ORIGINAL ARTICLES

Higher Infant Blood Lead Levels with Longer Duration of Breastfeeding

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Objective To determine whether longer breastfeeding is associated with higher infant lead concentrations.

Study design Data were analyzed from 3 studies of developmental effects of iron deficiency in infancy: Costa Rica (1981-1984), Chile (1991-1996), and Detroit (2002-2003). The relation between duration of breastfeeding and lead levels was assessed with Pearson product-moment or partial correlation coefficients.

Results More than 93% of the Costa Rica and Chile samples was breastfed (179 and 323 breastfed infants, respectively; mean weaning age, 8-10 months), as was 35.6% of the Detroit sample (53 breastfed infants; mean weaning age, 4.5 months). Lead concentrations averaged 10.8 μg/dL (Costa Rica, 12-23 months), 7.8 μg/dL (Chile, 12 months), and 2.5 μg/dL (Detroit, 9-10 months). Duration of breastfeeding as sole milk source and total breastfeeding correlated with lead concentration in all samples (r values = 0.14-0.57; *P* values = .06-<.0001).

Conclusions Longer breastfeeding was associated with higher infant lead concentration in 3 countries, in 3 different decades, in settings differing in breastfeeding patterns, environmental lead sources, and infant lead levels. The results suggest that monitoring lead concentrations in breastfed infants be considered. *(J Pediatr 2009;155:663-7)*.

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The marked mobilization of maternal bone lead stores during lactation[1,2] raises the issue of lead transfer to the infant via breast milk.[3-6] In 1994, we made the incidental observation that blood lead concentration was higher with longer breastfeeding in a sample of healthy full-term Costa Rican infants.[7] Here, we pursued the finding in 2 other samples and analyzed the Costa Rica data in more detail. These samples in 3 different countries were used to test the hypothesis that infants breastfed longer are at risk for higher lead concentrations.

Methods

Data on lead concentration and breastfeeding were obtained in the course of research on the behavioral and developmental effects of iron deficiency in infancy. The settings of all 3 studies—Costa Rica, Chile, and the United States—were urban or peri-urban. The study in Costa Rica was conducted between 1981 and 1984.[7] Lead-based paints were not in use, but gasoline was leaded. As established by the US Centers for Disease Control (CDC), the lead level of concern at that time was 25 μg/dL. The study in Chile was conducted between 1991 and 1996, as Chile made the conversion to unleaded gasoline.[8] Housing was of recent construction and generally unpainted. The study in Detroit was conducted in 2002 to 2003 in an inner-city population. Leaded paint and gasoline had been legally banned for several decades.[9] The CDC's cutoff level for concern was 10 μg/dL during the time of the Chile and Detroit studies.

Subject enrollment was restricted to full-term healthy infants in the Costa Rica and Chile studies. The Costa Rica sample consisted of 12- to 23-month-old infants enrolled through community-based door-to-door screening (n = 191).[10] The sample in Chile was enrolled in community clinics and well child care visits at 4 to 6 months. Lead concentrations were available for 331 infants.[11] In the United States, a sample of African-American infants was enrolled at 9-month health maintenance visits at an inner-city hospital. All infants were invited to participate

CDC	Centers for Disease Control
SES	Socioeconomic status

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over a 1-year period; lead concentrations were available for 167 of 198 infants.[9] For Costa Rica and Detroit, lead concentrations were determined on enrollment; for Chile, they were determined when infants were 12 months old.

Signed informed consent was obtained from parents in each study. Study protocols were approved by the institutional review boards of Case Western Reserve University for the Costa Rica study and the University of Michigan for the Chile and Detroit studies. Institutional review boards of the Hospital Nacional de Niños, the University of Chile, and Wayne State University also approved protocols for Costa Rica, Chile, and Detroit, respectively. Details of the studies have been reported.[9-11]

Procedures

Two variables reflected the duration of breastfeeding: weeks of breastfeeding as the sole source of milk and weeks of total breastfeeding (calculated from the age at complete weaning from the breast). In each sample, project personnel obtained information on infant feeding from the infant's mother. For the Detroit sample, the duration of breastfeeding as the sole source of milk was also determined from chart review of health care visits; pediatricians recorded feeding data from birth. Some data from mothers entailed recall, especially in the Costa Rica sample, in which infants were enrolled at 12 to 23 months of age. For Chile, contact with infants started at approximately 4 months, and feeding information was obtained prospectively afterward during weekly home visits. Because of the strength of this data collection (weekly and in-person), we will emphasize results from this sample. Data on age at starting juice and solids were not sufficiently complete across studies to be analyzed.

