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Metabolism of Lead-210 in Juvenile and Adult Rhesus Monkeys (*Macaca mulatta*)

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Many factors influence the susceptibility of experimental animals and man to lead intoxication. These factors include age, season of the year, calcium and phosphorus levels, iron deficiency, level of dietary protein, vitamin D, ascorbic acid, nicotinic acid, alcohol consumption, presence of other metals, coexisting diseases, and the ability of the body to form heterocellular complexes of lead. These factors have been reviewed by GOYER and MAHAFFEY (1972).

It has been shown that acute lead poisoning occurs most frequently in young children (INGOLLS et al. 1961; CHRISTIAN et al. 1964; RENNERT et al. 1970). The importance of age on susceptibility to lead poisoning has been demonstrated in rodents, monkeys and man. Lead absorption is greater in immature rats than in adults (FORBES and REINA 1972; GERBER and DEROO 1975), and in 5-7 day old rats, lead absorption may exceed 50% of the lead ingested (KOSTIAL et al. 1971). MUNRO et al. (1975) found 65-85% absorption of lead-210 nitrate in infant monkeys with only 4% absorption in mature animals. When exposed to lead acetate, infant rhesus monkeys developed overt acute lead encephalopathy while adolescent or adult monkeys exposed to similar levels did not (ALLEN et al. 1974). ZOOK et al. (1976) showed fecal excretion of chronic, high levels of ingested lead in a neonate to be much reduced compared to juvenile and adult rhesus monkeys. ALEXANDER et al. (1972) indicate that children 1-3 years of age may absorb 53% of ingested lead at low levels. In contrast, adults absorb about 10% of ingested lead (KEHOE 1961).

The present studies were designed to study the absorption, elimination and retention of a single dose of lead-210 acetate in infant and adult rhesus monkeys.

MATERIALS AND METHODS

Four infant (2 males and 2 females, 1.03-1.35 kg., 5-7 months of age) and four adult (females, 5.35-7.80 kg, 7-10 years of age) rhesus monkeys were given a single dose of lead-210 acetate. Radiolead acetate was prepared by mixing 400 mg lead acetate

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($Pb(C_2H_3O_2)_2 \cdot 3H_2O$) and 1.7 x 10^{-3} mg lead-210 nitrate [$^{210}Pb(NO_3)_2$] in fresh glass distilled water to make 100 ml, and allowing the solution to equilibrate overnight. Each animal was administered 10 mg (5 μCi) per kg body weight by stomach intubation. During the study, the animals were housed in stainless steel metabolism cages equipped with urine and fecal collection trays. The monkeys were fed Purina chow and water ad libitum.

Urine and feces were collected for 23 days at 24-hour intervals. The urine was acidified with hydrochloric acid to prevent precipitation of lead and adsorption of lead onto container walls. The feces were homogenized and packed into small polyethylene containers to maintain consistent geometry in the gamma counter. All samples were corrected for background counts and compared to appropriate standards. The amount of lead in each sample was calculated from the specific activity of lead-210 administered. The level of lead in urine and feces was determined by counting the 47 keV gamma rays in a Hewlett-Packard gamma scintillation counter.

Blood was drawn daily from the femoral vein in lead-free tubes for lead analysis. Blood lead concentrations were determined by using a modified Delves cup technique (EDIGER and COLEMAN 1972) and a Perkin-Elmer Model 306 Atomic Absorption spectrophotometer.

Definitions:

Elimination: amount of lead removed via defectation within 96 hours following intubation (Eliminated lead is assumed to be that portion of the administered dose which traverses the gastrointestinal tract unabsorbed.)

Absorbed dose: administered dose minus fecal elimination divided by administered dose x 100.

Administered dose: total lead intubated (10 mg/kg).

Excretion: the removal of lead from blood and tissues via urine and feces (after 96 hours for feces). Excretion is expressed as percentage of the absorbed dose.

RESULTS AND DISCUSSION

Absorption and elimination of orally administered lead-210. Infant rhesus monkeys absorbed 37.9±3.47% (mean ± standard error) of the intubated dose of lead-210 acetate compared to 26.4±4.72% absorption by the adult animals ($p<0.1$) (see Table I). The absorbed dose for each animal was calculated as the intubated dose less fecal elimination for 96 hours post-intubation.

