied Ecology Group meetings (Stanley *et al.*, 1974, 1975; Sutton *et al.*, 1977a, 1977b, 1977c; Patzer *et al.*, 1977a, 1977b; and Mullen *et al.*, 1977). The primary purpose of these metabolism studies has been to determine gastrointestinal uptake of the various nuclides, to determine the amount of activity that was trasnferred to the milk and to establish what fraction of the dose was retained by the tissues. In addition to administering oral nuclide doses to the dairy animals, several of the projects have also included intravenous dosing of one or two animals so as to establish plasma clearance characteristics and to provide an estimate of nuclide loss into the gastrointestinal tract (e.g., bile secretion).

The transport of ingested plutonium-238 to milk has been reported by Stanley *et al.* (1974, 1975). Following an acute oral plutonium nitrate dose, 2.0×10^{-4} percent of the ingested plutonium was recovered in milk. Multiple oral doses of plutonium dioxide resulted in 2.0×10^{-5} percent of the dose being transferred to milk. Information on gastrointestinal uptake of americium and the subsequent nuclide transport to milk is not currently available for dairy animals. Low gastrointestinal absorption values, e.g., <0.05 percent of dose (Hamilton, 1947), <0.01 percent of dose (Scott *et al.*, 1948) and 0.012 percent of dose (Sullivan and Crosby, 1975), have been reported following the administration of americium-241 to laboratory rats. Following intravenous nuclide doses to lactating Suffolk sheep, McClellan *et al.* (1962) noted that plutonium-239 and americium-241 both reached peak concentrations in the milk 7 hours after injection. However, americium was cleared more rapidly from the plasma and its subsequent transfer to milk was greater than was observed for plutonium.

Objectives of the current investigation were (1) to establish the gastrointestinal uptake of americium, (2) to determine the amount of activity transported to milk, (3) to examine the plasma clearance rate of americium, (4) to quantify the excretion characteristics of americium in urine and feces, and (5) to establish the tissue deposition pattern of americium in dairy animals. In pursuing the objectives, samples of blood, milk, urine and feces were taken from groups of cows and goats after the animals had received either oral or intravenous doses. Tissue collections were made at time of sacrifice.

METHODS AND MATERIALS

The study was conducted in two phases at the Nevada Test Site farm. Four lactating dairy cows, confined to individual metabolism stalls, were used in the initial phase. Two of the cows, average weight 575 kg, were each given single 41.7-mCi oral doses of americium-241 chloride. The oral doses were placed in gelatin capsules (doubly encapsulated) containing cellulose fiber and were administered using a balling gun. The other two cows, average weight 598 kg, were each given single intravenous doses (0.96 mCi) of citrate-buffered americium-241 chloride. Intravenous doses were approximately 5 ml in volume and were administered by jugular venipuncture. No intravenous or oral dose adjustments were made for individual variations in animal weight.

Daily milk, urine, fecal and blood samples were taken beginning 1 day prior to dosing and continuing until approximately 168 hours after dosing. The cows were each catheterized with an in-dwelling, inflatable urinary catheter and the urine drained through polyethylene tubing into 20-liter plastic bottles placed at the rear of each stall. A grid-covered pan, lined with polyethylene sheeting, was used to collect the feces. Milk was collected with individual bucket milkers twice daily and single blood samples were taken by jugular venipuncture. All urine, milk and fecal collections were weighed and then combined (a.m. + p.m.) into respective 24-hour composites for each animal. A Hobart mixer was used to mix the large fecal collections while respective composites of milk and urine were shaken thoroughly in plastic containers. Weighed subsamples were then taken from the respective composites and placed in individual 200-ml aluminum cans with formaldehyde added as preservative. On the second and fifth post-dosing day, three subsamples were taken of each composite to confirm the degree of sampling variability. Blood was collected at 8-hour intervals through the first day and then on a 24-hour basis. Samples were centrifuged and the plasma and cells separated using disposable pipettes. The packed cells were washed two times with physiological saline. Samples of plasma and cells were then individually diluted with distilled water and formaldehyde was added as a preservative. A limited number of whole blood samples was also taken.

The second phase of this study used five dairy goats and basically followed the same procedures as the bovine experiment. Two goats, average weight 35 kg, were each given a single oral dose (1.91 mCi) of americium-241 nitrate. A second pair of goats, average weight 36 kg, each received a single 41.7-μCi intravenous dose of citrate-buffered americium-241 nitrate. One goat served as a control animal and did not receive americium. As before, oral doses were placed in gelatin capsules and were administered using a balling gun. Intravenous doses were administered by jugular venipuncture.

The goats were maintained under conditions similar to those used during the bovine experiment, but in smaller and more elevated metabolism stalls which allowed easy access for the twice daily hand milkings. Urine was collected by catheter and the fecal pellets were collected in a modified tray. Twenty-four hour composite sampling was again conducted for milk, urine and feces. Due to the pellet nature of goat feces, an electric meat grinder (General

Slicing Company) was used to mix the daily collections. The grinder was dismantled and cleaned between each mixing. Commercially purchased soda crackers were also run through the grinder as part of the cleaning process. In a few cases, some of the ground crackers were subsequently analyzed for americium to check for cross-contamination. Blood was collected from the goats at 8-hour intervals for the first day followed by daily collections through the seventh day post-dosing.

