Low-Level Lead Exposure and Children's Cognitive Function in the Preschool Years

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ABSTRACT. In a cohort of 170 middle and upper-middle class children participating in a prospective study of child development and low-level lead exposure, higher blood lead levels at age 24 months were associated with lower scores at age 57 months on the McCarthy Scales of Children's Abilities. The mean blood lead level at age 24 months was 6.8 μg/dL (SD = 6.3; 75th, 90th, and 99th percentiles: 8.8, 13.7, 23.6, respectively) and for all but 1 child was less than 25 μg/dL, the current definition of an "elevated" level. After adjustment for confounding, scores on the General Cognitive Index decreased approximately 3 points (SE = 1.4) for each natural log unit increase in 24-month blood lead level. The inverse association between lead level and performance was especially prominent for visual-spatial and visual-motor integration skills. Higher prenatal exposures were not associated with lower scores at 57 months except in the subgroup of children with "high" concurrent blood lead levels (ie, ≥10 μg/dL). The concentration of lead in the dentine of shed deciduous teeth was not significantly associated with children's performance after adjustment for confounding. *Pediatrics* 1991;87:219–227; *lead, development, epidemiology, toxicology.*

ABBREVIATIONS. MDI, Mental Development Index; HOME, Home Observation for Measurement of the Environment; GCI, General Cognitive Index; DFFITS, the change in the predicted score for a child resulting from the deletion of that child from the data set used to calculate coefficients; DFBETAS, the change in the regression coefficients resulting from the deletion of a particular child.

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Findings from several prospective studies suggest that fetal or early postnatal lead exposure is associated with slower early cognitive development.[1-3] The Agency for Toxic Substances and Disease Registry[4] and the Environmental Protection Agency[5] of the United States have concluded that children's risk of developmental problems is increased at blood lead levels of 10 to 15 μg/dL, well below the current definition of an "elevated" level in young children.[6]

Although slower early cognitive growth is clearly an "adverse health effect," its usefulness in predicting children's later intellectual status is limited.[7] The public health risk posed by so-called "subclinical" lead exposures cannot be fully evaluated without knowing whether the associated developmental difficulties persist into the later preschool and school-age periods. Identifying factors that modify the development of a lead-exposed child is a critical part of this effort.

We studied a cohort of middle and upper-middle class children from birth to approximately 5 years of age, periodically assessing their development and lead exposure. Through 24 months of age, children with umbilical cord blood lead levels between 10 and 25 μg/dL displayed modest but persistent cognitive deficits on the Mental Development Index (MDI) of the Bayley Scales of Infant Development.[1] Blood lead levels measured postnatally were not associated with children's performance during this period. We report here that at age 57 months, the association between prenatal lead exposure and children's cognitive function diminished greatly in the cohort as a whole, except among children with higher concurrent lead exposure. Higher blood lead

levels at age 24 months were associated with significantly lower performance at age 57 months.

METHODS

Sample Selection

The children who participated in the 57-month follow-up assessment were part of a cohort of 249 children recruited from 1979 to 1981 from the delivery population of the Brigham and Women's Hospital (Boston, MA). Newborns meeting the following criteria were eligible for enrollment in the cohort: (1) umbilical cord blood lead concentration <3 μg/dL, 6 to 7 μg/dL, or ≥10 μg/dL (approximately the 10th, 50th, and 90th percentiles, respectively); (2) absence of a medical condition known to increase the risk of developmental problems; (3) English-speaking mother; and, (4) residence within 12 miles of Boston, but outside of specified inner-city neighborhoods or housing projects. Eligible children who were not enrolled differed minimally from children enrolled in the cohort.[8]

Follow-up assessments of this cohort were conducted when the children were 1, 6, 12, 18, and 24 months old. The 204 children who participated in the 24-month follow-up constitute the base population for the 57-month evaluation (Fig 1). Thirteen children were considered ineligible. Three infants had serious medical problems diagnosed within the first 2 years of life. Because the development of twins tends to differ from that of singletons,[9] five sets of twins were not followed up. These 13 children had been excluded from statistical analyses of previous evaluations.

