CALCIUM METABOLISM OF THE NORMAL RHESUS MONKEY *

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In research related to human nutrition, it has become a tradition first to conduct extensive studies on one or more species of experimental animal, and then to attempt to confirm the findings from these studies on relatively small groups of human beings. It is important that the animal species selected for study should closely resemble the human being with respect to the absorption, metabolism, degradation, and excretion of the nutrient under study. The species acceptable for the study of one nutrient is not necessarily the species of choice for the study of a different nutrient.

The rat and the dog have been used extensively in nutrition studies. These species appear to metabolize many nutrients in a manner similar to that of human beings, but Wanner and co-workers (1) presented preliminary data indicating that neither of these species is a satisfactory substitute for human beings in studies of calcium metabolism. They injected trace amounts of Ca^{45} intravenously, and observed that the ratio of Ca^{45} excretion in the urine and feces during the next 5 days was 1:22 in the rat, 1:10 in the dog, 2:1 in the monkey, and 2:1 in the human being. It has since been reported by Bronner, Harris, Maletskos and Benda (2) that the urine:feces excretion ratios of six young human subjects ranged from 0.50:1 to 3.2:1 and averaged 1.9:1. To our knowledge there are no other reports of similar studies on physiologically normal human subjects. Data obtained on patients with carcinoma, multiple myeloma, and thyroid disorders indicate that the excretion of Ca^{45} is disturbed in these situations, for the urine:feces excretion ratios ranged between 3:1 and 1:3 (3–6). In spite of these anomalies, the "endogenous" excretion of calcium by normal human beings and normal monkeys appears to be similar, and quite unlike that by the dog and the rat.

The data from studies of the calcium metabolism of 29 normal rhesus monkeys (*Macaca mulatta*) are being reported in this communication, and compared with the data from similar studies on human beings conducted by this (2, 7, 8) and by other (3–6, 9–16) laboratories.

EXPERIMENTAL PROCEDURES

All monkeys used in this research were received between 1955 and 1959 from Okatie Farms,[1] N. C. On arrival they were placed in individual monkey cages (27 × 27 × 30 inches) in an air-conditioned (78° F, 60 per cent relative humidity) laboratory designed for metabolic studies with radioactive isotopes. The body weights ranged between 1.8 and 4.9 kg, and all but 3 monkeys were male. The ages of these captive monkeys were not known. Van Wagenen and Catchpole (17) have suggested that a monkey's age may be calculated from his body weight. On this basis these monkeys ranged between 9 and 34 months, with 35 per cent of them just under 2 years old.

During a short period of acclimatization and observation, the monkeys were maintained on a nutritionally adequate diet [2] and distilled water *ad libitum*. All monkeys were fasted overnight before each experiment. Each was then given $Ca^{45}Cl_2$ by intravenous injection, by stomach tube with 200 or 400 mg calcium (as $CaCl_2$) in aqueous solution, or mixed in the diet after it had been

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[1] Maintained by The National Foundation for the quarantine of imported monkeys until cleared of parasites and infectious diseases.

[2] Composition of the maintenance diet (g/100 g): 44.0 farina (unenriched); 22.1 casein (Labco); 16.5 sucrose; 10.0 corn oil (Mazola); 4.0 salt mixture i.v. (18); 3.0 Celluflour; 0.1 *p*-aminobenzoic acid; 0.1 inositol; 0.2 choline chloride; 0.6 ml multivitamin (Vipenta, Roche) drops on alternate days (3 mg thiamine; 3 mg riboflavin; 20 mg niacinamide; 1 mg pyridoxine; 3 mg *d*-pantothenol; 75 mg ascorbic acid; 1 mg *d,l*-α-tocopherol acetate; 2 μg vitamin B_{12}; 5,000 USP U vitamin A; 1,000 USP U vitamin D).

triturated with 120 to 200 mg calcium as the chloride. This labeled meal was offered for 30 minutes and the uneaten residue was analyzed for Ca^{45} and total Ca content. Samples of blood, urine, and feces were collected at appropriate intervals, and analyzed for Ca^{45} and total Ca content. After the dose, blood samples were generally collected after 0.25, 2, 4, and 6 hours; 1, 2, 3, 5, 7 days; and then weekly. Urine and feces samples were collected daily during the first 7 days, and then 48-hour samples were collected at weekly or biweekly intervals until the end of the experimental period.

