Testing Lead's Limits

Time for Another Reassessment of Guidelines?

Cohort data during the 1980s linked blood lead levels of at least 10 µg/dL with low cognitive test scores in children, prompting the decision by the Centers for Disease Control and Prevention to redefine the action level for elevated blood lead from 25 to 10 µg/dL. Now, new data add to the growing evidence that the 10-µg/dL level may not be protective [***EHP* 116:243–248; Jusko et al.**].

The investigators recruited children aged 24–30 months who had been previously enrolled in a dust control study. All the children were born between July 1994 and January 1995 and lived in Rochester, New York, with parents expressing no plans to relocate. To reduce the possibility of misclassification of exposure, blood samples were collected for measuring blood lead on up to 8 occasions (at ages 6, 12, and 18 months, and annually from age 2 through 6 years).

The children were given the Wechsler Preschool and Primary Scale of Intelligence during their 6-year visit by an examiner trained in neurobehavioral testing and blinded to each child's blood lead level. These assessments were made at an age when IQ is measured reliably and is a significant predictor of IQ scores and educational and occupational success during adolescence and adulthood. The data analysis employed a regression model that controlled for family income; maternal education, race, prenatal smoking, and Stanford-Binet IQ score; child's birth weight; breastfeeding; crowding in the home; and quality of childrearing (using the Home Observation for Measurement of the Environment Inventory).

The average blood lead level was 7.2 µg/dL, and lead concentrations for more than half the children never exceeded the 10 µg/dL mark. Even at these concentrations, blood lead levels were inversely related to IQ scores. The association was most pronounced for the Full-Scale and Performance IQ scores. Children whose blood lead levels measured in the 5- to 9.9-µg/dL range had significantly lower IQ scores than children with levels below 5 µg/dL. A descriptive analysis of peak exposure throughout early childhood suggested an inverse association between maximal blood lead level and IQ at blood lead levels less than 3 µg/dL; levels as low as about 2 µg/dL were associated with significant IQ declines. These findings, reinforced by previous data gathered by the same research team, support the need for a further reassessment of standard guidelines for responding to blood lead in infants and children. **–M. Nathaniel Mead**

Arsenic Makes Its Mark

Using Biomarkers to Track Noncancer Respiratory Effects

Exposure to toxic levels of arsenic is a serious problem in many Asian countries, notably Bangladesh and India, where exposure to inorganic arsenic through naturally contaminated groundwater is widespread and often excessive. Scientists have long recognized the lung to be a major site of action of ingested arsenic, and most of the focus has been on risks associated with lung cancer. Nonetheless, habitual ingestion of high-arsenic drinking water also promotes many noncancer lung effects, and researchers are investigating the potential utility of biomarkers to identify such effects [***EHP* 116:190–195; Parvez et al.**].

One of the challenges of pursuing connections between arsenic and respiratory illness is that assessments of respiratory symptoms may be prejudiced by interviewer bias if study participants show visible skin lesions, a hallmark sign of chronic arsenic poisoning. To overcome this obstacle, researchers have begun exploring the use of biomarkers for chronic respiratory disease such as serum levels of Clara cell protein CC16. This serum marker runs low in individuals with compromised lung conditions induced by chronic environmental exposures such as cigarette smoking or ozone.

In the current study, investigators sought to determine the relationships of serum CC16 with well-water arsenic, total urinary arsenic, and urinary arsenic methylation indices in a population of 241 nonsmoking individuals exposed to arsenic-laden drinking water in Araihazar, Bangladesh. The mean arsenic concentration in drinking water was 134 µg/L, and individuals with skin lesions consumed significantly more arsenic than those without (159 versus 105 µg/L, respectively).

As it happens . . . Lung cancer isn't the only respiratory effect linked with drinking arsenic-contaminated water; noncancer effects also may occur.

In individuals with skin lesions (but not those without such lesions), there was a significant inverse association of CC16 with urinary arsenic as well as a marginally significant inverse association of CC16 with the cumulative arsenic exposure index, which estimates long-term exposure. The researchers speculate that individuals with skin lesions either are exposed to higher levels of arsenic or have a unique susceptibility to the respiratory effects of arsenic exposure for reasons unknown.

The analysis also revealed positive associations of CC16 levels with the secondary arsenic methylation index (an indicator of arsenic methylation capability), particularly among individuals without skin lesions. This suggests that individuals with better methylation capacity may be less susceptible to the adverse respiratory effects of arsenic. Moreover, the inverse association of CC16 with the percentage of monomethylated arsenic (a commonly measured arsenic metabolite) in urine indicates that individuals with incomplete methylation may be more vulnerable to arsenic-induced respiratory problems.

