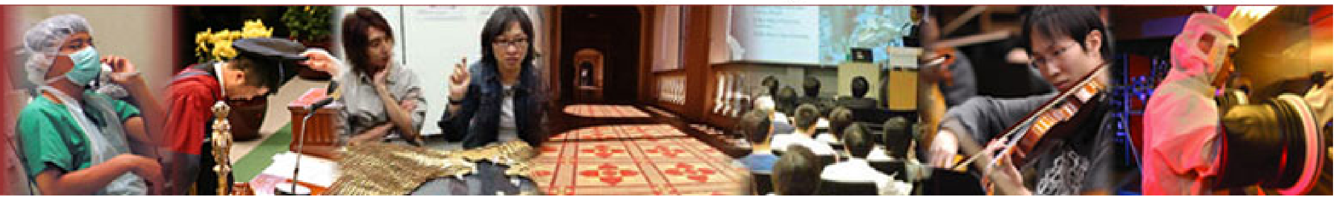

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Continual Decrease in Blood Lead Level in Americans: United States National Health Nutrition and Examination Survey 1999-2014

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ABSTRACT

BACKGROUND: Lead is toxic and affects neurodevelopment in children even at low levels. There has been a long-term effort in the United States to reduce exposure to lead in the environment. We studied the latest US population blood lead levels and analyzed its trend.

METHOD: Blood lead levels in 63,890 participants of the National Health Nutrition and Examination Survey 1999-2014 were analyzed using SPSS Complex Samples v22.0 (IBM Corp, Armonk, NY).

RESULTS: Mean blood lead levels and 95% confidence intervals (CIs) were 1.65 µg/dL (1.62-1.68), 1.44 µg/dL (1.42-1.47), 1.43 µg/dL (1.40-1.45), 1.29 µg/dL (1.27-1.32), 1.27 µg/dL (1.25-1.29), 1.12 µg/dL (1.10-1.14), 0.97 µg/dL (0.95-0.99), and 0.84 µg/dL (0.82-0.86) in 1999-2000, 2001-2002, 2003-2004, 2005-2006, 2007-2008, 2009-2010, 2011-2012, and 2013-2014, respectively. Blood lead levels decreased significantly ($P < .001$), and the trend remained significant when stratified by age, gender, ethnicity, and pregnancy status ($P < .05$). Estimated percentages of children with blood lead level ≥5 µg/dL were 9.9% (95% CI, 7.5-12.9), 7.4% (95% CI, 5.9-9.4), 5.3% (95% CI, 4.1-6.9), 2.9% (95% CI, 2.1-3.9), 3.1% (95% CI, 2.0-4.8), 2.1% (95% CI, 1.5-3.1), 2.0% (95% CI, 1.0-3.6), and 0.5% (95% CI, 0.3-1.0) in 1999-2000, 2001-2002, 2003-2004, 2005-2006, 2007-2008, 2009-2010, 2011-2012, and 2013-2014, respectively. The decreasing trend was significant ($P < .05$). In children aged 1 to 5 years in the National Health Nutrition and Examination Survey 2011-2014, the estimated 97.5 percentile of blood lead level was 3.48 µg/dL.

CONCLUSIONS: Blood lead levels have been decreasing in the US population. The reference level also should decrease. It is still important to monitor blood lead levels in the population, especially among pregnant women and children aged 1 to 5 years.

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KEYWORDS: Blood lead level; NHANES

Lead is ubiquitous in the environment but has no known biological role in humans.[1] It can form complexes with amino acids, proteins, and thiol-containing compounds, resulting in inhibition of enzymes and induction of oxidative stress.[2] In adults, lead is well known for causing toxicity to the bone marrow, liver, kidney, and central nervous system. Recent studies also showed that high blood lead levels are associated with an increase in systolic blood pressure and mortality.[3-5] Pregnant women with

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high blood lead levels are at risk of spontaneous abortion.[6,7] However, children are at the highest risk of lead poisoning. High blood lead levels are associated with reduced intelligence, attention deficit hyperactivity disorder, hearing impairment, and delayed puberty in girls.[7-9] Chelation therapy can be considered in children with a blood lead level of 45 µg/dL or greater,[10] but there is no evidence to show that chelation therapy is associated with any improvement in intelligence.[11] Because lead exposure can result in irreversible harm in children,[11,12] reducing blood lead levels in the population is desirable. This is best achieved by reducing lead in the environment.

