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Selected Persistent Organic Pollutants in Human Placental Tissue from the United States

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Abstract

Emerging and legacy environmental pollutants such as polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs) and organochlorine pesticides (DDE) are found in human placenta, indicating prenatal exposure, but data from the United States are sparse. We sought to determine concentrations of these compounds in human placenta as part of a formative research project conducted by the National Children's Study Placenta Consortium. A total of 169 tissue specimens were collected at different time points post delivery from 42 human placenta at three U.S. locations, and analyzed by gas chromatography coupled with mass spectrometry following extraction using matrix solid phase dispersion. PBDEs, PCBs, and DDE were detected in all specimens. The concentrations of 10 PBDEs (₁₀PBDEs), 32 PCBs (₃₂PCBs) and *p,p'*-DDE were 43–1,723, 76–856 and 10–1,968 pg/g wet weight, respectively, in specimens collected shortly after delivery. Significant geographic differences in PBDEs were observed, with higher concentrations in placenta collected in Davis, CA than in those from Rochester, NY or Milwaukee, WI. We combined these with other published data and noted first-order declining trends for placental PCB and DDE concentrations over the past decades, with half-lives of about 5

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^{*}The National Children's Study Placenta Consortium represents more than 100 investigators from twenty different institutions: University of Rochester (Lead Scientific Institution), Icahn College of Medicine at Mount Sinai, University of Illinois at Chicago, Columbia University, University of Utah, University of California at Davis, South Dakota State University, The Children's Hospital of Philadelphia, University of North Carolina, University of California at Irvine, University of Massachusetts, Duke University, Baylor College of Medicine, University of Arkansas, Medical College of Wisconsin, University of Wisconsin, National Institutes of Health, Placenta Analytics, and Westat. The co-authors of this paper were specifically involved in this investigation.

Conflict of interest statement The authors declare that there are no conflicts of interest.

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and 8 years, respectively. The effect of time to tissue collection from refrigerated placentae on measured concentrations of these three classes of persistent organic pollutants was additionally examined, with no significant effect observed up to 120 hours. The results of this work indicate that widespread prenatal exposure to persistent organic pollutants in the United States continues.

Keywords

Persistent organic pollutants; human placenta; polybrominated diphenyl ethers (PBDEs); polychlorinated biphenyls (PCBs); dichlorodiphenyldichloroethylene (DDE); National Children's Study (NCS)

1. Introduction

Polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs) and dichlorodiphenyl-dichloroethylene (DDE) are chemicals that are persistent, bioaccumulative and toxic. They have been widely used commercially – PBDEs as flame retardants, and PCBs mainly as dielectric or coolant fluids in electrical components. DDE is a breakdown product of the agricultural pesticide DDT. While their manufacture or use has been banned or restricted in the United States, these chemicals are detected in gravid human blood, newborn umbilical cord blood, and breast milk, indicating that prenatal and neonatal exposures to these chemicals are occurring (Al-Saleh et al., 2012; Frederiksen et al., 2009b; Shen et al., 2007; Hites, 2004; Schechter et al., 2003; Curley 1969; Rappolt and Hale 1968). Human and animal studies suggest that exposure to these chemicals *in utero* may have fetal developmental effects with potential life-long consequences (Jusko et al., 2012; Herbstman et al., 2010; Howdeshell, 2002; ATSDR, 2002; Darnerud et al., 2001; Aoki, 2001).

The placenta serves as a lifeline for the embryo and fetus, facilitating nutrient and gas exchange between mother and the fetus, and waste removal from the fetal environment. For bioaccumulative and toxic chemicals, the placenta may act as a diffusive barrier (Iyengar and Rapp, 2001) or a repository (Miller et al., 2007; Slikker and Miller, 1994). That placental transfer of PCBs occurs has been known for some time (Wang et al., 2006). Other toxic chemicals found in placentae include pesticides, drugs, and metals (Iyengar and Rapp, 2001; Myren et al., 2007; Shen et al., 2007; Eisenman and Miller, 1996; Zadorozhnaja et al., 2000). More recent studies have provided evidence for placental passage of PBDEs (Frederiksen et al., 2010; Gómara et al., 2007).

The National Children's Study (NCS) is a planned longitudinal study of 100,000 children in the United States, currently piloted in a number of U.S. locations. NCS will follow children from before birth to 21 years, to examine the influence of the environment on child health and development, in order to enhance understanding of the influence of environmental and other factors, both risk and protective, on health and development (Congress, 2000). Formative research is conducted as part of the NCS to address questions intended to inform the main study. We conducted a formative research project (LOI2-BIO-18) designed to establish for the NCS protocols for collection, management, utilization, examination, and storage of placental specimens for stem cell studies, morphologic/pathologic examination, genetic assessments, and analysis of environmental pollutants.

