Title

METABOLIC STUDIES WITH STRONTIUM-90 IN THE RHESUS MONKEY (PRELIMINARY REPORT)

Authors

Durbin, Patricia W.
Parrott, Marshall W.
Williams, Marilyn H.
et al.

Publication Date

1957-01-07

UCRL 3634

UNIVERSITY OF CALIFORNIA

Radiation Laboratory

METABOLIC STUDIES WITH STRONTIUM-90 IN THE RHESUS MONKEY

(Preliminary Report)

BERKELEY, CALIFORNIA

UCRL-3634
Distribution:
Health and Biology

UNIVERSITY OF CALIFORNIA

Radiation Laboratory
Berkeley, California

Contract No. W-7405-eng-48

METABOLIC STUDIES WITH STRONTIUM-90 IN THE RHESUS MONKEY

(Preliminary Report)

Patricia W. Durbin, Marshall W. Parrott, Marilyn H. Williams,
Muriel E. Johnston, C. Willet Asling, and Joseph G. Hamilton
with the technical assistance of Nylan Jeung and Sibyl A. Cole

January 7, 1957

Printed for the U. S. Atomic Energy Commission

METABOLIC STUDIES WITH STRONTIUM-90 IN THE RHESUS MONKEY
(Preliminary Report)

Patricia W. Durbin, Marshall W. Parrott, Marilyn H. Williams, Muriel E. Johnston, C. Willet Asling, and Joseph G. Hamilton
with the technical assistance of Nylan Jeung and Sibyl A. Cole

Division of Medical Physics, the Crocker Radiation Laboratory, and the Departments of Medicine, Anatomy, and Radiology
University of California, Berkeley and San Francisco

January 7, 1957

ABSTRACT

Adult rhesus monkeys eliminated 56% of administered Sr^{90}, compared with 28% of Ca^{45}, in the urine during the first 10 days after intravenous administration.

The Sr^{90} concentration in the vertebrae was found to be reasonably representative of the skeleton as a whole in two animals whose skeletal distribution of Sr^{90} was studied. Successive amputation of caudal vertebrae is therefore recommended as the simplest and safest method of acquiring information on long-term skeletal retention of Sr^{90} in valuable animals with long life spans.

Average half times for skeletal retention of Sr^{90} were calculated for an adult male, 470 days, and for an adult female that had experienced three closely spaced pregnancies, 315 days.

Half times for skeletal retention of Sr^{90} of 155 and 195 days were calculated for the first 10 months of life of two offspring born to an injected mother.

One infant monkey retained an average of 18% of Sr^{90} administered daily by mouth for 13 weeks, whereas six adolescents retained on the average less than 5% of a daily dose during the same period of time.

A measurable amount of Sr^{90}, 23.5 dpm/g bone ash, was found in the skeleton of an uninjected control animal.

Placental transfer from a mother with a fairly well-fixed skeletal burden of Sr^{90} amounted to about 3% of the Sr^{90} content of the mother's skeleton at term.

The Sr^{90} concentration in milk samples from an injected female taken shortly after the birth of her second offspring (402 days postinjection) was three to four times the Sr^{90} level of a plasma sample taken a few days later.

METABOLIC STUDIES WITH STRONTIUM-90 IN THE RHESUS MONKEY

(Preliminary Report)

Patricia W. Durbin, Marshall W. Parrott, Marilyn H. Williams, Muriel E. Johnston, C. Willet Asling, and Joseph G. Hamilton
with the technical assistance of Nylan Jeung and Sibyl A. Cole

Division of Medical Physics, the Crocker Radiation Laboratory, and the Departments of Medicine, Anatomy, and Radiology
University of California, Berkeley and San Francisco

January 7, 1957

INTRODUCTION

It is generally agreed that Sr^{90} is potentially the most dangerous of the fission products. It is produced in relatively high yield in the fission process, and has a long physical half life. Many of its compounds are quite soluble and are readily absorbed by both plants and animals. Once absorbed by an animal, Sr^{90} is retained for long periods in the skeleton.[1]

Dudley[2] has compiled a survey of the literature on Sr^{90} in mammals to mid-1954; this survey is in the form of tables setting forth the animals employed and their age, the dose administered, the length of the study, and the effects observed. Numerous investigations have been made or are under way of the absorption, distribution, and elimination of strontium isotopes under varying conditions in laboratory rodents,[1-7] dogs,[8] and domestic livestock.[9,10]

The most important animal from the standpoint of human society is necessarily man himself. Data currently being applied to human beings have been derived chiefly from three sources: (a) extrapolation from experience with laboratory animals, undependable at best; (b) studies of the behavior of stable strontium in normal man;[11-13] and (c) tracer experiments with shorter-lived radioisotopes of strontium in patients with advanced diseases, usually neoplastic.[14,15] For obvious reasons data on Sr^{90} in normal human beings can be obtained only from accidental contamination such as that reported by Cowan et al.[16] and the exposure of the Marshallese during Operation Castle.[17-19]

It was believed that another primate the rhesus monkey might provide valuable clues to the behavior and effects of Sr^{90} in man despite the differences in life span--20 years vs 65 years--and diet--herbivorous vs omnivorous. Edington et al.[20] reported that 0.5 mC/kilo of Sr^{90} was lethal to monkeys in 35 to 60 days. Using microradiographic and autoradiographic techniques, Jowsey et al.[21] found that in the tibiae of monkeys Sr^{90} was laid down quite unevenly, and apparently only in areas of bone growth.

This report is a summary of the data obtained during the past two and one-half years in the course of a series of investigations with Sr^{90} in the rhesus monkey (Macaca mulatta).

METHODS

General Care of the Animals

The animals used in these studies were adult, adolescent, and infant rhesus monkeys of both sexes. Adults and adolescents were maintained on the diet shown in Appendix I unless otherwise specified. They were fed early each morning; the entire daily ration was offered at that time. Upon receipt, each animal was tested for tuberculosis and x-rays were taken for age determination.* The TB tests were repeated at least annually. All animals in the colony were weighed once a month. Complete blood counts were also taken monthly. Periodically the colony was checked for intestinal parasites--chiefly worms. When necessary, "crystoid" tablets (0.1 g, Sharp and Dohme) and (or) gentian violet capsules (3/20 gr, Lilly) were administered until very few worm eggs could be found in three consecutive daily stool samples. Miscellaneous problems in care were handled with the help of a veterinarian and a dentist. Prior to use in an experiment, all animals were maintained in the colony for a conditioning period of 3 to 6 months.

