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Burden of higher lead exposure in African-Americans starts in utero and persists into childhood

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ABSTRACT

Background: Recent public health lead crises in urban areas emphasize the need to better understand exposure to environmental toxicants, particularly in higher risk groups. Although African-American children have the highest prevalence of elevated blood lead levels in the United States, little is known about when this trajectory of disproportionate burden of lead exposure first emerges.

Objectives: Using tooth-matrix biomarkers that directly measure fetal and early childhood metal levels, the primary goal of this study was to determine if there were racial disparities in lead levels during fetal development and early childhood. Manganese, an essential nutrient that modifies the neurotoxic effects of lead, was also measured.

Methods: Pregnant women served by the Henry Ford Health System and living in a predefined geographic area in and around Detroit, Michigan, were recruited during the second trimester or later into the Wayne County Health, Environment, Allergy and Asthma Longitudinal Study (WHEALS), a population-based birth cohort. Offspring born between September 2003 and December 2007 were studied in childhood. Child race was parent-reported. Lead and manganese during the second and third trimesters, early postnatal life (birth through age 1 year) and early childhood (age 1 through time of tooth shedding, which ranges from 6 to 12 years) were measured via high-resolution microspatial mapping of dentin growth rings, a validated biomarker for prenatal and childhood metal exposure.

Results: African-American children ($N = 71$) had 2.2 times higher lead levels in the second and third trimesters (both $p < 0.001$) and 1.9 times higher lead levels postnatally in the first year of life ($p = 0.003$) compared to white children ($N = 51$). Lead levels in African-American children were also higher during childhood, but this effect was only marginally significant ($p = 0.066$) and was attenuated after covariate adjustment. Additionally, we observed that African-American children had lower tooth-manganese levels during the third trimester ($p = 0.063$) and postnatally ($p = 0.043$), however these differences were attenuated after covariate adjustment.

Conclusion: The disproportionate burden of lead exposure is vertically transmitted (i.e., mother-to-child) to African-American children before they are born and persists into early childhood. Our results suggest that testing women for lead during pregnancy (or in pre-conception planning), may be needed to identify the risk to their future offspring, particularly for African-American women.

Abbreviations: BMI, Body Mass Index; ETS, Environmental Tobacco Smoke; GEE, generalized estimating equations; HFHS, Henry Ford Health System; LA-ICP-MS, laser ablation-inductively coupled plasma mass spectrometry; MI, Michigan; Mn, manganese; Pb, lead; QIC, Quasilikelihood under the Independence model Criterion; SES, Socioeconomic Status; WHEALS, Wayne County Health, Environment, Allergy and Asthma Longitudinal Study

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1. Introduction

In utero and early-life exposure to lead, and other environmental metal toxicants, even at very low levels, has long-term health implications (Haugen et al., 2015; Heindel et al., 2015). Studies have demonstrated racial, geographic and socioeconomic status (SES) differences in prenatal and early childhood exposure to metals using approaches that capture exposure either at a single point in time or one cumulative measure (Chatman and Wilson, 1975; Needleman et al., 1974; Wells et al., 2011). However, little is known about exposure patterns across early life, particularly at potential critical windows of development during prenatal and early postnatal periods (Selevan et al., 2000). Consequently, results from studies examining early-life exposure to metals and future health have been inconsistent (Grason and Misra, 2009) and hampered by lack of direct fetal markers of exposure. Recently-developed and validated tooth matrix biomarkers overcome these limitations and provide a direct measure of metal levels from the second trimester to early childhood (Arora et al., 2014). This method takes advantage of the incremental and archival nature of tooth development (similar to growth rings in trees), to reconstruct early life history of exposure to lead and other metals. Comparison with lead levels in umbilical cord blood and childhood blood has shown that teeth capture both the intensity and timing of exposure (Arora et al., 2014).

Here, we study lead, an established neurotoxicant, in Detroit, Michigan (MI), USA and its surrounding suburbs, an area just 70 miles from Flint, MI, which has recently been the focus of an acute drinking water crisis that included higher than average lead levels in the drinking water (Hanna-Attisha and Kuehn, 2016). The primary goal of this study was to determine if there were racial disparities in lead levels during fetal development and early childhood, even after accounting for SES or residential characteristics. Lead's effects on the nervous system can be modified by other metals, in particular manganese (Claus Henn et al., 2012; Kim et al., 2009), thus we also sought to examine if co-exposure to manganese modified the association between race and lead exposure. We used rigorously validated tooth-matrix biomarkers to directly measure fetal and postnatal lead and manganese levels (Arora et al., 2012; Arora et al., 2014; Austin et al., 2017; Gunier et al., 2013) in a racially and socioeconomically diverse birth cohort, the Wayne County Health, Environment, Allergy and Asthma Longitudinal Study (WHEALS) (Cassidy-Bushrow et al., 2012; Havstad et al., 2011; Wegienka et al., 2011)..

