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Hypospadias and halogenated organic pollutant levels in maternal mid-pregnancy serum samples

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Abstract

Background—Environmental contaminants that disrupt endocrine function may contribute to hypospadias etiology.

Objective—To compare levels of selected halogenated organic pollutants in women delivering infants with and without hypospadias.

Methods—This study examined levels of nine polybrominated flame retardants (PBDEs), 30 polychlorinated biphenyls (PCBs) and nine persistent pesticides in mid-pregnancy serum samples from 20 women who delivered infants with hypospadias and 28 women who delivered unaffected infants, in California. Analytes were measured using isotope dilution high-resolution mass spectrometry. Values below individual limits of detection (LOD) for each analyte were imputed based on a truncated multivariate normal distribution. Levels of 17 analytes for which at least 50% of cases and controls had values above the LOD were compared using t-tests and by generating odds ratios from logistic regression analyses.

Results—Means were greater for cases than controls for 11 of the 17 reported analytes (4 of 5 PBDEs, 7 of 9 PCBs, and 0 of 3 other persistent pesticides), but none of the differences were statistically significant. Eleven of the 17 odds ratios exceeded one (the same analytes that had greater means), but none of the confidence intervals excluded one. After adjustment for sample processing time and foreign-born Hispanic race-ethnicity, only four of the odds ratios exceeded one.

Conclusions—Levels of the PBDEs and PCBs were not statistically significantly different, but the sample size was small. The current study adds to a relatively limited knowledge base regarding the potential association of specific contaminants with hypospadias or other birth defects.

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Keywords

hypospadias; PCB; PBDE; DDE; pesticide; pregnancy

INTRODUCTION

Halogenated organic pollutants are ubiquitous in the environment. Concerns about their potential for harmful effects on human health abound and include various disruptions to the endocrine system. Concerns have led to bans on the use of many of them. For example, the pesticide p,p′-dichlorodiphenyltrichloroethane (DDT) and its metabolite p,p′-dichlorodiphenyldichloroethylene (DDE), as well as polychlorinated biphenyls (PCBs), were used industrially and had multiple uses. DDT and PCBs were banned in the 1970s. More recently, concerns have arisen regarding polybrominated diphenyl ethers (PBDEs), which are widely used as flame retardants (e.g., in the padding under wall-to-wall carpeting and the hard plastic casings of electronic equipment). PBDE use may currently be declining, due to voluntary suspension of production of penta-and octa-BDE mixtures [Great Lakes Chemical Corporation, 2003; Harrad and Diamond, 2006]. Nevertheless, human exposures to all of these contaminants continue because of their environmental persistence and long half-lives.

Hypospadias, a congenital malformation in which the urethral opening is on the ventral side of the penis, is one of the most common congenital malformations, affecting four to six males per 1,000 male births [Paulozzi et al., 1997; Paulozzi, 1999; Dolk et al., 2004]. Normal urethral closure, which occurs during the 7^{th}–15^{th} weeks of pregnancy (i.e., weeks after the last menstrual period) [Sadler, 2004], depends on fetal conversion of testosterone to dihydrotestosterone, binding of dihydrotestosterone to the androgen receptor, and proper subsequent androgen receptor signaling. Given the importance of endocrine function to urogenital development, it has been proposed that environmental contaminants that disrupt endocrine function may contribute to hypospadias etiology.

