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ARTICLE

Longitudinal Associations Between Blood Lead Concentrations Lower Than 10 μg/dL and Neurobehavioral Development in Environmentally Exposed Children in Mexico City

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ABSTRACT

OBJECTIVE. Increasing evidence suggests that 10 μg/dL, the current Centers for Disease Control and Prevention screening guideline for children's blood lead level, should not be interpreted as a level at which adverse effects do not occur. Using data from a prospective study conducted in Mexico City, Mexico, we evaluated the dose-effect relationship between blood lead levels and neurodevelopment at 12 and 24 months of age.

METHODS. The study population consisted of 294 children whose blood lead levels at both 12 and 24 months of age were <10 μg/dL; blood lead levels were measured by graphite furnace atomic absorption spectroscopy; Bayley Scales of Infant Development II were administered at these ages. The outcomes of interest were the Mental Development Index and the Psychomotor Development Index.

RESULTS. Adjusting for covariates, children's blood lead levels at 24 months were significantly associated, in an inverse direction, with both Mental Development Index and Psychomotor Development Index scores at 24 months. Blood lead level at 12 months of age was not associated with concurrent Mental Development Index or Psychomotor Development Index scores or with Mental Development Index at 24 months of age but was significantly associated with Psychomotor Development Index score at 24 months. The relationships were not altered by adjustment for cord blood lead level or, in the analyses of 24-month Mental Development Index and Psychomotor Development Index scores, for the 12-month Mental Development Index and Psychomotor Development Index scores. For both Mental Development Index and Psychomotor Development Index at 24 months of age, the coefficients that were associated with concurrent blood lead

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Key Words
lead, children, neurobehavioral

Abbreviations
BSID II—Bayley Scales of Infant Development II
MDI—Mental Development Index
PDI—Psychomotor Development Index

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level were significantly larger among children with blood lead levels <10 μg/dL than it was among children with levels >10 μg/dL.

CONCLUSIONS. These analyses indicate that children's neurodevelopment is inversely related to their blood lead levels even in the range of <10 μg/dL. Our findings were consistent with a supralinear relationship between blood lead levels and neurobehavioral outcomes.

UNCERTAINTY PERSISTS REGARDING the functional form of the dose-effect relationship between blood lead levels <10 μg/dL and neurodevelopment in children. The absence of a threshold long has been suspected,[1] and the results of recent studies provide increasingly compelling evidence to support this conjecture.[2–4] Moreover, recent debate has focused on whether the association within this range is best described as linear, sublinear, or supralinear. In an early meta-analysis, Schwartz[5] noted that studies in which cohorts had lower mean blood lead levels tended to report the greatest inverse linear slopes. The existence of a supralinear relationship is only 1 of several possible hypotheses to explain interstudy differences in slope, insofar as differences between study populations in the distributions of factors that modify lead neurotoxicity also could be contributory.[6] Using National Health and Nutrition Examination Survey data, however, Lanphear et al[7] showed that the magnitude of the estimated association between concurrent blood lead level and academic achievement in 6- to 16-year-olds was more steeply inverse when analyses were restricted to children with a blood lead level <2.5 μg/dL than when the analyses included all children with a blood lead level <10 μg/dL. The unavailability of data on critical confounders and on the participants' lead exposure histories limited the strength of the inferences that could be drawn from these analyses, however. In a subsequent prospective study in which such data were available among children whose blood lead levels, measured between 6 months and 5 years, never exceeded 10 μg/dL, a supralinear relationship was observed.[2] IQ at 5 years was estimated to decline 7.4 points up to 10 μg/dL but only 1.6 points between 10 and 30 μg/dL. A similar result was found in a reanalysis of the Boston prospective study that was limited to children whose blood lead levels never exceeded 10 μg/dL between birth and 10 years of age.[3] This pattern also was found in a pooled analysis of the data from 7 prospective studies.[8] Reanalyzing these pooled data, Rothenberg and Rothenberg[9] found that a log-linear relationship fit significantly better than did a linear model, consistent with a steeper slope at lower than at higher levels of lead. We report here on a subgroup of children who participated in a prospective longitudinal study in Mexico City, Mexico, for whom blood lead levels measured at both 12 and 24 months of age did not exceed 10 μg/dL, allowing us to contribute to the effort to characterize the functional form of the association between children's blood lead levels and neurodevelopment.