Cows and goats were sacrificed 8 to 9 days after dosing (Tables I and II) using intravenously administered euthanasia solution. Extensive precautions were taken in the sacrifice area (Nevada Test Site farm) to reduce any possibility of cross-contamination during tissue collection. Results of tissue analyses on the control goat suggested that cross-contamination or respiratory exposure was indeed minimal. All animals were weighed at time of sacrifice and partially exsanguinated before tissue samples were taken. Organs and tissues were removed from the animals within approximately 60 minutes of sacrifice. Extraneous tissue (adipose tissue or muscle associated with bone samples) was discarded and the required sample, plus formaldehyde, was sealed in 200-ml aluminum cans. Total weights were taken on most organs so that the percentage of administered dose retained by a specific tissue or organ could be calculated. When this was not practical (for muscle, bone, blood, etc.), total americium content was based on extrapolated organ weights using the respective percentage of body weight reported by Davis *et al.* (1975), Smith and Baldwin (1974) and Matthews *et al.*(1975). Americium concentrations from the femur (diaphysis and epiphysis), sternum, vertebra and rib were averaged to estimate the osseous retention values. Differences did exist, however, in the total number of individual samples that went into the average bone value. For bovine bone, the femur value was derived from two diaphysis and two epiphysis samples, and two samples each of vertebra and rib were collected. The same bones were sampled from the goats but only one diaphysis and one epiphysis sample per animal was collected as well as only one sample each of vertebra and rib. One sternum sample was taken from each cow and from each goat.

Americium-241 decays through the emission of alpha particles and 36 percent of its disintegrations are accompanied by a 60-keV gamma ray. Gamma counting was considered the most feasible analytical technique for use in conjunction with these experiments. Most samples were counted in 200-ml aluminum cans using a phoswich detector which consisted of a thin NaI scintillator backed by a thick CsI scintillator. Checks were made for gain shifts and changes in efficiency with an aliquot of the dosing solution. Backgrounds were taken before, during and after a series of counts to confirm that contamination of the counting chamber had not occurred. Various spiked standards (feces, milk, urine, plasma, blood cells, distilled water and agar) were also prepared. The amount of americium added (spike) was based on (1) the supplier's value for the stock solution and on (2) the calculated concentration range (percentage of dose per gram) likely to occur in milk, urine, etc., throughout the project. Different spiking levels within each group, e.g., milk, were separated by at least one order of magnitude and three replicates were prepared at each concentration. The americium-241 used in these experiments was obtained in the nitrate form from Amersham/Searle Corporation.

While the phoswich system was the primary detection method, other counting techniques were also employed during the study. Certain fecal samples from the orally dosed animals contained high concentrations of americium. For these assays the sample size was reduced to 25 grams (plus formaldehyde and a 2-percent agar solution) and they were analyzed using a FIDLER counting system, i.e., NaI(Tl) crystal and a single-channel analyzer. Furthermore, many samples of plasma, packed cells and whole boood were assayed in disposable 50-ml polypropylene centrifuge tubes using a NaI(Tl) well crystal. Selected samples were counted using both the phoswich system and the NaI(Tl) detector. Appropriate standards, blanks, duplicate assays and efficiency calculations were used to assess the results from all counting systems.

TABLE I

BACKGROUND INFORMATION ON THE FOUR DAIRY COWS DOSED WITH AMERICIUM

Animal Number	Americium Dose	Animal Weight* (kg)	Sacrifice Time Post-treatment (days)	Average Daily Output During Experiment (kg)		
				Milk	Urine	Feces
269	single oral dose (41.7 mCi) of americium-241 chloride	568	8	9.4	11.2	20.6
281	single oral dose (41.7 mCi) of americium-241 chloride	582	8	15.1	11.7	14.5
184	single intravenous dose (0.96 mCi) of citrate-buffered americium-241 chloride	677	9	20.3	20.3	30.3
280	single intravenous dose (0.96 mCi) of citrate-buffered americium-241 chloride	518	9	9.8	10.1	14.0

*Weight taken at time of sacrifice.

TABLE II

BACKGROUND INFORMATION ON THE DAIRY GOATS DOSED WITH AMERICIUM

Animal Number	Americium Dose	Animal Weight* (kg)	Sacrifice Time Post-treatment (days)	Average Daily Output During Experiment (kg) Milk	Urine	Feces
goat 1	single oral dose (1.91 mCi) of americium-241 nitrate	29.5	8	1.5	1.4	0.6
goat 2	single oral dose (1.91 mCi) of americium-241 nitrate	40.5	8	1.6	1.9	0.9
goat 3	control animal no dose administered	31.5	8	1.8	2.0	0.9
goat 4	single intravenous dose (41.7 μCi) of citrate-buffered americium-241 nitrate	30.9	8	2.6	3.4	1.4
goat 5	single intravenous dose (41.7 μCi) of citrate-buffered americium-241 nitrate	40.5	8	1.9	1.5	0.8

*Weight taken at time of sacrifice.

After assaying the samples by direct counting methods, radiochemical analyses (Eberline Instrument Corporation, Albuquerque, New Mexico) were performed on (1) a portion of the quality assurance samples, (2) on sets of samples that demonstrated considerable between-animal or within-animal variability and (3) on samples that contained less than 1 pCi of americium per gram of material. These radiochemical assays were conducted using alpha spectrometry. The total sample was ashed in a muffle furnace and then dissolved in acid with americium-243 added as a tracer. Following liquid extraction, the sample solution was passed through a cation exchange column and the americium was electroplated for analysis.

