

## THE LONG-TERM EFFECTS OF EXPOSURE TO LOW DOSES OF LEAD IN CHILDHOOD

### An 11-Year Follow-up Report

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**Abstract** To determine whether the effects of low-level lead exposure persist, we reexamined 132 of 270 young adults who had initially been studied as primary school-children in 1975 through 1978. In the earlier study, neuro-behavioral functioning was found to be inversely related to dentin lead levels. As compared with those we restudied, the other 138 subjects had had somewhat higher lead levels on earlier analysis, as well as significantly lower IQ scores and poorer teachers' ratings of classroom behavior.

When the 132 subjects were reexamined in 1988, impairment in neurobehavioral function was still found to be related to the lead content of teeth shed at the ages of six and seven. The young people with dentin lead levels >20 ppm had a markedly higher risk of dropping out of high school (adjusted odds ratio, 7.4; 95 percent con-

fidence interval, 1.4 to 40.7) and of having a reading disability (odds ratio, 5.8; 95 percent confidence interval, 1.7 to 19.7) as compared with those with dentin lead levels <10 ppm. Higher lead levels in childhood were also significantly associated with lower class standing in high school, increased absenteeism, lower vocabulary and grammatical-reasoning scores, poorer hand-eye coordination, longer reaction times, and slower finger tapping. No significant associations were found with the results of 10 other tests of neurobehavioral functioning. Lead levels were inversely related to self-reports of minor delinquent activity.

We conclude that exposure to lead in childhood is associated with deficits in central nervous system functioning that persist into young adulthood. (N Engl J Med 1990; 322:83-8.)

**W**ITHIN the past three years, the Environmental Protection Agency and the Agency for Toxic Substances and Disease Registry have concluded in policy statements that lead at low doses is a serious threat to the central nervous systems of infants and children.<sup>1,2</sup> These policy statements have been based on a growing convergence of results from both epidemiologic and experimental studies of lead toxicity in the United States, Europe, and Australia.<sup>3-8</sup> Whether the effects on the central nervous system of exposure to low doses of lead that have been observed in infants and children persist has received limited attention. Only three follow-up studies have been published to date, and the longest follow-up has been five years.<sup>9-11</sup> No data have yet been reported on whether early disturbances influence functional abilities in later life.

In 1979 we reported that first- and second-grade children without symptoms of plumbism, but with elevated dentin lead levels, had deficits in psychometric intelligence scores, speech and language processing, attention, and classroom performance.<sup>3</sup> When they were studied in the fifth grade, the children with high dentin lead levels had lower IQ scores, needed more special academic services, and had a significantly higher rate of failure in school than other children.<sup>9</sup> We have now evaluated the neuropsychological and academic performance in young adulthood of 132 of

the original sample of 270 subjects, and we report the relation of their recent performance to their exposure to lead, as measured 11 years earlier.

### METHODS

#### Sample

The initial sample was chosen from the population of 3329 children enrolled in the first and second grades in the Chelsea and Somerville, Massachusetts, school systems between 1975 and 1978. Of this population, 70 percent provided at least one of their shed primary teeth for lead analysis. From this sample of 2335 children, 97 percent of whom were white, we identified 270 from English-speaking homes whose initial dentin lead levels were either >24 ppm or <6 ppm. These children (mean age, 7.3 years) underwent an extensive neurobehavioral examination. More teeth were subsequently collected and analyzed, and the subjects whose teeth were discordant with respect to lead level according to a priori criteria were excluded from the data analysis. Also excluded from the analysis were children who had not been discharged from the hospital after birth at the same time as their mothers, who had a noteworthy head injury, or who were reported to have had plumbism.<sup>3</sup>

In a later reanalysis, conducted in response to suggestions from the Environmental Protection Agency,<sup>12</sup> the tooth lead level was treated as a continuous variable. A mean dentin lead level was computed for each subject from all the teeth collected. The exclusionary factors previously used were found not to be related to outcome scores. The subjects initially excluded were therefore not excluded from this follow-up sample.

