Variability in PCB and OH-PCB Serum Levels in Children and Their Mothers in Urban and Rural U.S. Communities

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ABSTRACT: Environmental exposures that affect accumulation of polychlorinated biphenyls (PCBs) in humans are complex and not fully understood. One challenge in linking environmental exposure to accumulation is determining variability of PCB concentrations in samples collected from the same person at different times. We hypothesized that PCBs in human blood serum are consistent from year to year in people who live in the same environment between sampling. We analyzed blood serum from children and their mothers from urban and rural U.S. communities (n = 200) for all 209 PCBs (median ΣPCBs = 45 ng/g lw) and 12 hydroxylated PCBs (median ΣOH-PCBs = 0.09 ng/g lw). A subset of these participants (n = 155) also had blood PCB and OH-PCB concentrations analyzed during the previous calendar year. Although many participants had similar levels of PCBs and OH-PCBs in their blood from one year to the next, some participants had surprisingly different levels. Year-to-year variability in ΣPCBs ranged from −87% to 567% and in ΣOH-PCBs ranged from −51 to 358% (5th−95th percentile). This is the first study to report variability of all PCBs and major metabolites in two generations of people and suggests short-term exposures to PCBs may be a significant component of what is measured in human serum.

INTRODUCTION

Polychlorinated biphenyls (PCBs) are a class of 209 anthropogenic, chlorinated organic compounds that were widely manufactured and used around the world in a variety of industries and products like electrical components and building materials. Production of commercial mixtures of PCBs ended in the United States in 1977, but PCBs are still widely manufactured and used around the world in a variety of industries and products like electrical components and building materials.

There are few recent studies of PCBs with repeat sampling of the same participants over time using congener-specific analysis, and no studies have evaluated all 209 PCBs and OH-PCBs over time. These few studies found an overall decrease in selected PCBs over periods ranging from 4 to 28 years, though trends for individual congeners and participants varied. In most cases, a major source of exposure (e.g., a nearby chemical plant or fish consumption) was identified as having been removed or reduced between the first and last sampling date.

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Congener-specific analysis for all 209 PCBs is optimal for determining the variability of PCBs in human serum over time because of humans’ exposure to a range of low to high chlorinated current and legacy PCBs and because PCB metabolism in the body is congener-specific depending on the number and position of chlorines. In this study we quantified blood concentrations of two groups of target analytes, 209 PCBs and 12 OH-PCBs, in mother/child pairs living in urban or rural locations.

Residents of our urban cohort live in East Chicago, Indiana. East Chicago was incorporated in 1893 as a railroad and steel community and is still heavily industrialized. East Chicago is bisected by the Indiana Harbor and Ship Canal (IHSC), an artificial waterway created to serve the manufacturing industries. The IHSC also flows near junior and senior high schools. Volatilization from IHSC contributes about 7.5 kg/yr of PCBs to the air.

Residents of our rural cohort live in the Columbus Community School District, which includes Columbus Junction, Columbus City, Conesville, Cotter, Fredonia, and surrounding rural areas with the schools located in Columbus Junction, IA. Columbus Junction was incorporated in 1874 as a railroad and steel town but in contrast to East Chicago, Columbus Junction is now predominantly an agricultural setting. The Columbus Community School District has no known current or historical industrial sources of PCBs.

Dietary habits, environmental exposures, and physiological changes like body composition and metabolism are expected to remain fairly consistent in a shorter period of time, and therefore we assumed that PCB concentration in an individual does not change significantly in a short period of time. We hypothesized that little variability from year to year would be measured in human serum. To address this hypothesis, we characterize the second annual data set of PCBs and OH-PCBs from children and their mothers living in East Chicago and the Columbus Junction area and compare them with the first annual data set, previously reported, in order to quantify the variability from one year to the next. We are the first to quantify variability of all PCBs and the major OH-PCBs in the same people.