TABLE I

Metabolism of Lead-210 in Juvenile and Adult Rhesus Monkeys[1]

Animal	Age	Elimination (%)	Absorption (%)	Excretion (%)			Body Burden[2] mg/kg body wt	Peak Blood[3] Lead (µg%)	Average Blood[4] Lead (µg%)
				Urine	Feces	Total			
28	juvenile	65.2	34.8	7.28	7.12	14.4	2.99	45	33
29	juvenile	69.0	31.0	3.07	3.26	6.33	2.90	20	17
30	juvenile	61.3	38.7	3.49	1.78	5.27	3.63	20	15
31	juvenile	52.8	47.2	1.50	1.66	3.16	4.75	14	14
	Mean	62.1	37.9	3.84	3.45	7.29	3.57	25	20
	S.E.	3.47	3.47	1.22	1.26	2.45	0.42		
		p<0.1	p<0.1		p<0.1		p<0.1	p<0.1	p<0.1
11	adult	71.5	28.5	3.44	1.99	5.44	2.69	43	28
21	adult	66.0	34.0	2.21	11.50	13.70	2.93	57	45
17	adult	69.7	30.3	5.37	21.80	27.20	2.20	73	57
45	adult	87.4	12.6	10.20	16.50	26.70	0.903	86	61
	Mean	73.7	26.4	5.31	13.0	18.30	2.18	65	47
	S.E.	4.72	4.72	1.75	4.1	5.29	.45		

[1]Each animal was orally administered 10 mg (5 µCi) lead-210 acetate per kg body weight.
[2]Body burden equals absorbed dose (mg) times excretion (%) divided by animal weight (kg).
[3]Peak blood lead (µg%) was 24 hours post-intubation.
[4]Average blood lead (µg%) was determined from days 1-4 post-intubation.
[5]Probability of T, student's T-test.

Fecal elimination patterns are given as percent of the intubated dose for 7 days post-exposure. Peak lead-210 elimination was observed in about 24 hours in both groups (Fig. 1). Clearance of lead from the gastrointestinal tract was shorter in the infant than in the adult monkey. This is undoubtedly due to the shorter length of the juvenile intestine and shorter resident time of the intestinal contents.

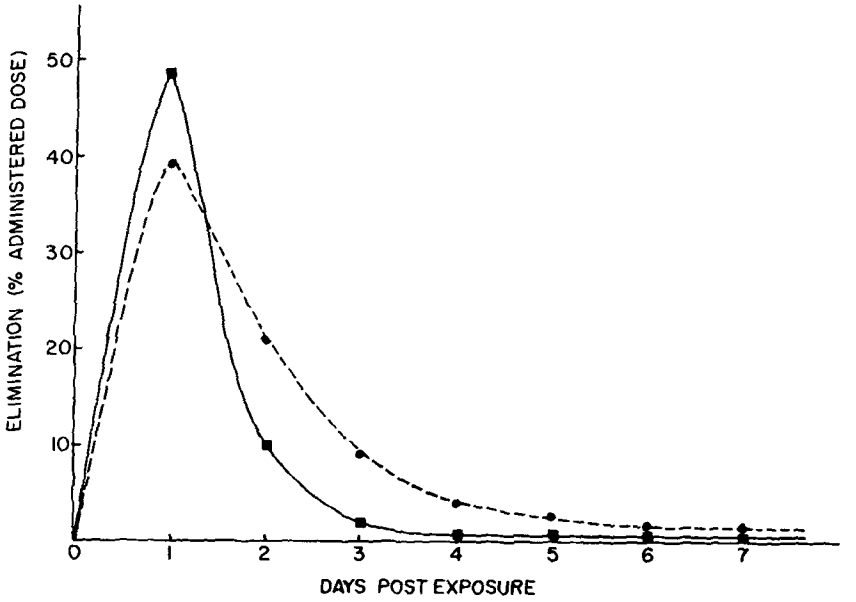

Fig. 1. Fecal elimination of administered lead-210 by infant ● , and adult ■ monkeys.

This increased lead absorption and decreased elimination by infant animals agrees with studies conducted with rats (KOSTIAL et al. 1973; GERBER and DEROO 1975). MUNRO et al. (1975) found 4% lead absorption in mature monkeys compared to 71% in animals 5 months old. Since these investigators used a different species (Macaca irus), younger infant animals (150 days compared to 170-200), and a high calcium diet (milk formula) which is known to increase lead absorption in rats (KELLO and KOSTIAL 1972), a direct comparison with the present study is limited.

Urinary and fecal excretion of absorbed lead-210. Infant monkeys excreted less of the absorbed lead in urine (3.84±1.22) than was excreted by adult animals (5.31±1.75%) (see Table I; Fig. 2). However, this difference was not significant statistically.

