COMMENTARIES

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Even Advantaged Children Show Cognitive Deficits From Low-Level Lead Toxicity

ABBREVIATIONS. CDC, Centers for Disease Control; LOAEL, lowest observed adverse effect level.

Over the past fifteen years, knowledge of the spectrum of lead neurotoxicity has increased dramatically. Since 1979, when Needleman and colleagues[1] showed that deciduous tooth lead levels were inversely related to intellectual performance and behavior in school-age children, many well-designed epidemiological studies have confirmed that low-level, subclinical lead exposure in early life is associated with decrements in childhood cognitive performance.[2] These human findings cohere with substantial primate evidence, which consistently demonstrates measurable and long-lasting neurodevelopmental deficits from exposure to low levels of lead.[3]

In response to compelling evidence of neurotoxicity from low-level lead exposure, the United States Centers for Disease Control (CDC) issued a revised lead statement—*Preventing Lead Poisoning in Young Children*—in October 1991.[4] This revision lowered the definition of an elevated blood lead level from ≥25 μg/dL whole blood to ≥10 μg/dL, the lowest blood lead level at which neurodevelopmental effects were believed to occur, and set the new medical intervention level at ≥20 μg/dL. The statement also recommended increased primary and secondary prevention efforts. Suggested primary prevention activities include removing lead from the environment before children are exposed and educating communities and families about identification and control of lead hazards. Suggested secondary prevention activities include phasing-in blood lead screening over several years, aggressively managing children known to have lead poisoning, and tracking the occurrence of childhood lead poisoning. The long-term goal of these efforts is to reduce all children's blood lead levels to less than 10 μg/dL.

The CDC screening recommendations are designed to meet the needs of children at both high and low risk for lead poisoning, with children at higher risk receiving more frequent blood lead screening than those at lower risk. The recommendations have two components: assessing likelihood of lead exposure and performing blood lead testing. The initial assessment of risk should occur in infants at 6 months of age, at which time their parents should be asked a series of questions. Any "yes" answer puts an infant in a high-risk group and blood lead testing should begin at age 6 months. Infants at low risk (a "no" answer to all questions) should have, at a minimum, a blood lead measurement performed at 1 year, and preferably again at 2 years of age. The goal of screening is to identify lead-burdened children early, stop their lead exposure, and prevent long-term neurodevelopmental compromise.

Despite strong evidence of lead's neurotoxic effects, many remain skeptical that low-level, subclinical lead exposure in early childhood impacts subsequent cognition and that the CDC's aggressive approach to eradicating lead poisoning, including universal screening, is warranted. Critics of the research on neurotoxicity associated with low-level lead exposure have claimed that these studies had biased and inadequate follow-up; insufficiently controlled for confounding variables, measuring the effect of some factor other than lead exposure such as socioeconomic status; were demonstrating an effect-cause relationship (that is, children with lower IQs were more likely to expose themselves to lead); or provided only limited data by restricting their study population to high-risk groups. Critics of the CDC lead statement have claimed that the CDC has created a false epidemic by lowering the definition of an elevated blood lead level to a point unjustified by current research; that the goal of lowering children's blood lead levels below 10 μg/dL is both impractical and overzealous; and that only children at high risk, rather than all children, should be screened for lead poisoning. The report by Bellinger and colleagues,[5] in this month's issue of *Pediatrics*, answers many of these criticisms.

Bellinger and colleagues present strong evidence that subclinical, very low-level, lead burden in early life impacts later cognitive performance, that this effect results from lead rather than some other factor, and that the CDC's goal of reducing children's lead exposures to the lowest possible levels is appropriate. This longitudinal study presents results of the 10-year neuropsychological evaluation of a cohort of middle-class and upper-middle-class children with low lifetime lead exposures. In the study population, mean blood lead levels collected between age 6 and 57 months ranged from 6.3 to 7.8 μg/dL with standard deviations ranging from 3.8 to 7.0 μg/dL; no blood lead levels exceeded 24 μg/dL. These blood lead levels are comparable with those of the general population.

