Dietary Lead Intakes for Mother/Child Pairs and Relevance to Pharmacokinetic Models

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Blood and environmental samples, including a quarterly 6-day duplicate diet, for nine mother/child pairs from Eastern Europe have been monitored for 12 to >24 months with high precision stable lead isotope analysis to evaluate the changes that occur when the subjects moved from one environment (Eastern Europe) to another with different stable lead isotopes (Australia). The children were between 6 and 11 years of age and the mothers were between 29 and 37 years of age. These data were compared with an Australian control mother/child pair, aged 31 and 6 years, respectively. A rationale for undertaking this study of mother/child pairs was to evaluate if there were differences in the patterns and clearance rates of lead from blood in children compared with their mothers. Blood lead concentrations ranged from 2.1 to 3.9 µg/dl in the children and between 1.8 and 4.5 µg/dl in the mothers, but the mean of differences between each mother and her child did not differ significantly from zero. Duplicate diets contained from 2.4 to 31.8 µg Pb/kg diet; the mean ± standard deviation was 5.5 ± 2.1 µg Pb/kg and total daily dietary intakes ranged from 1.6 to 21.3 µg/day. Mean daily dietary intakes relative to body weight showed that the intake for children was approximately double that for the mothers (0.218 vs. 0.113 µg Pb/kg body weight/day). The correlations between blood lead concentration and mean daily dietary intake either relative to body weight or total dietary intake did not reach statistical significance (p>0.05). Estimation of the lead coming from skeletal (endogenous) sources relative to the contribution from environmental (exogenous) sources ranges from 8 to 70% for the mothers and 12 to 66% for the children. The difference between mothers and children is not statistically significant (p = 0.28). The children do not appear to achieve the Australian lead isotopic profile at a faster rate than their mothers. These data provide evidence that the absorption or uptake of lead from dietary sources is similar in adult females and children of the age in this study. In spite of lower bone lead and faster bone remodeling and recycling in children compared with adult females, we see no differences between the mothers and their children in overall contribution of tissue lead to blood lead. Results from this study suggest that fractional absorption of ingested lead by children 6–11 years of age is comparable with absorption patterns observed among adult females in the 29–37-year-old age range. Because pharmacokinetic models apply a 40–50% absorption even for 7-year-old children, further investigations on fractional absorption of ingested lead by young children are warranted. Further investigations are especially needed in younger children than those who were subjects in the current study, particularly children in the 1–3-year-old age range. In addition, the effect of nutritional status and patterns of food intake on children's lead absorption require investigation, particularly given the increased prevalence of marginal nutritional status among low-income populations that are at increased risk of elevated blood lead levels. *Key words:* child, diet, lead isotopes, models, mother. *Environ Health Perspect* 105:1334–1342 (1997). *http//ehis.niehs.nih.gov*

Blood lead (PbB) levels decreased in developed countries between the late 1970s and the late 1980s to mid-1990s (*1–3*) as a result of decreased lead exposure from leaded gasoline, lead-soldered food cans, and other changes in manufacturing by the food industry. Consequently, lead from dietary sources has become progressively less important for the majority of children in the general population, especially for children having PbB concentrations less than 5 µg/dl. For example, the EPA and the Food and Drug Administration (FDA) estimated that over the period 1986–1990 the contribution of lead from dietary sources for a 2-year-old child decreased from 47 to 16% (*4*). These large decreases in the percentage contribution of dietary lead to overall lead ingestion are partly attributable to the belated recognition of the major contribution of dust and soil to PbB in young children (*5*). The contribution of dust to PbB is, however, most critical for children aged 1–3 years, typically the age group with the highest PbB levels (*6*) and greatest hand-to-mouth activity (*7*). In individuals older than 4 years, hand-to-mouth activity is much less predominant and diet assumes a greater importance as a source of lead. For example, for a female of child-bearing age the FDA estimates the contribution from diet is 65%, most of this coming from food (43%) and water (22%) (*4*).

All pharmacokinetic models for lead in humans differentiate between a lower absorption rate (uptake from the gastrointestinal tract) of 5–15% for adult male subjects versus 40–50% for children (*8–11*). In the EPA Integrated Exposure Uptake Biokinetic (IEUBK) model (*9*), the higher absorption values among adult males are applied to children up to 7 years old. The adult values for gastrointestinal lead uptake are fairly well validated using long-term mass balance studies (*12,13*), radioactive tracers (*14–19*), and stable isotope tracers (*20,21*). Most adult subjects were males. James et al. (*19*) determined the gastrointestinal absorption of tracer doses of [203]Pb in a group consisting of 12 women and 11 men at 26–77 years of age. The study primarily evaluated the influence of foods and beverages on lead absorption. Unfortunately, the report provided no discussion of whether or not the retention of [203]Pb differed between male and female subjects.

Uptake rates for children are much less well established and are based essentially on two mass balance studies with small numbers of children. Alexander et al. (*22*) conducted 11 balance studies with eight subjects ranging in age from 3 months to 8 years. Intakes averaged 10.6 µg Pb/kg body weight (bw)/day (range, 5–17 µg Pb/kg bw/day), with absorption averaging 53% of intake and retention averaging 18% of intake. In their investigation of 61 metabolic balance studies

with 12 infants ranging in age from 14 to 746 days and whose lead intakes were greater than 5 µg Pb/kg bw/day, Ziegler et al. (23) reported an average absorption of 41.5% and net retention of 31.7% of intake. Ziegler et al. (23) suggested that there was a higher absorption and retention of lead in younger infants compared with older children. The Glasgow Duplicate Diet study (24) is also cited as a data source for absorption of lead by young children. This study, largely aimed at evaluating the impact of drinking water on PbB in 131 mothers and infants, the age of the latter being up to 3 months (24), does not provide information on absorption of lead from food.

We have monitored a cohort of mother/child pairs as part of an investigation to compare the contribution of environmental and endogenous sources of lead to blood lead among female adults and children who immigrated to Australia. Gulson et al. (25) showed that there were significant differences in the isotopic composition of biological samples between Australian subjects and those from other countries. The isotopic composition in blood and urine of female adults migrating to Australia from Eastern Europe changed rapidly over a 3- to 4-month period towards Australian isotopic values. The rapid change is related to the approximately 120-day life of erythrocytes, the main store of lead in blood (26). Thereafter, an equilibrium was reached between skeletal lead and the Australian environmental lead with 41–73% of lead in blood derived from skeletal sources even after 12 months of residence in Australia.

We have monitored 10 mother/child pairs for up to 24 months to evaluate the impact of absorption of dietary lead during middle childhood compared with adults' absorption and to determine its impact on the lead burden of children versus adults. If there are significant differences in absorption rates in adults and children, the children's blood isotopic profile should be different than the maternal profile following establishment of an equilibrium with the Australian environment.