### MATERIALS AND METHODS

#### Sample Collection, Extraction, and Instrument Analysis

Serum samples and survey data were collected from junior high school-aged students and their mothers who were enrolled in the Airborne Exposures to Semivolatile Organic Pollutants (AESOP) Study between April 2009 and March 2010. In this second year of the study, serum was analyzed from 50 East Chicago mothers and their 50 enrolled children and from 46 Columbus Junction area mothers and their 54 enrolled children. Of those 200 participants, 155 had also provided blood for the year 1 (April 2008-March 2009) data set. Nine families enrolled more than one child. All AESOP subjects gave informed consent or assent in English or Spanish according to an established Institutional Review Board protocol. Participants generally did not fast prior to giving blood. The sample collection, extraction, separation, and cleanup methods are described in detail elsewhere, with minor improvements included here. Briefly, sera were weighed (~4 g) and spiked with 5 ng $^{13}$C-labeled PCBs and 4′-OH-PCB 159 (Supporting Information (SI) Table S1). The OH-PCB extract was derivatized to the methoxylated form (MeO-PCBs) using diazomethane. Immediately prior to instrument analysis, PCB extracts were spiked with 2 ng $^{13}$C-labeled internal standards and OH-PCB extracts were spiked with 5 ng PCB 209 (SI Table S1). Nine samples were removed from the PCB and OH-PCB data sets for having less than 4 g serum available for extraction, and 33 samples were removed from the OH-PCB data set following extraction errors.

GC-MS/MS (Agilent 7000 and Agilent 6890N with Waters Micromass MS) in multiple reaction monitoring mode was used for identification and quantification of 209 PCB congeners as 159 chromatographic peaks. GC-ECD was used for identification and quantification of 12 OH-PCB congeners as MeO-PCBs. Instrument operating parameters are in the SI. Instrument blanks of hexane were analyzed with each instrument run before and after the calibration and after the samples to ensure no cross-contamination.

Calibration standards were purchased from Cambridge Isotope Laboratories, Inc. (Andover, MA) and AccuStandard, Inc. (New Haven, CT, USA). The OH-PCB congeners were chosen based on the known metabolic pathways for the most common PCB congeners detected in the year 1 serum samples and commercial availability (as MeO-PCBs). Congener mass was calculated by applying a relative response factor obtained from each congener in the calibration.

A common congener list (SI and Table S7) was used when comparing the two data sets. Median change in PCB concentration from year 1 to year 2 was 8 ng/g lw (28%) considering all congeners and 6 ng/g lw (14%) using the common congener list. Median change in OH-PCB concentration from year 1 to year 2 was 0.032 ng/g fw (54%) considering all congeners and 0.004 ng/g fw (4%) using the common congener list.

#### Statistics

The concentration data set was first dichotomized at the threshold of the congener-specific LOQ (SI Tables S3–S4). Distribution of sum and individual congener concentrations were skewed to the right, and data did not exhibit a normal distribution following logarithmic transformation. Therefore, the nonparametric Wilcoxon Rank Sum test and Wilcoxon Signed Ranks test were used to compare sum and individual congener concentrations and paired mother-child sum concentrations, respectively.

Statistical analysis was carried out in R 2.13.1 and Minitab 16 (7.14.0.739). In all statistical tests, the level of significance was $\alpha = 0.05$.

#### Quality Control

Data were evaluated for representativeness, precision, reproducibility, and accuracy using a suite of quality control measures including method blanks, surrogate standards, and replicates of Standard Reference Material from the National Institute of Standards and Technology (NIST SRM 1957: Organic Contaminants in Non-Fortified Human Serum).

Method blanks consisting of 4 mL potassium chloride (1% w/w KCl in reagent water) were extracted, analyzed, and quantified with each batch of 10 samples. Most congeners were detected in the method blanks at low levels below 0.05 ng representing background noise (mean 0.012 ± 0.028 ng and mean 0.016 ± 0.042 ng for PCBs and OH-PCBs, respectively). A limit of quantification (LOQ) for each congener was determined as the upper limit of the 95% confidence interval (average mass in the method blanks plus two times the standard deviation). The sum of PCBs in five batches were higher than in the blank mass in the other 20 batches ($p = 0.0001$); consequently a separate LOQ was determined for those batches. PCB LOQ, ranged from 0.0021 ng for PCB 24 to
0.68 ng for PCB 52 (mean 0.035 ± 0.067 ng). OH-PCB LOQ ranged from 0.0039 ng for 3′-OH-PCB 118 to 0.066 ng for 4′-OH-PCB 107 (mean 0.025 ± 0.021 ng).

