

CASE RECORDS OF THE CHILDREN'S HOSPITAL PEDIATRIC ENVIRONMENTAL HEALTH CLINIC

## Lead Poisoning from an Unexpected Source in a 4-Month-Old Infant

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Childhood lead poisoning is characteristically a disease that occurs between the second and third years of life, generally resulting from the child's ingestion of lead-based paint or dust. However, lead poisoning may also appear in the first year of life. The case of a 4-month-old infant is reported in which the preparation of infant formula in a lead-soldered samovar (urn) resulted in venous blood lead levels as high as 46 µg/dl. The samovar had been brought into the United States by the parents while on a visit to Iran. The infant was placed on chelation therapy with parenteral CaNa<sub>2</sub>EDTA followed by oral *meso*-2,3-dimercaptosuccinic acid (DMSA) and *D*-penicillamine. This resulted in a rapid and substantial reduction in the blood lead level. Lead poisoning in infancy may have unusual etiologies such as *in utero* transmission of lead by lead-poisoned women. Because sources of lead poisoning in infancy may be unusual, a detailed environmental investigation may be necessary to identify the exact source. Children exposed to lead in the first 2 years of life have a special vulnerability to the neurotoxicity of lead, with the risk of enduring developmental handicaps. Continued public health initiatives to remove lead from the environment, in conjunction with routine lead screening of young children, will be key in meeting the goal of the Centers for Disease Control and Prevention to eliminate childhood lead poisoning by the year 2011. *Key words:* infancy, lead poisoning. *Environ Health Perspect* 106:313-316 (1998). [Online 11 May 1998]

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### Case Presentation

A 4-month-old male was referred to the Children's Hospital Lead Poisoning Treatment Program (LPTP) for management of a venous blood lead level of 46 µg/dl. The infant had an unremarkable past medical history. Recently the rented apartment in which he lived with his parents was scheduled to undergo deleading. The family promptly moved to alternate housing in another apartment building. After 2 weeks and prior to returning to their home, the parents requested a lead level on the infant as a baseline before reinhabiting the apartment. Unexpectedly, the infant's venous blood lead level was 44 µg/dl. When evaluated by the pediatrician, the child was asymptomatic and there were no reports of change in his behavior. An abdominal radiograph was negative for radiopaque material. He was immediately referred to the LPTP, where a repeat blood lead was 46 µg/dl. Because of his young age and uncertainty about the source of his lead poisoning, he was admitted to Children's Hospital for intravenous chelation and environmental protection.

While the infant was hospitalized, an environmental inspection was initiated by the

Massachusetts Childhood Lead Poisoning Prevention Program. The family's home, which was still undergoing deleading, was inspected and found to have residual lead hazards. However, the parents denied visiting the apartment during its deleading. The parents, who had emigrated from Iran 5 years earlier, were asked about occupations, hobbies, and ethnic remedies. The mother was a medical assistant and the father was a college student; neither had an occupation or avocation that involved lead. They denied use of ethnic remedies or lead-based cosmetics. Because of the possibility that the infant's lead exposure resulted from a source common to all family members, both parents and an 11-year-old brother were tested for lead. The father had a venous blood lead level of <5 µg/dl, the 11-year-old had a lead level of 8 µg/dl, and the mother's venous lead level was 29 µg/dl. Other than fatigue attributed to caring for her infant, the mother had no symptoms or signs of lead intoxication.

Upon further inquiry, the mother disclosed that for 2 months she had been feeding the infant formula supplemented with breast milk; before that the child was solely breast-fed. She denied applying any

