PRENATAL AND POSTNATAL EXPOSURE TO LEAD IN RELATION TO INFANT DEVELOPMENT: A REVIEW

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16. Abstract (Limit: 200 words) This report reviewed and evaluated the evidence concerning lead (7439921) exposure and infant development from prospective studies in Boston, Cincinnati and Cleveland in the United States as well as in Port Pirie, Australia; Kosovo, Yugoslavia; and Christchurch, New Zealand. The Boston and Cincinnati studies both found deficits in visual/motor skills in relation to prenatal and neonatal lead burdens. In the Port Pirie cohort the primary source of lead exposure was a smelter located upwind of the city. Blood lead levels of 8.3 micrograms/deciliter (microg/dl) prenatally and 2.1microg/dl in the postnatal period were determined in the mostly middle class population. Beginning at age 2 the blood lead levels were related to measurable deficits in the developmental assessment at age 4, primarily in nonverbal skills. A decrease of 7 points on the adjusted McCarthy GCI score was noted as postnatal blood lead levels rose from 10 to 30microg/dl. The Yugoslavian population was also residing near a lead smelter and demonstrated a mean of 17.1microg/dl prenatally and 35.5microg/dl in the postnatal period. Deficits were found in development at age 2 for prenatal as well as in postnatal blood lead. Each of the studied populations revealed that lead exposures sufficient to produce body burdens on the order of 10microg/dl in blood, either prenatally or postnatally, caused small reductions in infant and child cognitive ability as estimated by IQ tests.

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Background

In October of 1991, the Centers for Disease Control (CDC) issued new guidelines for allowable environmental lead exposures to children, replacing the previous single threshold value of 25 μg/dl in blood with several "levels of action," starting at blood lead concentrations of 10 μg/dl (1). Health and Human Services Secretary Louis Sullivan gave the following explanation for the revised guidelines: "...new data have shown that blood lead levels which were previously believed to be safe are in fact associated with significant adverse effects" (2). The effects referred to are (presumably) the findings from several recent studies that link prenatal and early postnatal lead concentrations in the 10-25 μg/dl range with losses of 4 to 6 points on tests of infant development.

The lowering of the environmental lead standard in response to data on neuropsychological deficits in infants exposed in-utero and postnatally raises the question of whether the occupational standard governing workplace exposure of parents also needs revision. Since lead accumulates in the body and readily crosses the placenta (e.g. 3-5), exposure to female workers could affect the intrauterine environment during any current or future pregnancy. In addition, since occupational lead has been found to "foul the nest" (6), exposures to male as well as female workers have the potential to influence a child's postnatal home environment. The purpose of this report is to review and evaluate the evidence concerning lead exposure and infant development from prospective studies in three U.S. cities (Boston, Cincinnati, and Cleveland), as well as in Port Pirie, Australia, Kosovo, Yugoslavia and Christchurch, New Zealand. Particular emphasis will be placed on aspects of the findings that carry implications for occupational risk assessment.

Early Studies

Studies describing effects of lead (Pb) on mental development in young children who had been diagnosed with Pb "poisoning" first appeared in the literature over 25 years ago (7-8). In spite of the fact that these studies lacked adequate control groups or evaluation of mental status prior to the diagnosis of Pb poisoning, the symptoms reported were sufficiently striking that high dose Pb exposure did indeed seem to be a cause of encephalopathy and severe neurological sequelae.

In the 1970s and 80s, studies began to appear that reported less severe but measurable adverse effects in connection with lead concentrations considerably below the 80 μg/dl level associated with frank Pb poisoning. A number of these studies, which used cross-sectional and retrospective cohort designs, suggested that, compared to their peers, children with an elevated Pb burden did less well both on standardized IQ tests and in terms of general classroom performance (9-18). However, numerous reviews of these studies (19-23) have raised doubts about their interpretation because of limitations that are inherent in cross-sectional study designs, and also to some extent in retrospective cohort studies. These limitations include, first, an ambiguity about the temporal sequence between exposure and effect. The issue of reverse causality (i.e., low IQ determining lead exposure) is a significant one in studies of Pb and infant development because of the phenomenon known as "pica." Pica refers to the hand-to-mouth behavior among infants and young children that can lead to Pb ingestion and which has been associated with mental impairment (24). Another notable limitation related to these study designs is the difficulty of clearly defining the population from which subjects are drawn (e.g., the problem of selective in- and out-migration as it affects cross-sectional studies, which view a population at a single point in time). A third important limitation is the difficulty of

