Lead Exposure and the Motor Developmental Status of Urban Six-Year-Old Children in the Cincinnati Prospective Study

Kim N. Dietrich, PhD*; Omer G. Berger, MD‡§; and Paul A. Succop, PhD*

ABSTRACT. The relationship between asymptomatic lead exposure and subtle deficits in intellectual attainment has been relatively well established by modern studies. However, neuromotor performance has rarely been the focus of these investigations. It was postulated that motor developmental outcomes may be more sensitive indicators of lead's adverse effects on the central nervous system as they are probably less confounded with social factors than cognitive and academic outcomes. A comprehensive neuromotor assessment battery was administered to 245 six-year-old urban inner-city children enrolled in the Cincinnati Lead Study. These children have been followed since birth with quarterly assessments of blood lead concentrations, medical status, and neurobehavioral development. Prior to covariate adjustment, neonatal, but not prenatal blood lead levels were associated with poorer scores on assessments of bilateral coordination, upper-limb speed and dexterity, and a composite index of fine-motor coordination. Averaged postnatal blood lead levels were also associated with lower scores on the aforementioned subtests as well as a measure of visual-motor control. Following statistical adjustment for covariates, neonatal blood lead levels were associated with poorer performance on a measure of upper-limb speed and dexterity and the fine-motor composite. Postnatal blood lead levels remained significantly associated with poorer scores on measures of bilateral coordination, visual-motor control, upper-limb speed and dexterity, and the fine-motor composite. Low to moderate lead exposure is associated with moderate deficits in gross and especially fine-motor developmental status. Results of this study provide support for recent initiatives to reduce the exposure of children to sources of environmental lead. *Pediatrics* 1993;91:301–307; *lead, motor development, toxicology, environmental health.*

ABBREVIATIONS. PbB, blood lead; BOTMP, Bruininks-Oseretsky Test of Motor Proficiency; PrePbB, maternal (first trimester) blood lead; NeoPbB, neonatal (10 day) blood lead; MPbB Life, mean lifetime blood lead.

Clinical epidemiologic investigation of the neurobehavioral effects of low-level lead and other environmental chemical exposures has been dominated by the assessment of cognitive outcomes.[1] The adverse effects of developmental exposure to another heavy metal, methylmercury, on neuromotor function have been well documented.[2] However, neuromuscular performance has rarely been intensively investigated in youngsters exposed to low to moderate levels of lead, despite the obvious fact that motor skills play an important role in influencing the quality of a child's daily activities and peer interactions.

In an early study, unsteadiness, clumsiness, and fine-motor dysfunctions were noted in a group of 58 mildly symptomatic lead-poisoned children in Boston, with such effects persisting long after medical treatment.[3] A recent study of 30 moderately exposed children living in the vicinity of a longstanding lead smelter in Greece found that children with blood lead (PbB) levels in the range of 1.7 to 2.9 μmol/L (35 to 60 μg/dL) had significantly lower scores on both the Gross and Fine Motor Composite subtests of the Oseretsky scales when compared to a group of control children residing in an unexposed area of the province.[4] An investigation of 26 children residing in a mixed rural and industrial area of eastern France found prenatal lead and cadmium exposure, as estimated by the levels of these metals in maternal and neonatal hair, significantly associated with lower scores on the Motor subscale of the McCarthy Scales of Children's Abilities.[5] A follow-up study of 63 New York children aged 8 to 11 years, who were screened previously as preschoolers for PbB elevations, found no statistically significant associations between McCarthy Motor subscale scores and lead exposure indices, despite the fact that children in the high-lead group had earlier PbB levels between 1.9 and 3.4 μmol/L (40 to 70 μg/dL).[6] Reports from two major prospective studies of lower-middle to upper-middle class children seem to suggest that while higher PbB levels are associated with lower scores on the McCarthy Motor subscale, cognitive outcomes are more sensitive and remain statistically significant following adjustment for confounding variables.[7,8]