Lead concentrations in infants were determined in venous blood, which was anti-coagulated with EDTA and stored frozen at −20 °C in lead-free vials when not assayed immediately. Laboratory procedures for lead assays in the Costa Rica and Chile samples were under direct CDC quality control specifications. All laboratories maintained strict quality control with internal and external standards. For the Costa Rica sample, lead levels were determined with a graphite furnace method by using a matrix modification procedure.[12] For the Chile sample, lead concentration was determined with electrothermal atomization (graphite furnace HGA700) atomic absorption spectrophotometry (Perkin Elmer 1100B, Boston, Massachusetts).[13] For the Detroit sample, the Detroit Medical Center University Laboratories performed lead assays with atomic absorption by using a graphite furnace.[14] Earlier analyses showed that measures of iron status did not relate to lead concentrations in these samples.[7-9]

Statistical Analysis

Information on feeding and lead levels has been published as part of sample descriptions for the iron deficiency studies.[8-10] In these secondary analyses, we focus on normal birth weight breastfed infants in each sample for whom lead concentrations were available. Three breastfed infants in the Detroit sample had birth weight <2500 g and were excluded from analysis. The associations between lead concentration and the duration of breastfeeding as the sole source of milk and total breastfeeding in weeks was analyzed with SAS software version 9.1 (Cary, North Carolina).[15] For infants who were still being breastfed when the lead concentration was obtained, their current age was used as the duration of total breastfeeding. A single unified analysis was not possible, because the samples did not overlap sufficiently in age, duration of breastfeeding at the longer end, or lead levels >5 μg/dL. Therefore, the association had to be determined within sample.

Pearson product-moment correlations were calculated when background factors were not associated with lead concentration and breastfeeding duration in a given sample. Multiple linear regression was used to calculate partial correlation coefficients when a background factor might be a confounder, that is, even weakly correlated ($P < .10$) with both these variables. In addition, we considered as a covariate any background variable that was correlated with lead concentration ($P < .10$). These background variables were considered: sex, age at testing, birth weight, gestational age, birth order, weight-for-age z-score, weight-for-length z-score, maternal age, maternal education, and family socioeconomic status (SES). We derived the most parsimonious models that included all background factors independently contributing to the models.

Table I. Characteristics of breastfed infants*

	Costa Rica (n = 179)	Chile (n = 323)	Detroit (n = 53)
Sex, % male (n)	55.3 (99)	52.6 (170)	45.3 (24)
Age at testing†, months	17.4 (3.2)	12.4 (0.2)	9.1 (0.5)
Birth weight, kg	3.26 (0.41)	3.61 (0.38)	3.55 (0.57)
Gestational age, weeks	39.4 (1.4)	39.6 (1.1)	39.5 (1.0)
Birth order	2.5 (1.6)	2.2 (1.2)	1.8 (1.0)
Breastfeeding as sole milk source, weeks	17.5 (18.1)	22.8 (13.0)	7.3 (11.8)
Total breastfeeding, weeks	32.0 (24.1)	41.5 (15.1)	18.7 (13.2)
Lead concentration, μg/dL whole blood	10.8 (2.6)	7.8 (3.6)	2.5 (1.5)
Weight-for-age z-score	−0.24 (1.01)	−0.03 (1.02)	0.12 (1.13)
Weight-for-length z-score	0.09 (1.03)	0.48 (1.00)	0.56 (1.01)

*Values are mean (SD) for continuous variables and % for categorical variables.
†For Costa Rica and Detroit, age of enrollment and age at testing for lead, weight-for-age z-score, and weight-for-length z-score were the same. For Chile, infants were enrolled at 4 to 6 months of age in a clinical trial of preventing iron deficiency anemia; blood lead levels were determined at the conclusion of the trial at 12 months; weight-for-age z-score and weight-for-length z-score at that age are shown.

