Published in final edited form as:

Clin Chim Acta. 2003 January ; 327(0): 109–113.

Blood lead concentrations in children: new ranges

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Abstract

Background—Lead exposure in young children may have adverse neurodevelopmental effects. Currently, an increased blood lead concentration is defined as 10 µg/dl for males and females of all ages, including children younger than 6 years. Using a large hospital population ($n = 11,145$), we define more specific ranges for pediatric blood lead concentrations.

Methods—Pediatric blood lead concentrations were determined (atomic absorption spectrophotometry) on patient samples accrued from January 2001 to June 2002, and the data was analyzed employing the Hoffman approach.

Results—For lead, the 2.5th and 97.5th percentiles for subjects aged 0 to 12 months were 2.3 to 4.7 µg/dl for females and 1.8 to 4.9 µg/dl for males. The 97.5th percentiles increased for the 1–2 years age group both for females (5.2 µg/dl) and males (5.6 µg/dl). There was a significant decrease in blood lead concentrations after age 10 years, the 97.5th percentile being 4.4 µg/dl in both female and male subjects. The values in all corresponding age groups were similar for females and for males. The medians of all age groups were similar for females and for male subjects.

Conclusion—The blood lead concentrations are much lower compared to previously published data.

Keywords

Blood lead; Diurnal variations; Environmental exposure/adverse effects; Lead poisoning/epidemiology; Lead poisoning/prevention and control; Pediatric; Human; Adolescent; Environmental monitoring; Urban

1. Introduction

Lead is an environmental toxicant that may deleteriously affect the nervous, hematopoietic, skeletal, renal, endocrine and reproductive systems. Lead exposure in newborn and in young children is of particular concern because of its adverse neurodevelopmental effects, which

can result in neurocognitive and neurobehavioral deficits. In addition, children are more susceptible to the effects of lead because they absorb lead more readily than do adults. The Centers for Disease Control and Prevention (CDC) has defined an increased blood lead concentration as $10 \mu\text{g/dl}$ ($0.48 \mu\text{mol/l}$) for male and female children [1]. Blood lead concentrations $< 10 \mu\text{g/dl}$ ($0.48 \mu\text{mol/l}$) can adversely affect the behavior and development of children [2]. Our group has more than two decades of experience in the area of pediatric reference ranges [3–7]. In order to define the current values for blood lead concentrations for both genders in the specific age groups, we calculated the pediatric concentration ranges for blood lead for age groups 0–12 months, 13–24 months, 2–4, 5–9, 10–11 and 12–18 years separately for female subjects and for male subjects.

2. Materials and methods

2.1. Patient selection and sample collection

Whole blood samples (EDTA) were obtained from a population of outpatient and hospitalized children at Children's National Medical Center, as part of routine diagnostic testing. The samples were collected between the dates of January 1, 2001 and June 8, 2002. The population included male and female aged 4 days to 18 years. The samples were organized by age and gender. Prior to performing the assay, the samples were kept refrigerated for no longer than 96 h at 2 to 4 °C. No effort was made to exclude subjects from the study based on prior chronic or acute lead exposure.

2.2. Lead assay

Blood lead concentrations were determined in 100- μl samples of whole blood containing EDTA with an electrothermal atomization atomic absorption spectrophotometric assay (AAAnalyst 600, Perkin Elmer, Wilton, CT). This assay is based on the rapid Zeeman graphite furnace atomic absorption method and has a high degree of accuracy [8,9]. Our laboratory routinely participates in lead proficiency testing. Three concentrations of control from Kaulson Laboratory were run prior to each batch of patient samples. In addition, a QC was run after every 10 samples. The analytical range for this assay extends from the minimum detectable concentration of $1 \mu\text{g/dl}$ to the concentration value of highest standard of $39 \mu\text{g/dl}$. In the case of subjects with a blood lead concentration $> 39 \mu\text{g/dl}$, the sample was diluted with diluent prior to analysis. We used the zero calibrator as diluent obtained from NIST (the National Institute of Standards and Technology, Gaithersburg, MD 20899) Standard Reference Material 955b.