The current upper reference level for blood lead is 5 µg/dL in the United States. This reference level was set in 2012 using the 97.5th percentile of blood lead levels in children aged 1 to 5 years in the National Health Nutrition and Examination Survey (NHANES) 2007-2010.[13] Previous studies have shown a decrease in blood lead levels in the US population over the years.[14-16]

However, as the events in Flint, Michigan, have shown, there is no room for complacency. The crisis was due to a decision made by the local government to use Flint River as the source for tap water. The proportion of children aged 1 to 5 years with a blood lead level ≥5 µg/dL was 2.5%.[17] Therefore, we analyzed the trend in blood lead levels in the US population using the latest data from NHANES and estimated the proportion of children with an elevated lead level, defined as 5 µg/dL or greater.

CLINICAL SIGNIFICANCE

- There has been a continuous decreasing trend in blood lead levels in the US population.
- The reference level should be revised to reflect the decrease in blood lead levels in the United States.
- The upper reference level for blood lead should be reduced to 3.5 µg/dL.

MATERIALS AND METHODS

NHANES is a continuous national survey conducted by the US Centers for Disease Control and Prevention. Detailed methodology and protocols are described on its webpage.[18] Each participant represents approximately 50,000 Americans. The study was approved by the Research Ethics Review Board at the National Center for Health Statistics. All participants gave informed consent.

We used the NHANES dataset from 1999 to 2014. For inclusion in the analysis, a blood lead level had to be available. Included participants were stratified according to the year of survey, age, gender, ethnicity, poverty income ratio, and pregnancy status.

Venous blood samples were obtained to measure blood lead levels according to a standard protocol. Samples were frozen at −20°C and shipped in dry ice until analysis. After thawing, samples were diluted and analyzed with an Inductively Coupled Plasma Dynamic Reaction Cell Mass Spectrometer (ELAN DRC II, PerkinElmer, Norwalk).[19] The limits of detection were 0.3 µg/dL in 1999-2002, 0.28 µg/dL in 2003-2004, 0.25 µg/dL in 2003-2012, and 0.07 µg/dL in 2013-2014. Blood lead levels below the lower limit of detection were assigned a value equal to the lower detection limit divided by $\sqrt{2}$.

Statistical Analysis

Results were analyzed using SPSS complex sample module version 22.0 (IBM Corp, Armonk, NY). Sample weights were applied to account for unequal probabilities of selection, nonresponse bias, and oversampling. Natural logarithm-transformed blood lead levels were used to normalize the distribution of blood lead levels.

The proportions of children aged 1 to 5 years and pregnant women with elevated blood lead level, defined as 5 µg/dL or greater, were estimated. Blood lead levels were expressed as geometric means and 95% confidence intervals (CIs). Categoric variables were expressed as percentages. Analysis of variance or *t* test was used to compare blood lead levels in different groups in the same sampling period. Multiple regression was used to analyze trends in blood lead level across sampling periods. A 2-tailed *P* value of <.05 was considered statistically significant. The 97.5th percentile of the blood lead level in children aged 1 to 5 years in NHANES 2011-2014 also was estimated.

RESULTS

We analyzed 7970, 8946, 8373, 8407, 8266, 8793, 7920, and 5215 participants in NHANES 1999-2000, 2001-2002, 2003-2004, 2005-2006, 2007-2008, 2009-2010, 2011-2012, and 2013-2014, respectively. The characteristics of these participants are summarized in **Table 1**. Mean blood lead levels decreased from 1.65 µg/dL (95% CI, 1.62-1.68) in 1999-2000 to 0.84 µg/dL (95% CI, 0.82-0.86) in 2013-2014 (**Table 1**). The decreasing trend of blood lead levels across the years was significant (*P* <.001).