Intravenous Studies

Three adults, Stupe (a normal healthy male), Tony (an older male with an arthritislike condition of the lower extremities), and Rosy (a 3-months-pregnant female**) were each given 35 μC of carrier-free Sr^{90} as the equilibrium mixture of Sr^{90}-Y^{90} and 135 μC of high-specific-activity Ca^{45} intravenously in isotonic sodium citrate.† One adolescent, Pat, received only Sr^{90}, 3 months after being placed on a low-calcium diet (the standard diet without the milk and vitamin supplements).

After injection of the radioisotopes all animals were placed in metabolism cages, and daily collections of urine and feces were made for 10 days. After the initial 10-day collection period the animals were returned to their regular cages. Fecal samples were obtained periodically without transfer of the animals from their regular cages.

Stupe and Rosy were kept for breeding and long-term study. Pat was sacrificed 94 days after injection, and Tony, 242 days after injection, both with overdoses of nembutal. Muscle was dissected from the various parts of the skeleton, which were ashed individually for radioactive assay. Muscle and soft-tissue balance were also prepared for assay. Bone biopsy samples were obtained from the two remaining adults and one uninjected adolescent female by amputation of two caudal vertebrae. The operations were performed under aseptic conditions and were followed by a course of antibiotics.

---

* Tabulation of the bone growth data is still incomplete.

** Gestation period for this species is 6 months.

† Both isotopes were obtained from Oak Ridge National Laboratory

Breeding Experiments

To date Rosy has been successfully mated with Stupe and has borne three apparently normal offspring. The first, Willie, was born 98 days after the mother received her Sr^{90} injection, Betty was born 402 days postinjection, and Henry was born 840 days postinjection. Daily milk samples of 1.2 to 8.3 ml were obtained from the mother with a breast pump from the third to the sixth day after the birth of the second infant, Betty. The Sr^{90} levels of the red blood cells and plasma of the mother were obtained 30 days later. All three infants were removed from the mother at birth and have been raised on formula by members of the staff. The formula and dietary supplements are shown in Appendix II. A careful record has been kept of the food intake, body weight, and blood counts of the infants.

The Sr^{90} burdens of the first two infants were checked when they were 3 months old by in vivo counting of the bremsstrahlung produced by the Y^{90} beta particles with two 2-inch sodium iodide scintillation counters. Bone biopsies (caudal vertebrae) were obtained from Willie and Betty at 20 and 10 months of age respectively. Fecal samples were obtained periodically from each animal for Sr^{90} assay.

The youngest, Henry, was checked for Sr^{90} content 8 days after birth by the above-mentioned in vivo method. This animal has worn plastic pants and a diaper (Fig. 1) since he was a few days old so as to facilitate collection of excreta. Pooled excreta were collected daily from birth until age 36 days to establish the rate of elimination of the Sr^{90} acquired in utero. When 36 days old he was put on a long-term low-level feeding program. For the past 5 months he has received daily in his first bottle 0.0043 μC of Sr^{90} as the equilibrium mixture except on week ends and holidays. Since the initiation of the feeding program, pooled daily excreta have been collected, ashed, and assayed for Sr^{90}.* Retention has been measured by (a) calculation from excretion data, (b) periodic in vivo counting, and (c) caudal vertebral biopsy.