As part of the LOI2-BIO-18 project, we analyzed the concentrations of 43 organic compounds, including 10 PBDEs, 32 PCBs, and p,p'-DDE, in 169 placental tissue samples from 42 placentae collected in three geographic regions of the United States. Results were compared among the three sampling locations and with those reported from other countries, examined for congener distribution patterns, and combined with other published data to

investigate temporal trends in contamination by these chemicals over the past decades. This work was also designed to determine how time elapsed from delivery to tissue collection influences chemical analysis. For this purpose, multiple placental parenchymal tissue samples were collected from each placenta at different time intervals after placental delivery, and the data were analyzed to investigate variation in analyte concentration with time in refrigerated storage of the placenta prior to tissue collection.

2. Materials and Methods

2.1. Sample Collection

Placenta samples were collected from hospitals in upstate New York, the Milwaukee area of Wisconsin, and Sacramento County in California, by NCS study centers and subcontractors located at the University of Rochester (UR), Medical College of Wisconsin (MCW), and University of California-Davis (UCD), respectively. Written informed consent was obtained as required by the Institutional Review Board (IRB) of record for the collecting institution. The study protocol was reviewed and approved by an Office of Human Research Protections registered IRB.

Placentae were sought from pregnant women with no history of maternal or fetal abnormalities and no labor complications. All specimens were collected from grossly normal areas of the villous parenchyma, with exclusion of the decidua basalis and chorionic plate. Each collection was restricted to a placental region. Collections were made into acid-washed 50-mL tubes using plastic (non-metallic) disposable forceps.

Repeated collection of specimens from each placenta occurred as per the sampling plan given in Table S1 of the Supplemental Material. Initial tissue specimen collection from placentae occurred within 15-30 minutes after birth (referred to as “t = 0” hereafter). All placentae were sampled at t = 0. The frequency of subsequent sampling at designated time points varied among sites (Table S1). A total of 169 specimens were collected from 42 placentae. During the repeated sampling procedure, placentae were kept at 4°C. Collected specimens were coded, frozen at -20°C, and transferred on dry ice to the NCS Placenta Processing Center in Rochester NY, where they were re-coded and express-delivered on dry ice to the Environmental Organic Chemistry Laboratory at the School of Public Health, University of Illinois at Chicago (UIC). The analysis laboratory was blinded to information associated with the coded specimens. The wet weights of individual samples ranged from 2.4 g to 42 g. Upon receipt, specimens were held at -20°C until processing.

2.2. Chemical Analysis

Detailed procedures including the extraction, cleanup, and instrumental analyses are described in the Supplemental Material. Briefly, freeze-dried tissues were extracted using matrix solid phase dispersion (MSPD), which was previously optimized for analyzing PBDEs in human placental tissue (Dassanayake et al., 2009). Cleanup of the extract was performed using multilayer silica gel column chromatography.

Individual compounds analyzed included BDEs 28, 47, 66, 85, 99, 100, 153, 154, 183, and 209, PCBs 8, 28, 37, 44, 49, 52, 60, 66, 70, 74, 77, 82, 87, 99, 101, 105, 114, 118, 126, 128, 138, 153, 156, 158, 166, 169, 170, 179, 180, 183, 187, and 189, and DDE. PCBs and DDE were analyzed with a gas chromatograph (Agilent 7890 GC) using a 30 m × 0.25 mm × 0.1 µm thickness column (Restek Rxi-XLB), coupled with a tandem mass spectrometer (Agilent 7000 MS/MS) equipped with an electron impact ionization source. PBDEs were analyzed with a gas chromatograph coupled with a single quadrupole mass spectrometer (Agilent 6890 GC / 5973 MS). A 15 m capillary column with a 0.25 mm ID and 0.10 µm thickness

(Restek Rtx-1614) was used for the separation. The MS was operated in the electron capture negative ionization (ENCI) mode with methane as the reagent gas.

