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Methyl mercury, but not inorganic mercury, associated with higher blood pressure during pregnancy

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Abstract

Prior studies addressing associations between mercury and blood pressure have produced inconsistent findings; some of this may result from measuring total instead of speciated mercury. This cross-sectional study of 263 pregnant women assessed total mercury, speciated mercury, selenium, and n-3 polyunsaturated fatty acids in umbilical cord blood and blood pressure during labor and delivery. Models with a) total mercury or b) methyl and inorganic mercury were evaluated. Regression models adjusted for maternal age, race/ethnicity, prepregnancy body mass index, neighborhood income, parity, smoking, n-3 fatty acids and selenium. Geometric mean total, methyl, and inorganic mercury concentrations were 1.40 µg/L (95% confidence interval: 1.29, 1.52); 0.95 µg/L (0.84, 1.07); and 0.13 µg/L (0.10, 0.17), respectively. Elevated systolic BP, diastolic BP, and pulse pressure were found, respectively, in 11.4, 6.8, and 19.8% of mothers. In adjusted multivariable models, a one-tertile increase of methyl mercury was associated with 2.83 mmHg (0.17, 5.50) higher systolic blood pressure and 2.99 mmHg (0.91, 5.08) higher pulse

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pressure. In the same models, an increase of one tertile of inorganic mercury was associated with a -1.18 mmHg (-3.72, 1.35) lower systolic blood pressure and -2.51 mmHg (-4.49, -0.53) lower pulse pressure. No associations were observed with diastolic pressure. There was a non-significant trend of higher total mercury with higher systolic blood pressure. We observed a significant association of higher methyl mercury with higher systolic and pulse pressure, yet higher inorganic mercury was significantly associated with lower pulse pressure. These results should be confirmed with larger, longitudinal studies.

Keywords

Mercury; methylmercury compounds; inorganic mercury compounds; blood pressure; pregnancy

Introduction

Cardiovascular health is a major public health concern. More than 1 in 3 United States adults have some form of cardiovascular disease; cardiovascular disease and stroke are the leading cause of mortality in the United States (Lloyd-Jones et al., 2010). Cardiovascular disease risk factors such as exercise, weight, and blood pressure are also of high prevalence; therefore, the burden of cardiovascular disease is expected to continue over the next several decades (Lloyd-Jones et al., 2010). Of particular concern is hypertension among pregnant women, as hypertension during this period has been associated with future cardiovascular disease risk (Wilson et al., 2003).

Methyl mercury is a recognized neurological toxin; however, cardiovascular toxicity may also be an important outcome of mercury exposure (Virtanen et al., 2007). The main route of methyl mercury exposure is from consumption of fish and seafood. Literature on the relationship of mercury exposure with cardiovascular related outcomes showed inconsistent results. A large cohort study (n=1857) from Finland identified significant associations between total mercury in hair and acute cardiac death (Virtanen et al., 2012a). Myocardial infarction was also associated with total toenail mercury in a multinational case-control study (Guallar et al., 2002). However, several nested case-control studies showed no association of total mercury in toenails (Mozaffarian et al., 2011; Yoshizawa et al., 2002), or blood with coronary heart disease, myocardial infarction, or cardiovascular disease.

A similar, mixed pattern appears with more subtle changes in cardiovascular health. Some studies have identified a link between total mercury in blood (Valera et al., 2009), hair (Yorifuji et al., 2010), or toenails (Choi et al., 2009) and worsening of cardiovascular risk factors such as blood pressure and heart rate variability; other studies using total whole blood (Nielsen et al., 2012) and urinary mercury (Park et al., 2013) have shown protective results. Of note is that none of the studies above focused on pregnant women. Although pregnancy is a lifestage of heightened susceptibility for cardiovascular risk, very few studies have focused on the potential effect of mercury exposures on cardiovascular health during pregnancy (Vigeh et al., 2006).

