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Health Effects of Lead at Low Exposure Levels

Expert Consensus and Rationale for Lowering the Definition of Childhood Lead Poisoning

Since the Centers for Disease Control (CDC) 1985 *Statement on Preventing Lead Poisoning in Young Children*[1] was published, an extensive database has provided a direct link between low-level lead exposure during early development and deficits in neurobehavioral-cognitive performance evident later in childhood through adolescence.[2-17] These consistent and conclusive studies, based on the strength of the science, have demonstrated the presence of a constellation of neurotoxic and other adverse effects of lead at blood lead (BPb) levels at least as low as 0.48 μmol/L (10 μg/dL). Accordingly, federal agencies and advisory groups have redefined childhood lead poisoning as a BPb level of 0.48 μmol/L (10 μg/dL).[18-23] These agencies arrived at this finding through consensus among informed lead experts and preparation of scientific documents evaluated through the peer review process. Furthermore, according to the CDC, no threshold for the lead-IQ relationship has been established.[18] Before discussing some of these studies in greater detail, the pervasiveness of this entirely preventable disease today in millions of American children must be recognized.[21]

See also pp 1257, 1259, and 1275.

Lead is a multimedia toxicant and provides, collectively, significant toxic risks even when specific sources appear, by themselves, to be relatively modest.[21,24] All sources of lead are integrated systemically into critical target tissues; the margin of safety, unlike other toxic pollutants, is extremely narrow. Today, as in previous decades, lead-based paint remains the major source of childhood lead exposure and poisoning.[18,19,21,22]

About 14 million or more children less than 7 years of age are at great risk because they live in pre-1959 housing that contains the highest concentration of lead-based paint.[21,25] Young children live in at least 54 million residential housing units, where there is an extant inventory of 3 million or more tons of lead-based paint.[18] According to the US Department of Housing and Urban Development, 20 million houses have peeling lead-based paint; nearly 4 million of these homes are currently occupied by families with children under 7 years of age.[25] White children 0.5 to 5 years of age constitute the largest group (over 11 million) of children at risk in the United States. About 4.5 million white children, from all sections and regions, are at high risk of developing adverse health effects of lead from lead paint exposure, because these children were estimated in 1984 to have BPb levels greater than 0.48 μmol/L (10 μg/dL) (Table). The Table indicates that the largest number of white children with BPb levels greater than 0.48 μmol/L (10 μg/dL) are from the highest social

Estimated Prevalence Rates and Numbers of Urban White Children (Aged 0.5 to 5 Years) With Blood Lead (BPb) Levels Greater Than 0.48 μmol/L (10 μg/dL) by Family Income*

Annual Family Income	Data
≥$15 000	
No. of children	7 643 900
No. with BPb >0.48 μmol/L (10 μg/dL)	2 473 700
Calculated prevalence	32.4%
$6000-14 999	
No. of children	2 666 300
No. with BPb >0.48 μmol/L (10 μg/dL)	1 332 900
Calculated prevalence	50%
<$6000	
No. of children	1 039 600
No. with BPb >0.48 μmol/L (10 μg/dL)	709 300
Calculated prevalence	68.2%
Total	
No. of Children	**11 349 800**
No. With BPb >0.48 μmol/L (10 μg/dL)	**4 515 900**
Calculated prevalence	39.8%

*From Crocetti et al,[32] Mushak,[33] and personal communication (A. F. Crocetti, PhD, May 10, 1992).

strata, although the prevalence rate is lower than among the other two groups. Collectively, about 40% of American white children between the ages of 0.5 to 5 years are estimated to have BPb levels greater than 0.48 μmol/L (10 μg/dL), the current definition of childhood lead poisoning.[18] These data demonstrate that virtually all children are at risk of lead poisoning.[18]

Evidence relevant to adverse effects of lead on central nervous system functioning at and below BPb levels of 0.48 μmol/L (10 μg/dL) is based on a large number of rigorously performed studies. Almost a dozen well-designed and carefully conducted cross-sectional and retrospective cohort studies converge on the strong, unequivocal conclusion that there is a negative association between BPb levels or other indexes of exposure and deficit in intellectual performance.[2-10,17-26] The pioneering study by Needleman et al[26] found an inverse correlation between dentine lead levels and IQ. Some of these children also had BPb levels between 1.45 and 2.41 μmol/L (30 and 50 μg/dL), levels higher than those found to produce adverse health effects in more recent studies.[2-5,8,12,16] The Needleman study[26] observed that intelligence test scores were approximately 4.5 points lower for school-aged children with moderately high dentine lead levels than for children with low dentine lead levels. This study[26] was recently criticized. However, when these criticisms were taken into account by including all subjects, controlling for age, and including mean values for each child's dentine lead level, mean dentine lead levels were a statistically more robust predictor of IQ ($P<.0069$) than initially reported.[17] The technique of nonparametric smoothing was used in this reanalysis.[17] In another cross-sectional study, Fulton et al[2] found a 5.8-point difference in scores on the British Ability Scales between the lowest and highest BPb level groups (range, 0.14 to 1.64 μmol/L [3 to 34 μg/dL]). The associations represented in the cross-sectional and retrospective studies are still significant when multiple covariates are accounted for. Based on currently published information, these IQ deficits are considered irreversible.[11,18]

