Title
Environmental chemicals in pregnant women in the United States: NHANES 2003-2004.

Permalink
https://escholarship.org/uc/item/4rp6z93t

Journal
Environmental health perspectives, 119(6)

ISSN
0091-6765

Authors
Woodruff, Tracey J
Zota, Ami R
Schwartz, Jackie M

Publication Date
2011-06-01

DOI
10.1289/ehp.1002727

Peer reviewed
Exposure to chemicals during fetal development can increase the risk of adverse health effects, and while biomonitoring studies suggest pregnant women are exposed to chemicals, little is known about the extent of multiple chemicals exposures among pregnant women in the United States.

**Objective:** We analyzed biomonitoring data from the National Health and Nutritional Examination Survey (NHANES) to characterize both individual and multiple chemical exposures in U.S. pregnant women.

**Methods:** We analyzed data for 163 chemical analytes in 12 chemical classes for subsamples of 268 pregnant women from NHANES 2003–2004, a nationally representative sample of the U.S. population. For each chemical analyte, we calculated descriptive statistics. We calculated the number of chemicals detected within the following chemical classes: polybrominated diphenyl ethers (PBDEs), perfluorinated compounds (PFCs), organochlorine pesticides, and phthalates and across multiple chemical classes. We compared chemical analyte concentrations for pregnant and nonpregnant women using least-squares geometric means, adjusting for demographic and physiological covariates.

**Results:** The percentage of pregnant women with detectable levels of an individual chemical ranged from 0 to 100%. Certain polychlorinated biphenyls, organochlorine pesticides, PFCs, phenols, PBDEs, phthalates, polycyclic aromatic hydrocarbons, and perchlorate were detected in 99–100% of pregnant women. The median number of detected chemicals by chemical class ranged from 4 of 12 PFCs to 9 of 13 phthalates. Across chemical classes, median number ranged from 8 of 13 chemical analytes to 50 of 71 chemical analytes. We found, generally, that levels in pregnant women were similar to or lower than levels in nonpregnant women; adjustment for covariates tended to increase levels in pregnant women compared with nonpregnant women.

**Conclusions:** Pregnant women in the U.S. are exposed to multiple chemicals. Further efforts are warranted to understand sources of exposure and implications for policy making.

**Keywords:** chemicals, environmental exposures, NHANES, pregnancy; Environ Health Perspect 119:878–885 (2011). doi:10.1289/ehp.1002727 [Online 14 January 2011]

Address correspondence to T.J. Woodruff, Program on Reproductive Health and the Environment, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, Oakland, California, USA.
Most chemical analytes were measured in subsets of the total NHANES sample. Each subset included about one-third the total number of participants, so not all chemical analytes were measured in each participant. Further, not every group of chemical analytes was measured in each cycle. Therefore, we analyzed the 2003–2004 cycle, because it represents the cycle with the highest number of chemical analytes measured across the sample of pregnant women. We limited our study population to those 15–44 years of age to be consistent with the definition used by the National Center for Health Statistics for women of childbearing age (Chandra et al. 2005). Therefore, our study population includes 268 pregnant women and 1,489 nonpregnant women 15–44 years of age included in at least one subsample for chemical analyte analysis.

Environmental chemical analyte analyses. Chemical analyte analyses were conducted at the National Center for Environmental Health laboratories (CDC, Atlanta, GA). Analytical procedures and summary statistics for the general population have been described in the Fourth National Report on Human Exposure to Environmental Chemicals and in the peer-reviewed literature (Calafat et al. 2008; Caldwell et al. 2009; CDC 2009a; Sjodin et al. 2008). We assessed 163 chemical analytes across 12 chemical classes (Table 1), measured in blood, urine, and serum.

Data analysis. We conducted analyses in SUDAAN (version 10.0; Research Triangle Institute, Research Triangle Park, NC) and SAS (version 9.2; SAS Institute Inc., Cary, NC). SUDAAN calculates variance estimates after incorporating the nonrandom sampling design and the sample population weights, which account for oversampling of certain subgroups.

We examined summary statistics and distributional plots for each chemical analyte. We calculated the following descriptive statistics (for further details on analysis, see Supplemental Material (doi:10.1289/ehp.1002727)): percentage of women with levels greater than the limit of detection (LOD), geometric mean (GM), geometric standard error (GSE), median, and 95th percentile estimates, and the coefficient of variation (CV; defined as the GSE divided by the GM). The GM, GSE, and CV were calculated only for chemical analytes with > 60% detection frequency. The median and 95th percentile were calculated for all chemical analytes. Concentrations below the LOD were substituted by the CDC with LOD/√2.