Methods

Nine of these mother/child pairs immigrated from Eastern Europe, with seven from the former Soviet Union, one from Poland, and one from Bosnia (Table 1). Their data are compared with an Australian control pair (referred to by their subject numbers 1044 and 2044). The ages of the children ranged from 6 to 11 years and the mother/child pairs were monitored from 12 to longer than 24 months. An age of 12 years was chosen as the cut-off limit because after this age the skeleton is considered to be in a relatively

Table 1. Personal information of subjects and mean blood lead (PbB)

Identifier	Country of origin	Sex	Age (years)	PbB (µg/dl) Mean ± SD	Number of samples
1015	Russia	F	37	4.46 ± 0.60	12
2015	Russia	F	9	2.63 ± 0.37	12
1023	Russia	F	34	1.81 ± 0.15	11
2023	Russia	F	8	2,41 ± 0.26	11
1029	Ukraine	F	36	2.94 ± 0.52	10
2029	Ukraine	M	11	2.62 ± 0.25	10
1031	Bosnia	F	39	3.33 ± 0.43	8
2031	Bosnia	F	9	3.59 ± 0.28	8
1046	Ukraine	F	30	1.80 ± 0.28	7
2046	Ukraine	M	10	4.10 ± 0.48	7
1047	Ukraine	F	29	1.87 ± 0.13	7
2047	Ukraine	F	6	2.82 ± 0.22	7
1052	Poland	F	29	2.03 ± 0.17	5
2052	Poland	M	6	2.83 ± 0.32	5
1054	Ukraine	F	33	2.73 ± 0.30	6
2054	Ukraine	M	7	4.26 ± 1.00	6
1064	Russia	F	29	2.77 ± 0.09	5
2064	Russia	F	8	2.06 ± 0.06	5
1044	Australia	F	31	1.86 ± 0.10	6
2044	Australia	F	6	3.84 ± 0.39	6

Abbreviations: F, female; M, male; SD, standard deviation.

dynamic state following the onset of rapid hormonally induced changes in growth and development (J. Eisman, personal communication).

Food sampling involved collection of a 6-day duplicate diet to coincide with the quarterly biological and environmental sampling. The diets for the mothers and children were collected and analyzed separately. Each daily sampling was blended in a cleansed blender. Several equal portions were then taken from each day's blended diet and composited in a single 6-day sample. Several food samples were analyzed in duplicate to determine the efficiency of homogenization of the blending.

Venous blood samples were collected following the protocol described by Gulson et al. (27). Fully flushed drinking water was collected from the kitchen faucet after an additional 30-sec flush. Dust was collected as dust fall accumulation using petri dishes placed in at least two locations in the residence for 3 months (28). The methods for sample preparation and analysis for blood and environmental samples have been reported previously (25,27). An aliquot of the blended food was analyzed by Australian Government Analytical Laboratory personnel (who perform the analyses of the Australian National Market Basket Survey) for concentrations of Ca, Mg, K, Na, Ba, Sr, Hg, Cd, Cu, Pb, and Zn.

Statistical calculations were performed using the S-Plus (Statistical Sciences, Seattle, WA) and Microsoft Excel Version 7.0 (Microsoft, Redmond, WA) packages.
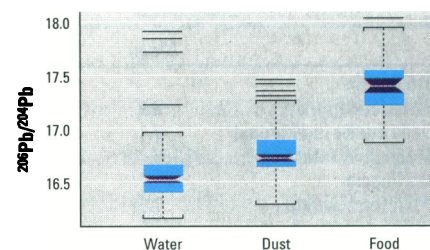

Figure 1. Notched box plots showing the $^{206}Pb/^{204}Pb$ in 6-day duplicate diets (n = 54), lead loading in house dust (n = 134), and tap water (n = 147). The upper and lower ends of the boxes (the rectangular areas) are the upper and lower quartiles. The distance between these two values (the interquartile range) is a measure of the spread of the distribution. The relative distances of the upper and lower quartiles from the median (the white rectangle at the notch) give information about the shape of the distribution of the data. (If one distance is much bigger than the other, the distribution is skewed.) The notches surrounding the median provide a measure of the rough significance of differences between the values. Specifically, if the notches about two medians do not overlap in the plots, the medians are roughly significantly different at about a 95% confidence level. The dashed appendages of the box plot encode the adjacent values, given by the following relationships. If r is the interquartile range, the upper adjacent value is the largest observation that is less than or equal to the upper quartile plus 1.5r. The lower adjacent value is the smallest observation that is greater than or equal to the lower quartile minus 1.5r. The horizontal lines are outliers.
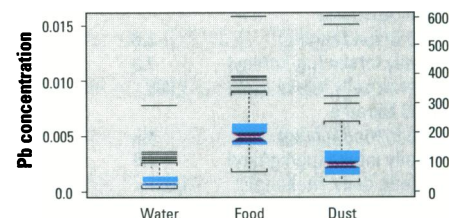

Figure 2. Notched box plots showing the lead concentrations in 6-day duplicate diets (n = 54; units in ppb or µg/kg), lead loading in house dust (n = 134; values in µg Pb/m²/30 days), and tap water (n = 147; units in ppb or µg/l).

Results

The data for the important environmental samples of drinking water, house dust, and 6-day duplicate diet are summarized in notched box plots in Figures 1 and 2. Air and drinking water contribute insignificantly to blood lead concentrations compared with dietary intake. Air lead concentrations for suburban Sydney are monitored by the NSW Environment Protection Authority and are routinely reported as <0.1 µg Pb/m³. Monthly isotopic measurements for particulates collected on high volume air monitors have $^{206}Pb/^{204}Pb$ ratios <17.0 for the period 1991–1996 (25,29). The lead concentrations in fully flushed drinking water were low and were already included