Of the 191 children considered eligible for the 57-month evaluation, at least partial data were obtained on 170. Evaluations were not conducted on the other 21 children because of a family residence change, our inability to obtain consent, or failure to locate a family. Nonparticipants and participants differed significantly on only two social class indicators or demographic characteristics (Table 1). Participants at 57 months were assigned significantly higher total scores than nonparticipants on the Home Observation for Measurement of the Environmnent (HOME) scale administered at 24 months, and a significantly higher percentage of participants were white. The postnatal blood lead levels of participants were generally higher than the levels of nonparticipants.

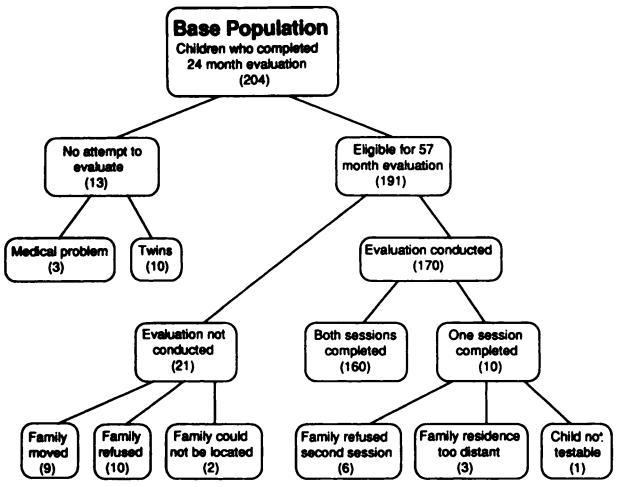

Fig 1. Attrition of the sample between ages 24 and 57 months.

Data Collection

The full battery of developmental tests was administered in a fixed order distributed over two sessions, the first at The Children's Hospital and the second in a child's home. To accommodate parents' wishes, first-session tasks were administered to 4 children in their homes. Second-session data were not obtained for 10 of the 170 children. Parents of 6 children agreed only to a single session. For three families who had moved to other states, the first session was scheduled to coincide with a return visit to Boston. Second sessions could not be scheduled within the limited time of these visits and the new homes of these families were too distant to conduct home visits. Second-session data were not collected for 1 child whose developmental difficulties precluded the completion of session 1.

A single examiner who was blind to all aspects of the children's lead exposure and developmental histories conducted the assessments. The median age of the children was 1777 days (SD = 63) at session 1 and 1796 days (SD = 63) at session 2. Children's performance on the McCarthy Scales of Children's Abilities,[10] the primary outcome in this evaluation, is the major focus of this report. It yields a General Cognitive Index (GCI) and five subscale scores: Verbal, Perceptual-Performance, Quantitative, Memory, and Motor.

At the conclusion of the first session, a 5-mL venous blood sample was obtained from 151 children. Parents of the remaining 19 children refused to grant consent for this procedure. Samples were collected using "butterfly" needles and Vacutainers treated with anticoagulant (Becton-Dickinson blue-top tubes). Lead was measured in duplicate by graphite furnace atomic absorption spectrophotometry (Perkins Elmer, Norwalk CT, model 5000 spectrophotometer). The sample was diluted threefold with 0.1% Triton X-100 and an ammonium phosphate matrix modifier. A L'vov oven platform and a Zeeman effect background corrector were used. An aliquot of a standardized blood sample provided