The 270 subjects tested from 1975 to 1978 constitute the base population for this report. From old research records, telephone directories, town records, and driver's-license rolls, we located 177 subjects. Of these, 132 agreed to participate, and the remaining 45 declined. The subjects were paid \$35 each and received travel expenses. Ten subjects tested in 1988 had been excluded from the analysis reported in 1979 because their parents stated at the time of testing that the children had elevated blood lead levels or had undergone chelation for lead poisoning. This group is discussed separately in this report. The mean age of the 132 subjects at the 1988 reexamination was 18.4 years; the mean length of time between the two examinations was 11.1 years. All but four subjects in the current follow-up study were white. No clinical manifestations of lead exposure were recorded in the earlier interviews for the 122 subjects who were not treated with chelating agents.

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The research protocol and informed-consent procedures were approved by the institutional review boards of the Children's Hospital of Pittsburgh and the Children's Hospital, Boston. Informed consent was given by all the subjects or their parents.

### Classification of Lead Exposure

All the dentin lead levels measured from 1975 through 1977 were used to compute an arithmetic mean lead concentration for each subject. The lead burden was treated in two ways: as an interval variable in linear regressions and as a categorical variable — i.e., high (>20 ppm), medium (10 to 19.9 ppm), and low (<10 ppm) — in the logistic regressions described below. Lead levels in venous blood were measured at the time of the reexamination to estimate current exposure. This practice was discontinued after the first 48 subjects were tested, because none had a lead level exceeding 0.34  $\mu\text{mol}$  per liter (7  $\mu\text{g}$  per deciliter), well below the Centers for Disease Control's definition of undue lead exposure of 1.25  $\mu\text{mol}$  per liter (25  $\mu\text{g}$  per deciliter).

### Behavioral Evaluation

The subjects were evaluated individually by a single examiner, who remained blinded to their lead-exposure status until all the data had been coded and entered into a computer data base. All assessments were carried out in a fixed order; the duration of the testing was about two hours.

#### Neurobehavioral Evaluation System

The subjects completed an automated assessment battery in which they used a personal computer, joystick, and response key.<sup>13</sup> We selected the following items from the battery for evaluation:

##### *Continuous-performance test.*<sup>14</sup>

*Symbol-digit substitution*, an adaptation of the Wechsler item for computer administration.

*Hand-eye coordination.* Using a joystick to move the cursor, the subject traced over a large sine wave generated on the monitor screen; deviations from the line (root mean square error) were recorded.

*Simple visual-reaction time.* Subjects pressed the response key when an O appeared on the screen; the interval before the stimulus was varied randomly.

*Finger tapping.* The subject pressed a response button as many times as possible during a 10-second period; both hands were tested.

*Pattern memory.* The subject was presented with a computer-generated pattern formed by a 10-by-10 array of dark and bright elements. After a brief exposure, the subject was presented with three patterns, only one of which was identical to the original pattern. The number of correct responses and the length of time to the correct choice were recorded.

*Pattern comparison.* The subject was presented with three computer-generated patterns on the 10-by-10 array. Two were identical, and one differed slightly from the other two. The subject was required to select the nonmatching pattern.

*Serial-digit learning.* The subject was presented with a string of 10 digits, then asked to enter the string into the computer. After an error, the same stimulus was presented, and the second trial began.

*Vocabulary.* For each of 25 words, the subject chose the word most nearly synonymous from a list of four choices.

*Grammatical reasoning.* The subject was presented with a pair of letters, A and B, whose relative position varied. Then the screen cleared, and the letters were replaced by a sentence that described the order of the letters. The sentence might be active or passive, affirmative or negative, true or false (examples are "A follows B" and "B is not followed by A"). The subject had to choose the correct sentences, and the number of errors was recorded.

