Low-Level Lead Exposure, Intelligence and Academic Achievement: A Long-term Follow-up Study

David C. Bellinger, PhD, MSc; Karen M. Stiles, PhD, MN; and Herbert L. Needleman, MD

ABSTRACT. The implications of low-level lead exposure for children's intellectual and academic performance at school age are uncertain. This issue was investigated in a prospective study of middle-class and upper-middle-class children with low lifetime exposures to lead. A battery of neuropsychological tests was administered at age 10 years to 148 children whose lead exposure and cognitive function had been previously assessed at ages 6, 12, 18, 24, and 57 months. Primary endpoints were Wechsler Intelligence Scale for Children-Revised (WISC-R) and the Kaufman Test of Educational Achievement (K-TEA). Higher levels of blood lead at age 24 months, but not at other ages, were significantly associated with lower global scores on both the WISC-R and the K-TEA after adjustment for potential confounders. Over the range of approximately 0 to 25 µg/dL, a 0.48-µmol/L (10 µg/dL) increase in blood lead at 24 months was associated with a 5.8-point decline in WISC-R Full-Scale IQ (95% confidence interval: 1.7 to 9.9, P = .007) and an 8.9-point decline in K-TEA Battery Composite score (95% confidence interval: 4.2 to 13.6, P = .0003). Mean blood lead level at age 24 months was 0.31 µmol/L (6.5 µg/dL; SD: 4.9, 90th percentile: 12.5). Slightly elevated blood lead levels around the age of 24 months are associated with intellectual and academic performance deficits at age 10 years. Pediatrics 1992;90:855-861; lead, intelligence, achievement, neuropsychological toxicology, environmental epidemiology.

ABBREVIATIONS. WISC-R, Wechsler Intelligence Scale for Children-Revised; K-TEA, Kaufman Test of Educational Achievement; Brief Form. HOME, Home Observation for Measurement of the Environment; GCI, General Cognitive Index; pb24, 24-month blood lead level. CI, confidence interval.

Lead poisoning is considered the most important pediatric environmental health problem in the United States. Blood lead levels in the range of 0.48 to 0.97 µmol/L (10 to 20 µg/dL) have been linked to a variety of adverse health effects and serve as reference points for recent revisions in the screening and treatment protocols recommended by the Centers for Disease Control. The long-term implications of exposures producing blood lead levels in this range remain uncertain. However, in primates, early exposures producing peak blood lead levels of 1.21 µmol/L (25 µg/dL) and steady-state levels of 0.63 µmol/L (13 µg/dL) impair performance up to 10 years later on a variety of cognitive tasks. Some ongoing prospective studies, but not all, report cognitive deficits at pre-school age among children with similar early exposures. The results of another study are mixed. No prospective study has yet reported to what extent any early deficits persist to school age. We report here on the association between early lead exposure and children's intellectual functioning and academic achievement at age 10 years.

METHODS

Sample

Infants born at the Brigham and Women's Hospital (Boston, MA) between August 1979 and April 1981 were provisionally eligible if the umbilical cord blood lead level was below the 10th percentile (<0.15 µmol/L or 3 µg/dL) approximately at the 50th percentile (0.31 µmol/L or 6.5 µg/dL), or greater than the 90th percentile (≥0.48 µmol/L or 10 µg/dL). Other eligibility criteria included (1) absence of medical conditions associated with developmental handicap, (2) English as the first language, (3) residence in the Boston area (<19 km from The Children's Hospital but not in certain public housing projects), and (4) maternal consent to be contacted. A total of 249 infants were enrolled. Postnatal blood lead levels and development were assessed at ages 6, 12, 18, 24, and 57 months. The base population for the 10-year follow-up assessment was the 169 children from the original sample who were tested at age 37 months. Assessments were completed on 148 children (87.6% of those considered eligible: 59.4% of the original cohort). Nine families refused or repeatedly failed to keep appointments (5.3%), 4 had moved from the area (2.4%), and 9 could not be located (4.7%). The cohort generally consisted of white, intact families with college-educated parents and relatively high-functioning children with low lifetime exposures to lead (Table 1). Compared with eligible families that did not participate in the 10-year assessment, participants tended to be of relatively higher socioeconomic status and to provide slightly more optimal developmental environments for their children.