Hypospadias can be induced experimentally by administration of several anti-androgenic pesticides, including vinclozolin, prochloraz and procymidone [Gray, Jr. et al., 2004; Noriega et al., 2005; Ostby et al., 1999]. A few human studies have attempted to assess the association between environmental contaminants and hypospadias. Most of these studies had limited exposure assessment (e.g., self-reported occupation), time windows of exposure that were not specific to urethral development, and/or case information that was passively reported {Pierik, 2004 1504/id; Weidner, 1998 951/id; Kristensen, 1997 481/id; Carbone, 2006 2126/id; Olshan, 1991 2127/id; Zhu, 2006 2128/id; Ormond, 2009 2474/id}. Three studies have measured maternal levels of DDE, which has known estrogenic and anti-androgenic properties, in populations with relatively high exposure [Bhatia et al., 2005; Longnecker et al., 2002; Flores-Luevano et al., 2003]. The odds ratios comparing high versus low values in these studies were 1.2 (95% confidence interval (CI) 0.6, 2.4) [Longnecker et al., 2002], 1.2 (0.5, 3.0) [Bhatia et al., 2005], and 0.5 (0.2, 1.6)[Flores-Luevano et al., 2003]. One study examined maternal serum PCBs and found that levels of individual congeners were not associated with hypospadias. Other studies observed that maternal serum PCB levels during pregnancy {McGlynn, 2009 2473/id} and historical maternal exposure to polybrominated biphenyl {Small, 2009 2475/id} were not associated with hypospadias.

The current study examined serum levels of selected potentially endocrine-disrupting environmental contaminants – PBDEs, PCBs, and several other persistent pesticides, including DDT and DDE – in routinely collected mid-pregnancy serum samples from women who delivered infants with and without hypospadias. The objective of the study was to compare levels of the contaminants in a small group of women delivering infants with and without

hypospadias. Our hypothesis was that these chemicals may affect fetal urogenital development by disrupting fetal endocrine function, by directly targeting the fetus or indirectly by targeting the placenta, which is integral to fetal endocrine function.

METHODS

This study examined mid-pregnancy serum samples from women in California. Specimens were collected from most women (70%) during the 15th–18th week of pregnancy, in southern California (primarily Orange and San Diego counties) [Shaw et al., 2009]. Specimens were collected as part of the California Expanded AFP (alpha-feto-protein) program that screens for neural tube defects and cytogenetic abnormalities. The collection and processing of specimens was as follows: 1) samples were taken at draw stations using BD™ Vacutainer 3.5 mL serum separator tubes with no anticoagulants or preservatives and centrifuged; 2) samples were received by designated clinical laboratories from draw stations at room temperature, on average 3.0 days after draw; 3) AFP assays were run on samples usually on the day received; 4) samples were refrigerated up to 7 days, in case further testing was necessary; 5) samples were sent on cold packs via overnight mail to the serum storage bank; and 6) samples were aliquoted, labeled with barcodes, and frozen at −70° C.

Each woman's serum specimen was linked with delivery outcome information to determine whether her fetus had a structural malformation, which was determined via medical record review by the California Birth Defects Monitoring Program [Shaw et al., 2009].

Among the more than 100,000 pregnancy specimens collected for testing in 2003 and that resulted in a liveborn delivery in 2003, we identified 63 cases with hypospadias. Among the 29 cases for which two serum specimens were available, we selected all 16 for whom the degree of severity was not specified and the four that were coronal, to give a total of 20 cases. As controls, we randomly selected 28 specimens that were collected at the same lab during the same time period and corresponded to non-malformed, liveborn male infants delivered in 2003. Thus, this was a nested case-control study. The selection of samples was limited to singletons. All samples were obtained with approval from the California Health and Welfare Agency Committee for the Protection of Human Subjects.

Specimens for the 48 subjects were sent on cold packs to the Centers for Disease Control and Prevention (CDC) for measurement in 2006. The serum samples were extracted by solid phase extraction (SPE) and after lipid removal analyzed by GC-IDHRMS (isotope dilution high-resolution mass spectrometry). The final analytic results were reported as fresh weight concentration (pg/mL serum) and lipid-adjusted concentration (ng/g lipid) [Sjodin et al., 2004b]. The measured analytes included nine polybrominated flame retardants (PBDEs), 30 polychlorinated biphenyls (PCBs) and nine persistent pesticides.

The limit of detection (LOD) was sample-specific, based on the sample volume. Values that were below the LOD were imputed based on a truncated multivariate normal distribution. This approach allowed us to incorporate information on correlations between related analytes and to restrict imputed values to being below the individual's LOD for each particular analyte. This type of imputation approach using truncated normal distributions has been applied previously in numerous settings [Lubin et al., 2004; Uh et al., 2008].

