Childhood Blood Lead Levels and Associated Risk Factors in Vietnam

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INTRODUCTION

The consequences of lead exposure have been documented for centuries. Childhood lead poisoning, in particular, is one of the most carefully studied and documented environmental exposures worldwide. However, despite awareness that lead exposure can compromise health, and that lead poisoning is completely preventable, lead continues to contribute significantly to the global burden of disease.

There are many sources of lead in the environment and these sources differ markedly between developed and developing countries. In developed countries such as the United States (US), children most at risk for lead exposure tend to be of a lower socioeconomic status and are most often exposed through peeling paint or leaded pipe solder. In developing countries, the exposures are frequently associated with smelting, mining or recycling efforts. Lead is still often added to paints, pigments, toys, traditional medicines and cosmetics—exposures that do not remain confined to their country of origin. The greatest exposure concern for the general population, leaded gasoline, has been removed from the majority of countries worldwide and subsequent blood lead levels have declined steadily as this process has been accomplished.

In some nations, such as the US, India and Indonesia, to name a few, studies have shown a precipitous drop in childhood lead levels after leaded gasoline has been outlawed. For instance, at the time US federal legislation was enacted in the 1970's to eliminate the use of leaded gasoline, the median blood lead level (BLL) of US children ages 1-5 was 15 µg/dL (from 1976 to 1980). In 1988-1991, the median was 3.6 µg/dL, and by 1999, the median BLL had decreased to 1.9 µg/dL (American Academy of Pediatrics 2005). Leaded gasoline was phased out in Vietnam in 2001. Unfortunately, no surveillance blood lead levels are available to confirm that Vietnamese children are now at decreased risk of complications due to lead exposure. Even with the elimination of leaded fuel, elevated pediatric blood lead levels have been found in neighboring Southeast (SE) Asian countries due to other environmental lead exposures such as lead battery recycling and electronic waste (e-waste) (Gottsfeld and Pokhrel 2011). Some of these same exposures can be found throughout Vietnam. Therefore, it is important to evaluate the current prevalence of elevated blood lead levels among children in Vietnam (Vietnews 2011). A range of environmental exposure sources are of increasing interest as it becomes clear that there does not appear to be a safe level of lead exposure in children.

Children often suffer greater effects from lead exposure than adults do for a variety of reasons: their intake of lead per unit of body weight is higher; they may be exposed throughout pregnancy; they are more likely to engage in hand-to-mouth behaviors that increase their ingestion of dust and soil; they are more likely to spend time in a single environment; they have greater potential for nutritional deficiencies that can lead to increased absorption of lead; they have more years of future life and potentially longer to develop consequences of exposures; and they tend to lack control over their environment (ATSDR 2007). All of these factors, combined with the fact that their systems are still developing, make them more vulnerable to the deleterious effects of lead.

There is a great deal of variation between countries in their approach to pediatric lead evaluation. The US has a fairly comprehensive approach with specific screening criteria for children who are most likely at risk (CDC 2002). Vietnam does not appear to have any form of routine surveillance in place, even though there has been increasing awareness of at-risk children, particularly around lead recycling and craft villages. I could not find any information in English medical literature or in discussion with Vietnamese personnel such as physicians and environmental scientists regarding any form of lead assessment or prevention programs in the country. There does not appear to be any public health movement to remediate any of the current lead exposures.

The present research project was developed to help increase awareness and information about lead in Vietnam. It used a cross-sectional study to gain better understanding of current lead exposures, blood lead levels, and risk factors for lead exposure in Vietnamese children. It is hoped that this study will be instrumental in assessing whether children are currently at risk for lead-related diseases and may be useful in making public health recommendations and determining the need for additional surveillance in Vietnam.

SOURCES OF LEAD

Sources of lead have been well described within the US, but are more difficult to characterize internationally. In the US, the two main causes of non-occupational lead exposure historically have been airborne lead from gasoline combustion and lead paint. Paint, which is typically ingested from lead containing dust, is the primary source of exposure for children. Occupational sources come from lead smelting and refining, soldering, steel welding and cutting, battery manufacturing, construction and demolition, radiator repair, and painting, particularly if it involves sanding or scraping of old painted surfaces. Hobbies that may predispose a person to lead exposure include working with stained glass, shooting with lead ammunition (or working at a shooting range), use or creation of lead fishing weights and painting pottery and ceramics. Although the US banned leaded gasoline (with tetraethyl and tetramethyl lead anti-knock additives) in 1996, it is still used in some developing countries. Tetraethyl lead gasoline also remains available for use in off-road vehicles and airplanes.

Reports on lead exposures internationally suggest additional sources. Liu, et al, note that in SE China, lead may be found in industrial emissions, lead-contaminated paints (houses, toys and stationery), parents' take-home lead from work, coal combustion, food and traditional medications (2011). Plumbing may contribute to lead ingestion. Acidic water can enable lead found in pipes, leaded solder and brass faucets, to be dissolved into the drinking water (ATSDR 2007).

Exposures may come from cosmetics such as *surma* and *kajal* from Asia, kohl from the Middle East, or, as recently described, in *tiro*, an eye cosmetic from Nigeria (Nasidi, 2012). Greta powder and *azarcon*, Mexican folk remedies, miniblinds from homes older than 1997, use of ceramic pots or water jars, and other culture-specific products such as spices have been found to be sources of lead. A study in Massachusetts evaluated over 150 imported powders used in the Indian community as spices, cosmetics (*aritha*, *henna*, *kajal*), or for religious ceremonies (*abil*, *gulal*, *kumkum*, *sindoor*). It was determined that a number of these products had elevated lead concentrations, which was placing children at risk due to the young age at which the powders are used, the extremely high lead concentrations often found, the chronic nature of the exposures (up to several times per week) and the hand-to-mouth behaviors common in children, even when the various powders were not intended to be directly ingested (Lin et al, 2010). Spices such as *swanuri marili* and *kharchos suneli* from the Republic of Georgia were also found to be sources of significant lead exposure (Woolf and Woolf, 2005). The circumstances by which these substances become contaminated are not always obvious. For instance, exposures in the Middle East and Turkey from wheat flour have been seen due to the use of molten lead to fill fissures in the worn drive shafts of millstones (Woolf and Woolf, 2005). Lead has also been added to commercial products to increase the value when they are sold by weight.

Figure 1. Products Containing Lead

Dumex lollipops from Mexico   Nigerian *tiro* container   Cambodian amulet with lead beads

Dumex brand lollipops from Mexico were a contributory factor in several lead exposures in California, leading to a public health warning from the Food and Drug Administration and California Department of Health Services. Other candies, containing tamarind, have also been implicated (Courtney, 2002). In particular, Margarita-brand Tamarindo Pulpa (with and without chili), Licona-imported Tamarindo, Picarindo-brand jellied Tamarindo candy, and Jarrita Chonita-brand jellied *tejocote* candy with chili from Mexico are often packaged in stoneware or terra cotta jars that have lead-based glazing. The fruits in these candies are acidic, which can increase the lead leaching from the jars. In the past, chilies could also be contaminated by air drying or fuel-assisted drying in areas where leaded gasoline was used (Dorfman, 1998).

Jewelry and amulets have been implicated in elevated lead levels in children. Wearing amulets for protection is a fairly common practice in certain countries such as Cambodia and other SE Asian cultures. Anecdotal reports have even suggested that lead bullets have been melted down to make some of the beads for the amulets. Several cases of imported jewelry with high lead content being ingested by children were reported to have caused lead toxicity (Mann, et al, 2011).

Many sources note lead battery manufacture and recycling exposure as a growing concern in developing countries (Gottesfeld and Pokhrel 2011). Global lead battery production is estimated to be worth about US $36.2 billion in 2010 with an overall lead consumption of greater than 10 million tons in 2011 (Occupational Knowledge International, 2009). Most lead batteries that are currently being made contain 60-80% recycled lead. The combination of rising prices of mined lead coupled with the ever-present demand has been a driving force for recycling ($1.20 per pound mined versus $0.70 or less for recycled lead). Thus far, there is not a good substitute for lead batteries, and newer substitutes for lead batteries may contain other heavy metals with potential health consequences (e.g., nickel, cobalt, manganese or lithium). Even environmentally friendly efforts may have unintended consequences. For instance, a growing number of electric bike sales in China have increased the demand for suitable lead batteries. These batteries typically have to be replaced yearly and disposal can be problematic (OKI, 2009). Most hybrid cars also include a conventional 12 volt lead battery along with a lithium or nickel battery.

In some countries, poor controls on the lead industry have led to occupational and environmental pollution. For instance, populations living near both conventional and cottage lead smelters and battery plants were found to have lead levels significantly higher than those in unexposed groups in Jamaica and Albania (Tong, et al, 2000). Kenya, which has a projected 24% annual growth rate for lead battery production, has no national workplace standards and limited testing of the environment for potential pollution (OKI, 2009). In Mexico, where a large number of US batteries have been shipped for recycling, particularly since the US decreased the acceptable air quality standard for lead in 2008, emissions from plants have been found that were 20 times higher than for similarly sized plants in the US, and well over the US standards (Rosenthall, 2011). Lead recycling can be associated with soil contamination in industrial and semi-industrial areas and garbage dumps, elevated BLL in workers, water contamination, air contamination in, and around, the industrial smelters and informal lead smelting operations, and may also effect populations that are exposed by living near these sources and those who recover materials from garbage dumps.