The investigators identified this cohort at birth; serially measured umbilical cord and postnatal blood

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lead; assessed development at age 6, 12, 18, 24, and 57 months and cognition at age 10 years; and collected detailed information on other factors that might impact intellectual performance. The most important result of this study is that relatively low blood lead levels at age 2 years—but not at other ages—independently predicted IQ at age 10 years. IQ was reduced by six points for every 10-μg/dL increase in blood lead. This association remained significant after adjustment for many confounding factors. Even the lowest lead levels, those below 10 μg/dL, were inversely related to IQ. These results indicate that even blood lead levels below 10 μg/dL may have measurable impact on subsequent cognition, that there may be no effect threshold for lead-associated cognitive toxicity, and that age at exposure may be important.

Bellinger and coworkers' study has several important new findings which warrant confirmation. Most important is the result that even blood lead levels below 10 μg/dL, the previous lowest observed adverse effect level (LOAEL), are associated with measurable long-term cognitive deficits. Also important is this study's suggestion of particular vulnerability at age 2 years for the cognitive effects of lead.

These findings directly address many previous concerns about the studies of low-level lead and neurodevelopment. The follow-up rate for the eligible population (those tested at 57 months) was high, 87.6% at 10 years. Children successfully evaluated at 10 years came from families within the cohort that were of higher socioeconomic status and provided the best developmental environments for their children. If these family characteristics created any bias, it would most likely be conservative, tending to underestimate the true risk of cognitive decrements from lead exposure. The authors adjusted for a large number of real and potential confounding variables and analyzed the data in a variety of ways; nevertheless, after adjustment and reanalysis, blood lead level at 2 years retained a reduced but still statistically significant independent effect on 10-year IQ. Because this study was prospective, collecting lead exposure data before assessing intelligence, it strongly supports a cause-effect relationship for lead exposure and subsequent cognitive decrements. And, even though this cohort consisted of children at low risk for long-term cognitive deficits from lead, lead was independently associated with IQ decrements in these children. In summary, the findings of this important longitudinal study refute many of the concerns raised about earlier reports of the cognitive deficits associated with low-level lead exposure.

The availability of long-term follow-up data from a low-risk cohort such as this one suggests that the CDC has not created a false epidemic. Instead, these data strongly support the current CDC goal of reducing all children's blood lead levels below 10 μg/dL, a standard that was developed to balance both health concerns and practical considerations. Furthermore, the findings suggest that future efforts are necessary to strive to eliminate childhood lead exposure entirely. Environmental health policy aims to reduce exposure levels well below the LOAEL, usually by a safety margin of 10 if the LOAEL is derived from human evidence. Following this standard, if the lowest blood lead level with observed effects is below 10 μg/dL, then the ideal childhood blood lead standard would be at or close to 0 μg/dL. However, a blood lead standard at or near zero is not a practically achievable goal now, because too many children in the United States currently have blood lead burdens well above 10 μg/dL. If confirmed, the evidence from this study indicating no threshold for lead-associated cognitive deficits suggests that future lead poisoning prevention efforts should strive for childhood blood lead levels at or near 0 when feasible.

The results of this study support the CDC recommendation to phase-in blood lead screening at or before 1 year of age. The CDC recommended screening for three reasons. First, substantial human data have demonstrated IQ reductions associated with low blood lead levels that are asymptomatic. Second, because lead contamination is widespread, all children are at risk for low-level lead exposure that is only detectable through screening. Third, in the past, screening recommendations targeted to high-risk groups have not been implemented. In 1985, the CDC lead statement recommended lead screening for high-risk children younger than age 6 years by measuring the erythrocyte protoporphyrin level; if this was elevated, the blood lead level was to be measured.[6] Despite this recommendation, very little screening was actually performed in the following years, even among the highest risk groups. For example, in California, among children receiving Medicaid-funded well-child care, fewer than 500 lead screening tests were performed annually between 1985 and 1991. The finding of long-term neurodevelopmental deficits from low levels of lead exposure in a low-risk population only reinforces the CDC's move toward universal screening. Furthermore, if age 2 is confirmed as a vulnerable age for lead exposure, then screening efforts to reduce lead exposure before age 2 are essential.