Table 2. Data for daily dietary intake

	Mean	Median	SD	Minimum	Maximum	Number
1015 Russia						
Pb in food (µg/kg)	6.2	4.3	4.2	2.5	14.9	9
Daily intake (µg/kg/day)	7.1	5.3	4.6	3.0	15.9	9
Mean daily intake (g)[a]	1,185	1,231	217	812	1,395	9
2015 Russia						
Pb in food (µg/kg)	7.8	5.4	4.6	3.9	15.8	10
Daily intake (µg/kg/day)	6.6	5.1	4.0	3.0	13.4	10
Mean daily intake (g)[a]	844	848	106	664	1,013	10
1023 Ukraine						
Pb in food (µg/kg)	4.7	4.4	1.6	2.8	7.3	8
Daily intake (µg/kg/day)	5.1	4.7	1.6	3.2	7.5	8
Mean daily intake (g)[a]	1,105	1,098	136	934	1,268	8
2023 Ukraine						
Pb in food (µg/kg)	4.2	3.8	1.5	2.1	6.8	8
Daily intake (µg/kg/day)	4.7	4.6	1.9	2.3	8.3	8
Mean daily intake (g)[a]	1,127	1,082	150	1,005	1,461	8
1029 Bosnia						
Pb in food (µg/kg)	6.4	6.1	1.9	3.9	9.5	8
Daily intake (µg/kg/day)	11.0	10.4	3.5	6.6	16.5	8
Mean daily intake (g)[a]	1,693	1,689	84	1,552	1,808	8
2029 Bosnia						
Pb in food (µg/kg)	5.6	4.7	1.7	4.0	8.6	8
Daily intake (µg/kg/day)	9.3	8.1	2.7	6.8	13.5	8
Mean daily intake (g)[a]	1,662	1,675	51	1,579	1,725	8
1031 Ukraine						
Pb in food (µg/kg)	5.8	5.7	2.3	2.9	9.4	8
Daily intake (µg/kg/day)	4.0	3.7	1.7	2.0	6.9	8
Mean daily intake (g)[a]	729	659	277	464	1,375	8
2031 Ukraine						
Pb in food (µg/kg)	12.6	6.7	12.1	3.7	31.9	8
Daily intake (µg/kg/day)	7.4	2.7	8.7	1.5	21.3	8
Mean daily intake (g)[a]	497	477	122	338	669	8
1044 Australia						
Pb in food (µg/kg)	4.0	4.0	0.9	2.8	5.4	5
Daily intake (µg/kg/day)	4.4	3.7	1.6	2.8	6.6	5
Mean daily intake (g)[a]	1,074	1,018	183	890	1,298	5
2044 Australia						
Pb in food (µg/kg)	6.6	6.5	0.9	5.7	7.6	4
Daily intake (µg/kg/day)	7.3	5.6	3.9	5.0	13.1	4
Mean daily intake (g)[a]	1,086	949	449	712	1,735	4
1046 Ukraine						
Pb in food (µg/kg)	4.6	4.3	1.0	3.6	5.9	5
Daily intake (µg/kg/day)	7.5	6.6	2.1	5.6	10.0	5
Mean daily intake (g)[a]	1,625	1,622	220	1,299	1,916	5
2046 Ukraine						
Pb in food (µg/kg)	5.3	5.4	1.1	3.7	6.5	6
Daily intake (µg/kg/day)	8.6	9.2	2.2	5.7	11.2	6
Mean daily intake (g)[a]	1,629	1,663	194	1,307	1,879	6
1047 Ukraine						
Pb in food (µg/kg)	5.1	4.8	1.3	3.9	6.8	5
Daily intake (µg/kg/day)	5.7	5.1	1.1	4.9	7.4	5
Mean daily intake (g)[a]	1,134	1,082	114	1,010	1,260	5
2047 Ukraine						
Pb in food (µg/kg)	5.5	5.6	1.0	4.3	7.0	5
Daily intake (µg/kg/day)	5.6	5.8	1.5	3.3	7.4	5
Mean daily intake (g)[a]	1,012	1,038	172	771	1,242	5
1052 Poland						
Pb in food (µg/kg)	7.7	6.6	3.0	5.3	12.6	5
Daily intake (µg/kg/day)	10.1	8.9	4.4	6.5	17.7	5
Mean daily intake (g)[a]	1,297	1,357	128	1,100	1,405	5
2052 Poland						
Pb in food (µg/kg)	6.5	6.2	1.1	5.6	7.6	3
Daily intake (µg/kg/day)	6.1	5.5	1.3	5.2	7.6	3
Mean daily intake (g)[a]	940	937	57	884	997	3
1054 Ukraine						
Pb in food (µg/kg)	5.1	4.6	1.6	4.0	7.4	4
Daily intake (µg/kg/day)	8.7	7.7	3.5	5.7	13.8	4
Mean daily intake (g)[a]	1,661	1,683	189	1,414	1,862	4
2054 Ukraine						
Pb in food (µg/kg)	4.8	4.9	1.6	2.8	6.4	4

(*continued, next page*)

as part of the 6-day diet. Dust collected as quarterly dust fall accumulation (*28*) in both residences and school classrooms generally have low lead loadings and $^{206}Pb/^{204}Pb$ ratios <17.0 (Fig. 2).

Information obtained from parents and children indicated that, except for school consumption, diet of the children was generally similar to the adults in the same family (Table 2). In testing the methods, several food samples were analyzed in duplicate. Even with complete digestion of the sample by the microwave, the reproducibility of results compared with that expected for other samples, such as blood, is poor (Table 3). The reproducibility of the isotopic ratios is satisfactory, but the lead concentrations are inconsistent, as found in early studies using a quarterly market basket survey (*27*). This is thought to arise from heterogeneity in the samples because of incomplete homogenization during blending. However, given the low concentrations of lead in the samples, the heterogeneity does not unduly affect the interpretations.

Mother/child bloods. The PbB concentrations in all subjects were <5 µg/dl. In 7 out of 10 cases, the mean PbB of the child was greater than that of the mother (Table 1) and the pooled mean PbB for the mothers and children had a *p*-value of 0.07 (Table 4). Correlation between the repeated measurements for mother/child bloods was examined by taking the differences between the mother and the child. Each component of the covariance of these differences was then plotted against the time interval between the readings (not shown). For most pairs, there was little pattern evident in the plots, which showed random scatter about the zero line. However there was a downward trend evident in the $^{207}Pb/^{206}Pb$ and $^{206}Pb/^{204}Pb$ isotope ratios for subjects 1023 and 2023. By assuming the time intervals were equally spaced, these plots were checked by plots of the autocorrelation for each series. These plots confirmed the correlation between repeated measures was not statistically significant (with the exception of the 1023/2023 pair). Similarly, the correlations between the paired blood and food repeated measures were examined. No evidence of correlation was found. We therefore omitted the data for the 1023/2023 pair and felt it was plausible to treat the remainder of the data as sets of independent observations. For 8 out of 10 mother/child pairs, there was a statistically significant positive correlation using the Kendall's Tau measure of rank correlation between the mother and her child's blood for the isotopic ratios. Only for the mother/child pairs 1029/2029 and 1052/2052 were there significant correlations between PbB concentrations (Table 5, Fig. 3).

Table 2. (*continued*)

	Mean	Median	SD	Minimum	Maximum	Number
Daily intake (µg/kg/day)	6.0	5.9	2.2	3.9	8.2	4
Mean daily intake (g)[a]	1,248	1,306	173	998	1,383	4
1064 Russia						
Pb in food (µg/kg)	4.9	5.2	0.6	4.1	5.3	3
Daily intake (µg/kg/day)	4.7	4.6	1.0	3.8	5.7	3
Mean daily intake (g)[a]	961	920	112	876	1,088	3
2064 Russia						
Pb in food (µg/kg)	5.7	5.7	0.9	5.1	6.3	2
Daily intake (µg/kg/day)	6.5	6.5	0.6	6.1	6.9	2
Mean daily intake (g)[a]	1,142	1,142	76	1,088	1,196	2

SD, standard deviation.
[a]Average intake over 6-day sampling period.