Lead exposure may also be related to e-waste. The US is estimated to discard 3 million tons of e-waste annually, while China contributes another 2.3 million tons. Once these devices near their end-of-life, they are exported for recycling and reuse. The effects of e-waste relate to the use of a variety of heavy metals and other substances in electronic devices such as cathode ray tubes from televisions (2-5 pounds of lead apiece), cell phones, circuit boards and other computer parts. As part of the recycling process, open air burning and acid baths can expose workers to lead or other toxic substances and these materials can also leach into the environment, affecting people who live nearby (EPA 2012). E-waste is frequently dismantled and recycled by unregulated and/or untrained individuals, often near landfill sites. Informal workers rarely use appropriate personal protective equipment, and high levels of arsenic, cadmium and lead contaminated dust and soil have been well documented near informal recycling sites in countries such as China, India and the Philippines (Fujimori 2012).

Although leaded paint has been discouraged, numerous countries still report high levels of lead in paint samples. It has been estimated that 2.5 billion people live in countries where lead paint is still used (OKI 2009). Several studies from Asia have assessed the lead concentration in new enamel paints. While the US has set its paint standard for lead at 90 ppm maximum for new paint, when five brands of new enamel household paint from Taiwan were analyzed, the median lead concentration was 2574 ppm. Lead levels tended to vary based upon color and brand (Ewers, et al, 2011). Lead levels tend to be higher in enamel than in water based paints. Lin, et al, confirmed this finding after testing numerous samples of new and existing paint in China. They similarly concluded that lead paint remains a threat to children in China despite regulations limiting lead content (Lin, 2009). Although it has been seen in many Latin American countries that leaded paint is likely not a significant source of exposure, lead-glazed ceramics can be (Tong, et al, 2000). Lead in paint is an extremely unfortunate source of exposure considering that there are many viable substitutes available such as titanium or zinc dioxide, which could provide the same advantages to the paint as are gained from lead use.

It is important to hunt down the sources of lead since the extent of its effects is now more fully recognized. Lead can potentially affect almost every organ, but the main body structures at risk for the chronic consequences of lead exposure are the central and peripheral nervous systems. Studies have shown a dose-response correlation between BLLs and IQ reduction. Blood lead levels as low as 1-3 µg/dL can be associated with subclinical neurobehavioral toxicities. It has been estimated that there is a loss of approximately a half of an IQ point for each 1 µg/dL increase in the BLL during the preschool years for children with levels of at least 10-20 µg/dL (WHO, 2010).

Lead exerts some of its toxic effects due to its ability to substitute for other cations such as calcium or zinc. As one example, lead can substitute for zinc and inhibit aminolevulinic acid dehydratase, one of the important enzymes in the biosynthesis of heme in red blood cells. This can contribute to a buildup of aminolevulinic acid. Aminolevulinic acid resembles γ-aminobutyric acid and can stimulate γ-aminobutyric acid receptors in the nervous system. According to Kelada, et al, this is thought to be one of the primary mechanisms of lead-induced neurotoxicity (2001). Lead can also form highly stable complexes with phosphate and replace calcium in the bony matrix. This process leads to lead deposition during the normal bone mineralization process. This also provides the mechanism for lead's very long half-life within the body as lead is slowly released and resorbed (ATSDR, 2007).

Since very little is known about the prevalence of elevated BLLs in Vietnam, the purpose of this study was to perform an initial screening process to determine if Vietnamese children overall may have elevated BLLs, or if high BLLs tend to be concentrated in areas with overt exposures such as lead battery recycling or other cottage industries. The general goal was to describe current BLLs and risk factors for lead exposure by surveying an urban pediatric population. Specifically, the project intended to estimate the prevalence of elevated BLLs and to identify the environmental risk factors for children whose levels are high.

METHODS

The hypothesis for this research project was that children in Vietnam are exposed to sufficient environmental lead that their BLLs are elevated above the current World Health Organization and (previous) Centers for Disease Control and Prevention (CDC) recommendations of <10 µg/dL. Although this level was formerly used to trigger public health activities, within the past year, the CDC in the US officially revised this level with ongoing recognition that BLLs lower than 10 µg/dL are associated with IQ deficits, attention-related behaviors and poor academic achievement. They have noted the evidence suggests that there is no safe or threshold BLL for toxicity in children. The CDC now recommends that a childhood BLL reference value based on the 97^{th} percentile of the US population for children ages 1-5 (5 µg/dL) be used to identify children and environments associated with lead exposure hazards (CDC Response to Advisory Committee 2012). Given that the effects of lead exposure appear to be irreversible and there is not a safe level of exposure, primary prevention is paramount, with the goal to reduce or eliminate lead sources before children come into contact with them.

This study evaluated a cross-sectional sample of children in Southeastern Vietnam, to measure blood BLLs and assess possible lead exposures through the completion of a questionnaire by the parents. All participants were recruited from those children hospitalized in the Respiratory Ward of Children's Hospital #2 in Ho Chi Minh City, Vietnam during April and May 2012. This study was a collaboration between the University of Washington and personnel at Children's Hospital #2, including attending and resident physicians. The study was approved by the Ethics Committee at Children's Hospital #2 and by the Institution Review Board (IRB) Human Subjects Division at the University of Washington.

Study Population and Sample Selection

Children's Hospital #2 is the second largest pediatric hospital in Ho Chi Minh City. It has a large population service area, primarily serving Ho Chi Minh City (the second largest city in Vietnam, with 7.2

million inhabitants) and the surrounding provinces in Southeastern Vietnam (additional combined population, 8.6 million) (General Statistics Office of Vietnam, 2009).

Children hospitalized in the Respiratory Ward, aged 0-15 years, whose parents or guardians provided informed and written consent, were eligible for the study. In order to minimize additional procedures on hospitalized children, the parents were only approached for enrollment in the study if the child would require further blood draws during their hospital stay. The Vietnamese resident physicians involved in the research project asked other doctors or nurses whether any patients who remained in the hospital overnight would be requiring additional lab testing. If a patient needed a test, then the parents and child were approached regarding participation in the study. The study was then described, along with its voluntary nature. Interested families completed written adult consent and child assent forms. The children and their guardians were not provided any remuneration for their participation. The child's blood sample was tested for lead using the LeadCare II Blood Lead Test System (Bionostics, Inc.). The questionnaire was completed either the same day as the consent form was completed or the next day. All of the parents or guardians were provided with educational materials regarding lead exposure. If the participant had a hemoglobin (HgB) and/or hematocrit (Hct) drawn during their hospitalization, those lab results were recorded. Heights and weights of the children were also obtained.

A total of 311 children participated in the study. Very few (less than approximately 10%) parents or children chose not to participate, when they were approached about possible participation.

Questionnaire

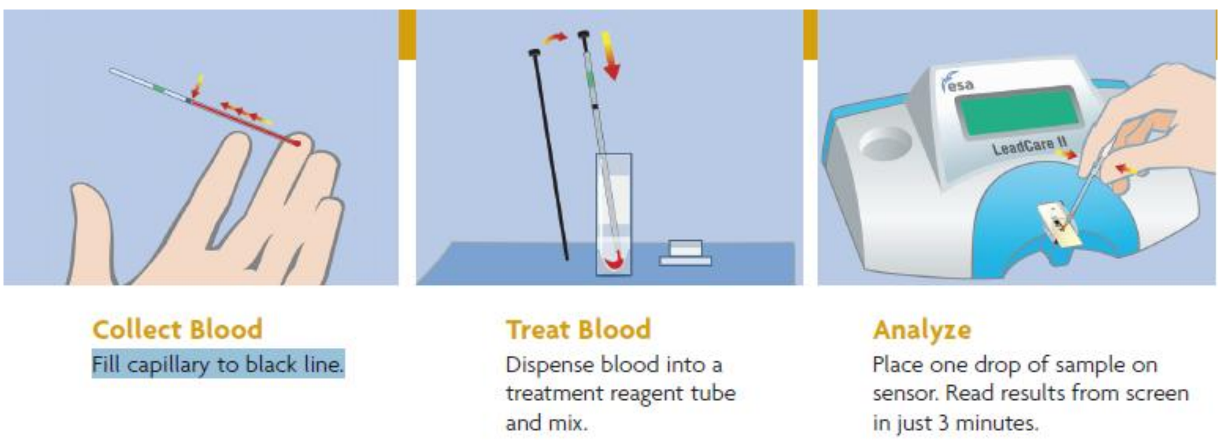
The questionnaire was designed by the study researchers based upon several sources: sample questionnaires used by other researchers, review of the literature, consultation with other researchers and interviews with the Vietnamese physicians involved with the study. The questionnaire was written in English and translated into Vietnamese. It was then back-translated in order to ensure accuracy and understanding. A number of the questions had been previously utilized in a similar study in Dong Mai village. These previously tested questions were initially written in Vietnamese by Vietnamese researchers. The questionnaires were administered by the Vietnamese resident physicians. Demographic information about the child, including age, sex, schooling, and symptoms was obtained. The questionnaire also asked about parental occupations and educational levels, potential lead recycling in the household or neighborhood, use of lead battery casings in or outside of the home, and use of lead cookware. Information was also collected about household sources of water, hobbies or craft work entailing potential lead exposure, and whether any individuals in the household had ever received a blood lead test.