Twenty-five of the 29 monkeys used in this research were used in subsequent studies of the effects of poliomyelitis paralysis upon Ca^{45} metabolism. Thus, only 4 of the monkeys may be considered as normal control animals at the time of sacrifice. Three monkeys were used in 3 successive experiments in which each received the Ca^{45} by intravenous injection, by stomach tube, and in a labeled meal. Several other monkeys were used in a second experiment after sufficient time had elapsed to permit the Ca^{45} levels in the tissues to stabilize.

At autopsy the gall bladder, heart, liver, kidneys, bone (radius, ulna, humerus, tibia, fibula, femur), and portions of gastrocnemius and biceps muscles were taken from each monkey for analysis. The dissected long bones were roentgenographed.

Samples were analyzed for Ca^{45}, total Ca, moisture, and ash content by the methods outlined by Bronner, and co-workers (8, 19). The data were statistically analyzed, when possible, by methods explained in Snedecor (20); SD in this paper refers to "standard deviation."

The monkeys usually defecated in the corners of the cages, and the stools were sufficiently firm to permit separate collection with little opportunity for the leaching of calcium into the urine. The urine was filtered and rinsed through coarse filter paper to remove food particles.

RESULTS AND DISCUSSION

1. Blood serum data. The total serum calcium content of the 29 monkeys averaged 10.4 mg per 100 ml. The specific activities [3] of the serum cal-

[3] Specific activity = % administered Ca^{45} per mg total calcium in tissue or fluid.

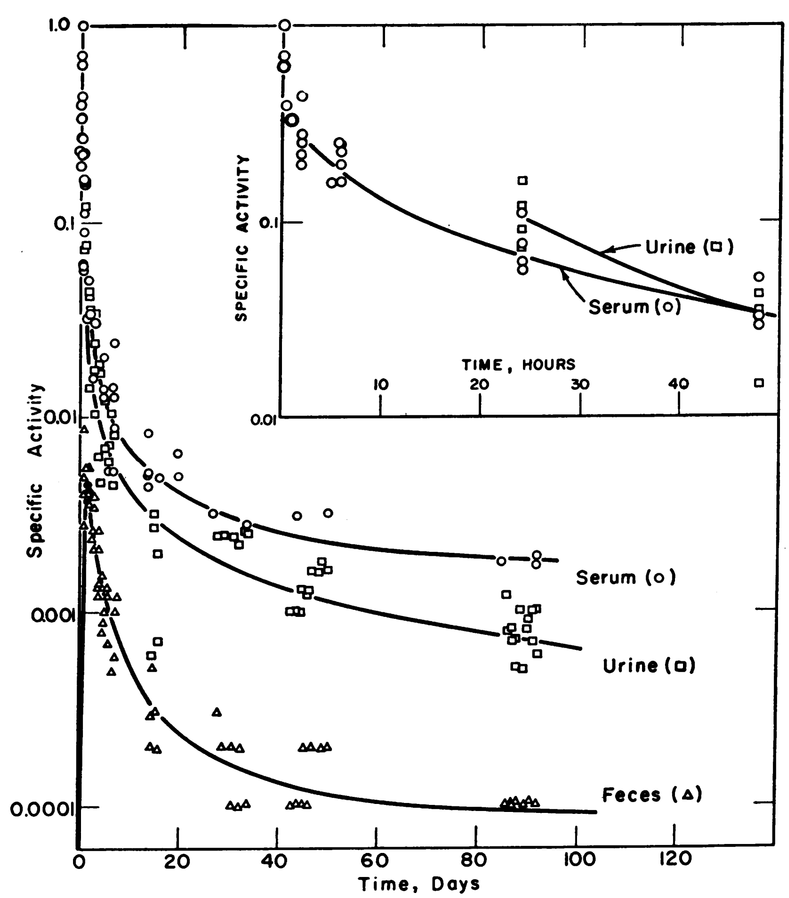

FIG. 1. SPECIFIC ACTIVITIES OF SERUM, URINE AND FECES OF NORMAL MONKEYS AFTER INTRAVENOUS INJECTION OF $Ca^{45}Cl_2$.