*Switching attention.* The subject was required to choose which key to press in response to three different instructions. In the "side" trials, the subject had to press the key on the same side as the stimulus. In the "direction" trials, the correct choice was the direction in which an arrow pointed. Before each trial in the third set, the subject was told whether to choose the side the arrow was on or the direction in which it pointed.

*Mood scales.* This test was derived from the Profile of Mood States.<sup>15</sup> Five scores were computed for tension, anger, depression, fatigue, and confusion.

The following tests were also used to evaluate neurobehavioral functioning:

#### California Verbal Learning Test

The California Verbal Learning Test<sup>16</sup> was used to assess multiple strategies and processes involved in verbal learning and memory. Scores for immediate and delayed recall were also obtained.

#### Boston Naming Test

In the Boston Naming Test,<sup>17</sup> the subject was presented with 60 pictures in order of increasing difficulty and asked to name the objects shown.

#### Rey-Osterreith Complex Figure Test

The Rey-Osterreith Complex Figure Test<sup>18</sup> was used to evaluate visual-motor and visual-spatial skills. The subject was asked to copy an abstract geometric figure and then to draw it from memory both immediately and after 30 minutes. Accuracy and organization scores were calculated.

#### Word-Identification Test

Form B from the Woodcock Reading Mastery Test was used to evaluate reading skill. Grade-equivalency scores were calculated from raw scores. Reading disability was defined as indicated by scores two grade levels below the score expected on the basis of the highest grade completed.

#### Self-Reports of Delinquency

The subjects completed a structured questionnaire from the National Youth Survey<sup>19</sup> that included scales for minor antisocial behavior and for violent crimes.

#### Review of School Records

High-school records were obtained for all but two of the subjects tested. Class size and rank, the highest grade completed, and the number of days absent and tardy in the last full semester were recorded. Students who were still in the 11th grade at the time of testing were not included in analyses of the highest grade completed. Class rank was computed as  $1 - (\text{class rank}/\text{class size})$ .

### Statistical Analysis

To evaluate whether the participants in this follow-up evaluation were representative of the original cohort, subjects who were tested and not tested in 1988 were compared in terms of variables reported in 1979, including dentin lead levels, covariates not related to lead exposure, teachers' ratings of classroom behavior, and IQ scores. In addition, we carried out separate regressions of dentin lead level against IQ score as measured between 1976 and 1978 for subjects tested and not tested in 1988. We then performed a regression on both groups taken together, entering both a dummy term for participation in the current follow-up (yes or no) and a lead-level-by-participation status term.

To evaluate the relation between early exposure to lead and each of the continuously distributed outcome variables, subjects were classified according to dentin lead-level quartiles, and mean scores, adjusted for covariates, were computed. Ordinary least-squares lin-

ear regression, with the mean or log-mean dentin lead level as the main effect, was used to estimate the significance of the relation. Outcomes that were significantly associated with lead exposure in these bivariate analyses were further evaluated by multiple regression analysis. Ten covariates were included in the model. They were the mother's age at the time of the subject's birth, the mother's educational level, the mother's IQ, family size, socioeconomic status (a two-factor Hollingshead index), sex, age at the time of testing, birth order, alcohol use, and whether the subject and the mother left the hospital together after the subject's birth. The lead measure (the mean or the log of the mean) that produced the best-fitted model (highest  $R^2$ ) is reported. Five of these covariates were employed in the first study of these subjects and shown to be influential. Five others (sex, age at testing, prolonged hospitalization as a neonate, birth order, and current alcohol use) were added to the model on the basis of prior knowledge of their effects on psychometric function. Logistic-regression analysis was used to model the association of lead level and two outcomes treated categorically (failure to graduate from high school and reading disability). In this analysis, we controlled for the covariates listed above. Two indicator variables were used to represent the three exposure groups. Odds ratios and 95 percent confidence intervals, adjusted for covariates, were computed for the high-lead-level group, with the low-lead-level group used as the reference group.

