

## **Chapter 5. Developmental Assessment and Interventions**

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**Table 5.1. Summary of Recommendations for Developmental Assessment and Interventions**

- Make long term developmental surveillance a component of the management plan for any child with a blood lead level (BLL)  $\geq 20$  g/dL, while recognizing that this will not necessarily result in referral for diagnostic assessment or intervention.
- Also consider developmental surveillance for a child who has a BLL that does not exceed 20 g/dL but who has other significant developmental risk factors.
- Do not base decisions regarding developmental assessment or intervention on a child's age at the time the child is found to have an elevated blood lead level (EBLL).
- If you wish to refer a child with an EBLL for intervention services, consider referring that child to early intervention/stimulation programs.
- Include a history of a child's EBLL in the problem list maintained in the child's medical record.
- Do not stop developmental surveillance when a child with an EBLL reaches age 6 or when the child's blood lead level is reduced. A responsible party (e.g., the child's PCP) should provide ongoing developmental surveillance of that child after the EBLL case is closed.
- In the developmental surveillance of children with EBLLs:
  - Watch for emerging difficulties at critical transition points in childhood: first, fourth, and sixth/seventh grades.
  - Watch for behaviors that interfere with learning, such as inattention and distractibility.
- Refer children experiencing neurodevelopmental problems for a thorough diagnostic evaluation.
- Be advocates for the child.

## Introduction

Since *Preventing Lead Poisoning in Young Children* was published in 1991 by the Centers for Disease Control and Prevention (CDC) (1), considerable new data have become available on the developmental and neurobehavioral effects of lead, including late results of a number of prospective longitudinal studies begun around 1980. These new data generally bolster the conclusion, reached in the 1991 statement, that lead adversely affects children's performance on tests of cognition at blood lead levels (BLLs) below 10 g/dL (2,3). New insights have been generated as well regarding both the most sensitive functional endpoints and the range of endpoints affected. Specifically, recent data suggest that lead toxicity may contribute to neurobehavioral, as well as cognitive, morbidities of childhood. Because of the consistency of these associations and the relatively high prevalence of BLLs in the range associated with these increased risks, it is important to address the issues involved in the identification and treatment of lead-related cognitive and neurobehavioral effects.

Any recommendations regarding neurodevelopmental assessments and interventions for children with elevated blood lead levels (EBLLs) must rest on a firm empirical foundation. Therefore, this chapter presents an overview of numerous studies of the association between children's BLLs and their neurodevelopment and behavior, as well as the recommendations based on the studies.

## Detailed Bases for Recommendations

### *BLLs and IQ*

Several older case series clearly demonstrate that children presenting with symptoms and findings of severe lead intoxication are at substantially increased risk for serious neurological sequelae (4-6). Asymptomatic children with BLLs in the 30- to 60- g/dL range also may suffer a variety of neurologic and neurobehavioral adversities (7-9).

Recent epidemiological studies provide a wealth of data on the nature of the dose-effect relationship for children with BLLs below 35 g/dL. The relationship between children's BLL and IQ appears to be linear, even at BLLs below 10 g/dL (2, 3). Some data suggest, however, that the slope for the dose-effect relationship is steeper for BLLs below 15 g/dL than it is for levels above 15 g/dL (3). Meta-analyses of the results of several studies indicate that an increase in average postnatal BLL from 10 to 20 g/dL is associated with a decrease of 1 to 3 points in the child's IQ measured at age 5 or older (3, 10, 11). The point estimates for the IQ change associated with a doubling of BLL from 10 to 20 g/dL were 2.57 points (standard error 0.41) in Schwartz' analysis of a mixed set of prospective and cross-sectional studies (3) and 2.53 points (standard error 0.41) in the analysis of cross-sectional studies by Pocock et al. (10).

The study cohorts were quite diverse ethnically, culturally, and sociodemographically. Children in some cohorts experienced chronic exposure by virtue of living near a smelter (12, 13), while children in other cohorts were impoverished and living in inner-city areas in old housing with leaded paint in poor repair (14, 15). Yet other cohorts consisted largely of children from relatively well-to-do families (16, 17). The likelihood that these interstudy differences were accompanied by differences in the nature and extent of confounding bias makes the overall consistency in the findings of the different studies even more impressive, and increases the plausibility of the conclusion that lead plays a causal role in a child's neurodevelopment. As in most areas of epidemiological research, however, interstudy variability is apparent in the strength of the association, with some investigators reporting that the association between children's BLLs and IQ scores was not statistically significant (15, 17-19). Nevertheless, the overall weight of evidence clearly supports the existence of an inverse association between children's BLLs and their IQ scores.