RESULTS AND DISCUSSION

Approximately 0.014 percent of the oral americium dose was absorbed from the gastrointestinal tract of dairy cows. Of this relatively small amount, essentially 3 percent was subsequently transported to milk, 8 percent was transported to urine and about 3 percent was probably returned to the digestive tract over the first 168 hours after dosing. At time of sacrifice (192 hours) 86 percent of the absorbed americium was recovered in the bovine carcass. A somewhat similar distribution resulted when the nuclide was introduced intravenously. Based on results from a single animal (goat 1), americium transport in the goat followed this general pattern after oral exposure. The estimated americium gastrointestinal uptake for this orally dosed goat was 0.016 percent of the administered nuclide. The above mentioned findings for the orally dosed animals are summarized in Table III. Carcass retention values used in this table were derived by summing the americium recovered in bone, liver, kidney, lung, spleen, heart, gonads, thyroid, muscle and plasma for the individual animals.

Values for goat 2 are also included in Table III. Relative to the carcass retention value (3.1×10^{-3} percent of dose), the total amount of americium transported to goat 2 milk (8.3×10^{-3} percent of dose) appears much too high. Milk and carcass values were confirmed by both direct counting techniques and by radiochemical assays. Possibilities of sample contamination were considered but americium concentrations in goat 2 milk followed the expected pattern (peak concentration at 48 hours with subsequent gradual decline) and americium concentrations in the sample replicates did not indicate irregularities. Tissue values also followed the expected deposition pattern but contained less americium than was noted for goat 1. Americium concentrations for urine, feces and blood plasma were similar between goats 1 and 2. The calculated gut absorption of americium (1.6×10^{-2} and 1.2×10^{-2} percent of the oral dose for goats 1 and 2 respectively) was also similar but the curious metabolic pattern suggests that for goat 2 the gut uptake may have actually been less than this calculated estimate.

The mean percentage of dose contained in plasma, milk, urine and feces for the two orally dosed cows is shown in Table IV. Values are given for each collection interval and for the total transport to milk, urine and feces during

TABLE III

GROSS ESTIMATE OF AMERICIUM TRANSPORT IN DAIRY ANIMALS
FOLLOWING A SINGLE ORAL AMERICIUM-241 DOSE

	Cow 281		Cow 269		Goat 1		Goat 2	
	% of Oral Dose	% of Absorbed Dose	% of Oral Dose	% of Absorbed Dose	% of Oral Dose	% of Absorbed Dose	% of Oral Dose	% of Absorbed Dose
Milk (168 h)	4.4×10^{-4}	2.8	4.5×10^{-4}	3.3	5.6×10^{-4}	3.6	8.3×10^{-3}	67.5
Urine (168 h)	9.0×10^{-4}	5.8	1.3×10^{-3}	9.6	1.6×10^{-3}	10.5	6.6×10^{-4}	5.4
Feces (168 h)	93.1	2.9*	81.5	2.9*	85.8	1.9*	85.5	2.0*
Carcass (192 h)	1.4×10^{-2}	87.7	1.1×10^{-2}	83.6	1.3×10^{-2}	84.0	3.1×10^{-3}	25.0
Estimated** G.I. Uptake	1.6×10^{-2}	-	1.3×10^{-2}	-	1.6×10^{-2}	-	1.2×10^{-2}	-

*Based on observed nuclide transport to feces for intravenously dosed animals.

**Preliminary summation composed of 1) the total transport (168 h) to milk and urine, 2) recovered activity estimate for each carcass (192 h) and 3) the extrapolated amount of absorbed americium returned to the gastrointestinal tract.

TABLE IV

MEAN PERCENTAGE OF ORAL AMERICIUM DOSE NOTED IN BLOOD PLASMA, MILK, URINE AND FECES FOR TWO DAIRY COWS DURING THE 168-HOUR SAMPLING PERIOD

Time After Dosing	Plasma*	Milk	Urine	Feces
8 h	3.22×10^{-5}	-	1.03×10^{-5}	3.10×10^{-2}
12 h	1.59×10^{-4}	-	-	-
24 h	2.33×10^{-4}	9.11×10^{-5}	8.61×10^{-5}	5.60
48 h	2.69×10^{-4}	9.37×10^{-5}	2.75×10^{-4}	9.59
72 h	1.32×10^{-4}	9.41×10^{-5}	2.68×10^{-4}	31.0
96 h	1.13×10^{-4}	7.44×10^{-5}	1.80×10^{-4}	20.5
120 h	1.99×10^{-4}	3.96×10^{-5}	1.24×10^{-4}	12.1
144 h	2.09×10^{-5}	2.88×10^{-5}	8.03×10^{-5}	6.57
168 h	2.34×10^{-5}	1.56×10^{-5}	6.12×10^{-5}	1.93
Total	-	4.37×10^{-4}	1.09×10^{-3}	87.3

*Extrapolated values

TABLE V

MEAN PERCENTAGE OF ORAL AMERICIUM DOSE NOTED IN BLOOD PLASMA, MILK, URINE AND FECES FOR TWO DAIRY GOATS DURING THE 168-HOUR SAMPLING PERIOD