The differences in observed impact from mercury exposure noted above may be explained in part by differences in study methodology. In addition to mercury, fish and seafood are also

sources of selenium and n-3 polyunsaturated fatty acids (n-3 PUFAs); both of these may provide benefits and act as negative confounders (Choi et al., 2008). It is known that different chemical forms of mercury have different toxicokinetics (Clarkson and Magos, 2006). However, studies to date mostly have relied on measurements of total mercury as a proxy for specific forms of mercury, which may result in errors of attribution. Additionally, the extent to which selenium and n-3 PUFAs have been included in the literature is variable; this makes it difficult to compare the studies to each other as well as to understand the true relationship of methyl mercury and cardiovascular risk (Karagas et al., 2012).

The goal of this research is to determine the association of total, methyl and inorganic mercury with blood pressure, while accounting for the potential for negative confounding by selenium and n-3 PUFAs. To evaluate this goal, we completed a cross-sectional study of pregnant women from Baltimore, Maryland.

Materials and Methods

The Baltimore THREE Study (Tracking Health through Environmental Exposures) is a cross-sectional birth cohort. This study was conducted with approval of the Johns Hopkins School of Medicine Institutional Review Board as well as the Johns Hopkins Department of Gynecology and Obstetrics' Maternal and Fetal Research Committee.

Details on the study design and data management have been published previously (Wells et al., 2012). Briefly, inclusion criteria included having a singleton birth at the Johns Hopkins Hospital from November 2004-March 2005 and availability of sufficient umbilical cord blood to conduct laboratory analyses; 300 out of 612 births met these criteria. Given our exclusion of infants from multiple births, and the fact that low birthweight infants were more likely to have insufficient cord blood for laboratory analyses, this study population had somewhat fewer low birth weight infants compared to all births at the hospital. Otherwise, the study population was representative of all births at Johns Hopkins Hospital during this time. However, it was not a representative sample of the community as a whole (Herbstman et al., 2007). For the current analysis, births without data on total mercury (n=8), smoking status (n=1), median household income (n=4), umbilical cord serum fatty acids (n=12), selenium (n=11), and blood pressure (n=3) were also excluded from analyses. Therefore, a total of 263 mothers were included in analyses.

Umbilical cord blood was collected by trained clinical staff, using standardized techniques (Witter et al., 2001). Metals were analyzed at the Inorganic and Radiation Analytical Toxicology Branch at the United States Centers for Disease Control and Prevention (CDC) using inductively coupled plasma mass spectrometry (ICP-MS). The method for total mercury (THg) was assessed using whole blood SRM955c standards; accuracy of measurements with this method are within 5% of target values (Jones et al., 2017). The limit of detection (LOD) for THg in our samples was 0.33 µg/L (THg); the six samples <LOD were replaced with LOD/ 2 for analyses.

Additionally, inorganic mercury (IHg), methyl mercury (MeHg) and ethyl mercury (EtHg) were measured using high performance liquid chromatography linked with inductively

coupled plasma mass spectrometry, this method is described in detail previously (Sommer et al., 2014; Verdon et al., 2008). Only one infant had an EtHg level > the LOD, so EtHg values are not included in this analysis. The other LODs for mercury compounds were 0.48 µg/L (MeHg) and 0.75 µg/L (IHg). The method accuracy was verified using whole blood reference materials from NIST (SRM 955c Level 3) and Centre de Toxicologie du Québec whole blood proficiency testing samples. The relative standard deviations were 8.3% (IHg) and 6.3% (MeHg); results analyzed by our method compared to certified target values with a slope of 1.05 and $r^2=0.986$, all falling within certified ranges (Sommer et al., 2014).

There were 44 MeHg and 201 IHg values below the limit of detection (LOD). Because MeHg and IHg had a high proportion (>10%) of values <LOD, we first imputed values <LOD using values that were observed via spectrometry even while being below the LOD; 24 of MeHg and 125 of IHg observations met this criterion. The remainder of values, 20 (7.6%) MeHg and 76 (28.9%) IHg observations that were not quantifiable (i.e., not detected) were imputed using the lowest observed value divided by the square root of two. Imputed values have a greater coefficient of variation in comparison to values >LOD. To minimize the potential impact of this uncertainty, mercury measurements were classified as tertiles for analyses (high/medium/low). Sensitivity analyses using mercury as a continuous variable were also conducted to confirm that the use of tertiles did not substantially influence our results.