TABLE 1. Comparison of Participants and Nonparticipants in 57-Month Assessment

Characteristic	Participant (n = 170)	Nonparticipant (n = 21)	*P* value†
Social class 1, %	53.0	47.6	.80
Mother employed, %	55.4	42.9	.19
Receiving nonparent care, %	42.3	47.6	.82
Male, %	51.2	47.6	.60
Mother not married, %	7.1	9.5	.65
Only child, %	45.2	42.9	.98
White, %	81.0	81.0	.024
Postcollege education, %			
Father	46.4	47.4	.90
Mother	31.0	23.8	23.8
Maternal age at child's birth, y (mean ± SD)	30.2 ± 4.4	30.4 ± 6.4	.92
Maternal IQ (mean ± SD)	123.9 ± 16.5	114.8 ± 24.7	.12
HOME total at 24 mo (mean ± SD)	37.3 ± 3.0	35.3 ± 2.7	.005
Family stress index* (mean ± SD)	87.2 ± 83.0	78.7 ± 55.5	.54
Birth weight, g (mean ± SD)	3442.8 ± 487.0	3482.8 ± 548.4	.73
Gestational age, wk (mean ± SD)	40.0 ± 1.7	39.9 ± 2.0	.70
Mental development index at 24 mo (mean ± SD)	116.3 ± 16.2	110.4 ± 17.3	.13
Prior blood lead			
High cord blood lead, % ≥ 10 μg/dL	32.7	20.0	
6 mo (mean ± SD)	6.8 ± 7.3	3.0 ± 3.0	.003
12 mo (mean ± SD)	7.8 ± 6.4	6.3 ± 8.1	.10
18 mo (mean ± SD)	8.0 ± 5.7	4.0 ± 3.7	.0003
24 mo (mean ± SD)	7.0 ± 6.6	4.0 ± 2.8	.035

* Social Readjustment Rating Scale (Holmes T, Rahe R. *J Psychsom Res* 1967;11:213–218).
† *P* value based on natural log transformation of measured values.

by the National Bureau of Standards was included in each batch of samples. Over the course of the analyses, the mean lead concentration in the standard was 12.9 μg/dL (SD = 0.98; SE = 0.30). The certified value of the standard was 13.0 μg/dL. Zinc protoporphyrin was measured by hematofluorometry (Environmental Sciences Associates Hematofluorometer model 4000, Bedford, MA).

One or deciduous teeth were obtained from 102 children (95 primary incisors, 7 uncertain). Two 10- to 15-mg samples of postnatal dentine were harvested by making two cuts from below the enamel-cementum junction to an area between the top of the pulp cavity and the crown. The lead content of these samples was determined by anodic stripping voltammetry (ESA model 3010A) using a method described elsewhere.[11] Laboratory performance was monitored by including blank tubes, aqueous lead standards, and a lead-enriched calcium-chloride standard in each batch of samples. The concentration of lead in the standards was determined by isotope dilution mass spectrophotometry by Professor William Manton. Using this reference method, the lead content of the calcium-based standard was determined to 5.52 μg/g (SD = 0.04). The mean of values obtained in our laboratory was 5.48 μg/g (SD = 0.38).

If the values obtained for the lead concentration in the two dentine specimens differed by less than 2.5 μg/g, they were averaged. If the difference was greater, two additional portions of tooth were analyzed and the three most similar values averaged.

As at previous assessments,[12] the children's blood lead levels were quite low (Table 2). Only 28 children (18.7%) had a level greater than 10 μg/dL. Six (4.0%) had a value greater than 15 μg/dL, and none exceeded 25 μg/dL. The correlations between a child's blood lead level at 57 months and blood lead levels at younger ages were modest, varying from .18 (for blood lead level at 6 months of age) to .29 (for blood lead level at 12 months of age).

The children's mean GCI score was nearly 1 SD above the expected population mean of 100 (Table 3). This is comparable with the children's performance on the MDI of the Bayley scales at age 24 months (mean = 115.6, SD = 16.4).

Statistical Analyses

In selecting variables to consider as potential confounders of an association between lead exposure and McCarthy scores, procedures described elsewhere were used.[13] Briefly, two sets of variables were identified. First, the associations between approximately 60 variables and both children's GCI scores and current blood lead levels were examined.