This cross-sectional investigation, the first to use biomarkers of arsenic exposure and lung injury in this way, is an important step toward further improving our understanding of arsenic-related nonmalignant respiratory illness. Serum CC16 shows promise as a biomarker for assessing early respiratory damage induced by arsenic, especially among individuals with skin lesions associated with the consumption of arsenic-contaminated drinking water. **–M. Nathaniel Mead**

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Revisiting the DDE–Lactation Question

Association Not Confirmed in Breastfeeding Mothers

Breastfeeding is known to be protective of newborn health, for example by lowering infant mortality and risk of infectious diseases. But breastfeeding is on the decline in some locales, especially in developing countries. Some studies have reported a link between elevated maternal serum DDE (the primary metabolite of the pesticide DDT) and shorter breastfeeding duration, suggesting that exposure to DDT affects the ability to breastfeed. New research does not confirm this hypothesis, however, and suggests possible ways to refine our understanding of the association previously reported with DDE [***EHP* 116:179–183; Cupul-Uicab et al.**].

Both DDT and DDE are retained in fatty tissue and excreted in breast milk. DDT was banned in the United States in 1972 but is still being used elsewhere to fight malaria. Given DDT's prominence in malaria prevention, it is important to determine whether it affects infant and maternal health.

The current study involved 784 mother–son pairs from Tapachula, Chiapas, Mexico, where DDT had been used for about 40 years. The pairs had previously participated in a study of DDE's antiandrogenic effects, in which the mothers' serum levels of DDT and DDE were measured shortly after delivery. For the current study, the researchers interviewed each mother about every 2 months until her baby was weaned to determine the length of lactation.

Good news for now. Data from a study of Mexican mothers do not support earlier concerns that DDT exposure might impede lactation.

The Tapachula women's serum levels of DDE were about 15 times higher than recently measured levels in U.S. women. The team was not surprised to find higher DDE levels in first-time breastfeeders, because experienced breastfeeders would already have transferred some of their DDE body burden to earlier children. In the group as a whole, few women reported problems starting breastfeeding, and the median nursing duration was 10.8 months.

The researchers found a statistically significant positive association between DDE and shorter duration of lactation, but only among women who had previously breastfed. This is consistent with some earlier research. But the team writes that it is probably an artifact rather than a causal link; otherwise, an association between DDE and shortened lactation would have been observed in both experienced and novice breastfeeders. Only 11 women could not breastfeed—too small a number for statistical significance—but these women did have higher median serum DDE concentrations than the other women in the study.

Although the authors found no link between DDE and shortened breastfeeding duration, they write that DDT exposure may make it more difficult to initiate breastfeeding, perhaps because of endocrine disruption early in lactation. For the first 2–3 days, lactation is controlled by hormones. If DDE behaves like estrogen, it could suppress initial milk production but have a weaker effect on established lactation. Future research could focus on this avenue by which DDE may affect successful breastfeeding. **–Valerie J. Brown**

Exposure Under Pressure

Lead Linked to Release of Cortisol in Children

Lead exposure is linked to cognitive deficits, cardiovascular disease risk, and behavioral problems, outcomes that potentially follow dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis. In animal studies, lead exposure has heightened the release of corticosterone, the counterpart to the human stress hormone cortisol. New research now reveals for the first time a similar response in children with blood lead levels below 10 µg/dL, the action level established by the Centers for Disease Control and Prevention [***EHP* 116:249–255; Gump et al.**]. This finding corroborates concerns that there is no safe level of lead exposure.

The researchers drew their study population from the ongoing Oswego Children's Study, a longitudinal study at the State University of New York at Oswego's Center for Neurobehavioral Effects of Environmental Toxics. Of the 169 children in the current study, blood lead levels were known for 154 prenatally (≤ 1.0–6.3 µg/dL) and for 120 during infancy or toddlerhood (1.5–13.1 µg/dL). At the time of their participation in the current study, children were 9.5 years old.

Cortisol levels vary diurnally, rising quickly after awakening and then declining steadily thereafter. To help control for this diurnal variation, tests always occurred in the late afternoon. Beginning with a brief rest period, each child's session involved submerging an arm in ice water for 1 minute (a standard protocol to assess neuroendocrine response to acute stress) and completing a series of simple tasks with intervening rest periods. Saliva was collected for cortisol measurements during the first rest period and at 21, 40, and 60 minutes after the cold stressor test.

The researchers controlled for numerous potentially confounding factors, including demographics, socioeconomic status, and the health, nutrition, and substance use of mothers and children. They also tested for the presence of other neurotoxicants such as polychlorinated biphenyls, DDE, and hexachlorobenzene in children's blood, as well as maternal mercury exposure.

Pre- and postnatal blood lead were not associated with any variation in baseline cortisol levels. However, increasing blood lead levels were independently and significantly associated with increasing cortisol responses to stress. Curiously, cortisol levels remained elevated throughout the test period instead of tapering off as expected. The authors suggest that the children may have already been stressed when the test began or that 60 minutes was insufficient for cortisol levels to return to baseline.

The precise mechanisms of lead's effect on the HPA axis are unclear. However, given the effects they found at relatively low lead exposures, the authors suggest that cortisol reactivity be considered in future studies as a potential mediator of lead-induced disorders. **–Julia R. Barrett**