Neuropsychological Assessment

The children were administered a battery of tests by a psychologist (K.M.S.) who was "blind" to all aspects of a child's developmental and lead exposure histories. In most cases, testing was conducted at The Children's Hospital (Boston) in a single session lasting approximately 3 hours. A second session was required to complete the testing of two children, and seven children were tested in their homes. The mean age (SD, range) of the children at testing was 9 years 9 months (41 days, 9 years 7 months to 10 years 2 months).
Measurement of Potential Confounders

Parents completed several questionnaires, including the McCarthv Scales of Children's Abilities, the Peabody Picture Vocabulary Test, the Social Readiustment Rating Scale, and the Home Observation for Measurement of the Environment. Information about other potential confounders was available in records from previous assessments (eg, maternal IQ, birth weight, HOME scores).

Blood Sampling and Analysis

A Children's Hospital phlebotomist drew 3-mL venous blood samples from 116 children on the day of testing. Samples were not obtained from 32 children because of refusal or because the assessment was conducted at home. In most cases, each sample was sent to the Clinical Laboratorics of the Children's Hospital for serum lead measurement by an immunoenzymatic assay using monoclonal antibodies. The remainder of the sample was sent to ESA Laboratories (Bedford, MA), where blood lead concentration was measured in duplicate using graphite furnace atomic absorption spectrophotometry with Zeeman Background correction using a Hitachi model 2-9000. Quality control samples (low and high) were analyzed with each batch. Blood lead level was assessed as high, moderate, or low, representing a child's average blood lead level across various age intervals; maximum blood lead level in the first year, the second year, or over the course of the study; interaction terms combining exposure with sociodemographic characteristics; and the estimated change in the lead coefficient produced more than a 10% change in the lead coefficient.

RESULTS

Overall Performance

Children's WISC-R and K-TTE scores were approximately 1 SD above the population average. Mean (SD, range) Full-Scale, Verbal, and Performance IQ scores were 119.1 (14.8, 71 to 147), 118.1 (14.9, 67 to 146), and 115.9 (14.2, 78 to 146), respectively. Mean (SD, range) Battery Composite, Mathematics Composite, Reading Composite, and Spelling scores were 118.8 (16.3, 69 to 160), 122.1 (18.7, 70 to 160), 117.0 (14.0, 71 to 140), and 113.5 (17.1, 68 to 153), respectively.

Wechsler Intelligence Scale for Children-Revised

Crude Analyses. All postnatal blood lead levels were inversely associated with Full-Scale IQ measured at 10 years of age, although only the associations in...
The analysis of blood lead levels at age 10 years, 57 months, and 24 months were statistically significant (Table 2). This was also true for both Verbal and Performance IQ scores.

**Adjusted Analyses** Adjustment for confounding reduced the magnitude of the coefficients associated with all blood lead levels. The coefficient associated with 24-month blood lead level (pb24) remained significant (Table 2). The decline in children's Full-Scale IQ corresponds to 0.24 μmol/L (5 μg/dL) increase in pb24 (95% confidence interval [CI]: 1.7 to 9.9 points). Adding pb24 to the covariate model accounted for an additional 3.2% of the variance in Full-Scale IQ scores. The partial regression residual plot indicated that this association was linear across Full-Scale IQ scores.

The sensitivity analyses indicated that the association between pb24 and Full-Scale IQ was robust to the introduction of additional variables, such as maternal IQ, HOME score, and family structure. The pb24 coefficient in this model was -0.42 (SE = 0.56) for children in the “low” cord blood lead group (<3 μg/dL), reference group is children in the “high” cord blood lead group.