Surrogate standards (SI Table S1) were used to evaluate extraction efficiency, and sample mass was corrected according to surrogate recoveries. Recovery of 13C-PCB 194 on the Agilent GC-MS/MS was consistently poor compared to the unlabeled standard, and therefore the 13C-labeled hepta-chlorinated surrogate standard (13C-PCB 180) was used instead of 13C-PCB 194 to correct the mass of octa-chlorinated PCBs. Quantification of the SRM confirmed the appropriateness of this substitution. Recovery of the remaining nine PCB...
surrogate standards ranged from 22 to 213% (mean 85 ± 25%). Recovery of the OH-PCB surrogate standard ranged from 40 to 113% (mean 70 ± 11%) (SI Table S5).

Analysis of PCBs in the SRM using the same extraction and quantification as the samples (SI Figure S1) resulted in a mean difference of 6 ± 17% between the NIST certified or reference values and our measured values for 22 congeners. Analytical variability of measurements between year 1 and year 2 can be approximated by the 22% difference in ∑PCBs in the NIST SRM 1957 extracted and analyzed in year 1 and again extracted and analyzed in year 2. Although their identity and concentration are not certified by NIST, we report values for OH-PCBs detected in the SRM (SI Table S6).

■ RESULTS AND DISCUSSION

PCBs and OH-PCBs in Year 2 Participants. 202 PCB congeners as 152 unique chromatographic peaks and all 11 OH-PCBs were detected in the samples (SI Tables S9–S11). Frequently detected PCBs included dioxin-like congeners 105, 118, 156 + 157, and 167. ∑PCBs concentrations ranged from 4 to 199 ng/g lipid weight (5th–95th percentile; median 45 ng/g lw). ∑OH-PCB concentrations ranged from 0.04 to 0.27 ng/g fresh weight (5th–95th percentile; median 0.09 ng/g fw). After removing one leverage point, a Columbus Junction mother with ∑PCBs and ∑OH-PCBs much higher than the other participants, there was a significant positive correlation between ∑PCBs and ∑OH-PCBs (Figure 1, R = 0.48, p < 0.0001).

Concentrations of sum and individual PCBs and OH-PCBs were not statistically significantly different between East Chicago and Columbus Junction participants except PCBs 11, 61 + 70 + 74 + 76, 178, 180 + 193, 194, 203, and 3′-OH-PCB 193 (SI Table S8). Concentrations of the 31 PCBs and 9 OH-PCBs that were detected in at least 20% of participants are shown in Figures 2 and 3, respectively. Our finding of similar concentrations between the urban and rural locations is consistent with the results from the first year of sample analysis.2

Children had lower levels of OH-PCBs in their blood than their mothers (p < 0.0001) and much lower levels of PCBs (p < 0.0001). East Chicago and Columbus Junction children had median ∑PCBs of 46% (8–155%, 5th–95th percentile) and 30% (2–110%, 5th–95th percentile), respectively of their mothers. In contrast, East Chicago and Columbus Junction children had median ∑OH-PCBs of 79% (28–181%, 5th–95th percentile) and 62% (13–140%, 5th–95th percentile), respectively of their mothers. This result could be due to children’s faster metabolism26 or our focus on higher molecular weight OH-PCBs with five to seven chlorines.

Children are enriched in low molecular weight PCBs (homologues 1–5) compared to their mothers. An average of 64% and 59% of ∑PCBs are from low molecular weight PCBs.
in East Chicago and Columbus Junction children, respectively, compared with an average of 42% and 40% in East Chicago and Columbus Junction mothers, respectively. Unlike their mothers, we presume the children have not yet accumulated the higher molecular weight PCBs associated with dietary intake. Therefore, low molecular weight PCB exposure in children is important to their blood PCB levels.

**Comparison between Year 1 and Year 2.** A subset of participants \( n = 155 \) also had blood PCB and OH-PCB concentration analyzed during the previous calendar year (April

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**Figure 4.** Change in concentration (left: ng/g lw; right: %) of total, low, and high PCBs, where low PCBs are the sum of homologues 1−5 and high PCBs are the sum of homologues 6−10. A positive value indicates an increase in concentration from year 1 to year 2. EC M and EC C represent East Chicago mothers and children, respectively. CJ M and CJ C represent Columbus Junction mothers and children, respectively.

