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Lead Exposure and Neurobehavioral Development in Later Infancy

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A prospective methodology was used to assess the neurobehavioral effects of fetal and postnatal lead exposure during the first 2 years of life. Lead was measured in whole blood prenatally in mothers and at quarterly intervals in the infant. Prenatal blood lead levels were low (*mean* = 8.0 μg/dL). However, approximately 25% of the study infants had at least one serial blood lead level of 25 μg/dL or higher during the second year of life. Multiple regression and structural equation analyses revealed statistically significant relationships between prenatal and neonatal blood lead level and 3- and 6-month Bayley Mental and/or Psychomotor Development Index. However, by 2 years of age, no statistically significant effects of prenatal or postnatal lead exposure on neurobehavioral development could be detected. Data consistent with the hypothesis that a postnatal neurobehavioral growth catch-up occurred in infants exposed fetally to higher levels of lead are presented.

Introduction

For most U.S. children, there has been a substantial reduction in lead exposure as a direct result of regulatory policies governing acceptable levels of the metal in atmosphere and diet (*1*). However, the level of lead exposure at which adverse effects to health are believed to occur has been correspondingly reduced. Much of these new data on the health effects of low-level lead exposure have come from prospective studies initiated at the beginning of this decade. Since most of these studies recruited pregnant women, the first available reports dealt with the effects of fetal lead exposure on perinatal outcomes and early postnatal development.

Lower level fetal lead exposure has been associated with poorer neonatal physical status in several prospective studies. Decreased gestational age or delayed fetal maturation (*2–4*), lower birth weight (*5,6*), and an increased risk for minor physical anomalies (*7*) have been associated with fetal lead exposure as assessed by prenatal, umbilical cord, or neonatal blood lead levels in the range common among women and neonates in developed countries.

Lead-related deficits in early postnatal neurobehavioral status have been reported by several prospective studies. Ernhart and her colleagues have reported a significant covariate-adjusted relationship between maternal blood lead level at delivery and the abnormal reflexes cluster on the Brazelton Neonatal Behavioral Assessment Scale and the soft signs and muscle tonus score on the Graham/Rosenblith Behavioral Examination of the Neonate (*8*). These same investigators found a significant covariate-adjusted negative relationship between maternal blood lead level at delivery and 6-month scores on the mental and psychomotor indexes of the Bayley Scales of Infant Development (*9*). However, there appeared to be no significant covariate-adjusted relationships between indexes of fetal or early postnatal lead exposure and Bayley scores at 1 or 2 years.

A somewhat different pattern of results were reported by Bellinger and his co-workers in Boston (*10*). As in the Cleveland study, a significant covariate-adjusted negative relationship between fetal lead exposure (in this case, cord blood lead level) and 6-month Bayley mental index was found (*10*). However, these investigators later reported a continuous inverse relationship between cord blood level and Bayley mental index through 2 years of age (*11,12*). In our own study, we have reported an inverse relationship between maternal prenatal blood lead level and covariate-adjusted Bayley mental index scores at 3 and 6 months. These effects appeared to be strongest in male infants and infants from the poorest families. In addition, deficits or delays in early mental development appeared to be partly mediated by lead-related lower birth weight, and decreased gestational maturity (*2*).

The prospective studies substantially differ from one another in terms of postnatal lead exposure during infancy. At the low end of the exposure spectrum is the Boston study, where the mean blood lead level was less than 8 μg/dL at

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all ages sampled (*12*). This was a middle-class sample at relatively low risk for undue pediatric intoxication. The Cleveland study and our own are somewhat intermediate in terms if postnatal blood lead level. In Cleveland, a mean 2-year blood lead level of 16.74 μg/dL was reported (*9*), while 2 year olds in the Cincinnati cohort had an average blood lead of 17.45 μg/dL (this report).

Among the published prospective studies, the highest postnatal lead exposures are found in a longitudinal investigation of children residing near a primary lead smelter in Port Pirie, Australia (*13*). In this cohort of over 600 children, a geometric mean 2-year blood lead level of 21.2 μg/dL was reported (*13*). Further, these investigators reported a statistically significant inverse relationship between prenatal, 6-month, and integrated postnatal blood lead level and 2-year Bayley mental index scores after controlling for 14 covariates, including maternal intelligence. However, in regression analyses controlling for both maternal intelligence and a standard measure of caretaking quality, only 6-month blood lead level continued to be inversely associated with Bayley scores at borderline significance (*14*).