Continuous blood pressure measurements were collected as part of routine care during labor and delivery with a General Electric Corometrics model 120 series fetal monitor (GE Healthcare, Little Chalfont, UK). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) at the time of admission to labor and delivery was extracted from medical records, as described previously (Wells et al., 2012). Elevated blood pressure was defined as SBP ≥ 140 mmHg or DBP ≥ 90 mmHg; given the differences in recommended data collection used in this study, these were not considered tantamount to the presence of hypertension. Pulse pressure (PP) was calculated from both the average and maximum estimates as SBP minus DBP. PP ≥ 60 mmHg was considered elevated. Medical records were used to identify diagnoses of chronic hypertension, pregnancy-related hypertension, and use of hypertensive medications; having any of these was considered having hypertension during pregnancy.

Umbilical cord serum was used to assess serum selenium, cotinine, and fatty acids. The CDC's Inorganic and Radiation Analytical Toxicology Branch measured umbilical cord serum selenium concentrations using inductively coupled plasma dynamic reaction cell mass spectrometry (ICP-DRC-MS); these measures were verified using serum reference materials. The LOD for selenium was 5 µg/L; all measurements were >LOD. Our previous work suggested that there is a nonlinear association between selenium and blood pressure; therefore, selenium was incorporated into models using a linear spline with a knot at the median value (70 µg/L) (Wells et al., 2012). CDC laboratories assessed umbilical cord serum cotinine using liquid chromatography in conjunction with atmospheric pressure ionization mass spectrometry; LOD was 0.015 ng/mL.

Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in umbilical cord serum were determined at the National Institute of Alcohol Abuse and Alcoholism using automated

fast gas chromatography (Lin et al., 2012). Accuracy for both fatty acids are >99% or higher in comparison to the conventional methods (Lepage and Roy assay), and both within-run and between-run coefficient of variance was <5% (Lin et al., 2012). All fatty acid values were above the LOD, which was 0.15 µg/L. The sum of EPA+DHA was used in analyses.

Additional information, including maternal age, race/ethnicity, height, prepregnancy weight, parity, self-reported smoking, and address, were extracted from maternal and infant medical records. Women were classified as smoking during pregnancy if this was noted in the medical record or umbilical cord cotinine concentration was ≥ 10 ng/mL (Hukkanen et al., 2005). Prepregnancy body mass index (BMI) was calculated from prepregnancy weight and height as kg/m². BMI was categorized using the World Health Organization standards: underweight or normal weight (<25.0 kg/m²), overweight (25.0-29.9 kg/m²), and obese (≥ 30 kg/m²). Maternal address of record was used to determine the mother's neighborhood of residence; median household income within these neighborhoods was determined using United States Census 2000 data. After being used to match to neighborhoods, addresses were expunged from the records.

All analyses were conducted using Stata 12.1 (College Station, TX). All mercury variables had lognormal distributions; therefore mercury data are described either in tertiles or as geometric means. Geometric mean mercury measurements were stratified by elevated versus normal blood pressure measurements, and these bivariate associations were evaluated using Student's t-test. Selenium and EPA+DHA were not lognormally distributed and are described using arithmetic means.

Multivariable linear regression models were constructed to evaluate the change in blood pressure measurement compared to mercury tertile, characterized as an ordinal variable. Models evaluated methyl and inorganic mercury jointly, but total mercury separately. Potential covariates were evaluated based on descriptive analyses within this dataset, as well as prior literature (Choi et al., 2008; Karagas et al., 2012). Adjusted models controlled for maternal age (continuous), maternal race/ethnicity (white/black/Asian), prepregnancy body mass index (continuous), median neighborhood household income (continuous), primiparous (yes/no), maternal smoking during pregnancy (yes/no), umbilical cord serum EPA+DHA (continuous) and umbilical cord serum selenium (continuous).