**Figure 5.** Change from year 1 to year 2 of each PCB congener in mothers and children. A positive value indicates concentration increased. Error bars represent the 5th−95th percentile ranges of change in concentration.
2008 to March 2009). Correlations between year 1 and year 2 concentrations are shown in SI Table S12. The median change in $\sum$PCBs from year 1 to year 2 was 6 ng/g lw but ranged from $-115$ to 164 ng/g lw (5th–95th percentile) indicating high variability in some participants (Figure 4). After removing seven participants with $\sum$PCBs < LOQ in year 1, this change represented a median of 14% of the participants’ year 1 $\sum$PCBs and ranged from $-87\%$ to $56\%$ (5th–95th percentile). Of all participants, 27% lost or gained more than 40 ng/g lw $\sum$PCBs (the median $\sum$PCBs in year 2). Of the 148 AESOP participants with $\sum$PCBs > LOQ in both year 1 and year 2, the vast majority (82%) had a change more significant than the estimated analytical variability. Concentrations of PCBs significantly changed from the first year to the second year in more children (88%) than mothers (76%), suggesting that children’s serum PCB concentrations especially reflect short-term exposures compared with their mothers. There is no meaningful correlation of percent change between mothers and their children ($R^2 = 0.061, p = 0.05$).

While the median variability for most PCBs was zero, large variability was found in several congeners (Figure 5). PCBs with the largest range of variability in concentration are shown in Table 1 along with the percent of mothers and children whose variability was greater than the estimated analytical variability. These congeners include higher molecular weight PCBs commonly reported in people (118, 138, 153, 180, and 187) that have been associated with dietary intake. It is possible that the large variability associated with these congeners reflects day-to-day variability from a large dietary intake of PCBs prior to sampling, although daily or monthly short-term variability is unexplored in the peer-reviewed literature. For all but one of these high variability congeners, more mothers had significant variability in concentration than children, and mothers gained more high molecular weight PCBs than their children. These differences between mothers and children could be a reflection of exposure or metabolism differences, or a combination. No difference in PCB concentration changes between boys and girls was observed.

A similar median variability but smaller range compared to our participants was observed in two published studies measuring changes in PCB levels across three and nine years. In two different cohorts of pregnant Californians sampled in 2008–2009 and 2011–2012, Zota et al. found that the geometric mean of sum of five tetra- to hepta-chlorinated congeners decreased 25% (range $−68\%$ to $7\%$), whereas PCB 180 declined 71% (range $−141$ to $−22\%$) between the earlier and later cohorts. Humblet et al. reported a pilot study of eight women who gave serum samples in 2000 and 2009 and found that concentration of sum of 36 PCBs decreased by an average of 19% (range $−48\%$ to $54\%$) during those 9 years. The women lived near a chlorinated chemical plant that ended operations in 2003, between the two sampling time points. These studies present important but incomplete observations about PCB trends in humans. In both cases there were externalities that may have caused a decrease in PCBs, and the decrease was observed over longer time periods. In our study examining the same cohorts, we observe significant individual variability but do not observe significant overall population declines in PCB concentration over the relatively short two year period.

| PCB | change in concentration (fifth to 95th) | % change (fifth to 95th) | estimated % change due to analytical variability | % mothers, with $\Delta > \text{analytical variability}$ | % children with $\Delta > \text{analytical variability}$ |
|-----|-----------------------------------------|-------------------------|-----------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| 20 + 28 | $-6 \text{ to } 5$ | $-32 \text{ to } 29$ | 87 | 10 | 3 |
| 66 | $-5 \text{ to } 8$ | $-13 \text{ to } 66$ | 136 | 1 | 1 |
| 83 + 99 | $-9 \text{ to } 7$ | $-85 \text{ to } 58$ | $-2$ | 85 | 64 |
| 105 | $-3 \text{ to } 5$ | $-20 \text{ to } 46$ | 58 | 10 | 1 |
| 110 + 115 | $-8 \text{ to } 12$ | $-26 \text{ to } 39$ | N/A | N/A | N/A |
| 118 | $-10 \text{ to } 13$ | $-57 \text{ to } 99$ | 8 | 71 | 29 |
| 129 + 137 + 138 + 163 + 164 | $-7 \text{ to } 9$ | $-71 \text{ to } 69$ | $-14$ | 44 | 21 |
| 146 | 0 to 3 | 0 to 61 | 50 | 8 | 2 |
| 153 + 168 | $-6 \text{ to } 9$ | $-75 \text{ to } 60$ | $-8$ | 49 | 31 |
| 156 + 157 | 0 to 4 | 0 to 53 | $-1$ | 60 | 8 |
| 170 | $-2 \text{ to } 5$ | $-18 \text{ to } 69$ | $-13$ | 35 | 4 |
| 180 + 193 | $-3 \text{ to } 7$ | $-30 \text{ to } 93$ | 4 | 71 | 32 |
| 187 | $-3 \text{ to } 4$ | $-22 \text{ to } 46$ | 1 | 81 | 25 |
| $\sum$PCBs | $-50 \text{ to } 83$ | $-87 \text{ to } 567$ | 22 | 76 | 88 |