2.3. Statistical analysis

Blood lead concentrations, reported in $\mu\text{g/dl}$ units (multiply by 0.0483 to convert to $\mu\text{mol/l}$), and child age and gender were entered into a spreadsheet program, the data sets were separated into female subjects and male subjects and stratified by age. Abnormal and outlier values were truncated from each individual age category according to the Hoffman method [10]. Generally, the top and bottom 10–20% of the data was discarded and a line was drawn to the central linear portion of the graph. The remaining data, which was of normal Gaussian distribution, was used to calculate the 2.5th and 97.5th percentiles for each of the age groups. We plotted percent cumulative frequency versus lead concentration on percent cumulative frequency paper so that the 2.5th and 97.5th percentiles could be calculated. These were used as the final reported blood lead concentration ranges.

For diurnal variation, a chi-square test was performed for determination of statistical significance between the male population tested early in the day and in the afternoon, and similarly for the female population.

3. Results

3.1. Lead ranges

Blood lead concentration ranges were determined separately for females and for males, and stratified by age groups (Table 1). Generally, ranges were higher for males in each of the age groups. In both male and females, lead values starting at age 13–24 months declined with age. The highest values were for males age 13–24 months. The medians for female and male subjects were similar and ranged between 3.1 (males 10–18 years) and 3.8 (females 13–24 months). Median values declined with age for both genders. Percentiles were calculated for all age groups using the Hoffman method (Table 2).

3.2. Seasonal and diurnal variations in blood lead concentrations

To determine if the blood lead concentrations of the subjects in the study changed significantly seasonally and with the time of day we studied the data according to month of blood lead test and the time, the sample was drawn. There did not appear to be any correlation between the month of the year and the blood lead concentrations of the patients.

To study the diurnal effects of lead, the data was divided into two groups for male subjects and two groups for female subjects. The first group had their blood drawn between 08:01 and 15:59 h. The second group had their blood drawn between 16:00 and 08:00 h. The results are summarized in Table 3.

It is interesting to note the diurnal differences in the percent of subjects with blood lead concentrations >6 and >10 $\mu\text{g/dl}$ blood lead. Both the male and female lead values show that the time of day has virtually no effect on the ranges for blood lead. However, differences were found in the mean blood lead concentration, the percent of subjects with blood leads >6 $\mu\text{g/dl}$ and the percent of subjects with blood leads >10 $\mu\text{g/dl}$. Similar patterns emerged with both male and female subjects, adding validity to the argument that the time of day may have some effect on the blood lead concentrations. A circadian rhythm for lead in plasma, erythrocytes and urine has been noted previously [11,12].

4. Discussion

This study summarizes data on 11,145 children screened for blood lead concentrations in the greater Washington, DC area and determines 2.5th to 97.5th percentile ranges for blood lead separately for females and for males. The ranges for both genders decrease as the child ages. A notable exception are both males and females in the 0–12 month group having lower blood lead concentrations than the 13–24 month age group. These age- and gender-related values are applicable to the population served by Children's National Medical Center in Washington, DC and may vary somewhat at other U.S. locations. The highest percentage of increased blood lead concentrations occurred in children 2–4 years of age, with slightly lower percentages in those younger and older age groups with blood lead concentrations >10 $\mu\text{g/dl}$ (>0.48 $\mu\text{mol/l}$). Overall, male subjects had higher blood lead concentrations than females.

CDC's National Health and Nutrition Examination surveys (NHANES), an ongoing series of national examinations of the health and nutritional status of the civilian, noninstitutionalized population, have published blood lead concentrations in the U.S. population [13–15]. Gender and age were two principal risk factors found for excessive blood lead concentrations in children in NHANES II and NHANES III in the U.S.

NHANES III, conducted during 1988 to 1994 and NHANES 1999 (published in 2002) [16], indicate that blood lead concentrations in the U.S. population continued to decrease and that

blood lead concentrations among children aged 1–5 years were more likely to be increased among those who were poor, non-Hispanic black, living in large metropolitan areas or living in older housing. The pediatric population in our study is mostly urban and a high percentage of the population is non-white (~ 60%). Comparison of our data with the NHANES III blood lead data shows a similar pattern, and as in the NHANES III survey, the 97.5th percentile values tend to decrease as the child ages. The overall mean blood lead concentrations for the U.S. population >1 year (including all adults tested) was 2.3 µg/dl [17]. In our study, the geometric mean for female subjects 0–18 years was 3.0 µg/dl and for male subjects 0–18 years 3.2 µg/dl. However, when the results were stratified by age, the geometric mean for subjects 10–18 years (both genders) was 2.4 µg/dl.