TABLE 2. Additional Characteristics of Participants

Characteristic	n	Mean	SD	Range
Blood measurements at 57 mo				
Blood lead, μg/dL	150	6.4	4.1	0–23.3
Erythrocyte protoporphyrin, μg/dL	151	6.7	5.6	0–33
Hematocrit, %	149	44.9	2.4	38–50
Serum ferritin, ng/mL	148	22.4	13.8	4.2–106.4
First tooth submitted				
Dentine lead, μg/g	102	2.8	1.7	0.3–12.8
Development at 57 mo				
General cognitive index	169	115.5	14.5	80–150
Verbal	169	59.7	10.0	32–78
Perceptual-Performance	169	57.6	8.7	32–78
Quantitative	169	57.8	8.0	37–78
Memory	169	56.4	9.0	34–77
Motor	169	50.6	8.5	29–74

TABLE 3. Least-Squares Adjusted Mean General Cognitive Index Scores (±SE) of Children Classified by Various Measures of Lead Exposure*

Age at Blood Lead Measurement	Blood Lead Category		
	Low (<3 μg/dL)	Medium (3.0–9.9 μg/dL)	High (≥10 μg/dL)
Birth	117.6 ± 1.8	114.6 ± 1.7	116.2 ± 1.8
6 mo	114.9 ± 1.7	118.3 ± 1.6	112.5 ± 2.4
12 mo	119.8 ± 2.0	114.5 ± 1.5	116.8 ± 1.9
18 mo	119.5 ± 2.1	114.2 ± 1.4	116.8 ± 1.9
24 mo	120.0 ± 2.1	115.5 ± 1.3	113.6 ± 2.3
57 mo	118.9 ± 2.6	114.9 ± 1.4	115.3 ± 2.8

* Adjusted for family social class, maternal IQ, marital status, preschool attendance, HOME total, hours per week of "out-of-home" care, number of family residence changes, recent medication use, number of adults in household, gender, race, birth weight, birth order.

This list was reduced to 23 variables that were related to both GCI and lead at a significance level of $P < .25$. An additional reduction was achieved by pruning from the list highly collinear sets of variables. For instance, the total score and all scale scores of the HOME except scale 2 were associated with both GCI and lead, as well as with one another. Therefore, the total score was used as a single expression for all that is measured by the HOME. Similarly, several indices of sociodemographic status (eg, father's and mother's occupations and educational achievements) were highly redundant and combined into a single index of family social class (Hollingshead Index of Social Class). This data-based method of selecting potential confounders resulted in a parsimonious set of 8 variables: family social class, maternal IQ, preschool attendance, HOME score (total), hours per week of "out-of-home" care, number of family residence changes since the child's birth, medication use in the preceding month, and the number of adults in the household.

Five additional variables were included in models of children's performance: gender, race (white/non-white), birth weight, maternal marital status, and birth order. These were selected based on subject matter considerations, regardless of the significance of their associations with lead exposure or GCI scores in this cohort.

Multiple regression was used to model children's GCI scores as well as the five subscale scores. All 13 potential confounders were included in each model, along with one or more lead variables. Umbilical cord blood lead group (low, medium, high) was coded by two indicator variables. The postnatal blood lead levels measured at 6, 12, 18, 24, and 57 months of age were transformed to natural logarithms.

Care was taken to ensure that the results were not unduly influenced by the data of individual children. Collinearity and influence diagnostics were computed for models in which the regression coefficient for a lead term was statistically significant. These included studentized residuals (the difference between a child's predicted and observed scores), the change in the predicted score for a child resulting from the deletion of that child from the data set used to calculate coefficients (DFFITS),

the change in the regression coefficients resulting from the deletion of a particular child (DFBETAS), and partial regression leverage plots (plot of McCarthy scale score vs lead after both are rendered statistically independent of the other variables in the model).[14] Models were refitted after deletion of highly influential observations (|studentized residual| ≥2, |DFFITS| ≥.622 in this data set, and |DFBETA| ≥.161 in this data set).

To appreciate nonlinearities in the association between lead level and development, additional models were fitted in which lead terms were coded as categorical variables ("low": <3 μg/dL; "medium": ≥3 but <10 μg/dL; "high": ≥10 μg/dL). Least-squares adjusted means were calculated to illustrate the level of performance of children in different lead exposure categories as well as the magnitude of performance differences between children in different categories.