identifying, measuring and adequately adjusting for all extraneous factors that might confound the relationship between Pb and infant development. In this connection, the main issue thus far has been disentangling effects of Pb exposure from those of low socioeconomic status (SES), since the two tend to be highly correlated. Low social class can affect infant IQ both because of a lack of stimulation in the home environment or because of low maternal IQ. A further complexity is that low maternal IQ and poor social circumstances may themselves be consequences of a mother's early exposure to a lead-contaminated environment. In addition to sociodemographic factors, biological factors such as iron deficiency may also confound the relationship between lead and infant development.

Because of their methodologic problems, these early studies will not be discussed in detail but the pattern of results is worth noting (see ref. 25 for a review and meta-analysis):

i. A fairly consistent inverse relationship was seen between BPb level and IQ scores (not necessarily significant).

ii. Although absolute IQ levels varied by study population, the relative magnitude of effect was similar -- about a 2-4 point decrease in IQ score per 10 μg/dl of BPb.

iii. There was no evidence for a threshold below which no harmful effects were seen.

iv. Results were <u>not</u> consistent across IQ test subscales, with some studies showing deficits in verbal IQ and others indicating deficits in visual acuity and motor skills.

v. The results from studies measuring dentine lead rather than BPb were generally similar in terms of the direction and magnitude of effect.

This early research raised the disturbing possibility that Pb exposure even at low levels might be harmful to cognition, learning and behavior in children, and served to motivate a new generation of prospective studies designed to improve on the previous work. It is the current generation of longitudinal cohort studies that will be the focus of this report.

Prospective Studies in Six Populations

Prospective studies of child development which follow a defined population longitudinally, from early pregnancy through the preschool and school years, provide the opportunity to measure lead exposure and outcome carefully over time. Since different developmental functions emerge at different time points, studies with such designs have the potential to indicate the ages at which the impact of Pb exposure first appears, the length of time during which effects persist, and, possibly, when and in what circumstances they disappear. Furthermore, longitudinal studies allow critical exposure periods to be identified. Such information about the relative impact of prenatal and postnatal exposures is clearly important for occupational risk assessment, as well as for understanding pathophysiologic mechanisms and for preventing and treating effects of lead on child development. In addition, and also important, is the opportunity prospective studies provide to carefully measure confounding and effect modifying variables and to deal with them through design and/or analysis.

The following text and tables describe and discuss ongoing prospective studies of child development in six different populations:

(1) a cohort of primarily white, upper-middle class families from a Boston suburb (26-28);

(2) a cohort of primarily black, single-parent, low SES households in Cincinnati (29-30);

(3) a cohort of primarily white low SES mothers from Cleveland, half of whom have a history of alcoholism (31-32);

(4) a cohort from Australia of white, primarily intact, lower- and middle-class families (33-34);

(5) a cohort from Yugoslavia, composed primarily of ethnic Serbians and Albanians (35); and

(6) a cohort of births from an urban region of New Zealand (36).

For each of the studies, Table 1 provides details on: the source population and sample for analysis; the oldest age reported on to date; the mean prenatal and postnatal BPb levels; the psychometric tests used to measure child development and the ages at which they were administered; average maternal IQ in each sample (a strong determinant of infant IQ); the approach to handling confounding variables and other data analytic issues; and the results reported over time in relation to measures of both prenatal and postnatal Pb exposure. Table 2 gives names and citations for the various IQ tests and subtests and the measure of the child's postnatal environment that have been used in these studies and are referred to in Table 1. Following is a brief discussion of each study's notable features and findings.