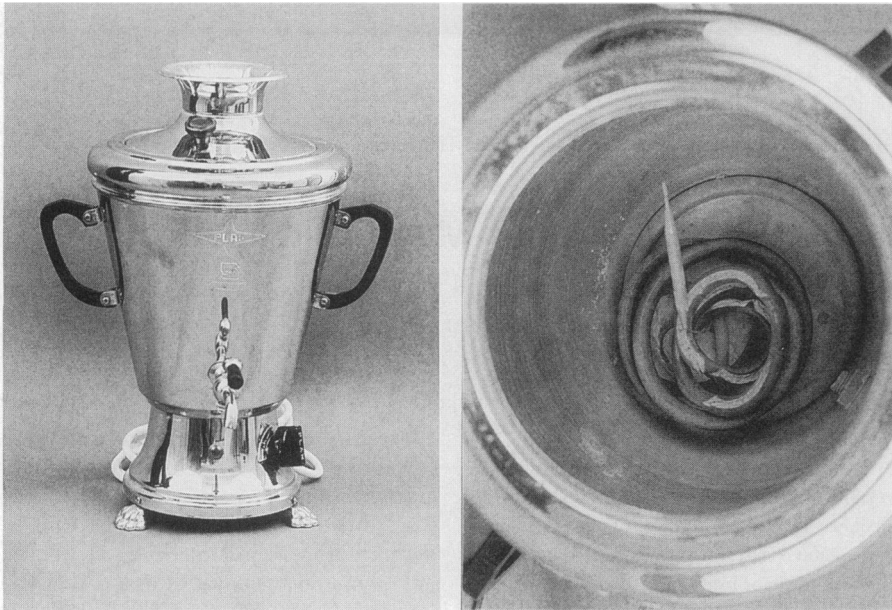
ointments, chemicals, or metal shields to her breasts. When asked to detail her methods of formula preparation, she stated that she routinely used powdered formula, reconstituting each bottle with water boiled for 10 min in a samovar (urn) that they had brought from Iran 6 months before. She also admitted that since the child's birth she had been regularly drinking tea with water from the same urn, a practice that the father and son did not have. She was asked to bring the vessel in for inspection. Visual inspection of the samovar (Fig. 1) showed that the segments of the urn, including its base and handles, were soldered into place. The samovar was investigated as a source of lead by placing 120 ml triple-distilled water in the urn for 15 min; the water was then decanted and analyzed for lead. The lead concentration of this unboiled water, tested by atomic absorption spectrophotometry (model Zeeman/3030, Perkin-Elmer Corp., Norwalk, CT) with graphite furnace and deuterium background correction, was 4,000 parts per billion (ppb, µg/l). Estimating the infant's daily formula intake at 1,000 ml, with a mean body weight of 6 kg, corresponded with a daily lead intake of greater than 600 µg/kg daily.

Upon admission to the hospital, the infant was alert and active. There was no history of lethargy, constipation, change in appetite, or change in behavior. Weight and length were at the 50% percentile for age. The physical examination was unremarkable. The admission hematocrit was 32.5%, electrolytes and urinalysis were within normal limits, zinc protoporphyrin was 181 µg/dl whole blood, and serum ferritin was 35.2 ng/ml (reference range 10-150 ng/ml). The child underwent a 5-day course of CaNa<sub>2</sub>EDTA, 50 mg/kg/day,

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**Figure 1.** The samovar and its interior. Each of the handles is soldered into place on the vessel wall, and a seam of solder also joins the base to the vessel.

at the end of which his lead level had fallen to 30  $\mu\text{g}/\text{dl}$ . During the hospitalization, his mother inquired about her ability to continue breast-feeding. To evaluate this, a specimen of her breast milk was expressed into a glass container that had been triple-washed with nitric acid. The lead content of the breast milk by atomic absorption spectrophotometry was  $<5 \mu\text{g}/\text{dl}$ . On the basis of this analysis, the mother was advised that she could continue breast-feeding.

The infant received further chelation as an outpatient. He was initially prescribed multiple courses of *meso*-2,3-dimercaptosuccinic acid (DMSA, succimer). This was followed by a several week course of *D*-penicillamine. These succeeded in bringing his lead level down to 8  $\mu\text{g}/\text{dl}$  after 9 additional months of treatment and monitoring. He was followed in the Lead Treatment Program for the next year. While his blood lead levels remained low (in the range of 10  $\mu\text{g}/\text{dl}$ ), concerns were raised and subsequently verified that the child had mild to moderate speech delay. Early intervention was promptly initiated. There were no further elevations in his lead level. At the age of 22 months, his lead level was 12  $\mu\text{g}/\text{dl}$ . A venous blood lead level at the age of 3 years was 7  $\mu\text{g}/\text{dl}$ .