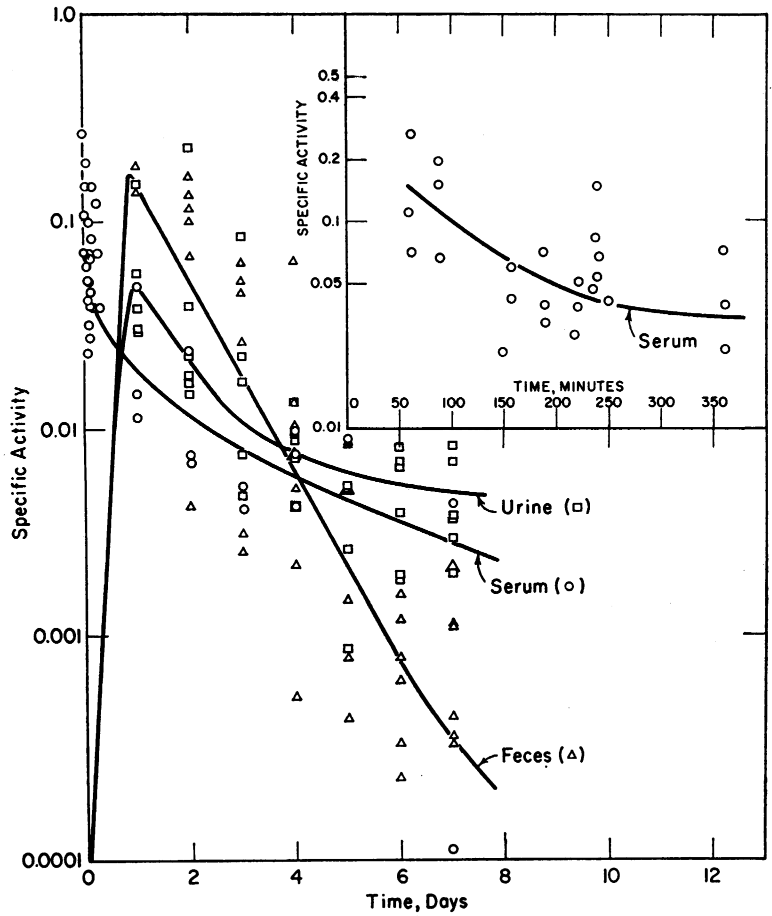

FIG. 2. SPECIFIC ACTIVITIES OF SERUM, URINE AND FECES OF NORMAL MONKEYS AFTER STOMACH TUBE FEEDING OF $Ca^{45}Cl_2$.

cium samples reached maxima immediately after intravenous injection, approximately 60 minutes after stomach feeding, and 200 minutes after dietary feeding of the Ca^{45} (Figures 1–3). In each case, the activities dropped at decreasing rates during subsequent hours.

The observation that less Ca^{45} was absorbed from the intestinal tract when it was fed in the diet than when given in aqueous solution by stomach tube conforms with the observation by Sharpe, Peacock, Cooke and Harris (21) that food solids interfere with the uptake of radioiron in children. Also, these data are in close agreement with data from similar studies in children, in which the specific activities reached a maximum of 0.6 within 15 minutes of intravenous injection, and a maximum of only 0.2 at 240 minutes after the ingestion of a labeled meal (7). Similarly, in human adults (5) a maximal specific activity of 0.12 was reached 15 minutes after injection, and a maximum of 0.04 was reached about 240 minutes after the ingestion of a labeled meal. Bauer, Carlsson and Lindquist (9) have suggested that the calcium of the body is contained in two fractions: a large relatively inert fraction (99 per cent) contained in the skeletal tissues, and a small amount (1 per cent) of readily exchangeable calcium. The serum specific activity data in Figures 1–3 were used to calculate the exchangeable calcium and the rate of accretion of calcium per day by 24 monkeys by using the method proposed by Bauer and co-workers. The exchangeable calcium, E, was found to be 1.19 g (SD 0.66) or 397 mg per kg body weight in these monkeys. Bauer and colleagues reported a value of 0.782 g exchangeable calcium in an infant weighing 4.3 kg

(182 mg per kg). Heaney and Whedon (14) reported that the exchangeable calcium in adult human beings was less than 100 mg per kg body weight. It appears that the amount of exchangeable calcium varies in relation to the size and age of the subject, being higher in the young child and monkey.

The average accretion rate, A, was calculated to be 0.243 g (SD 0.03) calcium per day in these monkeys, nearly the same as the 0.281 g calcium per day which Bauer and associates calculated for the infant. The accretion rate in the monkeys was about one-tenth that reported by Bronner and Harris (7) for adolescent boys, but the average body weight of the boys was ten times greater than that of the monkeys.