There appears to be general agreement among the prospective studies that low-level prenatal lead exposure may have some small effect on early neurobehavioral development (*2,8–12,14*). However, as others have noted (*11*), the implications of these adverse, low-level lead effects for regulatory policy depend on the magnitude of the inverse relationships and their stability over time. Therefore, one of the substantive issues for lead studies is whether such early deficits persist into later life. To address this important question, the Cincinnati Lead Program Project continues to follow study subjects into their early school years with a variety of regular biomedical and neurobehavioral assessments.

The primary purpose of this paper is to report on the relationship between prenatal/postnatal lead exposure and the development status of 2-year-old infants in the Cincinnati cohort. It was hypothesized that low to moderate prenatal and postnatal lead exposure would be adversely associated with indexes of 2-year neurobehavioral development after adjustment for relevant covariates or confounders.

Methods

The cohort at 2 years of age consisted of 297 infants for whom development data from the Bayley Scales of Infant Development were available. This sample included three sets of twins. Mothers of these infants were recruited prenatally between 1979 and 1984. Study families resided in predesignated lead-hazardous areas of Cincinnati, Ohio. This geographical area has a long history of cases of pediatric lead poisoning. Results of environmental studies with this cohort have shown conclusively that lead from paint, dust, and soil associated with poor housing stock is the major contributor to body burden (*15,16*). Informed consent for participation in the study was obtained at prenatal recruitment and again at delivery to obtain permission for infant follow-up. Women known to be drug addicted, alcoholic, diabetic, or those with a known neurological or psychological disorder were excluded from prenatal recruitment. Infants were excluded if they were less than 35 weeks gestation and/or 1500 g birth weight. Further, eligible infants must have had an Apgar score of 6 or greater at 5 min and have no serious medical condition or congenital anomaly. Descriptive statistics on mothers and infants excluded from the study and those families who refused to participate have been published elsewhere (*2*).

Table 1. Perinatal statistics on infants in study sample.

Study variable	Mean	SD	Lowest	Highest
Birth weight	3147.97	472.95	1814	4400
Gestational age, weeks[a]	39.57	1.69	35	43
Birth length, cm	49.25	2.47	42	56
Birth head circumference, cm	33.78	1.37	30	39
Obstretrical Complications Scale[b]	82.65	5.73	68	95
Postnatal Complications Scale[b]	94.44	9.47	30	100
APGAR score at 5 min.	8.85	0.40	6	9
Percent female	52.6%			
Percent black	86.2%			

[a]As assessed by standardized physical examination of the neonate (*12*).
[b]As assessed by Littman-Parmelee Obstetrical and Postnatal Complications Scales (*22*).

Table 2. Descriptive statistics on families in study sample.

Study variable	Mean	SD	Lowest	Highest
Maternal age at birth of child	22.55	4.40	15	37
Maternal IQ[a]	75	9.48	55	110
Socioeconomic status[b]	17.42	5.69	8	53
Number of children in the home	2.57	1.38	1	9
Total HOME score[c]	32.71	5.27	14	43
Percent unmarried	83.3%			

[a]Wechsler Adult Intelligence Scale-Revised (short form) (*25*).
[b]Hollingshead Four Factor Index of Socioeconomic Status (*23*).
[c]Home observation for measurement of the environment (HOME) (*24*).

Table 1 presents perinatal statistics on infants for whom 2-year developmental data were available. In general, study infants were healthy at birth, with a mean birth weight of 3147.97 g and gestational age (*17*) of 39.7 weeks. The sample was predominantly black (86.2%), with a nearly even percentage of male and female births. Table 2 presents descriptive statistics on study mothers and their families. Mothers were predominantly from the lower social classes (*23*), unmarried, and on some form of public assistance.