The Boston Cohort: One advantage of the Boston cohort that has frequently been bruited is that it represents a case in which lead exposure is not inextricably bound up with low social class; indeed, in the Boston cohort cord BPb levels tend to increase with increasing

SES. Subjects come from a suburb of Boston and the average maternal IQ score of 121 is an indicator of their reasonably advantaged social circumstances. Average blood lead levels (a mean of 6.6 μg/dl prenatally and 6.8 μg/dl in the postnatal period) are, on the other hand, at the low end of the spectrum represented by the six populations we are discussing; this is notable particularly in the postnatal period. Nonetheless, the range in lead exposure and social class within the cohort is sufficient for the data to indicate an important point about prenatal vs. postnatal exposure and the issue of recovery. The effect of prenatal Pb exposure on developmental test scores at 6 months through age 2 was reversed at the 57 month assessment, but this recovery depended on having low concurrent lead levels. Reversibility was also determined to some extent by social factors, with less improvement seen in children who were below the median on SES, HOME score and maternal IQ.

Two other findings from the Boston cohort are notable. First, BPb at age 2 was the strongest predictor of developmental deficit in visual-motor skills at 4 years, 9 months. This may reflect the fact that the second year of life is an important, perhaps even critical, period for brain growth and development. Second, no association was found between dentine lead levels and IQ scores (this was also true in the New Zealand study), yet tooth lead is generally held to be a better measure than BPb of cumulative exposure. If there is a critical period for exposure at say, age 2, than a measure that is cumulative over a longer period of time may not be as relevant.

The Cincinnati Cohort: The Cincinnati cohort, unlike the Boston cohort, is almost uniformly of low SES; mean lead levels are higher than in the Boston group, especially postnatally (17.4 μg/dl on average as compared with 6.8 μg/dl) and maternal IQ is

substantially lower (75 vs. 121). Yet there are important similarities in the pattern of results. Deficits in visual-motor skills (larger in males) were found at early ages in relation to prenatal and neonatal Pb burdens. Deficits increased as social class decreased. Postnatal Pb levels (4th year and cumulative) were a stronger predictor than prenatal BPb of neurodevelopmental deficits at age 4, although the effect of neonatal Pb levels persisted in low SES children.

The Cincinnati investigators carried out analyses designed to determine whether the developmental deficits they observed in connection with lead were mediated by effects of lead on pregnancy outcome. Based on a structural-equations approach, they suggest that the Pb-related developmental deficits in their cohort were partly the result of shorter gestations and lower birth weights among infants of mothers with higher BPb levels during pregnancy. This result emerged in spite of the fact that infants born in the early preterm period (< 35 completed weeks of gestation) and infants with very low birth weight (< 1500g) were excluded from the sample.

An interesting methodologic feature of the Cincinnati study is that they directly address the problem of missing values in longitudinal research (~25% in their case) by carrying out two analyses: one based only on subjects with complete data, and another using all subjects but imputing their missing BPb values. As there was no difference in the pattern of results, the Cincinnati group ultimately was able to use all the data collected and to retain all subjects in the final analysis.

The Cleveland Cohort: The Cleveland cohort, like the one in Cincinnati, is of low social class; lead levels are relatively high (a mean BPb of 6.5 μg/dl prenatally and 16.7 μg/dl postnatally). In contrast to the Cincinnati cohort, where the investigators were careful to

exclude alcohol and drug abusers from their sample, the Cleveland cohort was designed specifically so that half the mothers had a history of alcoholism. Yet no analyses testing for interactions between alcohol and BPb are presented. Thus it is difficult to interpret the results the investigators do report, which are described as "null" findings. In addition to the problem of including mothers with a history of alcohol abuse, this study excluded all premature infants from the sample; if the Cincinnati investigators are right in arguing that effects of lead on infant development are partially mediated through adverse pregnancy outcomes, this would introduce a bias towards the null.

The Port Pirie Cohort: The main source of lead exposure in this Australian cohort is a smelter upwind of the city. Consequently, there are substantial BPb levels (8.3 μg/dl prenatally and 21.2 μg/dl in the postnatal period) in a population that is mostly middle-class (average maternal IQ =95). Unlike most of the other studies, the Australians find no adverse effects of prenatal lead exposure and only a weak effect of early postnatal BPb, perhaps because social class advantage is a sufficient buffer. However, beginning at age 2, BPb levels are related to measurable deficits in the developmental assessment at age four, mainly in nonverbal skills. A decrease of 7 points on the adjusted McCarthy GCI score was seen as postnatal BPb rose from 10-30 μg/dl.