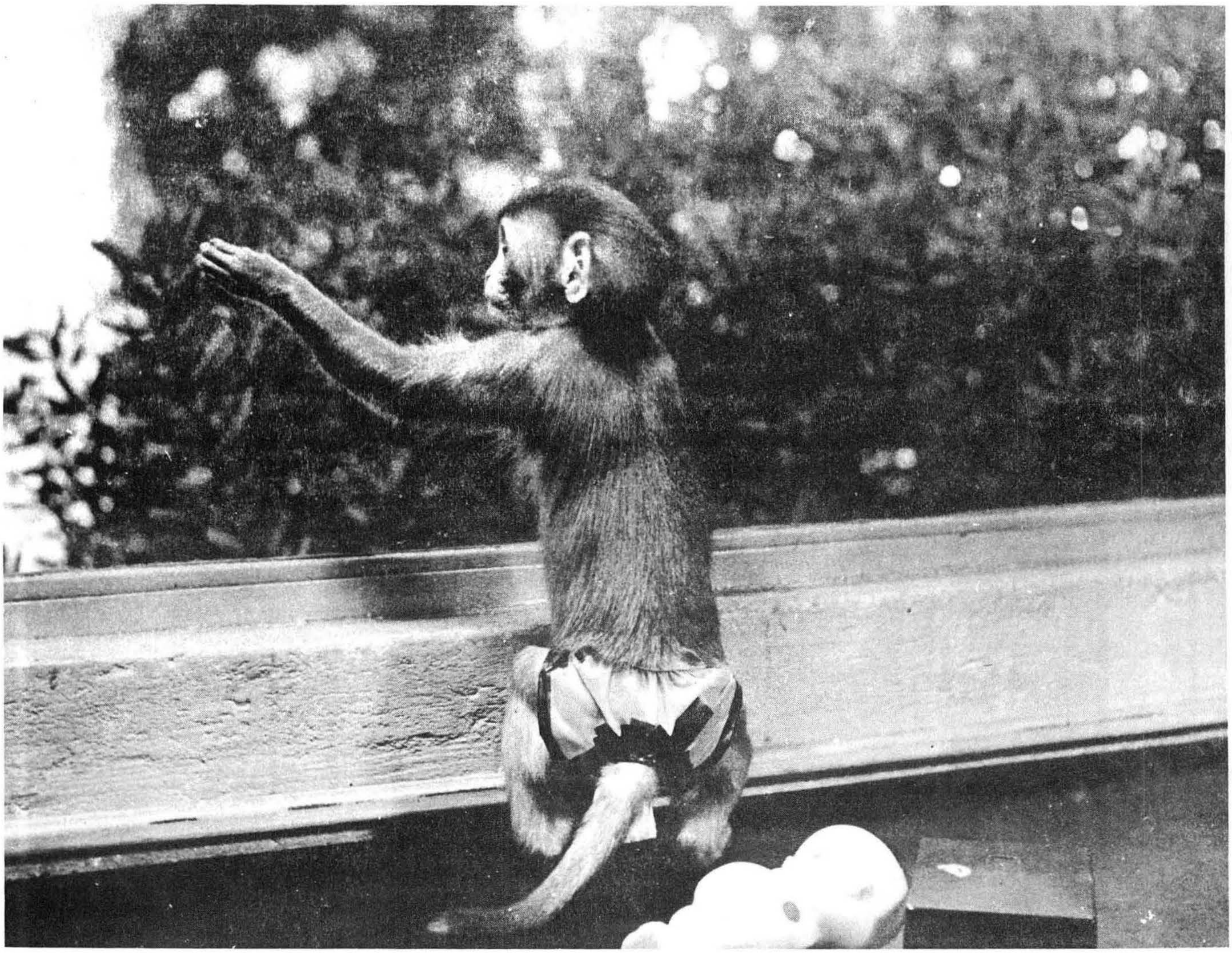
Absorption and Retention in Adolescents

Six adolescent monkeys,** two males and four females, have received daily 0.0066 μC of Sr^{90} as the equilibrium mixture except on week ends and holidays since June 26, 1956. A round slab of banana is scored with a knife, and 0.1 ml of a dilute saline solution of Sr^{90} is spread over the scored portion. The "spiked" banana is offered to each animal at least 10 minutes before the rest of the day's ration is presented. So far, there have been few difficulties in this feeding procedure because the animals are hungry, and banana is their favorite food. At the beginning of the feeding period the animals were housed in metabolism cages for collection of excreta. The separation of urine and feces is not complete because of the semiliquid nature of the stools, particularly after treatment for worms. Excreta are

---

* Unfortunately urine and feces are not readily separable.

** Estimated age at initiation of feeding program: 2 years.



ZN-1668

Fig. 1. Infant monkey with plastic pants and diaper.

collected every other day and pooled on a weekly basis for assay. Twelve weeks after the initiation of the feeding program three of the animals were placed on a low-calcium diet* consisting of fruit and vegetables; a milk substitute of butter, sugar, hydrolyzed casein and water (in the same proportions as are present in whole milk); and the usual supplement of vitamins and iron.

Radioactive Assay Procedures

Samples with very low levels of activity, such as blood and milk from injected animals and bones and excreta from the infants, were sent to Nuclear Science and Engineering Corporation, Pittsburgh, Pennsylvania, for assay. Bones and excreta from injected animals and those on the feeding program were assayed according to the following procedure: After dry ashing, the samples were digested with concentrated HNO_3 or aqua regia until solution was nearly complete and then evaporated to dryness. Dilute HNO_3 was added so that 10 ml of the final solution represented approximately 0.5 g of ash. Small aliquots were taken from samples containing both Ca^{45} and Sr^{90}, transferred to weighed gold plates, and treated according to a procedure described previously.[22] All samples were stored for at least 30 days to allow for attainment of radioactive equilibrium. The Ca^{45} and Sr^{90} beta-particle activities were measured with a thin-end-window G-M counter by differential filtration. Aliquots of samples containing only Sr^{90} were placed in weighed porcelain ashing capsules, evaporated to dryness, and counted with a G-M counter. In each case the appropriate corrections were made for self-absorption, and corrected counts were compared with an aliquot of the administered dose.

---

* The regular diet contains 1395 mg of calcium per day and the low-calcium diet, 696 mg calcium per day.

RESULTS

Distribution and Excretion of Intravenously-administered Sr^{90}

The decline in urinary excretion rate of intravenously administered Sr^{90} is shown in Fig. 2 for four adult rhesus monkeys. Because of the wide variations in the curve shapes for the individual animals, a scatter diagram with an average curve (broken line) is shown. The average urinary excretion curve (broken) has two components with half times of 0.8 and 4.2 days.

A comparison of the cumulative urinary excretion of Ca^{45} and Sr^{90} is shown in Fig. 3 for two of the adults. In contrast to the wide variation in the individual rate curves, the cumulative curves are quite similar for these two animals. Renal excretion of Sr^{90} was apparently more efficient than that of Ca^{45}. Similar results have been obtained for other species.[15, 23, 24] Figure 4 shows the fecal excretion rate of Sr^{90} in the two surviving adults to 900 days postinjection. The slope of the slowest component, which appears at about 200 days, was similar for the two animals despite the fact that the female had experienced three closely spaced pregnancies. It is quite unlikely that the urinary excretion-rate curve has a different shape, inasmuch as the Sr^{90} eliminated by either route is derived from the same source, namely, the circulating blood. Experiments are under way to test this point.

Table I shows the distribution of Sr^{90} in the various parts of the skeletons of an adult and an adolescent monkey. The ratios Sr^{90}:Ca^{45} for the skeletal parts are shown for the adult. As might be expected on the basis of age, differences in diet, and postinjection interval, the Sr^{90} level was generally higher in the bones of the adolescent. These differences were more striking in flat bones than in the long bones. The Sr^{90} content of the vertebrae seems to be reasonably representative of the skeleton as a whole. It was for this reason, as well as the simplicity of the operative procedure, that caudal vertebrae were selected for bone biopsy.

With the exception of scapulae, paw bones, and ribs, the Sr^{90}:Ca^{45} ratios were quite similar for the various bones. The mean Sr:Ca ratio for the entire skeleton of this animal was 0.52.

The body burdens of Sr^{90} in the two surviving adults, estimated from bone biopsy, are shown in Table II. Average half times for Sr^{90} were calculated for the male and female, based on retention 10 days after injection (57.7% and 36.3% at the administered dose respectively), and on the estimated body burdens at approximately 600 days. For the male the average half time was 470 days, and for the female, 315 days. The successive pregnancies of the female (but without lactation) appeared to hasten the elimination of Sr^{90}.

A measurable amount of Sr^{90}, 1.5 ± 0.5 dpm,* was found in a 63.8-mg sample of vertebral ash obtained in August 1955 from Alice, an animal that had not been given Sr^{90}. This Sr^{90} does not seem to be due to contamination, because a great deal of care was exercised to avoid contamination during the operative and ashing procedures.