Blood was collected for lead analyses prenatally from the mother and at quarterly intervals from the infant beginning at 10 gestationally corrected days. Lead was measured in whole blood using anodic stripping voltammetry. The microanalytical laboratory at the University of Cincinnati Department of Environmental Health participates in several quality control programs. The performance of this laboratory has been uniformly excellent throughout the course of the current study. Detailed descriptions of our collection methods, analytic methodology, and precision have been published elsewhere (*2,18*). Most blood samples were collected by venipuncture, although finger stick and heel stick methods were used when the physical or behavioral characteristics of the infant demanded it. Collection methods

Table 3. Descriptive statistics on blood lead variables.[a]

Blood lead variable	*n*	Mean	SD	Low	High
Prenatal (maternal) blood lead	261	8.09	3.64	1	27
Neonatal (10-day) blood lead	297	4.76	3.15	1	26
Neonatal (3-month) blood lead	297	6.18	3.75	1	26
Maximum first year blood lead	297	15.85	8.17	5	56
Maximum second year blood lead	297	21.11	11.38	6	85
24-Month (concurrent) blood lead	297	17.45	9.16	4	70

[a]In micrograms per deciliter, whole blood. All values have been normalized to a standard hematocrit of 35% packed cell volume.

other than venipuncture were used most often with neonates and younger infants. For example, at 10 days only 26.2% of the samples were collected by venipuncture, while at 2 years 90.9% of the samples were collected by this method. Environmental contamination of samples collected by methods other than venipuncture has not been a problem in this study due to the controlled clinical conditions under which phlebotomy takes place (*2*).

Table 3 presents descriptive statistics on blood lead variables for subjects in the 2-year follow-up sample. Prenatal and neonatal blood lead levels were low, with only a handful reaching or exceeding 25 μg/dL. Most subjects reached their highest blood lead level during the second year. Approximately 25% of study subjects had at least one serial blood lead determination of 25 μg/dL or greater during the second year.

Infants were given developmental assessments at 3, 6, 12, and 24 months of age. Our primary measure of infant neurobehavioral development was the Bayley Scales of Infant Development (*19*), which provides a three part assessment: a Mental Development Index (MDI) that assesses sensorimotor coordinations, perceptual acuities, objective and visual-spatial relations, imitation, prelinguistic and linguistic behaviors, and memory; a Psychomotor Development Index (PDI) designed to provide a measure of the coordination of the large body muscles and finer manipulatory skills of the hands and fingers; and an Infant Behavior Record (IBR) that is a 30-item rating scale completed by the psychologist after the MDI and PDI examinations. The IBR assesses the infant's social, objective, affective, and motivational behaviors. All biomedical and neurobehavioral evaluations took place at a prenatal and children's welfare clinic located in the heart of the study recruitment area. Behavioral evaluations always occurred before the medical examination and phlebotomy, and care was taken to ensure that the infant was healthy, fed, and unmedicated when tested. The Bayley scales were administered by Dietrich or by a trained assistant with whom adequate intertester reliability had been previously established. All examinations were conducted without knowledge of the infant's prenatal or postnatal blood lead level.

Table 4 presents descriptive statistics on the performance of study infants on the Bayley MDI at each age. The rather

Table 4. Descriptive statistics on Bayley Mental Development Index at 3, 6, 12, and 24 months.[a]

Bayley variable	*n*	Mean	SD	Low	High
3-Month MDI	273	100.38	9.91	60	125
6-Month MDI	288	107.69	16.28	61	150
12-Month MDI	296	111.89	14.46	50	137
24-Month MDI	284	88.08	13.77	50	132

[a]The Bayley Scales of Infant Development have a standardized population mean and SD of 100 ± 16.

dramatic drop in MDI at 2 years is not unusual for lower socioeconomic status infants and probably reflects the relatively greater number of items at this age that require a verbal or nonverbal response to representational stimuli, rather than some type of sensorimotor manipulation.

To reduce the Bayley IBR to a few meaningful psychologic factors, we factor analyzed the 30 rating variables and calculated factor scores for each subject using the factor scoring coefficients. For example, Table 5 presents results of a factor analysis of the Bayley IBR at 24 months. The factor structure found at 2 years revealed four interpretable behavioral dimensions: mood (factor 1), activity level (factor 2), attention span (factor 3), and reactivity (factor 4).