Blood Sampling and Analysis Technique

If the child was enrolled into the study, then, prior to drawing blood for the child's daily labs, his or her skin was wiped for approximately 30 seconds with a LeadTech™ (MEDTOX Scientific) wipe to remove any possible lead surface contamination. The skin was next disinfected with the usual methods used by the nursing staff (alcohol swab or cotton ball soaked with alcohol) prior to a fingerstick poke or venous blood draw, whichever their labs required. Subsequently, a small amount of whole blood (50 µL) was placed into a heparinized capillary tube (provided by the LeadCare II test kit). Once the heparinized tube was filled to the demarcated line with the blood, the sample was dispensed into the LeadCare II treatment reagent vial using the provided plunger. The treatment reagent vial contained 250 µL of a dilute hydrochloric acid solution in water. The reagent tube was capped and thoroughly mixed by inverting it repetitively. Once the sample was placed into the reagent tube, it was immediately refrigerated until analysis.

Initially the resident physicians who were involved in the study were taught how to properly operate the LeadCare II analyzer. The residents subsequently informed the nurses how to utilize the capillary tubes and testing reagents. The trained pediatric nurses were quite efficient at obtaining whole blood samples by capillary stick as it was the normal procedure for acquiring blood from infants and young children. The blood samples were obtained with the usual hospital blood draws, which occurred as early as 5:30 am each morning. The LeadCare II analysis was completed by approximately 6:30 pm on the same day that the blood was drawn. The product literature states that testing should occur within 48 hours if the sample had been mixed with reagent and stored at room temperature. The sample and reagent could be stored for up to seven days if they were refrigerated. No samples were stored in the refrigerator longer than two days. When the samples were removed from the refrigerator, they were allowed to equilibrate with ambient temperature for a minimum of 30 minutes prior to testing. Blood samples were analyzed using the LeadCare II portable analyzer.

Figure 2. LeadCare II Technique



Source: LeadCare II User’s Guide, ESA Biosciences, 2005

A sensor was placed in the analyzer and a drop of the blood and reagent mixture was applied to the sensor. Once a sufficient amount had been placed on the sensor, the analyzer beeped and the testing began. The testing time was three minutes once the sample had been placed into the analyzer.

Prior to each day’s testing, the analyzer was calibrated with the supplied calibration button. Each test kit was coded with a lot number. This lot number that accompanied the test kit and was associated with the specific reagents and calibration button was confirmed prior to any testing. For quality control, with each new test lot kit (48 samples), the analyzer was tested using the supplied control samples. The quality controls provided both high (25 +/- 4 µg/dL) and low ranges (9 +/- 3 µg/dL). The levels were found to be within the acceptable range with each lot.

Table 1. Quality Control Results for each Test Kit Lot

Lot #	Low control 9 +/- 3 µg/dL	High control 25 +/- 4 µg/dL
1	Within range but results not available	Within range but results not available
2	10.1	27.2
3	8.6	24.9
4	10.1	26.1
5	11.8	23.3
6	10.1	27.0
7	9.8	23.9

The LeadCare II analyzer is expected to work well at 54˚-97˚F (12˚-36˚C) and at 12-80% relative humidity. Due to concerns about instability of the test kit and reagents in the extremely warm and humid environment of Ho Chi Minh at the time, the LeadCare II analyzer was stored in the Children's Hospital #2 Neonatal Intensive Care Unit, which was an air conditioned area kept at approximately 21˚C, with humidity under the recommended 80%. The samples were analyzed under these conditions.

Reporting

The LeadCare II reports BLL to one decimal place with a reportable range between 3.3 and 65.0 µg/dL. If a result is less than 3.3 µg/dL, the analyzer reports it as "low". If the result is greater than 65.0 µg/dL, the result is displayed as "high". Oral and written results of the blood lead testing were provided to the family on the day after the testing occurred or via telephone if the child had left the hospital. If a child's level was found to be elevated, the family was interviewed regarding possible sources of lead exposure and recommendations were provided as appropriate. All of the families were given a pictorial handout that provided education regarding lead avoidance and ways to decrease lead exposure.

Additional testing was recommended for any children with levels greater than 10 µg/dL. Follow-up for other BLLs was performed according to the protocol listed in Table 2. Confirmatory venipuncture testing was conducted for any children with levels above 35 µg/dL, by the Can Tho branch of the Center of Analytic Services and Experimentation of HCMC (http://www.case.vn/ed-US/38/details.case). The cost of the confirmatory venipuncture testing was covered by the study. Three children required confirmatory testing.

Table 2. Protocol for Venipuncture and Follow-Up Testing

Level	**Actions**	
0-10 µg/dL	No additional testing necessary	
≥10-20 µg/dL	Repeat test in 1-3 months	Venous or capillary
>20-35 µg/dL	Repeat test immediately with capillary testing and thorough skin cleaning	Follow up with a venipuncture test in 1 week to 1 month
>35-44 µg/dL	Confirm within 48 hours	Venipuncture
>44 µg/dL	Confirm immediately, clinical assessment, discuss any relevant treatment options	Venipuncture

This protocol does vary from that recommended by the CDC, which is noted below in Table 3.

Table 3. CDC Protocol for Monitoring and Actions based on Blood Lead Level

Blood Lead Level (µg/dL)				
10-14	**15-19**	**20-44**	**45-69**	**>70**
Lead education -Dietary -Environmental Follow-up blood lead monitoring	Lead education -Dietary -Environmental Follow-up blood lead monitoring Proceed according to actions for 20-44 µg/dL if: -A follow-up BLL is in this range at least 3 months after initial venous test **or** -BLLs increase	Lead education -Dietary -Environmental Follow-up blood lead monitoring Complete history and physical exam Lab work: -Hemoglobin or hematocrit -Iron status Environmental investigation Lead hazard reduction	Lead education -Dietary -Environmental Follow-up blood lead monitoring Complete history and physical exam Lab work: -Hemoglobin or hematocrit -Iron status -Erythropoietic protoporphyria (EP) or zinc protoporphyria (ZPP) Environmental investigation Lead hazard reduction Chelation therapy	Hospitalize and commence chelation therapy Proceed according to actions for 45-69 µg/dL

Source: CDC, Managing Elevated Blood Lead Levels Among Young Children, 2002.

The study protocol was based on the CDC recommendations, but did deviate in several ways. The CDC encourages a confirmatory venipuncture sample after a LeadCare II test for all BLL ≥10 µg/dL. In this study, the LeadCare II was used for follow up testing unless the BLL was >35 µg/dL. The 35 µg/dL value was chosen out of concern for potential lack of precision in the LeadCare II values at higher BLL and the researchers' preference to avoid misclassifying any children with markedly elevated BLL. Additional blood tests as recommended by the CDC were difficult to obtain, outside of the HgB and Hct. Environmental investigation was not completed although environmental influences were thoroughly discussed with the families of children with elevated BLL. These deviations from the CDC protocol were primarily related to a number of practical issues:

1) Uncertainty regarding the ability of children, particularly those from outside of Ho Chi Minh to return to the hospital for follow-up testing, versus having venous BLL drawn by local health centers and appropriately shipped to qualified laboratories.

2) Balancing the availability of the LeadCare II testing supplies and the resources necessary (personnel, money) for venous blood testing and for additional lab tests such as the ZPP, EP or iron studies.

3) Lack of availability of resources (such as trained personnel) for environmental investigation.

4) Recognition that the LeadCare II, although quite reliable, can be less precise at higher lead levels, therefore the threshold for obtaining immediate confirmatory venipuncture blood tests was set at 35 µg/dL.

5) Uncertainties regarding the ability to locate children after their departure from the hospital.

Fortunately, it was possible to contact parents of all participating children and provide results of the BLL. However, not all (6 out of 22) of the children who required follow-up testing for BLL ≥10µg/dL were able to return to the hospital for completion of their evaluations. Only three out of the nine children with BLL > 20 µg/dL did not get follow up labs.