---

* Martell reports that the error in measurement of Sr^{90} by the "Chicago Sunshine Method" used by Nuclear Science Engineering Corporation is less than 10%.[25] The activity of this sample was well within their limits of sensitivity.

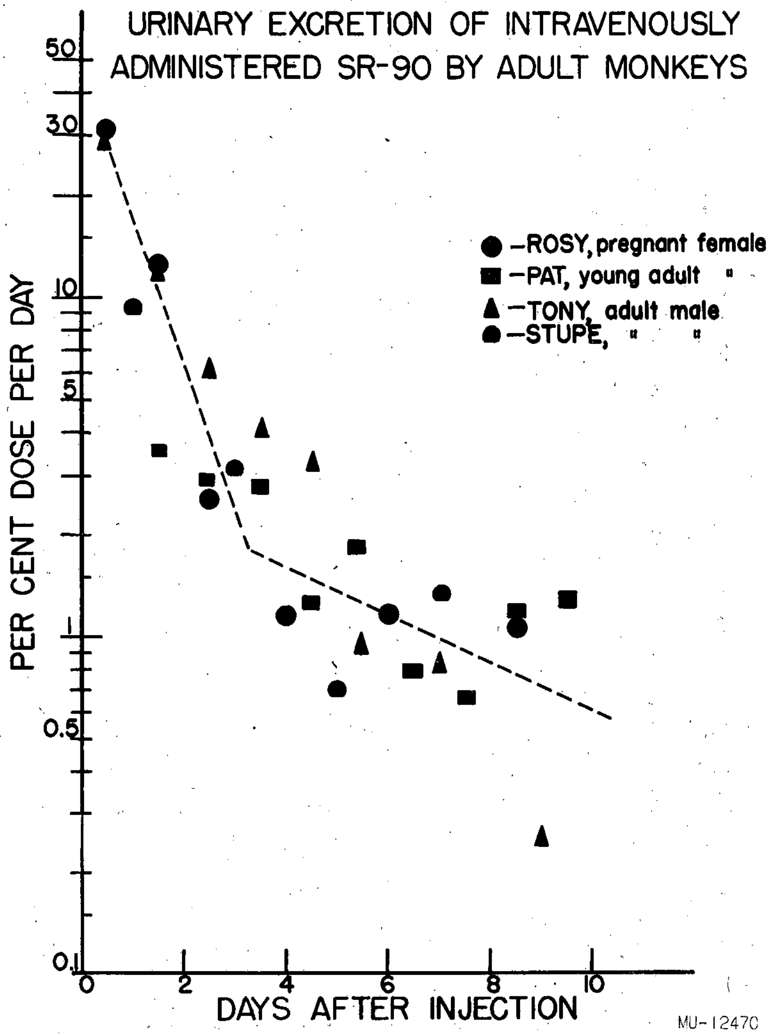


Fig. 2. Urinary excretion rate of Sr^{90} by adult rhesus monkeys.

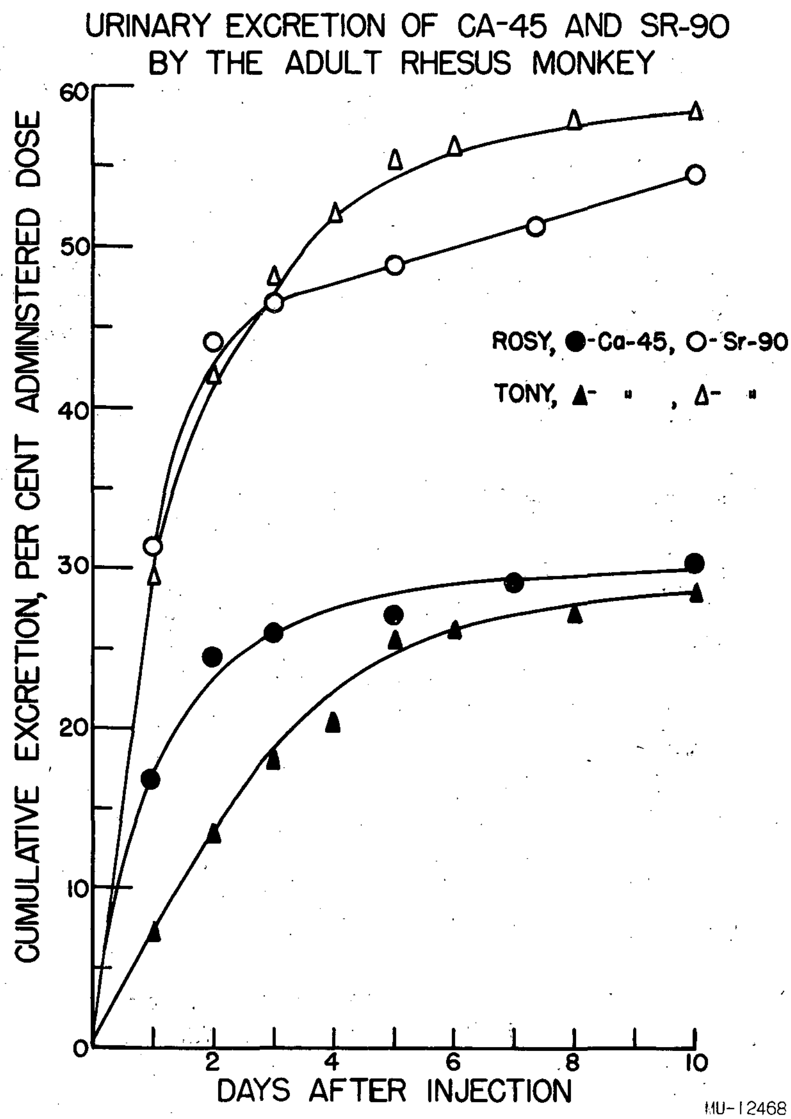


Fig. 3. Cumulative urinary excretion of Ca^{45} and Sr^{90} by adult rhesus monkeys.