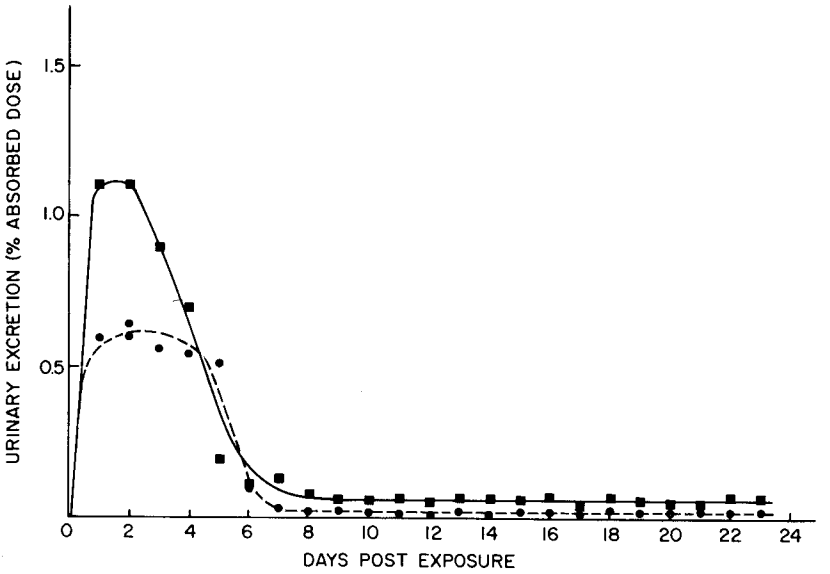

Fig. 2. Urinary excretion of absorbed lead-210 by infant ● , and adult ■ monkeys.

Fecal excretion of absorbed lead by infants (3.45±1.26%) was significantly less than fecal excretion by adult animals (13.0±4.1%). These data show that by 23 days post exposure the infant rhesus excretes a total of 7.29±2.45% of its absorbed dose of lead-210 as compared to 18.3±5.29% total excretion by the mature animals (Table I; Fig. 3). These values are greater than reported by COHEN et al. (1970) in the baboon. These investigators used lead injected intravenously rather than lead administered orally, and it is possible that the percent excretion in the present study could be inflated to a small degree by the elimination of unabsorbed lead along with the fecal excretion of the absorbed lead. It is apparent, however, that fecal excretion of lead-210 by adult animals is consistently greater than by infants.

Body burden of lead-210. The retention of lead-210 and body burden as mg lead-210 per kg body weight was calculated after 24 days. The infant monkeys carried a significantly higher body burden (3.57±0.42 mg per kg body weight) than the adult animals (2.18±0.45 mg per kg body weight) (Table I). These data indicate that increased absorption of orally administered lead, coupled with decreased fecal excretion of absorbed lead, results in a significantly greater body burden of lead in infant rhesus monkeys.

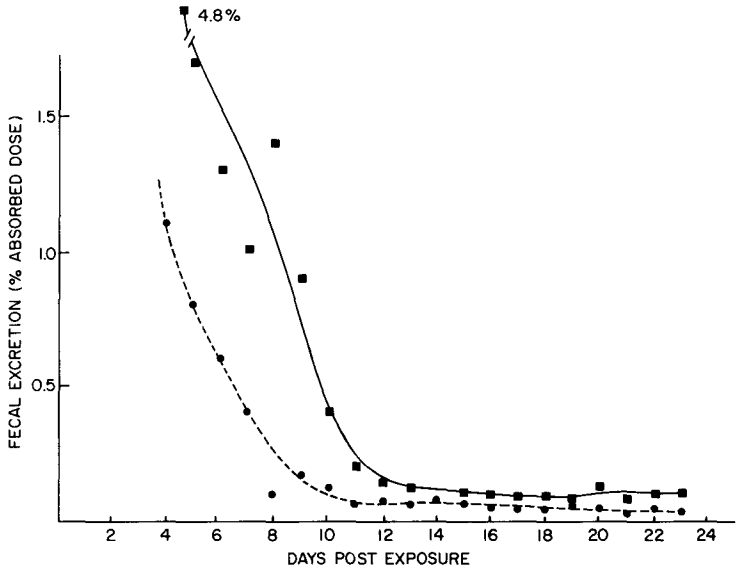

Fig. 3. Fecal excretion of absorbed lead-210 by infant ● , and adult ■ monkeys.

Blood lead concentrations. The blood lead concentration in juvenile monkeys was found to rise sharply to a higher level than in mature monkeys. The blood lead levels fell more slowly and remained higher in infant animals for the duration of the experiment. Linear regression analysis revealed a good inverse correlation between peak and average blood lead values with body burden and percent absorption (peak blood lead vs. body burden, $r = -.87189$; peak blood lead vs. percent absorption, $r = -.78699$; average blood lead vs. body burden, $r = -.82598$; and average blood lead vs. percent absorption, $r = -.71318$) (Table I)
These data indicate that lead-210 may have a greater affinity for tissue than blood components in infant as compared to adult monkeys. The deposition of lead within each individual animal may be as important as the animal's absorption and excretion parameters in determining lead toxicity.

Summary

Experiments were conducted measuring the gastrointestinal absorption and elimination of a single dose of lead-210 acetate in infant and adult rhesus monkeys. Urinary and fecal excretion of absorbed lead was followed for 23 days.

Infant monkeys eliminated less and absorbed more orally administered lead. Adult animals excreted more absorbed lead in feces, while urinary excretion between adults and infants was similar.

Increased absorption of administered lead and reduced fecal excretion of absorbed lead resulted in significantly greater body burden of lead-210 in infant animals. Blood lead values were increased in the infant animals, and were inversely correlated with body burden and percent absorption of ingested lead.

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