Results

Breastfeeding was near universal in the Latin American samples (93.7% and 97.6% in Costa Rica and Chile samples, respectively), whereas 35.6% of infants in the Detroit sample were breastfed. Table I shows the characteristics of breastfed infants in each sample (Costa Rica, n = 179; Chile, n = 323; Detroit, n = 53). For family characteristics, mothers in Costa Rica and Chile averaged 9.5 years of education, and 62% to 76% were married. Family SES was working- to middle-class. In the Detroit sample, maternal education averaged 12.8

Table II. Correlations among lead, breastfeeding, and background factors*

	Lead	Breastfeeding as sole milk source
	r (P value)	r (P value)
Sex		
Costa Rica	*.15 (.04)*	.09 (.24)
Chile	.07 (.18)	−.02 (.78)
Detroit	.05 (.73)	.03 (.82)
Age at testing		
Costa Rica	**.19 (.01)**	**.17 (.02)**
Chile	.01 (.89)	.04 (.48)
Detroit	−.15 (.28)	.08 (.56)
Birth weight		
Costa Rica	*−.16 (.04)*	.04 (.58)
Chile	.08 (.14)	.05 (.37)
Detroit	−.02 (.90)	.04 (.75)
Gestational age		
Costa Rica	.05 (.52)	−.09 (.23)
Chile	.08 (.15)	−.04 (.48)
Detroit	−.01 (.95)	−.003 (.98)
Birth order		
Costa Rica	.04 (.55)	.07 (.37)
Chile	.04 (.49)	.02 (.74)
Detroit	**.23 (.10)**	**.30 (.03)**
Weight-for-age z-score		
Costa Rica	**−.20 (.007)**	**−.24 (.001)**
Chile	−.01 (.93)	−.05 (.40)
Detroit	−.07 (.61)	.11 (.44)
Weight-for-length z-score		
Costa Rica	**−.17 (.02)**	**−.22 (.004)**
Chile	−.01 (.86)	−.004 (.95)
Detroit	−.005 (.97)	.002 (.99)
Maternal age		
Costa Rica	*−.15 (.05)*	.003 (.97)
Chile	.05 (.38)	.05 (.37)
Detroit	−.03 (.84)	.53 (<.0001)
Maternal education		
Costa Rica	*−.20 (.007)*	.04 (.56)
Chile	.03 (.56)	−.06 (.25)
Detroit	−.06 (.68)	−.08 (.58)
Family SES		
Costa Rica	*−.23 (.002)*	.05 (.51)
Chile	.06 (.28)	.02 (.67)
Detroit†	NA	NA

*Values in **bold** indicate a potential confounder (ie, correlated with both breastfeeding and lead); values in *italics* indicate a potential covariate (ie, correlated with lead). We included these variables in the appropriate multiple regression analyses and retained those that were statistically significant in the most parsimonious models.
†Almost all families received Medicaid insurance; data were not collected for a SES scale.

years. Only 14.7% were married, and 85% of families had Medicaid insurance, indicating considerable economic stress.

The patterns of breastfeeding differed markedly across samples (Table I). The mean duration of breastfeeding as the sole source of milk was 4 to 5 months in the Latin American samples, in contrast to <2 months in the Detroit sample. Complete weaning from the breast (duration of total breastfeeding) occurred on average at approximately 8 to 10 months in Costa Rica and Chile samples and 4.5 months in Detroit. In Costa Rica, 9.5% of the infants were still breastfed when enrolled at 12 to 23 months[10]; 29.8% of the Chilean infants were still breastfed when they completed the study at 12 months.[11] In the Detroit sample, <8% infants were nursing when enrolled at 9 to 10 months.

The mean lead concentrations were also distinctly different across studies (Table I). The mean lead concentration in the Costa Rica sample was approximately 11 μg/dL, and 53% of infants had concentrations $\geq$ 10 μg/dL. The mean in the Chile sample was approximately 8 μg/dL, and 26% of infants had concentrations greater than the cutoff level. The highest concentrations in both Latin American samples were 21 to 22 μg/dL. In contrast, the mean lead concentration in the Detroit sample was <3 μg/dL; the highest concentration was 8.0 μg/dL, and only 7.8% of values were >5 μg/dL.