A priori, we restricted comparisons of levels of the analytes among cases versus controls to analytes for which at least 50% of cases and controls had values above the LOD, i.e., 5 of 9 PBDEs, 9 of 30 PCBs, and 3 of 9 persistent pesticides. DDE had no values below the LOD and was therefore analyzed without multiple imputation. The distributions of the analytes (quartiles and means) were described based on considering the five imputed datasets as a single dataset. We examined the association of each analyte with case-control status by examining t-

tests for differences in the means, and by using logistic regression to estimate odds ratios (OR) and 95 percent confidence intervals (CI), using SAS PROC MIANALYZE (SAS 9.1, Cary, NC). We considered the following covariates for inclusion in the logistic regression analyses: maternal race-ethnicity (non-Hispanic white, U.S.-born Hispanic, foreign-born Hispanic, other); education (<, =, > high school); age (<35 years, versus 35 or older); number of previous live births (none versus any); time elapsed between blood collection and AFP analysis (i.e., time at room temperature); and time elapsed between AFP analysis and storage in the serum bank at −70° C (i.e., time under refrigeration). Two of these factors had an association with case-control status, based on univariate logistic regression analyses: foreign-born Hispanic race-ethnicity (OR 0.13, 95% CI 0.02, 1.2 for foreign-born Hispanic versus non-Hispanic white race-ethnicity, p-value 0.067) and time lapsed between blood collection and AFP analysis (OR for a one-day change was 0.6, 95% CI 0.3, 1.1, p-value 0.084); p-values for the other variables were all >0.1. Therefore, we considered incorporation of these two variables into the logistic regression analyses, as potential confounders.

RESULTS

Mean sample weights after removal of 250 μl for lipid analysis were 0.72 g (SD 0.17, range 0.33–1.01) among cases and 0.75 g (SD 0.10, range 0.49–0.93) among controls. Descriptive characteristics of study subjects are shown in Table 1. Mothers of cases were more likely to have higher education and be nulliparous and less likely to be Hispanic, and case infants were more likely to be low birthweight. The distribution of the analytes and percent of samples imputed are shown in Table 2.

Mean time elapsed between blood collection and AFP analysis was 2.9 days (SD 0.9) among cases and 3.5 (SD 1.2) among controls. Mean time elapsed between AFP analysis and storage at −70°C was 13.0 days (SD 2.0) among cases and 12.9 (SD 1.4) among controls. Among the controls, correlations of the studied analytes with time elapsed between sample collection and AFP testing were negative (ranging from −0.37 to −0.06), except for DDT and DDE (0.09 and 0.08, respectively) (data not shown). The confidence intervals for the coefficients all included one. Correlations of the analytes with time elapsed between AFP testing and storage at −70° C were more variable (ranging from −0.36 to 0.22), and all confidence intervals included one.

In comparisons of analyte levels among the cases and controls, means were greater for cases than controls for 11 of the 17 reported analytes (4 of 5 PBDEs, 7 of 9 PCBs, and 0 of 3 other persistent pesticides), but none of the differences were statistically significant (Table 2). Medians were greater for cases than controls for 9 of the 17 analytes. Eleven of the 17 odds ratios exceeded one (the same analytes that had greater means), but none of the confidence intervals excluded one (Table 3). After adjustment for foreign-born Hispanic race-ethnicity and time elapsed between sample collection and AFP analysis, confidence intervals still excluded one, but only four of the odds ratios exceeded one.

Imputing values below the LOD as the median LOD for a particular analyte divided by the square root of two did not result in a different pattern of results (data not shown).

DISCUSSION

This study examined whether levels of several environmental contaminants differed between hypospadias cases and non-malformed controls. The pattern of results suggested higher levels of PBDEs and PCBs among cases than controls (means were greater for cases and odds ratios exceeded one for four of five PBDEs and seven of nine PCBs), but after adjustment for potential confounders, this was not true. None of the comparisons were statistically significant.