We present statistical results for individual chemical analytes in the main text that are representative of each chemical class [for descriptive statistics and LODs for all 163 chemical analytes, see Supplemental Material, Table 1 (doi:10.1289/ehp.1002727)]. Representative chemical analytes were chosen based on public health relevance and expectation of relatively widespread exposure.

To assess extent of multiple exposures within a chemical class, we evaluated the

![Table 1. Chemical classes measured in biological tissue of pregnant women, NHANES 2003–2004.](doi:10.1289/ehp.1002727)

| Chemical class | Blood | Serum | Urine | Total |
|----------------|-------|-------|-------|-------|
| Cotinine       | 1     | 1     |       |       |
| Environmental phenols | 4     | 4     |       |       |
| Metals         |       |       |       |       |
| Organochlorine pesticides | 13    | 13    |       |       |
| Organophosphate insecticides | 6      | 6     |       |       |
| Perchlorate     | 1     | 1     |       |       |
| Phthalates      | 13    | 13    |       |       |
| PBDEs and other brominated flame retardants | 11    | 11    |       |       |
| PCBs and dioxin-like chemicals | 55    | 55    |       |       |
| PAHs            | 10    | 10    |       |       |
| PFCs            | 12    | 12    |       |       |
| VOCs            | 33    | 33    |       |       |

See Supplemental Material, Table 1 (doi:10.1289/ehp.1002727), for individual chemical analytes included in each chemical class.

![Table 2. Characteristics of reproductive-age women by pregnancy status, NHANES 2003–2004.](doi:10.1289/ehp.1002727)

| Demographic characteristic | Pregnant women (n = 268) | Nonpregnant women (n = 1,489) |
|----------------------------|--------------------------|-------------------------------|
| Age [years (mean ± SE)]** | 27 ± 0.8                 | 30 ± 0.37                     |
| Age [years (%)]**          | 15–17                    | 4                              |
|                            | 18–24                    | 30                             |
|                            | 25–29                    | 31                             |
|                            | 30–34                    | 25                             |
|                            | 35–44                    | 11                             |
| Race/ethnicity [%]**       |                          |                               |
| Non-Hispanic white         | 56                       | 67                             |
| Non-Hispanic black         | 18                       | 14                             |
| Mexican American           | 17                       | 10                             |
| Other Hispanic             | 2                        | 5                              |
| Other                      | 6                        | 5                              |
| Education (%)              |                          |                               |
| < High school diploma      | 26                       | 24                             |
| High school diploma        | 15                       | 22                             |
| > High school diploma      | 59                       | 54                             |
| Marital status [%]**       |                          |                               |
| Married or living with partner | 79                  | 50                             |
| Divorced, separated, or widowed | 2                  | 12                             |
| Never married              | 19                       | 38                             |
| Parity [%]**               |                          |                               |
| 0                          | 45                       | 44                             |
| 1                          | 34                       | 14                             |
| > 2                        | 21                       | 42                             |
| Smoking status [%]**       |                          |                               |
| Never                      | 59                       | 60                             |
| Former                     | 31                       | 11                             |
| Current                    | 9                        | 30                             |
| Trimester                  |                          |                               |
| First                      | 31                       |                               |
| Second                     | 32                       |                               |
| Third                      | 37                       |                               |
| Biochemical measurements   |                          |                               |
| Serum albumin [g/dl (mean ± SE)]** | 3.46 ± 0.04 | 4.23 ± 0.01 |
| Urinary creatinine [mg/dl (mean ± SE)] | 127.81 ± 6.00 | 130.86 ± 3.27 |
| Sampling characteristics   |                          |                               |
| Duration of food and drink fasting before blood collection [hr (mean ± SE)]** | 8.40 ± 0.73 | 10.67 ± 0.10 |

Data were missing in pregnant women for parity (n = 18), education (n = 3), smoking (n = 6), trimester (n = 41), and length of fasting (n = 21) and in nonpregnant women for parity (n = 160), education (n = 48), smoking (n = 151), and length of fasting (n = 26).