Time After Dosing	Plasma*	Milk	Urine	Feces
8 h	8.12×10^{-5}	2.18×10^{-6}	1.85×10^{-5}	5.86×10^{-5}
15 h	1.62×10^{-4}	-	-	-
24 h	1.44×10^{-4}	1.81×10^{-4}	2.59×10^{-4}	20.39
48 h	6.01×10^{-5}	3.80×10^{-3}	3.93×10^{-4}	48.05
72 h	3.56×10^{-5}	1.86×10^{-4}	1.91×10^{-4}	14.25
96 h	2.00×10^{-5}	6.87×10^{-5}	1.10×10^{-4}	2.39
120 h	1.86×10^{-5}	2.95×10^{-5}	4.39×10^{-5}	3.83×10^{-1}
144 h	1.30×10^{-5}	2.75×10^{-5}	8.12×10^{-5}	1.10×10^{-1}
168 h	1.07×10^{-5}	1.31×10^{-4}	5.49×10^{-5}	4.25×10^{-2}
Total	-	4.43×10^{-3}	1.15×10^{-3}	85.62

*Extrapolated values

the 168-hour collection period. Three days after dosing the largest daily amount of americium was excreted in the feces but the fecal nuclide content was relatively high from post-dosing day 2 through day 5. It will be noted that plasma levels rose to a peak plateau between 24 and 48 hours after dosing. Milk and urine concentrations, as expected, reflected this plasma increase with the greatest amount of americium being released (in milk and urine) during the 48- and 72-hour collection periods. Total nuclide transport to bovine milk and urine was 0.0004 and 0.001 percent of the administered oral dose, respectively. Table V presents the mean percentage of dose contained in plasma, milk, urine and feces for the two orally dosed goats. While results from both animals were used to compute the milk values, it should be remembered that for one goat the americium transport to milk was unexplainably high.

Americium concentrations decreased rapidly in the plasma of all intravenously dosed animals (Tables VI and VII). The initial plasma nuclide reductions were slightly more pronounced in the goats. However, in both groups of dairy animals the plasma retention of americium had dropped to below 1 percent of the original dose by the second day. A portion of the circulating americium had obviously been excreted in the urine during this initial time period and a much larger fraction had most likely been retained in the liver. At time of sacrifice the percentage of dose remaining in the plasma was quite close in both groups of animals (cows - 0.06 and goats - 0.03). Rapid plasma clearance rates have also been reported for rats (Taylor, 1962), sheep (McClellan *et al.*, 1962), dogs (Bruenger *et al.*, 1969) and baboons (Rosen *et al.*, 1972) following americium injections.

Bovine plasma extrapolations (to percentage of dose per total plasma weight) were based on the assumption that whole blood would be 8 percent of the body weight and subsequently that plasma represented 60 percent of the whole blood. Caprine plasma was calculated at 55.9 ml per kg of body weight (Klement *et al.*, 1955). However, some animal weight loss occurred during the study. This was especially evident in the dairy cows, thus introducing another extrapolation step to estimate total blood plasma. Multiple samples of bovine whole blood, plasma and cells collected at time of sacrifice and analyzed by both the direct counting and radiochemistry techniques, indicated that approximately 89 percent of the whole blood americium was found in the plasma. While this was the most thorough check on the distribution of americium in whole blood, it was evident from other bovine and caprine collections that, in spite of some fluctuation in the percentage distribution, the major fraction of whole blood americium was appearing in the plasma.

Tables VIII through XIII present a comparison of the mean americium transport to milk, urine and feces for all treatment groups. Values are expressed as both the percentage of the dose recovered per total collection and as the percentage of dose per gram of milk, urine or feces. Where the respective tables show a blank at an early post-dosing time (8 hours through 24 hours) it indicates a slight alteration in the sampling schedule. However, the blank shown at the 168-hour interval for bovine urine resulted from catheter displacement during a portion of this collection interval.

TABLE VI

PERCENTAGE OF AMERICIUM DOSE REMAINING IN BOVINE PLASMA FOLLOWING AN ACUTE 0.96 mCi INTRAVENOUS INJECTION OF CITRATE-BUFFERED AMERICIUM-241 CHLORIDE

Time post injection	Cow 184		Cow 280	
	% of Dose per Total Plasma*	% of Dose per Gram of Plasma	% of Dose per Total Plasma*	% of Dose per Gram of Plasma
8 h	2.82	8.07×10^{-5}	4.30	1.59×10^{-4}
12 h	2.74	7.82×10^{-5}	1.07	3.97×10^{-5}
24 h	9.90×10^{-1}	2.83×10^{-5}	1.43	5.30×10^{-5}
48 h	4.69×10^{-1}	1.35×10^{-5}	5.47×10^{-1}	2.10×10^{-5}
72 h	2.92×10^{-1}	8.46×10^{-6}	3.49×10^{-1}	1.34×10^{-5}
96 h	2.08×10^{-1}	5.96×10^{-6}	1.92×10^{-1}	7.35×10^{-6}
120 h	1.35×10^{-1}	4.10×10^{-6}	2.84×10^{-1}	1.09×10^{-5}
144 h	1.15×10^{-1}	3.37×10^{-6}	2.71×10^{-1}	1.08×10^{-5}
168 h	8.49×10^{-2}	2.57×10^{-6}	2.02×10^{-1}	8.06×10^{-6}
Sacrifice (approximately 216 h)	4.47×10^{-2}	1.40×10^{-6}	6.62×10^{-2}	2.65×10^{-6}

