**Determinants of prenatal exposure to polybrominated diphenyl ethers (PBDEs) among urban, minority infants born between 1998-2006**

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**ABSTRACT**

Polybrominated diphenyl ethers **(**PBDEs) are environmentally persistent chemicals that structurally resemble legacy pollutants, such as polychlorinated biphenyls (PCBs). PBDEs were added to consumer products for over 30 years, before being phased out due to evidence of toxicity. We examined temporal changes in prenatal exposure to PBDEs, as well as other sources of variation. We measured PBDEs in umbilical cord plasma from 327 minority infants born in New York City between 1998 and 2006.We used linear regression to examine changes in concentrations over time and in relation to lifestyle characteristics collected during pregnancy. We detected BDE-47 in 80% of samples with a geometric mean concentration of 14.1 ng/g lipid. Ethnicity was the major determinant of PBDE exposure; African American infants had 58% higher geometric mean cord plasma concentrations of BDE-47 (p<0.01) compared to Dominican infants. Notably, African American mothers were more likely to be born in the United States, which itself was associated with 40% (p<0.01) higher concentrations. We observed small decreases in PBDE concentrations by date of birth and no difference before and after their phase-out in 2004. Final multivariable models explained 8-12% of variability in PBDE concentrations depending on the congener. Our finding that prenatal exposure to PBDEs decreased only modestly between 1998 and 2006 is consistent with the lipophilic properties of PBDEs and their ongoing release from existing consumer products.

**Keywords**: PBDE, flame retardant, prenatal, exposure

**Capsule:** PBDEs are detectable in cord blood and concentrations decreased marginally between 1998 and 2006. U.S. compared to foreign born mothers deliver infants with higher PBDE concentrations.

Following a 1975 fire-safety law passed by the state of California, companies across the United States began adding polybrominated diphenyl ethers (PBDEs) to couches, chairs and other upholstered products, including those designed for infants and children (1, 2). Industry has primarily relied on three commercial formulations, which each consist of several PBDE congeners that vary in the number and location of bromine atoms around a diphenyl ether backbone (3). Over time, PBDEs migrate away from consumer products and enter house dust (4). In the United States, human exposure occurs primarily through incidental ingestion of dust, with consumption of meat, fish and dairy products considered secondary sources (5). PBDEs are classified as persistent organic pollutants (POPs). Structurally, they resemble several organohalogenated pollutants with known human toxicity, including polybrominated biphenyls (PBBs) and polychlorinated biphenyls (PCBs) (3). PBDEs are persistent, bioaccumulative and capable of long-range transport once released into the environment (6). Due to their lipophilic properties, PBDEs bioaccumulate in adipose tissue, cross the placenta, and partition into breastmilk (4, 5). As previously reviewed (7, 8), research examining human exposure has documented associations between PBDEs and endocrine disruption, reproductive problems and neurodevelopmental deficits. Owing to these health and environmental concerns, the three major commercial formulations were phased out of production in the United States between 2004 (PentaBDE, OctaBDE) and 2013 (DecaBDE) (9, 10). Despite these phase-outs, existing consumer products that are infrequently replaced, such as upholstered furniture, continue to release PBDEs, therefore, it is likely that only minimal reductions in human body burden will occur as these products progressively removed from the indoor environment. In this study, we examined time trends and other potential determinants of prenatal exposure to PBDEs, including ethnicity, in a low-income, minority cohort of infants born between 1998 and 2006.

**METHODS**

**Study population**

We conducted this study among a subset of 727 participants enrolled in the Columbia Center for Children’s Environmental Health (CCCEH) Mothers and Newborns birth cohort, which was designed to examine sub-clinical health effects associated with prenatal exposure to several environmental chemicals. Women with a singleton pregnancy were recruited from two prenatal clinics in Northern Manhattanbetween 1998 and 2006. Women were excluded if they were younger than 18 or older than 35 years, started prenatal care after the 20th week of pregnancy, were active smokers, had a history of drug abuse, or had diabetes, hypertension or known HIV infection (11). All study protocols were approved by the Institutional Review Board of Columbia University; it was determined that the Centers for Disease Control and Prevention were not engaged in human subjects’ research. Before each study visit, mothers were informed about all study procedures and provided written informed consent to participate.

**Data collection**

At the prenatal visit, trained research workers conducted structured interviews to ascertain information on demographic and several lifestyle factors, including material hardship and environmental tobacco smoke exposure. We defined material hardship as the inability to afford food, clothing or housing, and assessed environmental tobacco smoke (ETS) exposure by maternal report of smokers in the home as previously described (12). We assessed home cleaning habits by asking question about the frequency of vacuuming and mopping. After birth, we abstracted data related to the pregnancy, delivery, and newborn from hospital medical records.

**Umbilical cord blood collection and PBDE analysis**

At delivery, umbilical cord blood was collected by hospital staff and transported to the CCCEHlaboratory where samples were processed and stored in multiple aliquots at -70°C. Staff at the CDC measured 11 PBDE congeners (BDE-17, -28, -47, -66, -85, -99, -100, -153, -154, -183, and 209) in stored umbilical cord plasma (13, 14). Briefly, after fortification with internal standards, plasma samples were extracted using a Gilson 215 liquid handler (Gilson Inc., Middleton, WI) and lipids were removed on a Rapid Trace modular SPE work station (Biotage, Uppsala, Sweden). Final analytic concentrations were determined by gas chromatography isotope dilution high-resolution mass spectrometry on a DFS instrument (ThermoFisher, Bremen, Germany). Blanks (N=3) were processed with every 30 samples and the median blank value was subtracted from the final result. Serum lipids (total cholesterol and triglycerides) were measured using commercially available test kits (Roche Diagnostics, Indianapolis, IN) and total blood lipids were estimated using a recently developed cord blood-specific formula [total cord blood lipids = 2.657 × total cord blood cholesterol + cord blood triglycerides + 0.2680, in g lipids/L plasma] (A Sjodin, unpublished data, November 2016].