In a prospective study of low-socioeconomic status urban children at high risk for PbB elevations, we have not observed a consistent, statistically significant inverse association between repeated assessments of prenatal/postnatal PbB levels and measures of speech, language, or cognitive developmental status. This was particularly the case following statistical adjustment for such potential confounding variables as maternal IQ and measures of caretaking quality in the home environment.[9–11] This has been the experience of other investigators studying lower socioeconomic status samples.[12] We hypothesized that measures of motor development, as opposed to cognitive or other language-based indices, may be

From the *Departments of Environmental Health and ‡Pediatrics, University of Cincinnati College of Medicine, and the §Children's Hospital Medical Center, Cincinnati, OH.

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Reprint requests to (K.N.D.) University of Cincinnati College of Medicine, Dept of Environmental Health, Cincinnati, OH 45267-0056.

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less confounded with sociohereditary cofactors in lower socioeconomic status populations and, therefore, are likely to be more sensitive biobehavioral markers of lead's effects on the development of the central nervous system.

METHODS

Subjects were recruited for this study from consecutive births between 1979 and 1984 in a geographic area within Cincinnati, OH, where there has been a historically high incidence of childhood lead poisoning. This area has an abundance of pre-World War II vintage housing in various states of disrepair as well as newer public housing. Lead in paint, dust, and exterior soils has been demonstrated to be a major source of exposure for children residing in this area.[13] Women known to be addicted to drugs, alcoholic, or diabetic or those with proven neurologic disorders, psychoses, or mental retardation were excluded from prenatal recruitment. Excluded from prenatal recruitment on these bases were 487 women, and 23 refused to participate. Infants of less than 35 weeks' gestation and/or less than 1500 g birth weight were excluded from postnatal recruitment. Furthermore, recruited infants must have had an Apgar score of 6 or greater at 5 minutes and have no serious medical condition such as Down syndrome, phenylketonuria, or significant congenital anomaly. Excluded from postnatal recruitment based on these criteria were 76 neonates; 129 mothers recruited prenatally refused all aspects of the postnatal follow-up study. A comparison of mothers and infants who were excluded from the study with those enrolled showed that they were similar in terms of key sociodemographic characteristics such as maternal age, marital status, and gravidity. As one would expect, excluded neonates had lower birth weights, gestational ages, and Apgar scores. There was also a tendency for white and/or married families to refuse study participation.[14]

Three hundred five infants were developmentally evaluated at their second postnatal follow-up appointments at 3 and/or 6 months of age.[14] These children have been repeatedly assessed with quarterly determinations of PbB levels, general health, and neurobehavioral development. In addition, potential developmental cofactors such as obstetric complications, perinatal status, social class, quality of the rearing environment, maternal intelligence, and iron status have been assessed throughout the study.

Of these 305 babies, 245 were assessed at approximately 72 months of age (±30 days) with a comprehensive and standardized assessment of gross- and fine-motor functioning (the Bruininks-Oseretsky Test of Motor Proficiency [BOTMP][15]), which constitutes the principal developmental outcome variable in this report. The comprehensive form of the BOTMP consists of eight subtests and a Gross and Fine Motor Composite Score (see Table 1). Gross-motor skills are assessed with the subtests of Running Speed and Agility, Balance, Bilateral Coordination, and Strength, while fine-motor skills are indexed by the subtests of Response Speed, Visual-Motor Control, and Upper-Limb Speed and Dexterity.

Most blood samples for PbB analyses were obtained by venipuncture, although some were obtained by finger-stick if necessitated by the physical or behavioral characteristics of the child. Contamination of blood samples drawn by a method other than venipuncture was not a problem because of thorough presampling cleansing procedures and the controlled clinical conditions under which blood sampling took place.[14] Blood samples were analyzed for lead by anodic stripping voltametry. A detailed description of the analytical procedures and proficiency of the microanalytical laboratory in our institution has been published elsewhere.[16] All neurobehavioral and medical assessments took place at a pediatric clinic located in the heart of the recruitment area.