*Extrapolated values

TABLE VII

PERCENTAGE OF AMERICIUM DOSE RETAINED IN CAPRINE BLOOD PLASMA FOLLOWING A SINGLE INTRAVENOUS DOSE (41.7 μCi) OF CITRATE-BUFFERED AMERICIUM-241 NITRATE

Time After Injection	Percentage of Dose per Total Body Plasma*		Percentage of Dose per Gram of Plasma	
	Goat 4	Goat 5	Goat 4	Goat 5
8 h	6.86×10^{-1}	6.14×10^{-1}	2.81×10^{-4}	2.42×10^{-4}
15 h	3.89×10^{-1}	3.77×10^{-1}	1.62×10^{-4}	1.50×10^{-4}
24 h	2.85×10^{-1}	2.66×10^{-1}	1.21×10^{-4}	1.06×10^{-4}
48 h	1.63×10^{-1}	1.68×10^{-1}	7.19×10^{-5}	6.84×10^{-5}
72 h	1.15×10^{-1}	1.13×10^{-1}	5.32×10^{-5}	4.65×10^{-5}
96 h	5.28×10^{-2}	7.91×10^{-2}	2.57×10^{-5}	3.29×10^{-5}
120 h	4.08×10^{-2}	5.04×10^{-2}	2.08×10^{-5}	2.08×10^{-5}
144 h	5.52×10^{-2}	5.52×10^{-2}	2.85×10^{-5}	2.31×10^{-5}
168 h	3.84×10^{-2}	3.36×10^{-2}	2.16×10^{-5}	1.43×10^{-5}
192 h	2.64×10^{-2}	3.60×10^{-2}	1.54×10^{-5}	1.58×10^{-5}

*Extrapolated values

TABLE VIII

MEAN PERCENTAGE OF AMERICIUM DOSE TRANSFERRED TO MILK DURING THE 168-HOUR COLLECTION PERIOD

Time After Dosing	Oral Dose		Intravenous Dose	
	Cows	Goats	Cows	Goats
8 h	-	2.18×10^{-6}	-	1.13
24 h	9.11×10^{-5}	1.81×10^{-4}	1.41	3.18×10^{-1}
48 h	9.37×10^{-5}	3.80×10^{-3}	4.70×10^{-1}	1.95×10^{-1}
72 h	9.41×10^{-5}	1.86×10^{-4}	2.81×10^{-1}	1.09×10^{-1}
96 h	7.44×10^{-5}	6.87×10^{-5}	2.29×10^{-1}	7.20×10^{-2}
120 h	3.96×10^{-5}	2.95×10^{-5}	1.67×10^{-1}	6.72×10^{-2}
144 h	2.88×10^{-5}	2.75×10^{-5}	1.08×10^{-1}	5.76×10^{-2}
168 h	1.56×10^{-5}	1.31×10^{-4}	9.39×10^{-2}	4.44×10^{-2}
Total	4.37×10^{-4}	4.43×10^{-3}	2.76	1.99

TABLE IX

MEAN PERCENTAGE OF AMERICIUM DOSE TRANSFERRED PER GRAM OF MILK

Time After Dosing	Oral Dose		Intravenous Dose	
	Cows	Goats	Cows	Goats
8 h	-	3.32×10^{-9}	-	1.12×10^{-3}
12 h	1.09×10^{-8}	-	1.53×10^{-4}	-
24 h	1.88×10^{-9}	1.52×10^{-7}	1.25×10^{-4}	1.85×10^{-4}
48 h	8.87×10^{-9}	1.74×10^{-6}	3.95×10^{-5}	7.15×10^{-5}
72 h	7.98×10^{-9}	1.08×10^{-7}	2.48×10^{-5}	4.35×10^{-5}
96 h	6.10×10^{-9}	4.47×10^{-8}	1.71×10^{-5}	3.43×10^{-5}
120 h	3.33×10^{-9}	3.24×10^{-8}	1.30×10^{-5}	3.75×10^{-5}
144 h	2.06×10^{-9}	1.90×10^{-8}	9.28×10^{-6}	2.92×10^{-5}
168 h	1.48×10^{-9}	1.02×10^{-7}	8.77×10^{-6}	2.96×10^{-5}

TABLE X

MEAN PERCENTAGE OF AMERICIUM DOSE TRANSFERRED TO URINE DURING THE 168-HOUR COLLECTION PERIOD

Time After Dosing	Oral Dose		Intravenous Dose	
	Cows	Goats	Cows	Goats
8 h	1.03×10^{-5}	1.85×10^{-5}	1.93	2.07
24 h	8.61×10^{-5}	2.59×10^{-4}	1.31	6.07×10^{-1}
48 h	2.75×10^{-4}	3.93×10^{-4}	8.87×10^{-1}	6.55×10^{-1}
72 h	2.68×10^{-4}	1.91×10^{-4}	5.40×10^{-1}	2.95×10^{-1}
96 h	1.80×10^{-4}	1.10×10^{-4}	3.28×10^{-1}	2.14×10^{-1}
120 h	1.24×10^{-4}	4.39×10^{-5}	2.91×10^{-1}	2.00×10^{-1}
144 h	8.03×10^{-5}	8.12×10^{-5}	2.01×10^{-1}	1.32×10^{-1}
168 h	6.12×10^{-5}	5.49×10^{-5}	-	1.09×10^{-1}
Total	1.09×10^{-3}	1.15×10^{-3}	5.49	4.28