We further analyzed subgroups stratified by age, gender, and ethnicity. Mean blood lead levels stratified by age are summarized in **Figure 1**. There was a significant reduction in blood lead levels in all age groups (*P* <.001) (**Figure 1**). Blood lead levels stratified by age and gender are summarized in Supplementary Table 1, available online. There was a significant decrease (*P* <.001) in all age groups and genders. Blood lead levels stratified by ethnicity are summarized in Supplementary Table 2, available online. Other ethnicities have been further divided into non-Hispanic Asians and other race since NHANES 2011-2012 (Supplementary Table 2, available online). The decrease in blood lead levels was significant in all ethnicities

Table 1 Characteristics of Participants Included in Analysis

Year	1999-2000	2001-2002	2003-2004	2005-2006	2007-2008	2009-2010	2011-2012	2013-2014	P
N	7970	8946	8373	8407	8266	8793	7920	5215*	
Age, y	36.8 ± 0.29	36.7 ± 0.26	37.3 ± 0.26	37.9 ± 0.27	38.4 ± 0.26	38.8 ± 0.25	39.0 ± 0.31	29.4 ± 0.33	.551
Female (%)	4057 (50.9%)	4606 (51.5%)	4241 (50.7%)	4315 (51.3%)	4119 (49.8%)	4427 (50.3%)	3952 (49.9%)	2628 (50.4%)	.991
No. of children aged <20 y	3763 (47.2%)	4173 (51.5%)	3848 (46.0%)	3898 (46.4%)	2902 (35.1%)	3028 (34.4%)	2890 (36.5%)	2520 (48.3%)	.883
Ethnicity									
Mexican American (%)	2742 (34.4%)	2268 (25.4%)	2085 (24.9%)	2236 (26.6%)	1712 (20.7%)	1966 (22.4%)	1077 (13.6%)	969 (18.6%)	
Other Hispanic (%)	471 (5.9%)	403 (4.5%)	274 (3.3%)	277 (3.3%)	980 (11.9%)	949 (10.8%)	854 (10.8%)	9.8 (28.4%)	
Non-Hispanic white (%)	2670 (33.5%)	3768 (42.1%)	3436 (41.0%)	3310 (39.4%)	3461 (41.9%)	3760 (42.8%)	2493 (31.5%)	1848 (35.4%)	
Non-Hispanic black (%)	1807 (22.7%)	2175 (24.3%)	2225 (26.6%)	2193 (26.1%)	1746 (21.1%)	1593 (18.1%)	2195 (27.7%)	1119 (21.5%)	.949
Others (%)	280 (3.5%)	332 (3.7%)	353 (4.2%)	391 (4.7%)	367 (4.4%)	525 (6.0%)	1301 (16.4%)	767 (14.7%)	
Non-Hispanic Asian (%)	NA	NA	NA	NA	NA	NA	1005 (12.7%)	510 (9.8%)	
Other race, including multiracial (%)	NA	NA	NA	NA	NA	NA	296 (3.7%)	257 (4.9%)	
Pregnancy (%)	267 (3.4%)	322 (3.6%)	256 (3.1%)	353 (4.2%)	50 (0.6%)	65 (0.7%)	51 (0.6%)	28 (4.6%)	.001
Mean blood lead level (μg/dL)	1.65 (1.62-1.68)	1.44 (1.42-1.47)	1.43 (1.40-1.45)	1.29 (1.27-1.32)	1.27 (1.25-1.29)	1.12 (1.10-1.14)	0.97 (0.95-0.99)	0.86 (0.84-0.88)	.001

NA = not applicable.
*Fewer participants were selected to have blood lead measurements during this period.

(P <.05) except other race (P = .454) (Supplementary Table 2, available online).

The mean blood lead levels in pregnant women and in children aged 1 to 5 years are summarized in Supplementary Table 3, available online. The proportion of pregnant women with elevated blood lead level also decreased with marginal significance (P = .053) (**Table 2**). The proportion of children aged 1 to 5 years with an elevated lead level decreased from 9.9% (95% CI, 7.5-12.9) in 1999-2000 to 0.5% (95% CI, 0.3-1.0) in 2013-2014 (P <.001) (**Figure 2**). The estimated 97.5th percentile of the blood lead level in children aged 1 to 5 years in NHANES 2011-2014 was 3.48 μg/dL.