## RESULTS

### Selection Bias

The 132 subjects who were retested in 1988 (Table 1) were not representative of the group of 270 subjects tested in 1979. The subjects we retested tended to have slightly lower dentin lead levels, more highly educated families of higher socioeconomic status, and mothers with higher IQs and better obstetrical histories; a higher proportion of the retested subjects were girls. In addition, they had had fewer head injuries and had significantly higher IQ scores and better teachers' ratings as reported in 1979. The slope of the regression of childhood IQ on dentin lead level was steeper in the group not tested in the follow-up study, although the difference from the slope in the group we retested was not statistically significant ( $F = 1.82, 1,196$  df;  $P = 0.18$ ).

### Academic and Neurobehavioral Outcome

Table 2 shows the covariate-adjusted scores of the 122 subjects who did not have clinical plumbism, according to their dentin lead concentrations. Table 3 summarizes the results of modeling the relation between early exposure to lead and outcome by multiple regression. Earlier exposure to lead was significantly associated with diminished academic success. Among children with dentin lead levels  $>20$  ppm, as compared with those whose dentin lead levels were  $<10$  ppm, the unadjusted odds ratio for failure to graduate from high school was 4.6 (95 percent confidence interval, 1.2 to 17.4). Adjustment for

Table 1. Comparison of Subjects Tested and Not Tested in 1988.\*

| CHARACTERISTIC                       | TESTED<br>(N = 132) | NOT TESTED<br>(N = 138) | P VALUE |
|--------------------------------------|---------------------|-------------------------|---------|
| Lead-level group (%)                 |                     |                         |         |
| Low                                  | 50                  | 47.8                    | —       |
| Middle                               | 22.7                | 16.7                    | —       |
| High                                 | 27.3                | 35.5                    | 0.7†    |
| Birth order                          | 2.3±1.6             | 2.8±1.9                 | 0.016   |
| No. of live births                   | 2.8±1.5             | 3.2±1.6                 | 0.05    |
| Father's education (yr)              | 12.2±2.6            | 11.4±2.6                | 0.009   |
| Mother's education (yr)              | 12.0±2.2            | 11.1±2.1                | 0.0005  |
| Mother's IQ                          | 112±15              | 108±15                  | 0.017   |
| Mother's age at subject's birth (yr) | 25.5±5.9            | 25.3±5.8                | 0.7     |
| Father's age at subject's birth (yr) | 28.3±7.8            | 28.8±7.9                | 0.6     |
| Gestation (wk)                       | 39.9±2.0            | 40.0±1.7                | 0.7     |
| Birth weight (g)                     | 3776±608            | 3712±600                | 0.40    |
| Sex (%)                              |                     |                         |         |
| Female                               | 55.3                | 42.8                    |         |
| Male                                 | 44.7                | 57.3                    | 0.04    |
| Head injuries (%)                    | 3.8                 | 8.7                     | 0.09    |
| Teachers' ratings (1979 sum score)   | 9.3±2.8             | 8.2±3.6                 | 0.004   |
| Full-scale IQ (1979)                 | 107.5±14            | 99.5±15                 | 0.001   |

\*Plus-minus values are means ±SD.

†By chi-square test for all lead-level groups.

covariates increased the odds ratio to 7.4 (95 percent confidence interval, 1.4 to 40.8). Higher dentin lead levels were also associated with lower class rank, increased absenteeism, lower scores on vocabulary and grammatical-reasoning tests, significantly slower finger-tapping speed, longer reaction times, poorer hand-eye coordination, and lower reading scores. In subjects with dentin lead levels  $>20$  ppm, the unadjusted odds ratio for having a reading disability, defined by a score two grades below that expected for the highest grade completed, was 3.9 (95 percent confi-