METHODS

Study Population

Participants in this study are members of 2 cohorts of women and their offspring from the Mexico City metropolitan area. The first cohort was recruited from January 1994 through June 1995, and the second was recruited from May 1997 through July 1999. Both cohorts were recruited from maternity hospitals that serve a low- to middle-income population (Mexican Social Security Institute, Manuel Gea Gonzalez Hospital, and National Institute of Perinatology). Mothers in cohort 1 were recruited at the time of delivery. Mothers in cohort 2 were recruited during or before pregnancy.

The following exclusion criteria were applied to both cohorts: mother not a resident of Mexico City; mother planning to leave the area within 5 years; daily consumption of alcoholic beverages; addiction to illegal drugs; continuous use of prescription drugs; diagnosis of multiple pregnancy, preeclampsia, renal or heart disease, gestational diabetes, seizures that require medical treatment; and use of corticosteroids. In addition, eligibility for cohort 1 was restricted to women who were not anemic and who consumed no less than 860 mg of calcium per day by self-report on a food frequency questionnaire. A total of 588 mother-infant pairs met these criteria.

To be included in the analyses described below, a child had to meet the following additional criteria: venous blood lead concentration <10 μg/dL at both 12 and 24 months of age, gestation of 37 weeks or longer, and birth weight >2000 g. Finally, data had to be available on the following variables: neurodevelopmental status at 12 and 24 months, umbilical cord blood lead level, and maternal IQ. A total of 294 mother-infant pairs met all criteria.

All mothers were informed about the nature and the aims of the study and given information on ways to minimize lead exposure. All signed a letter of informed consent. The research protocol was approved by the Ethics and Research Committees of the National Institute of Public Health of Mexico and by the Institutional Review Board of Harvard University School of Public Health.

Blood Lead Measurement

Umbilical cord blood and infant venous blood samples at 12 and 24 months of age were collected in trace metal–free tubes. Samples were analyzed by means of a graphite furnace atomic absorption spectrophotometry (model 3000; PerkinElmer, Norwalk, CT) at the American Brit-

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ish Cowdray Hospital Trace Metal Laboratory in Mexico City, following the technique described by Miller et al.[10] External blinded quality control samples, provided throughout the study period by the Maternal and Child Health Bureau and the Wisconsin State Laboratory of Hygiene Cooperative Blood Lead Proficiency Testing Program (Madison, WI), were used to assess the precision and the accuracy of the analytical methods. The laboratory standardization program provided external quality control specimens that varied from 2 to 88 μg/dL. The laboratory maintained acceptable precision and accuracy (correlation = 0.98; mean difference = 0.71 μg/dL; SD: 0.68).

Measurement of Child Development and Potential Confounders

At 12 and 24 months of age, each infant's development was assessed using the Bayley Scales of Infant Development II (BSID II).[11] The instructions and prompts were translated into Spanish by L.S.-A., the chief neurodevelopmental examiner in our research group, who also trained and supervised the personnel who administered the BSID II. Standardization and quality control checks were conducted by reviews of videotaped evaluations. Information was collected via maternal interview on demographic characteristics, socioeconomic factors, and other potential confounders of the relationship between lead and child development. Maternal IQ was calculated on the basis of a mother's scores on the Information, Comprehension, Similarities, and Block Design subtests of the Spanish Wechsler Adult Intelligence Scale.

Data Analysis

Differences between participants and nonparticipants were evaluated using *t* tests or Kruskal-Wallis tests for continuous or discrete variables, and χ^2 tests for categorical variables. Mental Development Index (MDI) and Psychomotor Development Index (PDI) scores were the primary dependent variables. Blood lead levels measured at 12 and 24 months were the primary exposure variables. Mixed-effects regression models with a random intercept were used to estimate the associations between blood lead levels and MDI or PDI scores at 12 and 24 months of age. This approach takes into account the within-subject correlation structure as a result of the repeated measurements, reducing bias in the estimation of the SEs. An interaction term was included to evaluate whether the association between blood lead level and concurrent MDI and PDI scores at 12 months differed from the associations between blood lead level and concurrent MDI and PDI scores at 24 months. Nonlead variables that were related to BSID II scores with $P < .1$ in bivariate analyses were included in multivariate models. We also included variables that were considered to be biologically relevant to the association between children's blood lead levels and their BSID II scores, regardless of their statistical associations with BSID II scores, such as maternal age and IQ and children's gender and birth weight.