### TABLE 2. Regression Coefficients Associated With Blood Lead Levels and Children's Wechsler Intelligence Scale for Children-Revised IQ Scores at 10 Years of Age

<table>
<thead>
<tr>
<th>Blood Lead Measurement*</th>
<th>Full-Scale IQ</th>
<th>Verbal IQ</th>
<th>Performance IQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 y</td>
<td>-1.53 (0.56)</td>
<td>-0.39 (0.53)</td>
<td>-0.17 (0.55)</td>
</tr>
<tr>
<td>12 m</td>
<td>-0.20 (0.19)</td>
<td>-0.20 (0.19)</td>
<td>-0.17 (0.17)</td>
</tr>
<tr>
<td>18 m</td>
<td>-0.20 (0.19)</td>
<td>-0.20 (0.19)</td>
<td>-0.17 (0.17)</td>
</tr>
<tr>
<td>24 m</td>
<td>-0.20 (0.19)</td>
<td>-0.20 (0.19)</td>
<td>-0.17 (0.17)</td>
</tr>
<tr>
<td>57 m</td>
<td>-0.90 (0.33)</td>
<td>-0.07 (0.30)</td>
<td>-0.44 (0.31)</td>
</tr>
<tr>
<td>6 m</td>
<td>-0.20 (0.16)</td>
<td>-0.13 (0.16)</td>
<td>-0.03 (0.16)</td>
</tr>
</tbody>
</table>

* Age at which blood lead level was measured.
† Variables included in models:
20 years: HOME120 (sum of Scales V and VI of the Home Observation for Measurement of the Environment at age 10 years), family stress, child stress, maternal age, race (white/nonwhite), birth weight, mater nal IQ, number of day-care situations through 57 months, HOME57 (total score at 57 months), socioeconomic status (SES), sex, birth order (first, second, third or later), marital status (married/not married).
57 months: HOME120, family stress, child stress, race, maternal IQ, HOME57, SES, sex, birth order, marital status.
24 months: HOME120, child stress, maternal age, race, maternal IQ, HOME57, SES, sex, birth order, marital status, number of residence changes prior to age 57 months.
18 months: HOME120, family stress, child stress, maternal age, race, maternal IQ, HOME57, SES, sex, birth order, marital status, number of residence changes prior to age 57 months.
12 months: HOME120, child stress, race, maternal IQ, HOME57, SES, sex, birth order, marital status, family balance (Family Adaptability and Cohesion Evaluation Scales-III), parent's sense of competence.
6 months: HOME120, child stress, race, maternal IQ, HOME57, SES, sex, birth order, marital status, Cord blood: child stress, maternal age, maternal IQ, HOME57, SES, sex, birth order, number of residence changes prior to age 57 months, race.
‡ Regression coefficient (SE), representing the estimated change in score associated with each 0.48 μmol/L (1 μg/dL) increase in blood lead level.
§ Two-sided P value associated with the hypothesis that the coefficient is zero.
\* Coefficient (SE) associated with membership in the "low" cord blood lead group (<3 μg/dL); reference group is children in the "high" cord blood lead group.
\# Coefficient (SE) associated with membership in the "medium" cord blood lead group (3 to 7 μg/dL); reference group is children in the "high" cord blood lead group.
model reduction or confounder selection strategies, and to the deletion of influential observations. In most analyses, the change in the \( \text{pb24} \) coefficient was less than \( 15\% \). The largest change was a \( 40\% \) reduction (\( -0.08 \) to \( -0.20 \)) when observations with large impact on fitted values were deleted.

\( \text{pb24} \) was also significantly associated at \( P < 0.05 \) with Verbal IQ and five WISC-R subtest scores (Arithmetic, Comprehension, Similarities, Picture Completion, Block Design) and at \( P < 0.10 \) with two others (Vocabulary, Digit Span). It was not significantly associated with Performance IQ. Children with \( \text{pb24} \) levels greater than \( 10 \mu g/dL \) were less likely than children with lower levels to have Verbal IQs that were significantly higher (\( \geq 12 \) points) than their Performance IQs.\(^4\) No distinct pattern of relative strengths and weaknesses was apparent in subtest scores, however, nor was the amount of scatter in subtest scores (defined as the number of subtest scores deviating from the overall mean subtest score by at least \( 1 \) SD)\(^5\) associated with \( \text{pb24} \).