Undue lead exposure is known to covary with a number of social and biologic risks that may mimic, obscure, or otherwise interact with the effects of toxicant exposure on child development (*20,21*). Consequently, a substantial amount of social and medical background data were collected on all subjects and tested as potential confounders of the

Table 5. Factor analysis of the Bayley Infant Behavior Record at 24 months.[a]

Bayley variable	Factor 1	Factor 2	Factor 3	Factor 4
Emotional tone	0.79			
Endurance	0.75		0.35	
Social orientation to examiner	0.72	0.31		
Cooperativeness	0.68			
Fearfulness	−0.62	−0.44		
Manipulation of objects	0.34			
Goal directedness	0.33		0.51	0.35
Imaginative use of toys	0.32		0.31	
Vocalizations	0.31	0.48	0.33	
Activity level		0.87		
Body motion		0.87		
Energy		0.80		
Banging toys		0.46	−0.41	
Fine motor coordination			0.59	
Social orientation to persons			0.55	
Attention span			0.51	0.34
Social orientation to mother			0.49	
Interest in sounds			0.41	
Object orientation			0.36	0.48
Reactivity				0.57
Tension				0.54

[a]Infant Behavior Record variables with factor loadings of 0.30 or greater are shown.

blood lead-behavioral development relationship. Perinatal variables included birth weight, length, head circumference, ponderal index, gestational age (*17*), Obstetrical and Postnatal Complications Scale (*22*), 1- and 5-min Apgar scores, maternal age, parity, gravidity, number of cigarettes smoked per day during pregnancy, composite index of tobacco and alcohol consumption (a dichotomous variable indicating use or nonuse of tobacco and/or alcohol during pregnancy), maternal total iron binding capacity during pregnancy, child sex (0 = male, 1 = female), and child race (0 = white, 1 = black). Child health variables included current illness and iron status as assessed by hemoglobin, hematocrit, and total iron binding capacity. Sociohereditary variables included socioeconomic status (*23*), developmental stimulation in the home (*24*), maternal intelligence (*25*), and number of children in the home. Any covariable bivariately associated with Bayley outcomes at a liberal p value of 0.10 or less was classified as a potential covariate. Further, any covariable associated with both prenatal and/or postnatal lead exposure and Bayley outcomes at $p = 0.10$ or less was classified as a potential confounder.

Data Analyses

The data analytic procedures used in this series involved multiple regression analyses with both backward elimination of nonsignificant covariates and confounders (reduced model) and multiple regression analyses retaining all potential covariates and confounders regardless of their statistical significance in multivariable models. The latter strategy was employed to determine the statistical robustness of any blood lead-behavior relationship and if any positive findings were model-specific (*26*). Data analyses were conducted for singleton births as well as for the full cohort, which included three sets of twins. Results of both analyses were compared. Parameter estimates for independent variables in either reduced or original regression models did not differ as a function of whether twins were present or excluded from the sample.

Results

Earlier Findings

Our earliest series of studies dealt with the relationships between prenatal exposure to lead and fetal growth, maturation, and early postnatal neurobehavioral development (*2,5*). We have reported a statistically significant covariate-adjusted relationship between fetal lead exposure variables and Bayley MDI scores at 3 and 6 months (*2*). These reported effects appeared to be strongest among male infants and infants from the poorest families. For example, Table 6 presents results of multiple regression analyses examining the relationship between prenatal (maternal) and neonatal (10-day) blood lead level and performance on the Bayley MDI at 6 months. In this reanalysis, all covariates and confounders were retained in the final model regardless of their individual statistical significance. Lead variables were analyzed both in micrograms per deciliter and transformed to their natural logarithm. Prenatal blood lead was significantly related to 6-month MDI after statistical adjustment for all 10 potential covariates and confounders in untrimmed regression models. However, this relationship was only negative for male infants who exhibited a covariate-adjusted reduction of 0.867 MDI points for each microgram per deciliter of prenatal blood lead ($p = 0.0105$). The parameter estimate for female infants was positive and statistically insignificant. Neonatal blood lead level was also inversely related to 6-month Bayley MDI after adjustment for all potential covariates and confounders. In this instance, the effect was most evident among those infants from the poorest families. For example, for those infants with Hollingshead socioeconomic status (SES) scores at or below the sample median of 17, there was a covariate-adjusted reduction of 0.757 MDI points for each microgram per deciliter of neonatal blood lead ($p = 0.0316$). The parameter estimate for infants above the sample median was negative as well, but statistically insignificant.