Representative time–series plots of isotopic compositions expressed as the $^{206}Pb/^{204}Pb$ ratio and PbB concentrations are illustrated in Figures 4, 5, and 6 (mother/child pairs 1015/2015, 1023/2023, 1044/2044), and all data are summarized in Figure 7. The time–series plots often show approximately parallel trends. For example, the changes in isotopic profiles for the mother and child are parallel even in the case of mother/child pair number 1023/2023 when there was sharp increase in $^{206}Pb/^{204}Pb$ when they both visited Russia for a holiday (Fig. 5). The differences for each mother/child pair were calculated and then the differences between these adjacent differences were obtained. To test if the profiles are parallel, it is necessary for the variance of these adjacent differences to be similar for all mother/child pairs. Unfortunately this was not the case. It is therefore not possible to perform a statistical test to confirm or deny parallelism.

The data are relatively uniform over time (as shown by the means and standard deviations in Table 1). If anything, the data for each mother exhibited larger variations than for the corresponding child. However, F-tests on the variances for the isotopic ratios showed that none of the mother/child pairs attained significance (Table 5).

Blood–diet relationships. Lead concentrations in the 6-day duplicate diets were generally low, with a mean and standard deviation (SD) of 5.5 ± 2.1 µg Pb/kg diet and a range from 2.1 to 14.9 µg Pb/kg with exclusion of the data for the two outliers with lead concentrations greater than 15 µg/kg (15.8 and 31.9 µg Pb/kg). For the Pb isotope $^{206}Pb/^{204}Pb$ ratio, the mean ± SD = 17.41 ± 0.29 with a range of 16.6–18.4, excluding the data for the same two samples. The large isotopic variation in 6-day diets contrasts with quarterly market basket surveys carried out in 1990–1991 for the cities of Port Pirie, Adelaide, and Hobart in southern Australia. Lead concentrations in the market basket survey were generally less than 10 µg/kg diet and $^{206}Pb/^{204}Pb$ was less

Table 4. Summary of data for *t*-tests (2-tail)

Mother/child identifier	No.	Daily intake *p*-value	Child/mother daily intake (Pb/kg bw)
1015/2015	9	0.10	1.69
1023/2023	8	0.05	1.52
1029/2029	8	0.25	1.20
1031/2031	4	0.04	1.60
1044/2044	4	0.02	6.11
1046/2046	5	<0.01	1.97
1047/2047	5	<0.001	3.60
1052/2052	3	0.04	1.69
1054/2054	4	0.04	2.15
All data	51	<0.001	

bw, body weight. All data for blood lead, mothers versus children, *n* = 51; *p* = 0.07. All data for skeletal lead, mothers versus children, *n* = 10; *p* = 0.55.

Table 3. Lead isotopic composition and concentration data for repeat analyses of food samples

Sample	Days after arrival in Australia	$^{208}Pb/^{206}Pb$	$^{207}Pb/^{206}Pb$	$^{206}Pb/^{204}Pb$	Pb (µg/kg)
2015-1[a]	191	2.1459	0.9010	17.23	4
2015-2		2.1564	0.9079	17.09	4
1015-1	191	2.1571	0.9081	17.11	3
1015-2		2.1509	0.9048	17.16	2
2015-1	372	2.1519	0.9056	17.14	6
2015-2		2.1473	0.9014	17.23	5
1015-1	925	2.1466	0.9001	17.24	4
1015-2		2.1394	0.8959	17.32	3
1016-A$_1$[b]	36	2.1569	0.9088	17.09	5
1016-A$_2$		2.1513	0.904	17.17	6
1016-B$_1$	190	2.1443	0.8992	17.29	3
1016-B$_2$		2.1293	0.8908	17.47	3
1016-C$_1$	378	2.1373	0.8925	17.44	5
1016-C$_2$		2.1625	0.9121	16.98	9
1016-D$_1$	462	2.1467	0.8995	17.27	4
1016-D$_2$		2.1434	0.8972	17.32	4

[a]1 and 2 indicate duplicate analysis of a single sample.
[b]A$_1$, A$_2$, B$_1$, etc., indicate duplicate analysis of four samples from a subject from Armenia participating in the Biokinetics of Lead in Human Pregnancy.

Table 5. Statistical parameters for blood and diet of mother/child pairs

| Parameter/identifier	No.	$^{207}Pb/^{206}Pb$ Tau	$^{207}Pb/^{206}Pb$ *p*-Value	$^{206}Pb/^{204}Pb$ Tau	$^{206}Pb/^{204}Pb$ *p*-Value	PbB Tau	PbB *p*-Value	*F*-Test for $^{207}Pb/^{206}Pb$ *p*-Value
Blood from mother/child pairs (isotopic composition)								
1015/2015	12	0.49	0.01	0.52	0.01	0.30	0.09	0.26
1023/2023	11	0.56	<0.001	0.46	0.03	0.20	0.20	0.50
1029/2029	10	0.91	<0.001	0.82	<0.001	0.62	<0.01	0.48
1031/2031	8	0.57	0.02	0.36	0.11	0.64	0.01	0.94
1046/2046	7	0.21	0.23	0.21	0.23	-0.07	0.60	0.53
1047/2047	8	0.50	0.04	0.21	0.23	-0.29	0.84	0.52
1052/2052	5	0.80	0.03	0.80	0.03	0.80	0.03	0.50
1054/2054	6	0.87	<0.01	1.00	<0.01	-0.20	0.71	0.17
1064/2064	5	-0.20	0.69	0.00	0.50	0.40	0.16	0.42
1044/2044	6	0.73	0.02	0.73	0.02	-0.07	0.58	0.60
All data	79	0.58	<0.001	0.58	<0.001	-0.05	0.75	–
Blood-food (isotopic composition)								
All data	121	0.16	<0.01	0.17	<0.01	0.07	0.14	–
Mother	64	0.21	<0.01	0.24	<0.01	0.09	0.15	
Child	57	0.07	0.21	0.06	0.25	0.02	0.40	
PbB daily intake (µg Pb/day)								
All data	111	0.00	0.51	–	–	–	–	–
PbB daily intake (µg Pb/day/kg bw)								
All data	111	0.14	<0.01	–	–	–	–	–

PbB, blood lead.
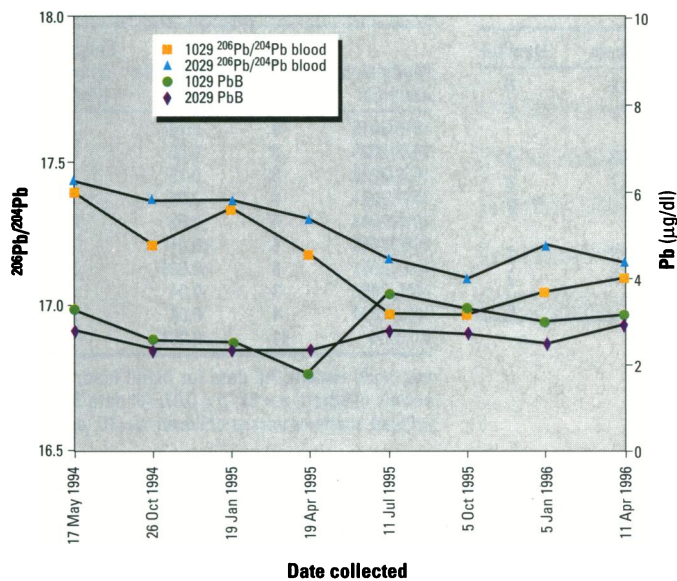
Figure 3. Time–series plot for $^{206}Pb/^{204}Pb$ and blood lead (PbB) for mother/child pair 1029/2029.