We chose to estimate the degree of prenatal lead exposure from the level of lead measured in maternal (first trimester) blood (PrePbB) and neonatal (10 day) blood (NeoPbB). Various methods for estimating postnatal lead exposure were examined, including peak or mean PbB levels in any given year. Although we have obtained PbB level data on these children on a quarterly basis since birth, it was not practical to examine exposures during any given year for evidence of a sensitive neurodevelopmental period. This is owing to the fact that PbB levels from any given year to another were very highly intercorrelated. However, data analyses revealed that mean lifetime PbB (MPbBLife) proved to be as good as any other characterization of postnatal exposure. MPbBLife is the mean of 20 quarterly PbB determinations beginning at 3 months of age and concluding at 60 months, and two additional PbB assessments at 66 and 72 months. The relationship between PbB level on the day of testing (72 months) and performance on the BOTMP was also examined. Duplicate data analyses were performed with both log-transformed and untransformed PbB data to determine whether this transformation affected the final regression models or statistical significance of the PbB variables. Since no major differences were found between these models, we only report findings of PbB expressed in micrograms per deciliter.

A statistical comparison of those evaluated at 72 months and subjects who were permanently or temporarily lost to follow-up revealed no differences in terms of obstetric complications, perinatal status, sex, social class, maternal intelligence, quality of rearing environment, earlier measures of neurobehavioral status, or prenatal or postnatal PbB levels. A higher percentage of white children were lost to follow-up.

Statistical analyses were performed with the Statistical Analysis System. Covariates were pretested for their confounding potential by examining their bivariate relationship with both PbB and the BOTMP scales. Following both backward and forward stepwise

TABLE 1. Subtests of the Bruininks-Oseretsky Test of Motor Proficiency[15]

Subtest	Description
Running Speed and Agility	Running speed is measured during a shuttle run.
Balance	Static balance is assessed by three items by asking the child to maintain balance while standing on one leg (floor and balance beam). Five items assess performance by requiring the child to maintain balance while executing various walking movements.
Bilateral Coordination	Seven items assess sequential and simultaneous coordination of the upper limbs with the lower limbs (eg, tapping foot and finger on same or opposite sides simultaneously). One item measures coordination of upper limbs only.
Strength	Arm, shoulder, abdominal, and leg strength are assessed in three items (broad jump, sit-ups, and push-ups).
Upper-Limb Coordination	Six items assess coordination of visual tracking with arm and hand movements (eg, catching and targeting a ball). Three items measure precise movements of the arms, hands, and fingers.
Response Speed	One item assesses the child's ability to respond quickly to and stop a moving stimulus (ruler placed on flat, 180° surface).
Visual-Motor Control	The ability to coordinate precise hand and visual movements is assessed by eight items (eg, use of scissors, pencil).
Upper-Limb Speed and Dexterity	Eight items measure hand and finger dexterity, hand speed, and arm speed (eg, object placement, pegboard, card sorting, stringing beads, drawing speed).

multiple regression analyses, those covariates that were independently related to one or more BOTMP subscales at $P \leq 0.10$ were included in all subsequent multiple regression analyses. With an N of 245 subjects, our power to detect a modest, statistically significant association of PbB level with neurobehavioral impairment (eg, $r = -.20$, $P \leq 0.05$) was approximately 0.88.

This study has been reviewed and approved by the Committee on Human Research, University of Cincinnati College of Medicine.

RESULTS

Table 2 presents descriptive statistics on the study sample, including prenatal, neonatal, and mean PbB levels for years 1 through 6. In general, the study sample consisted of healthy, term, normal birth weight infants. Sample families were predominantly black, single-parent households receiving public assistance. Prenatal (maternal first trimester) and neonatal PbB levels were low. Postnatal PbB levels began to rise after 6 months following the beginnings of prewalking progression and hand-to-mouth behaviors.[20] Blood lead levels in most subjects peaked at around 2 years of age and then very slowly declined thereafter. To provide a clearer picture of the range and levels of lead exposure experienced by this cohort, Fig 1 presents PbB levels obtained quarterly for children divided into four quartiles based on average lifetime PbB concentration. Eighty-seven children (35.5%) had at least one PbB level which equaled or exceeded 1.206 μmol/L (25 μg/dL) during the first 5 years of life, while 195 children (79.6%) had at least one PbB level equal to or in excess of 0.724 μmol/L (15 μg/dL) during this period. Only approximately 8.5% of the study sample underwent a diagnostic chelation, and only 5% were chelated therapeutically.