To assess the contributions of children's average level of lead exposure over various age spans to the multiple regression model of children's GCI scores, five additional exposure indices were calculated: the natural logarithm of the mean of blood lead levels at (1) 57 and 24 months; (2) 57, 24, and 18 months; (3) 57, 24, 18, and 12 months; (4) 57, 24, 18, 12, and 6 months; and (5) 57, 24, 18, 12, 6 months, and birth. Equal weight was given to blood lead levels at all ages, although the measurement interval is not constant and children's blood lead levels typically peak in the 18- to 36-month period. The strategy of equal weighting was considered acceptable in this cohort, however, in view of the consistency in the mean blood lead levels over this age span (Table 1).

RESULTS

Prenatal Exposure

Cord blood lead grouping (low, medium, high) was not significantly associated with GCI scores on the McCarthy scales (P = .49, Table 3) or with scores on any of the subscales.

Postnatal Exposure

Although children's MDI scores within the first 24 months were not associated with early postnatal measures of lead exposure, GCI scores at age 57 months were. In unadjusted analyses, higher blood lead levels at ages 18, 24, and 57 months and a higher tooth lead level were significantly associated with lower scores (Table 4). After adjustment for covariates, however, only the partial regression coefficient for blood lead level at 24 months of age remained statistically significant (P = .04). The least-squares (adjusted) mean GCI score of children with "low" blood lead levels at age 24 months (<3 μg/dL) was 6.4 points higher than the mean GCI score of children with "high" blood lead levels at that age (≥10 μg/dL). The coefficients for the other exposure indices remained negative, but for each the lower bound of the 95% confidence interval included 0. The impact of adjustment on the regression coefficient was particularly marked in the case of tooth lead level.

The partial regression coefficient for blood lead level at 24 months was not appreciably affected by deleting the 5 observations with large studentized residuals (−2.88, SE = 1.28), the 12 observations with large DFFITS (−2.44, SE = 1.30), the 8 obser-

TABLE 4. Mean Change in General Cognitive Index Scores (±SE) for Each Natural Log Unit Increase in Lead Level at Various Ages

Index of Lead Exposure	Regression Coefficient		
	Unadjusted (P Value)	Adjusted* (P Value)	95% Confidence Interval (Adjusted)
Blood			
6 mo	0.26 ± 1.37 (.85)	0.28 ± 1.29 (.83)	−2.3, 2.8
12 mo	−2.17 ± 1.32 (.10)	−1.43 ± 1.25 (.25)	−3.9, 1.0
18 mo	−3.02 ± 1.50 (.045)	−1.62 ± 1.39 (.25)	−4.3, 1.1
24 mo	−3.10 ± 1.49 (.039)	−2.95 ± 1.42 (.040)	−5.7, −0.2
57 mo	−4.27 ± 1.96 (.031)	−2.28 ± 1.88 (.23)	−6.0, 1.4
Dentine	−10.04 ± 3.78 (.009)	−2.51 ± 3.91 (.52)	−10.2, 5.2

* Adjusted for family social class, maternal IQ, marital status, preschool attendance, HOME total, hours per week of "out-of-home" care, number of family residence changes, recent medication use, number of adults in household, gender, race, birth weight, birth order.

vations with large DFBETAS for the 24-month lead term (−2.77, SE = 1.48), or the child with a 24-month blood lead level greater than 25 μg/dL (−2.88, SE = 1.49).

Much of the association between blood lead level at 24 months and GCI score appeared to be due to the association between this measure of lead exposure and children's scores on the Perceptual-Performance subscale of the McCarthy scales (Table 5). Blood lead level at 57 months was also significantly associated with scores on this subscale.

The indices of mean lead exposure integrated over various age spans were not more strongly associated with GCI (Table 6) than was blood lead level at 24 months alone (Table 4). The standard error of the partial regression coefficient for the lead term consistently increased as prior blood lead levels were added to the integrated index.