DISCUSSION

Data from NHANES were used because it is a large-scale survey representative of the US noninstitutionalized population.[20] Moreover, participants of all ages, including infants, children, and pregnant women, were included. The protocol in NHANES is standardized and therefore facilitates comparison across the years. Lead was measured in a centralized laboratory according to a strict protocol.

Previous studies have reported a decreasing trend in blood lead levels in the US populations among different age groups and ethnicities.[13,16,21,22] Our analysis confirmed this decreasing trend and showed that there were further decreases in recent years. This is encouraging and demonstrates the effectiveness of long-term measures to reduce lead exposure in the United States. Compared with the results of the Canadian Health and Measures Survey and the Korean National Health and Nutrition Examination Survey in the corresponding age groups, the mean blood lead levels in NHANES were lower.[23,24]

We found that less than 1% of children had a blood lead level ≥5 μg/dL in 2013-2014. There were no pregnant women in the sample population with an elevated blood lead level. It may be timely to revise the blood lead reference level to reflect the decrease in blood lead levels in the United States. Our analysis suggested that the upper reference level for blood lead should be reduced to 3.5 μg/dL.

In contrast to the declining blood lead levels across the United States, the switch to Flint River as the source of water resulted in increased release of lead in pipes and elevated blood lead level in the residents of Flint, Michigan.[25,26] In children, this is of particular concern because lead is detrimental to neurocognitive development. The lesson that should be learned is that public health measures to monitor and reduce population exposure to lead in the environment should not be relaxed. Continued vigilance is essential to good public health.

Study Limitations

Our analysis was not without limitations. The study population was not a cohort, and the participants, who were chosen randomly, differed in successive surveys. Blood samples were obtained only once in each participant, so

Table 2 Estimated Proportion of Pregnant Women and Children Aged 1 to 5 Years of Different Ethnicities and Poverty Income Ratios with Elevated Blood Lead Level in 1999-2014

Year	1999-2000	2001-2002	2003-2004	2005-2006	2007-2008	2009-2010	2011-2012	2013-2014	*P*
Pregnant women	0.7% (0.2-2.6)	0.2% (0.0-1.1)	0.9% (0.1-6.3)	0.0%	0.0%	0.0%	0.0%	0.0%	.053
Children aged 1-5 y									
Stratified by genders									
Male	7.9% (6.8-9.2)	5.9% (5.1-6.8)	4.5% (3.8-5.3)	3.4% (2.8-4.1)	3.9% (3.2-4.8)	2.9% (2.3-3.6)	2.5% (1.9-3.3)	2.4% (1.7-3.5)	.001
Female	2.8% (2.1-3.6)	1.9% (1.5-2.5)	1.6% (1.3-2.0)	1.3% (1.0-1.8)	1.1% (0.8-1.5)	0.8% (0.5-1.1)	1.2% (0.8-1.9)	0.3% (0.2-0.6)	.001
Stratified by ethnicities									
Mexican Americans	10.2% (7.2-14.2)	4.3% (2.5-7.4)	3.7% (2.0-6.7)	1.4% (0.5-3.9)	1.2% (0.5-3.3)	2.6% (1.3-5.1)	0.0%	0.5% (0.1-3.2)	.001
Other Hispanics	3.6% (1.2-10.4)	6.6% (3.1-13.5)	3.3% (0.4-20.4)	6.9% (2.9-15.4)	1.1% (0.1-7.2)	1.7% (0.4-6.8)	1.0% (0.1-7.2)	0.7% (0.1-4.7)	.049
Non-Hispanic white	9.4% (5.9-14.7)	5.5% (3.5-8.7)	2.9% (1.5-5.5)	1.6% (0.8-3.2)	3.1% (1.5-6.0)	1.65% (0.8-3.10)	2.8% (1.2-6.6)	0.0%	.001
Non-Hispanic black	19.1% (14.0-25.5)	18.0% (14.0-22.9)	16.4% (12.7-20.8)	7.8% (5.4-11.3)	7.1% (4.3-11.4)	3.8% (1.8-7.9)	3.2% (1.6-6.4)	1.6% (0.6-4.1)	.001
Others	2.6% (0.4-5.9)	8.8% (3.1-22.7)	4.9% (1.9-12.0)	3.8% (1.4-10.4)	1.2% (0.2-8.6)	1.7% (0.4-6.9)	0.0%	1.3% (0.4-4.0)	.027
Non-Hispanic Asian	NA	NA	NA	NA	NA	NA	0.0%	0.8% (0.1-5.4)	.267
Other race, including multiracial	NA	NA	NA	NA	NA	NA	0.0%	1.1% (0.3-3.9)	.001
Stratified by poverty income ratio									
<1.3	14.0% (10.2-18.9)	12.7% (9.8-16.1)	8.9% (6.7-11.7)	6.7% (4.8-9.2)	4.8% (3.3-7.1)	4.1% (2.7-6.0)	3.1% (1.6-5.9)	1.1% (0.5-2.0)	.001
≥1.3	6.2% (3.6-10.4)	2.7% (1.5-5.1)	2.5% (1.3-4.8)	0.9% (0.4-2.1)	1.9% (0.7-4.9)	0.6% (0.2-1.6)	0.8% (0.1-4.5)	0.0%	.001
Stratified by age									
1-2 y	11.8% (8.2-16.5)	12.1% (9.1-16.0)	7.7% (5.3-11.0)	3.6% (2.4-5.4)	3.4% (2.1-5.4)	2.9% (1.8-4.7)	3.3% (1.4-7.6)	0.9% (0.4-2.0)	.001
3-5 y	8.4% (5.5-12.6)	4.5% (2.9-6.8)	3.6% (2.5-5.4)	2.5% (1.5-4.0)	3.0% (1.6-5.6)	1.6% (0.9-2.9)	1.3% (0.5-3.3)	0.3% (0.1-0.9)	.001