Hypospadias is considered part of the testicular dysgenesis syndrome, which comprises several reproductive tract abnormalities – hypospadias, cryptorchidism, testicular germ cell cancer and impaired spermatogenesis – that may share a common etiology resulting from impairment in endocrine function during fetal development [Sharpe and Skakkebaek, 2008]. Accordingly, it has been proposed that these outcomes may be associated with many of the studied contaminants, given that PCBs and the other studied persistent pesticides have known effects on androgen-dependent reproductive health outcomes [Gray, Jr. et al., 2004; Cooke et al., 2001], and evidence for similar effects of PBDEs is accumulating [Legler and Brouwer, 2003; Stoker et al., 2005]. One recent study suggested increased risk of cryptorchidism was associated with higher maternal breast milk levels of PBDEs [Main et al., 2007]. In general, however, results of studies examining potentially endocrine-disrupting chemicals and male reproductive health outcomes are equivocal [Vidaeff and Sever, 2005].

Few studies have examined the association of hypospadias with any of the analytes considered in the current analysis. Two studies examined DDE and PCBs and included third trimester maternal serum samples from women enrolled from 1959–1965, a time when levels were much higher than today {McGlynn, 2009 2473/id}{Longnecker, 2002 960/id}. One study examined DDE and DDT and included serum samples that were primarily obtained soon after delivery, for deliveries from 1959–1967 {Bhatia, 2005 1346/id}. Another study of DDE, DDT and beta-hexachlorobenzene included serum samples obtained on average more than five years after delivery, among women in Mexico {Flores-Luevano, 2003 2334/id}. Maternal exposure to polybrominated biphenyl (congener 153) in the 1970s was measured many years before pregnancy by a study that included male offspring with genitourinary conditions, including five cases with hypospadias cases {Small, 2009 2475/id}. None of the studies found strong associations with hypospadias, although an interesting finding by McGlynn et al. was a potential association of hypospadias with the sum of PCBs {McGlynn, 2009 2473/id}. Thus, the literature includes studies that are not particularly comparable with regard to time period or geography, and none collected specimens at the time of urogenital development. Also, none of them had information regarding the location of the urethral meatus.

Although the current study is limited by its small sample size, it is strengthened by its inclusion of specimens from early pregnancy and its timeliness. Other strengths include the prospective study design; utilization of laboratory techniques that enabled detection of low levels of multiple analytes in a relatively small sample volume; and the multiple imputation approach to estimation of analyte levels below the limit of detection. Limitations included the small number of subjects, low sample volume, and unspecified location of the urethral meatus in most of the selected cases. In particular, a new study with 20 cases and 28 controls would have 80% power using a type 1 error rate of 5% to detect a 0.82 SD difference in exposure levels between cases and controls. Budgetary restrictions and sample availability restricted our ability to examine more subjects. Although the number of subjects was small – and thus the study was exploratory – it is noteworthy that some expected differences were observed between cases and controls, including fewer of the mothers of cases being Hispanic, more of the mothers of cases having higher education and being nulliparous, and more of the cases being low birthweight, relative to the controls [Carmichael et al., 2003; Carmichael et al., 2007]. Given the dearth of comparable data in the literature, a small-scale study seemed like a prudent first step toward understanding exposure levels in the study population and their association with hypospadias. Low sample volume resulted in a reliance on imputed data, which could lead to spurious results. The sample collection parameters also limited what compounds we could measure; for example, other potentially endocrine-disrupting contaminants, such as phthalates, bisphenol-A and other more volatile compounds, were not measurable. In addition, given the limited sample size and lack of association with individual compounds, we did not explore mixtures of compounds based on their known functions (e.g., examining analytes with known estrogenic effects as a single group), although this may be an important area of future inquiry

[Sharpe and Skakkebaek, 2008; Bloom et al., 2007; Rider et al., 2009]. We also were unable to examine genetic variability in biotransformation of halogenated organics and end-organ susceptibility, which would be an important consideration for future studies. Sample collection during mid-pregnancy was a strength (e.g., versus at delivery or post-partum), but nevertheless it occurred at the end of or shortly after completion of the urethral closure process. Given the persistence of the studied compounds, however, the levels are likely to be a good reflection of at least the few preceding weeks.