TABLE XI

MEAN PERCENTAGE OF AMERICIUM DOSE TRANSFERRED PER GRAM OF URINE

Time After Dosing	Oral Dose		Intravenous Dose	
	Cows	Goats	Cows	Goats
8 h	2.13×10^{-9}	3.65×10^{-8}	5.37×10^{-4}	3.33×10^{-3}
12 h	1.20×10^{-8}	-	1.60×10^{-4}	-
24 h	2.01×10^{-8}	4.01×10^{-7}	9.49×10^{-5}	5.47×10^{-4}
48 h	4.33×10^{-8}	1.77×10^{-7}	5.77×10^{-5}	1.87×10^{-4}
72 h	2.37×10^{-8}	1.05×10^{-7}	4.01×10^{-5}	1.08×10^{-4}
96 h	1.42×10^{-8}	8.49×10^{-8}	2.35×10^{-5}	1.15×10^{-4}
120 h	9.25×10^{-9}	5.34×10^{-8}	1.86×10^{-5}	1.05×10^{-4}
144 h	5.23×10^{-9}	4.59×10^{-8}	1.60×10^{-5}	6.10×10^{-5}
168 h	4.24×10^{-9}	3.25×10^{-8}	-	6.47×10^{-5}

TABLE XII

MEAN PERCENTAGE OF AMERICIUM DOSE TRANSFERRED TO FECES DURING THE 168-HOUR COLLECTION PERIOD

Time After Dosing	Oral Dose		Intravenous Dose	
	Cows	Goats	Cows	Goats
8 h	3.10×10^{-2}	5.86×10^{-5}	5.88×10^{-1}	3.11×10^{-2}
24 h	5.60	20.39	4.99×10^{-1}	3.19×10^{-1}
48 h	9.59	48.05	4.54×10^{-1}	5.80×10^{-1}
72 h	31.00	14.25	2.96×10^{-1}	3.35×10^{-1}
96 h	20.50	2.39	2.01×10^{-1}	2.86×10^{-1}
120 h	12.08	3.83×10^{-1}	1.52×10^{-1}	1.64×10^{-1}
144 h	6.57	1.10×10^{-1}	1.50×10^{-1}	1.98×10^{-1}
168 h	1.93	4.25×10^{-2}	8.10×10^{-2}	1.77×10^{-1}
Total	87.30	85.62	2.42	2.09

TABLE XIII

MEAN PERCENTAGE OF AMERICIUM DOSE TRANSFERRED PER GRAM OF FECES

Time After Dosing	Oral Dose		Intravenous Dose	
	Cows	Goats	Cows	Goats
8 h	4.76×10^{-6}	2.62×10^{-7}	9.47×10^{-5}	5.70×10^{-5}
12 h	5.85×10^{-4}	-	3.63×10^{-5}	-
24 h	1.18×10^{-3}	2.86×10^{-2}	3.08×10^{-5}	3.53×10^{-4}
48 h	1.97×10^{-3}	5.48×10^{-2}	2.45×10^{-5}	3.74×10^{-4}
72 h	2.28×10^{-3}	1.61×10^{-2}	1.46×10^{-5}	2.60×10^{-4}
96 h	1.00×10^{-3}	3.05×10^{-3}	1.11×10^{-5}	2.38×10^{-4}
120 h	6.28×10^{-4}	6.41×10^{-4}	8.21×10^{-6}	2.80×10^{-4}
144 h	2.41×10^{-4}	1.88×10^{-4}	7.16×10^{-6}	2.57×10^{-4}
168 h	7.20×10^{-5}	7.05×10^{-5}	6.36×10^{-6}	2.68×10^{-4}

Nuclide transport to milk, urine and feces was basically similar between orally dosed cows and goats. Peak americium concentration in bovine milk (Table IX) was considered to have occurred 48 hours after nuclide ingestion and the high 12-hour concentration resulting from an unexpectedly high value for one animal, does not appear to be an accurate reflection of the americium transport. For caprine milk, peak nuclide concentration also occurred 48 hours after dosing with somewhat of a peak plateau between post-treatment hours 24 and 72. Total americium transfer to milk for the individual goats was 5.67×10^{-4} and 8.28×10^{-3} percent of the oral dose. Peak americium concentrations in the urine (Table XI) following nuclide ingestion occurred at the 48-hour period for cows and at the 24-hour period for the goats. Americium concentrations in the feces (Table XIII) were highest at the 72-hour and at the 48-hour post-ingestion periods for cows and goats, respectively.

Americium transport to milk, urine and feces was also basically similar (between cows and goats) after intravenous dosing. The average percentage of injected americium transferred to milk, urine and feces was 3, 6 and 2 percent respectively for cows and 2, 4 and 2 percent respectively for goats. In both groups a large portion (approximately 30 percent) of all americium released from the body (milk, urine and feces) was found in the urine during the first 24 hours after injection. Taylor *et al.* (1961) noted that, during the early post-dosing stages, americium was excreted at a greater rate than was plutonium. Further studies have clearly shown that a large fraction of the total americium excretion from dogs is released via the urine 1 day after nuclide injection (Lloyd *et al.*, 1970).