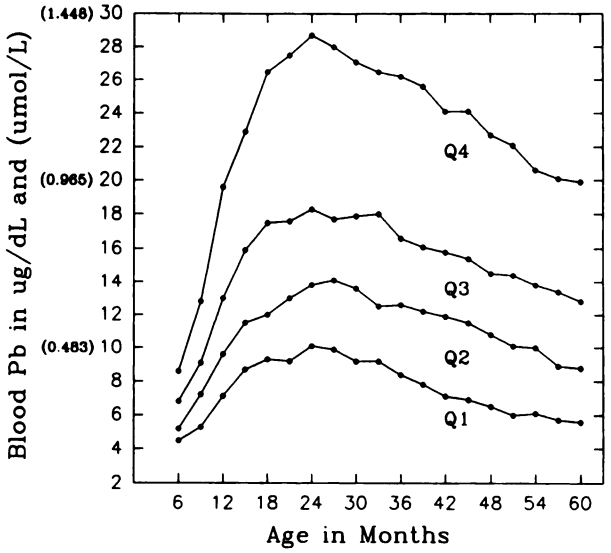

Fig 1. Blood lead concentrations obtained quarterly for children divided into four quartiles (Q1–4) based on average lifetime blood lead concentration (ie, the mean of 20 quarterly blood lead concentrations from 3 to 60 months). Age in months has been abbreviated to 6-month intervals rather than 3-month intervals for clarity of presentation.

TABLE 2. Descriptive Statistics on Selected Perinatal, Socioheredity, and Blood Lead Variables*

Variable	Mean	SD	Lowest	Highest
Perinatal				
Maternal age at birth, y	22.7	4.3	15	37
Birth weight, g	3133.0	464.2	1814	4400
Gestational age, wk†	39.6	1.7	35	43
5 Minute Apgar	8.8	0.4	6	9
% Male	50.2			
% Black	89.4			
Socioheredity				
Socioeconomic status‡	18.3	6.3	6	53
3 Year HOME score§	32.4	6.5	13	48
% Unmarried	84.0			
Highest grade completed by primary caretaker	11.3	1.4	7	16
Maternal IQ‖	75.3	9.4	55	110
Blood lead μmol/L (μg/dL)				
Prenatal PbB	0.406 (8.4)	0.184 (3.8)	0.044 (1)	1.293 (27)
Neonatal PbB	0.233 (4.8)	0.149 (3.1)	0.018 (1)	1.042 (22)
Mean 1st year PbB	0.506 (10.5)	0.238 (4.9)	0.150 (3)	1.690 (35)
Mean 2nd year PbB	0.824 (17.1)	0.395 (8.2)	0.275 (6)	2.380 (49)
Mean 3rd year PbB	0.783 (16.2)	0.369 (7.6)	0.207 (4)	2.428 (50)
Mean 4th year PbB	0.676 (14.0)	0.343 (7.1)	0.181 (4)	2.182 (45)
Mean 5th year PbB	0.574 (11.9)	0.307 (6.4)	0.156 (3)	1.847 (38)
Mean 6th year PbB	0.487 (10.1)	0.269 (5.6)	0.117 (2)	1.578 (33)

* N = 245 except for prenatal blood lead (PbB) level (n = 211), Home Observation for Measurement of the Environment (HOME) scores (n = 227), and maternal IQ (n = 243).
† Ballard Fetal Maturity Index.[17]
‡ Hollingshead Four-Factor Index of Social Status (unpublished manual).
§ Caldwell inventory.[18]
‖ Wechsler Adult Intelligence Scale-Revised.[19]

Table 3 presents subjects' performance on the BOTMP. As a group, study subjects exhibited average performance on the Bilateral Coordination, Strength, Upper-Limb Coordination, and Upper-Limb Speed and Dexterity subtests, but did poorly relative to national norms on the Balance, Response Speed, and Visual-Motor Control subtests. The Fine Motor Composite score was approximately 1.3 standard deviations below the national mean.

