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A multi-level model of blood lead as a function of air lead

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HIGHLIGHTS

- The objective of this study was to evaluate change in blood Pb–air Pb relationship after regulation.
- PbB was significantly associated with PbA during NHANES III for all age groups.
- The significance of the PbB-PbA association varied with age group during NHANES 1999–2008.

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ABSTRACT

National and local declines in lead (Pb) in blood (PbB) over the past several years coincide with the decline in ambient air Pb (PbA) concentrations. The objective of this work is to evaluate how the relationship between PbB levels and PbA levels has changed following the phase out of leaded gasoline and tightened controls on industrial Pb emissions over the past 30 years among a national population sample. Participant-level data from the National Health and Nutrition Examination Survey (NHANES) were employed for two time periods (1988–1994 and 1999–2008), and the model was corrected for housing, demographic, socioeconomic, and other covariates present in NHANES. NHANES data for PbB and covariates were merged with PbA data from the U.S. Environmental Protection Agency. Linear mixed effects models (LMEs) were run to assess the relationship of PbB with PbA; sample weights were omitted, given biases encountered with the use of sample weights in LMEs. The 1988–1994 age-stratified results found that ln(PbB) was statistically significantly associated with ln(PbA) for all age groups. The consistent influence of PbA on PbB across age groups for the years 1988–1994 suggests a ubiquitous exposure unrelated to age of the sample population. The comparison of effect estimates for ln(PbA) shows a statistically significant effect estimate and ANOVA results for ln(PbB) for the 6- to 11-year and 12- to 19-year age groups during 1999–2008. The more recent finding suggests that PbA has less consistent influence on PbB compared with other factors.

1. Introduction

A broad range of adverse health effects have been observed in children and adults exposed to lead (Pb). These well-known effects include neurological, hematological, and immune effects in children and neurological, hematological, cardiovascular, and renal effects in adults. Health effects have been shown to occur at blood Pb (PbB) levels less than 10 μg/dL (U.S. EPA, 2006). From 1991 to 2012, a PbB level of 10 μg/dL had been considered a "level of concern" for children aged 5 years and younger among health care practitioners and the scientific community. Based on the body of scientific evidence of effects at lower PbB concentrations, the Centers for Disease Control (CDC, 2012) have recently discontinued the use of the term "level of concern" and instead created a "reference value" equivalent to the 97.5th percentile PbB level among 1- to 5-year-old children from the most recent National Health and Nutrition Examination Survey (NHANES); this value is currently 5 μg/dL.

National and local data show declines in PbB over the past several years, which coincide with the decline in ambient air air Pb (PbA) concentrations (U.S. EPA, 2006). For example, calculations from the NHANES showed that between 1988–1991 and 2003–2004, geometric mean PbB among children ages 1–5 years dropped by 50% from 3.6 μg/dL to 1.8 μg/dL (Jones et al., 2009). Although NHANES data

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have demonstrated a decrease in PbB levels over time, important differences are apparent across different demographic groups. For example, Jones et al. (2009) found that, while PbB has decreased among all racial groups, non-Hispanic black children ages 1–5 years still had 2.8 times higher prevalence of PbB ≥ 10 μg/dL compared with either non-Hispanic white or Mexican American children for the NHANES 1999–2004 data. Although there have been substantial reductions in PbB over time, age, race, and environment may be important susceptibility factors with respect to increased PbB.

The objective of this work is to evaluate how the relationship between PbB levels and PbA levels has changed following the phase out of leaded gasoline and tightened controls on industrial Pb emissions over the past 30 years among a national population sample. This manuscript describes the statistical modeling techniques and compares results for effect estimates for PbA obtained using two different model formulations. One model formulation adjusts for a variety of covariates, and the other model only contains a term for PbA. The cross-sectional study results presented in this manuscript evaluate these relationships of PbB levels among children and adults with PbA concentrations for two time periods for the NHANES 1999–2008 and NHANES III surveys.

