

**Research Question:** Do population-focused treatment strategies influence the incidence of developmental delays in children age 0 to 7 yr., who have lead poisoning (blood lead levels of >10 mcg/ml)?

## Summary of Recommendations

**Recommendation I: Treatment:** The IPHA Nursing Section: Lead Evidence Base Committee found evidence that population-focused treatment strategies with the chelating agent, Succimer, does not influence the incidence of developmental delays in children age 0 – 7 years who have lead poisoning with BLL's >10mcg/ml and <45mcg/ml.  
*Rating: D*

*Rationale:* Of the three evidence based articles retrieved none reported any evidence that chelation with succimer will reverse cognitive impairment. The Treatment of Lead Exposed Children (TLC) was a randomized, double blind, placebo-controlled clinical trial that began in 1994. Findings from this large study of children beginning at ages 12 – 33 months from several parts of the country found no improvement in cognitive or behavior functioning in children treated with the oral chelating agent, Succimer, compared with the placebo group. The TLC group was tested again after school entry at ages 7 and 7 ½ and these results confirmed the earlier findings that chelation therapy with Succimer to reduce lead levels failed to improve cognitive and behavior outcomes when compared with the placebo group (Dietrich, K. N., Ware, J. H., Salganik, M., Radcliffe, J., Rogan, W. J., Rhoads, G. G., et al., 2004).

One part of the TLC study attempted to replicate findings from a New York study published in 1993 that showed a positive improvement in cognition of children with similar demographics and BLL's who were given chelation with EDTA and therapeutic iron when indicated. They were only followed for 6 months but at that time, those individuals whose BLL's fell the most had improved test scores. The authors of the final TLC study consider it improbable that another chelation regimen would have been more effective. However, they report that their results still must be viewed as specific to the treatment regimen followed by TLC, not all possible regimens (Dietrich, et. al., 2004).

Center of Disease Control guidelines (Centers for Disease Control, 2007) and the American Academy of Pediatrics (Committee on Environmental Health, 2005) both endorse chelation treatment at levels >45ug/dL. Routine chelation for lead levels of 25-45ug/dL is not recommended because there is no evidence that chelation avoids or reverses neurotoxicity (Centers for Disease Control, 2007). This leads us to consider the safety of Succimer in the treatment of BLLs of 20-45ug/dL.

Succimer has been found to be the most effective chelating agent currently available (Dietrich, et. al., 2004). There were however slightly concerning differences seen between the Succimer and placebo groups in the TLC studies. In the Succimer group of children in TLC, four differences were; a small but statistically significant deficit in linear growth, a modest but statistically significant excess of hospitalized and outpatient injury events, small but statistically non-significant deficits in the primary cognitive endpoints, and a statistically significant neuropsychological deficit seen in 7 year old children on the NEPSY test in the attention and executive functions core domain (Dietrich, et. al., 2004).

### **Recommendation II: Treatment:**

The Lead Evidence Base Committee found insufficient evidence to recommend for or against nutritional supplementations or chelation treatment with medications other than Succimer to prevent or reduce the incidence of developmental delays in children with elevated BLL's of >10mcg/ml and <45mcg/ml.

*Rating: I*

*Rationale:* Even though nutritional status can affect the body's absorption of lead a lack of information exists that was done on children in the United State about the benefits of nutrition to offset the neurologic/behavior effects of lead. Studies do exist that were done on lead poisoned children living outside of the United States but the results cannot be generalized to children in the U.S. The reasons are due to the differences in exposure times to lead, differences in nutritional status and age differences in children in the studies compared to children in the U.S.

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### **Recommendations Conclusion:**

The most important clinical significance to these findings is to know that once a young child has been identified as having an elevated lead level **there are no medical or nutritional treatments that are available that have been proven to prevent or reduce the neurological damage that may result.** Measures must be taken to remove the source of the lead. Sometimes that means moving the child to a different environment during clean up and/or

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renovation. Some health care providers choose to use chelation at levels lower than the recommended CDC guidelines of <45ug/dL but this should be done with caution.

Indeed, the first line of defense against this avoidable environmental disease should be the screening of homes with potentially hazardous sources of exposure. By the time a child is identified as lead poisoned, the damage already may have been done with possible irreversible consequences.

## Supporting Documents

Centers for Disease Control (2007). Lead poisoning prevention program. Department of Health and Human Services. Retrieved on April 25, 2008 from: <http://www.cdc.gov/nceh/lead/>

Committee on Environmental Health (2005). Lead exposure in children: Prevention, detection, and management. Policy statement. *Pediatrics*, 116(4), 1036-1046.

Dietrich, K. N., Ware, J. H., Salganik, M., Radcliffe, J., Rogan, W. J., Rhoads, G. G., et al. (2004). Effect of chelation therapy on the neuropsychological and behavioral development of lead-exposed children after school entry. *Pediatrics*, 114(1), 19-26.

Liu, X., Ragan, N. B., Rogan, W. J., Dietrich, K. N., Radcliffe, J., & Rhoads, G. G. (2002). Do children with falling blood lead levels have improved cognition? *Pediatrics*, 110(4), 787(5).

Rogan, W. J., Dietrich, K. N., Ware, J. H., Dockery, D. W., Salganik, M., Radcliffe, J., et al. (2001). The effect of chelation therapy with succimer on neuropsychological development in children exposed to lead. *The New England Journal of Medicine*, 344 (19), 1421-1426.