Table 4 presents unadjusted regression coefficients expressing the relationship between blood indices of prenatal and postnatal lead exposure and performance on the BOTMP. These coefficients are unstandardized and represent the estimated average change in BOTMP scores for each microgram-per-deciliter increment in prenatal or postnatal PbB.

Prenatal, neonatal, and postnatal PbB levels were unrelated to Balance, Strength, Upper-Limb Coordination, or Response Speed. Neonatal and/or postnatal PbB levels were significantly associated with lower scores on the Bilateral Coordination, Visual-Motor Control, and Upper-Limb Speed and Dexterity subtests as well as the Fine Motor Composite, which is a consolidation of the Upper-Limb Speed and Dexterity, Response Speed, and Visual-Motor Control subtests into one standard score.

A number of cofactors were significantly and independently related to BOTMP subtests, including several of the Home Observation for Measurement of the Environment[18] subscales, maternal IQ, social class, and child sex and race with male and African-American status being associated with superior performance on the Strength subtest and male status favoring performance on Response Speed. Model R^2 values were not large for any given regression analysis, accounting for approximately 5% to 17% of the variance in any particular subtest or scale.

As presented in Table 5, following covariate adjustment, Bilateral Coordination, Visual-Motor Control, Upper-Limb Speed and Dexterity, and the Fine Motor Composite retained some significant relationships to neonatal and/or postnatal PbB levels. As in the unadjusted regression analyses, prenatal (maternal) PbB levels were unrelated to BOTMP performance. However, neonatal (10 day) PbB levels were significantly associated with lower scores on the Upper-Limb Speed and Dexterity subtest and the Fine Motor Composite and marginally related to lower scores on the Bilateral Coordination subtest.

TABLE 4. Unadjusted Regression Coefficients for PbB Indices and Bruininks-Oseretsky Test of Motor Proficiency Subscales*

Scale	PbB	β	SE
Balance	PrePbB	0.03	0.10
	NeoPbB	−0.17	0.11
	MPbBLife	−0.04	0.05
	Current PbB	−0.05	0.06
Bilateral Coordination	PrePbB	−0.04	0.07
	NeoPbB	−0.15†	0.08
	MPbBLife	−0.12§	0.04
	Current PbB	−0.18§	0.04
Strength	PrePbB	0.07	0.09
	NeoPbB	−0.03	0.11
	MPbBLife	0.02	0.05
	Current PbB	−0.04	0.06
Upper-Limb Coordination	PrePbB	0.05	0.10
	NeoPbB	−0.02	0.11
	MPbBLife	−0.03	0.06
	Current PbB	−0.07	0.06
Response Speed	PrePbB	−0.07	0.08
	NeoPbB	0.02	0.10
	MPbBLife	−0.06	0.05
	Current PbB	−0.07	0.05
Visual-Motor Control	PrePbB	0.04	0.08
	NeoPbB	−0.10	0.10
	MPbBLife	−0.10‡	0.05
	Current PbB	−0.17§	0.05
Upper-Limb Speed and Dexterity	PrePbB	−0.19	0.12
	NeoPbB	−0.45§	0.14
	MPbBLife	−0.23§	0.07
	Current PbB	−0.34§	0.07
Fine Motor Composite	PrePbB	−0.26	0.21
	NeoPbB	−0.55‡	0.24
	MPbBLife	−0.41§	0.12
	Current PbB	−0.58§	0.12

* P values are two-tailed. PbB, blood lead; PrePbB, maternal (first trimester) blood lead; NeoPbB, neonatal (10 day) blood lead; MPbBLife, mean lifetime blood lead.
† $P \leq .10$.
‡ $P \leq .05$.
§ $P \leq .01$.