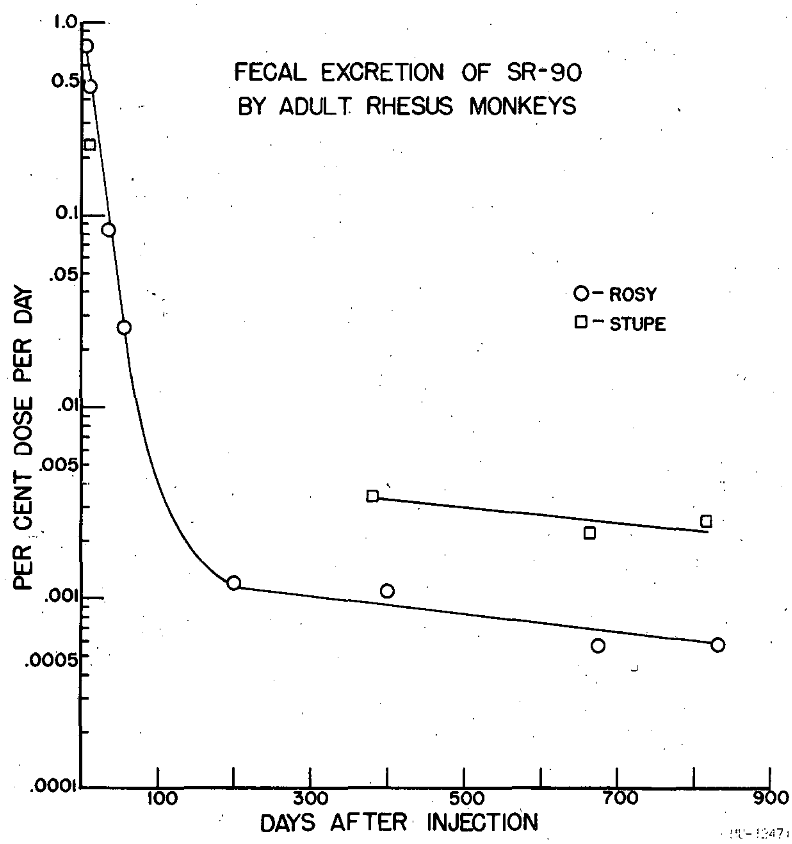


Fig. 4. Fecal excretion rate of Sr^{90} by adult rhesus monkeys.

Table I

The distribution of carrier-free Sr^{90} in the rhesus monkey after intravenous administration. Each animal received 35 μC Sr^{90}; Tony also received 135 μC Ca^{45}.

	Pat-3.5-yr-old female 94 days postinjection		Tony[a]-6.5-yr-old male 242 days postinjection		
	Sr^{90}		Sr^{90}		
	% dose	%/g ash	% dose	%/g ash	$\frac{\% Sr^{90}}{\% Ca^{45}}$
Skull	7.00	0.206	2.96	0.068	0.50
Mandible	2.76	0.264	1.31	0.113	0.57
Scapulae	1.77	0.294	1.28	0.138	0.62
Clavicles	0.29	0.290	0.31	0.135	0.57
Sternum	0.25	0.295	0.35	0.125	0.49
Ribs	2.00	0.278	0.90	0.106	0.63
Paw bones	2.53	0.141	2.05	0.116	0.60
Humeri	2.93	0.207	2.39	0.136	0.52
Ulnae	1.47	0.217	1.14	0.134	0.48
Tibiae	2.88	0.202	1.67	0.148	0.55
Femora	4.37	0.197	1.56	0.111	0.39
Radii and fibulae	1.82	0.191	1.20	0.122	0.42
Patellae	0.18	0.277	0.35	0.175	0.50
Cervical and thoracic vertebrae	2.56	0.224	2.80	0.135	0.54
Lumbar and caudal vertebrae	4.48	0.258	8.74	0.148	0.52
Pelvis	4.50	0.293	(b)	(b)	(b)
Teeth	0.96	0.106	0.27	0.016	0.49
Muscle	0.10	0.007	0.09	0.006	0.82
Soft tissue balance	0.08	0.009	0.11	0.007	0.61

[a] Arthritic (i.e. pelvis and lumbar and caudal vertebrae heavily calcified and fused).

[b] Included with lumbar and caudal vertebrae.

Table II

Sr^{90} content of biopsy samples of caudal vertebrae from injected adult male and female rhesus monkeys, the first two offspring of an injected female, and one control female. Injected animals received 35 μC Sr^{90} intravenously.

Animal	Estimated age at sampling	Days post-injection	Source	Body wt at sampling (kg)	dpm Sr^{90} per g ash of caudal vertebrae	Estimated Sr^{90} body burden[a] (μC)
Rosy	5–6 yr	638	Hooper Fdn.	4.85	2.95×10^4	3.2
Stupe	5.5–6 yr	623	"	11.1	5.95×10^4	8.2
Pat	3.5 yr	94	commercial	3.35	1.53×10^5	11.9[b]
Willie	20 mo.	(98 for mother)	Rosy and Stupe	2.95	5.5×10^2	3.6×10^{-2}
Betty	10 mo.	(402 for mother)	"	1.99	8.3×10^2	3.7×10^{-2}
Alice	3–3.5 yr	none-control	commercial	3.84	2.35×10^1	2×10^{-3}

[a] 1 μC = 2.22×10^6 dpm; body burden based on estimate from Table I that Sr^{90} concentration in caudal vertebrae is representative of total skeletal Sr^{90}; average ash content of monkey bone (plus marrow) taken as 27.5%; percent body weight of bone estimated at 18% for infants and females and 10% for adult males.

[b] Actual measured body burden 15 μC; error of estimate of this sort is thus in the range of 15%.

Samples of milk were obtained from Rosy for four successive days shortly after the birth of her second infant. Table III shows the Sr^{90} level in the milk, the daily fecal excretion rate at that time, and the Sr^{90} content of plasma 1 month later. Except for the first sample taken 3 days postpartum, the milk concentration was from three to four times that in the plasma.

The blook-count data have proved to be of little value because of the introduction into the colony late in 1954 of a blood parasite similar to Bartonella. The original infected animals were destroyed, but Rosy and Stupe apparently still remain carriers, and the parasite is now endemic in the colony.

Sr^{90} in Infant Monkeys

Table IV gives the Sr^{90} content of the first two infant monkeys 3 months after birth, and 8 days after birth of the third as determined by in vivo scintillation counting. The last two lines in Table II show the Sr^{90} burdens calculated from bone biopsy samples for the two older monkeys, Willie and Betty, at 20 and 10 months of age respectively.