DATA ANALYSIS

The questionnaire data was entered into a Microsoft Excel spreadsheet by the primary investigator. Approximately 10% of the data was reconfirmed to ensure reasonable accuracy. This data was analyzed using SPSS (Version 19). Descriptive statistics were used to summarize the demographic characteristics. BLLs were taken as dependent variables and the 30 investigated items from the questionnaire as independent variables. Since there were a large number of very young children enrolled in the study, age was recorded in months, not years. As BLLs were not normally distributed, and were truncated at the lower end of the distribution, the median and interquartile intervals (25th and 75th percentiles) were used to describe distribution, and nonparametric testing was used to compare BLLs between groups. However, to facilitate comparison with other studies, mean values are also presented. Between-group comparisons of numeric variables with normal distributions (such as HgB and Hct) used independent sample t tests. Bivariate logistic regression was used to examine the association between individual independent variable and dichotomized BLL (< 5 µg/dL versus > 5 µg/dL and also < 10 µg/dL versus ≥ 10 µg/dL. Some of the variables could not be evaluated due to limited numbers of individuals with BLLs ≥ 10 µg/dL.) Numeric variables that did have a normal distribution such as age, HgB, and Hct were analyzed using independent sample t tests. Although age was recorded in months, it was also evaluated as a categorical variable based on distinct years, and on larger groupings that included 0-1 years, 1-2 years, 2-3 years and greater than 3 years old.

Variables that were found by bivariate analysis to be associated with elevated BLLs were further considered by sequential entry into multivariate logistic regression models. This analysis was performed to fit a model of predictor variables that contributed to the BLL categories of ≥10 µg/dL versus <10 µg/dL and ≥ 5 µg/dL versus < 5 µg/dL. Variable entry ultimately included age (categorized), whether the child attended school outside the home water source, and whether the family participated in metal recycling activities. Because of interactions between age and school attendance, these two variables were combined into a new categorical variable.

RESULTS

Subject Characteristics

Table 4 displays characteristics of the children enrolled in the study, distinguishing between children who reside in Ho Chi Minh (HCM) city and children from all other provinces. Most of the children came from HCM (n=145, 47%), followed by Binh Duong (n=59, 19%), Dong Nai (n=39, 13%), Binh Phuoc (n=21, 7%), and Ba Ria-Vung Tau (n=16, 5%) provinces. The other 31 children (10%) came from regions outside Southeast Vietnam, including the Central Highlands (n=15), Mekong Delta (n=6), South Central Coast (n=2) and further north (n=2; see Figure 4). Overall, there were few substantial demographic differences between the children from Ho Chi Minh versus the children who live elsewhere in Vietnam, which might be expected, considering that the majority of the children who were from provinces that were not Ho Chi Minh, were from the regions closely surrounding it. Notable differences included the fact that there were more male (61%) than female (39%) children in the overall sample. Water sources varied between HCM and the other provinces. Piped water was more commonly used in HCM (n=65, 45%) than elsewhere (n=37, 22%), whereas well water use was more frequently in the other provinces (n=78, 47%) than in HCM (n=26, 18%). Another finding was the difference in the number of children who lived near a busy intersection, which was only 19% of the HCM children (n=27) but 35% of the children who lived outside of HCM (n=58).

Table 4. Characteristics of Participating Children and their Families, Comparing Children from Ho Chi Minh City and Other Provinces*

	HCM	Other Provinces	Total
Total	**144**	**165**	**309****
Male	**92 (64%)**	**98 (59%)**	**190 (61%)**
Female	**52 (36%)**	**67 (41%)**	**119 (39%)**
Age (months, mean)	**19.3 (22.0)**	**18.0 (19.0)**	**18.7 (20.4)**
Height (cm, mean)	**76.9 (17.1)**	**75.3 (14.6)**	**76.0 (15.8)**
Weight (kg, mean)	**10.2 (5.1)**	**9.8 (6.1)**	**10.0 (5.6)**
Hemoglobin (g/dL, mean)	**11.7 (1.5)**	**11.7 (2.6)**	**11.7 (5.6)**
Hematocrit (%, mean)	**36.1 (3.7)**	**35.6 (3.6)**	**35.9 (2.2)**
Potential Lead Exposures			
Household member recycles	**3 (2%)**	**2 (1%)**	**3 (1%)**
Child participates in recycling	**0**	**1 (<1%)**	**1 (<1%)**
Lead recycling in the house (in the past)	**0**	**2 (1%)**	**2 (<1%)**
Lead recycling in the home (currently)	**0**	**2 (1%)**	**2 (<1%)**
Using battery casings in the home for walls, furniture or other purposes	**0**	**1 (<1%)**	**1 (<1%)**
Using battery casings outside the home for driveway, fences or other purposes	**0**	**1 (<1%)**	**1 (<1%)**
Neighborhood lead recycling	**2 (1%)**	**2 (1%)**	**4 (1%)**
Neighborhood burning of lead recycling waste	**1 (<1%)**	**1 (<1%)**	**2 (<1%)**
Metal recycling or melting	**2 (1%)**	**4 (2%)**	**6 (2%)**

Table 4. Characteristics of Participating Children and their Families (continued)

Occupational Exposures (Parents)			
Parents do automotive work	**4 (3%)**	**4 (2%)**	**8 (3%)**
Parents do ceramics/glazing	**1 (<1%)**	**5 (3%)**	**6 (2%)**
Parents do welding	**19 (13%)**	**31 (19%)**	**50 (16%)**
Environmental Exposures			
Source of Drinking Water			
Piped	**65 (45%)**	**37 (22%)**	**102 (33%)**
Bottled	**52 (36%)**	**43 (26%)**	**95 (31%)**
Rainwater	**2 (1%)**	**7 (4%)**	**9 (3%)**
Well Water	**26 (18%)**	**78 (47%)**	**104 (34%)**
Peeling paint	**48 (34%)**	**47 (29%)**	**95 (31%)**
Live near a busy intersection	**27 (19%)**	**58 (35%)**	**85 (27%)**
Use traditional medicines	**117 (81%)**	**108 (65%)**	**225 (73%)**
Age of home (mean, years)	**10.8 (10.3)**	**8.67 (6.7)**	**9.7 (8.6)**
Home is painted-outside	**115 (80%)**	**125 (76%)**	**240 (78%)**
Home is painted-inside	**124 (86%)**	**131 (79%)**	**255 (83%)**
Years since home was most recently painted (mean)	**3.65 (4.3)**	**3.9 (4.0)**	**3.8 (4.1)**

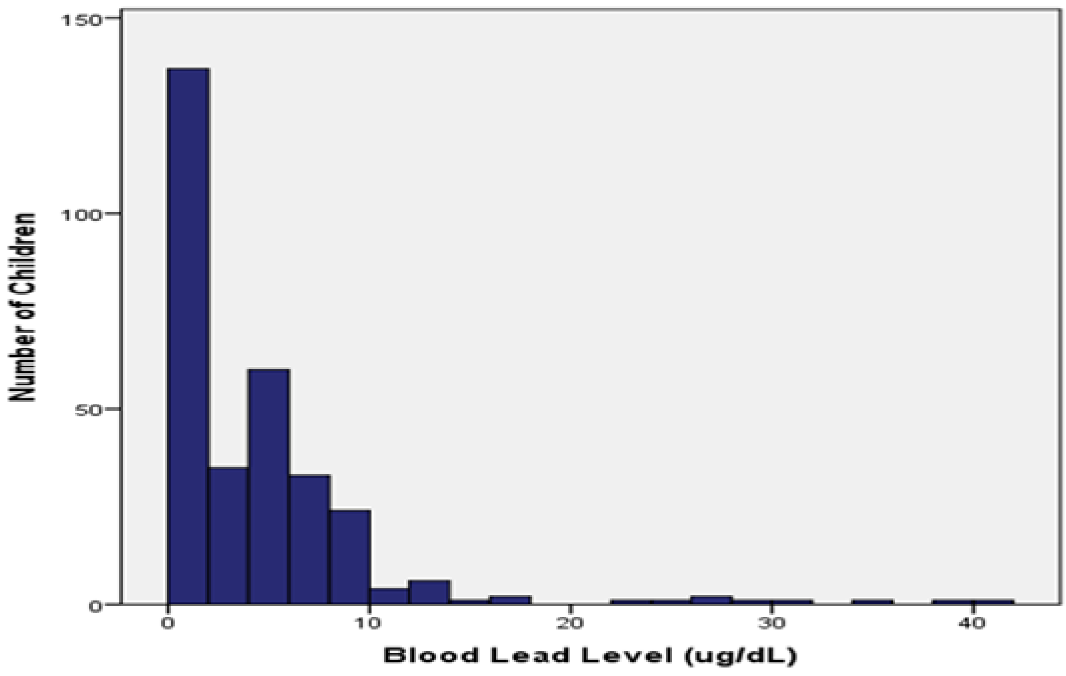
*Table displays counts (and percent of column total) or means (and standard deviations).

**Numerical discrepancies are due to missing information.

Overall distribution of BLL

The distribution of BLLs is shown in Figure 3. Of the 311 children tested, 289 children (92.9%) had BLLs <10 µg/dL. Twenty-two children had BLLs ≥ 10 µg/dL (7.1%) and only nine children had BLLs >20 µg/dL. Three children had levels >35 µg/dL.