TABLE 3. Performance on the Bruininks-Oseretsky Test of Motor Proficiency*

Variable	N	Mean	SD	Lowest	Highest
Balance	244	11.7	5.3	1	29
Bilateral Coordination	243	15.9	4.1	4	26
Strength	243	16.9	5.1	5	34
Upper-Limb Coordination	242	15.5	5.4	1	28
Response Speed	243	10.9	4.7	1	31
Visual-Motor Control	244	9.1	4.6	1	25
Upper-Limb Speed and Dexterity	243	16.5	6.7	1	32
Fine Motor Composite	242	36.8	11.7	7	73

* The Bruininks-Oseretsky subtests have an age-standardized mean of 15 and standard deviation of 5. The Fine Motor Composite has an age-standardized mean of 50 and standard deviation of 10. N values vary by subtests because of the presence of a few incomplete protocols. Space limitations did not permit administration of the Running Speed and Agility subtest, making calculation of a Gross Motor Composite score impossible. Fine Motor Composite standard score is based on subjects' performance on Response Speed, Visual-Motor Control, and Upper-Limb Speed and Dexterity subtests.

TABLE 5. Covariate-Adjusted Regression Coefficients for PbB Indices and Bruininks-Oseretsky Test of Motor Proficiency Subscales*

Scale	PbB	β	SE
Bilateral Coordination	PrePbB	−0.04	0.08
	NeoPbB	−0.15†	0.09
	MPbBLife	−0.11‡	0.04
	Current PbB	−0.18§	0.04
Visual-Motor Control	PrePbB	0.06	0.08
	NeoPbB	−0.10	0.10
	MPbBLife	−0.05	0.05
	Current PbB	−0.12‡	0.05
Upper-Limb Speed and Dexterity	PrePbB	−0.20	0.12
	NeoPbB	−0.45§	0.14
	MPbBLife	−0.19§	0.07
	Current PbB	−0.31§	0.07
Fine Motor Composite	PrePbB	−0.14	0.21
	NeoPbB	−0.49‡	0.24
	MPbBLife	−0.28‡	0.12
	Current PbB	−0.46§	0.13

* P values are two-tailed. Abbreviations are explained in the first footnote to Table 4.
† $P \leq .10$.
‡ $P \leq .05$.
§ $P \leq .01$.

To clarify the dose-effect relationship between lifetime postnatal lead dose and performance on the BOTMP, least-square means were calculated from an analysis of covariance procedure to examine the relationship between MPbBLife quartile dose categories and the Bilateral Coordination subtest and Fine Motor Composite. The results of these analyses are presented in Figs 2 and 3. Children having an average mean lifetime PbB level of approximately equal to or exceeding about 0.435 μmol/L appeared to experience a deficit on both of these scales relative to children in the lowest PbB quartile. Figure 2 shows that, on average, children in the highest MPbBLife quartile had scores on the gross-motor subtest assessing bilateral coordination of approximately 0.5 standard deviations (2.5 points) lower than their counterparts in the lowest quartile. Figure 3 shows that children in the highest MPbBLife quartile also scored more poorly in fine-motor functioning, having scores of approximately 0.6 standard deviations lower (6.3 points) than those in the lowest quartile.