A quality control protocol was implemented. No target chemicals were found in the tissue collection tubes using deionized water as matrix. One procedural blank was analyzed with each batch of 10-15 samples. ^{13}C -labeled PCB52 (as PCB surrogate) and two fluorinated PBDEs (FBDEs 47 and 208, as surrogates for PBDEs) were spiked into each sample before extraction. Their recoveries were $67\pm 18\%$ ($N=125$), $105\pm 21\%$ ($N=170$), and $96\pm 24\%$ ($N=124$), respectively. Limits of detection (LOD) and quantitation (LOQ) are listed in Table S2, calculated as the concentrations 3 and 10 times, respectively, of the instrument signal-to-noise ratio. Additional detailed quality control results are described in the Supplemental Material.

2.3. Statistical Analysis

Mixed effect models were used to test the hypothesis that, at the population level, the logarithms of the $_{10}\text{PBDEs}$, $_{32}\text{PCBs}$ and DDE concentrations did not change with time to tissue collection. Logarithm transformed concentrations were used to improve normality in the residuals. Mixed effects models were used rather than ANOVA because not all placentae were sampled at all time points. Mixed effects models were used rather than standard linear regression to account for repeated measures from each placenta. Specifically, placenta was treated as a random intercept effect to account for repeated measures from each placenta. The placenta random intercept was also nested within the study site variable to address the hierarchical study design. Models were implemented using the *lme* function with the maximum likelihood method in the R Project for Statistical Computing. The location hierarchical random effects were retained for location interclass correlation $\geq 1\%$. Models with random slope effects were compared to the random intercept models using the log-likelihood (logL) test, and were preferred when $p < 0.05$.

3. Results and Discussion

The measured concentrations of $_{10}\text{PBDEs}$, $_{32}\text{PCBs}$ and p,p'-DDE are presented in Table 1 and Figure 1. Descriptive statistics for individual analytes are summarized in Table S3. All concentrations are reported on a wet weight (ww) basis. Due to the nature of the MSPD extraction method, simultaneous lipid content determination was impossible, and the small quantity of tissue available did not allow for a separate lipid measurement. The concentrations of all analytes showed near log-normal distributions.

3.1. PBDEs

The median of $_{10}\text{PBDEs}$ in 42 placental tissue samples from initial collection time ($t = 0$) is 330 pg/g ww, with a range of 43–1,723 pg/g ww. Compared to those in European countries and Japan, PBDE levels in human placentae in the United States are significantly higher (see Table S4-a). The median (291 pg/g ww) of tri- to hepta- BDEs ($_{3-7}\text{BDEs}$) is about seven times that reported from a highly polluted e-waste recycling region in China (41 pg/g ww) (Zhao et al., 2013). Our finding aligns with reports that PBDE concentrations in various human samples from North America are generally one to two orders of magnitude higher than those in Europe and Asia (Hites, 2004; Sjödin et al., 2003).

The only previously published study in the United States of PBDEs in human placentae focused on analytical method development and involved only five placenta specimens collected in Chicago, IL during 2007 to 2008 (Dassanayake et al., 2009). While small sample numbers in that study make a direct comparison inconclusive, the range of the total concentration of the same ten congeners (367–2,317 pg/g wet wt) reported there

(Dassanayake et al., 2009) nonetheless overlaps with the range observed from the present study. Compared to Dassanayake et al., (2009), the median of the total tri- to hepta-BDEs in this study is significantly lower, while the concentration of BDE209 is 56% higher. These differences may reflect the impact of phasing-out commercial penta mixture in 2004, and continued use of commercial deca product.

For Σ_{10} PBDEs and almost all PBDE congeners, the median concentration values are higher in samples collected by UCD than those collected by UR or MCW (Table 1 and Figure 2-A). The median and mean concentrations of BDEs 47, 153 and 183 in UCD samples were approximately double those at the other two collection sites (Figure 2-B). Unpaired t-test using the natural log concentrations demonstrates that the differences between UCD and MCW are statistically significant for BDE47 ($p = 0.039$) and likewise between UCD and UR for BDE153 ($p = 0.0069$). For Σ_{10} PBDEs, p -values for t-tests comparing UCD with UR and MCW were 0.062 and 0.094, respectively, while $p = 0.46$ for the difference between UR and MCW. The higher levels of PBDEs in human placenta from UCD are consistent with elevated PBDE concentrations in house dust and serum observed in northern and central California, and may reflect unique furniture flammability standards in California (Zota et al., 2011, 2008). Interestingly, the range between the 25th and the 75th percentiles of Σ_{10} PBDEs at UCD is narrower than those at the other two locations (Figure 2-A), suggesting a lower variability in exposure to PBDEs among individuals living in northern California than in the areas of upstate New York or Milwaukee, Wisconsin. To our knowledge, this is the first report of geographic differences in placental PBDEs in the United States.

