
LEAD POISONING PREVENTION & TREATMENT UPDATES

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Welcome

This newsletter will provide you with information from the current research literature and updates on available resources related to lead poisoning prevention. With your help we will strive to reach the goal of eliminating lead as an environmental hazard for children by 2010. This quarterly newsletter is a collaborative effort between the Virginia Department of Health's Lead-Safe Virginia Program and the University of Virginia's Division of Medical Toxicology.

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PHONE NUMBERS TO KNOW

- **Lead-Safe Virginia, Virginia Department of Health**
(877) 668-7987 or Director at (804) 864-7694
- **24-hour Healthcare Professional Lead Emergency Hotline** (866) SOS-LEAD

Lead Poisoning and Chelation Therapy: An Article Review

This article refers to the following study:

Rogan WJ, Dietrich KN, Ware JH, et al. **The effect of chelation therapy with succimer on neuropsychological development in children exposed to lead.** N Engl J Med. 2001 May 10; 344(19):1421-6.

In 1991, the Food and Drug Administration licensed succimer (dimercaptosuccinic acid), the first approved oral lead chelator, for use in children with blood lead levels of at least 45 µg per deciliter. Succimer reduced blood lead levels at least as well as parenteral treatment with edetate calcium disodium in children with levels of 30 µg per deciliter (1.4 µmol per liter) or higher. Also in 1991, universal screening of children for elevated blood lead levels was recommended by the Centers for Disease Control (CDC), and the threshold of concern was lowered from 25 µg per deciliter to 15 µg per deciliter — a level associated with cognitive impairment but not symptoms of lead poisoning. However, the CDC made no specific recommendation about chelation therapy in children with blood lead levels of 20 to 44 µg per deciliter. Because of the increase in screening, the wide availability of an oral chelator, and the lack of data on lead chelation for the prevention of cognitive impairment, Rogan et al. conducted a multicenter, randomized, placebo-controlled clinical trial. This was designed to test the hypothesis that

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RESOURCES

Lead-Safe Virginia

<http://www.vahealth.org/leadsafe/>

Download copies of the *Guidelines for Childhood Lead Poisoning Screening in Virginia*:

[Guidelines for Childhood Lead Poisoning Screening in Virginia](#)

Virginia “*Care Coordination Manual: Children with Elevated Blood Lead Levels for Public and Private Practitioners*”

[Care Coordination Manual for Public and Private Practitioners](#)

CDC Spotlights on Lead

<http://www.cdc.gov/nceh/lead/>

Search for recalled lead items:

[U. S. Consumer Product Safety Commission](#)

<http://www.cpsc.gov/>

EPA Lead Page

<http://www.epa.gov/opptintr/lead/index.html>

Children's Environmental Health

<http://www.niehs.nih.gov/health/topics/population/children>

National Lead Information Center

<http://www.epa.gov/opptintr/lead/pubs/nlic.htm>

National Center for Lead Safe Housing

<http://www.cehn.org/cehn/resourceguide/nclsh.html>

American Academy of Pediatrics' Position Statement on Lead Screening

<http://aappolicy.aappublications.org/cgi/reprint/pediatrics;101/6/1072.pdf>

American Academy of Pediatrics' Position Statement on Lead Levels < 10 ug/dL

<http://pediatrics.aappublications.org/cgi/content/full/120/5/e1285>

ONLINE LEAD EDUCATION

Education in lead poisoning topics for health care professionals. Free CME for Virginia health care providers. <http://www.leadpoison.org/>

Current courses:

- Lead Pathophysiology
- Sources of Lead Poisoning

More courses to follow. Archived issues of this newsletter are also available.

children with moderate blood lead levels who were given succimer would have better scores than children given placebo on a range of tests measuring cognition, neuropsychological function, and behavior at 36 months of follow-up.

The authors of this study accepted referrals of children 12 to 33 months of age (a range that includes the age at which lead levels peak) who had blood lead levels of 20 to 44 µg per deciliter, had no more than two main residences, and could be tested in English (or Spanish, at one site). They measured lead levels in venous blood, serum ferritin levels, blood counts, renal function, and serum enzyme levels. They also inspected the children's homes to determine whether cleaning and minor repairs could be expected to reduce exposure to lead dust.

Using supplies known to be lead-free, venous blood was collected for measurement of blood lead levels twice before randomization and then on days 7, 28, and 42 after the beginning of each course of treatment. After treatment was stopped, blood lead levels were measured every three to four months. A total of 780 children were enrolled; they randomly assigned 396 to succimer and 384 to placebo. Treatment assignments were stratified according to clinical center, body-surface area, blood lead level, and language.

The two treatment groups were balanced with respect to base-line characteristics so the estimates of the effect of treatment are similar for the adjusted and unadjusted scores. According to the parents' reports, over 90 percent of the assigned doses of study drug were given. When the pills were counted, about 76 percent of the capsules had been removed from the bottles. Forty percent of the families whose children were given succimer and 26 percent of the families of children given placebo reported difficulty administering the drug. Interruptions in the administration of the drug occurred at similar rates in the succimer group (30 percent) and the placebo group (27 percent). Of the children in whom administration of the drug was interrupted, 39 percent of those receiving succimer and 45 percent of

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those receiving placebo resumed taking the study medication. Scores were obtained or imputed on the WPPSI-R for 745 of the 780 enrolled children (96 percent), on one or more of the NEPSY subscales for 688 (88 percent), and on the CPRS-R for 721 (92 percent).

Unadjusted mean scores on the WPPSI-R, NEPSY, and CPRS-R were similar in the two treatment groups. After adjustment for the variables listed in the Statistical Analysis section above, the mean full-scale IQ score on the WPPSI-R for children given succimer was 1.1 points (95 percent confidence interval for the difference, -2.6 to 0.5) lower than that for children given placebo. The children given succimer scored slightly higher on four of the five domains of the NEPSY; the differences did not vary according to age at testing. For the CPRS-R, the behavioral index was 1.2 points (95 percent confidence interval for the difference, -0.5 to 2.8) higher (i.e., worse) in children given succimer. None of these differences approached statistical significance. Adjustment had little effect on the estimates of the differences in means, as would be expected given the similarity of the groups at base line. Treatment with succimer in this study did not lead to better scores.

The results of this study suggest that chelation therapy is not of benefit for young children with blood lead levels below 45 µg per deciliter. The treatment in this study did not improve the cognitive, behavioral, or neuropsychological outcome. The regimen is expensive and a significant burden on the families. In addition, the slight slowing of linear growth and the evidence of more frequent trauma in children receiving succimer are not reassuring. Since lead poisoning and its sequelae are entirely preventable, the inability to demonstrate effective treatment lends further impetus to efforts to protect children from exposure to lead in the first place.

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