The Yugoslavia Study: As in the Australian study discussed above, the Yugoslavia study is based on a population living near a lead smelter. Blood lead burdens are highest in this cohort (a mean of 17.1 μg/dl prenatally and 35.5 μg/dl in the postnatal period), which appears to be of lower social class than the Australian sample, judging from maternal IQ and HOME scores. Here, deficits are found in development at age 2 for prenatal as well as

postnatal BPb (again, this may support the modifying effects of social class on neuropsychological development). However, BPb at age 2 was the strongest predictor of deficits, which were mainly in the visual realm although some effects were seen on verbal IQ. The investigators also report data implicating iron deficiency as harmful to infant development.

The New Zealand Cohort: Like the Port Pirie cohort (and unlike many of the others), this is a well-defined fairly complete birth cohort (N = 1265). It has, however, experienced substantial attrition over time; the sample with complete data at 9 years includes only 664 children (52% of the original cohort). A strength of the New Zealand study is that the analysis actually models the effects of sample selection factors and takes account of them in estimating the association between Pb exposure and child development. As in Boston, lead levels are rather low and SES fairly high. The estimate of Pb exposure is the mean of two dentine chip values; the outcome measures include school performance (teacher ratings, scores on a standardized reading test) as well as IQ. An adjustment has been made for pica behavior to control for the possibility of reverse causality. The authors report clearcut, significant effects of cumulative Pb exposure on school attainment at ages 8 and 9, but only small nonsignificant effects on cognitive ability (as measured by IQ). They suggest this pattern may be coherent with an effect of lead on attentional processes.

In Sum:

The results to date reported from these six ongoing cohort studies are:

i. reasonably consistent as to the direction of effect on neuropsychological development (i.e. inverse);

ii. reasonably specific (i.e., observed deficits are mainly in perceptual-performance skills, particularly after age 2);

iii. reasonably consistent as to the magnitude of the effect (i.e., small and within the range of repeated testing on the same child);

iv. reasonably consistent in showing that the magnitude of the effect and the potential for reversibility are both social-class dependent;

v. reasonably consistent in suggesting a dose-response relationship (even the advantage of high SES is smaller at high BPb levels);

vi. reasonably consistent in suggesting that exposure during the second and third year of life may be a critical period (and, therefore, that postnatal exposure may be more important in the long term than prenatal exposure);

vii. reasonably consistent in indicating that if a threshold for developmental effects does exist, it must be at least as low as 10 μg/dl.

If, as seems to be the case, children with elevated lead exposure do less well on measures of cognitive ability and attainment, what might the neurobiological basis for such an association be, and is it of any clinical or public health consequence? One interpretation of the effects that have been seen -- at this point, merely a speculation -- is that lead affects neurons in the hippocampus, an area of the brain which controls spatial ability, perseverance and emotionality. As to significance, while the effects of low level lead exposure on cognition, learning and behavior are small and perhaps not important from the clinical standpoint, the public health consequences of even a slight shift in the population distribution of IQ scores is potentially large.

Some Methodologic Concerns and Comments

The intent in undertaking prospective studies of Pb and infant development was to address methodologic concerns about inadequate measures of Pb body burden and cognitive ability and inadequate control of confounders. To some extent, the studies have been successful on this score. Certainly we are learning something from the data on repeated measures of BPb and the estimates of cumulative exposure represented by tooth lead or, better yet, by an integrated average of serial BPbs. As mentioned previously, it appears to me that exposure between ages 1 and 3 may be critical.

The reliability and validity of IQ tests as measures of cognitive ability have long been debated and the truth of the matter is beyond my expertise as an epidemiologist. However, the investigators in Australia, New Zealand and Yugoslavia appear to be aware of issues related to applicability of these tests in their populations (e.g., using carefully trained testers and restricting evaluation to raw scores). Moreover, in every case the scores are analyzed within populations. Reporting results of subscales as well as overall scores serves to increase the sensitivity of IQ tests in detecting effects of PB on particular aspects of neuropsychological functioning. As follow-up of the cohorts continues into the elementary school years, it may be useful to include measures of school performance as well as cognitive ability.