## Discussion

Lead is among the most ubiquitous environmental toxins in the world. Mined and used extensively for more than 7,000 years, this potent heavy metal has been cited as a contributor to such important historical events as the fall of the Roman Empire, epidemics of lead poisoning among moonshiners, epidemic gout,

peripheral neuropathy in painters, and deaths among young children (1,2).

Lead poisoning in children was first identified by Turner (3) and Gibson (4) in 1892 when cases of encephalopathy, often fatal, were associated with the ingestion of "white paint" chips from old porches. In the United States well into the 20th century, childhood lead poisoning and paint chip ingestion became synonymous with lead poisoning characterized as an illness of the poor, found only among children living in ghettos or other dilapidated housing. It has been only recently, as lead poisoning has begun to occur from renovation of old homes among upper socioeconomic groups, that this disease has been able to shed its reputation as a disease of poverty. In the United States, the phaseout of lead from gasoline, paint, food, and water over the last 20 years has dramatically reduced the exposure of Americans to lead and remains one of the greatest public health successes in American history (2).

Epidemiologic data from the National Health and Nutrition Examination Survey (NHANES) have documented the effectiveness of reduced lead exposure on blood lead levels in the United States. There was a 77% fall in mean blood lead levels between the second and third (phase 1) NHANES studies (1976–1980 and 1988–1991) (5,6). Recent data from phase 2 of the the third NHANES indicate that the geometric mean blood lead level of children 1–5 years of age is 2.7  $\mu\text{g}/\text{dl}$  (7). It is important to note that there are little data on blood lead levels in children less than 6 months of age; therefore, among infants such as the child in this case, lead poisoning has unknown prevalence,

although congenital and neonatal lead poisoning have been well described.

Developmentally, childhood lead poisoning has its peak occurrence between the ages of 18 and 24 months for a variety of reasons (5,7,8). First, this is an age range in which children are the most curious, mobile, and oral; it is also a time when adult supervision begins to lessen. Additionally, by this age the child has mastered the pincer grasp necessary to pick up and mouth a paint chip. Finally, this age range is notable for being a period during which children become very interested in windows as a source of play (because they represent an at-level table and because of the toddlers' interest in observing outdoor activities). Within homes, windows are most likely to have flaking paint and highly absorbable lead dust; they have been identified as an important vector for childhood lead poisoning (5,7,8).

Because lead paint and dust remain the most common causes of lead poisoning in children, the environmental assessment of a lead-poisoned child should begin with an investigation of the child's residence (9). In this case, there was no lead in the alternate housing. The family home did have lead hazards, but the parents denied entering the home. Also, the young age of the child meant he had neither the mobility nor the dexterity to grasp a paint chip or mouth a dust-laden object. Nonetheless, in a review of the etiologies of lead poisoning in the first year of life, we found that epidemiologically the most common cause was household renovation (10). Another potential source of lead in the first 6 months of life is congenital lead poisoning. The kinetics of lead in pregnancy are such that it is efficiently transmitted across the placenta; fetal blood lead levels are 80–100% those of the mother (11,12). The postnatal rate of decline in blood lead levels among congenitally lead-poisoned neonates has not been defined. Theoretically, the rapid growth and bone development of the infant should promote a rapid fall in blood lead levels. In this case, the finding of an elevated lead level in the mother was in fact strongly suggestive of congenital lead poisoning as an etiology (13–15).

Other potential sources of lead poisoning in infants are the use of folk remedies and lead-contaminated water. Folk remedies, nutritional supplements, and cosmetics may be very high in lead (16,17). Water is a component of background daily lead exposure but can also occasionally result in frank lead poisoning. A phenomenon occurring almost solely in infants who are fed powdered or concentrated formula (because these require the addition of large amounts of water), lead poisoning from contaminated water has been previously described (18,19).