**PBDE predictors**

We reviewed published literature to identify potential determinants of PBDE exposure related to: 1) the mother (ethnicity, country of birth, residential history, age at delivery, education, relationship status, parity, time since previous pregnancy, and employment during pregnancy); 2) the newborn (sex, birthweight, gestational age); and 3) the household (material hardship, cleaning habits, environmental tobacco smoke) for which we had collected information during the prenatal period.

**Statistical analysis**

*Distribution-based multiple imputation of non-detected concentrations*

We focused our analysis on BDEs-47 (detection frequency: 80%), -99 (50%), -100 (42%) and -153 (38%), which, consistent with previous research, were the most frequently detected congeners. We natural-log transformed each congener concentration to better approximate a normal distribution and examined each as a continuous, lipid-adjusted variable. We imputed concentrations below the limit of detection (LOD) using a distribution-based multiple imputation approach (R function available in Supplemental Information Table 1 and LODs available in Supplemental Information Table 2). Specifically, to account for each sample’s unique LOD, which is proportional to the available plasma volume and lipid content, we randomly drew a value from a congener-specific distribution of detected data for which the LOD was less than or equal to that of the non-detected concentration. We repeated the imputation procedure 10 times and pooled parameter estimates for all subsequent analyses using the Multiple Imputation by Chained Equations (MICE) R package.

*Predictors of cord plasma PBDE concentrations*

We examined descriptive statistics for each potential determinant identified from our review of the literature. To evaluate whether children without a measure of PBDEs were different from those with a measure of PBDEs, we conducted student’s t, Wilcoxon-Mann-Whitney, and Pearson’s chi-square tests to identify differences in predictors among participants included and those excluded from this analysis for not having a measure of PBDEs.

We used linear regression to model the association between the child’s date of birth and natural-log transformed PBDE concentrations (ng/g lipid). We treated date of birth as a continuous variable and examined units of both days and years. In addition to time, we examined effect estimates and p-values from models between PBDE concentrations and other potential predictors, which we included in a multivariable model if the univariate p-value was less than 0.1. We visualized our findings by plotting geometric mean PBDE concentrations within levels of each predictor, with continuous variables dichotomized at the median.

A woman’s ancestry, geography, language, religion, lifestyle and cultural traditions shape her ethnicity. In turn, these factors may influence individual determinants of PBDE exposure. For example, PBDEs sorb to dust particles and ethnicity may influence home cleaning habits. Therefore, to better understand the impact of ethnicity on exposure, we examined potential determinants of cord blood PBDE concentrations among African American and Dominican participants in separate models. These models included the same predictors examined in unstratified models. We further identified demographic and lifestyle differences between African American and Dominican participants using student’s t-tests and Pearson’s chi-square tests for categorical and continuous variables, respectively.

Finally, several characteristics that have been previously associated with PBDE concentrations, such as maternal age (15), may affect cord blood lipid levels (16). Therefore, we used linear regression to model the association between each potential determinant and total cord blood lipid levels (mg lipid/dL blood). We performed all analyses using RStudio (v0.99.891) or SAS (v9.4).

**RESULTS**

**Study population**

Of the 727 children fully enrolled in the Mothers and Newborns cohort, 577 (79%) had a cord blood sample collected at delivery. We quantifiedPBDEs in umbilical cord plasma from 327 of these 577 infants (57%), which included cord blood from all available stored samples. Table 1 presents demographic and lifestyle characteristics of the study sample. All maternal-child pairs are African American (n=121) or Dominican (n=206) and at delivery all mothers resided in Northern Manhattan or the South Bronx. Among the African American mothers, 96% were born in the United States, compared to only 22% of Dominican mothers; of mothers born outside of the United States, 86% were born in the Dominican Republic. At delivery, 35% of mothers had less than a high school education and 39% reported experiencing material hardship. On average, infants with a measure of PBDEs were born earlier during the enrollment period (p<0.01), weighed more at birth (p<0.01) and were more often born to a nulliparous mother (p<0.01) compared to infants without a measure of PBDEs. We detected no other significant differences between mother-child pairs included in the present analysis and those excluded. Among participants with a PBDE measure, we found several significant differences by ethnicity. On average, African American mothers were younger (p=0.01), had a higher pre-pregnancy body mass index (p<0.01), gained less weight during pregnancy (p=0.04), delivered lower birthweight babies (p<0.01) with shorter gestations (p<0.01), were less frequently in a stable relationship while pregnant (p<0.01) and were enrolled earlier during the study period (p<0.01). With regard to the home environment, African American mothers were less likely to experience material hardship (p<0.01) or use a wet mop for cleaning (p<0.01), but more likely to use a damp mop (p<0.01), vacuum (p<0.01) and be exposed to environmental tobacco smoke (p<0.01).

**Distribution of cord plasma PBDEs**

We detected BDEs-47, -99, -100 and -153 in 80%, 50%, 42% and 38% of cord plasma samples, respectively. Supplemental Table 3 presents detection frequencies for all 11 congeners measured. As illustrated by Figure 1, BDEs-47, -99, -100, and -153 concentrations were log-normally distributed with geometric means of 14.1 ng/g lipid, 3.7 ng/g lipid, 2.9 ng/g lipid, and 2.6 ng/g lipid, respectively. As expected given their shared use in the PentaBDE mixture, these four congeners were moderately to highly correlated (mean rspearman between congeners across 10 imputed datasets: 0.42-0.80, p<0.01; see Supplemental Table 4, which provides correlation coefficients for each congener comparison).