A benefit of this study is that it establishes the feasibility of measuring the selected analytes under the given sample collection and handling conditions. Although sample volume was limited, it was adequate to allow detection of reasonable levels of many of the analytes in most samples. A potential concern was contamination of the samples with ambient PBDEs (e.g., from dust). However, the median ratio of PBDE-99 to PBDE-47 was 0.31 among cases and 0.32 among controls, which is consistent with previous studies and suggests that substantial contamination did not occur during sample processing (exogenous PBDEs tend to have a higher ratio) [Bradman et al., 2007; Sjodin et al., 1998; Sjodin et al., 2005]. Also consistent with other studies, the correlations of PBDEs with PCBs were low (e.g., among controls, the correlation of PBDE-47 with PCB-153 was 0.05) and support the idea that exposure pathways differ for the two classes of compounds [Bradman et al., 2007; Schecter et al., 2006].

This study also documents baseline levels in the study population, albeit in a relatively small group. Table 4 shows levels of some of the analytes observed in other recent study populations for comparison. Few previous studies have examined levels during pregnancy, especially in the U.S. Most have been limited to relatively small sample sizes and tend to include fewer individual compounds or classes of compounds than the current study. Median levels of PBDEs in our study were comparable to levels observed by NHANES among U.S. females [Sjodin et al., 2008] and levels among pregnant women in a small study in Indiana [Mazdai et al., 2003]. Most levels were at least two-fold higher than levels among pregnant women in another California study [Bradman et al., 2007], and most were many-fold higher than levels among pregnant women in Sweden [Guvenius et al., 2003]. In contrast, PCBs in our study tended to be lower than in the other studies, although PCB-153 was about 2-fold higher in our study than in the other California study [Bradman et al., 2007]. As for the other persistent pesticides, our study had lower levels than another study of pregnant women in California [Fenster et al., 2006] and levels that were more similar to a study of pregnant women in New York [Wolff et al., 2005]. Explanations for the differences are unknown. It is noteworthy that most of the women in the other California studies were Mexican immigrants, residing in central California, which may account for some of the differences in exposures with our study.

CONCLUSIONS

Current knowledge regarding the potential effects of the studied compounds on infant health – especially birth defects – is limited. Although the current study had certain limitations, it does add to our knowledge regarding exposure to the selected contaminants among pregnant women and regarding potential associations with hypospadias. Based on this study, in conjunction with the few other available studies, it appears that if the analytes we examined are associated with hypospadias, the associations with individual compounds may be small. Confirmation by larger studies of more contemporaneous groups of subjects is needed. Examining exposure to combinations of compounds – whether within classes of compounds or across classes, especially those that may have similar endocrine effects – is also important to explore in the future.

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Table 1

Characteristics of mothers of 20 hypospadias cases and 28 non-malformed control infants.

	Percent (n)	
	Cases	**Controls**
Maternal race-ethnicity		
Hispanic – U.S.-born	5 (1)	21 (6)
Hispanic – foreign-born	5 (1)	29 (8)
Non-Hispanic white	50 (10)	32 (9)
Other	40 (8)	18 (5)
Age (years)		
<25	15 (3)	25 (7)
25–34	70 (14)	61 (17)
35 or greater	15 (3)	14 (4)
Education		
< 12 years	10 (2)	29 (8)
= 12 years	25 (5)	21 (6)
> 12 years	60 (12)	46 (13)
Number of previous live births		
0	50 (10)	43 (12)
1 or more	50 (10)	57 (16)
Birth weight		
<2500 gm	25 (4)	0 (0)
2500 gm or more	75 (16)	100 (28)

Table 2

Distribution of lipid-adjusted levels of analytes, percent of subjects with imputed data for each analyte, and p-value for differences in means, in mid-pregnancy serum samples from mothers of 20 hypospadias cases and 28 non-malformed control infants.