**p < 0.01.
number of individual PBDEs, perfluorinated compounds (PFCs), organochlorine pesticides, and phthalates detected in each pregnant woman. We chose these chemical classes to represent banned persistent chemicals (organochlorine pesticides), persistent chemicals (PBDEs and PFCs), and currently used nonpersistent chemicals (phthalates).

We then evaluated the extent of multiple chemical exposures across chemical classes in three different subsamples. These three subsamples were the primary subsamples of the pregnant women. Pregnant women in subsample A were assessed for metals, cotinine, and PFCs (17 chemical analytes in 76 women); in subsample B, for metals, cotinine, organochlorine pesticides, phthalates, PBDEs, and polycyclic aromatic hydrocarbons (PAHs) (52 chemical analytes in 54 women); and in subsample C, for metals, phenols, polychlorinated biphenyls (PCBs), organophosphate insecticide metabolites, perchlorate, and cotinine (71 chemical analytes in 59 women) [for subsample composition, see Supplemental Material, Table 2 (doi:10.1289/ehp.1002727)]. Volatile organic compounds (VOCs) were measured only in a subsample of pregnant women that partially overlapped with subsamples A, B, and C. Consequently, we did not include VOCs in analyses of multiple chemical exposures.

To compare chemical analyte concentrations between pregnant and nonpregnant women, we constructed multivariate regression models, which included our main effect (binary pregnancy status variable) along with covariates. We log-transformed chemical analytes before regression analysis to account for the nonnormal distributions. From these models, we calculated the least-squares geometric means (LSGMs), which provide GM estimates after adjustment for other covariates. For every chemical analyte in the main analysis, we used the same set of covariates. Covariates were included if they were significant predictors of more than one chemical analyte.
analyte or if their inclusion in the model changed the β-coefficient for the main effect by > 20%. The following covariates were evaluated: age (continuous), race/ethnicity (Mexican American, non-Hispanic white, non-Hispanic black, or other), education (high school diploma or less vs. more than high school diploma), marital status (married/living with a partner, divorced/separated, or never married), parity (number of pregnancies resulting in live births, nulliparous vs. one or more child), current body mass index (BMI; continuous), smoking status (never, former, or current), serum albumin (continuous), length of food and drink fasting before blood collection (0–4.5 hr, 4.5–8.5 hr, or 8.5–24 hr), and urinary creatinine (continuous). All regression models were adjusted for the same covariates except for creatinine (included in models for urinary chemicals only). We excluded 12 non-pregnant women who reported fasting times > 24 hr. We defined statistical significance as p < 0.10 for all analyses because of relatively small number of pregnant women sampled for each chemical analyte and, consequently, small degrees of freedom.

As a sensitivity analysis, we performed multivariate regression in women < 35 years of age, because the age distribution differed between the two groups. For this analysis, we selected model covariates separately for each individual chemical analyte using the covariate selection method described above. Thus, the covariates in the sensitivity analysis may differ from that used in the main analysis. We conducted sensitivity analyses for lead (n = 215 pregnant; n = 885 nonpregnant), BPA (n = 63 pregnant; n = 275 nonpregnant), and p,p’-dichlorodiphenyldichloroethene (DDE) (n = 65 pregnant; n = 380 nonpregnant).

Results

Although most pregnant and nonpregnant women were white, there was a higher percentage of Mexican-American pregnant women compared with nonpregnant women, reflecting higher birth rates among Hispanic women in the United States (Table 2) (Martin et al. 2007). Nonpregnant women were older, less likely to be married or with a partner, and more likely to smoke than were pregnant women (Table 2). In addition, pregnant women had lower levels of albumin and shorter fasting times before blood collection than did nonpregnant women.