Table 2. Outcomes in Young Adulthood According to Dentin Lead Concentration in Childhood.\*

| OUTCOME VARIABLE                           | LEAD CONCENTRATION      |                      |                        |                           |
|--|-------------------------|----------------------|------------------------|---------------------------|
|  | LOWEST<br>( $<5.9$ ppm) | LOW<br>(6.0–8.2 ppm) | HIGH<br>(8.3–22.2 ppm) | HIGHEST<br>( $>22.2$ ppm) |
| No. of subjects                            | 30                      | 31                   | 30                     | 31                        |
| Reading score (words read correctly)       | 143.8                   | 142.7                | 140.2                  | 135.2                     |
| Reading grade equivalent (grade level)     | 12.2                    | 11.9                 | 11.2                   | 10.1                      |
| Highest grade achieved (grade level)       | 11.7                    | 11.9                 | 11.5                   | 11.3                      |
| Class standing (percentile)                | 0.60                    | 0.59                 | 0.48                   | 0.45                      |
| Absence from school (no. of days/semester) | 12.0                    | 12.0                 | 17.9                   | 20.8                      |
| Vocabulary (words correct)                 | 18.0                    | 16.4                 | 17.6                   | 14.6                      |
| Grammatical reasoning (no. incorrect)      | 13.1                    | 13.0                 | 12.8                   | 15.8                      |
| Hand-eye coordination†                     | 5.1                     | 5.4                  | 5.5                    | 6.2                       |
| Reaction time (msec)                       |                         |                      |                        |                           |
| Preferred hand                             | 246.6                   | 255.5                | 267.3                  | 275.1                     |
| Nonpreferred hand                          | 241.2                   | 238.2                | 258.4                  | 261.2                     |
| Finger tapping (no./10 sec)                | 46.6                    | 47.2                 | 45.9                   | 43.5                      |

\*The subjects were divided into groups according to lead-level quartiles. The values shown are least-square mean scores, after adjustment for covariates. Subjects with clinical plumbism have been excluded.

†For hand-eye coordination, larger numbers indicate more errors.

Table 3. Regression of Outcomes in Young Adulthood on Dentin Lead Levels in Childhood.\*

| OUTCOME VARIABLE           | BIVARIATE REGRESSION |                    |       |         | MULTIPLE REGRESSION |                    |       |         |
|----------------------------|----------------------|--------------------|-------|---------|---------------------|--------------------|-------|---------|
|                            | R <sup>2</sup>       | PARAMETER ESTIMATE | SE    | P VALUE | R <sup>2</sup>      | PARAMETER ESTIMATE | SE    | P VALUE |
| Highest grade achieved     | 0.061                | -0.027             | 0.009 | 0.008   | 0.319               | -0.027             | 0.01  | 0.013   |
| Reading grade equivalent   | 0.121                | -0.07              | 0.018 | 0.0001  | 0.229               | -0.072             | 0.021 | 0.001   |
| Class standing             | 0.039                | -0.006             | 0.003 | 0.048   | 0.248               | -0.006             | 0.003 | 0.048   |
| Absence from school†       | 0.071                | 4.8                | 1.7   | 0.006   | 0.209               | 4.73               | 1.8   | 0.01    |
| Grammatical reasoning      | 0.051                | 0.159              | 0.062 | 0.012   | 0.197               | 0.178              | 0.068 | 0.011   |
| Vocabulary                 | 0.108                | -0.124             | 0.032 | 0.000   | 0.324               | -0.122             | 0.033 | 0.001   |
| Finger tapping             | 0.031                | -0.104             | 0.05  | 0.05    | 0.336               | -0.133             | 0.05  | 0.01    |
| Hand-eye coordination      | 0.043                | 0.041              | 0.018 | 0.02    | 0.195               | 0.048              | 0.019 | 0.01    |
| Reaction time†             |                      |                    |       |         |                     |                    |       |         |
| Preferred hand             | 0.025                | 11.8               | 6.66  | 0.08    | 0.242               | 12.9               | 6.3   | 0.042   |
| Nonpreferred hand          | 0.03                 | 11.5               | 0.05  | 0.056   | 0.229               | 10.3               | 5.5   | 0.06    |
| Minor antisocial behavior† | 0.025                | -0.639             | 0.36  | 0.082   | 0.306               | -0.739             | 0.35  | 0.038   |

\*The following covariates were controlled for in the multiple regression analysis: age, sex, birth order, family size, mother's age at the subject's birth, length of the neonatal stay in the hospital, mother's education level, mother's IQ, socioeconomic status, and current alcohol use.