In the past 5 to 8 years, cross-sectional studies have been supplemented by prospective studies in which investigators gain information about the timing and extent of exposure, as well as many other covariates, in longitudinally designed protocols.[12-16] Additional strengths of prospective studies, pointed out by Mushak et al,[24] include the use of standardized and sophisticated methods for assessing exposure and various outcomes, systematic employment of statistical methods to control for multiple covariates and potential confounders, enrollment of cohorts of sufficient size to yield more than enough power to detect subtle effects, and assessment of the full scope of childhood development longitudinally from birth to several years of age.[16] Furthermore, through the use of consistently applied outcome measures, prospective studies can be compared directly.[24] These international prospective studies have further changed how public health and regulatory federal agencies approach childhood lead poisoning[18-23]; the results of these studies unequivocally confirm evidence linking low levels of lead exposure (≤0.48 μmol/L [10 μg/dL]) to neurobehavioral-cognitive impairments. The Cincinnati (Ohio) study[15] found effects of prenatal lead exposure on Mental Developmental Index scores that amounted to an eight-point deficit for each 0.48-μmol/L (10-μg/dL) increase in BPb levels. The study in Port Pirie, Australia,[12] evaluated children up to 4 years of age and related integrated BPb levels to the McCarthy Scales of Children's Abilities. Blood lead levels were inversely related at 4 years of age, with children having cognitive scores 7.2 points less, once BPb levels reached 1.45 μmol/L (30 μg/dL), compared with children with BPb levels less than or equal to 0.48 μmol/L (10 μg/dL).[12]

Perhaps the most unique prospective study, now in its 10th year, is being carried out in Boston (Mass).[13,14,16] The Boston cohort is composed of advantaged middle- and upper-class children living in optimal circumstances.[14,16] Relatively few children have access to the social and economic advantages in the Boston cohort. These advantaged children could be expected to be at the least risk for having lead-induced cognitive deficits. The effect of lead on cognitive functioning of these children at extremely low exposure levels is remarkable. Higher BPb levels (mean, 0.33 μmol/L [6.8 μg/dL]) at 24 months of age were associated with a decrease of 5.9 points on the General Cognitive Index of the McCarthy Scales at 57 months of age, when the mean BPb level was 0.31 μmol/L (6.4 μg/dL). In short, the General Cognitive Index decreased by about three points for each natural log unit increase in BPb level at 24 months. This cohort was characterized by maternal IQ scores of 124±16 (mean±SD), Mental Development Index scores on the Bayley Scales of 116±16 at 24 months, and General Cognitive Index of 115.5±14.5 at 57 months. Further analyses between BPb levels and General Cognitive Index fail to reveal a threshold down to BPb levels of 0.10 μmol/L (2.0 μg/dL) or less.[17]

The socioeconomically advantaged Boston cohort has now been assessed at 10 years of age, when the mean BPb level was 0.14 μmol/L (2.9 μg/dL).[16] Slight elevations in BPb levels (about 0.24-μmol/L [5-μg/dL] increments) at 2 years of age were associated, without an apparent threshold, with significant impairments in intellectual and academic performance, assessed by the Wechsler Intelligence Scale for Children–Revised and the Kaufman Test for Educational Achievement, at 10 years of age. An increase in BPb levels of 0.48 μmol/L (10 μg/dL) at 24 months was associated with a 6.0-point decline in full-scale IQ on the Wechsler Intelligence Scale for Children–Revised and an 8.9-point decrease on the Kaufman Test for Educational Achievement.[16]