At time of sacrifice nuclide retention differences were noted between cows and goats. Bovine bone retained the greatest fraction of the administered dose (Table XIV) followed by the liver. However, liver retained the greatest amount of americium in the goats following both oral and intravenous doses. Differences in nuclide deposition are quite evident in the intravenously dosed animals. Caprine bone contained only 13 percent of the injected americium, an observation that contrasted with the intravenously dosed cows where nearly 51 percent of the dose was retained in the skeleton. In the orally dosed cows, approximately 48 percent of all americium retained in the carcass was found in the skeleton. For the orally dosed goats, 24 percent of the carcass americium was recovered in bone. However, it should be remembered that total carcass retention following oral dosing has been based on the americium recovered in only liver, bone, kidney, lung, spleen, thyroid, gonads, muscle, heart and plasma. Small amounts of americium were undoubtedly present in other tissues and organs which, if included in the total carcass value, would reduce these relative percentages of skeletal retention.

The mean percentage of americium dose retained per gram of tissue is shown for all treatment groups in Table XV. In each case the femur shaft contained less americium per gram than did the epiphysis, and the sternum contained more americium per gram of tissue than did the vertebra. The relatively high concentration in goat rib following intravenous injections is somewhat surprising at this early sacrifice time. In general, the skeletal deposition pattern in goats is more difficult to interpret than that for the

TABLE XIV

MEAN PERCENTAGE OF AMERICIUM DOSE RETAINED IN DAIRY ANIMALS AT TIME OF SACRIFICE

	Oral Dose		Intravenous Dose	
	Cows	Goats	Cows	Goats
Bone	5.66×10^{-3}	1.67×10^{-3}	50.5	12.7
Liver	4.08×10^{-3}	5.43×10^{-3}	40.8	47.4
Kidney	3.75×10^{-4}	1.51×10^{-4}	2.4	0.9
Lung	2.82×10^{-4}	9.96×10^{-5}	1.7	0.5
Spleen	7.84×10^{-5}	8.04×10^{-6}	0.7	0.4
Thyroid	5.67×10^{-7}	3.55×10^{-7}	0.2	0.02
Muscle	9.55×10^{-4}	6.69×10^{-4}	5.4	4.4

TABLE XV

MEAN PERCENTAGE OF AMERICIUM DOSE RETAINED PER GRAM OF TISSUE

	Oral Dose		Intravenous Dose	
	Cows	Goats	Cows	Goats
Diaphysis	3.47×10^{-8}	8.54×10^{-7}	3.05×10^{-4}	3.58×10^{-3}
Epiphysis	5.77×10^{-8}	1.01×10^{-6}	6.07×10^{-4}	6.33×10^{-3}
Sternum	8.69×10^{-8}	1.01×10^{-6}	6.79×10^{-4}	5.43×10^{-3}
Vertebra	7.32×10^{-8}	5.50×10^{-7}	6.58×10^{-4}	4.67×10^{-3}
Rib	4.48×10^{-8}	8.53×10^{-7}	4.38×10^{-4}	6.83×10^{-3}
Liver	4.30×10^{-7}	7.96×10^{-6}	3.82×10^{-3}	5.66×10^{-2}
Kidney	1.54×10^{-7}	1.23×10^{-6}	1.15×10^{-3}	6.97×10^{-3}
Lung	5.15×10^{-8}	1.20×10^{-7}	2.64×10^{-4}	1.09×10^{-3}
Spleen	3.34×10^{-8}	6.44×10^{-8}	2.71×10^{-4}	2.93×10^{-3}
Thyroid	1.22×10^{-8}	8.11×10^{-8}	7.08×10^{-5}	3.78×10^{-3}
Muscle	3.60×10^{-9}	4.36×10^{-8}	1.93×10^{-5}	2.85×10^{-4}
Mammary Gland	4.26×10^{-8}	4.37×10^{-7}	4.81×10^{-4}	2.49×10^{-3}
Heart	7.29×10^{-8}	1.21×10^{-7}	2.88×10^{-4}	1.05×10^{-3}

cows which revealed a similar pattern after both the oral and intravenous doses. Short term americium metabolism in rats (Taylor, 1962) also demonstrated the increased americium deposition in the epiphysis relative to the diaphysis. Vertebra and sternum had greater americium concentrations per gram than did either the femur or rib in an intravenously dosed baboon sacrificed 1 month after nuclide injection (Rosen *et al.*, 1972). However, the sternum retained less americium per gram than either the rib, femur or vertebra in dogs (Lloyd *et al.*, 1972) sacrificed at various time intervals. Variations in total skeletal retention have also been related to the particulate characteristics of the americium dose (Lindenbaum *et al.*, 1970).

In both intravenously and orally dosed dairy animals, the liver retained the greatest amount of americium on a per gram of tissue basis. Following the liver, americium concentrations were second highest in the kidney. The extent of americium retention in the liver has been shown to be affected by animal age and sex (Durakovic *et al.*, 1973). Furthermore, since americium retention may be influenced by the absolute size of various organs, it should be noted that livers of lactating cows have been projected to be approximately 20 percent heavier than livers from non-lactating cows (Smith and Baldwin, 1974). Hollins and Durakovic (1972) reported americium retention differences in the livers of lactating and non-lactating rats following intravenous doses on or before the day of parturition. While there were no liver differences in americium concentration between lactating and control rats, liver weights were greater in the lactating animals. During the current americium experiment using cows and goats, actual liver weights were taken for all animals and the americium retention has been reported on a per organ basis and on a per gram of tissue basis.