†The natural log of the mean dentin lead level was used as the main effect.

dence interval, 1.5 to 10.5). Adjustment for covariates increased the odds ratio to 5.8 (95 percent confidence interval, 1.7 to 19.7). For most outcomes, neither the size of the lead regression coefficients nor their standard errors were substantially changed by adjustment for covariates.

Of the 10 children with clinical plumbism (who either underwent chelation or were reported to have had elevated blood lead levels), 3 of 7 (43 percent) dropped out before graduating from high school (3 others are still in school), and 5 of 10 (50 percent) have reading disabilities. When the children with plumbism were grouped with the other subjects ac-

ording to quartiles for dentin lead levels, a dose-response relation was evident for both outcomes (Fig. 1 and 2).

Early exposure to lead was not significantly associated with performance on the symbol-digit or serial-digit tests, the continuous-performance test, pattern memory or pattern comparison, switching attention, the California Verbal Learning Test, the Rey-Osterreith figures, the Boston Naming Test, or mood scores. The lead level was inversely related to the summed score on the self-report of delinquency questionnaire, which consisted primarily of reports of minor antisocial behavior.

When subjects were divided into two groups according to their dentin lead levels (<10 ppm vs. ≥10 ppm), high dentin lead levels predicted future failure to graduate from high school with a sensitivity ( $\pm$ SE) of  $0.71 \pm 0.12$  and a specificity of  $0.61 \pm 0.05$  (Table 4).

## DISCUSSION

In this extended follow-up study, in which the mean length of follow-up was 11.1 years, we found that the associations reported earlier between lead and children's academic progress and cognitive functioning persisted into young adulthood. The persistent toxicity of lead was seen to result in significant and serious impairment of academic success, specifically a seven-fold increase in failure to graduate from high school, lower class standing, greater absenteeism, impairment of reading skills sufficiently extensive to be labeled reading disability (indicated by scores two grades below the expected scores), and deficits in vocabulary, fine motor skills, reaction time, and hand-eye coordination.

A number of issues require consideration when one is interpreting the data reported here. The first is the influence of selection bias on the associations we observed. The subjects retested in 1988 had more favorable characteristics than those who could not be located or who declined to participate. The subjects who were not retested tended to have had higher lead lev-

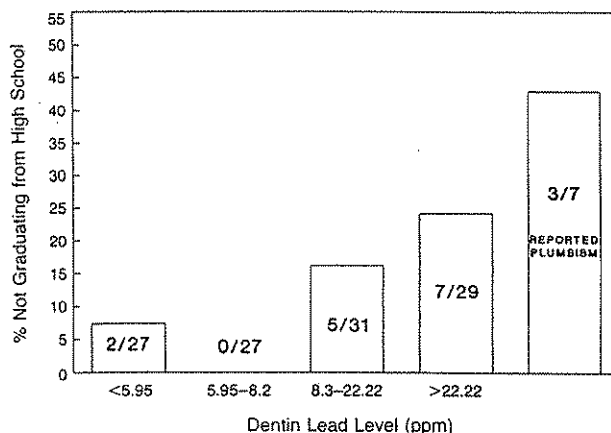


Figure 1. The Proportion of Subjects Who Did Not Graduate from High School, Classified According to Their Past Exposure to Lead.