BDE47 is the most abundant PBDE congener, accounting for 37(± 13)% of Σ_{10} PBDEs (Figure 3-A). It is followed by BDEs 153, 99, 100, and 209 (Figure 3-A). The relative abundance of congeners varies around the world. In Europe, Japan and China, BDE209 is found to be the most abundant congener, accounting for more than 50% of the total concentrations in human placenta (Zhao et al., 2013; Frederiksen et al., 2009a; Gómara et al., 2007; Takasuga et al., 2006). In the United States, however, BDE47 is the most prevalent in human and other biota. The concentration of BDE47 in placenta is about one order of magnitude higher in the United States than in Europe, consistent with relatively high concentrations of BDE47 found in dust in the U.S. (Frederiksen et al., 2009b). Differences in congener distribution between the continents are not surprising, given the fact that Americans consumed 98% of pentaBDEs but only 44% of decaBDE on the global market (Hites, 2004). In addition, the lower BDE congeners, namely BDEs 28+33, 47, 66, 85, 99, 100, 153, and 154, all of which are components of commercial penta mixture (La Guardia et al., 2006), are significantly positively correlated (Table S5).

The limited number of observations over past decades makes time trend analysis difficult. Overall, the trend is one of increasing concentrations over time (Figure 4-A). In the year 2000, BDE47 levels in human serum of the U.S. population exceeded that of PCB153 (Sjödin et al., 2004). Among all the analytes we examined, BDE47 had the highest level. The median concentration ratios of BDE47 to PCB52, PCB153, and DDE were 2.2, 6.5 and 1.3, respectively.

3.2. PCBs

The median of Σ_{32} PCBs in the 42 placenta tissue samples initially collected ($t = 0$) was 371 pg/g ww, ranging from 76 to 856 pg/g ww (Table 1). The set of PCBs analyzed in this study included 7 “indicator” congeners (PCBs 28, 52, 101, 118, 138, 153 and 180), which are often the most abundant congeners found in the environment and in humans. The set of targeted PCBs also contains 8 of the 12 “dioxin-like” congeners (PCBs 77, 105, 114, 118, 126, 156, 169 and 189).

Using an ANOVA single factor test on the means of log-transformed concentrations from the initial collection time, no significant differences between collection sites were found for the seven indicator PCBs and $\Sigma 32$ PCBs, although both the mean and median for UCD are higher than those at the other sites (Figure 2-A). Additionally, no significant correlation was found between $\Sigma 32$ PCBs and $\Sigma 10$ PBDEs ($p = 0.43$). This was not unexpected based on the differences between PCBs and PBDEs with regard to their sources of human exposure and time scales of production and use.

The homolog distribution pattern of PCBs is shown in Figure 3. Among the 32 PCBs analyzed, PCB52 was found to have the highest median concentration, followed by two other indicator congeners, PCBs 28 and 101. PCB126 was detected least frequently and was present in only 48% of the samples. Gómara et al., (2012) also found PCB52 concentrations higher than others. A number of studies found PCB153 to be the most abundant congener in placenta (Bergonzi et al., 2009; Reichrtová et al., 1999). In the serum of pregnant and non-pregnant women in the U.S. in 2003-2004, PCB153 was higher than PCB52 (Woodruff et al., 2011). Most of the major congeners are strongly correlated with each other, except PCB180 (Table S5). These variations in PCB congener patterns in human samples warrant further study.

Table S4-b summarizes the PCB concentrations reported in the literature. Caution is needed in comparing the data, due to the different congeners included as well as possible variations in detection limits and data quality. Generally, PCB concentrations in human placenta appear to be higher in North America and Europe than in Asia. This spatial distribution pattern for PCBs in placental tissue may reflect the fact that about 80% of global PCB production occurred in the U.S. and European countries (Breivik et al., 2002).

Since its ban in the 1970s, the PCB burden in humans has been declining. Using the wet weight based concentration data in Table S4-b with exclusion of studies from Asia and/or using only dioxin-like PCBs, we modeled time trends based on first-order kinetics, i.e., $\ln C$ vs. year of placental collection (Figures 4-B). Despite the differences in the number of PCB congeners used and the geographical regions among individual studies, the regression statistics are remarkably strong ($R^2 = 0.93$ and $p = 0.0001$; Table S6). The apparent half-life of the decline, estimated from the slope, is 5.2 ± 0.6 years. Long-term declining trends in PCB concentrations have been reported in numerous studies, with apparent half-lives of, for example, about 7 years in air (Sun et al., 2006) and 3-6 years before 1990 then 15-30 years in fish (Carlson et al., 2010) of the Great Lakes. In humans, reported congener-specific apparent half-lives of PCBs range from 0.1 to >40 years (Ritter et al., 2011).