To estimate the effect of lead on the change in mental and psychomotor development from 12 to 24 months, we generated linear regression models of both MDI and PDI at 24 months that included MDI and PDI at 12 months of age, respectively, as covariates. These allowed us to estimate the effect of recent lead exposure (ie, that reflected by the 24 month blood lead level) on neurodevelopment independent of any effects that were attributable to past exposures (as reflected by the 12-month blood lead level). Also, to evaluate the possibility of a lagged effect of lead on neurodevelopment, we also considered models of MDI and PDI at 24 months, which included lead concentration at 12 months of age, as the exposure variable.

Log-e transformed lead concentrations were used in modeling the relationships between concurrent blood lead and BSID II scores insofar as this parameterization provided the best model fits. The presence of nonlinearity in the relationship between concurrent blood lead and MDI or PDI was evaluated further by additional analyses of the 294 children, comparing them with 90 children who met all inclusion criteria but for whom blood lead level at 12 or 24 months was >10 μg/dL. In these last models, measured blood lead concentration, rather than log-transformed concentration, was used because it allows us to compare β coefficients in the various lead concentration ranges (which under the hypothesis of linearity should be the same). To test for differences in coefficients at various lead concentrations, we used a dummy variable to code blood lead range (<10 vs ≥10 μg/dL). The same approach was followed to compare regression coefficients in the ranges of 0 to 5 and 5 to 10 μg/dL blood lead. Analyses were performed using Stata 8.0 statistical software (Stata Corp, College Station, TX).

RESULTS

The analyses included 294 mother-infant pairs: 71 pairs from cohort 1 and 223 pairs from cohort 2. The characteristics of these 294 pairs are compared, in Table 1, with the characteristics of all pairs that were recruited into the 2 cohorts as well as with the characteristics of the pairs that did not fulfill the eligibility criteria for inclusion in the analyses. The most common reasons for exclusion from the analyses were an infant blood lead level >10 at 12 or 24 months or missing data on 1 or more critical variables. Women who participated were slightly older and more highly educated than those who did not, and mean umbilical cord blood lead level was significantly lower among participants.

In cohort 1, the mean blood lead level was 56% higher than that of cohort 2 at 12 months and 46% higher at 24 months. In cohort 1, the mean blood lead

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TABLE 1 **Characteristics of the Study Population**

Characteristics	Eligible		Nonparticipants		Participants ($N = 294$), Mean (SD)	P
	n	Mean (SD)	n	Mean (SD)		
Mothers						
IQ	794	87.38 (12.94)	500	87.04 (12.79)	87.97 (13.19)	.33[a]
Age, y	814	25.39 (5.20)	521	25.15 (5.25)	25.82 (5.08)	.07[b]
Years in school	815	10.26 (2.91)	522	10.09 (2.86)	10.57 (2.98)	.03[b]
Children						
Male gender, %	419	51.29	142	52.96	48.30	.20[c]
Birth weight, kg	814	3.12 (0.44)	294	3.11 (0.47)	3.16 (0.40)	.47[b]
Cord lead, μg/dL	583	5.49 (3.43)	294	6.14 (3.70)	4.85 (3.00)	<.01[b]
12 mo						
MDI	817	97.29 (9.36)	523	97.20 (9.41)	97.44 (9.29)	.74[b]
PDI	814	91.46 (9.86)	520	91.67 (10.43)	91.09 (8.77)	.94[b]
Blood lead, μg/dL	566	4.66 (2.87)	272	5.08 (3.44)	4.27 (2.14)	.08[b]
Hemoglobin, g/dL	472	12.05 (6.19)	263	11.64 (1.47)	11.96 (1.18)	.06[b]
24 mo						
MDI	817	91.59 (12.74)	523	90.92 (12.52)	92.78 (13.06)	.07[b]
PDI	815	95.16 (10.25)	522	94.43 (10.29)	96.46 (10.09)	.01[b]
Blood lead, μg/dL	752	5.78 (4.10)	458	6.74 (4.70)	4.28 (2.25)	<.01[b]
Hemoglobin, g/dL	688	12.48 (1.18)	432	12.52 (1.20)	12.40 (1.15)	.09[b]

[a] Student's t test.
[b] Kruskall-Wallis equality-of-populations test.
[c] χ^2 test.

level increased by 11% between 12 and 24 months, whereas the mean blood lead level in cohort 2 decreased by 6% during the same interval.