Figure 4. Time–series plot for $^{206}Pb/^{204}Pb$ and blood lead (PbB) for mother/child pair 1015/2015.

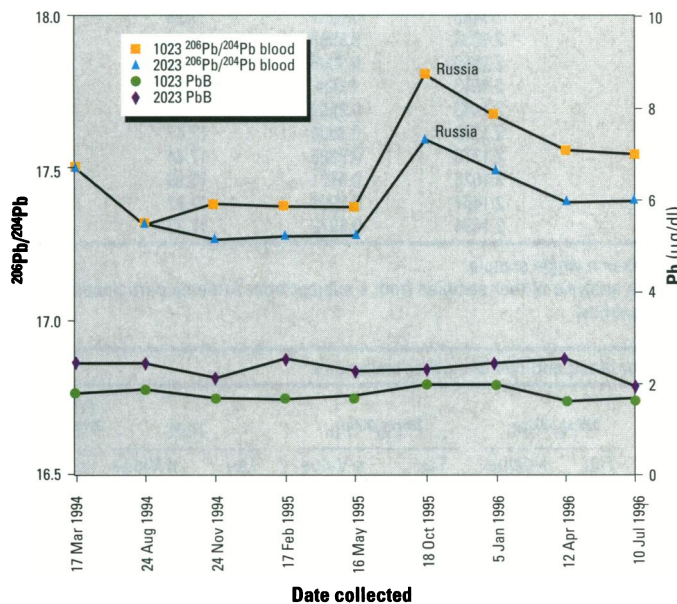**Figure 5.** Time–series plot for $^{206}Pb/^{204}Pb$ and blood lead (PbB) for mother/child pair 1023/2023. The time at which the mother and child returned for a visit to Russia is indicated.
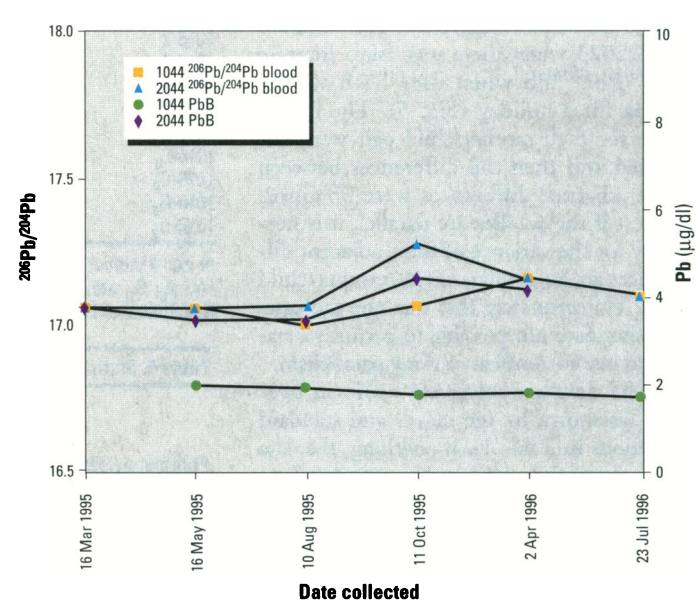
Figure 6. Time–series plot for $^{206}Pb/^{204}Pb$ and blood lead (PbB) for mother/child pair 1044/2044.

than 17.0 (27). The larger isotopic variations and increasing $^{206}Pb/^{204}Pb$ ratios in the 6-day diets over time are probably a reflection of the desire to consume food from the country of origin of the subjects and globalization of the food market.

The 6-day averaged daily weight of consumed dietary material varied from a low 338 g in subject 2031 to 1,929 g for subject 1046. The daily weights were relatively consistent for each subject over the period of monitoring. The 6-day averaged daily lead intake varied from 1.5 to 21.3 μg Pb/day

(Table 2), and this range applied for subject 2031.

The mean daily intake of lead for the children was 0.21 ± 0.11 μg Pb/kg bw/day compared with 0.11 ± 0.06 μg Pb/kg bw/day for the mothers. The mean daily intake of Pb for the children was overall approximately twice that of the mothers; the ratio of dietary intake for child/mother was from 1.20 to 6.11 μg/kg bw/day (Table 4). The combined data for mothers and children showed that there were significant differences in mean daily intake ($p < 0.001$; Table 4). For matched
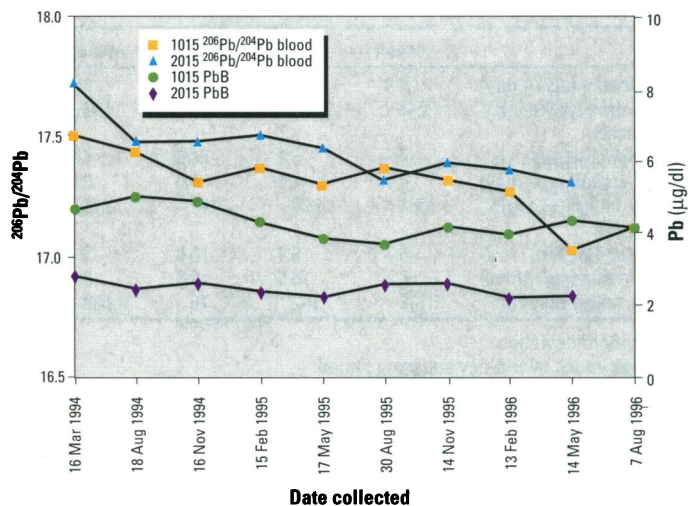
mother/child pairs, the daily intake was also significantly different in six of the nine pairs (Table 4). There did not appear to be any relationship between child/mother daily intake and PbB and isotopic composition.

Except for subjects 1015, 1044, and 2046, the correlations of individual mother blood-food and individual child blood-food for isotopic composition failed to reach statistical significance ($p > 0.05$). There was not a statistically significant ($p > 0.05$) association between blood lead and food lead concentrations. When the data were pooled (Table 5),

there was a statistically significant correlation for mother blood-food in isotopic composition ($p<0.01$ for $^{206}Pb/^{204}Pb$ and $^{207}Pb/^{206}Pb$) but not for the child blood–food data ($p \approx 0.2$).

