

Reducing Blood Lead Levels

Benefits and Strategies

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DESPITE DRAMATIC REDUCTIONS IN POPULATION LEAD exposure over the past 2 decades, nearly 900 000 US children younger than 6 years still have elevated blood lead levels ($\geq 0.483 \mu\text{mol/L}$ [$\geq 10 \mu\text{g/dL}$]).^{1,2} The problem disproportionately affects low-income children living in older dwellings. Available data suggest that subtle health effects, such as lower IQ scores in children, may extend to blood lead levels well below the $0.483\text{-}\mu\text{mol/L}$ ($10\text{-}\mu\text{g/dL}$) threshold.³ While not as well studied, an association between blood lead levels in this range and cognitive function of middle-aged and elderly men has also been reported.⁴ Further research may continue to redefine what constitutes an entirely “safe” level.

Much of the reduction in lead exposure to date has come from eliminating uses of lead, such as in gasoline, soldered cans, and housepaint, that were causing widespread, ongoing exposures.⁵ The opportunity for such relatively simple but powerful interventions has waned as the most hazardous uses of lead have been largely phased out in the United States (although not, unfortunately, in many developing nations). The remaining challenge is far more complex: to address the large reservoirs of lead in paint and exterior soil and dust contaminated from past uses. Some further declines in exposure may occur with turnover in the housing stock and dilution of existing soil and dust contamination. However, without additional efforts to reduce lead hazards at the level of individual homes and neighborhoods, such changes will come too slowly to avoid harm to many cohorts of children.

Consequently, as the distribution of blood lead levels has shifted downward, policy makers and researchers continue to address 2 questions: (1) what impact do blood lead levels prevailing in the population today have on human health; and (2) what interventions can further reduce the risk of lead toxicity, especially among those at highest risk? Two reports in this issue of THE JOURNAL address aspects of these questions.

Moss and colleagues⁶ add data on dental caries to other findings supporting health effects of lead at levels common in the general population, including lower IQ scores and

reductions in stature. Based on data from the Third National Health and Nutrition Examination Survey (NHANES III),⁷ the authors report a direct relation of blood lead levels in children to the prevalence and extent of dental caries,⁶ even for levels well below $0.24 \mu\text{mol/L}$ ($5 \mu\text{g/dL}$). The authors estimate that variation in lead exposure could account for perhaps 20% or more of the prevalence of dental caries among older children.

In addition to the usual limitations of cross-sectional data, at least 2 caveats should be kept in mind when interpreting these findings. First, it is not clear whether other nutritional or behavioral factors might confound the observed association between lead and caries. The roles of iron⁸ and ascorbic acid,⁹ for example, can and should be assessed with data available in NHANES III. In addition, the authors are perhaps too quick to minimize the possibility of potential confounding of their findings by exposure to fluoridated drinking water. Lead exposure is influenced by both individual-level factors and community characteristics (such as urbanization).¹⁰ If lead exposure and lack of fluoridation are correlated at the community level, this could explain some of the dental caries risk gradient reported by Moss et al. Despite these limitations, the strength of the relationship reported by Moss et al, its consistency across age groups, and supporting animal data bolster a causal explanation.

The study by Simon and Hudes¹¹ concerns the second question of potential interventions to reduce the risk of lead toxic effects. The authors report an inverse relationship of serum ascorbic acid levels to blood lead levels in both children and adults. As in the study by Moss et al, Simon and Hudes used NHANES III data to examine in the general population an association suggested by animal and limited human data. The association of both high blood lead levels¹⁰ and low dietary ascorbic acid intake (in adults) with poverty¹² raises the possibility of confounding by socioeconomic status. Since the authors largely addressed this possibility, their results imply that the impact of increasing ascorbic acid intake on blood lead levels could be greatest in the highest-risk populations.

Ascorbic acid intake is but 1 of several nutritional factors that may influence lead toxicity through an influence

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on absorption, elimination, transport, tissue binding, or secondary mechanisms of toxicity.¹³ Irregular food intake, high dietary fat intake, low dietary calcium, and iron deficiency can increase the risk of lead toxicity in a contaminated environment.¹⁴ As Simon and Hudes point out, however, causal inference from observational studies of isolated nutrient effects is difficult, given the tendency of any nutrient to covary with others and with social or lifestyle factors associated with lead exposure. An additional, unfortunate limitation of this study is the lack of data on the group of greatest interest—children younger than 6 years. Even though a beneficial effect of ascorbic acid supplements on lead levels is supported by a recent report from a small randomized trial in adult smokers,¹⁵ more evidence from controlled intervention trials is needed to demonstrate the real value, if any, of increased ascorbic acid intake, especially in young children.

Even if a nutritional manipulation is proven effective in reducing blood lead levels, reliance on such an intervention places most of the burden for prevention on those most affected and least responsible for the underlying environmental causes of lead toxicity.¹⁶ Nutritional interventions, therefore, must never substitute for efforts to reduce lead exposure to safe levels. On the other hand, when used as an adjunct to environmental measures, some nutritional changes may prove to have benefits beyond any impact on lead toxicity. For example, studies have suggested benefits of higher ascorbic acid intake on blood pressure,¹⁷ blood lipid profiles,¹⁸ and respiratory symptoms.¹⁹

What needs to be done to hasten the reduction of lead exposure, especially for the populations most affected? While existing efforts, such as screening and responding to lead-poisoned children, need to continue, it would seem reasonable to propose expanded activity on 2 fronts in particular.