Table 6. Results of multiple regression analyses examining the relationship between prenatal and neonatal blood lead level and performance on the Bayley Mental Index at 6 months of age.[a]

Blood lead variable	n	β	SE	t	p
Log prenatal blood lead	249	−5.9103	2.6758	−2.21	0.0281
Log prenatal blood lead by child sex		11.2481	4.0686	2.76	0.0061
Prenatal blood lead, μg/dL		−0.8859	0.3400	−2.60	0.0099
Prenatal blood lead, μg/dL by child sex		1.5335	0.5146	2.98	0.0032
Log neonatal blood lead	283	−11.9301	5.0188	−2.38	0.0181
Log neonatal blood lead by socioeconomic status		0.5836	0.2820	2.07	0.0395
Neonatal blood lead, μg/dL		−3.1544	1.2999	−2.43	0.0159
Neonatal blood lead, by socioeconomic status		0.1626	0.0762	2.13	0.0338

[a] Covariates and confounders in regression models included birth weight, gestational age, Obstetrical Complications Scale, Postnatal Complications Scale, child sex, child race, composite index of tobacco and alcohol consumption, maternal age, socioeconomic status, and parity.

In a structural equation analysis, we also found an indirect effect of prenatal blood lead on both 3- and 6-month MDI and PDI through lead-related lower birth weight and decreased gestational maturity (*2*). For example, in a structural analysis of relationships among prenatal blood lead, covariates, and 6-month Bayley variables, each log increment in prenatal blood lead was associated with a reduction of 157 g birth weight and about one-half week gestation. In turn, birth weight and gestation were positively related to both Bayley MDI and PDI. Another structural analysis was conducted in an interim analysis of 12-month Bayley data with similar results (*28*).

These results have been previously published or presented at scientific meetings (*2,5,28*). They are reviewed here in order to put our new findings into their appropriate context. The primary focus of this paper is on the relationship between fetal and postnatal lead exposure and the developmental status of infants in the Cincinnati cohort at 2 years of age. The substantive issue at hand is whether the lead-related reductions in earlier indices of neurobehavioral status persist in evaluations of the older infant.

Two-Year Follow-Up

Table 7 presents results of multiple regression analyses examining the relationship between prenatal and postnatal blood lead level and performance on the Bayley MDI at 24 months. No statistically significant relationships between prenatal or postnatal blood level variables and Bayley MDI were found. Indeed, in many cases the parameter estimates were positive rather than negative. For prenatal (maternal) blood lead expressed in micrograms per deciliter, this positive relationship was statistically significant ($p = 0.0217$).

Although not presented in Table 7, we also examined the potential interactions among prenatal and postnatal exposure variables. These analyses tested the hyphothesis that those infants with both higher prenatal and higher postnatal blood lead levels may exhibit a deficit in 2-year MDI when compared to their less exposed peers. The results forthcoming from these statistical analyses were similarly insignificant.

Analyses of the relationship between prenatal and postnatal blood lead level and Bayley IBR factor scores also yielded statistically insignificant results. Unfortunately, we could not adequately examine the relationship between lead exposure variables and 2-year Bayley PDI, since only 170 of these examinations could be completed. The rather lengthy and demanding nature of the MDI protocol conducted first in the assessment series prevented many 2 year olds from completing the PDI. Structural equation analyses were also conducted to determine if there was a continued, adverse impact of prenatal lead exposure on Bayley MDI through fetal growth and maturational variables. The results of these analyses were consistently negative.