NA = not applicable.

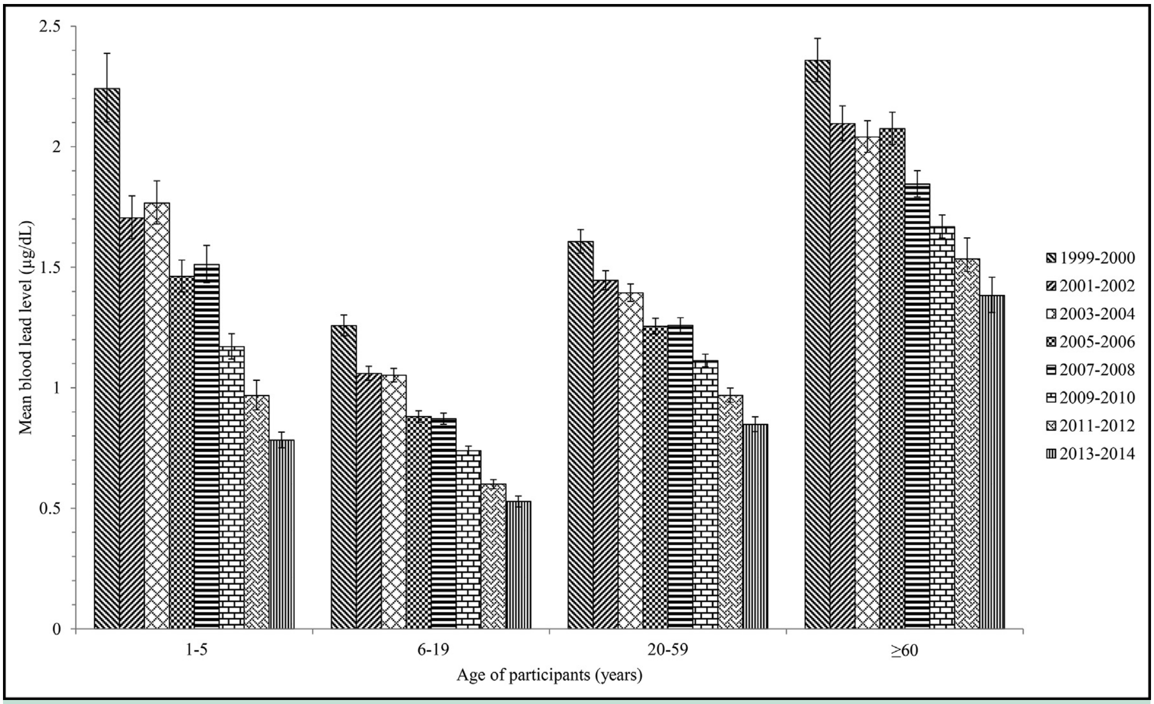

Figure 1 Estimated mean blood lead level in participants in different age groups in 1999-2014.