2. *Urine data.* The Ca^{45} and the total calcium content of the urine recovered from the monkeys which had received Ca^{45} by the three routes are presented in Table I and Figures 1–3. Although the day-to-day excretions of total calcium were varied, the specific activity data were not. As each experiment progressed, the specific activities of the urine and of the serum dropped at approximately parallel rates, when calculated according to the method of Krane, Brownell, Stanbury and Corrigan (5) and Bender (22). This is in agreement with data obtained by us on children (2) which indicated a parallelism between serum and urine specific activity values during 28 days. The peak urinary excretion of Ca^{45} occurred during the first day, whatever the route of Ca^{45} administration.

The total excretion of Ca^{45} in the urine during 5 days after intravenous injection of the radioactive substance averaged 7.56 per cent (SD 7.73). This is in agreement with data obtained by us in similar experiments in children (2) wherein adolescent boys excreted 5.1 per cent of the intravenously injected Ca^{45} within 5 days. The urinary

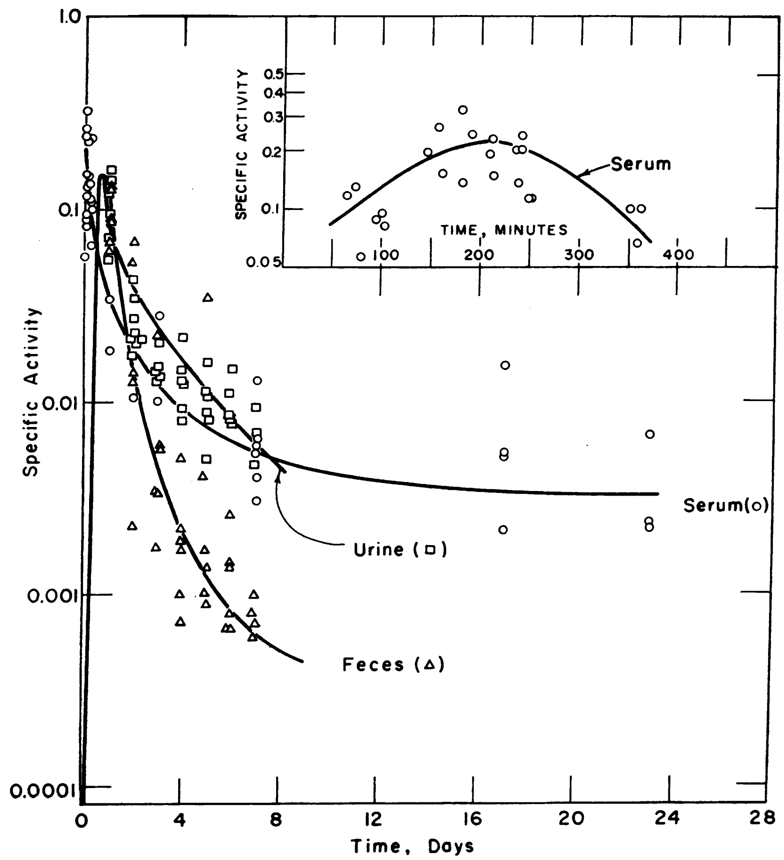

FIG. 3. SPECIFIC ACTIVITIES OF SERUM, URINE AND FECES OF NORMAL MONKEYS AFTER INGESTION OF $Ca^{45}Cl_2$ IN A LABELED MEAL.

TABLE I

Total calcium and Ca^{45} excreted in the urine and feces after Ca^{45} administration to monkeys (averaged values)