2. Methods

2.1. Study population

WHEALS recruited pregnant women with due dates from September 2003 through December 2007, and who were seeing a Henry Ford Health System (HFHS) obstetrics practitioner at one of five clinics to establish an unselected birth cohort (Cassidy-Bushrow et al., 2012; Havstad et al., 2011; Wegienka et al., 2011). All women were in their second trimester or later, were aged 21–49 years, and were living in a predefined geographic area in Wayne and Oakland counties of Michigan that included the city of Detroit as well as the suburban areas immediately surrounding the city. A total of 1258 maternal-child pairs were included in WHEALS.

WHEALS families were asked if they would donate an exfoliated primary tooth to the WHEALS Tooth Fairy Study. Between December 2011 and January 2015, 373 teeth were received from 156 participants. Teeth were selected for measurement if the child had at least some outcome data available and the tooth was relatively intact. A few children ($N = 17$) had multiple teeth analysed for quality control; metals levels were averaged over teeth within each child. Teeth from 152 children underwent analysis. After excluding 30 children who were non-African-American or non-white, due to small sample sizes within other groups (13 Middle Eastern, 7 Hispanic, 6 Asian and 4 Multi-racial), our final analytic sample consisted of 122 children. All participants provided written, informed consent. Study protocols were approved by the HFHS Institutional Review Board.

2.2. Covariate measurement

Maternal race was self-reported and child race was parent-reported, usually by the mother. Household income, marital status, exposure to environmental tobacco smoke (ETS), smoking during pregnancy, exposure to indoor pets prenatally, year the residence was built and infant feeding practices at 1 month (formula feeding, exclusive breast-feeding or mixed formula/breastfeeding) were self-reported. Year residence was built was dichotomized as 1980 or after or before 1980, to indicate risk of lead exposure due to lead-based paint (Dixon et al., 2009). Address during pregnancy/early childhood was recorded and used to define whether the fetus/child spent most of his/her time in an urban residence (defined as within the confines of the city of Detroit) or a suburban residence. Prenatal and delivery records for WHEALS women were abstracted to obtain antibiotic and antifungal use (Wegienka et al., 2015), prenatal hemoglobin levels, body mass index (BMI) at the first prenatal care visit, delivery type, birth weight and gestational age at delivery. The American College of Obstetricians and Gynecologists definitions for maternal anemia vary by trimester of measurement (11 g/dl in first and third trimester; 10.5 g/dl in second trimester) (ACOG Practice Bulletin No. 95, 2008); because some women had multiple measures of hemoglobin over the course of pregnancy and potential uncertainty in pregnancy dating, we used ever having a hemoglobin < 10.5 g/dl as our definition of ever anemic. Gender- and gestational-age adjusted birth weight *Z*-scores were calculated using the US population as a reference (Oken et al., 2003). Children's medical records were abstracted to obtain hemoglobin values and were used to define anemia during childhood.

2.3. Analysis of metals in tooth samples

We directly measured metals in teeth using laser ablation-inductively coupled plasma mass spectrometry (LA-ICP-MS) and assigned developmental times as detailed elsewhere (Arora et al., 2012; Arora et al., 2014). Teeth were sectioned and the neonatal line (a histological feature formed in enamel and dentine at the time of birth) and incremental markings were used to assign temporal information to sampling points. We used an ArF excimer laser ablation system (ESI, USA) attached to an Agilent Technologies 8800 triple-quad ICP-MS. Data were analysed as metal-to-calcium ratios (e.g. $^{208}Pb{:}^{43}Ca$) to control for variations in mineral content within a tooth and between samples. Samples were analysed in two batches. Metal levels were measured at four times: second trimester, third trimester, early postnatal life (through ~age 1 year), and childhood (from ~age 1 year to time of tooth shedding which ranges from 6 to 12 years). National Institute of Standards and Technology SRM 612 was used for calibration and quality control. The detection limit was 0.05 μg/g for lead and manganese.

2.4. Statistical analysis

For descriptive purposes, maternal and child characteristics were compared by race (African American compared to white) using a chi-square test for discrete characteristics and ANOVA for continuous characteristics. Intraclass correlation coefficients (ICC) were calculated to determine the agreement in lead and manganese levels between teeth shed from the same child.

Racial differences in the time-specific metal levels were examined using GEE (Zeger and Liang, 1986) linear regression models with the individual metal as the outcome variable and race as the predictor variable. GEE accounts for potential correlation in measurements in the same tooth at different time points; an autoregressive working