Thyroid glands, composed of spherical follicles and an interfollicular area of highly vascular connective tissue, have been found to retain relatively high concentrations of americium in beagle dogs. Taylor *et al.* (1969), using autoradiographic techniques, showed that the americium was being retained extracellularly in the interfollicular regions. High thyroid concentrations were not noted in the dairy animals used for the current experiment.

Tables XVI, XVII, and XVIII present some comparisons between the transport of americium-241 and plutonium-238 in Holstein dairy cows. Twenty-four-hour collections of urine and milk (Table XV) contained noticeably higher nuclide concentrations when the animals were injected with americium, as opposed to plutonium. Nuclide retention in the liver (Table XVII) was also greater for animals that had been dosed with americium. There was a marked similarity in the nuclide deposition pattern following ingestion of either americium-241 chloride or citrate-buffered plutonium-238 nitrate (Table XVIII).

TABLE XVI

COMPARISON OF AMERICIUM-241 AND PLUTONIUM-238 TRANSPORT TO MILK, URINE AND FECES IN HOLSTEIN DAIRY COWS (Values Expressed as a Percentage of the Respective Intravenous Doses)

Time post-injection	Americium-241*			Plutonium-238**		
	Milk	Urine	Feces	Milk	Urine	Feces
24 h	1.41	3.25	1.09	0.450	0.991	0.272
48 h	0.470	0.887	0.454	0.434	0.476	0.605
72 h	0.281	0.540	0.296	0.273	0.393	0.514
96 h	0.229	0.328	0.201	0.186	0.278	0.423
120 h	0.167	0.291	0.152	0.142	0.243	0.391
Total	2.56	5.30	2.19	1.49	2.38	2.21

*Average values from two cows each given an intravenous dose (0.96 mCi) of citrate-buffered americium-241 chloride.

**Average values from four cows each given an intravenous dose (16.0 mCi) of citrate-buffered plutonium-238 nitrate (Sutton *et al.*, 1977b).

TABLE XVII

COMPARISON OF AMERICIUM-241 AND PLUTONIUM-238 RETENTION IN HOLSTEIN DAIRY COWS APPROXIMATELY ONE WEEK AFTER RECEIVING SINGLE INTRAVENOUS DOSES
(Values Expressed as a Percentage of Dose per kg of Tissue)

Tissue	Americium-241*	Plutonium-238**
Diaphysis	3.05×10^{-1}	2.56×10^{-2}
Epiphysis	6.07×10^{-1}	8.26×10^{-2}
Sternum	6.79×10^{-1}	8.25×10^{-1}
Liver	3.82	2.48
Kidney	1.15	2.97×10^{-1}
Muscle	1.93×10^{-2}	2.63×10^{-2}
Lung	2.64×10^{-1}	4.36×10^{-1}
Thyroid	7.08×10^{-2}	3.36×10^{-1}
Spleen	2.71×10^{-1}	1.95×10^{-1}
Heart	2.88×10^{-1}	9.59×10^{-2}

*Average values from two cows sacrificed nine days after receiving an intravenous dose (0.96 mCi) of citrate-buffered americium-241 chloride.

**Average values from two cows sacrificed six days after receiving an intravenous dose (16.0 mCi) of citrate-buffered plutonium-238 nitrate (Patzer *et al.*, 1977b).

TABLE XVIII

TRANSPORT OF ORALLY ADMINISTERED PLUTONIUM-238 AND AMERICIUM-241 TO EDIBLE BOVINE PRODUCTS

Nuclide Dose	No. of Animals	% of Dose Secreted in Milk (Cumulative)	% of Dose/Liter of Milk at Peak Concentration	Time of Sacrifice	% of Dose in Liver	% of Dose/g of Liver	% of Dose in Muscle (Skeletal)	% of Dose/g of Muscle
Citrate-Buffered Plutonium 3 mCi/animal acute dose (Stanley *et al.*, 1974)	4	2.0×10^{-4}	4.9×10^{-6}	2 animals sacrificed 93 days post-treatment	3.5×10^{-3}	3.7×10^{-7}	2.0×10^{-3}	6.7×10^{-9}
Plutonium Dioxide 1 mCi/animal/day for 19 consecutive days (Stanley *et al.*, 1975)	4	2.0×10^{-5}	2.7×10^{-7}	2 animals sacrificed 42 days post-treatment	5.3×10^{-4}	5.3×10^{-8}	8.7×10^{-5}	3.3×10^{-10}
				2 animals sacrificed 73 days post-treatment	6.2×10^{-4}	5.8×10^{-8}	1.3×10^{-4}	3.4×10^{-10}
Americium Chloride 41.7 mCi/animal acute dose	2	4.4×10^{-4}	8.6×10^{-6}	2 animals sacrificed 8 days post-treatment	4.1×10^{-3}	4.3×10^{-7}	9.6×10^{-4}	3.6×10^{-9}

FUTURE PLANS

In addition to preparing a final report on the curium-243 metabolism studies, summary comparisons will be presented on the biological transport of plutonium, americium, curium and neptunium in dairy animals. One comparative report has already been presented (Patzer *et al.*, 1977b). Results will also be compiled and presented from a recently conducted study (Patzer *et al.*, in preparation) on the relative transport of plutonium-238 and plutonium-239 in dairy cows.

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