Serum ferritin was measured to evaluate the hypothesis that any developmental problems associated with higher lead exposure are due not to lead but to the adverse effects of iron depletion on children's cognition. Because ferritin was not significantly associated with either concurrent blood lead level or GCI score, it is not a confounder in this data set. Children with low ferritin values (<15 ng/mL) had a mean blood lead level of 6.7 μg/dL (SD = 3.9), and children with ferritin values in the normal range had a mean blood lead level of 6.4 μg/dL (SD = 4.3) (t = 0.47, df = 143, P = .64). The mean GCI scores of the children in the two groups were 116.1 (SD = 14.3) and 115.1 (SD = 15.1), respectively (t = 0.36, df = 145, P = .72).

TABLE 5. Mean Change in McCarthy Subscale Scores (±SE) for Each Natural Log Unit Increase in Blood Lead Level at 24 and 57 Months of Age*

McCarthy Subscale	Age at Blood Lead Measurement	
	24 mo	57 mo
Verbal	−0.41 ± 1.04 (.69)	−1.06 ± 1.38 (.44)
Perceptual-Performance	−2.58±0.88 (.004)	−2.33 ± 1.13 (.042)
Quantitative	−1.45 ± 0.85 (.09)	0.13 ± 1.13 (.91)
Memory	−0.66 ± 0.94 (.49)	0.49 ± 1.25 (.70)
Motor	−0.90 ± 0.92 (.33)	−1.89 ± 1.15 (.10)

* Adjusted for family social class, maternal IQ, marital status, preschool attendance, HOME total, hours per week of "out-of-home" care, number of family residence changes, recent medication use, number of adults in household, gender, race, birth weight, birth order. P values are given in parentheses.

TABLE 6. Mean Change in General Cognitive Index Scores (±SE) Associated with Each Natural Log Unit in the Mean of Blood Lead Levels Over Various Age Spans

Interval for Which Blood Lead Levels Integrated	Adjusted* Regression Coefficient	P Value
Birth to 57 mo	−2.76 ± 2.41	.25
6 to 57 mo	−2.33 ± 2.22	.30
12 to 57 mo	−2.17 ± 1.98	.28
18 to 57 mo	−2.94 ± 1.91	.13
24 to 57 mo	−2.80 ± 1.59	.08

* Adjusted for family social class, maternal IQ, marital status, preschool attendance, HOME total, hours per week of "out-of-home" care, number of family residence changes, recent medication use, number of adults in household, gender, race, birth weight, birth order.

DISCUSSION

Up to age 24 months, children's scores on the MDI of the Bayley scales were inversely related to level of prenatal lead exposure. Between 24 and 57 months, however, the association attenuated. At age 57 months, children's scores on the McCarthy Scales of Children's Abilities were not significantly related to their umbilical cord blood lead levels. Whereas no measure of children's postnatal lead exposure was associated with MDI scores at 24 months, blood lead level at 24 months of age was inversely related to GCI score at 57 months.

We conducted an additional set of analyses to understand better why the association between prenatal exposure and cognitive performance changed during the interval between 24 and 57 months. We modeled change in children's performance over this period as a function of umbilical cord blood lead level and lead levels at different postnatal ages. Briefly, a child's MDI score at 24 months was subtracted from his or her GCI score at 57 months. These difference scores were then regressed on MDI at 24 months (as a measure of initial level) and various postnatal lead terms, including interaction terms combining lead levels measured at different ages (eg, cord blood lead group × 57-month blood lead level). (This analysis was carried out using a simple difference score rather than the difference between z-transformed scores because GCI and MDI are both scaled to have a mean of 100 and a standard deviation of 16.)

