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Body burdens of mercury, lead, selenium and copper among Baltimore newborns☆,☆☆

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ABSTRACT

Umbilical cord blood or serum concentrations of mercury, lead, selenium and copper were measured with inductively coupled plasma mass spectrometry in a population of 300 infants born in Baltimore, Maryland. Geometric mean values were 1.37 μg/L (95% confidence interval: 1.27, 1.48) for mercury; 0.66 μg/dL (95% CI: 0.61, 0.71) for lead; and 38.62 μg/dL (95% CI: 36.73, 40.61) for copper. Mean selenium was 70.10 μg/L (95% CI: 68.69, 70.52). Mercury, selenium and copper levels were within exposure ranges reported among similar populations, whereas the distribution of lead levels was lower than prior reports; only one infant had a cord blood lead above 10 μg/dL. Levels of selenium were significantly correlated with concentrations of lead (Spearman's $\rho=0.20$) and copper (Spearman's $\rho=0.51$). Multivariable analyses identified a number of factors associated with one of more of these exposures. These included: increase in maternal age (increased lead); Asian mothers (increased mercury and lead, decreased selenium and copper); higher umbilical cord serum $n-3$ fatty acids (increased mercury, selenium and copper), mothers using Medicaid (increased lead); increasing gestational age (increased copper); increasing birthweight (increased selenium); older neighborhood housing stock (increased lead and selenium); and maternal smoking (increased lead). This work provides additional information about contemporary prenatal element exposures and can help identify groups at risk of atypical exposures.

1. Introduction

In utero environmental exposures can have long term consequences to health and development. Mercury and lead are toxic metals that serve no useful purpose for human health and are recognized for their association with deficits in neurological development with early life exposure (Grandjean et al., 1998; Lanphear et al., 2005). On the other hand, selenium and copper are essential nutrients that are components of several proteins, including glutathione peroxidase (selenium) and cytochrome c oxidase (copper)

Abbreviations: BMI, body mass index; CI, confidence interval; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; ICP-MS, inductively coupled plasma mass spectrometry; ICP-DRC-MS, inductively coupled plasma dynamic reaction cell mass spectrometry; LOD, limit of detection; THREE, tracking health related to environmental exposures; CDC, United States Centers for Disease Control and Prevention

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(Navarro-Alarcon and Lopez-Martinez, 2000; Uriu-Adams et al., 2010). The possibility that selenium is protective against the toxic effects of methyl mercury through binding to mercury has been explored (Chen et al., 2006; Yoneda and Suzuki, 1997), but not confirmed in longitudinal epidemiology studies (Choi et al., 2008a; Saint-Amour et al., 2006). Outside of beneficial intake ranges, either elevated or reduced levels of selenium or copper can adversely affect health (Keen et al., 1998; Rayman, 2000; Stern et al., 2007). $n-3$ fatty acids are essential for healthy neurological development and may counteract negative effects of methyl mercury (National Research Council, 2007). Since fish is a source of methyl mercury, $n-3$ fatty acids, and selenium, these nutrients and toxicants may co-vary in the bodies of people who eat fish.

Little is known about fetal levels of toxic metals and elements that may be beneficial. While in the US there is a large-scale surveillance effort to track levels of mercury, lead, selenium and copper among older children and adults, in the United States Center for Disease Control and Prevention (CDC)'s National Health and Nutrition Examination Survey, there is no routine evaluation of fetal exposures. Recent epidemiology studies among non-Arctic European and North American populations have reported average umbilical cord blood or serum concentrations between 0.5 and 4.4 μg/L for mercury, 1–15.7 μg/dL for lead, 35–86 μg/L for selenium and 22–52 μg/dL for copper (Bjornberg et al., 2003; Devereux et al., 2007; Jedrychowski et al., 2007; Jones et al., 2010; Koppen et al., 2009; Lorenzo-Alonso et al., 2005; Morrissette et al., 2004; Osman et al., 2000; Palkovicova et al., 2008; Perveen et al., 2002; Rhainds et al., 1999; Schell et al., 2003; Schulpis et al., 2004; Takser et al., 2005; Vahter et al., 2000).

Blood lead levels in the U.S. generally are higher among minorities, people with lower socioeconomic status, and those living in older housing; sources of lead exposure include contaminated dust, water and food (Bernard and McGeehin, 2003; Rastogi et al., 2007). In the U.S. population, 80–90% of total mercury in blood is in the form of methyl mercury. Methyl mercury levels are the highest among those with higher fish and shellfish consumption, including coastal populations, health-conscious populations, and those of Asian ethnicity (Mahaffey, 2005; Tsuchiya et al., 2008). Volatilization of mercury from dental amalgams is a source of exposure to elemental mercury, which is transformed to inorganic mercury (Palkovicova et al., 2008). Selenium and copper intake occurs through dietary sources, primarily meats, fish and eggs for selenium, and cereals, nuts, organ meats and water for copper (Leblanc et al., 2005; Navarro-Alarcon and Cabrera-Vique, 2008). The relative importance of dietary sources varies by geographic region (Navarro-Alarcon and Cabrera-Vique, 2008).

Inadequate maternal seafood intake has been reported to have detrimental effects on child development (Hibbeln et al., 2007). A number of studies indicate that there are both risks of methyl mercury and benefits of nutrients unique to seafood consumption in child neurodevelopment (Strain et al., 2008; Choi et al., 2008b). Thus, both the World Health Organization and the United States Food and Drug Administration have drafted risk–benefit evaluations of seafood consumption (World Health Organization, 2010; US Food and Drug Administration, 2009).