Route of Ca^{45} adminis.	Day collected	Urine: Total Ca per day	Urine: Ca^{45}	Feces: Total Ca per day	Feces: Ca^{45}
		mg	*% total dose*	*mg*	*% total dose*
Expt. A Intravenous	0–1	33.8	3.16	221	1.15
	1–2	36.6	1.24	182	0.66
	2–3	52.1	0.90	287	0.73
	3–4	22.0	0.36	210	0.28
	4–5	26.9	0.34	210	0.28
Expt. B_1 Intravenous	0–1	30.7	3.64	210	1.85
	1–2	27.3	1.12	251	1.42
	2–3	31.4	0.74	235	0.80
	3–4	65.5	1.10	206	0.44
	4–5	87.8	1.09	358	0.54
	5–6	75.8	0.55	243	0.29
	6–7	62.5	0.55	317	0.38
	14–15	51.9	0.16	213	0.10
	15–16	46.8	0.15	280	0.08
	27–28	82.7	0.20	112	0.03
	28–29	113.8	0.27	422	0.08
	29–30	113.8	0.26	422	0.08
	30–31	81.4	0.20	327	0.05
	31–32	81.2	0.18	326	0.04
	32–33	87.4	0.23	346	0.06
	33–34	87.3	0.22	345	0.05
	44–45	84.4	0.11	163	0.03
	45–46	84.3	0.10	162	0.02
	46–47	38.1	0.06	214	0.04
	47–48	38.0	0.06	214	0.03
	48–49	45.2	0.08	347	0.08
	49–50	45.2	0.07	346	0.06
	85–86	36.8	0.03	168	0.02
	86–87	37.8	0.03	124	0.01
	87–88	37.7	0.02	124	0.01
	88–89	58.4	0.06	302	0.04
	89–90	58.4	0.05	301	0.03
	90–91	61.7	0.06	210	0.02
	91–92	61.7	0.06	210	0.02
Expt. B_2 Intravenous	0–1	57.0	4.09	204	0.82
	1–2	36.8	0.98	163	0.66
	2–3	41.5	0.42	118	0.30
	3–4	85.3	0.40	247	0.36
	4–5	37.0	0.26	230	0.21
	5–6	51.2	0.31	203	0.20
	6–7	45.4	0.24	380	0.20
	14–15	46.3	0.13	142	0.04
	15–16	78.1	0.16	383	0.09
Expt. C Intravenous	0–1	21.2	1.66	158	0.85
	1–2	28.6	0.41	186	0.67
	2–3	54.5	0.19	173	0.34
	3–4	68.3	0.44	211	0.25
	4–5	63.9	0.46	250	0.21
	5–6	69.8	0.37	250	0.17
	6–7	71.2	0.32	252	0.14
	14–15	49.2	0.03	152	0.03
	15–16	98.1	0.07	166	0.03
	42–43	60.2	0.06	246	0.02
	43–44	130.8	0.14	311	0.02
	44–45	61.0	0.06	162	0.02
	45–46	27.7	0.04	96	0.01
	85–86	51.4	0.06	352	0.02
	86–87	57.8	0.04	387	0.03
	87–88	44.4	0.03	474	0.03
	88–89	36.6	0.02	288	0.02
	89–90	46.1	0.04	222	0.02
	90–91	29.9	0.02	370	0.04
	91–92	107.2	0.06	410	0.02
Expt. D Intravenous	0–1	89.8	13.65	218	0.62
	1–2	96.1	4.27	215	1.13
	2–3	117.4	3.97	269	1.06
	3–4	131.3	2.50	468	1.22
	4–5	121.1	1.72	531	0.88
	5–6	136.5	1.44	293	0.36
	6–7	136.0	1.10	504	0.48
Expt. E_1 & E_2 In diet	0–1	28.8	2.83	188	17.88
	1–2	45.8	1.34	252	7.32
	2–3	37.5	0.63	225	1.74
	3–4	25.9	0.30	169	0.44
	4–5	18.8	0.18	176	1.04
	5–6	29.8	0.26	247	0.32
	6–7	38.8	0.23	250	0.20
Expt. F_1 & F_2 By stomach tube	0–1	52.0	2.72	301*	23.06*
	1–2	24.4	1.32		
	2–3	21.5	0.32	250	7.88
	3–4	35.2	0.38	236	3.10
	4–5	37.4	0.29	320	1.32
	5–6	17.3	0.10	278	0.19
	6–7	27.0	0.15	293	0.16

* Two-day collection was pooled.

excretion data from monkeys are more in agreement with the values for adolescent boys than for adults (2, 13) who averaged between 13 and 20 per cent excretion of Ca^{45} in the urine during 5 days. This may be taken as confirmatory evidence that the monkeys were immature.

The total urinary excretions of Ca^{45} during 5 days by the three monkeys which had received the radioactivity successively by intravenous injection, stomach tube, and in the diet were 6.00 per cent (SD 4.15), 5.02 per cent (SD 4.51), and 5.28 per cent (SD 4.29), respectively. The urinary excretion was significantly higher at the 5 per cent level after intravenous injection than after enteral feeding. This is a reflection of the reduced rate at which the Ca^{45} entered the blood stream due to incomplete uptake of the Ca^{45} after feeding by gastric tube and in the diet.