MDI

Results of the multivariate modeling of MDI, adjusting for birth weight, gender, age, and mother's IQ, are presented in Table 2. Blood lead level at 12 months was not significantly associated with 12-month MDI score ($P = .32$), but blood lead level at 24 months of age was inversely associated with 24-month MDI score ($P < .01$). The model predicted that an increase of 1 logarithmic unit in 24-month blood lead level was associated with a reduction of 4.7 points in MDI score at 24 months. The covariate-adjusted relationships between concurrent blood lead levels and their respective MDI scores are shown in Fig 1. A separate regression of 24-month blood lead level (untransformed) and 24-month MDI was conducted to permit comparison of the magnitude of the coefficient for 24-month blood lead level in 2 strata: <5 μg/dL and 5 to 10 μg/dL. The regression coefficient that was associated with blood lead concentrations in the range of <5 μg/dL was −1.71 ($P = .01$). Although the coefficient that was associated with concentrations in the range of 5 to 10 μg/dL was negative (−0.94), it was not significant ($P = .12$). Furthermore, the difference between the coefficients was not significant ($P = .34$).

The indicator variable that represented cohort was significant ($P = .04$), indicating that the MDI scores of the children in cohorts 1 and 2 differed. Stratified analyses showed that in neither cohort was 12-month blood lead level significantly associated with 12-month MDI

TABLE 2 **Longitudinal Models of MDI and PDI Scores at 12 and 24 Months ($n = 294$)**

Variable	MDI				PDI			
	β	P	95% CI		β	P	95% CI	
Blood lead level, μg/dL[a]								
At 12 mo[b]	−1.14	.32	−3.4	1.11	−0.42	.66	−2.31	1.46
At 24 mo	−4.70	<.01	−6.97	−2.44	−5.44	<.01	−7.35	−3.54
Birth weight, kg	1.24	.33	−1.27	3.74	2.37	.03	0.29	4.44
Gender (1 = male, 2 = female)	3.23	<.01	1.2	5.27	1.3	.13	−0.39	2.99
Age (1 = 24 mo, 0 = 12 mo)	−0.04	.98	−3.97	3.89	11.9	<.01	8.59	15.21
Mother's IQ	0.09	.03	0.01	0.16	0.02	.51	−0.04	0.09
Cohort	−2.73	.04	−5.31	−0.15	−2.64	.02	−4.78	−0.49
Intercept	87.4	<.01	75.23	99.57	84.95	<.01	74.84	95.07

CI indicates confidence interval.
[a] Log_e transformed.
[b] P value of the age × lead interaction: MDI model, $P = .01$; PDI model, $P < .01$.

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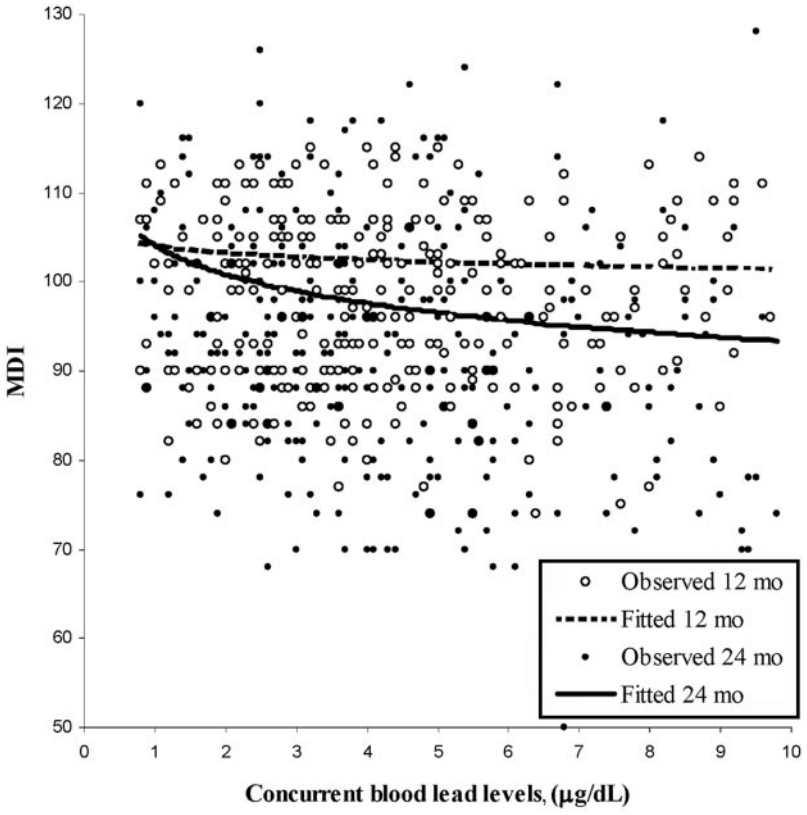