**Kaufman Test of Educational Achievement**

**Crude Analyses.** Blood lead levels measured at ages 10 years, 24, 18, and 12 months were significantly related to children's Battery Composite scores (Table 3). Each of these blood lead levels was also significantly associated with one or more of the subtest scores (data not shown).

**Adjusted Analyses.** Only blood lead levels at 24 months of age were significantly associated with adjusted K-TEA scores. Battery Composite score declined \( 8.9 \) points for each \( 0.48\mu mol/L \) increase in \( \text{pb24} \) (95% CI: 4.2 to 13.6) (Table 3) (Figure). Including Full-Scale IQ in the model reduced but did not eliminate the association (coefficient = \( -5.1 \), SE = 0.20, \( P = 0.13 \)). Exposure-related decreases were also noted in Spelling scores (95% CI: 4.2 to 15.3 points per \( 0.48\mu mol/L \) increase) and Mathematics Composite scores (95% CI: 3.4 to 14.8 points per \( 0.48\mu mol/L \) increase). \( \text{pb24} \) was more strongly associated with performance on the more advanced Concepts Applications items (coefficient = \( -2.4 \), SE = 0.8, \( P = 0.04 \)) than on the Computation items (coefficient = \( -0.08 \), SE = 0.5, \( P = 0.99 \)).

**DISCUSSION**

The most striking finding in this long-term follow-up study is the continued presence at age 10 years of an association noted at age 3 years between a child's blood lead level at 24 months of age and cognitive function. Terms integrating blood lead level over various intervals beginning at 24 months of age were also associated with children's performance. These associations were evident in broad-based assessments of both intelligence and academic achievement. Because the association between \( \text{pb24} \) and IQ was apparent even with adjustment for GCI scores achieved at 57 months, the underlying process may involve more than simple persistence of the performance deficits noted at that time. One possibility is that lead exposure around the age of 24 months has adverse impact on cognition that is not yet fully expressed at age 5 years. A second possibility, not supported by additional analyses, is that different subsets of children were responsible for the associations at the two ages. A third possibility is that this is a measurement artifact stemming from differences in the functional domains assessed by the WISC-R and the McCarthy Scales of Children's Abilities. The associations between \( \text{pb24} \) and K-TEA scores were still evident after we adjusted for IQ, suggesting that lead-sensitive behavioral or neuropsychological factors not reflected in WISC-R IQ scores may contribute to reduced performance on academic tasks.

At 24 months of age, children in this cohort had a mean blood lead level of less than \( 0.34 \mu mol/L \) (7 \( \mu g/dL \)). 90% had levels below 0.63 \( \mu mol/L \) (13 \( \mu g/dL \)), and all had levels below 1.21 \( \mu mol/L \) (25 \( \mu g/dL \)). The exposure-related performance differences are approximately twice the size of that observed at 57 months, corresponding to declines of 5.8 and 8.9 points in Full-Scale IQ and K-TEA Battery Composite scores, respectively, for each \( 0.48\mu mol/L \) increase in \( \text{pb24} \). To provide a context for evaluating the relative importance of lead as a predictor of IQ, children whose mothers achieved IQ scores in the top quartile (in this cohort) had IQ scores that averaged 13.4 points higher than those of children whose mothers' IQ scores were in the bottom quartile. IQ scores of firstborn children averaged 9.0 points higher than those of children born third or later.

Children's performance was much more strongly associated with \( \text{pb24} \) than with blood lead levels at other ages. It is unclear whether this reflects a special vulnerability of the nervous system during this period\(^6\) or simply the fact that blood lead levels tend to peak in the second year.\(^4\)\(^4\)\(^4\) Our finding that \( \text{pb24} \) was more predictive of performance than was maxi...
mum blood lead level supports the hypothesis of an age specific vulnerability.