Table 3 summarizes statistics for pregnant and nonpregnant women for select chemical analytes [for all 163 chemical analytes in pregnant women, see Supplemental Material, Table 1 (doi:10.1289/ehp.1002727)]. We found that 0–100% of pregnant women had a detectable level across the individual chemical analytes. Eight of 12 classes of chemicals included individual chemical analytes detected in 99–100% of pregnant women (PFCs, PBDEs, PCBs, organochlorine pesticides, phenols, phthalates, PAHs, and perchlorate). Four classes (VOCs, PFCs, PCBs, and organochlorine pesticides) included
Among pregnant women, DDE had the highest GM concentration (140.4 ng/g lipid) of the persistent, lipophilic compounds measured in serum (PCBs, PBDEs, and organochlorine pesticides), whereas concentrations of most of the other measured chemical analytes in the class were an order of magnitude lower (PCBs, 4–8 ng/g lipid; PBDEs, 5–23 ng/g lipid). Perfluorooctane sulfonic acid (PFOS) had the highest GM among the persistent chemical analytes that do not accumulate in lipids (e.g., lead, cadmium, and PFCs). Of the nonpersistent chemical analytes measured in urine (organophosphate metabolites, phensols, phthalates, PAHs, and perchlorate), triclosan, benzophenone-3, and monothylphthalate (MEP) had the highest GMs (17.00, 25.49, and 226.53 μg/L, respectively).

Although the GM for cotinine was < 1 μg/L, the range of concentrations spanned three orders of magnitude (CV = 0.31). Variability in other chemical analyte levels measured in pregnant women was generally low (CV < 0.25), except for some phenols (CV = 0.25–0.51), phthalates (CV = 0.22–0.35), MTBE (CV = 0.40), triclosan (CV = 0.51), and PBDE-153 (CV = 0.31).

Figure 1 shows the numbers of individual PFC, PBDE, organochlorine pesticide, and phthalate chemical analytes detected in individual pregnant women. At least two organochlorine pesticides, one PBDE, two PFCs, and four phthalates were measured in each pregnant woman. The median number of chemicals detected for organochlorine pesticides, PBDEs, PFCs, and phthalates were 6, 6, 4, and 9, respectively. For PBDEs and phthalates, 7% and 2%, respectively, had detectable levels of ≥ 90% of the chemical analytes in the class.

The median number of chemical analytes detected among women in subsamples A, B, and C were 8 (range, 4–12), 37 (range, 28–45), and 50 (range, 35–60), respectively (Figure 2). We found generally that the overall number of chemicals detected was not dominated by detects within a particular chemical class (Figure 3). For example, several participants in subsample B at the median detected level (37 chemicals) had 10 phthalates, 10 PAHs, 7 PBDEs, 6 organochlorine pesticides, 3 metals, and cotinine detected.

GM and median levels for most chemicals were similar to or lower than those in pregnant than in nonpregnant women, except for PBDEs, DMTP, triclosan, and perchlorate (Table 3). About half the LSGM estimates for pregnant women (Table 4) increased after adjusting for covariates (Tables 3 and 4). For a few chemicals, the LSGM estimates for pregnant women decreased after adjustment, such as PBDEs, some phthalates, perchlorate, and BPA. In general, adjusted LSGMs were comparable between pregnant and nonpregnant women (Table 4). Nonpregnant women had significantly higher levels of cadmium, lead, PFOS, BPA, and cotinine, but pregnant women had significantly higher levels of DDE, DMTP, MTBE, and perchlorate (Table 4). The most pronounced differences between pregnant and nonpregnant women were for MTBE and DMTP (levels in pregnant women were about two times those of nonpregnant women) and cotinine (levels in pregnant women were about half those of nonpregnant women).

Serum albumin influenced the comparison between pregnant and nonpregnant women for 28 of the 32 compounds evaluated in regression analyses (the b-coefficient changed by > 20%); however, direction of the effect varied by type of compound. In general, for chemical analytes measured in blood, effect estimates for albumin were positive, and their inclusion increased the LSGMs for pregnant women; in contrast, for nonpersistent urinary chemical analytes, the albumin effect estimates were more often negative, and their inclusion...
Levels of chemicals measured during pregnancy can be influenced by physiological (e.g., changes in BMI, plasma volume expansion, and bone mobilization) and behavioral factors. For example, previous research has found an inverse relationship between weight gain during pregnancy and levels of persistent organic pollutants in pregnant women (Bradman et al. 2006). We found that plasma volume expansion, using the level of albumin as a surrogate, may also influence chemical levels measured in pregnant women. Plasma volume begins to expand in pregnant women at around 8 weeks of gestation and increases progressively until 30–34 weeks gestation, when it plateaus. This expansion may dilute environmental chemical concentrations in blood (Faupel-Badger et al. 2007). Accurately measuring plasma volume expansion is expensive and ideally requires multiple measurements throughout pregnancy (Faupel-Badger et al. 2007). However, albumin measurements may provide a reasonable surrogate because previous studies suggest that blood volume expansion dilutes circulating levels of albumin during pregnancy (Honger 1968). We found that, in general, adjusting for albumin increased GM estimates of persistent compounds, such as DDE, in pregnant women, suggesting that the concentration is diluted by increased plasma volume. However, adjustment for albumin generally decreased estimates for nonpersistent compounds, such as BPA, in pregnant women, suggesting that lower albumin may be associated with an increased clearance of environmental contaminants. Albumin may affect metabolism and transport of chemicals by mechanisms other than plasma volume expansion. For example, previous research has shown that PFCs actually bind to albumin in the blood (Jones et al. 2003). BPA also binds to plasma proteins, such as albumin, in humans (Teeguarden et al. 2005), so reduced albumin during pregnancy may influence the amount of BPA that undergoes phase II conjugation and subsequent elimination through urine. The role of albumin, and other transport proteins, in the transport and metabolism of environmental chemicals, particularly during pregnancy, is an important topic and requires further research.