As pediatricians move toward full implementation of the CDC screening recommendations, they must learn to interpret and manage blood lead levels, both between 10 and 20 μg/dL and even higher in their patients. When discussing lead screening with parents, pediatricians should explain that the primary goal of blood lead screening is to find children currently being exposed to lead and to prevent further exposure. When the pediatricians identify a lead-burdened child, they should ask about possible lead sources in the child's environment, identify and treat iron and calcium deficiencies (the most common nutritional deficiencies that increase lead absorption), and teach parents simple actions they can take to reduce exposure. To reduce lead exposure, parents can identify and contain sources of lead in the home, use cleaning procedures such as damp mopping with a high-phosphate detergent to remove lead dust, feed their children a diet rich in iron and calcium, and teach their children to wash their hands frequently.

Effectively communicating the meaning of blood lead results to parents is perhaps the most challenging task in management of low-level lead exposure. Parents need to know the implications of low-level lead exposure, without becoming overly alarmed. Pediatricians can assure parents that the IQ decrements associated with low-level lead exposure, though important for the entire population, are subtle and generally cannot be measured in individual children. Most important, pediatricians should advise parents to strive to provide an optimal developmental environment for their children which does not limit but instead provides ample opportunities for cognitive growth.

To successfully implement universal lead screening and perform case management, pediatricians will need new and better tools for identifying and managing lead poisoning in their practice. These include a blood lead screening test that is reliable, easy to perform, accurate at very low levels, and low cost; counseling materials for patients; and knowledge, obtained from properly designed randomized controlled trials, about whether chelation therapy has long-term cognitive benefit. Strategies for enhanced clinical primary prevention activities need development. In addition, pediatricians will require adequate support from the public health sector, which is responsible for identifying the sources of lead poisoning in individual children. And, since most lead poisoning is from exposure to leaded paint, families will need resources for abatement, including properly trained contractors and financial resources.

Bellinger and his colleagues have demonstrated long-term cognitive effects associated with low-level lead exposure in a cohort of advantaged American children. These findings strongly support national efforts to identify and eradicate childhood lead poisoning. For this wide-reaching eradication effort to be successful, all segments of society will need to participate, and pediatricians will play a major role.

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How Much Resuscitation Is Enough Resuscitation?

One of the problems facing all of us when we perform cardiopulmonary resuscitation on children is deciding when enough is enough, and when it is perhaps too much. We want to give any child experiencing a sudden, unexpected catastrophe with cardiopulmonary arrest the fullest benefit of our skills and techniques, but if we persist too long, we risk resuscitating the heart but not the brain and creating a fate worse than death: the neurologically devastated or persistently vegetative state. I am as guilty as others of losing track of time and have found myself trying to resuscitate a patient for more than an hour. The question is, is there a time limit to cardiopulmonary resuscitation beyond which all efforts should be ceased in all cases?

In this issue of *Pediatrics*, Quan and Kinder[1] present data on predictors of outcome in pediatric submersion accidents and recommend that victims who do not respond to advanced life support within 25 minutes be declared dead at the scene by emergency medical services personnel and have all efforts ceased. I have problems with this conclusion and recommendation.

First of all, the recommendation to pronounce dead in the field is based on only 29 victims in this study[1] and 38 victims in the previous study.[2] Although the chance for survival is exceedingly small, the 95% confidence interval allows that 1 in 11 victims might still survive in a normal state or with mild neurologic impairment with a resuscitation duration in excess of 25 minutes. Similar recommendations in the adult literature for the termination of cardiopulmonary resuscitation in the field have chosen 45 minutes of resuscitation,[3–6] which is almost twice as long, before giving up. These same guidelines specifically exclude children and drowning victims from the discontinuance of resuscitative efforts in the field.

It is evident from the authors' own cases that the 25-minute limit to resuscitation is, perhaps, splitting hairs. A 1.5-year-old girl required 23 minutes of advanced life support in the field before spontaneous circulation returned, and she was normal at follow-up evaluation.[1] If 23 minutes can be this successful, why stop at 25 minutes?

An even more important question is whether the field is ever the appropriate place for the discontin-

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