Results

Multiple population characteristics were considered (Table 1). Mean maternal age was 25.8 years (95% confidence interval (CI): 25.0, 26.6). The majority of mothers were African American; less than 10% of mothers were of Asian race/ethnicity. Mean neighborhood household income was approximately \$35,000/year. Slightly less than 20%, 10% and 50% of mothers smoked during pregnancy, had hypertension during pregnancy and were overweight or obese prior to pregnancy. Mean maternal blood pressure measurements were 122.3 mmHg (95% CI: 120.5, 124.1) for SBP; 71.5 mmHg (95% CI: 70.1, 73.0) for DBP; and 50.8 mmHg (95% CI: 49.4, 52.1) for PP.

The ranges of blood mercury concentrations for total, methyl and inorganic mercury were <LOD-16.8 µg/L, ND-15.4 µg/L and ND-2.17 µg/L, respectively (Table 2, Supplemental Figures S1-S2). There were 5 (1.9%) MeHg measurements higher than the reference dose for MeHg proposed by the National Research Council, 5.8 µg/L (National Research Council, 2000). Overall, the percentage of MeHg to THg is 74.6% (95% CI: 71.2, 78.1); for IHg to THg this is 29.1% (95% CI: 23.6, 34.6). The percentage of MeHg to THg increased with increasing concentrations of THg. Average MeHg/THg was 66.2% (95% CI: 58.0, 74.4) for those in the lowest tertile of THg, 69.9% (95% CI: 65.4, 74.4%) for those in the middle tertile of THg, and 87.9% (95% CI: 85.2%, 90.6%) for those in the highest tertile of THg.

Umbilical cord serum selenium ranged from 42 to 114 µg/L (Table 2, Supplemental Figures S1-S2). The majority of EPA+DHA (Table 2) consisted of DHA: mean EPA was 1.7 µg/mL (95% CI: 1.6, 1.8) and mean DHA was 47.3 µg/mL (95% CI: 45.7, 49.0).

Table 3 presents correlations between mercury species, selenium and fatty acids. THg and MeHg are very highly correlated (Spearman's $\rho=0.91$) and IHg is somewhat correlated with both THg ($\rho=0.53$) and MeHg ($\rho=0.51$). Scatterplots of THg, MeHg, and IHg are presented as Supplemental Figure S3. There was a smaller correlation of EPA+DHA with all of the other compounds (ρ ranging from 0.19 to 0.27); but selenium was not correlated with any mercury species.

Bivariate associations of mercury compounds with demographic characteristics were assessed using unadjusted regression models or Fisher's exact tests (Supplemental Figure S4). Increasing age was significantly associated with increased THg and IHg and was approaching significance with MeHg ($p=0.08$). African American and Asian mothers had significantly higher THg and MeHg, but not IHg, compared to Caucasian mothers. No other significant correlations of mercury species with demographic characteristics were observed. Increased selenium was significantly associated with decreased maternal age, lower median household income, and there was a non-significant trend towards increased selenium correlated with African American race/ethnicity (compared to Caucasian). No association of EPA+DHA was observed with age or race/ethnicity. Increased EPA+DHA was observed with the highest category of median household income (vs. the lowest category), but this did not reach statistical significance ($p=0.09$).

Bivariate relationships between blood pressure measurements and mercury levels are presented in Table 4. A significant bivariate association was observed only between PP and IHg.

Unadjusted associations between mercury species and blood pressure are presented in Supplemental Tables 1a, 2a, and 3a. Multivariable model results are presented in Table 5 and Supplemental Tables 1b, 2b, and 3b. In adjusted models, there was a statistically significant association between a one-tertile increase in MeHg with higher SBP and PP at each tertile. A one-tertile increase in IHg was associated with significantly lower PP in adjusted models. Higher THg was related to higher SBP in adjusted models ($p=0.066$). No measure of mercury was associated with DBP. Results from sensitivity analyses using continuous measures of mercury instead of tertiles are shown in supplementary material. Results using

continuous measures of mercury were similar, although somewhat reduced in magnitude, compared to models using tertiles of mercury.