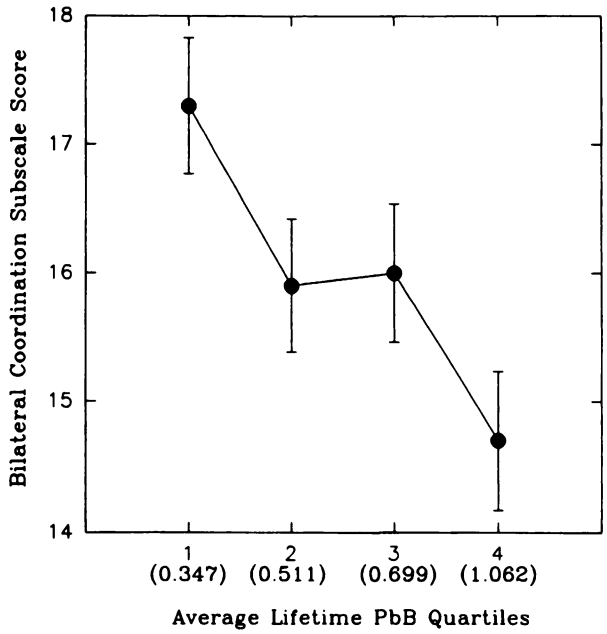

Fig 2. Covariate-adjusted dose-effect relationship between average lifetime blood lead (PbB) level quartile and standard scale score on the Bilateral Coordination subtest. Numbers in parentheses are mean PbB levels within each quartile in micromoles per liter. Lifetime mean PbB levels in quartiles 1 to 4 were in the following ranges: (1) 0.227 to 0.435 μmol/L; (2) 0.441 to 0.594 μmol/L; (3) 0.598 to 0.806 μmol/L; (4) 0.807 to 1.841 μmol/L. Two-way bars represent standard errors.

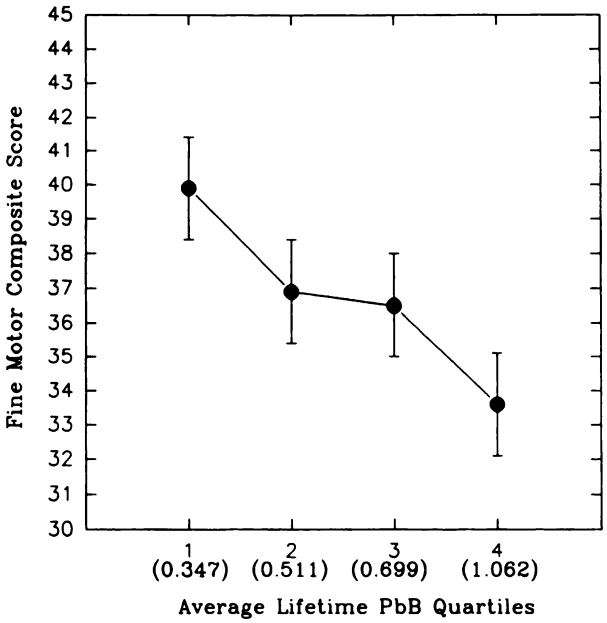

Fig 3. Covariate-adjusted dose-effect relationship between average lifetime blood lead (PbB) level quartile and standard scale score on the Fine Motor Composite. Numbers in parentheses are mean PbB levels within each quartile in micromoles per liter. See legend to Fig 2 for PbB ranges in each quartile. Two-way bars represent standard errors.

DISCUSSION

Previous studies of the neurotoxic effects of lead on development have tended to focus on mental rather than motor functions. In this investigation of the effects of low to moderate lead exposure on motor development, we obtained a mixed pattern of findings. Prenatal and postnatal PbB levels were unrelated to both the Balance and Response Speed subtests of the BOTMP. The findings for balance skills were unexpected, as we have previously observed a significant association between postnatal PbB levels and standing postural sway, as quantified by an apparently more sensitive computer-based force platform technique.[21] Past studies have also reported a significant relationship between various indices of lead exposure and reaction time.[1] However, the Response Speed subtest of the BOTMP contains only one item and, therefore, may not be reliable.[22] Furthermore, previous lead studies have assessed reaction time within the context of more complex and challenging attentional performance tasks, which are

likely to be substantially more sensitive than this single item from the Bruininks battery.[23–26]

Nevertheless, we observed statistically significant inverse associations between neonatal and postnatal PbB levels and some elements of both gross- and fine-motor functioning as assessed by the Bruininks. Following statistical adjustment for covariates, NeoPbB levels were significantly associated with lower scores on the subtests assessing upper-limb speed and dexterity as well as the composite score for fine-motor performance. After adjustment for covariates, MPbBLife levels were associated with lower scores on subtests measuring aspects of bilateral coordination of the gross musculature, upper-limb speed and dexterity, and the composite score for fine-motor performance.