Table II shows background factors and their correlations with lead concentration and the duration of breastfeeding as the sole milk source in each sample (correlations with duration of total breastfeeding available on request). For the Costa Rica sample, the most parsimonious model included infant age (potential confounder), birth weight, and SES. For Detroit, birth order was a potential confounder; there were no other covariates. For Chile, no background variable related to either breastfeeding or lead concentration.

As reported earlier as an incidental finding,[7] there was a positive correlation between the total duration of breastfeeding and infant lead levels in the Costa Rica sample. The partial correlations between lead and the duration of breastfeeding as the sole milk source and total breastfeeding were 0.19 and 0.16, respectively, controlling for infant age, birth weight, and SES. Even stronger correlations were observed in the Chile and Detroit samples for the duration of breastfeeding as the sole source of milk (r values = 0.23 and 0.56, respectively, controlling for birth order in the Detroit sample). The corresponding r values for total breastfeeding were 0.17 and 0.31. All data points and the regression lines in the 3 samples are shown for the associations between lead and duration of breastfeeding as the sole source of milk (Figure 1) and total breastfeeding (Figure 2), controlling for background factors as indicated.

Discussion

Longer breastfeeding was associated with higher infant lead concentrations in 3 different countries, in 3 different decades, in settings that differed in the prevalence and duration of breastfeeding, the use of unleaded gasoline, and mean infant lead levels. The findings in the Chile and Detroit samples confirm our earlier observation in the sample from Costa Rica.

The association between lead concentration and duration of breastfeeding as the sole milk source was weakest in Costa Rica, perhaps because the infants were considerably older than in Detroit and Chile samples. This difference is plausible because breast milk is likely to contribute less to infants' lead burden as they get older and have longer periods of environmental exposure and normal developmental behaviors, such as mouthing and independent locomotion. The Costa Rica sample was also the only one with a wide age range, compared with the other studies, and largely retrospective data on breastfeeding, which could introduce inaccuracy and potential bias. We also emphasize that the Detroit sample, in particular, was small, and breastfeeding was shorter and

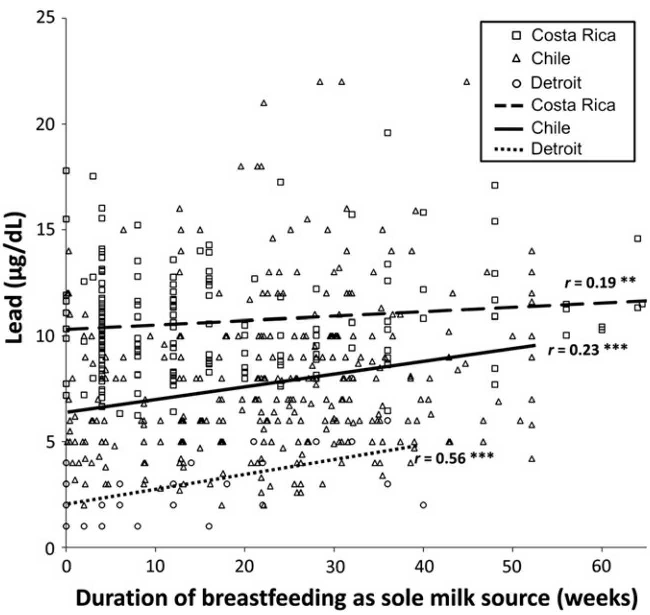

Figure 1. Relation between lead concentration and duration of breastfeeding as the sole source of milk. All data points are shown □ Costa Rica, Δ Chile, ○ Detroit. Regression lines are shown for each sample (*dashed line*, Costa Rica; *solid line,* Chile; *dotted line,* Detroit) as is the Pearson correlation coefficient for Chile and partial correlation coefficients for Costa Rica and Detroit. $^{**}P < .01$; $^{***}P < .001$.