FIGURE 1
Concurrent blood lead levels versus MDI by age. Curves indicate the best-fit model for the association between concurrent blood lead levels and MDI scores, adjusting for gender, birth weight, cohort, and mother's IQ, by age.

score, and the overall association between 24-month blood lead level and 24-month MDI was attributed largely to the significant inverse association in cohort 2. The regression coefficient in cohort 2 was −4.7 ($P < .01$), compared with −0.1 ($P = .98$) in cohort 1.

Inclusion of umbilical cord blood lead level in the model indicated that it was not a significant predictor of MDI ($P = .5$); neither did its presence alter appreciably the coefficient for 24-month blood lead level as a predictor of 24-month MDI ($\beta = -4.58$, $P < .01$). Excluding the 15 children for whom umbilical cord blood lead level was >10 μg/dL also had little impact on the coefficient ($\beta = -4.4$, $P < .01$).

Concurrent blood lead levels seemed to have an impact on MDI scores independent of any effect that was associated with previous exposure to lead. Adjusting for MDI at 12 months, a log-unit increase in blood lead level at 24 months was associated with a 4-point drop in MDI scores ($\beta = -4.0$, $P < .01$), after adjustment for covariates. Also, concurrent blood lead levels seemed to be more strongly related to MDI scores at 24 months than was the blood lead level measured 1 year before insofar as lead level at 12 months did not significantly predict MDI score at 24 months ($\beta = -2.0$, $P = .16$), after adjustment for covariates.

At 12 months of age, the regression coefficient that was associated with concurrent blood lead levels <10 μg/dL did not differ significantly from the regression coefficient that was associated with blood lead levels ≥10 μg/dL (Table 3). At 24 months of age, however, the coefficient that was associated with concurrent blood lead levels <10 μg/dL was significantly larger (−1.04 vs 0.07; $P = .01$).

PDI

A similar series of analyses were conducted to assess the relationships between concurrent blood lead levels and PDI scores. In many respects, the findings were similar to those for MDI. Blood lead level at 24 months was inversely and significantly associated with PDI at 24

TABLE 3 **Comparison of the Coefficients of Concurrent Blood Lead in a Fitted Longitudinal Model of MDI and PDI at 12 and 24 Months of Age, at Various Lead Concentrations ($n = 384$ Children, 768 Observations).**

Model	<10 μg/dL		≥10 μg/dL		P^a
	β	P	β	P	
MDI					
12 mo	−0.15	.57	−.71	0.17	.33
24 mo	−1.04	<.01	.07	0.84	.01
PDI					
12 mo	−0.01	.98	−1.19	0.01	.02
24 mo	−1.18	<.01	.04	0.89	<.01

Lead concentrations were adjusted for gender, birth weight, and maternal IQ.
[a] *P* value for the comparison in coefficients at various ranges of lead concentration.

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months ($P < .01$), but 12-month blood lead level was not associated with 12-month PDI ($P = .66$; Table 2). The model indicated that an increase of 1 logarithmic unit in 24-month blood lead level was associated with a 5.4-point reduction in PDI at 24 months. The covariate-adjusted relationships between concurrent blood lead levels and PDI scores are shown in Fig 2. The estimated decline in PDI for blood lead levels <5 μg/dL ($\beta = -0.63$, $P = .26$) did not differ significantly ($P = .49$) from the estimated decline in the range of 5 to 10 μg/dL ($\beta = -1.09$, $P = .03$).

The indicator variable that represented cohort also was significant for PDI ($P = .02$), indicating that PDI scores of the children differed in the 2 cohorts. Stratified analyses showed that in neither cohort was 12-month blood lead level significantly associated with 12-month PDI score, although the association approached significance in cohort 2 ($\beta = -1.72$, $P = .06$). Although the inverse associations between 24-month blood lead level and 24-month PDI score were similar in magnitude in cohort 1 ($\beta = -4.1$, $P = .34$) and cohort 2 ($\beta = -4.0$, $P < .01$), the association was significant only in cohort 2.

