

## COMMENTARY

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### Lead Toxicity in the 21st Century: Will We Still Be Treating It?

Clinical pediatric practice has not kept pace with the explosive growth in scientific understanding of lead poisoning during the past decade. The report by Glotzer and Bauchner in this issue<sup>1</sup> demonstrates the widely differing approaches to treatment of lead toxicity found at many centers. Primary prevention of lead poisoning, the most effective response, continues at a pedestrian pace, even though in the United States we now possess both the knowledge and means to eradicate the disease permanently.

Our understanding of lead's role in human health has changed profoundly during the past five decades. In that period, pediatricians have discarded the once widely held belief that affected children either died or recovered completely from lead poisoning. They now are confronted with data demonstrating that 3 to 4 million lead-exposed children, most of whom have no symptoms, may have impaired neurobehavioral function.<sup>2</sup> This new information has drawn the Public Health Service to declare that "Lead Poisoning remains the most common and societally devastating environmental disease of young children."<sup>3</sup>

In 1988, the Agency for Toxic Substances and Disease Registry issued "The Nature and Extent of Lead Poisoning in Children in the United States: A report to Congress."<sup>2</sup> This historic report estimated that 16% of *all* American children have blood lead levels in the neurotoxic range. Being well off does not protect children against lead hazards; 7% of economically favored white children were estimated to have blood lead levels greater than 15  $\mu\text{g}/\text{dL}$ . But being poor radically increases the risk; 55% of African American children in poverty have blood lead levels greater than 15  $\mu\text{g}/\text{dL}$ . There is no other serious disease with this prevalence. It is a disgrace that more than half of the Black children in poverty in the United States enter the first grade with this preventable handicapping condition. It is also a real danger to the polity.

As a result of these data, the announced federal strategy has shifted from finding cases and then treating them, to finding the toxicant in the environment, removing it, and breaking the exposure link. On February 21, 1991, Dr James Mason, the Assistant Secretary of Health, issued the "Strategic Plan to

Eliminate Childhood Lead Poisoning."<sup>4</sup> This initiative represents the first authentic step toward primary prevention.

As recently as 1969, a blood lead less than 60  $\mu\text{g}/\text{dL}$  was thought to be safe. In 1970, the Surgeon General reset the definition of toxicity from 60  $\mu\text{g}/\text{dL}$  to 40  $\mu\text{g}/\text{dL}$ . Many studies, beginning early in the 1970s, showed that lead at "silent" levels was associated with deficits in psychometric intelligence.<sup>5</sup> Once thought to be exclusively a disease of inner city African-American children, the impact of lead exposure on intelligence came under international study. As a result, in the 1980s, well-designed and well-executed investigations from Scotland, Denmark, Greece, Italy, Germany, England, Australia, and New Zealand reported effects of lead on children's IQ, academic achievement, and behavior.<sup>6-13</sup> These studies, which capitalized on previous work, tended to use larger samples, better outcome measures, better covariate control, and more sophisticated multivariate models.

Not all studies report an effect; some reviewers, after counting the number of positive and negative reports, have concluded that the issue of silent lead neurotoxicity is still a matter of controversy. It is important to recognize that simple tallies of studies are weak and unsatisfactory ways to draw conclusions from a group of investigations. If there were no effect of lead on children's IQs, one would expect about one study in 20 to report an association on the basis of chance. In fact, more than half of the published studies show an effect at  $P < .05$ . Meta-analysis, a quantitative approach to synthesis, offers a stronger method to draw conclusions from a group of studies. Three recent meta-analyses all showed a strong effect of lead on IQ.<sup>14-16</sup>

Do children have elevated blood lead levels because of preexisting intellectual deficit? Is lead an effect rather than a cause? These questions were answered by prospective studies of children from birth onward. These showed that prenatal lead levels, or early infancy lead levels, were related to latter psychologic scores,<sup>12,17,18</sup> after adjustment for other variables such as maternal IQ and socioeconomic status.