The significant positive correlation found between body weight and urinary Ca^{45} excretion may be a reflection of differences in the maturity of the bones of these adolescent monkeys. Bronner and Harris (7) observed that an adult man excreted nearly five times as much Ca^{45} in the urine as a teen-aged boy during the 5 days after intravenous injection. The 5-day excretion of Ca^{45} and total calcium in the urine increased as the estimated age of the monkeys increased. This correlation was significant at the 5 per cent level. Similar results have been obtained with mature and aged rats [Hironaka, Draper and Kastelic (23, 24)]. In summarizing the literature on this subject, Harrison (25) presented a graph indicating an inverse correlation between age and calcium absorption.

After the injection of Ca^{45}, the specific activity of the serum averaged higher than that of the urine (Figure 1).[4] This observation is in accord with the results of Bronner, Benda, Harris and Kreplick (19) who worked with children and with a young man. It agrees in general with the finding of Dow and Stanbury (4), who reported consistently higher specific activity in the urines of patients with thyroid and parathyroid disorders, osteoporosis, and Paget's disease.

Lower specific activities were observed in the sera than in the urine of those monkeys which had received the Ca^{45} by gastric intubation or in the diet.

If the data of Day 1 and Day 7 are assumed to be typical, it is to be noted that the specific activities of the sera were significantly higher (1 per cent level) in those monkeys which received the Ca^{45} intravenously rather than enterally. No significant differences were found in the specific activities of the urines.

3. Feces data. The data on the amounts of Ca^{45} and of total Ca excreted in the feces of the three groups of experiments are presented in Table I and Figures 1–3. Although the daily excretions of calcium were quite variable, the specific activities were rather constant. After intravenous injection the peak excretion of Ca^{45} occurred in 17 of 29 trials on Day 1, in 10 trials on Day 2, and in 1 trial each on Days 3 and 4. After the gastric intubation, the peak occurred on the first day in one trial and on the second day in two of the three trials. Similarly, after the ingestion of Ca^{45} in the diet, the peak excretion occurred on Day 1 in five of six trials, and on Day 2 in the remaining trial. These differences are mainly due to the diet ingested, the peristaltic activity of the intestinal tract, and the frequency of defecation. The passage of Ca^{45} through the intestinal tract appears to have been more rapid in these monkeys than in the human being (2).

The results of 29 trials on 27 monkeys which received Ca^{45} intravenously indicate that the average fecal excretion during 5 days totaled 3.70 per cent (SD 1.76) of the injected dose. Similar data have been reported in studies of adolescent boys who excreted 2.5 per cent of the injected dose, and of one young adult male who excreted 6.8 per cent of the injected dose, within 5 days (7).

The three monkeys receiving Ca^{45} by the three routes in successive experiments excreted 3.09 per cent (SD 0.58), 35.36 per cent (SD 22.13), and 28.43 per cent (SD 9.50) of the administered Ca^{45} in the feces during 5 days after intravenous injection, stomach tube feeding, and dietary ingestion, respectively. The last two values are not significantly different. The results with ingested Ca^{45} in monkeys are in agreement with data obtained in 18 trials on nine adolescent boys, which showed that 24 to 47 per cent of the ingested Ca^{45} was excreted in the feces in 5 days (7). It may be concluded that the high fecal excretion of Ca^{45} after enteral feeding is due mainly to poor absorption.

The average daily excretion of total calcium in the feces after the intravenous injection of Ca^{45} increased with the estimated age of the monkey. This correlation was significant at the 1 per cent level. The total Ca^{45} excretion during the first 5 days also increased significantly (at the 1 per cent level) with the age and weight of the monkey.

Relatively small amounts of Ca^{45} were excreted in the feces when it was administered intravenously, and this excretion occurred mostly during the first few days (Table I). The serum data in Figures 1 to 3 indicate that most of the Ca^{45} taken either intravenously or enterally entered the calcium depots within 1 week. Bronner and coworkers (8) have suggested that studies of the uptake, retention, and excretion of Ca^{45} administered by various routes and in various carriers may be completed within 10 days.