Table 7. Results of multiple regression analyses examining the relationship between prenatal and postnatal blood lead level and performance on the Bayley Mental Index at 24 months of age.[a]

Blood lead variable	n	β	SE	t	p
Log prenatal blood lead	237	3.2956	1.7123	1.92	0.0555
Prenatal blood lead, μg/dL		0.5058	0.2188	2.31	0.0217
Log neonatal 10-day blood lead	270	0.2434	1.2049	0.20	0.8400
Neonatal 10-day blood lead, μg/dL		−0.0162	0.2483	−0.07	0.9480
Log neonatal 3-month blood lead	270	1.3452	1.3306	1.01	0.3129
Neonatal 3-month blood lead, μg/dL		0.2351	0.2090	1.12	0.2618
Log maximum blood lead, 1st year	270	2.2155	1.6277	1.36	0.1747
Maximum blood lead, 1st year, μg/dL		0.1338	0.0962	1.39	0.1655
Log maximum blood lead, 2nd year	270	2.3227	1.6498	1.41	0.1603
Maximum blood lead, 2nd year, μg/dL		0.0961	0.0692	1.39	0.1663
Log blood lead, 24-months	270	3.1969	1.6971	1.88	0.0607
Blood lead 24-months, μg/dL		0.1270	0.0877	1.45	0.1490

[a]Other significant covariates and confounders in reduced aggression models included child sex, maternal intelligence (IQ), and birth length.

The only significant independent predictors of 2-year Bayley MDI were child sex ($\beta = 5.184$, $t = 3.25$ $p = 0.0013$) with females outperforming males; birth length ($\beta = 1.0694$, $t = 3.28$, $p = 0.0012$); and maternal intelligence ($\beta = 0.1860$, $t = 2.20$, $p = 0.0288$). Other covariables that were bivariately associated with 2-year Bayley MDI but eliminated from the trimmed regression models were birth weight, head circumference, gestational age, Postnatal Complication Scale score, and Home Observation for Measurement of the Environment (HOME) score.

The lack of inverse relationships between measures of fetal lead exposure and 2-year MDI and IBR factors suggests that those infants of mothers with higher prenatal blood lead levels may have recovered from their very early developmental deficits. The phenomenon of catch-up in physical growth has been well documented by auxologists who have studied infants compromised by intrauterine or early extrauterine influences (*29*). Further, studies of the neurobehavioral development of infant twins have shown corresponding catch-up growth in neurobehavioral development (*30*).

We examined the possibility of lead-related catch-up neurobehavioral growth in an exploratory analysis. Bayley MDI raw scores were used as a measure of behavioral growth. Bayley MDI raw scores represent the number of items passed at the age of testing and thus provide a rough gauge of the accrual of sensorimotor and cognitive skills over the first 2 years of life. A ratio was calculated to express the relative change or increase in MDI raw score between 3 and 24 months [i.e., $100*(MDI_{raw}24 - MDI_{raw}3)/(MDI_{raw}3)$]. The mean percent increase in MDI raw score in the study sample was 275.43% ± 72.5. The relative increase in MDI_{raw} between 3 and 24 months ranged from a low of 144.68% to a high of 892.31%.

Our primary interest was in the relationship among these change scores and fetal lead exposure and fetal growth and maturational variables such as birth weight and gestational age. We were particularly interested in these fetal developmental factors because the effects of prenatal lead exposure on early neurobehavioral development were shown to be partly mediated through them (*2*). The results of these analyses are presented in Figure 1. For this analysis, the variables of prenatal blood lead, birth weight, gestation, and head circumference were grouped by quartiles. The means and standard deviations for groups 1 through 4 are given in the figure legend. Analysis of variance revealed that all four perinatal variables were significantly associated with the percent increase in MDI raw score at $p < 0.05$. Those infants with the highest prenatal lead exposure or those having the lowest birth weight, shortest gestational age, or smallest head circumference showed the greatest degree of postnatal neurobehavioral growth catch-up.

It is interesting to compare the prenatal blood lead and birth weight variables in this figure. Their relationships to the neurobehavioral growth index appear to mirror each other. This is as one might expect given that prenatal blood lead and birth weight were related to early neurobehavioral