In our own series, 24% of lead poisoning cases were due to water contamination (10). We measured lead concentrations in water samples as high as 200,000 ppb, either from water that was placed in a lead-containing vessel, from excessive boiling, or from use of lead-contaminated tap water. The EPA has recently established a maximum contaminant level of zero for lead in water, with an action level of 15 ppb. In a recent national evaluation of water supplies, the EPA found that more than 130 municipalities exceeded the action level (20).

Lead intoxication in infants from water has several unique features. First, with the administration of formula daily, this vector guarantees a high daily intake of lead for a protracted period of time. Second, lead absorption from the gastrointestinal tract is inversely related to age; an estimated 30–50% of ingested lead is absorbed by the gastrointestinal tract of a child versus approximately 10% in an adult (21). This observation implies that lead absorption from the gut would be maximal in the first months of life. Finally, because absorption of lead is inversely related to particle size, lead in water is more absorbable than lead from paint or dust. The quantity of lead administered by this route can be enormous. For example, a 4-month-old child would drink approximately 1,000 ml of water daily if given powdered or concentrated formula. If that water has a lead concentration of 100 ppb, a concentration exceeded in many U.S. communities, the child's daily intake of lead would be 100 µg. At an average body weight of 6 kg, the child would be exposed to more than 15 µg/kg of lead daily. Positive lead balance in infants is associated with daily intakes of greater than 5 µg/kg (22). Given the slow rate of elimination of lead from the body (a half-life of 20 years) (23,24), there would be accumulation such by the first birthday, the lead burden would be substantial, with the child having been exposed to 36,500 µg of lead from water alone.

In the case under discussion, the source of lead was traced to an imported cooking vessel. Lockitch et al. (19) described a similar case of an infant who presented with seizures in association with a blood lead level of 155 µg/dl as a result of parents using a samovar. That case, like this one, illustrates that alternate sources including lead-glazed ceramics and cooking vessels must be considered in the evaluation of infants with lead poisoning (25).

Early signs of lead poisoning in children are highly variable and can be very difficult to discern in the young nonverbal child. Children can be completely asymptomatic across a wide range of blood lead levels.

Typically children have no overt signs of toxicity until blood lead levels exceed 25–30 µg/dl. Early signs of toxicity are nonspecific and may include sleeping difficulties, decreased appetite, and hyperactivity (26,27). Once blood lead levels exceed 50 µg/dl, manifestations become more obvious, e.g., marked irritability and anorexia. Seizures may occur at blood lead levels as low as 50–60 µg/dl (28). When lead levels exceed 80–100 µg/dl, frank encephalopathy with lethargy, seizures, cerebral edema, and death can occur (29,30).

Because children can remain asymptomatic for extended periods of time, the practice of routine lead screening has assisted in reducing the incidence of severe lead poisoning by identifying children as their exposure is just beginning and by preventing exposure in siblings and playmates. Interestingly, because lead screening does not typically begin until the child is at least 6 months old, this infant's lead poisoning might not have been discovered if the mother had not requested lead screening.

Severe lead poisoning is treated with hospitalization and chelation therapy (9). Chelation therapy has several potential advantages. First, it has been proven to reduce the mortality associated with lead poisoning. Second, it can rapidly reduce the overall lead burden by promoting lead elimination; with lead's profound biological persistence, minimal elimination occurs in the absence of chelation. Third, chelation can more rapidly ameliorate toxic effects of lead such as impaired vitamin D activation, diminished nerve conduction velocity, and hematologic toxicity (as manifested by elevated erythrocyte protoporphyrin) (31,32). Finally, there is evidence, which requires further validation, that chelation may minimize the extent of neurodevelopmental injury the child will sustain (33).