We found that, generally, the levels in pregnant women were similar to or lower than levels measured in nonpregnant women. Adjusting for physiological factors that may influence levels of chemicals in pregnant women tended to increase the levels in pregnant women compared with nonpregnant women. This suggests that generally levels of chemicals in nonpregnant reproductive-age women are reasonably representative of levels found in pregnant women. However, for several chemicals, levels in pregnant women remain lower than those in nonpregnant women. Behavioral factors may explain this difference (e.g., cotinine and smoking), or other physiological factors may be important (e.g., chemical levels concentrating in the fetus such as for BPA (Takahashi and Oishi 2000)).

The NHANES study design, where groups of chemicals were analyzed in approximate one-third–sized subsamples, meant that we could not evaluate more than 71 chemical analytes in any individual pregnant woman, or about 44% of chemical analytes measured.
during 2003–2004. This also limited our ability to assess exposures to multiple chemical analytes that may be acting on the same adverse outcome (e.g., PBDEs and PCBs, which can affect neurodevelopment, were not measured in the same women). Given that several chemical analytes within each of the classes were detected almost ubiquitously, pregnant women have more detectable chemical analytes than we could assess in any individual pregnant women. The number and types of chemicals sampled changes by cycle. Another challenge is that LODs vary among the cycles. Mostly they decreased, such as with PCBs, which can increase the number of chemicals detected. However, a few LODs increased; for example, certain urinary phthalate esters, such as mono-2-ethylhexyl phthalate (MEHP) and MEP, increased between 2003–2004 and 2005–2006.

Chemical analyte concentrations in NHANES participants should be representative of typical U.S. concentrations. Thus, highly exposed subpopulations may be underrepresented. For example, women living in the agricultural Salinas Valley of California had higher measurable levels of several pesticides than did NHANES pregnant women (Castorina et al. 2010). Other subpopulations may have nonrepresentative exposure patterns, such as high fish consumption or higher use of certain personal care products.

Our analysis indicates high variability in exposures for some chemical analytes, shown by the relatively high CV for phenols, phthalates, cotinine, and MTBE. For some of these analytes, with almost an order of magnitude difference between the median and the 95th percentile, variation may reflect geographic variability in exposure sources. For example, MTBE was used in reformulated gasoline starting in 1995. Reformulated gasoline was required for use year-round in cities with significant smog problems (Energy Information Administration 2008), so it was not used in

### Table 4. Comparison of chemical analyte concentrations between pregnant and nonpregnant women after adjustment for covariates, calculated from multivariate regression models.