The extent to which children with "high" levels of prenatal exposure "recovered" from deficits manifested at age 24 months varied with level of concurrent lead exposure. Among these children, performance change between 24 and 57 months varied in a dose-effect fashion with 57-month blood lead level (Fig 2) (partial regression coefficient: −0.46, SE = 0.18, P = .013). Among children with "low" or "medium" prenatal exposure, the partial regres-

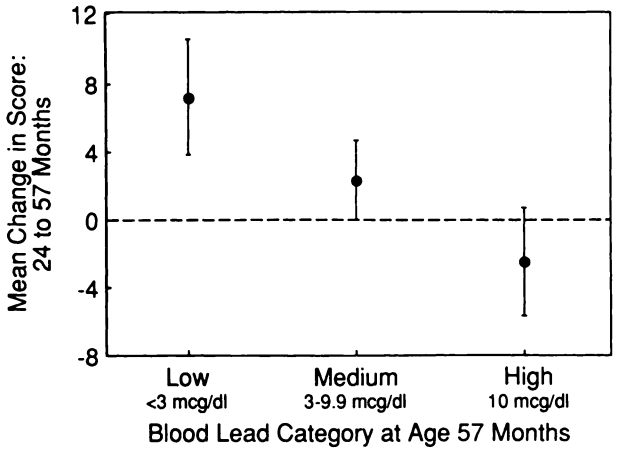

Fig 2. Mean change between Mental Development Index scores at age 24 months and General Cognitive Index scores at age 57 months in children classified by blood lead level at age 57 months. Only children whose umbilical cord blood lead levels exceeded 10 μg/dL (i.e., "high") are included. The numbers of children in the low, medium, and high 57-month blood lead groups are 5, 28, and 14, respectively.

sion coefficients were −0.16 (SE = 0.14, P = .26) and −0.14 (SE = 0.22, P = .52), respectively. A similar "recovery" phenomenon among children with high prenatal lead exposure was recently reported by Shukla et al[15] in a study of early postnatal growth.

Social factors were also associated with degree of recovery. Males improved less than females between 24 and 57 months, and children below the median in terms of social class, HOME score, and maternal IQ improved less than children with values above the median. These data are consistent with previous observations suggesting that children from less advantaged circumstances express deficit at lower blood lead levels than do children in higher social strata.[2,16] These data furthermore suggest that the deficit is more persistent, at least in the preschool years. A more complete description of the methods and results of these analyses is available elsewhere.[17]

Our overall findings are similar to those reported by McMichael et al.[3] In a cohort of children living near a lead smelter in Port Pirie, South Australia, GCI score at age 4 years was inversely related to an integrated average of postnatal blood lead levels, especially blood lead levels at 2 to 3 years of age. Scores were not significantly related to umbilical cord blood lead level, maternal blood lead level at delivery, or an index of average antenatal exposure. Although the exposures of the Australian children were considerably greater than those of the children in the Boston cohort, the slopes of the regression lines describing the relationship between postnatal lead levels and GCI score are similar in the two studies. In the Australian study, an increase in blood lead level from 10 to 31 μg/dL was associated with a decrease of 7.2 GCI points at age 4 years. In the Boston cohort, an increase from 3 to 20 μg/dL (ie, 2 natural log units) at 24 months of age was associated with a decrease of 5.9 GCI points at 57 months.

In both the Port Pirie study and ours, the association between higher postnatal lead levels and lower scores was especially strong for the Perceptual-Performance subscale of the McCarthy scales. Most of the items contributing to this subscale assess visual-spatial and visual-motor integration skills. In our cohort, item analyses of children's performance on the Bayley scales at previous assessments have consistently identified nonverbal skills as the domain of function most strongly associated with lead exposure.[8,18]

Discrepant findings have been reported from a prospective study of disadvantaged children in Cleveland. In that cohort, children's cognitive performance in the preschool years was not significantly associated with any measure of prenatal or postnatal lead exposure.[19] Differences between the findings of the Cleveland study, and both the Port Pirie and Boston studies, may be due to the high prevalence (50%) of alcohol abuse among mothers in the Cleveland sample.