Inclusion of umbilical cord blood lead level in the model indicated that it was a significant predictor of PDI, independent of concurrent lead exposure ($\beta = -1.5$, $P = .04$). Its inclusion, however, did not alter appreciably the association between 24-month blood lead level and 24-month PDI score ($\beta = -5.5$, $P < .01$). Excluding the 15 children for whom umbilical cord blood lead level was >10 μg/dL also had little impact on the coefficient for 24-month blood lead level ($\beta = -5.1$, $P < .01$).

As seen with respect to MDI, concurrent blood lead levels had an impact in the change in PDI score from 12 to 24 months. An increase in 1 log unit of lead level at 24 months was associated with a 2.5-point drop in PDI score, adjusting for PDI at 12 months of age. However, in contrast with the findings for MDI, blood lead level at 12 months was significantly associated with a 3-point drop in PDI score at 24 months of age ($\beta = -3.0$, $P = .01$), after adjustment for covariates.

At 12 months of age, the regression coefficient for concurrent blood lead level was significantly larger in the range of ≥10 μg/dL than in the range of <10 μg/dL (−1.19 vs −0.01; $P = .02$; Table 3). At 24 months of age, however, the coefficient was significantly larger in the range of <10 μg/dL (−1.18 vs 0.04; $P < .01$).

DISCUSSION

The major finding of these analyses is that among infants whose blood lead levels did not exceed 10 μg/dL at 12 or 24 months of age, scores on both the MDI and the PDI of the BSID II were inversely related to blood lead level at 24 months, adjusting for such covariates as maternal IQ, birth weight, gender, age, and umbilical cord blood lead level. The associations between MDI and PDI scores at 12 months and blood lead level at 12 months were consid-

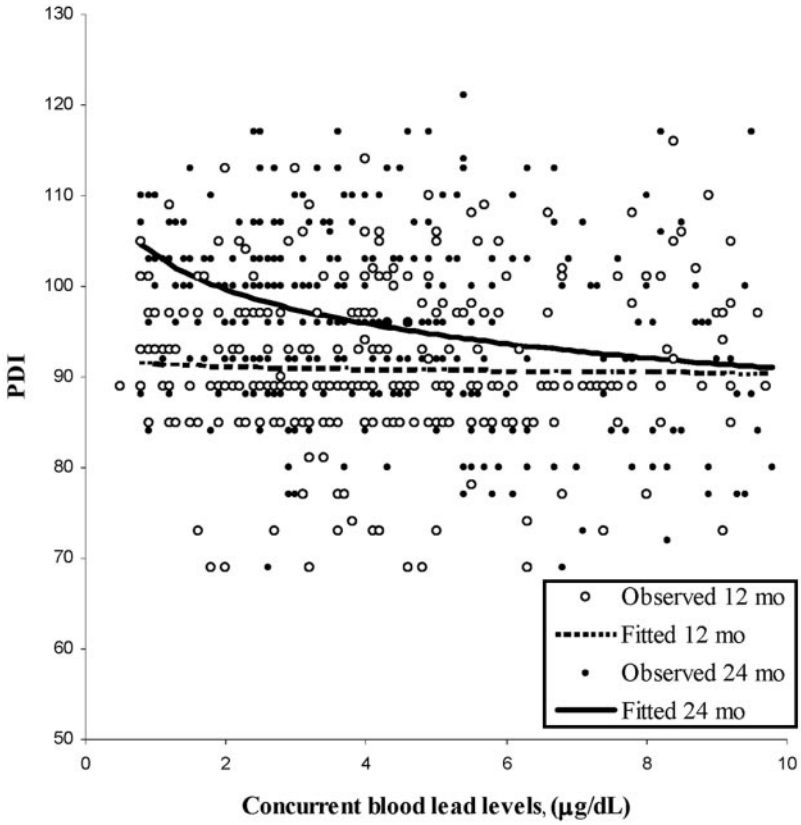

FIGURE 2
Concurrent blood lead levels versus PDI by age. Curves indicate the best-fit model for the association between concurrent blood lead levels and PDI scores, adjusting for gender, birth weight, cohort, and mother's IQ, by age.