It should be acknowledged that, on average, the apparent effects of lead exposure as estimated by PbB levels on motor developmental status were moderate, amounting to an average difference of approximately one half of a standard deviation between the lowest and highest PbB quartiles. Furthermore, it is difficult to reconcile the inconsistent findings for measures of prenatal lead exposure. NeoPbB was inversely associated with measures of fine-motor performance, but results for PrePbB were completely negative. We have previously observed this discrepancy in cognitive evaluations of the Cincinnati cohort[10] and have suggested that neonatal PbB levels may be a better measure of the actual amount of lead that is crossing the placenta and absorbed by the fetus. The low correlation between prenatal and neonatal PbB levels suggests that they do reflect different aspects of lead dose, absorption, and retention ($r = .26$, $P = \leq .01$). Nevertheless, the inconsistency in these findings should be acknowledged and should temper any overinterpretation of the NeoPbB association with the development of fine-motor functions.

From these results, it appears that low to moderate postnatal lead exposure is associated with some small deficit in gross- and fine-motor development. Motor outcomes may be more appropriate biobehavioral markers of lead's effects on the developing central nervous system than cognitive or academic measures, particularly in populations where significant confounding exists. This appears to be true in this cohort as we have failed to observe any substantial effect of lead on preschool-age intellectual outcomes following adjustment for such covariates as Home Observation for Measurement of the Environment scores and maternal IQ,[9–11] but note here some statistically significant associations when motor outcomes are considered in the same cohort of children.

The exact mechanisms that may be involved in lead-associated motoric developmental deficits at lower levels of exposure are not yet clear. The cerebellum has been observed to be particularly sensitive to very high-level lead intoxication.[27] Developmental neurobiologic studies have reported profound lead-related reductions in cerebellar transplant electrophysiologic activity in rodents.[28] Low levels of lead have recently been reported to precociously induce rat cerebellar glial cell development and impair embryonic to adult conversion of the neural cell adhesion molecule,[29,30] both processes that are intimately involved in the orchestration of brain histogenesis. Whatever the mechanism, the results of this study, as well as many that have preceded it, provide support for recent initiatives to reduce environmental lead exposure in children.[31]

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SHOULD WE USE DEXAMETHASONE IN MENINGITIS?

In conclusion then, it seems probable that children with haemophilus meningitis may benefit from the use of early adjunct treatment with dexamethasone, particularly in the reduction of deafness. Almost all the evidence for this comes from a single unit in North America, and different parameters have shown benefit in different trials. The advantages of steroid treatment here probably outweigh the disadvantages. The case for pneumococcal meningitis is minimal, based in a retrospective study from Dallas and on a subgroup of a Cairo study performed in a mixed group of adults and children. Very limited information is available for meningococcal meningitis. What evidence there is suggests steroids may not help. As there are well established risks associated with steroid administration to septic patients, especially those in shock, there is an urgent need for further studies to confirm or refute this potentially major change in our management of a widely and justly feared infection.

How easy would these be?

It would be necessary to recruit very large numbers of patients and controls (many hundreds) into a placebo controlled trial of dexamethasone designed to confirm or refute a 50% reduction of moderate/severe deafness in bacterial meningitis. The patients would need careful monitoring and audiological follow up over a prolonged period. We may be approaching the point at which this type of controlled study can no longer easily be performed in Britain alone.

A European multicentre trial may be the answer.

The Meningitis Working Party of the British Paediatric Immunology and Infectious Diseases Group. Should we use dexamethasone in meningitis? *Archives of Disease in Childhood.* 1992;67:1398–1401.

Noted by J. F. L., MD