The proportion of the Ca^{45} that was recovered in the feces during 5 days after enteral administration can be used as a measure of the efficiency of Ca^{45} uptake. A small portion of the excreted Ca^{45} represents radioactivity that was absorbed and later re-excreted as "endogenous" calcium. The correction for this endogenous Ca^{45} excretion by monkeys during 5 days is about 3 per cent. Thus the true uptake of Ca^{45} after ingestion in the diet was about 75 per cent. This result is similar to that reported by Bronner and Harris (7) for boys whose uptake varied between 55 and 78 per cent. Blau, Spencer, Swernov and Laszlo (11) reported somewhat lower values of 44 and 67 per cent in two adult patients with carcinoma.

[4] The apparent exception in the Day 1 values is not real, since Fisher's *F* test showed them not be be significantly different.

Since approximately 35 per cent of the Ca^{45} administered to the monkeys by stomach tube was excreted in the feces, the total uptake was only about 68 per cent. This lower uptake may be a reflection of the emotional stress observed in these monkeys during intubation, and which Malm (26) considered to be a factor in human subjects.

4. *Urine : feces ratios of Ca^{45} excretion.* The data on the excretion of Ca^{45} in the urine and feces of the 29 monkeys after administration of the Ca^{45} by intravenous injection reveal that an average of twice as much Ca^{45} was excreted in the urine as in the feces during the first 5 days. The same trend continued throughout the experimental period. Thus, the urine : feces ratio of Ca^{45} excretion is 2 : 1 in monkeys, confirming the preliminary report based on only three monkeys (1). The results of these studies in comparison with similar studies on children, adults, rats, and dogs are summarized in Table II. Analyses made in these laboratories indicate that the urine : feces ratio in the human is 2 : 1 (2). Spencer, Li, Samachson and Laszlo (6) reported that the average urine : feces ratio of 5 human females with carcinoma was 2 : 1. Anderson, Emery, McAlister and Osborn (3), reporting therapeutic treatment of a patient with multiple myeloma, gave values which indicate that the urine : feces ratio was about 2.2 : 1. Bellin and Laszlo (10) gave Ca^{45} to two patients with carcinoma. After 7 weeks the average urine : feces ratio was 1.4 : 1. These values resemble those found in normal children and adults (1) but are not like the data reported by Dow and Stanbury (4) from patients who had previously had thyroid disorders but were considered to be euthyroid at the time of study; their urine : feces ratios were much lower, and ranged between 0.6 : 1 and 0.3 : 1. Krane and colleagues (5) studied the calcium excretions of four patients and observed the following urine : feces excretion ratios: one patient with Friedrich's ataxia, 1.5 : 1; one patient with coronary disease, 0.90 : 1; and two patients with treated thyroid disorders, who were considered normal, 1.2 : 1. Since these calcium excretion ratios by patients are quite different from the ratios of normal subjects, it may be concluded that their disorders had produced disturbances in calcium metabolism.

Thus, the monkey resembles the normal human being in relation to the ratios of calcium excreted by the urinary and fecal routes. The rat and the dog are strikingly different in this respect.

5. *Tissue data.* Four of our monkeys were autopsied and selected tissues were analyzed. The tissue data are summarized in Table III. The radioactivity data are not alike, since the monkeys received different amounts of radioactivity at different times before sacrifice. The specific activities of the soft tissues were not significantly different within each experiment, indicating that the Ca^{45} turnover rates of these tissues were the same; this also was true of the various bones.

TABLE II

Species differences in the excretion of intravenously injected Ca^{45}

Species	Age	Subjects	Condition	Ca^{45} injected	Excreta collected	Excreted	Urine Ca^{45} / Feces Ca^{45} ratios	References
	yrs	*no.*		*μc*	*no. days*	*% dose*		
Human								
♂	12–15	65	Normal	0.7–1.0	5	8	2/1	(2)
♂	21	1	Normal	3.4	5	20	2/1	(7)
♂	adult	1	Multiple myeloma		7	37.4	2.3/1	(3)
♂	65	1	Euthyroid	5	9	24.73	0.6/1	(4)
♀	38	1	Euthyroid	5	9	16.87	0.3/1	(4)
♂	26	1	Friedrich's ataxia	5–7	9	21.17	1.54/1	(5)
♂	50	1	Coronary disease	5–7	9	13.19	0.91/1	(5)
♀	42	1	Euthyroid	5–7	9	26.59	1.16/1	(5)
♀	39	1	Euthyroid	5–7	9	21.74	1.22/1	(5)
♀	59	1	Carcinoma		7	31.0	3.2/1	(6)
♀	52–56	4	Carcinoma		12	23.0	0.8/1	(6)
Monkey	9–34 mo.	29	Normal	1.2–170.2	5	11.3	2/1	This paper
Dog	adult	8	Normal	1.5	5	42.0	1/10	(1)
Rat	120 days	20	Normal	1.0	5	15.0	1/20	(1)