| Chemical analyte                          | β-Coefficient (90% CI) | Pregnant women | Nonpregnant women |
|-------------------------------------------|------------------------|----------------|-------------------|
| **Metals (blood [μg/L])**                 |                        |                |                   |
| Cadmium                                  | -0.20 (–0.36 to -0.04)*| 0.27           | 0.33              |
| Lead (μg/dL)                              | -0.16 (–0.27 to -0.05)*| 0.80           | 0.94              |
| Mercury (total)                           | -0.11 (–0.33 to 0.10)  | 0.71           | 0.79              |
| VOCS (blood [μg/L])                       |                        |                |                   |
| MTBE                                      | 0.97 (0.03 to 1.90)*   | 0.02           | 0.006             |
| Toluene                                   | 0.15 (–0.14 to 0.43)   | 0.11           | 0.09              |
| **PFCs [serum (μg/L)]**                   |                        |                |                   |
| Perfluorooctanoic acid                    | -0.18 (–0.37 to 0.02)  | 2.99           | 3.22              |
| PFOS                                      | -0.23 (–0.35 to –0.12)**| 12.81         | 16.28             |
| **PBDEs [serum (ng/g lipid)]**            |                        |                |                   |
| PBDE-47                                   | 0.02 (–0.32 to 0.35)   | 21.76          | 21.33             |
| PBDE-99                                   | -0.11 (–0.47 to 0.26)  | 4.62           | 5.10              |
| PBDE-100                                  | 0.24 (–0.22 to 0.70)   | 5.21           | 4.10              |
| PBDE-153                                  | 0.51 (–0.10 to 1.12)   | 8.85           | 5.31              |
| **PCBs [serum (ng/g lipid)]**             |                        |                |                   |
| PCB-118                                   | -0.02 (–0.31 to 0.28)  | 4.39           | 4.44              |
| PCB-138 and -158                          | -0.07 (–0.33 to 0.19)  | 8.25           | 8.85              |
| PCB-153                                   | -0.11 (–0.39 to 0.17)  | 9.67           | 11.02             |
| PCB-180                                   | -0.27 (–0.65 to 0.11)  | 5.64           | 7.39              |
| Organochlorine pesticides [serum (ng/g lipid)] |                      |                |                   |
| DDT                                       | -0.10 (–0.32 to 0.13)  | 3.49           | 3.86              |
| DDE                                       | 0.33 (0.12 to 0.53)*   | 198.34         | 142.59            |
| Hexachlorobenzene                         | -0.02 (–0.14 to 0.10)  | 13.74          | 14.01             |
| Organophosphate insecticide metabolites [urine (μg/L)] |      |                |                   |
| DMTF                                      | 0.85 (0.34 to 1.35)*   | 4.39           | 1.88              |
| Environmental phenols [urine (μg/L)]      |                        |                |                   |
| BPA                                       | -0.55 (–0.97 to -0.13)*| 1.63           | 2.83              |
| Triclosan                                 | 0.47 (–0.60 to 1.54)   | 23.81          | 15.03             |
| Benzo(ghi)fluoranthene-3                  | -0.07 (–1.26 to 1.12)  | 38.09          | 40.85             |
| Phthalates [urine (μg/L)]                 |                        |                |                   |
| Monobenzyl phthalate                      | -0.02 (–0.53 to 0.50)  | 14.73          | 15.03             |
| Monoisobutyl phthalate                    | -0.37 (–0.76 to 0.03)  | 2.83           | 4.06              |
| Mono-n-Butyl phthalate                    | -0.26 (–0.62 to 0.11)  | 18.36          | 23.81             |
| MEP                                       | -0.13 (–0.93 to 0.66)  | 221.41         | 254.68            |
| PAHs [urine (μg/L)]                       |                        |                |                   |
| 9-Hydroxyfluorene                         | -0.15 (–0.50 to 0.19)  | 0.20           | 0.23              |
| 2-Naphthol                                | -0.15 (–0.57 to 0.27)  | 3.00           | 3.49              |
| 2-Hydroxyphenanthrene                     | -0.12 (–0.27 to 0.02)  | 0.05           | 0.06              |
| 1-Hydroxypropene                          | -0.14 (–0.46 to 0.19)  | 0.08           | 0.09              |
| Perchlorate [urine (μg/L)]                | 0.25 (0.05 to 0.45)*   | 3.35           | 2.67              |

CI, confidence interval. Sample sizes for chemical classes are approximate because sample sizes vary slightly by chemical. *Models adjusted for age, race/ethnicity, education, smoking, parity, BMI, albumin, duration of fasting before specimen collection, and creatinine (only urinary chemical analytes adjusted for creatinine). §Reference group is nonpregnant women. Chemical analyte concentrations are log-transformed. ¶LSGM (least-squares geometric mean) estimates are < LOD (see Table 3). *p < 0.10; **p < 0.01.
every U.S. location. Thus, the geographic variation in MTBE use may play a role in the wide exposure variability (Energy Information Administration 2008). PBDE-153 is another example of how geographic use variation can influence exposures levels. The 95th percentile of PBDE-153 levels is 15 times greater than the median, and previous research has found PBDE concentrations to be around two times higher in Californians than in others in the United States, likely because of California’s unique flammability standard (Zota et al. 2009). Variation in exposure to chemical analytes used in consumer and personal care products (e.g., triclosan, where the 95th percentile is 35 times greater than the median) could be driven by unique product uses (Allmyr et al. 2009). Although biomonitoring studies can demonstrate variation in exposures within populations, they generally are limited in their ability to identify sources of exposures. Consequently, additional exposure assessment research is needed to identify the dominant sources of exposure among pregnant women and the general population.