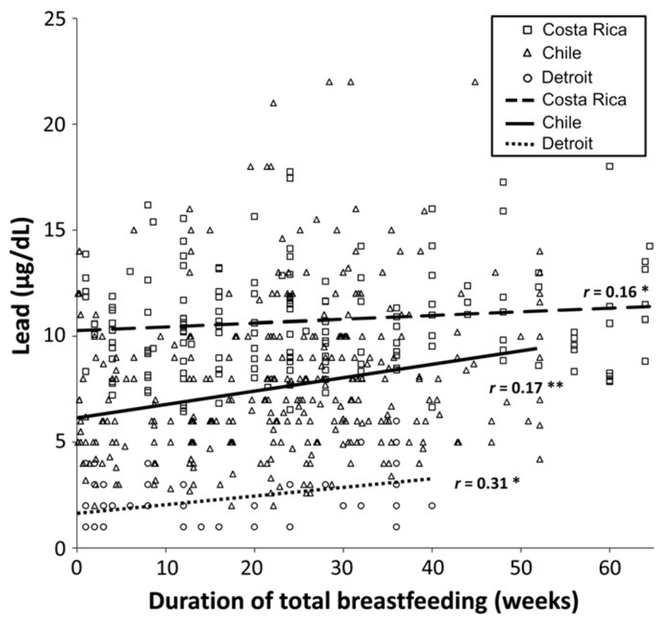

Figure 2. Relation between lead concentration and total duration of breastfeeding. All data points are shown □ Costa Rica, Δ Chile, ○ Detroit. Regression lines are shown for each sample (*dashed line*, Costa Rica; *solid line,* Chile; *dotted line,* Detroit) as is the Pearson correlation coefficient for Chile and partial correlation coefficients for Costa Rica and Detroit. $^{*}P < .05$; $^{**}P < .01$.

less intense than the other samples. Thus, we have the most confidence in the associations observed in the Chile sample. It was not only the largest, but also the one with the best data on breastfeeding (ie, obtained prospectively beginning at 4 to 6 months during weekly home visits).

Some investigators have reported low lead levels in breast milk or noted that formula contributes similar, if not more, lead to the infant's diet[3,4] and concluded that increased lead levels in breastfed babies are not a significant public health concern. However, the physiologic rationale for concern is strong. Even with no current environmental exposure, lead accumulates in maternal bones from past exposure. During lactation, a period of heightened bone turnover, maternal bone lead redistributes from bone into plasma and into breast milk.[1,2] Our results are consistent with this physiology mechanism. With a longer duration of breastfeeding, the infant would have an opportunity to accumulate more lead as maternal blood lead is redistributed into breast milk. Our findings support the conclusion of Ettinger et al[5] that "[t]his phenomenon constitutes a potential public health problem in areas where environmental lead exposure is continuing as well as in areas where environmental lead exposure has recently declined." Our observations should be confirmed and extended in future studies. Longitudinal intergenerational studies are needed to understand how maternal lead burden in infancy and childhood affects lead in breast milk and infant lead levels. Interactions between minerals, such as calcium and lead, also warrant further investigation.

Our study has important limitations. As the figures show, there was insufficient overlap between samples in lead concentrations or breastfeeding duration to support a unified analysis. Rather, each sample had to be analyzed separately. Furthermore, we could not analyze cumulative lead burden, because lead was measured at a single point in the Chile and Detroit samples and only in a 3-month period for the Costa Rica sample. The Costa Rica data were collected at what is typically the age period for peak lead levels, but infants in the Chile and Detroit samples were younger, and we have no data on their lead levels in the second year of life. We also had no data on maternal lead levels in bone or blood. Thus, we could not directly test the hypothesized mechanism or address fundamental questions about the relations between lead in maternal bone, maternal blood, breast milk, and infant blood. Our results point to a need for further research on these relations and the mechanisms that account for them. We also could not determine whether maternal blood lead concentrations during pregnancy could be used in a selective screening process (ie, to identify infants at particular risk for higher lead concentrations with longer breastfeeding).

Our findings do not detract from the many known benefits of breastfeeding. Rather, they suggest that monitoring lead concentrations in breastfed infants should be considered. There is increasing concern about adverse developmental effects of lead at even very low levels,[16,17] which has contributed to updated policy statements. Some recommend lowering the blood lead action level.[18] The American Academy of Pediatrics recommends that pediatric health care providers consider universal screening when there are no state guidelines other than for infants participating in Medicaid or the Women, Infants, and Children program.[19] However, state guidelines vary, and many breastfed infants do not meet state criteria for screening. If our results are born out in other samples, additional monitoring of breastfed infants may be indicated until there are generations of mothers who grow up with little lead exposure and infants with little environmental exposure themselves. ■

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