The lack of statistical significance is obvious when the data are plotted in various ways. For example, the blood and diet isotopic data for subjects 1015 and 2015 are plotted in Figures 8 and 9 compared with the PbB and 6-day averaged dietary intake. In both mother and child for the May 1996 sampling, there was a marked increase in dietary intake, but totally contrasting isotopic compositions in the diet; yet, the PbB showed very little change and, for the child 2015, even the isotopic composition showed little change. The isotopic composition of the mother 1015 showed a decrease. In the case of mother/child pair number 1029/2029, there was a marked increase in dietary intake in the middle of the monitoring, but minimal effect was observed in the blood isotopic composition or concentration (Fig. 10 and 11). Variability in either isotopic composition of the diet and/or dietary intake but with minimal change in blood isotopic composition or blood was observed in most of the other mother/child pairs (Fig. 3, 5, 6).

Blood lead concentrations and, commonly, the isotopic composition exhibited very little variation over time, even when the isotopic composition of diet was markedly different from the blood isotopic composition and the dietary intake was >10 µg Pb/day, as shown for 1029/2029 in Figures 10 and 11 and summarized for all subjects in Figure 7.

As expected, the 6-day diets show considerable variation in the elements such as Ca, Mg, Sr, Ba, etc., but at this stage there does not appear to be any systematic trends between mothers or children.

Discussion

Clearance rate of lead from blood and skeletal contribution to blood lead. This study evaluates differences in the patterns and clearance rates of lead from blood in children compared with their mothers. Gulson et al. (*25*) showed that there was an exponential decrease in the $^{206}Pb/^{204}Pb$ ratio over a 3- to-4-month period in female adults migrating from Eastern Europe to Australia, which was related to the mean life of lead in the red blood cell. That is, the European lead in blood was exchanging with Australian lead. Furthermore, after equilibrium with the Australian environment was attained after 3 to 4 months, about 41–73% of lead in the blood derived from endogenous (predominantly skeletal) tissues. In most cases it was not possible to evaluate the clearance rates of lead from
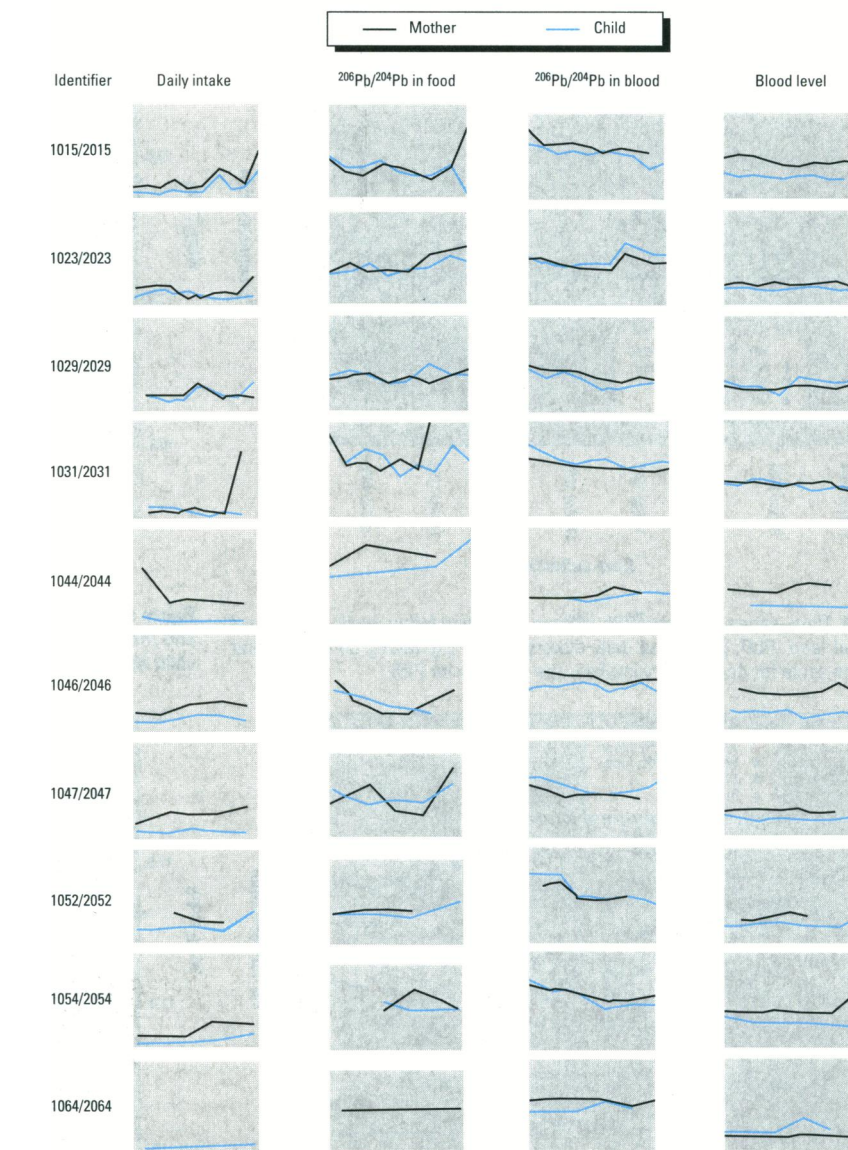

Figure 7. Summary of time–series plots for all subjects for $^{206}Pb/^{204}Pb$ in food and blood, lead daily intake (µg/kg body weight), and blood lead (µg/dl).

blood in the children in the present study because they were usually recruited at least 1 month or longer after the mother had been recruited. The similar blood lead isotopic and concentration trends shown in Figures 3 through 6 and summarized in Figure 7 for the mother/child pairs indicates that the nine clearance rates for lead from blood are similar for the children and their mothers. Further evidence for this hypothesis comes from the subjects 1023/2023 who visited Russia for 3 months and then returned to Australia. The trends in both isotopic composition and pre- and post-Russia are identical and would suggest that the clearance rate of lead from blood is similar for both mother and child (Fig. 5).

When equilibrium was reached between skeletal lead and Australian lead, the skeletal contribution to PbB for the mothers ranged from 16 to 70% and for children varied from 26 to 64% (Table 6). There was no consistency between mothers and children as to whether or not body stores contributed more than environmental sources to PbB. Three of nine mother/child pairs showed a higher contribution of skeletal lead to blood lead for the mother compared with the corresponding child, two pairs had the same, and four mother/child pairs showed the child having a larger contribution than the mother.