Higher SBP or DBP were also significantly associated with higher prepregnancy BMI, primiparity, and smoking during pregnancy. Higher DBP was also associated with older age. Higher pulse pressure was significantly associated with higher prepregnancy BMI. Point estimates for the relationship of EPA+DHA with blood pressure suggests an inverse relationship (i.e., a protective effect); however, this was not statistically significant. The relationship of selenium with blood pressure appears to be nonlinear; for those with selenium below median values (70 µg/L) increasing selenium was associated with decreased blood pressure; however, for those with selenium higher than 70 µg/L increasing selenium was associated with increased blood pressure. However, these relationships were not statistically significant. Full results for each model are presented in the supplementary information.

Discussion

We report a significant association between higher concentrations of MeHg in cord blood with higher SBP and PP among mothers in regression models controlling for IHg, selenium, and EPA+DHA. In the same models we also observed a significant association of higher IHg with lower PP. We did not observe a statistically significant association of total mercury with any measure of blood pressure nor any measure of mercury with diastolic blood pressure. The magnitude of the changes we observed are relatively small; however, given that exposure to mercury is widespread in the population, these small changes among individuals can result in substantial changes to population prevalence of elevated blood pressure.

PP appeared to be more strongly related to blood methyl mercury concentrations than SBP. PP may be elevated as a result of increased arterial stiffness and/or increased mean blood pressure. PP has been found to be an independent predictor of future cardiovascular risk (Safar et al., 2003). PP is widely used in the literature, including several recent studies on whole blood total mercury (Valera et al., 2011a; Valera et al., 2011b) toenail mercury (Mordukhovich et al., 2012), or hair mercury (Valera et al., 2011a; Virtanen et al., 2012b); however, only one reported an association of PP with mercury, and this was only observed in unadjusted analyses (Valera et al., 2011a).

Several studies report no association of SBP or DBP with THg in blood among women (Nielsen et al., 2012), in both sexes (Bautista et al., 2009; Valera et al., 2011b), or among fish consumers (Vupputuri et al., 2005); with THg in hair (Bautista et al., 2009; Virtanen et al., 2012b); or with toenail mercury (Mordukhovich et al., 2012). While Valera et al. observed a crude association of blood mercury with both SBP and DBP in a population of Canadian Cree, this did not persist after adjustment for confounders, including serum n-3 PUFAs and selenium (Valera et al., 2011a). Additional studies found significant associations of SBP but not DBP with blood THg among non-fish consumers in the United States (Vupputuri et al., 2005); hair mercury taken from adults in the Brazilian Amazon (Fillion et al., 2006); and Nunavik Inuit (Valera et al., 2009). Similarly, Xun and colleagues reported that the combination of high toenail mercury and low Se appeared to attenuate the protective

effect of n-3 PUFAs on hypertension (Xun et al., 2011). As noted earlier, none of these studies evaluated MeHg and IHg exposures; therefore these data are most appropriately compared with our models of that include total blood mercury only, which was weakly associated with systolic blood pressure.

Among populations with very high fish consumption, measurements of THg biomarkers have been hypothesized to reflect a higher proportion of MeHg (Oskarsson et al., 1996). This could be one explanation for why studies of populations with high fish consumption – villagers along the Amazon River (Fillion et al., 2006), Inuit (Valera et al., 2009), or Faroese whaling men (Choi et al., 2009) – observed significant associations of THg measurements with SBP or DBP where general population studies did not. This would be consistent with our models that included methyl mercury and inorganic mercury.

Urinary mercury concentrations, reflecting exposure to IHg, have been associated with a lower SBP among United States adults in the 2003-2006 NHANES (Park et al., 2013) and dental professionals (Goodrich et al., 2013); the latter study notes this was driven by associations among males. This is consistent with our observations that inorganic mercury was associated with a lower in PP. A mechanism to explain why total and methyl mercury are associated with higher blood pressure whereas increases in urine or inorganic mercury appear to be associated with lower blood pressure is currently unknown. Nor is it understood whether a similar distinction exists with neurological impairment related to mercury exposure. However, given that several studies have now consistently observed these associations, further research incorporating measurements of speciated mercury in cardiovascular as well as neurological studies is recommended.