Our analysis of the NHANES pregnancy data shows ubiquitous exposure to multiple chemicals during a sensitive period of fetal development. The NAS recommends accounting for both multiple exposures and exposures that occur during vulnerable developmental periods in improved approaches for assessing chemical risks across the population, which includes shifting to a risk assessment approach that presumes no threshold of effect on the population unless shown otherwise (National Research Council 2008b). Data, such as from NHANES, should be used to enhance our understanding of risks among the U.S. population and to inform further policy and research activities.

**References**

Allmyr M, Panagiotidis G, Sparve E, Diczfalusy U, Sandberg-Englund G. 2009. Human exposure to triclosan via toothpaste does not change CYP3A4 activity or plasma concentrations of thyroid hormones. Basic Clin Pharmacol Toxicol 105(5):339–344.

Barr DB, Bishop A, Needham LL. 2007. Concentrations of xenobiotic chemicals in the maternal-fetal unit. Reprod Toxicol 23(3):260–266.

Blount BC, Silva MJ, Caudill SP, Needham LL, Pirikle JL, Sampson EJ, et al. 2000. Levels of seven urinary phthalate metabolites in a human reference population. Environ Health Perspect 108(5):579–582.

Bredman A, Barr DB, Claus Hann BG, Drumheller T, Curry C, Eskenazi B. 2003. Measurement of pesticides and other toxicants in amniotic fluid as a potential biomarker of prenatal exposure: a validation study. Environ Health Perspect 111:1779–1782.

Bredman A, Schwartz JM, Fenster L, Barr DB, Holland NT, Eskenazi B. 2006. Factors predicting organochlorine pesticide levels in pregnant Latina women living in a United States agricultural area. J Expo Sci Environ Epidemiol 17(4):388–399.

Calafat AM, Ye XY, Wong LY, Reidy JA, Needham LL. 2008. Exposure of U.S. women to bisphenol A and 4-tert-octyl-cysteophenol: 2003–2004. Environ Health Perspect 116:39–44.

Caldwell KL, Jones RL, Verdon CP, Jarrett JM, Caudill SP, Osterloh JD. 2009. Levels of urinary total and specified arsenic in the US population: National Health and Nutrition Examination Survey 2003–2004. J Expo Sci Environ Epidemiol 19(1):59–68.

Castorina R, Bredman A, Fenster L, Barr DB, Bravo R, Vedov M, et al. 2010. Comparison of current-use pesticide and other toxicant urinary metabolite levels among pregnant women in the CHAMACOS cohort and NHANES. Environ Health Perspect 118:856–863.

CDC Centers for Disease Control and Prevention. 2009a. Fourth National Report on Human Exposure to Environmental Chemicals. Atlanta, GA:Centers for Disease Control and Prevention, National Center for Environmental Health.

CDC Centers for Disease Control and Prevention. 2009b. NHANES 2007–2008 Public Data General Release File Documentation. Available: http://www.cdc.gov/nchs/nhanes/nhanes2007-2008/generaldoc_e.htm [accessed 31 March 2010].

CDC Centers for Disease Control and Prevention. 2010. National Health and Nutrition Examination Survey. Available: http://www.cdc.gov/nchs/nhanes.htm

Chandra A, Martinez GM, Mosher WD, Abma JC, Jones J. 2005. Fertility, family planning, and reproductive health of U.S. women from the 2002 National Survey of Family Growth: National Center for Health Statistics. Vital Health Stat 23(25):1–160.

Chesley LC. 1972. Plasma and red cell volumes during pregnancy, Am J Obstet Gynecol 112(3):440–450.

Chevrier J, Eskenazi B, Holland N, Bredman A, Barr DB. 2008. Effects of exposure to polychlorinated biphenyls and organochlorine pesticides on thyroid function during pregnancy, Am J Epidemiol 168(3):298–310.