#### *Other Neurodevelopmental Deficits Associated with EBLs*

Children presenting with severe symptomatic lead intoxication are known to suffer from neurobehavioral problems such as impulsivity, aggression, and short attention span (4). Results of a number of studies support the hypothesis that the spectrum of low-level lead effects on children includes neurobehavioral problems (20-23). At present, there is no compelling evidence that an EBL increases a child's risk for attention deficit hyperactivity disorder (ADHD) (24). However, because the studies mounted to address this question have been cross-sectional or retrospective, children's lead exposure status at earlier developmental periods may have been misclassified. It is noteworthy that elevated blood or tooth lead levels have been repeatedly linked to the types of behavioral problems pertinent to the diagnosis of attention deficit disorder inattentive subtype, a diagnosis included for the first time in the fourth (and most recent) edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (25). These behaviors include distractibility, poor organization, a lack of persistence, and daydreaming (26-29). Elevated bone lead levels have also been linked to an increased risk of engaging in antisocial behaviors in middle childhood (29).

Efforts to identify a "neurobehavioral signature" for children with EBLs have generally been unsuccessful (30), although several studies have found that among preschool children, EBLs were most strongly associated with deficits in nonverbal functions, particularly visual-motor skills (13, 31-33). However, the nature of the deficits identified when children reach school age are less consistent. It is likely that the manner in which lead toxicity is expressed depends on many factors, including the timing and chronicity of exposure, the child's age when outcomes are assessed, and the context of the assessment (30). Given the absence of specificity in the findings associated with an EBL, a child's specific deficits are of little use in making a diagnosis of past or present EBL.

### *Interchild Variability*

The BLLs at which individual children show signs of clinical lead intoxication vary widely, and despite the consistent inverse association between children's BLL and IQ noted above, children have varying sensitivity to the more subtle functional impairments associated with EBLLs (30). Although, on average, children with higher BLLs tend to score lower on IQ tests than do children with lower BLLs, some children seem to be more affected than others by a given lead dose (34). This suggests that not all children with a given BLL should be considered at equivalent neurodevelopmental risk. In other words, an EBLL should be viewed as a risk factor for neurodevelopmental problems, not a diagnosis.

### *Importance of Age*

Identifying the age at which children are most sensitive to the neurodevelopmental effects of lead is complicated by the relatively high degree of stability in children's BLLs and the frequent confounding of age and peak BLL (32, 35). However, data from cohorts in which these obstacles to inference are less severe indicate that children's IQs may be particularly sensitive to lead-associated effects when the children are about 2 years old (16). Pocock et al. for example, found that EBLLs in children from 1 to 3 years of age appear to be the most predictive of children's later development (10). On the other hand, data from several of the prospective studies suggest that recent or concurrent BLLs are among the strongest predictors of children's neurodevelopmental function at school-age (12, 32). Furthermore, primate studies indicate that the period of greatest susceptibility to EBLLs may depend upon the specific deficit being evaluated (36). There is some limited evidence for this from human studies as well (37).

### *Time Lag Associated with the Effects of EBLLs*

For the most part, the evidence from prospective studies regarding the time course of the association between a child's BLL and neurodevelopment is consistent with a lag effect (16, 31). It is much more common to find a significant association between children's previous BLLs and their current neurodevelopmental status than between their current BLLs and current developmental status. This pattern is less clear under circumstances in which children's BLLs remain elevated for extended periods of time, such as when they live near smelters or in hazardous housing; under such conditions, children's current and past BLLs tend to be strongly correlated. The lag may be the result of a toxicological process in which some period of time is required for past lead exposure to affect the central nervous system function. Another explanation is that lead may primarily affect higher-order neurodevelopmental processes that are best tested at later ages when children's response modalities are more highly differentiated. One implication of this lag is that neurodevelopmental assessments conducted when a child has an

EBLL may produce many false-negative results and fail to identify a child who is at risk for later neurodevelopmental dysfunction. Careful long-term surveillance of behavior and neurodevelopment is thus needed to ensure that such children are identified.