The Sr^{90} burdens of these animals apparently had no ill effect upon their growth rate, as shown in Fig. 5. The growth rates of the three siblings were very close to that reported by Pickering et al.[26] for infant monkeys of this species raised under similar conditions. During the first 6 months to a year the blood counts of all three infants were within normal limits.*

Samples of pooled urine and feces from Betty at 14 and 140 days of age contained 260 dpm/day and 38.6 dpm/day, indicating that the Sr^{90} acquired by placental transfer was eliminated fairly rapidly. Nearly a year after birth (305 days), Willie, the oldest, was still excreting Sr^{90} in the feces at a relatively high level: 205 dpm/day. More recent excretion samples from these two animals have not yet been analyzed.

On the basis of the data in Table IV, and the calculated body burdens shown in Table II, approximate half times for elimination of Sr^{90} during the first 10 months of life were calculated for the two older infants: 195 days for Willie, and 155 days for Betty. Extrapolation back to the time of birth of these two infants provides a rough estimate of the placental transfer of Sr^{90}. In the first-born, Willie, placental transfer accounted for about 0.3 μC Sr^{90}, or 3% of the mother's retained dose; the retention by the mother was calculated from her half-time value of 315 days. Rosy received her Sr^{90} injection halfway through the second trimester of her first pregnancy. The extrapolated Sr^{90} content for the second offspring, Betty, was slightly more than 0.15 μC, 2.9% of the mother's retained dose 402 days postinjection. When Henry, the third offspring, was 8 days old, an in vivo count was on the border line of the

---

* At age 14 mo Betty's red blood cell count dropped to less than one million. A few days later she succumbed, apparently as the result of infection with the blood parasite mentioned above. Her skeleton is currently being processed for assay. Willie was infected at the same time but responded to a heroic course of treatment with "Aralen," chloroquin hydrochloride (Winthrop-Stearns), and massive injections of liver, iron, and folic acid. His red cell count has remained at from 4.1 to 4.5 million for the past 3 months, and he has continued to gain weight at an apparently normal rate.

Table III

The blood level, fecal excretion rate, and milk concentration of Sr^{90} in an adult female rhesus monkey, Rosy, 3 to 40 days after the delivery of her second offspring on the 402nd day after receiving 35 μC of Sr^{90} intravenously.

Sample	Days postinjection	Sr^{90} concentration (%/ml)
Plasma	449	3.7×10^{-6}
Red blood cells	449	1.6×10^{-6}
Milk	(second offspring born 402 days postinjection)	
3 days post partum	405	2.6×10^{-6}
4 days post partum	406	6.5×10^{-6}
5 days post partum	407	9.1×10^{-6}
6 days post partum	408	1.7×10^{-5}
Fecal excretion rate	397 to 407	1.1×10^{-3}%/day

Table IV

Placental transfer of Sr^{90} in the rhesus monkey estimated by in vivo scintillation count of the infants

	Vital Statistics		Counting		
Animal	Birth date	Day after mother injected	Date	Age (days)	Estimated Sr^{90} content[a] (μC)
Willie	7/7/54	98	10/29/54	104	0.22
Betty	5/7/55	402	8/12/55	97	0.10
Henry	5/20/56	840	5/28/56	8	$<$ 0.10

[a] Low counting rate makes for probable error of at least 25%.

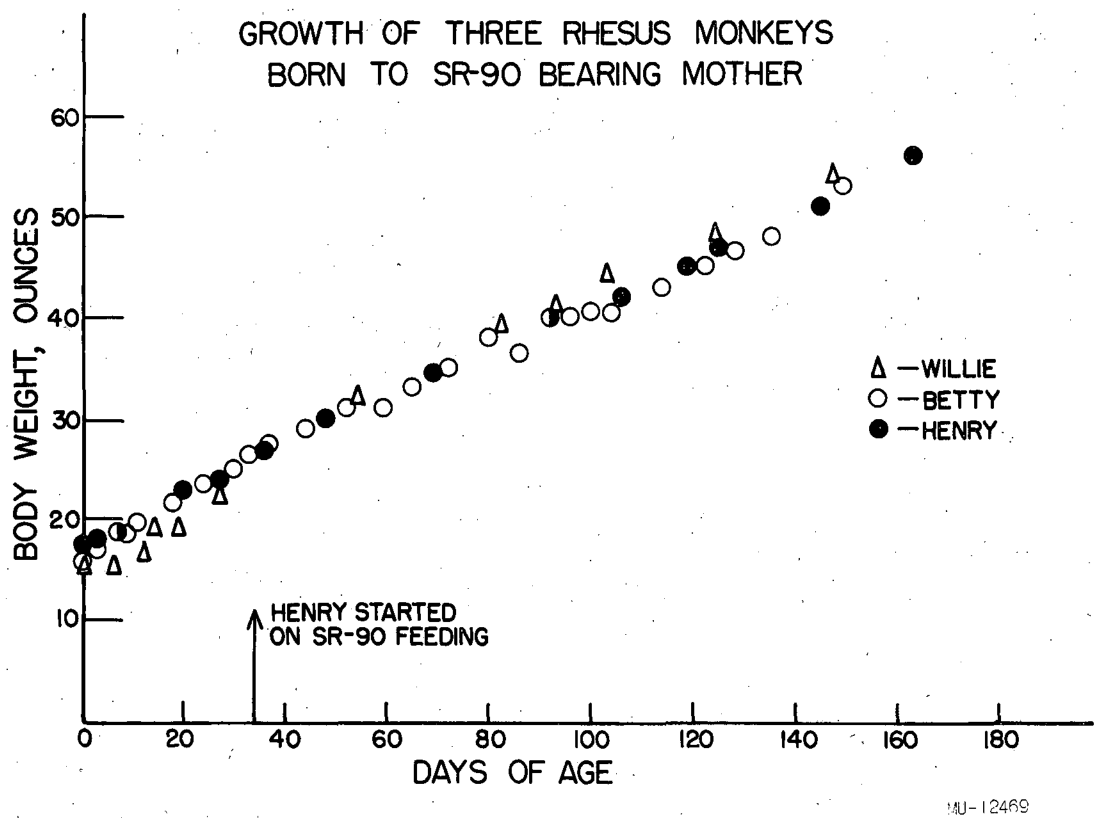


Fig. 5. Growth of three infant rhesus monkeys born to Sr^{90}-injected mother. Note lack of influence of low-level Sr^{90} feeding on body weight of Henry (solid circle).

sensitivity of the counting method, and the Sr^{90} burden was estimated at something less than 0.1 μC, or slightly more than the 3% calculated for the other two. Although the number of individuals was small, and the measurements subject to errors of about 15%, placental transfer of a gradually declining burden of Sr^{90} can be estimated at something close to 3% of that in the mother shortly before the birth of the infant.