Asymptomatic subjects are classified according to lead-level quartiles. Seven of the 10 subjects who were earlier reported to have clinical plumbism are shown in a separate column. No school records were found for two subjects. One subject was not tested but reported that she had graduated from high school. (There are therefore 121 subjects represented in this figure.) Ten subjects (three with reported plumbism and seven asymptomatic subjects) are still attending high school and are therefore not shown here. The numbers in each column indicate the number who did not graduate and the total number in the category.

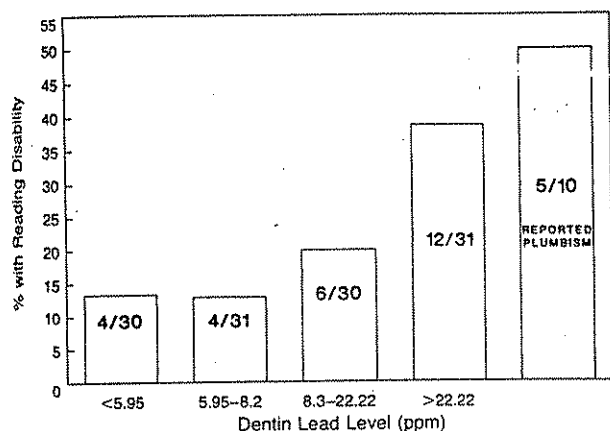


Figure 2. The Proportion of Subjects with Reading Disabilities, Classified According to Their Past Exposure to Lead.

Asymptomatic subjects are classified according to lead-level quartile, and 10 children with a history of clinical plumbism are shown separately. Reading disability is defined as indicated by a reading level two or more grades below the expected level. The numbers in each column indicate the number with a reading disability and the total number in the category.

els, lower socioeconomic status, and lower IQ scores and teachers' ratings of classroom behavior. The inverse relation between dentin lead levels and IQ reported in 1979 was stronger for the subjects who were not retested in 1988 than for those we retested, although the difference did not reach statistical significance. This finding is in agreement with the observation, made by us and others, that children from families in lower socioeconomic groups are more vulnerable to the effects of lead than children from more favored economic backgrounds.<sup>20</sup> We infer that the estimates made on the basis of the data on the 132 subjects we restudied are likely to be conservative. Indeed, had all the original subjects been located and retested, the magnitude of the effect of lead exposure might have been even greater.

Is the nature of the relation between lead and later outcome causal, or does it result from confounding by other variables? The association between lead and outcome reported here meets six criteria for valid causal inference: proper temporal sequence, strength of association, presence of a biologic gradient, non-spuriousness, consistency, and biologic plausibility.<sup>21</sup>

In this study, the exposure to lead preceded the school failure and the reading disabilities measured. The strength of the association, as measured by adjusted odds ratios of 7.4 and 5.8, was substantial. A dose-response relation has been demonstrated between exposure and numerous outcome variables (Table 2, Fig. 1 and 2). "Nonspuriousness" indicates that the association observed is not due to confounding. In this analysis, we controlled for both the covariates that were identified in 1979 as potential confounders and others we suspected were important. The magnitude of the effect of lead was reduced only slightly, if at all, by this procedure. The zero-order correlation between socioeconomic status and dentin lead levels

in this sample was not great ( $r = 0.04$ ). Many covariates that were important contributors to performance in the early grades (e.g., the mother's IQ and the mother's educational level) had less effect on the subject's performance in young adulthood. The results, moreover, are consistent with those of several other studies by workers who have reported lead-associated deficits in reading<sup>4,22,23</sup> and early classroom behavior.<sup>24,25</sup> The lead-related deficits in IQ, speech and language processing, and attention reported in 1979 provide plausible mechanisms by which lead could impair performance in class and produce eventual failure. Similar effects on learning have been demonstrated in the experimental studies by Gilbert and Rice of subhuman primates.<sup>7</sup> In these investigations, rhesus monkeys, administered lead only in the first 100 days of life, had impairments in learning as adolescents. In adolescence, the mean blood lead level of these monkeys was  $0.73 \mu\text{mol per liter}$  ( $15 \mu\text{g per deciliter}$ ).