*Change in concentration of cord plasma PBDEs over time.*

As illustrated by Figure 2, we observed small reductions in BDEs-47 (3%), 99 (5%), and 100 (3%) per year of birth when examined over the entire enrollment period (1998 to 2006), however, this decrease was only statistically significant for BDE-99 (p=0.04). When we adjusted for ethnicity, decreases in concentrations were attenuated and the association with BDE-99 was no longer significant. When stratified by ethnicity, temporal decreases in concentration were larger among African American (2% decrease in BDE-47 per 8 years) compared to Dominican (0.5% decrease in BDE-47 per 8 years) infants (see Supplemental Material Figure 1). We detected no change in BDE-153 concentration over the enrollment period. We did not find significantly different PBDE concentrations among infants born before compared to after the PentaBDE phase-out in 2004 (p=0.13-0.60).

*Predictors of cord plasma PBDE concentrations.*

Our final multivariable models included 12 predictors, which are detailed below and collectively explained a low amount of variability in cord plasma BDE-47 (12%), BDE-99 (11%), BDE-100 (10%), and BDE-153 (8%) concentrations. Figure 3 presents geometric mean PBDE concentrations from univariate models between predictors and each congener. We found that higher concentrations were associated with (1) African American [vs. Dominican] ethnicity, (2) maternal birth in [vs. outside] the United States, (3) younger maternal age at delivery [continuous in days], (4) lower maternal educational attainment [less than high school vs. high school degree or equivalent], (5) single relationship status [vs. married or in a stable relationship for 7 or more years], (6) male sex of study child [vs. female], (7) longer gestation [continuous in weeks], (8) earlier date of birth of study child [continuous in days], and (9) prenatal environmental tobacco smoke exposure [any vs. none]. With regard to maternal cleaning habits, (10) vacuuming [ever vs. never] was associated with higher concentrations and (11) damp mopping [ever vs. never] was associated with lower concentrations. (12) Wet mopping [ever vs. never] was associated with higher BDE-153 concentrations, but not with the other three congeners studied (see Supplemental Table 5, which provides effect sizes and p-values for each association).

Ethnicity was the major determinant of PBDE exposure; African American infants had 58%, 56% and 35% higher geometric mean cord plasma concentrations of BDE-47 (p<0.01), BDE-99 (p<0.01) and BDE-100 (p<0.01) compared to Dominican infants, respectively. Notably, African American mothers were more likely to be born in the United States, which itself was associated with 40% (p<0.01), 31% (p=0.01) and 24% (p=0.04) higher concentrations of BDE-47, BDE-99, and BDE-100. We did not find relations between BDE-153 and ethnicity or maternal birthplace. Among a subset of 167 Dominican mothers (81%) with information about lifetime residential history, we found that for every 10% of life lived in the United States, her infant’s cord plasma BDE-47 concentration increased by 4% (p=0.03). We detected similar, but statistically insignificant changes for BDE-99 (p=0.11) and BDE-100 (p=0.10). We did not detect an association between residential history and BDE-153.

Of the other 10 variables included in our final multivariable model, six significantly varied by ethnicity, with Dominican mothers typically having characteristics associated with lower PBDE concentrations (older, more likely to be in a stable relationship, less likely to be exposed to environmental tobacco smoke, less likely to vacuum). The exceptions were that Dominican mothers had longer pregnancies and were more likely to use a wet mop. When stratified by ethnicity, depending on the congener, our multivariable models explained 11-19% of variability in PBDE concentrations among Dominican mothers and 15-18% of variability among African American mothers. We did not detect significant associations between any variable included in our final models and cord plasma total lipid levels.

**DISCUSSION**

We measured cord plasma PBDE concentrations in 327 minority infants born in New York City between 1998 and 2006; this is the largest United States-based study of umbilical cord PBDE concentrations. We detected BDE-47, which is typically the dominant congener found in humans, in 80% of samples and BDEs-99, -100, and -153 each in at least 35% of samples. These four congeners are components of the PentaBDE mixture, which was voluntarily phased out of United States commerce in 2004 (9).

PBDE concentrations in our samples were similar to levels detected in umbilical cord (15, 19, 20) or maternal blood (17, 18, 21, 22) within seven other United States-based studies (see Supplemental Table 6, which compares mean concentrations across studies). While enrollment in previous studies spanned only one to three years, we were able to examine time trends in exposure over an eight-year period that overlapped with the phase-out of PentaBDE. We found modest reductions in PBDE concentrations by year of birth (3-5% depending on the congener) and no significant difference in concentrations among infants born before versus after the PentaBDE phase-out in 2004. In a recent analysis of PBDE stocks and flows, Abbasi et al estimated that approximately 46,000 tons of PentaBDE were used in consumer products in the United States and Canada between 1970 and 2004, with a peak application of approximately 17,000 tons in 2004 (1). Given these trends and the use of PBDEs in products that are infrequently replaced, it is not surprising that we detected only modest decreases over time and no significant difference between children born before versus after the 2004 phase-out. We expect exposure will continue to decrease and dominant sources of exposure may shift as PBDE-containing products enter end-of-life stages and are removed from the indoor environment. For example, as PBDE-containing furniture enters waste streams, contamination of air and water may occur via volatilization and leaching from landfills. Given these shifting exposure sources, monitoring landfills for PBDE emissions will be an important step in understanding the environmental burden of PBDEs in coming decades. Additionally, as time since the PBDE phase-out progresses, socioeconomic disparities in PBDE exposure may widen, as lower income families may infrequently replace furniture or may purchase older, second-hand items manufactured before the phase-out.

Among the sociodemographic and lifestyle factors considered, ethnicity was the most important determinant of cord plasma BDE-47, -99 and -100, with Dominican infants typically having lower concentrations. Notably, the majority of Dominican mothers were born in the Dominican Republic, where PBDEs may not have been routinely used as flame retardants in consumer products. The importance of the mother’s birthplace is further supported by our finding of a positive association between cord plasma BDE-47 and proportion of lifetime lived in the United States. However, the modest size of this relation (4% increase in concentration for every 10% increase in proportion of life lived in the United States) suggests that exposure conditions present during the mother’s early life may be important determinants of body burden during adulthood. Our findings are consistent with results from a California-based study that found PBDE concentrations were higher among pregnant women born in the United States compared to Mexico or Latin America and increased with the duration of time lived in the United States (17). Likewise, an independent New York City-based study of pregnant women found PBDE concentrations in maternal blood were higher among African American women compared to Hispanic women (18).

