EXECUTIVE SUMMARY

In March 2002, the Centers for Disease Control and Prevention (CDC) Advisory Committee on Childhood Lead Poisoning Prevention (ACCLPP) established a work group (WG) to review the available evidence of possible health effects of blood lead levels (BLLs) of below 10 micrograms per deciliter (µg/dL), the level of concern currently established by CDC. The WG was charged with designing and following a rigorous protocol to review studies of the health effects of lead exposure at very low BLLs. The workgroup intended to focus on studies of the effects of peak BLLs at <10 µg/dL in children never known to have a BLL exceeding 10 µg/dL. However, there are relatively few such studies and the workgroup decided to review the larger number of studies that could indirectly support or refute the existence of a threshold near 10 µg/dL. Although the workgroup was the primary author of this report, the ACCLPP reviewed the document and it was revised to reflect their comments. The ACCLPP unanimously endorsed the findings in this report.

Methods

The following criteria were used for selecting relevant studies to review:

- BLLs were measured using graphite furnace atomic absorption spectrometry (GFAAS) or anodic stripping voltammetry (ASV);
- the study was published in English;
- for studies in which IQ or General Cognitive Index (GCI) was a measured outcome, an assessment of the association between BLLs in children and IQ or GCI was included; and
- for studies in which IQ or GCI was not a measured outcome, an assessment of the association between BLLs in children and a specified health outcome was included.

For each relevant study, a structured abstraction was performed that captured the following:

- study location and sample size;
- age at which BLL and cognitive or health outcome was measured;
- the distribution of BLLs (mean or other measure of central tendency and variance) and percentage of participants with BLL <10 μg/dL;
- crude and adjusted regression coefficients relating BLLs to outcome;
- other measures of association (e.g., correlation coefficients); and
- model type and covariates included in adjusted models.

When reviewing the evidence, including indirect evidence from IQ studies, the workgroup considered both alternate explanations for study findings and potential effect of residual confounding.

Conclusions

The main conclusions reached by the WG are summarized as follows.

1. **Does available evidence support a negative association between measured BLLs <10 μg/dL and children's health?**
    - The overall weight of available evidence supports an inverse (negative) association between BLLs <10 μg/dL and the cognitive function of children.
    - A steeper slope in the dose-response curve was observed at lower rather than higher BLLs.
    - The available evidence has important limitations, including the small number of directly relevant cohort studies and the inherent limitations of cross-sectional studies (i.e., the lack of data regarding both BLLs earlier in life and key covariates).

- For health endpoints other than cognitive function (i.e., other neurologic functions, stature, sexual maturation, and dental caries), consistent associations exist between BLLs <10 µg/dL and poorer health indicators.

2. **Are the observed associations likely to represent causal effects of lead on health?**
    - Though not definitive, the available evidence supports the conclusion that the observed associations between BLLs <10 µg/dL and cognitive function are caused, at least in part, by lead toxicity.
    - The strength and shape of the causal relationship are uncertain because of limitations of the available evidence.
    - The health effects of lead are uncertain in individual children who have BLLs measured at a single point in time. Thus, scientific evidence does not provide a basis for classifying individual children with BLLs <10 µg/dL as "lead poisoned," as the term is used in the clinical setting.
    - The greatest source of uncertainty in evidence concerning the relationship between BLLs <10 µg/dL and children's cognitive function is the potential for residual confounding, especially by socioeconomic factors.
    - The available data for health endpoints other than cognitive function, taken mostly from cross-sectional studies, are limited; therefore, firm conclusions concerning causation can not be made.

Future Research Needs

The WG identified the following research needs to address gaps in the existing base of evidence and to allow for more definite conclusions about the strength and shape of the causal relationship.

- Prospective observational studies designed to minimize the chance of residual confounding.
- Randomized trials to test interventions designed to reduce BLLs in the range <10 µg/dL and assess the impact on children's cognitive development.
- Animal and in vitro studies to identify mechanisms of lead toxicity at low BLLs that could explain the observed steeper slope at lower compared with higher BLLs.