Alternatively, the apparent importance of pb24 as a predictor may be due to methodological factors such as differences in the power of hypothesis tests involving blood lead levels measured at different ages. The extremely low levels, restricted range, and smaller number of 10-year blood lead levels reduced the likelihood of finding an association between current exposure and performance. Analyses involving all other postnatal blood lead levels had about 80% power to detect roughly the same effect size ($f = 0.48$) increase in blood lead level. Other considerations are relevant to this issue, however. The coefficient of variation was substantially greater for pb24 than pb57 (75.0 vs 60.4%), suggesting that a greater proportion of the observed variation in pb24 than pb57 reflects differences in children's exposures rather than analytical variation, which was relatively constant over time. Moreover, unlike blood lead levels at 57 months and 10 years, pb24 was not strongly associated with sociodemographic characteristics and psychosocial environment. Nevertheless, our findings suggest that, after adjustment for confounding, only blood lead level measured at 24 months was significantly associated with children's function should be interpreted cautiously until confirmed by other studies.

The association was robust to changes in analytical strategy and model composition. Although we cannot exclude the possibility that confounding by some unmeasured or inadequately measured variables produced a spurious association, the estimated decline in children's scores with increasing pb24 was relatively unaffected by adjustment for a variety of factors germane to the psychological, emotional, and intellectual climate within a family. Nevertheless, measures of such factors are fallible. To the extent that these factors are true confounders and the instruments failed to measure them accurately, our adjustment for confounding bias is incomplete.

Another factor to be weighed in evaluating these results is the possibility of bias in terms of the children available for follow-up. The key issue is whether the associations we observed between lead exposure and development among participants are similar to those we would have observed had we been able to evaluate the entire cohort. We determined that the estimated associations noted at earlier assessments between cord blood lead level and Mental Development Index Scores at 6, 12, 18, and 24 months of age were comparable among children who participated in the 10-year follow-up and those who did not. The degree of similarity in the relationship between pb24 and GCI scores at 57 months is more uncertain because of the relatively small number of children lost to follow-up between 57 months and 10 years. Although the coefficients for participants and nonparticipants were not significantly different, the association between pb24 and performance at 10 years may have been somewhat diminished had we achieved 100% follow-up.

Analyses of WISC-R subtest scores indicated that pb24 was most strongly related to children's scores on verbally mediated tasks. In contrast, at age 57

<table>
<thead>
<tr>
<th>Blood Lead Measurement*</th>
<th>Crude Battery Composite</th>
<th>Adjusted* Battery Composite</th>
<th>Mathematics Composite</th>
<th>Reading Composite</th>
<th>Spelling</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 y</td>
<td>$-1.43 (0.31)$</td>
<td>$-0.44 (0.61)$</td>
<td>$-0.46 (0.71)$</td>
<td>$-0.71 (0.54)$</td>
<td>$-0.24 (0.73)$</td>
</tr>
<tr>
<td>12 mo</td>
<td>$-0.90 (0.37)$</td>
<td>$-0.15 (0.34)$</td>
<td>$0.00 (0.41)$</td>
<td>$-0.15 (0.31)$</td>
<td>$-0.35 (0.41)$</td>
</tr>
<tr>
<td>18 mo</td>
<td>$-0.99 (0.27)$</td>
<td>$-0.53 (0.24)$</td>
<td>$-0.91 (0.29)$</td>
<td>$-0.15 (0.21)$</td>
<td>$-0.37 (0.28)$</td>
</tr>
<tr>
<td>57 mo</td>
<td>$-0.09 (0.21)$</td>
<td>$-0.15 (0.21)$</td>
<td>$-0.31 (0.25)$</td>
<td>$0.08 (0.19)$</td>
<td>$-0.44 (0.25)$</td>
</tr>
<tr>
<td>6 mo</td>
<td>$-0.14 (0.21)$</td>
<td>$-0.00 (0.18)$</td>
<td>$-0.11 (0.22)$</td>
<td>$0.02 (0.16)$</td>
<td>$0.09 (0.21)$</td>
</tr>
</tbody>
</table>