Figure 3. Distribution of Blood Lead Levels (n=311)



Geographic distribution of BLL

There was a nearly two-fold difference across the range of median BLL values observed for children from each of the provinces represented in the study sample, and these differences were statistically significant (Table 5;p=0.009, Kruskal-Wallis). There was no substantial difference when BLL values were aggregated according to conventional Vietnamese regional groupings (see Figure 4 and Table 6; p=0.87).

Table 5. Mean and Median Blood Lead Levels by Province

Province	Number and % of total (n=311)	Mean BLL (µg/dL)	Median BLL µg/dL) and IQI
Binh Duong	59 (19%)	6.0	5.4 (1.65-7.90)
Binh Phuoc	21 (6.8%)	4.2	1.7 (1.65-4.35)
Dong Nai	39 (12.5%)	6.7	4.0 (1.65-7.70)
Dak Nong	5 (1.6%)	4.9	3.8 (1.65-8.70)
HCM	145 (46.6%)	4.4	1.7 (1.65-5.35)
Lam Dong	8 (2.6%)	3.3	3.6 (1.65-4.38)
Ba Ria-Vung Tau	16 (5.1%)	3.4	4.6 (1.65-4.08)
Other*	18 (5.8%)	5.2	1.7 (1.65-7.33)
Total	311		

*Other includes: Binh Thuan (3), Dak Nong (4), Kien Giang (2), Long An (2), Phu Yen (2), Ben Tre (1), Dak Lak (1), Kon Tum (1), Lang Son (1), Quang Nam (1), Thanh Hoa (1), Tien Giang (1), Vinh Long (1)

Figure 4. Vietnamese Regions

Table 6. Median Blood Lead Level by Region

Region	Number/% of total	Median BLL/IQR
Southeast	284 (91.3%)	3.60 (1.65-6.08)
Mekong Delta	6 (1.9%)	4.53 (1.65-8.45)
Central Highlands	15 (4.8%)	3.70 (1.65-4.60)
South Central Coast	2 (0.6%)	5.35
North Central Coast	1 (0.3%)	3.50
Northeast	1 (0.3%)	6.00

Location of residence was also obtained at the district level. There were only a few districts with more than 1 child who had an elevated BLL ≥ 10 µg/dL. These districts included: Q1 (n=2), Q12 (n=3), Di An (n=4), and Binh Hoa (n=3). Q1 and Q12 are districts in Ho Chi Minh City. Both Di An and Bien Hoa adjoin Ho Chi Minh and are in close proximity with one other.

The median BLLs (Table 7) also did not differ significantly when comparing children from HCM city with children from all other locations (HCM 1.65 µg/dL, IQI 1.65-5.35; non-HCM 3.8 µg/dL, IQI 1.65-6.70;p=0.059; note, BLL 1.65 is the value assigned for test results that were below the analytic level of detection with the LeadCare II system.

Table 7. Mean and Median BLL for Ho Chi Minh and Other Provinces

	Total (µg/dL)	**Ho Chi Minh** (µg/dL)	**Other Provinces** (µg/dL)
Blood Lead Level			
Male (mean, SD)	5.2 (5.9)	4.8 (6.0)	5.5 (5.9)
Female (mean, SD)	4.6 (4.8)	3.7 (3.0)	5.4 (5.8)
Median BLL (IQI)	3.60 (1.65-6.00)	1.65 (1.65-5.35)	3.80 (1.65-6.70)

Child and Family Characteristics and Distribution of Blood Lead Levels

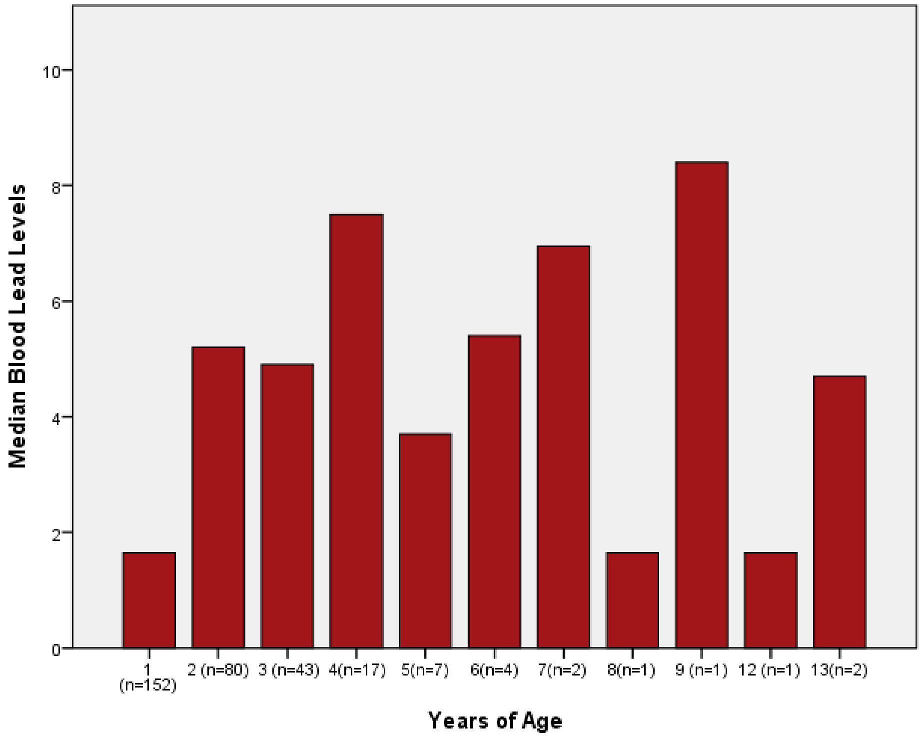
In general, BLL were significantly lower in the youngest children (0-12 months old) compared to all older children (Table 8). The relationship between age and BLL was less monotonic when viewed relative to individual years of age (Figure 5), instead of age groups, although this may be at least partially attributable to the small numbers of older children. BLL was also significantly higher among children who attended school outside the home (Table 8). There were no significant differences in BLL relative to gender or any of the other environmental or occupational variables.

Table 8. Distribution of Blood Lead Levels Relative to Major Child and Family Characteristics (n=311)

	Mean (μg/dL)	Median (μg/dL) and IQI	Significance*
Gender			
Male	5.19	3.70 (1.65-6.52)	
Female	4.63	3.60 (1.65-5.80)	0.773
Age (months)			<0.001
0-12	3.75	1.65 (1.65-3.60)	
13-24	6.71	5.20 (3.63-7.60)	
25-36	5.39	4.90 (1.65-7.40)	
37+	5.70	5.50 (3.70-7.90)	
Location			0.014
Ho Chi Minh	4.41	1.65 (1.65-5.35)	
All other locations	5.43	3.80 (1.65-6.70)	
Water source			0.116
Piped	4.54	1.65 (1.65-5.20)	
Bottled	4.88	4.00 (1.65-6.20)	
Rainwater	5.62	5.40 (3.28-7.95)	
Well water	5.39	3.65 (1.65-6.68)	
Use traditional medicines	5.12	3.80 (1.65-6.20)	0.431
Have peeling paint in the home	4.84	3.50 (1.65-5.70)	0.607
Attends school outside the home	6.54	5.70 (4.10-8.15)	<0.001
Parents do metal recycling	10.64	5.45 (4.39-14.55)	0.109
Live near a busy intersection	5.14	3.60 (1.65-6.35)	0.430

* Significance (p value) based on Mann Whitney U or Kruskal Wallis tests.

Figure 5. Median Blood Lead Level by Years of Age



Although the differences between years does appear to be quite striking for certain years of age on the graph, many of the older groups are represented by a very small number of children. These differences are still apparent when considering the mean and median BLL. Overall, there are statistical differences between these large age groups ($p<0.001$), which are listed in Table 9.

Table 9. Mean and Median Blood Lead Level by Age Groups

Age	Number	Mean BLL	Median BLL/IQI
0-1 years	152	3.75	1.65 (1.65-3.60)
1-2 years	80	6.71	5.20 (3.63-7.60)
2-3 years	43	5.39	4.90 (1.65-7.40)
Over 3 years	35	5.70	5.50 (3.70-7.90)

Risk Factors for Relatively High Blood Lead Levels

Bivariate Analysis

In general, analyses of BLL dichotomized at 5 µg/dL showed no substantial differences compared to analyses of BLL dichotomized at 10 µg/dL, and measures of risk for the latter were much less robust because of the smaller number of children who had BLL ≥ 10 µg/dL and the relatively low prevalence of some risk factors of concern. Therefore, results of risk factor assessment are presented only for dichotomization at 5 µg/dL (Table 10). A relatively higher BLL (> 5 µg/dL) was significantly more likely to occur if the child attended school outside of the home, used rain or bottled water, or had parents who were engaged in metal recycling or melting. Because of evident interactions between child age and school attendance, we created a combined age-school variable for use in subsequent multivariate analyses. A number of variables, such as use of traditional medicines, engaging in activities considered likely to be high risk such as having a household member or child participate in lead recycling, using recycled battery casings in or outside of the home for furniture, fences or other purposes, having parents who were poorly educated, or having symptoms suggestive of lead exposure, did not show a significant association.