In addition to birthplace, the PBDE concentration disparity between African Americans and Dominicans may relate to differences in lifestyle and daily habits. For example, African American mothers were more likely to vacuum, which was associated with higher cord plasma PBDE concentrations. This is consistent with a recent study that reported household vacuuming frequency was positively associated with PBDE concentrations measured in silicon wristbands worn by children (23). It is plausible that the physical agitation of dust particles that occurs during the vacuuming process contributes to increased ingestion and inhalation of dust. Using a damp mop was associated with lower concentrations, especially for BDEs-100 and -153; in contrast to the direction observed with other predictors, this behavior was significantly more common among African American mothers. Conversely, Dominican mothers were more likely to use a wet mop, which was associated with higher BDE-153 concentrations. While poorly understood, this finding is consistent with the results from a recent study based in Spain, which found housekeeping frequency was positively associated with cord blood BDE-153, but not BDEs-47, -99 or -100 (24).

Dominican mothers were significantly less likely to be single or exposed to environmental tobacco smoke, both of which were associated with higher PBDE concentrations. Our finding of lower concentrations among children born to older mothers is consistent with previous research (15). While it is plausible that older women have lower body burdens due to increased child bearing, we did not find significant associations between PBDE concentrations and parity or time since previous delivery. Alternatively, this finding may reflect the older age of Dominican compared to African American mothers in our sample. In contrast to these patterns, African American infants had shorter gestations, which was associated with lower concentrations, possibly related to the reduced time opportunity for *in utero* transfer.

Other determinants of PBDE exposure included in our final multivariable model that did not vary by ethnicity included maternal education and infant gender. We found mothers with less than a high school degree delivered infants with higher PBDE concentrations. This is consistent with the results of a Baltimore-based study (15), but in contrast to findings from a cohort in California (17). Notably, the California study found maternal education was positively associated with years of residency in the United States, which itself was associated with higher PBDE exposure. Conversely, they found that higher income, which was not related to residency, was associated with lower exposure. Other studies measuring PBDEs in child or adult blood have reported similar trends, with higher neighborhood poverty, lower household income and lower educational attainment typically associated with higher exposure (25, 26).

Finally, boys had higher cord plasma concentrations of BDE-153 compared to girls. This finding is consistent with results from the National Health and Nutrition Examination Survey, which found higher serum concentrations of BDE-153, but not other congeners, among male compared to female participants (27). While the mechanisms underlying these findings are poorly understood, placental transfer of PBDEs is known to vary by bromination status, with lower brominated congeners characterized by faster and more extensive passage (4). Furthermore, while little information exists on placental gene expression in relation to PBDEs, expression of genes involved in regulation of nutrient transport has been shown to be sexually dimorphic (28), thus it is plausible that placental transfer of BDE-153, which is the highest molecular weight congener we studied, is impeded to a greater extent among girls compared to boys due to differential expression of transport genes. Importantly, however, this putative mechanism is inconsistent with findings from a recent study that reported higher concentrations of BDE-209, which is fully brominated, in placentas from male pregnancies (29). More research is needed to understand how sex may contribute to differences in fetal exposure to PBDEs and other environmental chemicals.

In contrast to previous studies, we found no associations between PBDE concentrations and pre-pregnancy body mass index (15, 17). Likewise, we found no relation between concentrations and weight gain during pregnancy or birthweight, and between any maternal characteristic and cord plasma lipid levels.

We identified several important predictors of PBDE exposure, including ethnicity, however, the majority of variation in cord plasma concentrations remained unexplained by our final models. Additional factors that may be plausibly associated with PBDE exposure that we did not measure include breastfeeding of previous children, bedroom and living room floor type, the number of electronics and furniture pieces containing polyurethane foam in the home, and personal behaviors, such as handwashing and nail biting. While we did have information on kitchen floor type for 84% of participants, we found little variability, with the majority (77%) of homes having a smooth surface. We did collect limited information on the mother’s diet, including meat and fish consumption, during pregnancy, however, these data focused on cooking styles rather than consumption quantity and did not include information on dairy products. In addition to these other exposure sources and pathways, individual concentrations may vary due to inter-individual differences in genes involved in metabolism and excretion of PBDEs.

Over 95% of PentaBDE produced globally has been used in North America, where the general population has the highest body burden in the world (7). In 2004, PentaBDE was phased-out of United States commerce owing to evidence of environmental persistence and human toxicity. In 2009, it was added to the Stockholm Convention’s list of persistent organic pollutants, prompting member countries to eliminate production and new use (3). Despite these measures, exposure to PBDEs will continue for decades due to their continued release from furniture and other consumer products. Indeed, we detected only modest reductions in cord plasma concentrations over an eight-year period. Further, we found that maternal birthplace was an important predictor of exposure, with foreign-born mothers delivering babies in the United States with significantly lower cord plasma PBDE concentrations compared to U.S. born mothers.

Future research is needed to better understand modifiable behaviors that may reduce exposure to PBDEs in the home environment. For example, while vacuuming might reasonably be assumed to reduce exposure, we found vacuuming frequency during pregnancy was associated with higher cord plasma PBDE concentrations, likely due to the emission of dust into the air. We did not have information about personal vacuum characteristics, however, it is plausible that high efficiency particulate air (HEPA) filters may help reduce exposure during the vacuuming process. Importantly, HEPA vacuums are generally more expensive than standard filtration vacuums and may be less affordable for lower income households. Moreover, we found lower maternal education, an indicator of socioeconomic status and resource availability, was associated with higher exposure, echoing concerns by other research groups that disparities in PBDE exposure may be an environmental equity issue (26).