The effects of EBLLs on the skills required for academic success may not be appreciated until a child reaches critical transition points in school: 1) first grade, when children are expected to begin acquiring basic academic skills such as reading words or performing arithmetic operations; 2) fourth grade, where the emphasis begins to shift from acquiring basic skills to using those skills to learn new material (“reading to learn” as opposed to “learning to read”); and 3) sixth or seventh grade, when students are expected to use higher-order planning and organizational skills in order to complete long-term projects. Increased BLLs have been associated with difficulties with all three types of skills (20, 26, 38).

#### *Persistence of Neurodevelopmental Effects*

Results from a variety of studies indicate that neurodevelopmental problems associated with elevated postnatal BLLs are persistent (8, 16, 38-43). The natural history of these problems appears to correspond to a “constant decrement” model, with the deficits associated with higher BLLs neither increasing nor decreasing over time (44), although few data are available on the persistence of effects. In contrast, the findings from most of the prospective studies are consistent with the hypothesis that neurodevelopmental effects associated with elevations in biomarkers of prenatal lead exposure attenuate during a child’s early years of life (10).

#### *Factors Affecting a Child’s Risk for Neurological Sequelae*

Increased exposure to lead frequently occurs in the context of other factors that also place a child at increased neurodevelopmental risk (e.g., poverty, single-parent household, teen-age mother, child abuse, poor nutrition). From this perspective, lead represents an additional “hit,” adding to a child’s cumulative neurodevelopmental risk (45). In multivariate statistical models, children’s BLLs tend to account for a relatively small amount of the variance in their neurodevelopmental status. The amount varies across outcomes measured and across studies, ranging from 0% (i.e., accounting for no variance in neurodevelopmental measurements) to as much as 11% (46), although usually on the order of 1% to 3%. For instance, in the set of cross-sectional studies included in the meta-analysis of Needleman and Gatsonis (47), children’s BLLs accounted for 2.3% of the variance in their IQ scores (based on a weighted partial correlation of  $-0.152$ ). Other factors, particularly social class and parental intelligence, typically account for much larger percentages of outcome variance.

Some evidence suggests that certain characteristics of children and their families are associated with the children’s increased risk for neurodevelopmental impairments from a given level of lead exposure. Several studies, although not all, have identified family social class as one

such characteristic, with children from lower social strata appearing to express the neurodevelopmental effects of lead at a lower BLL (48-51). A sex difference is also sometimes found, although in some studies it is girls (52, 53) and in others it is boys (10, 50, 54) who are found to be at greater risk. One implication of these findings is that lead's association with children's neurodevelopment cannot be accurately expressed as a single number because the magnitude of the association may vary depending on the characteristics of a particular child and his or her environment. A more promising implication, however, is that the effects of lead on a child might be reduced by modifying critical aspects of the environment. For example, indirect observational evidence indicates that the persistence of the link between an EBLL and reduced function varies with factors such as family social class, maternal IQ, and quality of the home environment (54). Specifically, if two children with the same early BLL achieve the same developmental score at time 1, but one child's environment offers greater cognitive stimulation, that child's developmental status at time 2 is likely to be better than that of the child from the less stimulating environment. Thus certain factors might help children to weather the developmental insult of early lead exposure, either preventing neurodevelopmental effects from being expressed or facilitating subsequent recovery of function. Social class is often found to be such an effect modifier, although higher social class is presumably a surrogate for the more proximal influences that confer this greater resilience (e.g., better nutrition, greater access to academic supports, more varied experiences).

### *Effectiveness of Reducing BLLs*

It has not been shown that lowering a BLL after it has been elevated prevents lead-induced cognitive defects. In one study, children with BLLs between 25 and 55 g/dL were chelated if a test dose of EDTA increased their urinary lead excretion. Chelation did not change their neurodevelopmental test scores or BLLs at 6 months of follow-up. However, the children whose BLLs fell the most, whether they had chelation or not, had the greatest improvement in test scores at their 6-month follow-up evaluation (55). It is noteworthy that children's test scores increased one point for each decline of 3 g/dL in their BLL, a slope that is consistent with the slope for the dose-effect relationship from several observational studies that did not involve any intervention. However, the only large-scale randomized trial assessing the effects of chelation-induced BLL reductions on neurotoxicity showed that oral chelation with succimer (dimercaptosuccinic acid) lowered children's BLLs but did not improve their scores on a range of cognitive, neuropsychological, and neurobehavioral tests. Conducted among children living in deteriorating housing in four inner-city areas, this study involved 780 children (12 to 23 months of age) with BLLs from 20 to 44 g/dL who were randomly assigned to receive either a placebo or up to three courses of succimer. While the mean BLL of the treated group was 4.5 g/dL lower than that of the control group 6 months after treatment, there were no significant

differences between them in any of the mean test scores 3 years after treatment began, when the children were, on average, 5 years old (56).