There were 16 positive responses to the "other" questions about activities that potentially involved lead use or exposure (with 13 of these children having BLL >5 µg/dL) and there were 12 children with a "yes" answer to one or more activity. It is unknown whether any of these positive responses represent duplicates from the same household. This paucity of positive responses does become relevant when engaged in a regression analysis, especially when attempting to find associations with higher lead levels (> 10 µg/dL), which were also represented by a very small number of children (n=22).

Table 10. Risk of Relatively High Blood Lead Level (> 5µg/dL), Relative to Child and Family Characteristics, including Activities with Potential Lead Exposure

Variable	Number and % of Children (n=311)	Odds Ratio and 95% Confidence Interval	Significance
Gender			
Male	67 (22%)	1	
Female	42 (14%)	.99 (0.6-1.6)	0.99
Age (months)			
0-12	152 (49%)	1	
13-24	80 (26%)	0.1 (0.1-0.2)	<0.001
25-36	43 (14%)	0.6 (0.3-1.4)	0.25
37+	35 (11%)	0.6 (0.2-1.4)	0.56
School Outside the Home	48 (15%)	4.7 (2.7-8.1)	<0.001
Busy Intersection near Home	27 (9%)	0.8 (0.5-1.4)	0.49
Traditional Medicine	46 (15%)	1.1 (0.7-1.7)	0.68
Welding	21 (7%)	1.4 (0.8-2.7)	0.25
Metal Recycling or Melting	5 (2%)	9.8 (0.1-85)	0.04
Water Source			
Piped	27 (9%)	1	
Bottled	38 (12%)	1.9 (1.0-3.4)	0.05
Rainwater	6 (2%)	5.6 (1.3-23.8)	0.02
Well	38 (12%)	1.6 (0.9-2.9)	0.12
One or more other listed activities*	13 (4%)	1.6 (0.5-5.0)	0.40

*Odds ratio and 95% confidence interval (95% CI) determined by bivariate logistic regression. A variable category with odds ratio=1 is the reference category for that variable.

**Other activities: household member recycles (n=5), child participates in recycling (n=1), lead recycling occurs in the home, either currently (n=2) or in the past (n=2), battery casings are used in or around the home (n=2), neighborhood lead recycling is present (n=4), or neighborhood burning of lead recycling waste is occurring (n=2).

Multivariate Analysis

Three variables were significantly associated with relatively higher BLLs (> 5 µg/dL) in the multivariate logistic regression model: province, water source and a combined variable that included age and whether the child attended school outside the home. The other variables either made no significant additional contribution to the model, or there were too few children who had the risk factor and BLL > 5 µg/dL.

Table 11. Risk of Relatively High Blood Lead Level (>5 µg/dL); Multivariate Analysis

Variable	Number with BLL >5µg/dL	Odds Ratio	95% Confidence Interval	Significance
Province				0.03
Ho Chi Minh	41	1		
Binh Duong	33	2.9	1.4-6.1	0.01
Binh Phuoc	4	0.7	0.2-2.6	0.56
Dong Nai	18	2.2	0.9-5.3	0.07
Dak Nong	1	0.4	0.0-4.4	0.47
Lam Dong	1	0.2	0.0-2.6	0.25
Ba Ria	3	0.6	0.1-2.6	0.49
Other	8	1.5	0.4-4.7	0.53
Water Source				0.11
Piped	27	1		
Bottled	38	1.7	0.8-3.4	0.14
Rainwater	6	7.2	1.3-40.8	0.03
Well Water	38	1.6	0.8-3.3	0.22

Table 11. Risk of Relatively High BLL, continued

Age and School Attendance				<0.001
0-12 months	24	1		
13-24 months	42	6.0	3.1-11.8	<0.001
25-36 months				
Attends school	17	7.5	2.8-19.9	<0.001
Not in school	2	0.9	0.2-5.0	0.90
37 months and up				
Attends school	17	12.6	4.6-34.3	<0.001
Not in school	7	16.8	3.8-74.7	<0.001
Other High Risk Factors	6	2.5	0.7-9.1	0.17

* A variable category with odds ratio = 1 is the reference category for that variable.

Two provinces in particular, Binh Duong and Dong Nai, appeared to be associated with elevated BLLs. The "Other High Risk Factors" variable did not show a significant association with elevated BLLs in the multivariate analysis. When "Metal recycling or melting" was added to this variable, there was not a notable change in the odds ratio. The age and school variable did provide evidence that as age increases, BLL increases. In this project, except for the 25-36 month old children who did not attend school outside the home, the odds ratio for elevated BLL increased with age. Why the 25-36 month old category did not show the same trend is unclear, but it is represented by a very small number of children.

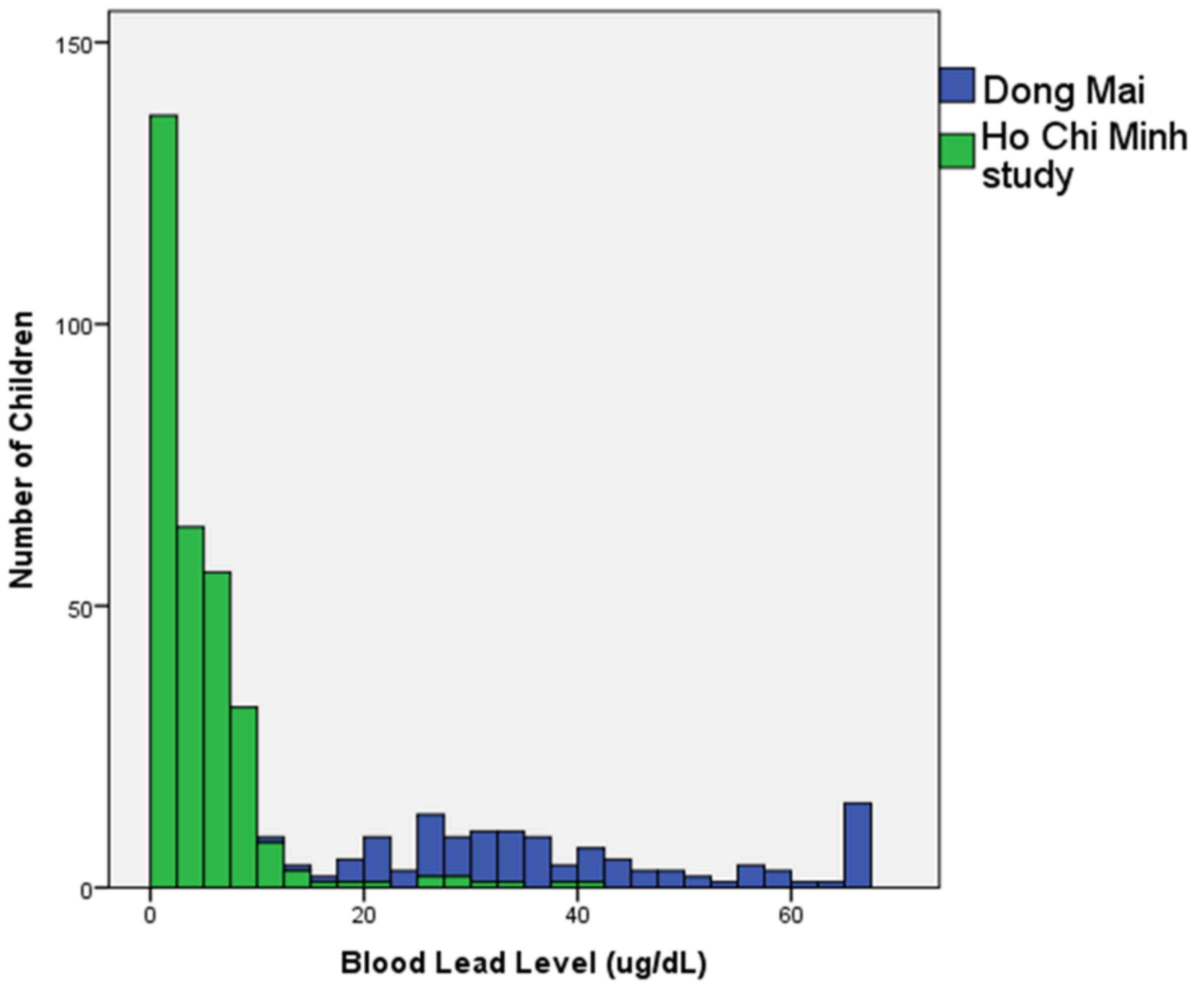
DISCUSSION

Findings from this study support the idea that, although leaded gasoline has been phased out, there are still sources of lead exposure in the environment in Vietnam more than a decade later. It is now known that elevated BLLs are not ubiquitous throughout Vietnam since the prevalence of BLLs> 10 µg/dL from this study was 7.1%. It is also known that the mean and median BLL from this study were much lower than that seen in the Dong Mai lead recycling village in northern Vietnam (Wallace, 2012). But 7% is clearly too high, particularly in light of the health effects that can be caused by having elevated levels of lead. For those children who are in the 7%, there may be the acute symptoms of lead poisoning, which can be treated and hopefully resolved, but worse, there may be the chronic effects that they cope with throughout their entire life. The goal is that children will not be exposed to lead at all.