2. Methods

2.1. Data sets

Participant-level data were obtained from the NHANES III and Continuous NHANES survey, for the years 1999–2008 in 2-year cycles (CDC, 2010). NHANES III was conducted from 1988 to 1994, and data from the Continuous NHANES (hereafter referred to as NHANES 9908) were obtained in 2-year cycles between 1999 and 2008. NHANES is a nationwide U.S. survey developed to draw national inferences about nutrition, health, demographics, socioeconomics, and other factors. All publicly available (non-geocoded) NHANES variables are listed in Table 1 along with the type of information represented. NHANES III and NHANES 9908 covariates used in the analysis include demographic information, socioeconomic status, body storage and Pb mobilization, housing (Pb paint), drinking water exposures, and occupational exposures. Most of these variables were employed in an analysis of the PbB–PbA relationship using NHANES II data, when the associations between blood Pb and gasoline consumption were examined (Schwartz and Pitcher, 1989). Previous studies also showed that PbB levels were associated with calcium (Ca) and iron (Fe) levels (Mahaffey et al., 1986; Bradman et al., 2001; Schell et al., 2004; Wolf et al., 2003). Therefore, variables available in NHANES III and NHANES 9908 reflecting Ca and Fe levels were also incorporated in the model. The analysis of data from several cycles of NHANES made the analysis more challenging because the number and definition of relevant variables changed among the cycles. Small differences existed between the variables included in the 2-year cycles during NHANES 9908. In comparing NHANES III with NHANES 9908, the definitions of the variables changed slightly between cycles. All NHANES variables were reviewed for these differences, and where appropriate, categorical variables were recoded to make the value definitions consistent. The NHANES oversamples certain population centers by design; the data can be adjusted by sample weights to develop results from which a national inference can be drawn. Unweighted data are used here because the linear mixed effects (LME) model analysis may be biased by their incorporation, as described in the Statistical Analysis section.

Some of the publicly available NHANES records had missing or uncertain data. For NHANES 9908, 19% of data were missing for PbB, and 0.076% of PbB data were below the method detection limit (MDL) of 0.2 μg/dL for the analysis of Pb in blood. For NHANES III, 8.7% of the PbB data were missing, and 0% of PbB data were below the MDL of 0.7 μg/dL. If an NHANES participant's record did not contain a value for PbB, it was omitted from the file because PbB is the dependent value in the statistical analysis. For all other variables in NHANES, statistical imputation was used with an in-house program developed in MATLAB R2009a (The Mathworks, Inc., Natick, MA). The fractional probability of each categorical value was measured from non-missing frequency data. Then a random seed between 0 and 1 was used to assign a categorical value based on the probability of each category. For continuous variables, the statistical distribution was estimated based on the non-missing data. A value was next calculated based on the

Table 1
Listing of publicly available variables from NHANES used in the mixed effects model analysis.

Information Type	Variable Description	Values[a]
Demographic	Age	Continuous
	Sex	Male Female
	Race/ethnicity	Mexican American Other Hispanic and Other Races White Black or African American
	Country of birth	50 U.S. States Mexico Other
Socioeconomic status	Head of household education level	Less than 9th grade Some high school High school grad Some college or associate's degree College grad or above
	Income-to-poverty line ratio	Continuous
	Household size	Integer (7 = 7 or more)
Body storage and Pb mobilization	Past 30 days milk consumption	Never Less than once per week At least once per week, less than once per day At least once per day Varied (NHANES 9908 only)
	Mother's age at child subject's birth (for subjects ages 19 and under)	Continuous
	Blood levels of cadmium (CdB), calcium (CaB), iron (FeB), lead (PbB), and phosphorus (PB)	Continuous
Housing	Years living in home	Less than 1 year 1–2 years 3–5 years 6–10 years More than 10 years
	When home was originally built	NHANES III: NHANES 9908: Before 1946 Before 1950 1946–1973 1950–1977 After 1973 After 1977
Drinking water exposures	Source of tap water	Private/public water company Private/public well
Occupation (ages 20 and over)	Type of business and work at present employment (recoded variables)	No likely current occupational Pb exposure Likely current occupational Pb exposure
	Type of business and work performed for the longest interval of a subject's career (recoded variables)	No likely long-term occupational Pb exposure Likely long-term occupational Pb exposure
	Length of time the subject has done the work performed over the longest interval of his/her career	Continuous

[a] Categorical variables also have “do not know” and “refused” options.