Finally, despite amendments to California’s flammability standard (30) and the availability of chemical-free fire safety approaches, including the use of smoke detectors, sprinkler systems, reduced ignition propensity cigarettes and fire safe candles, evidence indicates companies have been replacing PBDEs with alternative flame retardant chemicals that have unknown toxicity (31). Development of federal and state requirements for testing replacement chemicals, especially those that have properties similar to PBDEs and other POPs, before they are added to consumer products is critical for preventing future global contamination with toxic and environmentally persistent chemicals.

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| **Table 1 -** Demographic and Lifestyle Characteristics of Study Participants with a Measure of PBDE Exposure Enrolled between 1998 and 2006 in a New York City-Based Birth Cohort |
| N (%) or Mean±SD | All (n=327)a | African American (n=121) | Dominican (n=206) |
| Maternal characteristics at delivery |  |  |  |
|  African American | 121 (37) | (100) |  |
|  Dominican | 206 (63) |  | 206 (100) |
|  Born in the United States\* | 161 (49) | 116 (96) | 45 (22) |
|  Age (years)\* | 25.1±4.9 | 24.2±4.9 | 25.6±4.8 |
|  Less than high school education | 114 (35) | 43 (36) | 71 (34) |
|  Married or in a stable relationship\* | 81 (25) | 16 (13) | 65 (22) |
|  Office work during pregnancy | 36 (11) | 13 (11) | 23 (11) |
|  Pre-pregnancy body mass index\* | 26.0±6.1 | 27.3±6.7 | 25.2±5.6 |
|  Weight gain during pregnancy (kg)\* | 17.1±6.8 | 16.1±6.6 | 17.8±6.9 |
|  Nulliparous | 166 (51) | 58 (48) | 108 (52) |
|  Years since previous pregnancyb | 2.2±2.3 | 2.3±2.2 | 2.1±2.3 |
| Child characteristics |  |  |  |
|  Male | 149 (46) | 51 (42) | 98 (48) |
|  Gestational age (months)\* | 39.4±1.3 | 39.1±1.4 | 39.5±1.2 |
|  Birth weight (kg)\* | 3.4±0.4 | 3.4±0.5 | 3.5±0.4 |
|  Birth year: 1998-2000\* | 176 (54) | 81 (67) | 95 (46) |
|  Birth year: 2001-2003\* | 88 (27) | 24 (20) | 64 (31) |
|  Birth year: 2004-2006\* | 63 (19) | 16 (13) | 47 (23) |
| Household characteristics |  |  |  |
|  At least one material hardship\* | 127 (39) | 35 (29) | 92 (45) |
|  Tobacco smoke exposure in home\* | 115 (35) | 56 (46) | 59 (29) |
|  Ever vacuum to clean floors\* | 56 (18) | 32 (27) | 24 (12) |
|  Ever damp mop to clean floors\* | 183 (57) | 81 (68) | 102 (51) |
|  Ever wet mop to clean floors\* | 189 (59) | 57 (48) | 132 (66) |
| aMissing (n): pre-pregnancy BMI (10), weight gain (36), ever vacuum (11), ever damp mop (8), ever wet mop (9); bincludes all previous pregnancies carried to the third trimester.\*African American and Dominican participants significantly different at the p=0.05 level.  |

**Figure 1.** Measured and imputed concentrations (ng/g lipid) measured in cord plasma collected from infants born in New York City between 1998 and 2006.



Note: plots generated using data from 1 of the 10 imputed datasets.



**Figure 3. PBDE concentrations in umbilical cord plasma collected from children born in New York City between 1998 and 2006 stratified by lifestyle and demographic and lifestyle characteristics (n=327).**



**REFERENCES**

1. Abbasi G, Buser AM, Soehl A, Murray MW, Diamond ML. Stocks and flows of PBDEs in products from use to waste in the U.S. and Canada from 1970 to 2020. Environ Sci Technol 2015;49(3):1521-8.

2. Stapleton HM, Klosterhaus S, Keller A, Ferguson PL, van Bergen S, Cooper E, et al. Identification of flame retardants in polyurethane foam collected from baby products. Environ Sci Technol 2011;45(12):5323-31.

3. UNEP. Listing of POPs under the Stockholm convention. In. Chatelaine, Switzerland: The Stockholm Convention, United Nations Environmental Programme; 2012.

4. Frederiksen M, Vorkamp K, Thomsen M, Knudsen LE. Human internal and external exposure to PBDEs--a review of levels and sources. Int J Hyg Environ Health 2009;212(2):109-34.

5. Lorber M. Exposure of Americans to polybrominated diphenyl ethers. J Expo Sci Environ Epidemiol 2008;18(1):2-19.

6. Law RJ, Covaci A, Harrad S, Herzke D, Abdallah MA, Fernie K, et al. Levels and trends of PBDEs and HBCDs in the global environment: status at the end of 2012. Environ Int 2014;65:147-58.

7. Fromme H, Becher G, Hilger B, Volkel W. Brominated flame retardants - Exposure and risk assessment for the general population. Int J Hyg Environ Health 2016;219(1):1-23.

8. Linares V, Belles M, Domingo JL. Human exposure to PBDE and critical evaluation of health hazards. Arch Toxicol 2015;89(3):335-56.

9. Corportation GLC. Great Lakes Chemical Corporation completes phase-out of two flame retardants. In. Indianapolic, IN: Great Lakes Chemical Corportation; 2005.

10. USEPA. DecaBDE Phase-out Initiative. In; 2010.

11. Perera FP, Rauh V, Whyatt RM, Tsai WY, Tang D, Diaz D, et al. Effect of prenatal exposure to airborne polycyclic aromatic hydrocarbons on neurodevelopment in the first 3 years of life among inner-city children. Environ Health Perspect 2006;114(8):1287-92.

12. Rauh VA, Whyatt RM, Garfinkel R, Andrews H, Hoepner L, Reyes A, et al. Developmental effects of exposure to environmental tobacco smoke and material hardship among inner-city children. Neurotoxicol Teratol 2004;26(3):373-85.