These findings prompted the Centers for Disease Control to lower the definition of lead toxicity to 30  $\mu\text{g}/\text{dL}$  in 1978, and then to 25  $\mu\text{g}/\text{dL}$  in 1985.<sup>19</sup> This was a contentious process, and on both occasions the lead industry attempted to retard the decision making.<sup>20</sup> The Centers for Disease Control Advisory Committee now has reviewed the latest data and has concluded that lead toxicity is found at levels of 10  $\mu\text{g}/\text{dL}$  and that the effect may occur at levels below this.<sup>21</sup>

This new standard raises difficult questions for the clinician. The first is how to implement lead screening

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in practice. Many pediatricians serving middle class patients believe that lead exposure has too low a prevalence to warrant the expense. Yet tuberculosis tine tests, phenylketouria, and galactosemia screening are conducted routinely in busy practices, even though the prevalence of these diseases is less than 1/10 000. In the average pediatric practice of 3000 children, if the prevalence of blood lead levels greater than 25  $\mu\text{g}/\text{dL}$  is 0.5% and those greater than 10  $\mu\text{g}/\text{dL}$  is 3%, 15 children with blood leads greater than 25  $\mu\text{g}/\text{dL}$  and 90 children with blood lead levels greater than 10  $\mu\text{g}/\text{dL}$  can be expected. This may be a conservative scenario. A random survey of a racially and economically diverse private practice in a mid-western city recently showed that 22% of the patients had blood lead levels greater than 15  $\mu\text{g}/\text{dL}$ , and 3% had blood lead levels greater than 25  $\mu\text{g}/\text{dL}$  (T. Schlenker, MD, personal communication, Dec 16, 1991).

Clinicians are reluctant to screen because, at levels of lead less than 25  $\mu\text{g}/\text{dL}$ , no pharmacologic treatment is currently available. Management of lead exposure is not limited to prescribing drugs. The pediatrician has much to offer: testing siblings; finding the source; detection of risky behaviors such as pica, nail biting, or finger sucking; education about the hazards and control of lead in paint, dirt, dust, and water; nutritional counseling; and finally, systematic follow-up. A child with a blood lead level between 10 and 14  $\mu\text{g}/\text{dL}$  should be retested at 3-month intervals to determine if the level is rising.

Another reason is the nature of the screening test for lead. The Free Erythrocytic Protoporphyrin test has no screening value for blood lead levels less than 25  $\mu\text{g}/\text{dL}$ . Venous blood lead levels are reliable in reflecting actual body burdens, but phlebotomy of 1-year-olds is difficult. Capillary blood lead tests using a finger stick require scrupulous quality control; contamination must be avoided, and venous blood follow-up is needed to eliminate false positive results. X-ray fluorescence of bone lead, as well as micro-methods for detecting erythrocyte lead levels, are on the research horizon and should enhance the ease of lead screening.

Some clinicians cite the lack of environmental health and housing resources as reasons not to screen. When no children are screened, no cases are found, and the myth that there is no lead problem becomes fixed. When screening is put in place, community lead problems have been identified consistently.

Glutzer and Bauchner<sup>1</sup> show that the choice of treatment and the criteria for instituting it vary widely across institutions. There are many reasons for this. Most prominent is the lack of data about the efficacy of chelation at levels of lead, that while toxic, are not associated with severe symptoms. It is startling to realize that 48 years after the introduction of chelation therapy with edathamil ( $\text{CaNa}_2\text{EDTA}$ ),<sup>22</sup> we still do not know if it conveys any benefits to children with moderate elevations of blood lead. Nor do we know the long-term consequences of penicillamine therapy. A new oral chelating agent, succimer, chemically related to British anti-lewisite, has been released by the Food and Drug Administration. It is a safe bet

that unless a multicenter trial of all three agents, with a rigorous randomized design and standard set of outcome measures is conducted, the current *Laissez faire* intuitive approach to chelation will continue, and that our successors will know as little about the benefits and hazards of these drugs as we do today. There are no data on the long-term effects of succimer on blood lead levels.