	Cases			Controls			p-Value for Difference in Means
Analyte (ng/g lipid)	Mean (Standard Error)	Median (Interquartile Range)	Percent Imputed*	Mean (Standard Error)	Median (Interquartile Range)	Percent Imputed*	
Brominated Flame Retardants							
PBDE-28	2.0 (0.5)	1.0 (0.5–2.3)	50.0	1.8 (0.4)	1.30 (0.8–2.6))	32.1	0.74
PBDE-47	49.9 (16.6)	19.1 (9.5–57.1)	15.0	31.8 (14.0)	18.8 (12.5–39.0)	3.6	0.41
PBDE-99	26.3 (11.6)	5.2 (2.8–14.2)	45.0	9.6 (9.8)	6.5 (4.6–11.6)	21.4	0.28
PBDE-100	12.1 (4.4)	3.7 (2.2–11.2)	35.0	9.3 (3.7)	5.1 (3.2–10.6)	17.9	0.63
PBDE-153	12.4 (4.1)	4.7 (3.7–11.4)	5.0	12.7 (3.5)	6.9 (3.3–14.3)	3.6	0.96
Polychlorinated Biphenyls							
PCB-52	2.1 (0.4)	1.6 (0.9–2.4)	25.0	1.9 (0.3)	1.5 (0.9–2.6)	21.4	0.70
PCB-99	2.0 (0.4)	1.7 (1.0–2.3)	20.0	1.7 (0.3)	1.2 (0.6–2.5)	42.9	0.56
PCB-153	10.3 (1.4)	9.7 (5.5–12.9)	5.0	9.0 (1.2)	8.0 (4.1–12.7)	10.7	0.49
PCB-180	8.3 (1.4)	6.6 (4.4–9.9)	5.0	8.1 (1.3)	6.5 (3.4–10.7)	0.0	0.92
PCB-187	2.6 (0.6)	2.0 (1.0–2.8)	30.0	2.5 (0.5)	1.2 (0.6–3.1)	42.9	0.89
PCB-194	2.3 (0.6)	1.6 (0.8–2.7)	35.0	2.1 (0.5)	1.1 (0.5–2.7)	46.4	0.81
PCB-199	1.7 (0.5)	0.9 (0.5–2.0)	45.0	1.8 (0.4)	0.9 (0.5–2.7)	46.4	0.88
PCB-138_158	7.7 (1.4)	6.1 (1.6–11.0)	30.0	8.4 (1.2)	7.1 (3.8–11.7)	7.1	0.70
PCB-196_203	2.5 (0.6)	1.8 (0.9–3.2)	25.0	2.3 (0.5)	1.2 (0.6–3.2)	46.4	0.78
Other Persistent Pesticides							
Hexachloro-benzene	4.8 (1.3)	4.4 (2.7–5.5)	35.0	7.0 (1.1)	4.9 (2.6–9.9)	35.7	0.19
p,p′-DDT	20.5 (27.5)	2.6 (1.4–3.9)	25.0	34.4 (23.3)	2.2 (0.8–5.0)	39.3	0.70
p,p′-DDE	344.5 (367.6)	168.5 (113.6–226.5)	0	624.3 (310.7)	168.5 (95.0–312.5)	0	0.56

[a]Values were imputed for samples that were below the LOD; see Methods for details.

Table 3

Association of maternal mid-pregnancy levels of analytes with risk of hypospadias among offspring.