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erably weaker in magnitude, and neither was statistically significant. The inverse association between blood lead level at 12 months of age and PDI score at 24 months of age was significant, however. In addition, 24-month blood lead level remained a significant predictor of both MDI and PDI scores at 24 months even when adjustments were made for the MDI or PDI scores that children achieved at 12 months. This suggests that the associations reflect deficits that are attributable to recent lead exposure (eg, exposure that occurred between 12 and 24 months) rather than to exposures that occurred before 12 months of age.

The magnitudes of the inverse associations between 24-month blood lead level and both 24-month MDI and PDI were not the same across the blood lead range. The regression coefficients were significantly larger among children whose blood lead levels were <10 μg/dL than among children for whom blood lead level at 12 and/or 24 months was ≥ 10 μg/dL. The findings were not consistent in the 12-month data. For MDI, the coefficients within the 2 blood lead ranges did not differ. For PDI, the coefficient was significantly greater at blood lead levels ≥ 10 μg/dL. These findings in some respects are similar to those in previous studies, suggesting a possible supralinear functional form.[2,3] The primary mechanism of lead neurotoxicity is likely to differ depending on dose. It is possible that neurotoxicity at doses that correspond to blood lead levels <10 μg/dL involves an exquisitely sensitive pathway that is saturated rapidly and that other mechanisms are involved at doses that correspond to higher blood lead levels. A set of dose-dependent mechanisms that might account for supralinearity in the dose-effect relationship has not been identified, however.

The inverse association between 24-month blood lead level and 24-month BSID II scores was more evident in cohort 2 than in cohort 1. Cohort 2 contributed >75% of the mother-infant pairs included in these analyses, resulting in considerably greater power in the analyses that involved cohort 2 than in those that involved cohort 1. This disproportionate representation between the cohorts is attributable to the decline in lead exposures in Mexico City during the 1990s, with a larger proportion of infants in cohort 2 than in cohort 1 having blood lead levels that remained <10 μg/dL. The mean umbilical cord blood lead level of infants in cohort 2 also was only two thirds that of infants in cohort 1. Although we adjusted for umbilical cord blood lead level, it is possible that the higher prenatal exposures of infants in cohort 1 reduced our ability to appreciate the association between infants' postnatal blood lead levels and their BSID II scores.

In most prospective studies, children's blood lead levels were not significantly associated with their PDI scores.[12–14] Nevertheless, assessments that have conducted at older ages often have revealed inverse associations between children's blood lead levels and their scores, at later ages, on tests of motor development or visual-motor skills.[15–18]

Limited consensus exists on the nature of age-dependent variation in vulnerability to lead neurotoxicity. In the Boston prospective study, blood lead level at 24 months of age was more predictive of IQ at 5 and 10 years of age than were levels that were measured before or after 24 months. In that study, however, 24-month blood lead level did not predict concurrent MDI score, as it did in the present analyses. In the Port Pirie prospective study, lifetime lead exposure through 24 months of age consistently predicted neurodevelopmental scores between 24 months and 11 to 13 years.[19] In other studies, 24-month blood lead level did not seem to be more predictive than levels that were measured at other ages.[2,20,21] Factors such as pattern and level of lead exposures, co-exposures to other developmental risk factors, and other differences between study cohorts might account for inconsistencies across studies.

Because blood lead level was measured only twice between birth and 24 months of age, it is possible that, for some children, the level exceeded 10 μg/dL but had fallen below 10 μg/dL by the time of our measurement. To the extent that such exposure misclassification occurred, the coefficients that we estimated will not describe accurately the association between neurodevelopment and blood lead levels <10 μg/dL. Because our study necessarily was observational, the possibility of residual confounding by unmeasured or poorly measured factors cannot be dismissed. Adjustments were made, however, for many of the variables that were identified as key potential confounders in previous lead studies.

CONCLUSIONS

Among infants whose blood lead levels at 12 and 24 months were <10 μg/dL, we found inverse associations between 24-month blood lead level and concurrent MDI and PDI scores on the BSID II. These findings thus provide additional evidence that 10 μg/dL should not be viewed as a biological threshold for lead neurotoxicity. Furthermore, for MDI but not PDI, the association seemed to be supralinear, with the steeper inverse slope over the range up to 5 μg/dL than over the range between 5 and 10 μg/dL.

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