Crofton KM. 2008. Thyroid disrupting chemicals: mechanisms and mixtures. In J Anim Androl 31(2):209–223.

Energy Information Administration. 2008. Status and Impact of State MTBE Ban. Available: http://www.eia.doc.gov/oilينا/servlet/mb/103/11466/5415 [accessed 12 April 2010].

Fauvel-Badger JM, Hsieh CC, Trosi R, Lagiou P, Polschuns M. 2007. Plasma volume expansion in pregnancy: implications for biomarkers in population studies. Cancer Epidemiol Biomarkers Prev 16(9):1720–1723.

Gluckman PD, Hanson MA. 2004. Living with the past: evolution, development, and patterns of disease. Science 305(5691):1733–1736.

Herbstman JB, Sjodin A, Kurzon M, Lederman SA, Jones RS, Rauh V, et al. 2010. Prenatal exposure to PBDEs and neurodevelopment. Environ Health Perspect 118:712–719.

Honger PE. 1966. Albumin metabolism in normal pregnancy. Scand J Clin Lab Invest 21(1):2–9.

Jones PD, Hu W, De Coen W, Newstedt JL, Giesy JP. 2003. Binding of perfluorinated fatty acid esters to serum proteins. Environ Toxicol Chem 22(11):2639–2649.

Kortenkamp A. 2007. Ten years of mixing cocktails: a review of combination effects of endocrine-disrupting chemicals. Environ Health Perspect 115(suppl 1):98–105.

Lederman SA, Jones RL, Caldwell KL, Rauh V, Sheets SE, Tang D, et al. 2008. Relation between cord blood mercury levels and early child development in a World Trade Center cohort. Environ Health Perspect 116:1085–1091.

Martin J, Hamilton B, Sutton P, Ventura S, Menacker F, Kirmeyer S, et al. 2007. Births: Final Data for 2005. Hyattsville, MD:National Center for Health Statistics.

Mirel LB, Curtin LR, Gahche J, Burt V. 2009. Characteristics of pregnant women from the 2001–06 National Health and Nutrition Examination Survey. In: JSM Proceedings. Alexandria, VA:American Statistical Association, 2592–2601. Available: https://www.amstat.org/membersonly/pavings/2009/papers/304032.pdf [accessed 26 April 2011].

National Research Council. 2008a. Phthalates and Cumulative Risk Assessment: The Task Ahead. Washington, DC:National Academies Press.

National Research Council, Committee on Improving Risk Analysis Approaches Used by the U.S. EPA. 2008b. Science and Decisions: Advancing Risk Assessment. Washington, DC:National Academies Press.

Pirani BBK, Campbell DM. 1973. Plasma volume in normal first pregnancy. J Obstet Gynaecol Br Commonw 80(10):884–887.

Sjodin A, Wong LY, Jones RS, Park A, Zhang Y, Hodge C, et al. 2008. Variation in exposure to current-use pesticides and organochlorine pesticides others (PBDEs) and polybrominated biphenyl (PBB) in the United States population: 2003–2004. Environ Sci Technol 42(13):1377–1384.

Stilleman KP, McKee DR, Giudice LC, Woodruff TJ. 2008. Environmental exposures and adverse pregnancy outcomes: a review of the science. Reprod Sci 15(7):831–850.

Swan SH, Main KM, Liu F, Stewart SL, Kruse RL, Calafat AM, et al. 2005. Decrease in anogenital distance among male infants with prenatal phthalate exposure. Environ Health Perspect 113:1056–1061.

Takahashi O, Ushio S. 2000. Disposition of orally administered 2,2-bis(hydroxyethyl)propylene (bisphenol A) in pregnant rats and the placental transfer to fetuses. Environ Health Perspect 108:931–935.

Teeguarden JG, Waechter JM, Clewell HJ, Covington TR, Barton HA. 2005. Evaluation of oral and intravenous route pharmacokinetics, plasma protein binding, and uterine tissue dose metrics of bisphenol A: a physiologically based pharmacokinetic approach. Toxicol Sci 85(2):829–838.

Zota AR, Rudel RA, Morello-Frosch RA, Brody JG. 2008. Elevated house dust and serum concentrations of PBDEs in California: unintended consequences of furniture flammability standards? Environ Sci Technol 42(21):8156–8164.