In several studies, tooth lead level has proved to be a significant predictor of certain aspects of children's neuropsychologic function.[20–24] There are several possible explanations for why this was not the case in our study. First, the dentine lead concentrations in our subjects' teeth were lower than those measured in most studies. Children's cognition may be unaffected by lead at these levels. Second, teeth were available for only 102 children, so inadequate power may have contributed to our failure to observe an association. Children for whom teeth were not available had slightly lower GCI scores. Their exclusion from the analyses resulted in some range restriction, further reducing the likelihood of detecting a significant association between GCI scores and tooth lead levels. Children who provided teeth differed little from those who did not in terms of blood lead histories or family characteristics, however. A third explanation concerns the information about exposure history that is conveyed by a child's tooth lead level. Although it is usually assumed that tooth lead is an index of a child's cumulative postnatal exposure, data from our cohort do not fit a simple accumulation model. Instead, dentine lead level is most strongly associated with children's relatively recent exposure (ie, 57-month blood lead level), supporting a model that

permits lead to be removed from dentine. Thus, discrepancies in the results of studies examining the association between dentine lead level and children's neuropsychologic function may reflect differences in dose and in the extent to which dentine lead level truly reflects exposure at younger ages.

Our ability to detect associations between prenatal lead exposure and early cognitive development may have been increased by the unusual patterns of covariance between prenatal lead exposure and potential confounders in our cohort. In contrast to the usual pattern, higher exposures were associated with the absence of other risk factors for developmental difficulties. Therefore, at earlier ages, adjustment tended to increase rather than decrease the estimate of lead's association with development.[25] The covariance pattern in this cohort has changed over time, however, and now resembles more closely the pattern seen in other cohorts. For example, the 6-month HOME score was positively related to umbilical cord and early postnatal blood lead level. The HOME score at 57 months, however, was inversely related to tooth lead level ($r = -.49$). Once 57-month HOME score was included in the regression model, the coefficient for dentine lead, which was highly significant in bivariate analyses, became indistinguishable from zero. This suggests that in a prospective study, it is important to remeasure covariates that may vary over time, as well as to reevaluate as potential confounders variables not found to be confounders at previous assessments.

Our findings suggest that early developmental problems associated with umbilical cord blood lead levels exceeding 10 μg/dL may not persist until age 57 months in children whose postnatal lead exposures are low (ie, below 10 μg/dL). In addition, high social class standing is associated with greater recovery from early developmental problems. On the other hand, higher postnatal exposures, particularly at 24 months of age, were associated with poorer performance at age 57 months regardless of children's social standing. The mean blood lead level in our cohort at 24 months of age was 6.8 μg/dL (SD = 6.3; 90th percentile: 13.7).

The Agency for Toxic Substances and Disease Registry estimated that in 1984 the blood lead levels of 3 to 4 million US preschool children exceeded 15 μg/dL.[4] Unfortunately, a relatively small percentage of children enjoy the social and economic advantages of the children in our cohort. Moreover, most children who suffer high exposure to lead early in life have comparable exposure opportunities throughout childhood. Thus, our findings, which pertain to children living in optimal circumstances, reflect the "best case" scenario. They may be largely irrelevant to the task of predicting the developmental prognosis for the large population of children at greater risk of having lead-induced cognitive problems.

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POTTER'S FIELD 1990

Inmates in orange jumpsuits moved briskly, spoke little and didn't smile. In armfuls of three, they unloaded 53 foot-long pine boxes from the rear of a Ford dumptruck onto the muddy ground. For 50 cents an hour, they were burying New York City's poorest infants...

The little coffins had pink labels pasted on them. Some had names...

Burials of indigent infants are increasing considerably faster than those of poor adults, also on an upswing. Last year 1,606 babies were buried on Hart Island; in 1986, the number was 1,128.

"There is no question that it is directly linked to the drug epidemic"...

The name potter's field comes from the Bible, Matthew 27:6–7. The chief priests of Jerusalem said that it was wrong to put the 30 pieces of silver that Judas had received for betraying Jesus into the general treasury. So the money was used to buy a field from a potter "to bury strangers in."

Martin D. A heavy burden: Burying Eileen, Sam, Liz and F/C. *The New York Times.* March 29, 1990.

Noted by J.F.L., MD