The goal of this research was to describe concentrations of mercury, lead, selenium and copper in umbilical cord blood among an urban population, in the context of serum levels of $n-3$ fatty acids and other personal and demographic characteristics. Understanding the extent and correlations of current prenatal exposure to these elements is a key step in designing and implementing targeted public health actions to protect fetal health.

2. Materials and methods

The Baltimore THREE (Tracking Health Related to Environmental Exposures) Study is a cross-sectional study of births at the Johns Hopkins Hospital, Baltimore, Maryland. This study was conducted with the approval of the Maternal and Fetal Research Committee, Department of Gynecology and Obstetrics and the Johns Hopkins School of Medicine Institutional Review Board.

There were 603 deliveries (612 births) at the Johns Hopkins Hospital in Baltimore, Maryland, between November 2004 and March 2005. Some of these were ineligible for the THREE study because they were twin births ($n=24$ births, $n=12$ pairs), did not have umbilical cord blood available ($n=250$) or there was too little umbilical cord blood collected ($n=41$). This left a total of 300 births in the study. Of these, 294 samples were analyzed for mercury and lead and 287 samples were analyzed for selenium and copper.

Trained clinical staff obtained umbilical cord blood using standardized procedures. Cord blood was temporarily stored (<3 h) at 4 °C, after which aliquots of whole blood and serum were transferred to 2 mL cryovials. Samples were stored at −80 °C except during shipment to offsite laboratories for analyses, when they were packed in dry ice. Specimen containers and syringes were prescreened for elements and found to be free of contamination by mercury, lead, selenium and copper, which would be significant to the planned measurements. No maternal biological samples were collected for this study.

Total mercury and lead were measured in umbilical cord whole blood using inductively coupled plasma mass spectrometry (ICP-MS) (CDC, 2008a), and selenium and copper were measured in umbilical cord serum using inductively coupled plasma dynamic reaction cell mass spectrometry (ICP-DRC-MS) (CDC, 2008b) at CDC laboratories. Limits of detection (LOD) for elemental analyses were 0.33 μg/L (total mercury), 0.25 μg/dL (lead), 5 μg/L (selenium) and 4 μg/dL (copper). There were seven mercury and 13 lead samples below their respective limits of detection; these were set equal to $LOD/\sqrt{2}$. CDC laboratories also measured umbilical cord serum cotinine using liquid chromatography in conjunction with atmospheric pressure ionization mass spectrometry. This method has a limit of detection of 0.015 ng/mL, and 75 samples were below the limit of detection. Umbilical cord serum fatty acids, including $n-3$ fatty acids, were measured at the National Institute for Alcohol Abuse and Alcoholism in umbilical cord serum using fast gas chromatography in an automated system featuring a robotic apparatus. This automated method has been thoroughly tested against standard analytic techniques (Masood and Salem, 2008). The present analysis used a combination of the two most commonly detected $n-3$ highly unsaturated fatty acids: eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

Study personnel abstracted data from maternal and infant medical records and study clinicians reviewed a 10% random sample for accuracy. Maternal prepregnancy body mass index (BMI) was calculated as kilograms/meter from maternal height and prepregnancy weight data. Smoking status of mothers was based on a combination of self report and umbilical cord cotinine concentrations. Women who reported smoking during pregnancy and/or had an umbilical cord serum cotinine measurement >10 ng/mL were considered active smokers; the remainder were considered passive smokers or nonsmokers (CDC, 2005).

Maternal addresses were geocoded by GeoLytics, Inc. (East Brunswick, NJ) and study staff using TerraServer USA (Microsoft Corporation and the United States Geological Survey) or ESRI ArcMap 9.0 (Redlands, CA). These were matched with United States Census 2000 block group data to obtain the median year of housing construction. A block group is a subset of a census tract consisting of several contiguous blocks. On average, 1500 people reside in a block group. Median household income was based on 1999 values from the US Census.

Stata 11.1 (College Station, Texas) was used for statistical analyses. Mercury, lead and copper all had lognormal distributions; therefore, their means were reported as geometric means. In contrast, selenium had a normal distribution, so arithmetic means were used. Correlations between elements were analyzed using Spearman's correlation coefficients, as this method is independent of the distribution of the variables. Analysis of variance, nonparametric tests for trend and nonparametric smoothing curves (lowess curves) were used to evaluate concentrations of elements across categories of personal or neighborhood characteristics (data not shown).

Descriptive multivariable models were used to describe which characteristics were independently associated with concentrations of elements in umbilical cord blood or serum. Four different linear multivariable regression models were constructed, each using a different element as the dependent variable. Individual characteristics thought *a priori* to be potential confounders were included in every model. These were maternal age, race, insurance, prepregnancy weight, smoking status, gestational length and infant birth weight. To account for possible exposure via fish and seafood, levels of $n-3$ fatty acids (as measured by the sum of DHA+EPA) were included in the model for mercury. Since U.S. homes built before 1955 are more likely to contain leaded paint (Rabin, 1989), average year of neighborhood home construction was included in the model for lead. As little is known regarding descriptors of selenium and copper in umbilical cord serum, both $n-3$ fatty acid levels and average year of neighborhood home construction were included in selenium and copper models. Covariates were described categorically if the variable was inherently categorical (race, insurance, smoking status, etc.) or differences are reasonably expected to be observed by categories as described above (smoking, age of housing, etc.). Other covariates were tested to determine whether linear, quadratic or a cubic spline provided the best fit, based on Akaike's and Schwarz's Bayesian information criteria. Linear terms were the best fit for all covariates.