### *Effects of Early Enrichment on Children with EBLs*

No studies have been published on the effectiveness of non-medical interventions, such as early enrichment programs, in ameliorating the effects of EBLs on children's neurodevelopment. In the absence of such data, it is reasonable to hypothesize that children with neurodevelopmental problems associated with an EBL would benefit from the types of interventions shown to be effective in facilitating the neurodevelopment of other groups of children with idiopathic neurodevelopmental problems or those known to be at increased risk for such problems, such as low birth weight infants. Evaluations of interventions to foster the development of preschool children at risk for neurodevelopmental problems because of socioeconomic disadvantage, nonorganic failure to thrive, or low birth weight indicate that such programs can produce IQ increases on the order of 8 points (57). Although the magnitude of these IQ effects might attenuate after children complete the programs, participation in such programs is associated with lower rates of grade retention and need for special education (58). Some evidence suggests that programs in which participation begins prior to age 3 are more effective than those in which participation begins later (59). Programs that include procedures to foster both child development and parenting skills tend to be more effective than programs that are solely child-focused or parent-focused (57). Examples of such programs are the Mother-Infant Transaction Program (60-64) and the Infant Health and Development Program (65-67).

### **General Recommendations**

*Make long-term developmental surveillance a component of the management plan for any child with a BLL  $\geq 20$  g/dL.*

The precise BLL that one identifies as a "trigger" for neurodevelopmental surveillance will depend on the type and magnitude of deficit that one considers sufficiently large to warrant concern. Current CDC guidelines recommend that a child whose BLL is  $\geq 20$  g/dL or above receive environmental and medical evaluations. It makes both clinical and logistical sense to integrate neurodevelopmental surveillance and possible referral for diagnostic assessment or intervention into the overall management plan of such a child. The PCP and case manager, working in close collaboration, are best positioned to organize and oversee these processes. A BLL that exceeds  $20$  g/dL should not necessarily result in a referral for diagnostic assessment or intervention. This clinical decision should be made on a case-by-case basis, taking into account whether other neurodevelopmental risk factors are present (e.g., teen-age mother, poor parenting skills, inadequate cognitive or emotional stimulation, child abuse, poverty, genetic disorder, poor

nutrition, other medical issues). Under some circumstances, such as persistent BLLs of 15 to 19 g/dL or the presence of other significant neurodevelopmental risk factors, it would be appropriate to place a child with a lower BLL under increased neurodevelopmental surveillance. The case manager is in a unique position to assist the PCP in this regard by virtue of his or her knowledge of a child's risk factors gleaned from visits to the home or other contacts. Thus, the case manager can serve as a critical information resource to the PCP regarding contextual factors germane to the PCP's decisions about a child's neurodevelopmental needs. Furthermore, a case manager with training in neurodevelopmental assessment can conduct screening evaluations and bring potential problems to the PCP's attention.

The usual absence of associations between concurrent BLLs and risk for neurobehavioral deficits among children aged 0 to 3 years suggests that neurodevelopmental assessment of children while they have an EBLL might not identify children who will later experience cognitive problems (false-negatives). If a child currently has or has ever had an EBLL, however, the PCP and case manager should take a more aggressive approach in assessing that child's neurodevelopment and referring that child for follow-up. Under ordinary circumstances, the PCP is in the best position to follow up with long-term monitoring of a child with an EBLL. The developmental and behavioral screening that PCPs conduct at well-child visits, including taking a clinical history and administering brief instruments such as the Denver Developmental Screening Test, may be sufficient to identify children who are failing to make age-appropriate progress and transitions and who thus require additional diagnostic evaluation. Kindergarten-readiness evaluations generally are not designed to identify vulnerabilities that may be expressed as serious academic problems once children enter school. Because they produce many false negatives, kindergarten evaluations are not sufficiently sensitive to identify potential lead-associated learning difficulties.

*Do not base decisions regarding developmental assessment or intervention on a child's age at the time of the EBLL.*

Age is an inappropriate criterion for determining which children with EBLLs need referral for developmental evaluation. The neurodevelopmental effects of EBLLs are persistent and may be delayed. Also, there is no way of knowing how long a child may have had an EBLL. A child first identified as having an EBLL at age 4 might well have also had an EBLL at age 2 or 3 and, on the basis of a presumed chronic exposure, could be regarded as being in greater need of developmental assessment than a child with an EBLL at age 2. Because detailed information about children's blood lead history is often not available, a child of any age who is found to have a BLL of 20 g/dL or greater should be placed under increased surveillance in order to identify any emerging neurodevelopmental problems as early as possible.