Several prior findings are inconsistent with our results, specifically: among the 2003-2006 NHANES study blood THg was associated with decreased SBP (Park et al., 2013); blood THg was associated with decreased DBP among 1,861 Inuit men from Greenland (Nielsen et al., 2012); and blood THg was associated with increased DBP, but not SBP among 2,114 healthy Korean adults (Eom et al., 2014). There are several possible explanations for these differences. There is substantial variation in the methods used to control for selenium and/or n-3 PUFAs. Several studies used fish consumption (Bautista et al., 2009; Choi et al., 2009; Eom et al., 2014; Mordukhovich et al., 2012; Mozaffarian et al., 2012), or dietary recall questionnaires (Park et al., 2013) instead of quantitative measures of Se or n-3 PUFAs, which may result in misclassification of these variables. Our study population Another potential contributor to differences in study results could be differences in underlying genetic, such as genetic susceptibility for cardiovascular disease, between the different populations studied. Finally, only a few prior reports include a longitudinal component (Choi et al., 2009; Mozaffarian et al., 2012; Xun et al., 2011). Also, two of these studies evaluated mercury in much higher ranges of exposure than our study (Eom et al., 2014; Nielsen et al., 2012). Geometric mean blood THg levels were: Greenland males 20.5 µg/L; Greenland females 14.7 µg/L; and Korean adults, 3.90 µg/L.

This study has several limitations. It is cross-sectional, thus exposures and outcomes were measured concurrently. It used umbilical cord blood mercury levels as a proxy biomarker of maternal mercury exposure; however, this may be interpreted as a minor limitation, as there

is a high correlation between umbilical cord mercury and maternal blood mercury concentrations (Sakamoto et al., 2010). Given the observations that mercury tends to concentrate in umbilical cord blood as compared to maternal blood (Sakamoto et al., 2010), our measurements of mercury may be somewhat elevated; however, our approach of classifying mercury exposure into tertiles served to minimize bias due to choice of biomarker and this limitation thus should not affect the validity of our overall conclusions. Blood pressure measurements were taken in a clinical setting, at admission to labor and delivery, where participants may have been experiencing some stress. These measurements are likely somewhat higher than blood pressures taken using recommended protocols for hypertension. However, as reported previously these blood pressure measurements were highly correlated with assessment of hypertension in the medical record (Wells et al., 2012). Thus, we feel there is sufficient justification to use these measurements to distinguish relative blood pressure among these women.

This study also has several strengths. We obtained high-quality laboratory measurements for selenium, n-3 PUFAs, and total mercury. We were able to obtain speciated mercury measurements and thus to assess methyl mercury and inorganic mercury levels specifically. Additionally our study focuses on a sample of women with mercury exposure which is somewhat above average compared with United States estimates, but substantially lower than studies conducted in populations with very high seafood consumption and/or located in arctic regions. Thus, our results are more reflective of the range of exposures potentially faced by a larger segment of the population. Our results suggest that assessment of the specific form of mercury, as well as selenium and n-3 PUFAs as potential confounders, is worth considering in the development of future studies on mercury and cardiovascular health.

In conclusion, among this cross-sectional study of women during childbirth, we observed a statistically significant association of higher MeHg with higher SBP and PP and of higher IHg with lower PP. Our results provide supporting information for the potential impact of methyl mercury with higher blood pressure and are consistent with prior reports that inorganic mercury may be associated with lower blood pressure; however, they should be confirmed with larger, prospective studies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

LOD	Limit of detection
BMI	Body mass index
CDC	United States Centers for Disease Control and Prevention
CI	Confidence interval
DBP	Diastolic blood pressure
DHA	Docosahexaenoic acid
EHg	Ethyl mercury
EPA	Eicosapentaenoic acid
Hg	Mercury

ICP	DRC-MS-Inductively coupled plasma dynamic reaction cell mass spectrometry
ICP	MS-Inductively coupled plasma mass spectrometry
IHg	Inorganic mercury
MeHg	Methyl mercury
ND	Not detected
PP	Pulse pressure
SBP	Systolic blood pressure
THg	Total mercury
THREE	Tracking Health Related to Environmental Exposures
US EPA	United States Environmental Protection Agency

Highlights

- We compared total, methyl and inorganic mercury with blood pressure in pregnancy.
- Models controlled for n-3 fatty acids, selenium, and other variables.
- Methyl mercury was associated with higher systolic blood pressure and pulse pressure.
- Inorganic mercury was associated reduced pulse pressure.
- There were no significant associations of total mercury with blood pressure.