The link between low-level lead exposure during early development and later deficits in intellectual and academic performance is remarkably consistent with few exceptions[27]; there is compelling consistency in effect-size estimates in BPb-IQ-neurobehavioral outcomes. If large variations existed, this would suggest confounding by an omitted variable or an omitted effect modifier.[17] If effect-size estimates are available from multiple studies, the weighted average effect size is a highly significant summary of the weight of these data. In this approach, individual studies are treated as data points in a larger "meta-study." This technique

is known as meta-analysis. The usefulness of this technique resides in the fact that it permits the investigator to combine the results of studies that differ in some respect, while examining the same research questions.[28] Seven studies were so analyzed, and the effect-size estimates were quite similar and highly significant.[17] Overall, these data indicated an average decrease of 0.25 IQ points for each 0.05-μmol/L (1.0-μg/dL) increase in BPb levels.[17] This inverse relationship between IQ and BPb levels continued well below 0.48 μmol/L (10 μg/dL).[17] Another meta-analysis of 13 such studies[29] yielded a joint probability of obtaining the reported results of less than three in a trillion. Thus, the overall pattern, further confirmed by another meta-analysis of 24 studies,[26] strongly supports the conclusion that low-level lead exposure is related directly to neurobehavioral and cognitive deficits. Collectively, the results of the prospective and cross-sectional studies and the meta-analyses indicate causality between remarkably low levels of lead exposure and neurobehavioral-cognitive-IQ deficits in young children.

The public health implication of four- to six-point deficits on various tests of neurobehavioral and cognitive functioning may not be clinically devastating to an individual child. However, a downward shift of four points in the normal distribution of mental developmental indexes on the Bayley Scales or other neurobehavioral-cognitive outcome measures for a population of children would result in 50% more children scoring in the borderline range of 80.[30] Similarly, such a downward shift in neurobehavioral-cognitive-academic functioning would result in an absence of children who achieved superior scores (greater than 125).[18]

In large part, based on the evidence cited above, the CDC lowered the definition of childhood lead poisoning in 1991 from 1.21 to 0.48 μmol/L (25 to 10 μg/dL)[18]; this consensus decision was based on the strength and consistency of data detailed above. Other new initiatives were also included in the CDC's guidelines.[18] The recommendation for universal screening of all children 6 years of age or under included testing BPb levels at 12 and 24 months of age; more frequent assessments of BPb levels were strongly recommended if children fell into priority groups reflecting age and condition of housing, age of the child, occupation of the parents, etc. A multitier approach for environmental and medical intervention was outlined based on the results of testing BPb levels. A fundamentally new focus of these guidelines[18] was a reorientation of public health and pediatric communities toward approaches *to prevent* young children from being exposed to lead, rather than to treat them after the fact. A critical component of the CDC's overall strategy,[18,19] therefore, is to markedly increase abatement of lead hazards in children's homes.

The CDC's *Strategic Plan for the Elimination of Childhood Lead Poisoning*[19] recognized that prevention of childhood lead poisoning would be an important public health activity, even if no economic benefits could be demonstrated. However, based on the demonstrated efficacy of abatement to prevent lead poisoning and estimated costs of medical care, special education, the effect of loss of IQ points on wage rate and on educational attainment, etc, the net dollar benefits to prevent childhood lead poisoning are substantial. Based on this cost-benefit analysis, similarly carried out by the US Environmental Protection Agency as part of the phasedown of lead in gasoline,[31] a net annual benefit of over $1.4 billion (in 1989 dollars) would be achieved by systematically deleading just the worst of pre-1959 housing.[19] This analysis provides, in addition to benefits for children's health, an economic justification for a national program of abating lead-contaminated housing to prevent childhood lead poisoning.[19]

A dedicated role by the pediatric community is a critical ingredient to eradicate this entirely preventable disease.[18] To ensure the health of children under their care, it is highly recommended that pediatricians educate parents concerning sources of lead and implement testing for BPb levels according to established schedules,[18] as if a BPb level test was as routine in pediatric practice as a tuberculin skin test, hematocrit, or immunization. Furthermore, pediatricians should be able to interpret test results of BPb levels according to the need for comprehensive medical and environmental interventions. Moreover, it is important for pediatricians to ensure that lead-poisoned children receive appropriate medical and environmental treatment both initially and in comprehensive follow-up that include ongoing education, BPb level testing, medical and environmental evaluations, possible pharmacologic intervention, and definitive environmental abatement.[18] If these tasks prove to be difficult for individual pediatricians, then referral of lead-poisoned children to centers that have experience in the treatment (medical and environmental) of lead poisoned children is necessary.[18]

The pediatric community, in collaboration with other disciplines must play a central role to ensure that America's most cherished resource, young children, reach adulthood free from the conclusively documented consequences of childhood lead poisoning. By so doing at a very early age in a child's life, pediatricians can make a significant contribution to a child's future academic success and productivity in the workplace.

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