Table V shows the retention by the infant monkey, Henry, of orally administered Sr^{90} for the first 13 weeks of the feeding program. The daily excretion pattern is not tabulated, but is of some interest because it is so consistent. Values for a typical week were as follows: Monday, 36.5 cps; Tuesday, 39.4 cps; Wednesday, 42.3 cps; Thursday, 43.4 cps; Friday, 49.8 cps; Saturday, 6.0 cps; and Sunday, 5.1 cps. The dose averages 62 cps/day Monday through Friday. The mean weekly retention during this 13-week period was 18.2% of the administered Sr^{90}, or 0.048 μC. Although the level of activity in the animal is still too low for accurate in vivo counting, a Sr^{90} measurement was made by this method after 12 weeks of Sr^{90} that agreed fairly well with the retention calculated by difference in administered and excreted Sr^{90}.

The data on retention by the adolescent monkeys of oral Sr^{90} are being analyzed at the present time, and accurate values cannot be given as yet. Based on the initial calculations, an upper limit of something less than 5% can be set for the retention of oral Sr^{90} by 2- to 2.5-year-old monkeys.

Table V

Retention of 0.0043 μC Sr^{90} fed daily as the equilibrium mixture of $Sr^{90} \cdot Y^{90}$ in milk to an infant monkey (Henry). Feeding was started at age 36 days.

Weeks	Sr^{90} fed dpm x 10^4	Retention dpm/week x 10^3	Retention % weekly dose
1	4.42	6.63	15
2	3.67	8.15	22.2
3	4.65	5.25	11.3
4	4.77	9.16	19.2
5	4.72	13.92	29.5
6	4.75	6.74	14.2
7	4.75	10.83	22.8
8	4.75	6.32	13.3
9	4.65	3.63	7.8
10	4.70	10.81	23.0
11	3.78	10.05	26.6
12	4.75	6.94	14.6
13	4.75	9.02	19.0

DISCUSSION

Most of the results described above were obtained from measurements on only a few individuals; nevertheless, some tentative conclusions may be drawn. The metabolism of Sr^{90} in the monkey followed qualitatively the pattern described for other species.[1-10] Early elimination was chiefly urinary; later, excretion occurred in urine, feces, and milk.

Retention was prolonged, and in the adults the half time was on the order of 400 days. The most widely quoted half time for skeletal retention of Sr^{90} (>200 days) is that derived by Hamilton[1] from experiments with adult rats. This figure was rechecked recently in this laboratory in a double labeling experiment with Ca^{45} and Sr^{90} in rats, and the half time obtained was on the order of 350 days or about one-half of the animal's remaining life expectancy.[27] The biological half life for Sr^{90} in man currently accepted by the International Commission on Radiological Protection[28] is 11.2 years and is based on the original work by Hamilton[1] and by Sullivan et al.[29] with rats. With corrections for the difference in life expectancy--20 to 25 years for the rhesus monkey and 65 to 70 years for man--a biological half time based on the monkey data presented in this report would be in the neighborhood of three years, or about one-fourth of the currently accepted value.

The turnover of Sr^{90} was much more rapid in the infant monkeys; the half time can be set tentatively at about 6 months.

Placental transfer from a mother with a relatively firmly fixed Sr^{90} burden was roughly 3% of the Sr^{90} retained by the mother at term. The concentration of Sr^{90} in the milk of the breeding female was two to four times the plasma level, indicating that for this species a significant amount of Sr^{90} would be transferred to the nursing young. Secretion of Sr^{90} in milk and its subsequent accumulation in the bones of the young has been demonstrated for rats and mice[4,30] and for cows.[31]

In the infant monkey with a rapidly developing skeleton, 18% of orally administered Sr^{90} was retained, compared with less than 5% for adolescent monkeys with presumably nearly complete skeletal growth. It should be noted that the diet of these latter animals was much richer in calcium, phosphorus, and protein (designed to resemble the diet of Western Man) than what would be available to them in their natural habitat.

Acknowledgments

The authors wish to thank Dr. John H. Lawrence and the staff of the Donner Laboratory for the use of the in vivo counting apparatus; Dr. Charles Riggs, University of California Radiation Laboratory veterinarian, for help and advice in the care and maintenance of the monkey colony; Dr. Gordon Fitzgerald, D.D.S., University of California Medical Center, for assistance with the dental problems of the colony, and Mrs. Grace Walpole for the preparation of the manuscript.

This work was done under the auspices of the U. S. Atomic Energy Commission.

Bibliography

1. J. G. Hamilton, "Metabolism of the Fission Products and the Heaviest Elements," Radiology 49, 325-343 (1947).

2. R. A. Dudley, "Biological Hazard of Radioactive Strontium," Second Annual Conference on Plutonium, Radium and Mesothorium, Univ. of Utah, College of Medicine, June 17-19, 1954.

3. C. Pecher, "Biological Investigations with Radioactive Calcium and Strontium," Proc. Soc. Exptl. Biol. Med. 46, 86-91 (1941).

4. C. Pecher and J. Pecher, "Radio-Calcium and Radio-Strontium Metabolism in Pregnant Mice," ibid 91-94.

5. Gross, Taylor, Lee, and Watson, "The Availability of Radio-Strontium to Mammals by way of the Food Chain," UCLA-259, June 1953.

6. Jowsey, Rayner, Tutt, and Vaughan, "The Deposition of Sr^{90} in Rabbit Bones Following Intravenous Injection," Brit. J. Exptl. Path. 34, 384-391 (1953).