Table 1
Study population characteristics, Baltimore THREE Study, 2004-2005

Characteristic	<i>n</i>	Percent	95% Confidence Interval
Entire population	263	100.0	--
Age			
< 20 years	55	20.9	16.4, 26.3
20-29 years	127	48.3	42.3, 54.4
30 years	81	30.8	25.5, 36.7
Race/ethnicity			
White/Caucasian	54	20.5	16.1, 25.9
Black/African American	188	71.5	65.7, 76.6
Asian	21	8.0	5.2, 12.0
Median household income			
< \$25,000	80	30.4	25.1, 36.3
\$25,000-\$50,000	142	54.0	47.9, 60.0
> \$50,000	41	15.6	11.7, 20.5
Parity			
Primiparous	110	41.8	36.0, 47.9
Multiparous	153	58.2	52.1, 64.0
Hypertension during pregnancy			
No	239	90.9	86.7, 93.8
Yes	24	9.1	6.2, 13.3
Smoking during pregnancy			
No	214	81.4	76.2, 85.7
Yes	49	18.6	14.3, 23.8
Prepregnancy BMI			
< 25 kg/m ²	133	50.6	44.5, 56.6
25-29 kg/m ²	65	24.7	19.8, 30.3
30 kg/m ²	65	24.7	19.8, 30.3
	<i>n</i>	Mean	95% Confidence Interval
Age, years	263	25.8	25.0, 26.6
Median household income, thousands	263	35.1	32.7, 37.5
Prepregnancy BMI, kg/m ²	263	26.5	25.7, 27.4
Serum cotinine (nonsmokers), ng/mL ^a	213	0.06	0.05, 0.08
Serum cotinine (smokers only), ng/mL ^a	49	29.2	16.0, 53.2
Systolic blood pressure	263	122.3	120.5, 124.1
Diastolic blood pressure	263	71.5	70.1, 73.0
Pulse pressure	263	50.8	49.4, 52.1

THREE = Tracking Health Related to Environmental Exposures; BMI = body mass index.

^aGeometric mean is presented.

Table 2
Concentration of mercury, selenium, and EPA+DHA in umbilical cord blood or serum, Baltimore THREE Study, *n*=263

Compound	Mean (95% CI)	Geometric mean (95% CI)	Range, by tertile of compound		
			1 st tertile	2 nd tertile	3 rd tertile
Total mercury, µg/L	1.77 (1.58, 1.97)	1.40 (1.29, 1.52)	< LOD – 1.12	1.13–1.76	1.77–16.8
Methyl mercury, µg/L	1.45 (1.26, 1.65)	0.95 (0.84, 1.07)	ND – 0.78	0.79–1.44	1.45–15.4
Inorganic mercury, µg/L	0.43 (0.38, 0.48)	0.13 (0.10, 0.17)	ND – 0.07	0.08–0.57	0.58–2.17
Selenium, µg/L	69.8 (68.4, 71.3)	68.8 (67.3, 70.3)	42.0–64.0	65.0–75.0	76.0–114.0
EPA+DHA, µg/mL	49.0 (47.3, 50.8)	47.2 (45.7, 48.8)	21.6–41.6	41.7–52.2	52.3–116.9

THREE = Tracking Health Related to Environmental Exposures; CI = confidence interval; LOD = limit of detection; ND = not detected; EPA = eicosapentaenoic acid; DHA = docosahexaenoic acid

Table 3

Spearman's correlation coefficient (p-value) for mercury, selenium, and EPA+DHA in umbilical cord blood or serum, Baltimore THREE Study, $n=263$

	THg, µg/L	MeHg, µg/L	IHg, µg/L	Selenium, µg/L	EPA+DHA, µg/mL
THg, µg/L	--				
MeHg, µg/L	0.907 (<0.001)	--			
IHg, µg/L	0.528 (<0.001)	0.506 (<0.001)	--		
Selenium, µg/L	0.021 (0.738)	-0.018 (0.767)	-0.055 (0.371)	--	
EPA+DHA, µg/mL	0.268 (<0.001)	0.234 (<0.001)	0.160 (0.008)	0.188 (0.002)	--