Succimer has been approved for use in children with blood lead levels greater than 45  $\mu\text{g}/\text{dL}$ , but many pediatricians are already using it at lesser concentrations. Administration of succimer should not be considered a substitute for environmental control; the drug must not be administered until the patient has been separated from the source of lead. Because the drug is administered orally, many physicians will be tempted to give it on an outpatient basis, and there is already some evidence that insurance carriers are encouraging this. It is dangerous to give an oral chelating agent while the child continues to reside in the presence of lead.

The current experience with this agent is less than 200 cases, and the postmarket surveillance protocol issued by the manufacturer cannot be described as rigorous. In the face of limited experience, statements about the lack of side effects must be considered tentative and subject to revision. To rely on physicians' reports of untoward effects of any agent is to accept a notoriously weak scheme of detection. Physicians who employ succimer should inquire carefully for allergic reactions, neutropenia, and test renal and kidney function at regular intervals.

Treatment begins and ends with removing lead from the child's environment, and the most important source is old leaded paint. Removing lead safely from houses takes time and trained workers. The residents should not be on the premises while the work is carried out.

Finding and treating patients can only be thought of as a temporary response to a problem of such dimensions. The Centers for Disease Control Strategic Plan to Eliminate Childhood Lead Poisoning<sup>4</sup> outlines the first 5 years of a 15-year effort to reduce the prevalence rate to zero. But at this time the Plan is merely an important document, and will remain so until the required steps to implement it have been put in place. The costs of such an effort are formidable, and will be counted in billions of dollars. There are four lead bills in congress requesting additional funds for lead control. It is critical that the Administration, having declared that it considers lead at the top of the list of serious environmentally related childhood diseases, provide the federal funds to match its rhetoric.

We will not end this man-made epidemic until we understand the reasons for its curious persistence in the face of considerable data about what lead does, and what is needed to rid ourselves of it. Among the reasons for desultory attention to this epidemic is the stubborn belief that this is an affliction of only poor minority children. Related is the tendency on the part of some to blame the mother's rearing style for the elevated blood lead. Many people believe that with the passage of the Lead Paint Poisoning Prevention

Acts, and the removal of lead from gasoline, the problem somehow disappeared. Academic pediatrics, with some exceptions, has not found this commonplace low technology malady as fascinating as molecular disorders. Most academic pediatric departments give more attention, resources, and urgency to much rarer diseases. Private pediatric practitioners generally believe that this is not a problem for their patients. The lead industry since at least as early as 1939 has worked to obscure the effects of lead on human health; this practice continues today. Finally, the size of the problem and the amount of dollars and effort involved result in a reflex wave of pessimism. Self-styled realists, when confronted with a 10-billion-dollar estimate to delead and improve the 2 million dangerous houses in which children live and the paint is peeling, shrug and turn away.

The Centers for Disease Control Strategic Plan<sup>4</sup> contains an econometric analysis of the costs and benefits of lead prevention. The Plan estimates the costs for deleading homes and the benefits that accrue from reduced need for medical care, for special education and the increase in wages that goes with having a higher IQ. The model does not include other potentially related benefits such as increased tax returns, reduced spending for delinquency, and reduced medical costs for hypertension and cardiovascular disease. The conclusion of the analysis, described as conservative by Centers for Disease Control, is that the net return to our society for deleading the housing stock in the United States would be \$28 billion more than the costs of the abatement.

It should not be necessary to place a price tag on the eradication of a serious childhood illness; the presence of the disease and owning the means to eliminate it should be enough. But this is the era of self-satisfied pragmatism, and metrics are often required to justify undertaking moral actions. The eradication of lead, this blunter of children's cognition and silent thief of their futures, meets the pragmatic test. The numbers are clear; it makes unequivocal fiscal sense to make this investment in human capital, and in achieving this end, we might learn something important about our ability to control our personal destinies.

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