As Vietnam strives to become an economic powerhouse in SE Asia, the loss of ingenuity and productivity from 7% of their potential workforce is a significant cost that is unrecognized. On the other hand, universal pediatric blood lead testing is also a costly expenditure and likely not economically feasible. Therefore targeted screening of at-risk populations remains the preferred approach. This study did help identify possible at-risk groups, but increased characterization of potential sources of lead exposure is needed. From a public health standpoint, knowing these sources is crucial in determining what is placing children at risk and how to avoid those exposures.

It is known that living in or near a lead recycling village places children at risk. BLL results from a similar study completed in the lead recycling village of Dong Mai in early 2012 were quite elevated, clearly indicating that children in lead recycling villages warrant closer attention (Wallace, 2012). However, the children in this study, which largely represent populations resident in or near Ho Chi Minh City had markedly lower BLLs on average. This can be seen by the following histogram which indicates the result of BLL testing from Dong Mai along with the BLL results from Ho Chi Minh.

Figure 6. Histogram of Blood Lead Levels from the Dong Mai and Ho Chi Minh Studies



It can be seen that there is not a great deal of overlap between these two populations. In the Dong Mai study, *all* children except for seven had BLL > 20 µg/dL, whereas in the Ho Chi Minh study, *only* nine children had levels greater than 20 µg/dL.

Outside of proximity to lead recycling efforts, the risk factors for elevated BLL in Vietnam based on this study appear to include: increasing age, attending school outside the home, drinking rainwater and residing in Binh Duong and Dong Nai provinces. For screening purposes, these risk factors could be applied to the general pediatric population if it is assumed that the children in this study were a reasonable representation of the public as a whole. It might be argued that this is more representative of an urban population, and admittedly the questionnaire did not assess whether children were living in urban or rural settings, which may be a contributing factor to lead exposure. Indeed, although many of the children were not from Ho Chi Minh, they may have been living in urban settings. It was interesting that a larger number of families from provinces other than Ho Chi Minh indicated that they lived near a busy intersection (35%) than did the families that said they lived in Ho Chi Minh (only 19%). Considering that Ho Chi Minh is a city of approximately 7 million people and nearly as many motorbikes, this was somewhat surprising. However, it is a fairly non-specific question and does not take into account what the general layout of streets or communities may be like in Vietnam.

It could also be argued that this population of children, being ill and hospitalized, does not well represent the general population who might be exposed to lead. Researchers involved in the study felt that if the children were hospitalized for respiratory concerns, these were not symptoms or diseases that tend to be associated with elevated BLLs, therefore the children likely had no greater risk factors for lead exposure. Additionally, if the children were frequently hospitalized, this could decrease the environmental lead exposure from their home or neighborhood. On the other hand, if the children were often ill and treated with traditional medicines containing lead, this might increase their potential lead exposure. Ultimately it was decided to recognize that while this was a convenience sample, it offered a useful starting point in the process of evaluating whether Vietnamese children were being exposed to lead.

The questionnaire included many variables that have been associated with elevated pediatric BLLs in SE Asian countries. In Thailand, the predictors have included: peeling paint, eating paint chips, geographic location, and age (Chomchai, et al, 2005). In Malaysia, the primary predictor was living in an urban setting (Hashim, et al, 2000). In a study from the Philippines, it was noted that, "After adjustment for covariates, our model showed that roof material, water source, haemoglobin, a history of breastfeeding, age, expenditure on cell phones and home province were all associated significantly with increasing BLL ($p < 0.05$)" (Riddell, et al, 2007). In Indonesia, Albalak, et al, found an association with level of education of the child's primary caregiver, water collection method, home varnishing, and living near a highway or major intersection (2003). A recent study from China in 2011 indicated an association with being male, age, living in a crowded neighborhood and smoking within the home (Liu, et al). It is intriguing that there are so many apparent associations that have been found, and yet the primary predictor in the US, lead-based paint, was seen in few of these other countries.

Similar to other studies from the region, there was an association between age and BLL. The mean BLL was highest in 2 year olds (6.71 µg/dL) compared to other age groups, consistent with the notion that mouthing activities are expected to put children around that age at high risk for elevated BLL. The fact that the odds ratio for high BLL continues to increase with age does suggest that there are ongoing lead exposures over time. Since the half-life of lead is measured in years, and leaded gasoline was phased out in 2001, it remains a possibility that some of this this effect relates to the ongoing legacy of leaded gasoline exposure. However, it does seem less likely since there were very few children (n=2 for children > 12 years old) included in the study who were alive at that time. The process implemented by Vietnam to minimize leaded gasoline is not known.

The significance of rainwater as a factor associated with elevated BLL is unclear. Information about income was not obtained as part of the research process, but rainwater use may be a surrogate marker for poverty or for living in a rural area. Another surrogate marker for poverty is education. The highest educational level in the households that used rainwater did not appear to be any lower than that of households that used other water sources. Also, educational levels in general did not have an association with elevated BLL. The information regarding water source was obtained during April and May, which is the dry season in Vietnam, and complicates understanding of the potential widespread nature of this variable. Explanations for elevated lead with rainwater use may include: household storage containers that contain lead, collecting devices with lead or lead solder, or possibly large containing devices that have been made with lead contaminated ingredients/soils, especially if there has been historical contamination of a particular site.

Having such a broad assortment of variables associated with elevated BLL in numerous countries, yet so few that reached statistical significance in this study in Vietnam, argues for the need to have very community-specific evaluations, by researchers who are culturally astute. This study clarified that wide-ranging questions of risk determination presented to the general populous did not yield particularly useful results. Future questionnaires should be improved using additional input from local community advisors to enhance any routine screening or surveillance process.

Prior to this study, it was unknown what the potential prevalence of elevated BLL in Vietnamese children without obvious significant sources might be. This study estimated that the prevalence of elevated BLL $\geq$ 10 µg/dL in Vietnam is around 7%. This is consistent with nearby SE Asian countries such as Thailand, China and others, as seen in Table 11. The mean BLL (4.95 µg/dL) is also comparable with surrounding countries.

Table 12. Prevalence of BLL >10 μg/dL and Average BLL for Countries in SE Asia

	Number	Prevalence BLL >10 μg/dL	Average BLL (μg/dL)
Thailand[1]	296	8.1%	5.7
Malaysia (KL)[2]	346	6.4%	5.3
Philippines[3]	2861	21%	6.9
China[4]	1344	8%	6.2
India[5]	754	32%	8.4

1. Chomchai (2005) J Med Assoc Thai, pg S53-S58.
2. Hashim (2000) Asia Pac J Public Health, pg 75-70.
3. Riddell (2007) Bull WHO, pg 674-680.
4. Liu (2012) Paediatr Perinat Epidemiol, pg 61-69.
5. Nichani (2006) Sci Total Environ, pg 95-106.

One way to assist children who are at risk for lead exposure would be to implement a lead surveillance system in Vietnam. Screening is necessary since individuals with elevated levels are rarely symptomatic. Ideally this system would be focused, accurate and inexpensive. By Western standards, the LeadCare II is relatively inexpensive; hence it is widely used throughout the US. However, the cost is likely prohibitive if it were to be applied to all children in Vietnam. Therefore dedicated screening of only high risk children would be optimal, using the LeadCare II. Initial screening of BLL in aggregate could be used to identify areas where additional interventions should be concentrated. The LeadCare II is felt to be reasonably accurate for screening purposes and its use has been encouraged by the CDC. See Appendix 1 for further discussion of lead testing methods. Using the LeadCare II in a limited fashion should provide a cost-effective approach to evaluating pediatric populations at risk for elevated BLL.

Cases with elevated BLL greater than 35 µg/dL

Case 1: A 9 month old female presented with an initial LeadCare II result of 39.9 µg/dL on 04/30/2012. Her weight was 9.5 kg, height 78 cm, HgB 13.4 g/dL and Hct 41.9%. Her BLL was tested at EAC on 05/03/2012 with a result of < 10 µg/dL. A second measurement by LeadCare II on 05/05/2012 was 15.7 µg/dL. According to the lab manager, the EAC result was likely not accurate. This result may have been due to incorrect procedures performed by an employee unfamiliar with the test. Another explanation in this scenario is surface lead contamination that dissipated by the time of the second LeadCare II test, or was properly removed at the time of the second test. This could have been an important factor since the child's father's profession was "metal analysis". In review of her questionnaire responses, her family had been engaging in lead and metal recycling activities. They answered positively on the questions asking about lead recycling in the home, both current and past, whether a household member recycles, and that lead cooking does occur in the home. This child was not symptomatic and, particularly in light of the unusual test results, she was not treated. Environmental evaluation and modification would be crucial in ensuring that this child would have decreased lead exposure in the future.