fluctuations of blood levels with time among individuals could not be captured. Because lead is mainly deposited in bones, the cumulative exposure of lead could not be measured simply by blood test. This is especially relevant to immigrants, who may have been exposed to lead before living in the United States. Immigrants and refugees within 6 months of arrival in the United States are more likely to have elevated blood lead levels.[27-29] The Centers for Disease Control and Prevention has introduced a program to monitor population groups. Previous studies showed elevated blood lead levels in Mexican Americans[25] and the poor,[20] but this was not evident in the latest NHANES data.

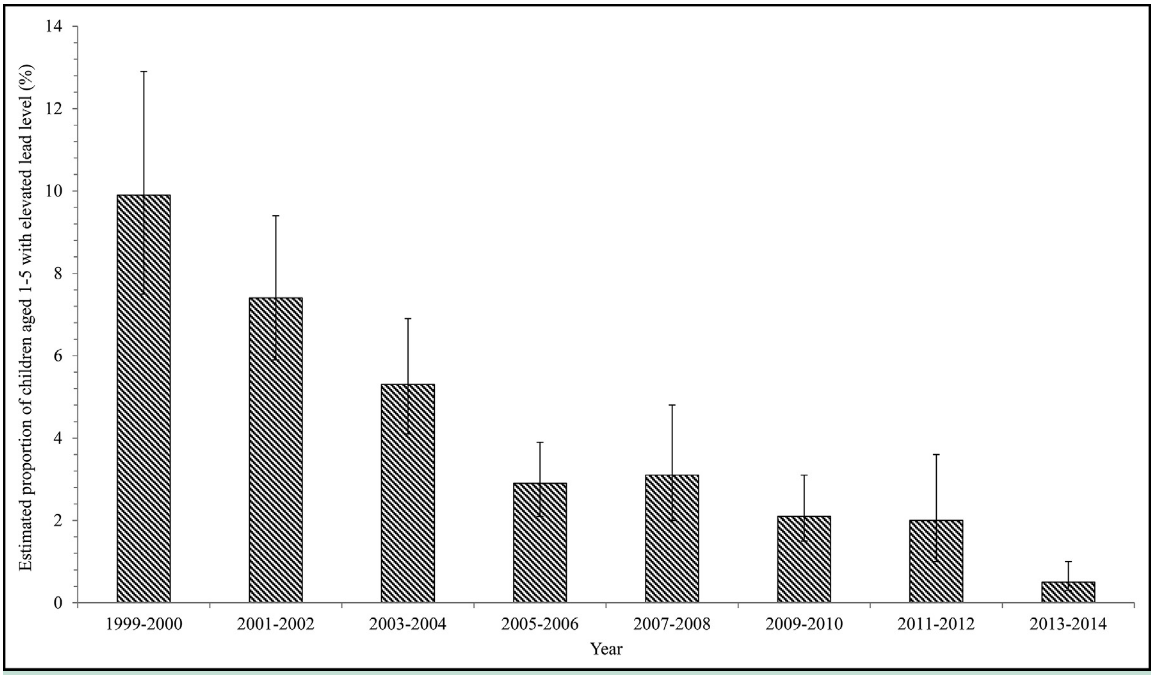

Figure 2 Estimated proportion of children aged 1 to 5 years with elevated lead level in 1999-2014.

CONCLUSIONS

There has been a continuous decreasing trend in blood lead levels in the US population. Because blood lead level in young children is a very important health issue, monitoring of blood lead levels at the population level should be continued.

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SUPPLEMENTARY DATA

Supplementary tables accompanying this article can be found in the online version at http://dx.doi.org/10.1016/j.amjmed.2016.05.042.