First, public and private efforts should be made to increase the testing and remediation of residential lead hazards from deteriorated paint and contaminated dust before children develop lead toxic effects. Interior dust lead measurements, available at relatively low cost, can now be used to help identify the most immediately hazardous dwellings,²⁰ and interventions are available to substantially reduce residential lead exposure.²¹ The use of this relatively inexpensive test should be expanded, thus decreasing the reliance on elevated blood lead levels in children to identify hazardous home environments.

Second, additional research is needed regarding the sources, fate, and remediation of contaminated exterior dust and soil, which can have major effects on blood lead levels.^{20,22} Approximately 11% of pre-1980 homes are estimated to have soil lead concentrations exceeding 1000 ppm,²³ and lead levels in some urban communities may be comparable to those found in communities contaminated by smelting and mining operations.²⁰ Practical interventions and the resources to implement them in large urban areas are currently lacking.

The studies by Moss et al⁶ and Simon and Hudes¹¹ add to existing knowledge of the benefits of reducing lead exposure and of the potential role of nutrition in augmenting environmental efforts. These reports do not fundamentally alter current understanding of the causes of the remaining lead exposure problem or the actions required for its elimination. Until recently, the perceived scope of the problem—some 57 million pre-1978 private dwelling units are estimated to have at least some leaded paint²⁴—and its connection to the deeper problems of poverty and substandard housing made its elimination seem an elusive goal. However, by focusing prevention efforts on vulnerable populations exposed to immediate lead hazards, progress toward the virtual eradication of childhood lead toxicity can be greatly accelerated.

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Hypoxia Is the Cause of Brain Damage in Hyponatremia

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THERE HAS BEEN AN ONGOING CONTROVERSY REGARDING the treatment of chronic hyponatremia. The initial reports^{1,2} suggesting that overzealous treatment of hyponatremia with hypertonic saline may cause central pontine myelinolysis or osmotic demyelination in the brain provoked a voluminous literature that continues to be just as lively now as it was at the time the first reports were published.³ Today, most clinicians who deal with electrolyte disorders appear to agree that acute symptomatic hyponatremia, or more precisely, acute water intoxication, imposes the risk of cerebral edema, uncal herniation, and death. In these patients, when hyponatremia is of recent onset, immediate administration of hypertonic saline in a quantity calculated to increase serum sodium levels by approximately 10 mmol/L may be lifesaving.⁴ However, total correction or overcorrection may result in irreversible damage to the brain.⁵

Experimentally, studies have shown that brain cells adapt to hypotonicity by expelling potassium, some sodium and chloride, amino acids, and certain osmotically active metabolites such that the volume of the cell, initially expanded by hypotonicity, returns toward normal.⁶ This process approaches completion after approximately 2 days. At this point, the hyponatremia is arbitrarily called chronic.^{7,8} If brain cell adaptation occurs in humans as predictably as in animals, then simple water deprivation should allow gradual recovery with less risk. However, not all patients with chronic hyponatremia do well even when they have had time to undergo adaptation. When pondering treatment options in hyponatremic patients, the pivotal issue is to determine if the patient displays encephalopathic symptoms of hyponatremia. These symptoms may be mild and difficult to sort out in an elderly person who may have subtle disturbances in baseline cognitive function. These include a mild change in mental status that may be noticed only by a close acquaintance, or peculiar behavioral changes, illusions, confusion, incontinence, tremulousness, clumsiness, ataxia, or falls. Seizures also may occur and signal the need for urgent treatment with saline. If none

of these symptoms is present, conservative treatment, consisting of eliminating the precipitating cause of hyponatremia if one is evident and simple water deprivation, generally is the preferred course to follow.

In this issue of THE JOURNAL, Ayus and Arieff⁹ describe 53 postmenopausal women with chronic hyponatremia who were all encephalopathic. Seventeen of these patients were seen before evidence of hypoxia or respiratory failure supervened. The remainder had already become hypoxic and required intubation and ventilatory assistance. The 17 patients without respiratory failure and 22 of the 36 patients with hypoxia were treated with saline or hypertonic saline to increase their plasma sodium concentration by no more than 0.8 mmol/L per hour but not greater than an end point of 133 mmol/L. The average absolute change in plasma sodium concentration was 22 and 30 mmol/L in patients without and with hypoxia, respectively. An exception was made for patients with seizures, who were given sufficient hypertonic sodium chloride to increase serum sodium concentration by 8 mmol/L during the first hour. The remaining 14 hypoxic patients who were treated conservatively with water deprivation showed an average increase of plasma sodium concentration of 3 mmol/L during the entire course of their treatment.

All patients without hypoxia recovered completely. None of the patients available for magnetic resonance imaging 1 year later showed cerebral abnormalities. Six of the 11 patients treated with saline who had imaging studies performed before treatment showed evidence of cerebral edema. Of the saline-treated patients who were hypoxic, 2 recovered completely, 6 recovered partially, and the remainder either developed irreversible disabling brain damage or died. In contrast, each hypoxic patient treated with simple water deprivation either died or experienced permanently disabling brain damage. The study by Ayus and Arieff offers several important observations and clinical lessons.

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