Case 2: A 2 month old male had an initial LeadCare II result of 34.9 µg/dL on 05/04/2012. His weight was 4.2 kg, height 59 cm, HgB 9.3 g/dL and Hct 28.4%. His BLL was verified by the EAC which obtained a result of 59 µg/dL on 05/05/2012. A repeat BLL measured by LeadCare II on 05/11/2012 was 29.3 µg/dL. This child's mother was a tailor, and his father was an electrician. This child or this child's mother consumed traditional medicine (described as a powdered orange medicine) one month before admission. No additional history of lead exposure in his environment was discovered. His mother's BLL by LeadCare II on 05/11/2012 was 19.1 µg/dL. This scenario is consistent with an acute lead exposure. Admittedly, the source of the lead may never be entirely certain, although the family was discouraged from using the traditional medicine since it could have been the means of exposure. The initial LeadCare II result and the EAC both indicated quite elevated BLL, but it is worthwhile to note that the LeadCare II is less accurate at higher lead levels, which could account for the initial discrepancy. The half-life of lead in the body is quite long and is typically considered in days, months or even years. But it is possible, with an acute exposure, to see the rapid drop in the lead level that appeared to occur with this boy, as the lead is metabolized or bound to hemoglobin and removed from the bloodstream. An additional follow-up level of 26.1 µg/dL was seen on 5/30/2012. Although apparently asymptomatic, there was initial consideration for treating this child, purely on the basis of a BLL of 59 µg/dL, which is consistent with current CDC recommendations. Unfortunately, the medications to chelate and treat elevated BLL are not easily obtained in Vietnam. Fortunately, the follow up BLL indicated marked improvement prior to any intervention occurring.

Case 3: A 13 month old breastfeeding male had a BLL by LeadCare II on 05/15/2012 that was 40.8 µg/dL. When he was tested by venipuncture on 05/16/2012 at the EAC laboratory, his level was 36 µg/dL. It was found that his mother had been using a powdered medicine of unknown origin to treat her sinusitis, apparently on a regular, if not daily, basis. No other history of lead exposure in his environment was discovered. This child was also asymptomatic. His mother's BLL was not obtained but could have been useful in determining whether her intake may have led to the child's elevated level. However, had there been a simultaneous environmental exposure, her BLL would not have fully clarified the situation. Testing all members of the household would likely have helped to better understand this scenario. Limitations on the availability of testing supplies and on the desire of the family to undergo venipuncture testing through the EAC did not allow the source to be fully defined.

Treatment of Lead Toxicity

The primary treatment for any child with an elevated BLL is to remove him or her from the source of lead. For an acute exposure, such as may be due to ingestion of a lead-laden substance like traditional or folk medicines, this can be a simple intervention. For chronic exposures, this may be more problematic, particularly since environmental remediation can be expensive or difficult to modify, or the exposure may be tied to the family's livelihood. Environmental evaluation is crucial for any children who have elevated BLLs.

The medical interventions will vary depending upon the BLL and presenting symptoms. Clinical signs and symptoms rarely present until children have markedly elevated levels. Even children with levels above 50 µg/dL rarely present with the classical symptoms and laboratory findings. These classical features of lead toxicity include colicky abdominal pain, constipation and anemia, with basophilic stippling of red blood cells. At lower BLLs, the symptoms tend to be subtle or easily misconstrued as originating from an alternate cause. The clinical presentation of a child with extremely elevated lead levels may also include coma, encephalopathy or seizures. Initial management of these high lead levels involves routine stabilization, followed by considerations for other interventions such as chelation. The CDC has set a level of 45 µg/dL as the point at which children should be chelated. Particularly with small children, it is advisable to confirm with abdominal radiograph that enteral lead is not present.

Chelation therapies, which are medicines that remove lead from the blood or tissues by binding it, have limited impact on overall body stores due to the long half-life of lead in the body (particularly bone, where the $t^{1/2}$ is measured in years). The lead reservoirs in bone account for 70% of the lead in children. Chelation is not a single therapy, but typically will need to be done repetitively, with close follow up of the BLL. Chelation will create a temporary decrease in the BLL, but these levels often rebound. It can take a considerable amount of time for the BLL to decline to a lower steady state that is safer for the child. A study from New York City showed that, using medical and environmental management consistent with CDC recommendations, it generally takes 6-12 months for children's BLLs to decline from ≥ 20 µg/dL to < 10µg/dL (Dignam, et al, 2008).

There is no controversy that children with extremely high BLLs should be chelated, although the potential for rebound elevation in the BLL needs to be closely monitored and taken into consideration with the treatment protocols. There is debate about the risks and benefits of chelating children with lower BLLs. For instance, Rogan, et al, found that chelating children with levels between 20 and 45 µg/dL lowered their BLLs but did not improve their neuropsychiatric scores (2001).

In this study, there were several limitations with respect to treatment. First, the Vietnamese physicians had limited access to chelating medications. It was never clear whether any of the first line medications, particularly succimer, which can be delivered orally, were available. Lacking access to these medications, the Vietnamese physicians had limited knowledge regarding their delivery, side effects, and use in practice. Secondly, separating the children from the environmental cause of their high BLL is the mainstay of treatment. However, awareness of the environmental etiologies of lead exposure in this study's participants was limited to the information obtained from the questionnaire or by the resident physicians. Optimally, there would be individuals trained at environmental evaluation who could more closely examine the households or neighborhoods of the children with elevated BLLs. To the extent it was feasible, the CDC protocol outlined in Table 3 above was followed.

The CDC recommendation includes environmental investigation beginning at BLL >20 µg/dL, along with lead hazard reduction and chelation beginning at 45 µg/dL. Except for the child who had the marked variation in BLL (case 2 above), none of the participants in this study required chelation based purely on their BLL. There was serious consideration of chelating the child who had an initial level of 40.8 µg/dL due to the potential lack of precision with the LeadCare II, however without being able to truly modify the environment, without knowing whether this was an acute or chronic exposure, and due to the lack of medication availability, it is certainly questionable whether the benefits of treatment would have been worth the potential risk to the child.

CONCLUSIONS

Reflecting upon this study allows for several conclusions to be made. There appears to be minimal awareness or activity in Vietnam regarding assessment for potential childhood lead exposures. An additional complicating factor in this situation is that even once children were diagnosed with elevated BLL, they did not have easy access to treatment or environmental evaluation. This study was useful in bringing up the issue of lead exposure and initiating an effort to understand the extent of the problem. However, in addition to further lead testing in children, another aspect of alleviating this public health concern would be to provide education and training for the public health and medical personnel who may be caring for them. The goal of these efforts is to find ways to minimize BLL in children, ideally by understanding potential exposures well enough that they can by completely avoided.

Another learning point is that if the questionnaire were to be used again, it should be further refined to improve its ability to discern various potential exposures. It was, however, an initial attempt and was based upon previous instruments that appeared reasonable, although they had not been tested on this particular population. Certainly there may have been difficulties with translation that hampered our ability to assess for particular lead exposures. For instance, in discussion with the Vietnamese research personnel, there seemed to be particular confusion in either translating the question regarding the use of traditional medicines or obtaining accurate answers. It would have been useful to specifically ask how long the children had been hospitalized, in order to better understand their severity of illness. Questions to better assess year round water sources would have been useful. Also, more thorough questioning regarding socioeconomic status and living in a rural versus urban setting may have clarified a few variables. Additional useful future questions could include proximity to industries such as cement plants or mining, second hand smoke, or better understanding of possible aviation influences with leaded gasoline.

This study could be better refined with additional environmental analysis and possible testing if warranted. The old adage which states that, "A picture is worth a thousand words" likely applies to this situation. Being able to examine the households or neighborhoods and possibly test paint chips or ingested substances such as water or medicine would probably be very revealing, although it may be cost prohibitive. It is possible that another method to achieve this end would be detailed discussions with local personnel who are knowledgeable regarding local industry and practices; however with the notable lack of awareness currently regarding lead related issues, this would probably not be fruitful in this situation.

A third concern is that of accuracy of the venipuncture testing. To a certain extent we had to rely on the practices of the Vietnamese physicians, who obtained the services of a local laboratory. There simply were not enough paired samples (EAC lab and LeadCare II) to truly get a sense of whether the testing methods correlated well or if there were significant discrepancies. It also would have also been useful to know how many children had their BLL from capillary fingerstick versus venipuncture samples. Further discussion of the laboratory techniques while in country with relevant laboratory personnel would also be useful.

Despite a few complications, this study was an initial attempt at furthering awareness regarding lead related issues in a country that has yet to focus attention on this problem. It is ironic that often the countries that are in greatest need of surveillance are those with the fewest resources to address the problems once they have been created. Although awareness is a critical first step in addressing lead related concerns, encouraging efforts to avoid environmental lead exposures, whether through public or private efforts, is ultimately the best approach to solving the lead problem.

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