Concerning the matter of control of covariates: although the definition of and approach to controlling confounding varies somewhat from study to study, the tendency is in the direction of overcontrol rather than omission of important covariates. Maternal IQ is clearly important as is the HOME score and in most studies their inclusion attenuates the estimates of lead effects. Social factors are also suggested to modify the effect of lead and should not simply on principle be treated as confounders without first examining

whether there is effect modification. Also worthy of attention in future analyses (or reanalyses) is the suggestion that prematurity or low birth weight may mediate effects of lead on infant development.

The issues of sample selection bias and bias arising from missing values are, I believe, serious ones and have not received sufficient attention. In any longitudinal study there are bound to be subjects who drop out as well as subjects who are missing values for at least some time points. Rarely will they be "missing at random." Simply ignoring the issues and restricting analysis to a subgroup of "survivors" with complete data is not only wasteful but risks introducing a bias of unknown direction and magnitude. The Cincinnati and New Zealand studies are all the more compelling for having taken steps to deal with this -- the first by imputing missing values and then comparing results with those from analyses based only on observed data, and the second by including an estimated sample selection hazard in the regression equation following the method of Berk (37).

Overall Summary

In conclusion, the evidence provided by six ongoing prospective studies suggests that lead exposures sufficient to produce body burdens on the order of 10 μg/dl in blood, either prenatally or postnatally, can cause small reductions in infant and child cognitive ability as estimated by IQ tests. It may be necessary to reassess occupational risks in light of these recent data concerning lead levels previously thought to be innocuous.

TABLE 1

Prospective Studies of Lead Exposure and Infant Development

Study Site (refs)	Population; Sample (N)	Oldest Age Reported On	Mean BPb (µg/dl)		Psychometric Tests and Age at Administration	Average Maternal IQ	Handling of Confounding and Other Analytic Issues	Results Reported
			Prenatal	Postnatal				
Boston (26-28)	Births at one Boston hospital (N=249), divided into three exposure groups on the basis of cord BPb: low (<3 µg/dl) med (6-7 µg/dl) hi (≥ 10 µg/dl) 958 births excluded for birth complications, language, distance from Boston, refusals and failure to locate	4 yr,9mo	6.6	6.8	Bayley at 6 mo	121	Adjustment using multiple regression modeling; confounders defined using p-value (0.05) as criterion. Quality of the postnatal environment measured with the HOME scale.	(26): At 6mo, a 6 point difference in adjusted mean MDI scores of the high and low cord blood lead group (visual-motor subtests); no association with 6 mo BPb level.
					at 12mo, 18mo, 24mo		Confounders defined a priori and on the basis of change-in-estimate.	(27): Effect maintained at 12 mo, 18 mo and 24 mo (ave. decrement between high and low = 4.8 points) No association with postnatal BPb.
	at 57 mo follow-up (N=170). Losses due to medical problems, change in residence, refusals, failure to locate and exclusion of twins.			Dentine Pb= 5.5µg/g	McCarthy at 57mo		Confounding defined using both substantive and statistical criteria ($p<0.025$).	(28): At 57 mo, no association with cord BPb except for those whose concurrent BPb were ≥ 10µg/dl; 3 point decrease per log unit increase in 24 mo BPb (on visual-motor subtest mainly). Recovery from prenatal lead exposure was less in children in disadvantaged circumstances. No association with dentine Pb.
Cincinnati (29-30)	Births to mothers residing in high-lead areas (N=305). Alcohol or drug-addicted mothers excluded, as were preterm, very low BW or seriously ill or malformed infants. Prenatal and cord BPb (available for only one-third of subjects); postnatal BPb at 10 da, 3 mo, and 6 mo.	4 yr	8.3	17.4	Bayley at 3mo, 6mo	75	Adjustment for "perinatal health factors" in multiple regression models. Confounding defined using $P \leq .10$ as the criterion. HOME score was the measure of postnatal environment. Structural equations were used to examine relations among prenatal BPb, perinatal outcomes and infant development.	(29): At 3 mo, prenatal and cord BPb were associated with deficits in the adjusted MDI score (0.3-0.6 points per µg/dl). At 6mo, prenatal BPb also related to reductions in MDI scores; effect stronger in males. Newborn BPb also showed an association; deficits larger at low SES. Structural equations suggested that developmental effects were partly mediated by birthweight and gestation.
	4 yr follow-up (N=263). Postnatal BPb assessed quarterly from 3 mo to age 4. Missing BPb values were imputed.				Kaufman (K-ABC) at 4 yr		Same analytic strategy. HOME score and maternal IQ were important predictors of cognitive performance at age 4. Sex and SES were examined as potential effect modifiers.	(30): Inverse relations between late postnatal BPb and K-ABC (SIM subscale measuring visual-motor skills), not significant after adjustment for maternal IQ and HOME scale. Maximum effect size is 5.6 point decrease on SIM subscale. Neonatal BPb affected 4yr cognitive status only in low SES children.