7. Kidman, Tutt, and Vaughan, "The Retention and Excretion of Radioactive Strontium and Yttrium in the Healthy Rabbit," J. Path. Bact. 62, 209-227 (1950).

8. W. E. Kisieleski, "The Distribution and Excretion of Sr-Y in the Dog," ANL-5247, April 1954, p. 68.

9. Comar, Lotz, and Boyd, "Autoradiographic Studies of Calcium, Phosphorus and Strontium Distribution in the Bones of the Growing Pig," Am. J. Anat. 90, 113-129 (1952).

10. S. L. Hansard, "Conference on the Use of Isotopes in Plant and Animal Research," U. S. Atomic Energy Commission, Report No. TID-5098, April 1953, p. 88-98.

11. R. A. McCance and E. M. Widdowson, "The Fate of Strontium after Intravenous Administration to Normal Persons," Biochem. J. 33, 1822-1825 (1939).

12. Hodges, MacDonald, Nusbaum, Stearns, Ezirlian, Spain, and McArthur, "The Strontium Content of Human Bones," J. Biol. Chem. 185, 519-524 (1950).

13. Harrison, Raymond, and Tretheway, "The Metabolism of Strontium in Man," A.E.R.E. (Great Britain), SPAR/2, 1955.

14. R. S. Stone and J. G. Hamilton, Private Communication [data tabulated by Dudley[2]].

15. Spencer, Brothers, Berger, Hart, and Laszlo, "$Strontium^{85}$ Metabolism in Man and Effect of Calcium on Strontium Excretion," Proc. Soc. Exptl. Biol. Med. 91

16. Cowan, Farabee, and Love, "Health Physics and Medical Aspects of a Strontium^{90} Inhalation Incident," Am. J. Roentgenol. Radium Therapy Nuclear Med. 67, 805-891 (1952).

17. Cohn, Rinehart, Robertson, Gong, Milne, Chapman, and Bond, "Nature and Extent of Internal Radioactive Contamination of Human Beings, Plants and Animals Exposed to Fallout," Operation Castle, WT-936, 1955.

18. Cohn, Rinehart, Robertson, Gong, Milne, Chapman, and Bond, "Internal Radioactive Contamination of Human Beings Accidentally Exposed to Radioactive Fallout Materials," USNRDL-TR-86, May 1956.

19. Bond, Conard, Robertson, and Weden, Jr., "Medical Examination of Rongelap People Six Months after Exposure to Fallout," Operation Castle, WT-937, 1955.

20. Edington, Judd, and Ward, "Toxicity of Radio-Strontium in Monkeys," Nature 172, 122-123 (1953).

21. Jowsey, Owen, and Vaughan, "Microradiographs and Autoradiographs of Cortical Bone from Monkeys Injected with Strontium^{90}," Brit. J. Exptl. Pathol. 34, 661-667 (1953).

22. G. Barr, "A Method for Uniform Mounting of Samples Emitting Soft Radiations," in Medical and Health Physics Quarterly Progress Report, UCRL-2881, Feb. 1955, p. 15.

23. P. S. Chen, Jr., and W. F. Neuman, "Renal Reabsorption of Calcium Through its Inhibition by Various Chemical Agents," Am. J. Physiol. 180, 632-636 (1955).

24. Comar, Wasserman, and Nold, "Strontium-Calcium Discrimination Factors in the Rat," Proc. Soc. Exptl. Biol. Med. 92, 859-863 (1956).

25. E. A. Martell, "The Chicago Sunshine Method," Univ. of Chicago, AECU-3262, May 1956.

26. Pickering, Smyth, Van Wagenen, and Fisher, "Growth and Metabolism in Normal and Thyroid-ablated Infant Rhesus Monkeys (Macaca Mulatta) I," Am. J. Diseases Children 86, 1-10 (1953).

27. Durbin, Hamilton, Williams, Jeung, and Gee, "Tracer Studies with Calcium and Strontium," in Medical and Health Physics Quarterly Progress Report, UCRL-2881, Feb. 1955, 10-14.

28. International Commission on Radiological Protection Recommendations, Brit. J. Radiol., Supp. No. 6, 1955.

29. Sullivan, Doull, and DuBois, "Metabolism and Toxicity of Radioactive Materials. III. Strontium-89, Tantalum-182 and Yttrium-91," University of Chicago Toxicity Lab Quarterly Prog. Report TID-365, Jan. 1950.

30. M. P. Finkel, "The Transmission of Radiostrontium and Plutonium from Mother to Offspring in Laboratory Animals," Physiol. Zool. 20, 405-421 (1947).

31. L. Erf and C. Pecher "Secretion of Radiostrontium in Milk of Two Cows Following Intravenous Administration," Proc. Soc. Exptl. Biol. Med. 45, 762-764 (1940).

Appendix I

Standard monkey diet

Item	Source	Daily ration[a]
Fruit and vegetables:	local	
Apple		3/4
Orange		3/4
Banana		1/2
Carrot		3 med.
Peanuts		1 doz
Chim Biscuits-2 oz	Kennel Food Supply Co., Fairfield, Conn.	2
Whole milk, reconstituted, powdered	Golden State Co.	1 pt
Dietary supplements added to milk:		
"Meritene"-protein supplement	Dietene Co., Minneapolis, Minn.	1 1/2 tbsp[b]
"Vi-mix Drops"-Vit. A, B complex, D	Lilly	0.5 cc[c]
"Zymatinic Drops"-Vit. B complex, iron, liver	Upjohn	0.5 cc[c]

[a] Average amounts for 2- to 5-kg monkey, adjusted upward for larger animals.

[b] One-half human adult minimum daily protein requirement.

[c] Approximately equal to human infant minimum daily requirement.

Appendix II

Infant monkey diet

Item	Source	Daily ration
Formula:		8 to 9 oz[a]
Whole cow's milk (16 oz)	local	
Sucrose (3 tbsp.)		
Fresh fruit (orange, apple, banana)	local	20 g
Dietary supplements:		
"Vi-daylin" (Multivitamin mixture)	Abbott	1 cc[b]
"Feosal" (Fe_2SO_4)	Squibb	1 cc[b]

[a] Formula constitution given for infants 2 months of age and older. A more dilute formula is used for the first two months.

[b] Approximately one-half human infant minimum daily requirement.