3.3. DDE

p,p'-DDE was detected in 100% of placenta samples, with mean concentration of 168 pg/g ww and median concentration of 74 pg/g ww for samples collected at $t=0$ (Table S3). The corresponding mean and median for samples from all collection time points were 205 pg/g ww and 81 pg/g ww, respectively, ranging from 10 ww to 3,223 pg/g ww (Table 1). Although large scale production of the pesticide DDT commenced and ended earlier than it did for PCBs and PBDEs, the DDT metabolite DDE is still more prevalent and abundant in human placenta than any individual PCB or PBDE congener except BDE47, based on the medians found in this work (Table S3).

DDE concentrations reported in the literature range from 58 pg/g lipid to 5×10^6 pg/g lipid (Table S4-c). The averages in Table S4-c indicate a declining trend over time (Figure 4-C) despite high variability in recent years. The overall DDE half-life, calculated from the slope of the regression based on first order kinetics using the mean concentrations summarized in Table S4-c, is about 8.3 ± 3.4 years. If only data from the U.S. are used, the half-life is

5.5±0.5 years. The widespread use of DDT from the 1940s to the 1970s around the world, and the fact that DDE is highly persistent, make DDE a global pollutant. Despite differences in the scale of DDT application among countries, the overall declining trend on a global scale is clear and strong. Similar trends in air, soil, wildlife, and human DDE concentrations have been widely reported in many regions of the world, including the Arctic.

In this work, the highest DDE concentrations (>1,000 pg/g ww at t = 0) were found in two placentas collected by UCD and MCW, respectively. The two next highest (>300 pg/g ww at t = 0) were both from UR. The 90th percentile of all the samples was 270 pg/g ww. In contrast to PBDEs and PCBs, access to DDT stored in the individual home environment could dominate overall personal exposure in these cases. Nonetheless, placental tissues collected by UCD had comparatively higher DDE concentration than those from UR (p = 0.03), based on a one-tail t-test for t = 0 data, implying the existence of regional differences. The Spearman rank correlation of DDE with Σ PCBs was strong (p = 0.003) but not with Σ PBDEs (p = 0.46). The correlation between DDE and PCBs could be the result of similar time periods (1940s to 1970s) for human exposure. DDE does not share any sources or time scale with PBDEs.

3.4. Variation of measured concentrations with placenta storage time

Variations of the concentrations of Σ PBDEs, Σ PCBs and DDE over increasing delays in placental tissue sampling were analyzed. The results demonstrated that, in general, the variation was within ±50% up to 48 h, and did not show significant difference among collection sites. Greater variations in concentration were observed in samples stored 72 h or longer (Figure 5).

Final mixed effects models are presented in Table 2. The hierarchical random intercept effect was included for ln(Σ PBDE) only, indicating that the mean concentrations differed among the study locations. Of the unexplained variance in ln(Σ PBDE) concentrations, 4.6% was explained at the level of study site and 43% at the level of individual placenta, which means that the variability between study sites was smaller than the variability among placenta. Of the unexplained variance in ln(Σ PCBs) and ln(DDE) concentrations, 30% and 85% was explained at the level of individual placenta, respectively. This means that, for all three chemical classes studied, pollutant concentrations vary widely among placenta.

Our specific objective with these models was to test if the concentrations changed with increasing time to sample collection (0–120 h). The event of no change with sample collection time was indicated by a regression coefficient equal to zero, $\beta_1 = 0$, and tested against a two-sided alternative hypothesis, $\beta_1 \neq 0$. The addition of a random slope effect was considered, but this model did not converge (e.g., Σ PCBs and DDE), or provided no improvement relative to random intercept models (e.g., Σ PBDE, log-likelihood test p-value = 0.09). For all pollutants, the change with time, β_1 , is slightly positive, but not statistically significantly different from zero (Table 2). This indicates that at the population level and for these data, the concentrations of ln(Σ PBDE), ln(Σ PCBs), ln(DDE) do not change significantly with delays of up to 120 h in tissue sample collection from refrigerated placenta.