The value accepted as the threshold for lead-engendered neurotoxicity in children has declined steadily over the past decade as more sophisticated population studies, with larger samples, better designs, and better analyses, have been conducted.<sup>4,5,11,22,24,26-29</sup> When this study was begun in 1975, the toxic level of lead in the blood was defined by the Centers for Disease Control as  $2.0 \mu\text{mol per liter}$  ( $40 \mu\text{g per deciliter}$ ). In 1973, the mean blood lead level in a subsample of 23 children chosen from among those with the highest dentin lead levels in an earlier study was  $1.7 \mu\text{mol per liter}$  ( $34 \mu\text{g per deciliter}$ ).<sup>3</sup> None of our subjects were symptomatic. That these subjects were exposed to high doses of lead after the original study was completed is unlikely. Lead exposure, the incidence of pica, and hand-to-mouth behavior diminish after the fifth year of life. The low blood lead levels found in these subjects in young adulthood (all  $<0.034 \mu\text{mol per liter}$ ) provide convincing evidence that their later exposure to lead was not excessive.

The consensus on what level of lead is toxic has changed in recent years. After reviewing the studies published up to 1987, the Agency for Toxic Substances and Disease Registry defined the threshold for neurobehavioral toxicity as  $0.5$  to  $0.7 \mu\text{mol per liter}$

Table 4. Sensitivity and Specificity of the Dentin Lead Level in Childhood as a Predictor of Failure to Graduate from High School.\*

| HIGH-SCHOOL GRADUATION            | LEAD LEVEL    |            |
|-----------------------------------|---------------|------------|
|                                   | $\geq 10$ PPM | $< 10$ PPM |
| No                                | 10            | 4          |
| Yes                               | 39            | 61         |
| Sensitivity = $10/(10+4) = 0.71$  |               |            |
| Specificity = $61/(61+39) = 0.61$ |               |            |

\*Of the 122 asymptomatic subjects studied, 7 subjects who were still attending school at the time of this analysis were excluded. One subject's school records were not found. Of the 132 subjects retested in 1988, the 10 with clinical plumbism have been excluded.

(10 to 15  $\mu\text{g}$  per deciliter).<sup>1</sup> The agency estimated that 3 to 4 million American children have blood lead levels in excess of 0.7  $\mu\text{mol}$  per liter. The mean blood level among our subjects with high tooth lead levels, estimated in 1979 from a limited lead-screening program, was 1.6  $\mu\text{mol}$  per liter (34  $\mu\text{g}$  per deciliter) (range, 0.87 to 2.6  $\mu\text{mol}$  per liter [18 to 54  $\mu\text{g}$  per deciliter]). For subjects with low tooth lead levels, it was 1.2  $\mu\text{mol}$  per liter (24  $\mu\text{g}$  per deciliter) (range, 0.58 to 1.7  $\mu\text{mol}$  per liter [12 to 36  $\mu\text{g}$  per deciliter]). Thus, the lead levels in the reference sample used in the calculation of the odds ratios for one high-lead-level group were relatively high by contemporary standards.

The data presented here indicate that exposure to lead, even in children who remain asymptomatic, may have an important and enduring effect on the success in life of such children and that early indicators of lead burden and behavioral deficit are strong predictors of poor school outcome. For the small group of 10 subjects who were diagnosed earlier as having plumbism, the outcome was especially dire; half of these young people have reading disabilities, and almost half left high school before graduation. Given the federal estimates that 16 percent of children in the United States have elevated blood lead levels ( $>0.7$   $\mu\text{mol}$  per liter [15  $\mu\text{g}$  per deciliter]), the implications of these findings for attempts to prevent school failure are intriguing. The practical importance of early detection and abatement of lead in the environment, before it enters the bodies of children, is borne out by these long-term findings in young adults.

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