Absorption rates. The PbB concentrations in these subjects are low; hence, any changes in blood lead due to diet should be more easily discernible than among subjects with elevated body stores of lead (e.g., persons having PbB levels over 10 µg/dl). If there was a 40–50% absorption for a child
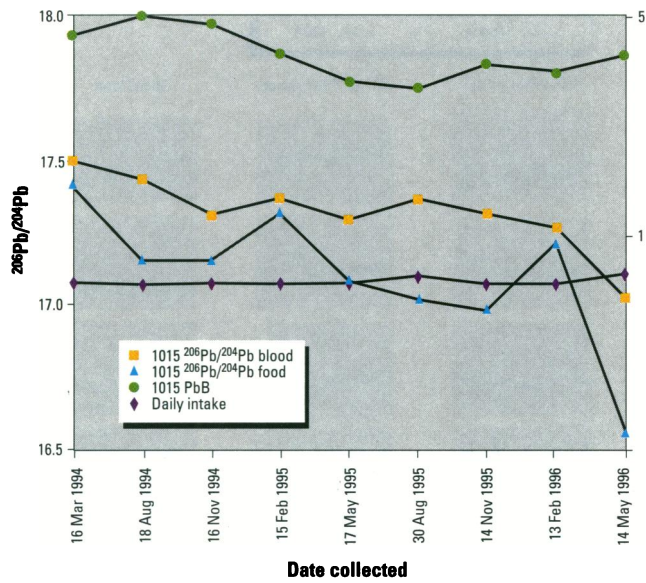
Figure 8. Time–series plots for $^{206}Pb/^{204}Pb$ in blood and 6-day duplicate diet and for blood lead (PbB; μg/dl) and daily dietary intake (μg/day/kg bw) for mother 1015. The scale for daily dietary intake is the same as for PbB.

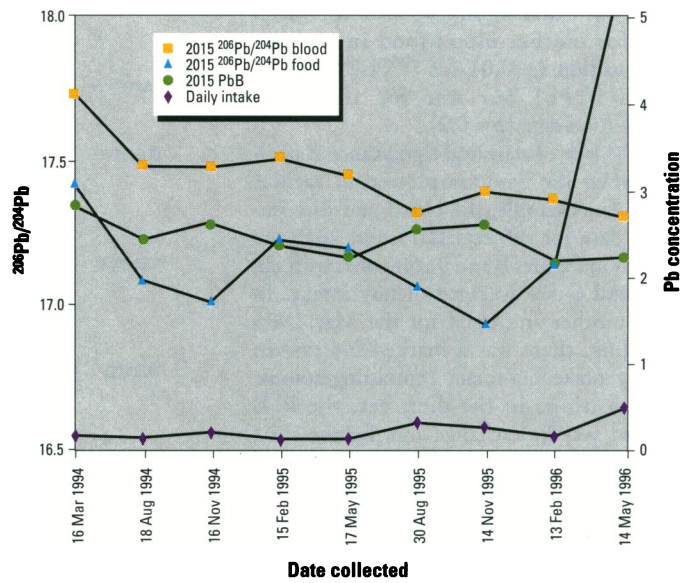**Figure 9.** Time–series plots for $^{206}Pb/^{204}Pb$ in blood and 6-day duplicate diet and for blood lead (PbB; μg/dl) and daily dietary intake (μg/day/kg bw) for child 2015. The scale for daily dietary intake is the same as for PbB.

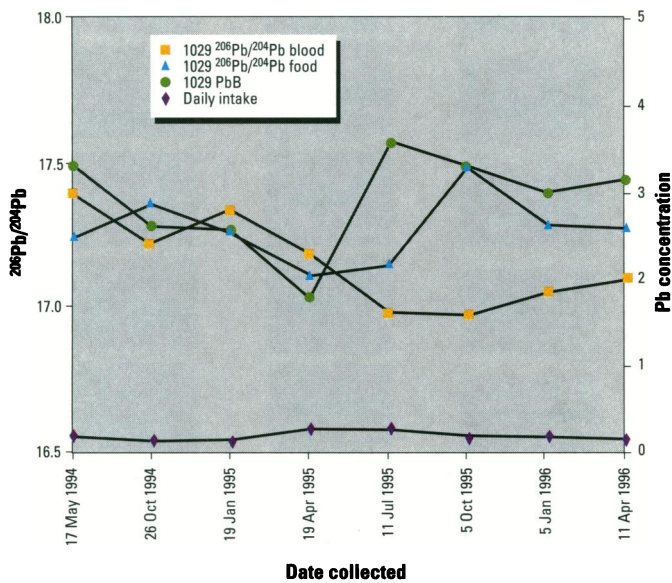**Figure 10.** Time–series plots for $^{206}Pb/^{204}Pb$ in blood and 6-day duplicate diet and for blood lead (PbB; μg/dl) and daily dietary intake (μg/day/kg bw) for mother 1029. The scale for daily dietary intake is the same as for PbB.

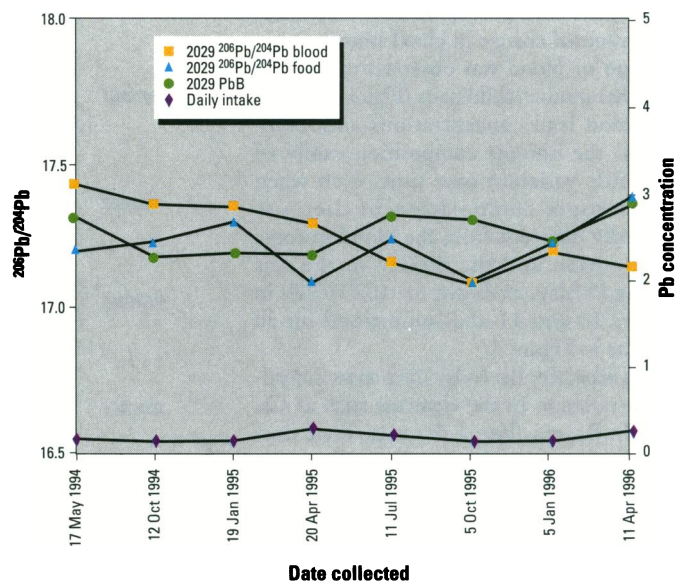**Figure 11.** Time–series plots for $^{206}Pb/^{204}Pb$ in blood and 6-day duplicate diet and for blood lead (PbB; μg/dl) and daily dietary intake (μg/day/kg bw) for child 2029. The scale for daily dietary intake is the same as for PbB.

and if the isotopic composition in the diet changes markedly, this should be reflected by a more rapid change in the child's blood isotopic composition towards the Australian values. This more rapid change in the children's blood isotopic composition does not occur in spite of 1) a greater intake of Australian lead from lunches consumed away from home, and potentially a greater intake of lead from dust/dirt with the Australian isotopic composition compared with adult women; 2) the children are dosed with dietary lead at approximately

two times the rate (i.e., daily intake Pb per kilogram body weight) compared with their mothers; and 3) the children have lower body lead stores than adults (30,31) so that they have less lead of European origin to counter the input of dietary lead of Australian isotopic composition. Increased bone turnover in the children (32) as an argument also fails to explain the cases in which the diet shows an increase in both intake and isotopic composition, such as for subjects 2015 (Fig. 9), 2023, and 2031.

In all cases, the patterns for the isotopic

composition of blood are similar for mothers and children (Fig. 4–7) or the change is in the opposite direction to the change in isotopic composition of the diet (Fig. 7, 9, 10).