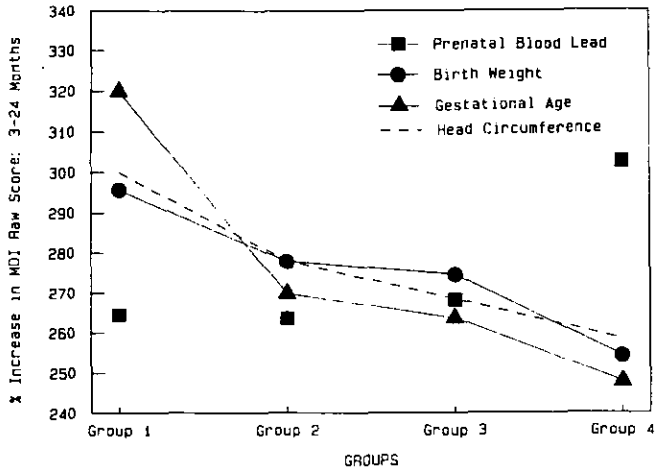

FIGURE 1. Percent increase in MDI raw score by fetal biological risk groups. Percent change in MDI raw score between 3 and 24 months was calculated as $[100*[MDI_{raw}24 - MDI_{raw}3]/MDI_{raw}3]$. Prenatal blood lead is measured in micrograms per deciliter, birth weight in grams, gestational age in weeks, and head circumference in centimeters. Group means: prenatal blood lead, group 1, 4.25 ± 1.16, group 2, 6.61 ± 0.61, group 3, 8.53 ± 0.63, group 4, 13.00 ± 3.28; birth weight, group 1, 2553.58 ± 235.32, group 2, 2977.43 ± 75.29, group 3, 3303.24 ± 107.05, group 4, 3757.35 ± 228.26; gestational age, group 1, 37.03 ± 0.94, group 2, 39.26 ± 0.44, group 3, 41.00 ± 0, group 4, 42.36 ± 0.50; head circumference, group 1, 31.89 ± 0.53, group 2, 33.29 ± 0.29, group 3, 34.17 ± 0.23, group 4, 35.50 ± 0.83.

status at 3 and 6 months, and the influence of prenatal blood lead on early developmental indices appeared to be mediated through birth weight (*2*). These findings are consistent with a hypothesis of neurobehavioral catch-up growth for infants whose central nervous system growth and development may have been compromised by lead exposure or other factors that influenced prenatal growth and maturation.

Discussion

We failed to find a persistent effect of fetal lead exposure on infant neurobehavioral development over the first 2 years of life. These results are in accord with one previous study (*9*), but not with studies conducted by Bellinger and his associates, who have reported a continuous inverse relationship between cord blood lead level and Bayley MDI between 6 months and 2 years (*10–12*). Our results also do not confirm those reported by Port Pirie, Australia, investigators who found a significant inverse relationship between early postnatal blood lead level and 2-year Bayley MDI (*14*). However, this relationship was no longer statistically significant after the HOME variable was entered.

We also failed to find a statistically significant relationship between indexes of postnatal lead exposure and Bayley MDI or IBR factors. These findings are in agreement with those reported by the Cleveland and Boston studies (*9–12*) but are somewhat discordant with findings from the Port Pirie, Australia, study (*14*). These investigators reported a statistically significant inverse relationship between integrated postnatal blood lead level and 2-year Bayley MDI after adjustment for 14 covariates, including maternal intelligence. However, after inclusion of the HOME variable, this relationship was no longer statistically significant. The more positive nature of the Port Pirie findings may suggest a threshold for an effect on 2-year Bayley MDI since mean postnatal blood lead levels in this sample were somewhat higher than those reported in the Cleveland study and our own. Nevertheless, we were somewhat surprised by the absence of an association between postnatal lead exposure and Bayley variables, especially given the fact that a substantial number of subjects in the Cincinnati cohort had at least one serial blood lead level that equalled or exceeded the current level of concern as established by the Centers of Disease Control (*31*).

Although we did not find any significant relationship between lead exposure indexes and the neurobehavioral status of older infants, two caveats are probably in order. First, the Bayley scales may be somewhat limited in their ability to measure more complex perceptual-performance, information processing, and linguistic skills, which may indeed be compromised by early exposure to lead. Fetal and postnatal lead exposure at low to moderate levels may produce adverse neurobehavioral sequelae that may only be measurable in the older child. The evaluation of such effects must await maturation of the Cincinnati cohort. Second, at least two major longitudinal studies have reported a significant relationship between early lower level lead exposure and the neurobehavioral status of infants at 2 years (*12,14*). Public health officials, governmental agencies, and industry must make policy decisions based upon all of the available scientific data, not any single study. Our negative findings at 2 years do not imply that lower level pediatric lead exposure is without any continuing harmful effects.

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