Until recently, the only chelators available for moderate to severe lead poisoning were NaCa<sub>2</sub>EDTA and 2,3-dimercapto-1-propanol (dimercaprol, BAL). Because these are parenterally administered agents, hospitalization is usually necessary. In 1991, DMSA became the first oral chelator approved for the treatment of moderate lead poisoning in children (34,35). This chelator has proven to have a favorable profile of safety and efficacy, offering the possibility of outpatient management (36,37). Data by Graziano et al. (34,35) suggest that DMSA has an efficacy comparable to EDTA and can serve as an outpatient alternative to EDTA chelation. However, in cases such as this, where the source of exposure is unclear, hospitalization may be necessary to prevent ongoing exposure. *d*-Penicillamine is an oral lead chelator that has been used since the 1970s for the treatment of lead poisoning (38). Like DMSA, it is also

very efficacious in reducing blood lead levels in children (39). However, because it is not approved by the Food and Drug Administration for this indication and has a significant side effect profile, there remains considerable reluctance to use this chelator.

The natural history of blood lead levels after chelation therapy, as demonstrated in this case, is one of frequent rebound in blood lead levels, representing continued diffusion of lead from bone and soft tissues back into blood. With the goal of chelation therapy being to lower and maintain the lead level below 10–15 µg/dl in this case, repeated courses were necessary. Childhood lead poisoning is therefore a chronic illness for which treatment may be needed for a year or more. Efficient, successful management requires a multidisciplinary approach that includes pediatricians, toxicologists, community advocates, and housing specialists.

The lead poisoning unexpectedly found in the mother presented several management difficulties. First, the finding suggested that the child was a victim of congenital lead poisoning. This was unlikely, given the history the mother provided of not drinking tea from her samovar until the child was born. A second concern was that the mother probably acquired a substantial lead burden during her childbearing years. This had implications for future children. We felt it advisable to counsel the mother against having another child for at least a year, assuming that in such a period of time her blood lead concentration would fall, thereby minimizing the extent of transplacental lead diffusion. Finally, the safety of continued breast-feeding became a concern. Elevations in the concentration of lead in breast milk may normally occur in lactating women either from the lead mobilization that accompanies the bone mobilization of pregnancy or from low-grade environmental exposure during pregnancy (40,41).

Studies of the diffusion of lead into breast milk have produced somewhat inconsistent results. Milk to plasma ratios of lead in milk range from 0.1 to 0.3 (42). Nahimira et al. (43) found a high linear correlation ( $r = 0.88$ ) between blood and breast milk lead levels when maternal blood lead was greater than 40 µg/dl (43), but others have not found such a correlation (44). In an examination of this mother and in a similar case, we found that with women who have blood lead levels <35 µg/dl there is minimal excretion of lead into breast milk (45). We were therefore able to counsel this mother that breast-feeding could continue.

Among the toxicities of lead, the effect with the greatest potential long-term impact is injury to the developing brain (46–48). It is the neurodevelopmental toxicity of lead



that led to its recognition as a hazard of great public health impact. Over the last 20 years, the lead levels at which these neurodevelopmental toxicities can occur has been lowered, as rigorous longitudinal studies have demonstrated such effects at low blood lead levels. Studies by Baghurst et al. (49,50), Bellinger et al. (51–54), Needleman et al. (55–59), and others have firmly established that lead neurotoxicity may occur in children who have blood lead levels as low as 10 µg/dl (2). The infant in this case was therefore in a high risk category for neurodevelopmental sequelae. It is notable that at an early age concerns were raised about his development. Data by Bellinger et al. (51–54) and others have suggested that cognitive performance among school-aged children who have high level lead exposure early in life is best predicted by the blood lead level at the age of 24 months. In the case under discussion, the child's residual lead burden plus ongoing background environmental exposures resulted in a lead level of greater than 10 µg/dl at the age of 22 months, placing the child at risk for long-term neurodevelopmental weaknesses (53).

This unfortunate case exemplifies the multifaceted nature of childhood lead poisoning: lead epidemiology, unusual lead sources, the kinetics of lead in young children, chelation therapy, neurodevelopmental consequences, and lead kinetics in lactating women. In 1991, the Centers for Disease Control and Prevention announced a 20-year goal for the elimination of childhood lead poisoning in the United States. While the incidence of childhood lead poisoning continues to fall due to the combination of environmental reduction and lead screening, the approximately 1 million lead-poisoned American children remaining (7) are a clear indication that the issues which arose in this case will continue to occur.

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