This analysis suggests that, when placenta are refrigerated at 4°C under clean conditions, delays of <120 h in tissue collection may not significantly alter results of measurements of PBDEs, PCBs, and DDE in placental tissue. However, variation of pollutant concentrations with prolonged storage without proper preservation may occur due to contamination from air or collection containers, loss of blood, and other unknown factors. The observed variation of concentration over time may also be explained by tissue heterogeneity of the placenta. This effect would be eliminated by homogenization of the placenta prior to

specimen collection. In this study, homogenizing the placenta was in conflict with the study design to simulate undisturbed placental tissue prior to tissue collection. To minimize potential changes in pollutant concentrations, tissue collection within 72 h of delivery is strongly recommended for analysis of trace level persistent organic chemicals.

In conclusion, the results of this work indicate that widespread and geographically varied prenatal exposure to persistent organic pollutants in the United States continues. Future study of the sources, influencing factors, and health consequences of such exposure is warranted. Investigation of temporal trends in concentrations of these chemicals in placental tissue suggests continued decline for PCBs and DDE but an increasing overall trend for PBDEs. Our findings indicate additionally that procedures developed for NCS collection, transport, processing, shipment, and storage of placental tissue preserve relative stability for measurement of PBDEs, PCBs, and DDE for at least 72 hours.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- We measured 10 PBDEs, 32 PCBs, and DDE in 169 placenta specimens from 42 placentae.
- Significant geographic differences in placental PBDEs in the U.S. were found.
- Worldwide first-order declining trends for PCBs and DDE were identified.
- The concentrations did not vary much for specimens collected <72 h after delivery.

Figure 1.

Box and whisker plot of concentrations of (A) PBDEs and (B) PCBs and DDE in placentae collected at $t = 0$ ($N = 42$). Shown are average (cross), median (lines inside the box), 25th to 75th percentiles (box), 10th and 90th percentiles (whiskers), and the minimum and maximum (circles). Missing data points indicates the presence of non-detect results.

Figure 2.

Comparison of concentrations at time = 0 among placenta collection sites (N = 13 for UCD, N = 17 for UR, and N = 12 for MCW). Shown are average (cross), median (lines inside the box), 25th to 75th percentiles (box), 10th and 90th percentiles (whiskers), and the minimum and maximum (circles). In (B) two major components in the commercial product “penta” BDEs 47 and 153 and a representative congener of product “octa” BDE183 are selected.

Figure 3. PBDE congener and PCB homolog distributions (as % of Total) based on the averages of specimens collected at $t = 0$ ($N = 42$).

Figure 4.

Temporal trends of concentrations in human placenta tissue. Data are from Table S4. The median concentrations were used for PBDEs and PCBs; while for DDE the mean was used due to the limited number of reported medians. For PCBs, studies from Asia and/or using only “dioxin-like” congeners are excluded. Regression statistics are given in Table S6.

Figure 5. Relative change of concentrations with placental storage time. Symbol shape indicates study location, and color indicates each unique placenta.

Table 1

Median and range of concentrations (pg/g ww) by sampling site.

Analyte	Rochester NY	Davis CA	Waukesha WI	All Sites
Specimens collected at time = 0 h				
n *	17	13	12	42
₁₀ PBDEs	266 (43–848)	343 (172–1723)	317 (76–1493)	330 (43–1723)
₃₂ PCBs	395 (174–856)	412 (76–848)	344 (185–577)	371 (76–856)
DDE	56 (10–397)	120 (51–1968)	63 (33–1039)	74 (10–1968)
All specimens collected				
N **	76	52	41	169
₁₀ PBDEs	266 (43–6083)	431 (155–1779)	191 (31–1554)	313 (31–6083)
₃₂ PCBs	409 (164–876)	406 (76–1572)	360 (134–902)	395 (76–1572)
DDE	69 (10–637)	122 (12–3223)	77 (14–1951)	81 (10–3223)

*
n = the number of placentae collected.

**
N = the number of specimens received by the analytical laboratory.

Table 2

Mixed effects models of pollutant concentrations as a function of sample collection time with a random intercept effect of placenta or placenta nested within study location.

Estimate	ln(₁₀ PBDEs)		ln(₃₂ PCBs)		ln(DDE)	
	Estimate	SE	Estimate	SE	Estimate	SE
intercept β_0	5.75	0.160	5.92	0.0557	4.46	0.150
time slope β_1	1.7×10^{-3}	2.0×10^{-3}	5.9×10^{-3}	1.1×10^{-3}	2.0×10^{-3}	1.2×10^{-3}
location intercept variance σ_γ^2	0.0372		-		-	
placenta intercept variance σ_0^2	0.347		0.0623		0.860	
error variance σ^2	0.426		0.148		0.152	
-2logL	390.16		190.12		285.18	