TABLE 1 (continued)

Prospective Studies of Lead Exposure and Infant Development

Study Site (refs)	Population; Sample (N)	Oldest Age Reported On	Mean BPb (µg/dl)		Psychometric Tests and Age at Administration	Average Maternal IQ	Handling of Confounding and Other Analytic Issues	Results Reported
			Prenatal	Postnatal				
Cleveland (31-32)	Births from a Cleveland cohort (N=359) selected so that half the mothers are alcohol abusers. Preterm and seriously ill infants excluded. 25% attrition during period of follow-up (6 mo to age 4).	4 yr, 10 mo	6.5	16.7	Bayley at 6mo, 1yr, 2 yr Kent Infant Development (KID) Scale at 6 mo Stanford Binet at age 3	74	Adjustment for a pre-specified set of covariates chosen on the basis of "a recognized relationship with the outcome measure." HOME scores of the postnatal environment were included as covariates at 1,2, and 3 yrs. Tested the reverse causality hypothesis (i.e., that earlier developmental scores would predict later BPb. Race (but not maternal alcohol abuse) was examined as a potential effect modifier	(31): Fetal BPb showed a significant inverse relationship with 6 mo Bayley and KID scales, but no association with developmental tests at later ages. BPb at 6 mo was significantly associated with higher 6 mo KID scores. No associations were seen with BPb at 2 and 3 yrs. No consistent support for reverse casualty hypothesis. No interactions reported.
	Follow-up at 4 yr, 10 mo (N = 242).				WPPSI at 4 yr, 10 mo		Same hierarchical data analysis to control for confounding. Race and also sex were examined for effect modification.	(32): Small, not significant, but fairly consistent inverse associations were found for both prenatal and postnatal BPb and IQ scores. No interaction effects reported.

TABLE 1 (continued)

Prospective Studies of Lead Exposure and Infant Development

Study Site (refs)	Population; Sample (N)	Oldest Age Reported On	Mean BPb (µg/dl)		Psychometric Tests and Age at Administration	Average Maternal IQ	Handling of Confounding and Other Analytic Issues	Results Reported
			Prenatal	Postnatal				
Port Pirie, Australia (33-34)	Births in Port Pirie (a lead smelter town) between 1979-82; Analysis based on ~600 of 723, because of losses to follow-up. Pb = cord, 6 mo, 15 mo, 2 yr.	4 yr	8.3	21.2 (18.1 for integrated postnatal value).	Bayley at 2 yr	95	Adjustment using multiple regression for 13 sociodemographic, neonatal and behavioral variables associated with the MDI score, plus maternal IQ, and HOME score of the postnatal environment.	(33): No association of prenatal BPb and MDI scores up to age 2, but a 1.6 point decrease in 24 mo MDI score for every 10 µg/dl of BPb at 6 mo. (of borderline statistical significance after adjustment for maternal IQ and HOME score).
	Again, at 4 yr (N = 537).				McCarthy at 4 yr		Same analytic strategy.	(34): At age 4, an inverse association between BPb at 2 and 3 yr, and an integrated postnatal BPb, and McCarthy GCI score (7.2 point decrement as BPb rises from 10-31 µg/dl); again, mainly nonverbal skills affected.
Kosovo, Yugoslavia (35)	From 1502 index pregnancies in a lead smelter and control town, 1008 with complete delivery data were eligible for analysis. After exclusions for twins, major malformations, and distant residence, N=706 infants were selected for follow-up. Of these, N=392 infants were assessed at age 2. BPb measured prenatally and at 6, 12,18 and 24 mo.	2 yr	17.1	35.5	Bayley (used in Yugoslavia for over a decade)	31.9 (Raven Raw Score)	Adjustment by regression analysis for variables associated with MDI at 2 yr (at p <0.20). Postnatal environment assessed with the HOME scale.	(35): Both prenatal and postnatal Pb exposure led to small deficits in development at age 2. Comparing prenatal vs. postnatal Pb exposure, the greatest decrement in 24 mo MDI score was found for BPb at age 2 (-2.5 MDI points as BPb rises from 10-30 µg/dl). An inverse association was also found between iron stores (Hbg concentration) and adjusted mean MDI.