	Crude		Adjusted	
Analytes (ng/g lipid)	**Odds Ratio**	**p-value**	**Odds Ratio[c]**	**p-value**
Brominated Flame Retardants				
PBDE-28[a]	1.05 (0.78, 1.42)	0.73	0.95 (0.68, 1.31)	0.74
PBDE-47[b]	1.04 (0.94, 1.14)	0.44	1.01 (0.93, 1.11)	0.73
PBDE-99[b]	1.10 (0.87, 1.38)	0.44	1.06 (0.90, 1.22)	0.50
PBDE-100[b]	1.08 (0.79, 1.47)	0.63	1.02 (0.74, 1.35)	0.90
PBDE-153[b]	0.99 (0.71, 25.03)	0.96	0.95 (0.67, 1.35)	0.76
Polychlorinated Biphenyls				
PCB-52[a]	1.07 (0.77, 1.48)	0.69	1.04 (0.74, 1.48)	0.80
PCB-99[a]	1.10 (0.79, 1.54)	0.56	1.00 (0.70, 1.42)	0.99
PCB-153[b]	1.39 (0.54, 3.53)	0.49	0.84 (0.30, 2.46)	0.72
PCB-180[b]	1.05 (0.39, 2.82)	0.91	0.66 (0.22, 2.01)	0.46
PCB-187[a]	1.02 (0.82, 1.25)	0.88	0.95 (0.76, 1.19)	0.63
PCB-194[a]	1.03 (0.81, 1.31)	0.80	0.93 (0.71, 1.21)	0.58
PCB-199[a]	0.98 (0.74, 1.29)	0.87	0.90 (0.66, 1.22)	0.47
PCB-138_158[b]	0.83 (0.32, 2.15)	0.70	0.61 (0.22, 1.65)	0.33
PCB-196_203[a]	1.03 (0.82, 1.30)	0.77	0.97 (0.76, 1.23)	0.78
Other Persistent Pesticides				
Hexachlorobenzene[a]	0.92 (0.80, 1.05)	0.21	0.95 (0.79, 1.13)	0.53
p,p′-DDT[a]	1.00 (0.99, 1.00)	0.70	1.00 (0.99, 1.01)	0.72
p,p′-DDE[b]	1.00 (0.99, 1.00)	0.59	1.00 (0.95, 1.00)	0.80

[a] OR for a 1 ng/g lipid change in the analyte (presented for analytes with an interquartile range spanning <5 ng/g lipid, as shown in Table 1).

[b] OR for a 10 ng/g lipid change in the analyte (presented for analytes with an interquartile range spanning ≥5 ng/g lipid, as shown in Table 1).

[c] ORs adjusted by sample processing time and foreign-born Hispanic race-ethnicity.

Table 4

Previously reported median levels of analytes (ng/g lipid).

		Analyte									
Study	**Study description**	**PBDE-28**	**PBDE-47**	**PBDE-99**	**PBDE-100**	**PBDE-153**	**PCB-52**	**PCB-153**	**PCB-180**	**HCB[a]**	**DDE**
Current study	28 women (controls), mid-pregnancy, Southern CA, 2003	1.3	18.8	6.5	5.1	6.9	1.5	8.0	6.5	4.9	168.5
Bradman et al. 2007 [Bradman et al., 2007]	24 women, late pregnancy, Salinas Valley, CA, 1999–2001	11	2.8	1.8	1.5			4.4			
Fenster et al., 2006 [Fenster et al., 2006]	385 women (85% Mexican immigrants), late pregnancy, Salinas Valley, CA, 1999–2000									64.8	1004
Guvenius et al. 2003 [Guvenius et al., 2003]	15 women at labor and delivery, Stockholm, 2000–01	0.1	0.8	0.2	0.2	0.6	<0.5	56	29		
Mazdai et al. 2001	12 women at labor and delivery, IN, 2001		28	5.7	4.2	2.9					
Petreas et al. 2003 [Petreas et al., 2003]	50 Laotian women, age 19–40, San Francisco Bay Area, 1997–99	10						41			
Sjodin et al. 2008 [Sjodin et al., 2008]	~1064 females, NHANES – U.S., 2003–04	1.0	19.1		3.2	4.0					
Sjodin et al. 2004 [Sjodin et al., 2004a]	7 pooled blood samples, TN and WA, 2000–02		34	11	5.9	7.3		35			
Wolff et al., 2005 [Wolff et al., 2005]	385 women, third trimester, NY, 1998–2002										111

[a]HCB = Hexachlorobenzene