THREE = Tracking Health Related to Environmental Exposures; THg = total mercury; MeHg = methyl mercury; IHg = inorganic mercury; EPA = eicosapentaenoic acid; DHA = docosahexaenoic acid

Table 4
Geometric mean umbilical cord methyl mercury and inorganic mercury concentrations
by blood pressure status, Baltimore THREE Study, 2004-2005, $n=263$

Blood pressure measurement	n (%) ^a	Geometric mean (95% CI)		
		Total mercury	Methyl mercury	Inorganic mercury
Systolic blood pressure				
< 140 mmHg	233 (88.6)	1.40 (1.28, 1.52)	0.94 (0.82, 1.07)	0.14 (0.10, 0.18)
140 mmHg	30 (11.4)	1.42 (1.08, 1.87)	1.04 (0.72, 1.50)	0.10 (0.04, 0.22)
Diastolic blood pressure				
< 90 mmHg	245 (93.2)	1.38 (1.27, 1.51)	0.94 (0.83, 1.06)	0.13 (0.10, 0.17)
90 mmHg	18 (6.8)	1.62 (1.18, 2.23)	1.11 (0.67, 1.84)	0.10 (0.03, 0.32)
Pulse pressure				
< 60 mmHg	211 (80.2)	1.42 (1.30, 1.56)	0.96 (0.84, 1.10)	0.15 (0.12, 0.20) ^b
60 mmHg	52 (19.8)	1.31 (1.08, 1.59)	0.90 (0.67, 1.20)	0.07 (0.04, 0.13) ^b

THREE = Tracking Health Related to Environmental Exposures; CI = confidence interval

^aPercents may not sum to 100 due to rounding

^bSignificant difference in mercury levels between elevated versus non elevated blood pressure, Student's *t*-test, $p<0.05$.

Table 5
Change (95% confidence interval) in blood pressure measurement with a one-tertile increase in mercury, Baltimore THREE Study, 2004-2005, $n=263$

Model	Variable	Change in mmHg (95% CI)		
		SBP	DBP	PP
THg only, unadjusted ^a	THg	1.57 (-0.63, 3.77)	1.29 (-0.46, 3.05)	0.28 (-1.42, 1.98)
THg only, adjusted ^b	THg	2.13 (-0.14, 4.40) ^e	1.43 (-0.40, 3.26)	0.70 (-1.10, 2.50)
MeHg and IHg, unadjusted ^c	MeHg	2.23 (-0.35, 4.81) ^e	-0.04 (-2.10, 2.02)	2.27 (0.30, 4.23) ^f
	IHg	-1.56 (-4.13, 1.02)	1.23 (-0.83, 3.30)	-2.79 (-4.76, -0.83) ^f
MeHg and IHg, adjusted ^d	MeHg	2.83 (0.17, 5.50) ^f	-0.16 (-2.32, 2.00)	2.99 (0.91, 5.08) ^f
	IHg	-1.18 (-3.72, 1.35)	1.32 (-0.73, 3.38)	-2.51 (-4.49, -0.53) ^f

THREE = Tracking Health Related to Environmental Exposures; CI = confidence interval; SBP = systolic blood pressure; DBP = diastolic blood pressure; PP = pulse pressure; THg = total mercury; MeHg = methyl mercury; IHg = inorganic mercury

^aUnadjusted model with total mercury as the independent variable.

^bModel includes covariates for total mercury, age, race/ethnicity, median neighborhood household income, prepregnancy body mass index, smoking during pregnancy, EPA+DHA and selenium.

^cUnadjusted model with methyl and inorganic mercury as independent variables.

^dModel includes covariates for methyl mercury, inorganic mercury, age, race/ethnicity, median neighborhood household income, prepregnancy body mass index, smoking during pregnancy, EPA+DHA and selenium.

^e p -value < 0.10

^f p -value < 0.05