TABLE III

*Ash, Ca^{45} and total Ca of tissues from four normal monkeys after intravenous injection of Ca^{45} **

Tissue	Ash weight		Total Ca		Ca^{45}, % total dose		% Ca^{45} dose/mg Ca†	
	Expt. B	Expt. C	Expt. B	Expt. C	Expt. B	Expt. C	Expt. B	Expt. C
	g	*g*	*mg*	*mg*	%	%		
Heart	0.176	0.152	0.71	0.73	0.0033	0.0010	0.0046	0.0014
Kidney	0.184	0.159	1.10	1.06	0.0050	0.0023	0.0046	0.0022
Liver	1.348	1.523	5.48	3.69	0.0267	0.0046	0.0049	0.0012
Gall bladder	0.048	0.038	0.66	0.61	0.0026	0.0007	0.0039	0.0012
Biceps muscle		0.144		0.78		0.0010		0.0013
Gastrocnemius muscle	0.295	0.239	1.29	0.91	0.0061	0.0012	0.0047	0.0013
Humerus	4.59	4.57	1692	1762	5.46	3.23	0.0032	0.0018
Ulna		2.43		946		1.39		0.0015
Radius		1.89		762		1.30		0.0017
Femur	6.60	7.28	2488	2972	8.41	4.34	0.0034	0.0015
Tibia	4.42	4.89	1584	1890	4.92	2.65	0.0031	0.0014
Fibula		1.05		397		0.40		0.0010
Serum (at autopsy)							0.0050	0.0010

* Monkeys in Experiment B received Ca^{45} at 120 days and again at 3 weeks before sacrifice; those in Experiment C received one injection 13 weeks before sacrifice.

† Specific activity = % administered Ca^{45}/mg total calcium

Experiment B involved two monkeys which had received 170 μc Ca^{45} at 120 days and 133 μc Ca^{45} at 16 days before sacrifice. The specific activities of the bones were significantly (1 per cent level) lower than the soft tissues and the sera. This difference may be a reflection of a slower uptake of the recently injected Ca^{45} by the bones.

Experiment C was concerned with two monkeys which had received 160 μc Ca^{45} 13 weeks before sacrifice. The specific activity of the serum was lower than that of the bones and soft tissues. The specific activities of the soft tissues were significantly (5 per cent level) lower than those of the bones, indicating that once the bones had taken up the radioactivity they released it more slowly than did the soft tissues. The conclusion that there is a difference in Ca^{45} turnover rates of the hard and soft tissues is in agreement with data reported by Bronner and co-workers (19) from a study of a child with gargoylism.

SUMMARY AND CONCLUSIONS

The metabolism of Ca^{45} was studied in 29 rhesus monkeys (26 male, 3 female) maintained on a nutritionally adequate diet. The Ca^{45} was administered by intravenous injection, by gastric intubation, and in the diet. Samples of blood serum, urine, and feces were collected at intervals and analyzed for total Ca and Ca^{45} content. Samples of soft and hard tissues were taken at autopsy and analyzed for Ca^{45}, total calcium and ash content.

Serum Ca^{45} activity reached a maximum within 15 minutes after intravenous injection, 60 minutes after gastric intubation, and 200 minutes after ingestion in the diet.

The average amount of the more readily exchangeable fraction of body calcium was calculated to be 1.19 g per monkey. The accretion rate averaged 0.243 g of calcium per monkey per day.

The excretions of Ca^{45} during 5 days after intravenous injection, gastric intubation, and ingestion in the diet were, respectively: 7.6, 5 and 5.3 per cent in the urine; and 3.7, 35 and 28 per cent in the feces.

The data on the appearance and disappearance rates of Ca^{45} in the sera, the amounts of exchangeable calcium, the amounts of Ca^{45} excreted in urine and feces, and the urine: feces ratios of Ca^{45} excretion reported in this study of 29 monkeys are in close agreement with data previously obtained in similar studies on 65 children. They are in disagreement with data from studies on rats and dogs. The evidence indicates that the monkey is the best substitute for the human being in studies of calcium metabolism.

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