*If you wish to refer a child with an EBLL for intervention services, consider referring that child for early intervention/stimulation programs that are available for children at increased developmental risk.*

Although there is no empirical basis for recommending interventions with specific characteristics for children with neurodevelopmental problems resulting from an EBLL, it is reasonable to hypothesize that such children would benefit from the types of interventions shown to be effective in facilitating the neurodevelopment of other groups of children with idiopathic neurodevelopmental problems. Programs in which participation begins prior to age 3 or those that include procedures to foster both child development and parenting skills may be most effective. Examples of such programs are the Mother-Infant Transaction Program and the Infant Health and Development Program.

*Include a history of a child's EBLL in the problem list maintained in the child's medical record.*

If a child changes his or her PCP, ensure that this information, along with other pertinent aspects of the child's medical history, is transmitted to the next provider. The PCP should work with the case manager to ensure appropriate follow-through.

*For the purposes of developmental surveillance, do not consider a child's case "closed" when the child reaches age 6 or when his or her BLLs are reduced.*

The period of increased risk for the expression of lead-associated neurodevelopmental problems continues after lead exposure has been remediated and BLLs reduced. Closure of a child's case by the case manager does not mean that the need for neurodevelopmental monitoring has ended.

*Be especially vigilant for emerging difficulties at critical transition points in childhood.*

There are three periods when different types of learning difficulties are typically expressed:

1. *First grade:* Children begin acquiring basic academic skills.
2. *Fourth grade:* They use these basic skills to learn new material.
3. *Sixth or seventh grade:* They need higher order planning and organizational skills.

A child with a history of EBLs who experienced difficulties making earlier transitions should be viewed as being at increased risk of experiencing difficulties with later transitions. Even children who made early transitions smoothly should be under increased surveillance at later transition points, as they may have problems when new educational demands are placed on them.

*Be alert for behaviors that might interfere with learning.*

An EBLL in early childhood is associated with an increased risk for behaviors such as inattention, distractibility, and impulsivity that can interfere with learning. These behaviors are characteristic of the recently recognized inattentive subtype of ADHD. Even if the behaviors a child presents are not sufficient to warrant the diagnosis of ADHD, the child may be helped by the types of classroom and work accommodations routinely made for children with an attention disorder.

*If you suspect that a child might be experiencing neurodevelopmental problems, consider arranging a thorough diagnostic (as opposed to screening) evaluation.*

The procedures used for assessment and intervention for a child with a history of EBLL and neurodevelopmental problems should be the same as those for a child with neurodevelopmental problems due to known and unknown causes. Ideally, assessments should be conducted by multidisciplinary teams, which might include developmental-behavioral pediatricians, educators, neuropsychologists, neurologists, speech/language pathologists, and child psychiatrists.

*Be advocates for the child.*

This might involve assisting the family in arranging diagnostic evaluations, interpreting the results, and petitioning third parties to pay for the evaluation on the grounds that the evaluation might reduce special education or specialized therapy costs in future years. In regions where access to specialized neurodevelopmental clinics is limited, diagnosis and treatment planning can also be achieved by means of school-based evaluations or private practitioners. It is important to recognize the complexities of school-system involvement in this process. Some school systems may be unwilling to commit resources to evaluate a child in the absence of a complaint that includes reduced academic progress. Furthermore, expecting schools to conduct such evaluations places them in a position of possible conflict of interest insofar as they would have to pay for remedial services deemed necessary as a result of the evaluations.

### **Recommendations for Future Research**

1. Conduct studies to characterize in greater detail the neurodevelopmental presentation associated with an EBLL, including analyses of the degree to which the presentation varies with factors such as the child's age at exposure and the magnitude and chronicity of the exposure.
2. Conduct studies to characterize the associations between EBLLs and learning disabilities.

3. Conduct studies to evaluate the role of EBLs in causing or exacerbating behaviors associated with ADHD, conduct disorder, and other psychiatric diagnoses.
4. Conduct studies to evaluate the potential psychosocial vulnerabilities of children with EBLs (e.g., self-esteem, self-concept, social competencies, aggression).
5. Conduct randomized trials to evaluate the efficacy of specific interventions in ameliorating lead-associated neurodevelopmental problems.

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