13. Jones R, Edenfield E, Anderson S, Zhang Y, Sjodin A. Semi-automated extraction and cleanup method for measuring persistent organic pollutants in human serum. Organohalogen Comp 2012;74:97-98.

14. Sjodin A, Jones RS, Lapeza CR, Focant JF, McGahee EE, 3rd, Patterson DG, Jr. Semiautomated high-throughput extraction and cleanup method for the measurement of polybrominated diphenyl ethers, polybrominated biphenyls, and polychlorinated biphenyls in human serum. Anal Chem 2004;76(7):1921-7.

15. Herbstman JB, Sjodin A, Apelberg BJ, Witter FR, Patterson DG, Halden RU, et al. Determinants of prenatal exposure to polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) in an urban population. Environ Health Perspect 2007;115(12):1794-800.

16. Kazemi SA, Sadeghzadeh M. Lipid Profile of Cord Blood in Term Newborns. J Compr Ped 2014;5(4):e23759.

17. Castorina R, Bradman A, Sjodin A, Fenster L, Jones RS, Harley KG, et al. Determinants of serum polybrominated diphenyl ether (PBDE) levels among pregnant women in the CHAMACOS cohort. Environ Sci Technol 2011;45(15):6553-60.

18. Horton MK, Bousleiman S, Jones R, Sjodin A, Liu X, Whyatt R, et al. Predictors of serum concentrations of polybrominated flame retardants among healthy pregnant women in an urban environment: a cross-sectional study. Environ Health 2013;12:23.

19. Herbstman JB, Sjodin A, Kurzon M, Lederman SA, Jones RS, Rauh V, et al. Prenatal exposure to PBDEs and neurodevelopment. Environ Health Perspect 2010;118(5):712-9.

20. Mazdai A, Dodder NG, Abernathy MP, Hites RA, Bigsby RM. Polybrominated diphenyl ethers in maternal and fetal blood samples. Environ Health Perspect 2003;111(9):1249-52.

21. Stapleton HM, Eagle S, Anthopolos R, Wolkin A, Miranda ML. Associations between polybrominated diphenyl ether (PBDE) flame retardants, phenolic metabolites, and thyroid hormones during pregnancy. Environ Health Perspect 2011;119(10):1454-9.

22. Vuong AM, Webster GM, Romano ME, Braun JM, Zoeller RT, Hoofnagle AN, et al. Maternal Polybrominated Diphenyl Ether (PBDE) Exposure and Thyroid Hormones in Maternal and Cord Sera: The HOME Study, Cincinnati, USA. Environ Health Perspect 2015;123(10):1079-85.

23. Kile ML, Scott RP, O'Connell SG, Lipscomb S, MacDonald M, McClelland M, et al. Using silicone wristbands to evaluate preschool children's exposure to flame retardants. Environ Res 2016;147:365-72.

24. Costa O, Lopez-Espinosa MJ, Vizcaino E, Murcia M, Iniguez C, Navarrete-Munoz EM, et al. Dietary and Household Sources of Prenatal Exposure to Polybrominated Diphenyl Ethers (PBDEs) in the INMA Birth Cohort (Spain). Environ Sci Technol 2016;50(11):5935-5944.

25. Darrow LA, Jacobson MH, Preston EV, Lee GE, Panuwet P, Hunter RE, Jr., et al. Predictors of Serum Polybrominated Diphenyl Ether (PBDE) Concentrations among Children Aged 1-5 Years. Environ Sci Technol 2017;51(1):645-654.

26. Zota AR, Adamkiewicz G, Morello-Frosch RA. Are PBDEs an environmental equity concern? Exposure disparities by socioeconomic status. Environ Sci Technol 2010;44(15):5691-2.

27. Sjodin A, Wong LY, Jones RS, Park A, Zhang Y, Hodge C, et al. Serum concentrations of polybrominated diphenyl ethers (PBDEs) and polybrominated biphenyl (PBB) in the United States population: 2003-2004. Environ Sci Technol 2008;42(4):1377-84.

28. Rosenfeld CS. Sex-Specific Placental Responses in Fetal Development. Endocrinology 2015;156(10):3422-34.

29. Leonetti C, Butt CM, Hoffman K, Hammel SC, Miranda ML, Stapleton HM. Brominated flame retardants in placental tissues: associations with infant sex and thyroid hormone endpoints. Environ Health 2016;15(1):113.

30. Technical Bulletin 117-2013. In. Sacramento, CA: State of California, Department of Consumer Affairs; 2013. p. 1-13.

31. Stapleton HM, Sharma S, Getzinger G, Ferguson PL, Gabriel M, Webster TF, et al. Novel and high volume use flame retardants in US couches reflective of the 2005 PentaBDE phase out. Environ Sci Technol 2012;46(24):13432-9.

**SUPPLEMENTAL INFORMATION**

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**Supplemental Figure 1** – Temporal change in BDE-47 Concentrations Measured in Umbilical Cord Blood Collected from Infants Born in New York City between 1998 and 2006, Stratified by Ethnicity (n=327)

**Supplemental Table 1** –Steps to Distribution-Based Multiple Imputation

For each sample with a concentration less than the limit of detection (LOD), count the number of congener-specific detected samples with a concentration less than the LOD of the non-detected sample.