* Age at which blood lead level was measured.
* Adjustment made for the same variables listed in footnote f of Table 1.
* Regression coefficient (SE), representing the estimated change in score associated with each 0.48-μmol/L (1-μg/dL) increase in blood lead level.
* Two-sided P value associated with the hypothesis that the coefficient is zero.
* Coefficient (SE) associated with membership in the "low" cord blood lead group; reference group is children in the "high" cord blood lead group.
* Two-sided P value associated with the hypothesis that there are no differences among the scores of children in the three cord blood lead groups.
months pb24 was more strongly associated with nonverbal skills. Verbal deficits among children with higher pb24 levels may not have been apparent at 57 months because of the relative insensitivity of the language assessments available for evaluating children at that age. Greater compensatory effects of environmental stimulation on language performance at younger ages, or both. Alternatively, a common underlying neurological substrate (eg, attention, state) that affects performance on psychometric tests may be expressed differently over time. This hypothesis is speculative, although other follow-up studies have reported that the behavioral and developmental correlates of early biological insult may change over time.  

There is little evidence that lead exposure has a distinctive "behavioural signature." Measures of lead exposure have been significantly related to both Verbal and Performance IQ, only Verbal IQ, only Performance IQ, or neither. Findings are also inconsistent with respect to lead and academic achievement. The explanation for this is not clear, although differences in study power may be contributory. In addition, the manner in which toxicity is expressed may depend on a number of factors, including the timing and level of exposure, its chronicity, and other aspects of a child's developmental context. Retrospective and cross-sectional studies provide only limited opportunities to discern associations between specific characteristics of exposure history and neuropsychological outcome.

At present, other prospective studies provide only partial support for our findings. It is unclear whether this reflects instability of the association between lead exposure and development, methodological differences among studies, or both. The cohorts being followed differ substantially in terms of exposure characteristics. On the basis of toxicokinetic principles, different patterns of associations between exposure and function should be expected. Functional deficits have consistently been noted at lower blood lead levels in our cohort than in the others. We attribute this, at least in part, to the low background risk of intellectual handicap in this cohort relative to others. Most US lead studies focus on poor inner-city children for whom lead exposure is only one of many developmental risk factors. The high socioeconomic standing of our cohort may have provided us greater opportunity to perceive lead-related variance in cognitive function. It may also restrict the population to which our findings may be generalized. Early insults tend to be expressed more severely among populations at high socioeconomic risk. The associations we observed may underestimate those that, with adequate control of confounding, would be observed in a group more representative of children with higher levels of lead exposure.

In summary, this follow-up study of socioeconomically advantaged children with relatively low lifetime exposures to lead suggests that slight elevations of blood lead at around the age of 2 years are associated, without an apparent threshold, with significant decrements in intellectual and academic performance at 10 years of age.

ACKNOWLEDGMENTS

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REFERENCES

FAT FACTS

McDonald's merits praise for introducing a lower-fat version of its large hamburger. But by promoting its new "McLean Deluxe" as "91% fat free," it reinforces the trend of using misleading fat-free claims.

Such claims, expressing fat content as a percentage of weight, are a powerful selling tool in a health-conscious market. But much of the weight may be water, so the implication that a product is low in fat can be deceptive. The McLean's 9 percent fat content, for example, though only about half that of standard burgers, still packs 10 grams of fat—five times the FDA definition of low fat.

McDonald's is hardly the only offender. Misleading percentage claims are a powerful marketing ploy for fat-laden products ranging from frozen sausages and French fries to ice cream. The FDA could help consumers by immediately calling for a fat content, for example, though only about half that of standard burgers, still packs 10 grams of fat—five times the FDA definition of low fat.

McDonald's is hardly the only offender. Misleading percentage claims are a powerful marketing ploy for fat-laden products ranging from frozen sausages and French fries to ice cream. The FDA could help consumers by immediately calling for a moratorium on such claims, even while the agency prepares new restrictions to carry out last year's Federal nutrition labeling reform.


Submitted by Kurt Metzl, MD