TABLE 1 (continued)

Prospective Studies of Lead Exposure and Infant Development								
Study Site (refs)	Population; Sample (N)	Oldest Age Reported On	Mean BPb (μg/dl)		Psychometric Tests and Age at Administration	Average Maternal IQ	Handling of Confounding and Other Analytic Issues	Results Reported
			Prenatal	Postnatal				
Christchurch, New Zealand (36)	Birth cohort of children delivered in the Christchurch urban region in mid-1977, and assessed at birth, 4 mo and annually to age 9. Measure of Pb= average of 2 dentine chip values. N ~660	9 yr		Dentine Pb =6μg/g	WISC-R Burt Reading Test Teacher Ratings at 8 and 9 yr	NA	Adjustment by regression analysis for 12 covariates apparently chosen a priori (including family environment measured by the HOME inventory among other variables). An additional model was fitted to take account of pica behavior (reverse causality). Sample selection factor and unreliability in Pb and outcome measures were addressed analytically.	(36): After correction for covariates and reverse causality, there are small nonsignificant inverse associations between IQ scores and dentine lead. The inverse correlations between dentine lead levels and school performance measures remain significant even after these adjustment

Table 2

Measures of IQ, School Performance and Home Environment Used in Ongoing Prospective Studies of Lead Exposure and Infant Development in Six Populations

I. Scale Measuring Intelligence, Developmental Competence and Relevant Age Ranges

1. Bayley Scales (infancy -36 mo)
   Mental Development Index
   Psychomotor Development Index
   (Bayley N, Bayley scales of infant development. New York: The Psychological Corporation, 1969.)

2. Kent Infant Development (KID) Scales (infancy -12 mo)
   Parent report inventory on 5 domains: cognitive; language; social; motor; and self-help
   Total Score
   (Reuter J, Beckett L. The Kent infant development scale manual, 2nd ed. Kent, OH: Kent Development Metrics, Inc., 1985.)

3. McCarthy Scales (2-9 yr)
   Verbal, Perceptual-Performance, Quantitative, Memory and Motor Subscales
   General Cognitive Index Score (GCI)
   (McCarthy D. Manual for the McCarthy scales of children's abilities. New York: The Psychological Corporation, 1972.)

4. Kaufman Assessment Battery for Children (K-ABC) (2.5 - 12.5 yr)
   Mental Processing Composite Score (MPC)
   Sequential Processing Standard Score (SEQ)
   Simultaneous Processing Stand Score (SIM)
   Nonverbal Standard Score (NONVB)
   Achievement Standard Score (ACHIV)
   (Kaufman A, Kaufman N. Kaufman assessment battery for children. Circle Pines, MN: American Guidance Service, 1983.)

5. Wechsler Preschool and Primary Scales of Intelligence (WPPSI) or WISC-R (4-10 yr)
   Verbal IQ, Performance IQ
   Total IQ
   (Wechsler D. Wechsler Intelligence Scale for Children - revised. New York: The Psychological Corporation, 1974.)

II. Measure of School Performance

1. Burt Reading Test
   (Gilmore A, Craft C, Reid N. Burt Word Reading Test, New Zealand Revision. Wellington: New Zealand Council for Educational Research, 1981.)

III. Measure of Home Environment

1. Home Scale (different scales for infants, preschool and school age children)
   Observer inventory of 6 domains: emotional and verbal responsiveness of parents; parental acceptance of the child; maternal involvement with the child; organization of the home environment; play materials; and variety in daily stimulation
   (Bradley R, Caldwell B. Home observation for measurement of the environment. Little Rock, Arkansas: University of Arkansas, 1977.)

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