* If the number of available observations ≥ 2
	+ Calculate the mean and variance of ln(PBDE) from the available observations
	+ Draw a random value from the normal distribution with the same mean and variance
		- BDE-47: 98%, BDE-99: 98%, BDE-100: 99.5%, BDE-153: 100%
* If the number of available observations = 1
	+ Use the available ln(PBDE) to fill in the non-detected value
		- BDE-47: 0%, BDE-99: 0%, BDE-100: 0.5%, BDE-153: 0%
* If the number of available observations = 0
	+ Replace non-detected concentration with ln(LOD/2)
		- BDE-47: 2%, BDE-99: 2%, BDE-100: 0%, BDE-153: 0%

**R Function**

PBDE: PBDE concentration

LOD: limit of detection

Ln\_PBDE: natural log transformed PBDE concentration

impute.func=function(pbde, lod, ln\_pbde){

  missing.index=which(is.na(pbde))

  for(i in missing.index){

    n.available=sum(pbde<lod[i], na.rm=T)

    if(n.available>1){

      mu=mean(ln\_pbde[which(pbde<lod[i])], na.rm=T)

      sd=sd(ln\_pbde[which(pbde<lod[i])], na.rm=T)

      ln\_pbde[i]=rnorm(n=1, mean=mu, sd=sd)

    }else if(n.available==1){

      ln\_pbde[i]=ln\_pbde[which(pbde<lod[i])]

    }else if(n.available==0 & !is.na(lod[i])){

      ln\_pbde[i]=log(lod[i]/2)

    }else if(is.na(lod[i])){

      ln\_pbde[i]=mean(log(pbde), na.rm=T)

    }

  }

  return(ln\_pbde)

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| **Supplemental Table 2** - Limits of Detection for Detected and Not Detected Concentrations of Four Polybrominated Diphenyl Ether (PBDE) Congeners Measured in Umbilical Cord Plasma Collected from Infants Born between 1998 and 2006 in New York City (n=327)  |
|  | DetectedRange, ng/g lipid (n) | Not-DetectedRange, ng/g lipid (n) | Percent of Non-Detected Samples with LODs in the Range of Detected Sample LODs |
| BDE-47 | 0.69-9.14 (261) | 2.60-11.59 (66) | 98 |
| BDE-99 | 0.41-5.46 (165) | 0.91-5.40 (161) | 98 |
| BDE-100 | 0.29-5.46 (136) | 0.94-5.40 (191) | 100 |
| BDE-153 | 0.29-5.10 (123) | 1.14-5.46 (204) | 100 |

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| **Supplemental Table 3** - Detection Frequencies for 11 Polybrominated Diphenyl Ether (PBDE) Congeners Measured in Umbilical Cord Plasma Collected from Infants Born between 1998 and 2006 in New York City (n=327) |
|  | Detected, n (%) | Not Detected, n (%) | Not Reportable, n (%) |
| BDE-17 | 0 (0) | 327 (100) | 0 (0) |
| BDE-28 | 48 (15) | 279 (85) | 0 (0) |
| BDE-47 | 261 (80) | 66 (20) | 0 (0) |
| BDE-66 | 16 (5) | 310 (95) | 1 (<1) |
| BDE-85 | 31 (9) | 296 (91) | 0 (0) |
| BDE-99 | 165 (50) | 161 (49) | 1 (<1) |
| BDE-100 | 136 (42) | 191 (58) | 0 (0) |
| BDE-153 | 123 (38) | 204 (62) | 0 (0) |
| BDE-154 | 11 (3) | 316 (97) | 0 (0) |
| BDE-183 | 10 (3) | 317 (97) | 0 (0) |
| BDE-209 | 6 (2) | 321 (98) | 0 (0) |

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| **Supplemental Table 4** – Correlationsa (RSpearman, p-values) between Four PBDE Congeners (ng/g lipid) Measured in Umbilical Cord Plasma Collected from Infants Born between 1998 and 2006 in New York City (n=327) |
|  | BDE-47 | BDE-99 | BDE-100 | BDE-153 |
| BDE-47 |  | 0.80 (<0.01) | 0.70 (<0.01) | 0.44 (<0.01) |
| BDE-99 | 0.80 (<0.01) |  | 0.68 (<0.01) | 0.42 (<0.01) |
| BDE-100 | 0.70 (<0.01) | 0.68 (<0.01) |  | 0.52 (<0.01) |
| BDE-153 | 0.44 (<0.01) | 0.42 (<0.01) | 0.52 (<0.01) |  |
| aValues are the mean correlation coefficient across 10 imputed datasets |