Lead exposure adversely affects the neurocognitive development and behavior of young children. Lead toxicity is not only a function of the developmental vulnerability of the child, it is also a function of the dose, the duration of exposure and the nutritional status of the child. The current CDC reference cut-off for children aged < 6 years is < 10 µg/dl. Children are particularly vulnerable to lead exposure because their neurocognitive system is more susceptible to lead insults and because they absorb lead more readily. Children living in urban areas and in older homes are more exposed to increased environmental lead concentrations [18].

A statistically significant higher percentage of male subjects whose blood was drawn in the morning and blood lead concentrations tested >6 µg/dL and >10 µg/dL than those who were tested in the afternoon and evening (Table 3). The same was true for females with blood lead concentrations >6 µg/dL but the difference was not statistically significant for those females who tested higher than 10 µg/dL (>0.48 µmol/L) ($p = 0.407$).

Blood lead concentrations in children in the United States have declined steadily. [13,14,16] The downward trend in blood lead concentrations in the greater Washington, DC area seems to continue as illustrated in our study of >11,000 children in 2001–2002. The means reported here are significantly lower than those reported in 1993 for a similar population in the greater Washington area [18]. Although the mean blood lead concentrations of children have been declining in the U.S. for more than two decades, even low concentrations of lead may continue to affect the growth of some children.

Acknowledgments

The authors would like to thank Dr. John C. Pezzullo, Georgetown University, for assistance with some of statistical analysis. Mr. Brian Hanak was supported by the Colaco Foundation for students of excellence.

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Table 1

Pediatric ranges of blood lead concentrations ($\mu\text{g/dl}$)^a for females and males age 0–18 years

Age groups	Blood lead concentration ranges ($\mu\text{g/dl}$)		<i>n</i>	
	Males	Females	Males	Females
0–12 months	1.8–4.9	2.3–4.7	1072	710
13–24 months	1.7–5.6	2.2–5.2	593	455
2–4 years	1.6–5.5	2.2–5.1	2513	3004
5–9 years	1.6–5.2	2.5–4.8	1053	1025
10–11 years	1.3–4.9	1.9–4.5	232	161
12–18 years	1.8–4.4	2.1–4.4	121	207

^aTo convert to ($\mu\text{mol/l}$) multiply by 0.0483.

Table 2

Percentiles of blood lead concentrations ($\mu\text{g}/\text{dl}$)^a for females and males age 0–18 years

Age groups	Percentiles											
	10%		25%		50%		75%		90%		n	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
0–12 months	2.3	2.7	2.8	3.1	3.3	3.5	3.8	3.9	4.3	4.3	1072	710
13–24 months	2.4	2.7	2.9	3.2	3.6	3.8	4.3	4.3	4.9	4.8	593	455
2–4 years	2.3	2.8	2.9	3.3	3.6	3.7	4.4	4.2	5.0	4.6	2513	3004
5–9 years	2.2	2.9	2.8	3.2	3.4	3.6	4.0	4.0	4.6	4.4	1053	1025
10–11 years	1.9	2.3	2.5	2.7	3.1	3.2	3.7	3.6	4.3	4.0	232	161
12–18 years	2.2	2.5	2.6	2.8	3.1	3.2	3.5	3.6	4.0	4.0	121	207

^aTo convert to $\mu\text{mol}/\text{l}$ multiply by 0.0483.

Table 3
Diurnal effects on blood lead concentrations males and females aged 4 days to 18 years

Characteristic	Gender and time period					
	Males			Females		
	8:01–15:59	16:00–08:00	<i>p</i>	8:01–15:59	16:00–08:00	<i>p</i>
Number of subjects	3280	2303		3438	2125	
% of subjects with blood lead>6 µg/dl ^a	9.57%	7.03%	0.001	9.51%	6.59%	< 0.001
% of subjects with blood lead>10 µg/dl ^a	4.27%	2.21%	< 0.001	3.26%	2.82%	0.407
Median blood lead (µg/dl) ^a	3	3		3	3	
Concentration Range for Blood Lead (µg/dl) ^a	1.7–5.4	1.4–5.3		2.4–5.0	2.2–5.0	

^aTo convert to µmol/l multiply by 0.0483.