The above data indicate that the lead absorption from the gastrointestinal tract in these children is essentially the same as for the adult females. That is, the absorption rate is around 10–15% rather than 40–50%. Our interpretations are supported by data of Angle et al. (33) in which they suggested that absorption of ingested lead among 2- to 3-year-old children was 10–15%. Even though

Table 6. Percentage skeletal contribution to blood lead

Identifier	Mother (%)	Child (%)
1015/2015	34	44
1023/2023	51	40
1029/2029	16	26
1031/2031	70	57
1046/2046	42	61
1047/2047	56	42
1052/2052	53	49
1054/2054	58	63
1064/2064	48	64
1044/2044	NA	NA

NA, not available.

the average age of 8 years for the children in the present study is slightly older than the limits of 6–7 years in, for example, the IEUBK model, the data are still considered relevant for use in pharmacokinetic models, especially given the paucity of information on dietary absorption of lead in children.

The daily intakes of lead from dietary sources in both mothers and children varies from 1.5 to 21.3 µg Pb/day, with a mean and SD of 6.8 ± 3.7 µg/day (based on 111 analyses of composited 6-day diets) and are comparable with those used in the IEUBK model (version 0.9) of 5.5–7.0 kg/day (*9*). Calculation of PbB using the IEUBK model for a child 6-7 years of age results in an increase in PbB from 2.7 to 3.2 µg/dl (approximately an 18% increase over the initial value) when the daily intake is increased from 7 to 14 µg/day. This increase in PbB is almost twice the variation observed in the children in this study ranging over periods from 12 to over 24 months (Table 1). As an additional example of differences between observed and modeled changes, using the IEUBK model, the calculated PbB for subject 2031 changes from 2.3 to 3.8 µg/dl (approximately 65% higher than the initial value) when the daily dietary intake is increased from 1.5 µg Pb/day to 21.3 µg Pb/day. Some of the differences between calculated and observed blood lead values may be explained by the assumption in the IEUBK model that dietary lead intake had been constant in the previous 12-month period. The measured change in PbB over the whole period of monitoring subject 2031 was 3.0–3.8 µg/dl (SD = 0.28; Table 1).

Generalizability to disadvantaged subpopulations. The women and children evaluated in this study were natives of Eastern Europe consuming diets available in Australia, with food choices likely to be representative of their Eastern Europe origins. No specific dietary advice had been provided by the investigators to the families to encourage or discourage them from selecting any particular foods. The fractional absorption of lead by the children who were subjects in this study has been considered representative of children consuming nutritionally adequate diets, although we do not have specific assessments of nutritional status for these children.

The prevalence of elevated blood lead levels is higher among children from low-income and socially disadvantaged families, although lead toxicity can occur among any situation if lead exposures are elevated. Nutritional status varies within the general population. For example, data from the third National Health and Nutritional Examination Survey (NHANES III) conducted in the United States showed that 4.5% of all 1- to 2-year-old children had blood lead levels greater than 10 µg/dl; however, 21.6% of 1- to 2-year-old non-Hispanic black children had blood lead levels over 10 µg/dl (*34*). Among non-Hispanic black 3–5-year-old children, the prevalence of blood lead levels of 10 µg/dl was 20.0% compared with 3.7% among non-Hispanic children (*34*). Nutritional status for minerals (especially low-calcium and low-iron status), quantity and type of macronutrients (e.g., high-fat intake), and less than adequate overall food intakes have been found to increase lead absorption [for a review, see Mahaffey (*35*)]. The same low-income subpopulations at risk of increased prevalence of elevated blood lead levels are also at risk of increased prevalence of inadequate nutrition. Reporting on data gathered by the National Nutrition Monitoring and Related Research Programs, an analysis of nutritional problems in the United States raises concerns about iron and calcium status, as well as overall food sufficiency among low-income families (*36*). Marginally adequate calcium intakes have been identified more commonly among nonwhite populations, particularly children with higher blood lead levels (*37*), and recently identified as a risk factor for elevated blood lead levels among pregnant women in Mexico City (*38*).

When dietary iron intake is low, tissue lead levels are higher and lead absorption is increased [for a review of data describing this interaction, see Mahaffey (*35*)]. In nationally based surveys conducted in the United States, median iron intakes from food were below recommended values for young children 1 to 2 years of age, as well as for adolescent and adult females (*36*). Recent reports provide specific examples of the influence of iron status on blood lead levels. Hammad et al. (*39*) identified a statistically significant negative association between blood lead concentrations and dietary iron intake among a group of 299 urban preschool children aged 9 months to 5 years. Granado et al. (*40*) have found an increased prevalence of elevated blood lead levels among iron-deficient Spanish children. A significant decrease in mean blood lead levels (from a mean of 14.1 µg/dl to 7.5 µg/dl) was observed following iron therapy (*40*).

There is a general concern that dietary fat intake is higher than recommended, primarily reflecting concern about risk factors for cardiovascular diseases but also because high-fat diets facilitate absorption of lead in experimental animals (*41*). Significant positive associations between blood lead concentrations and dietary fat intake (as well as total caloric intake) were reported among 296 children aged 9–72 months (*42*).

Metabolic studies among adults show that when lead is ingested during fasting the fractional absorption increases from the range of 5–20% to approximately 60–80% (*16,18,19,21*). Consequently, national data from the United States that indicate occurrence of food insufficiency among low-income families raise profound concerns for many reasons, including increased susceptibility to lead toxicity. The national nutrition situation described in the Life Sciences Research Office report (*36*) indicated that

> although the availability of food and nutrients in the U.S. food supply is, on a per capita basis, generally adequate to prevent undernutrition and deficiency-related diseases, about 9–13% of people living in low-income households or families experience some degree of food insufficiency.

Specifically,

> in 1988–1991, Mexican Americans and non-Hispanic blacks were more likely than non-Hispanic whites to report that they sometimes or often did not have enough food to eat... For low-income households, the prevalence of food insufficiency in 1989–91 was higher among blacks than whites, and Food Stamp Program participants were more likely to report a food-insufficiency problem than nonparticipants....

Conclusions

If the absorption rate of lead from diet for children was four to five times greater than that of adults, this should be reflected by a faster rate of accumulation of Australian lead isotopic profile in the blood of children compared with their mothers. In spite of considerable changes in average dietary intake, changes in the dietary isotopic composition, and the dietary intake lead per kilogram body weight of the children being approximately twice that of the mother, the similarity in patterns for isotopic composition and PbB for mother/child pairs in this investigation suggest that the absorption rate of lead from dietary sources is similar for adults and children 6 years of age and older. As dietary intake is a significant contributor to

PbB for children over 5 years of age and in adults, our results have importance for the values of dietary absorption employed in pharmacokinetic models, especially those such as the IEUBK model, which is used for remediation purposes. As pharmacokinetic models apply a 40–50% absorption even for 7-year-old children, further investigations on fractional absorption of ingested lead by young children (especially those of 1–3 years of age) are warranted. Additional information on the increased risk of lead toxicity among marginally nourished children will help target public resources toward subpopulations at highest risk of adverse health effects.

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