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| **Supplemental Table 5** - Associations between Umbilical Cord Plasma PBDE Concentrations (ng/g lipid) and Several Demographic and Lifestyle Factors Measured in a Sample of Mothers and Infants Born between 1998 and 2006 in New York City (n=327) |
| Significantly higher levels at p ≤ 0.10 | Ln BDE-47 | Ln BDE-99 | Ln BDE-100 | Ln BDE-153 |
| Significantly lower levels at p ≤ 0.10 | β±SE | p | β±SE | p | β±SE | p | β±SE | p |
| African American vs. Dominican ethnicity | 0.45±0.08 | <0.01 | 0.44±0.11 | <0.01 | 0.30±0.10 | <0.01 | 0.07±0.08 | 0.36 |
| Born in the United States vs. foreign born | 0.34±0.12 | <0.01 | 0.27±0.11 | 0.01 | 0.22±0.11 | 0.05 | 0.01±0.07 | 0.91 |
| Age (per year) | -0.04±0.01 | <0.01 | -0.02±0.01 | 0.09 | -0.01±0.01 | 0.28 | 0.00±0.01 | 0.72 |
| High school or more vs. less | -0.27±0.13 | 0.03 | -0.10±0.11 | 0.38 | -0.11±0.10 | 0.28 | 0.00±0.08 | 0.97 |
| Stable relationship  | -0.51±0.14 | <0.01 | -0.36±0.12 | <0.01 | -0.28±0.12 | 0.02 | -0.12±0.09 | 0.18 |
| Office work during pregnancy  | -0.26±0.19 | 0.18 | -0.23±0.17 | 0.19 | -0.11±0.16 | 0.51 | -0.19±0.13 | 0.14 |
| Pre-pregnancy body mass index (kg/m2) | 0.01±0.01 | 0.22 | 0.01±0.01 | 0.51 | 0.00±0.01 | 0.67 | -0.01±0.01 | 0.17 |
| Weight gain during pregnancy (kg) | 0.00±0.01 | 0.92 | 0.01±0.01 | 0.55 | 0.00±0.01 | 0.92 | 0.00±0.01 | 0.58 |
| Multiparous vs. nulliparous | -0.08±0.12 | 0.50 | 0.03±0.11 | 0.77 | -0.03±0.10 | 0.74 | 0.02±0.07 | 0.78 |
| Previous pregnancy within 4 years | 0.09±0.12 | 0.47 | 0.10±0.11 | 0.34 | 0.04±0.10 | 0.70 | -0.02±0.07 | 0.75 |
| Male | 0.13±0.12 | 0.29 | 0.06±0.11 | 0.55 | 0.12±0.10 | 0.24 | 0.12±0.07 | 0.10 |
| Gestational age (weeks) | 0.08±0.05 | 0.09 | 0.04±0.04 | 0.35 | 0.06±0.04 | 0.13 | 0.04±0.03 | 0.12 |
| Birth weight (kg) | 0.01±0.13 | 0.93 | -0.06±0.12 | 0.61 | 0.00±0.11 | 0.97 | -0.02±0.08 | 0.81 |
| Born after October 18, 2000 (median) | -0.22±0.12 | 0.07 | -0.19±0.11 | 0.08 | -0.15±0.10 | 0.15 | 0.01±0.07 | 0.91 |
| At least one material hardship vs. none | -0.14±0.13 | 0.27 | -0.15±0.11 | 0.17 | -0.10±0.10 | 0.33 | -0.04±0.08 | 0.56 |
| Yes environmental tobacco smoke vs. none | 0.31±0.13 | 0.02 | 0.24±0.11 | 0.03 | 0.15±0.11 | 0.15 | 0.00±0.07 | 0.96 |
| Ever vacuum during pregnancy vs. never | 0.34±0.16 | 0.04 | 0.19±0.14 | 0.19 | 0.28±0.13 | 0.04 | 0.13±0.09 | 0.17 |
| Ever damp mop during pregnancy vs. never | -0.08±0.13 | 0.53 | -0.11±0.11 | 0.31 | -0.17±0.10 | 0.10 | -0.19±0.08 | 0.01 |
| Ever wet mop during pregnancy vs. never | -0.01±0.13 | 0.92 | -0.03±0.11 | 0.81 | 0.08±0.10 | 0.41 | 0.16±0.07 | 0.03 |

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| **Supplemental Table 6 –** PBDE Concentrations (Median, ng/g lipid) and Detection Frequencies (%) Measured in Maternal or Umbilical Cord Blood Collected by Eight United States-Based Studies Conducted between 1998 and 2010 |
| Location (Ref) | Enrollment Period | Blood type | Study size | BDE-47 | BDE-99 | BDE-100 | BDE-153 |
| New York, NYa | 1998-2006 | UCB | 327 | 14.1 (80) | 3.7 (50) | 2.9 (42) | 2.6 (38) |
| Monterey, CA (1)a | 1999-2000 | MB | 416 | 15.8 (100) | 4.4 (99) | 2.8 (98) | 2.4 (98) |
| Indianapolis, IN (2) | 2001 | UCB | 12 | 25 (100) | 7.1 (100) | 4.1 (100) | 4.4 (100) |
| New York, NY (3) | 2001-2002 | UCB | 201 | 11.2 (81) | 3.2 (60) | 1.4 (64) | 0.7 (50) |
| Cincinnati, OH (4)a | 2003-2006 | MB | 274b | 20.5 (100) | 4.9 (99) | 4.1 (98) | 5.5 (99) |
| Baltimore, MD (5) | 2004-2005 | UCB | 297 | 13.6 (90) | 4.3 (47) | 2.3 (65) | 2.6 (60) |
| Durham, NC (6)a | 2008-2010 | MB | 137 | 16.5 (95) | 4.7 (64) | 4.2 (89) | 5.9 (96) |
| New York, NY (7) | 2009-2010 | MB | 316 | 7.9 (99) | 1.6 (84) | 1.7 (91) | 3.0 (98) |
| MB: Maternal blood; UCB: Umbilical cord bloodaConcentration is geometric mean, not medianbSample size: BDE-47=305, BDE-99=204, BDE-100=275 |

**Supplemental Table 6 References**

1. Castorina R, Bradman A, Sjodin A, Fenster L, Jones RS, Harley KG, et al. Determinants of serum polybrominated diphenyl ether (PBDE) levels among pregnant women in the CHAMACOS cohort. Environ Sci Technol 2011;45(15):6553-60.
2. Mazdai A, Dodder NG, Abernathy MP, Hites RA, Bigsby RM. Polybrominated diphenyl ethers in maternal and fetal blood samples. Environ Health Perspect 2003;111(9):1249-52.
3. Herbstman JB, Sjodin A, Kurzon M, Lederman SA, Jones RS, Rauh V, et al. Prenatal exposure to PBDEs and neurodevelopment. Environ Health Perspect 2010;118(5):712-9.
4. Vuong AM, Webster GM, Romano ME, Braun JM, Zoeller RT, Hoofnagle AN, et al. Maternal Polybrominated Diphenyl Ether (PBDE) Exposure and Thyroid Hormones in Maternal and Cord Sera: The HOME Study, Cincinnati, USA. Environ Health Perspect 2015;123(10):1079-85.
5. Herbstman JB, Sjodin A, Apelberg BJ, Witter FR, Patterson DG, Halden RU, et al. Determinants of prenatal exposure to polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) in an urban population. Environ Health Perspect 2007;115(12):1794-800.
6. Stapleton HM, Eagle S, Anthopolos R, Wolkin A, Miranda ML. Associations between polybrominated diphenyl ether (PBDE) flame retardants, phenolic metabolites, and thyroid hormones during pregnancy. Environ Health Perspect 2011;119(10):1454-9.
7. Horton MK, Bousleiman S, Jones R, Sjodin A, Liu X, Whyatt R, et al. Predictors of serum concentrations of polybrominated flame retardants among healthy pregnant women in an urban environment: a cross-sectional study. Environ Health 2013;12:23.