*Note: Concentration is in units of ng/g lipid weight. The estimated % change due to analytical variability was determined from extraction and analysis of NIST SRM 1957 in both year 1 and year 2, where N/A means not available because congener concentrations are not certified by NIST. The 10 coeluting groups (containing 19 congeners) with biggest decrease in concentration (as indicated by the 5th percentile of the difference between year 1 and year 2) and 10 coeluting groups (containing 18 congeners) with the biggest increase in concentration (as indicated by the 95th percentile of the difference between year 1 and year 2) were selected for this table. Seven coeluting groups (containing 14 congeners) had both the biggest decrease and biggest increase.*

**Table 1. Sum and Individual PCBs with Largest Change from Year 1 to Year 2**
these studies are related to declines in the PCB levels in their food source (fish) or due to loss of PCBs through childbirth, whereas our cohorts were not selected as fishers or pregnant women. Furthermore, PCB decline observed in these studies were in higher molecular weight PCBs, whereas our study also included lower molecular weight PCBs.

The change in $\Sigma OH$-PCBs in our cohort from year 1 to year 2 was an order of magnitude less variable than found for $\Sigma$ PCBs. The median change was 0.004 ng/g fw but ranged from $-0.07$ to 0.10 ng/g fw (5th–95th percentile), again indicating high variability in some participants (Figure 6). After removing one participant with $\Sigma OH$-PCBs < LOQ in year 1, this change represented a median of 4% of the participants' $\Sigma OH$-PCBs and ranged from $-51$ to 358% (5th–95th percentile). Of all participants, only 6% lost or gained more than 0.09 ng/g fw OH-PCBs (the median $\Sigma OH$-PCBs in year 2). The median change was nonzero for three of four OH-PCBs in mothers and only one of four OH-PCBs in children. Of the four OH-PCBs, year to year variability was largest for 3′-OH-PCB 138 for mothers and 4-OH-PCB 107 for children (Figure 7). No difference in OH-PCB concentration changes between boys and girls were observed.

The only other study that quantified variability in OH-PCB concentrations, (although in different people from year to year) supports our finding that OH-PCB concentrations are less variable. Zota et al. found that the sum of the three measured congeners were not different between the two cohorts across three years, although most of the pregnant Californians had concentrations of the three OH-PCBs measured below the detection limit which makes their results harder to interpret.

A quartile analysis of the PCB and OH-PCB year to year variability within each participant subgroup was also performed. Most participants' PCB concentrations remained in the same quartile rank from year 1 to year 2, or changed only by one quartile. A small number (8%) of East Chicago mothers' concentrations increased or decreased more than one quartile compared with 32% of East Chicago children. PCB concentrations in Columbus Junction mothers and children were more similar year to year, with 24% and 21%, respectively increasing or decreasing by more than one quartile. Participants' OH-PCB concentrations changed quartiles in about the same percentage in each subgroup (27% East Chicago mothers, 25% East Chicago children, 20% Columbus Junction mothers, and 20% Columbus Junction children).

**Figure 6.** Change in concentration (left: ng/g fw; right: %) of sum of four OH-PCBs. A positive value indicates an increase in concentration from year 1 to year 2. EC M and EC C represent East Chicago mothers and children, respectively. CJ M and CJ C represent Columbus Junction mothers and children, respectively.

**Figure 7.** Change from year 1 to year 2 of each OH-PCB congener in mothers and children. A positive value indicates concentration increased. Error bars represent the 5th–95th percentile ranges of change in concentration.
We assumed that PCB concentration does not change much from year to year because dietary habits, environmental exposures, and physiological changes like body composition and metabolism are thought to remain fairly consistent in a shorter period of time. Our data show this assumption is not true for most participants in this study. In this paper we examined variability in the same population from one year to the next, and we are the first to quantify variability for all 209 PCBs and the commonly reported OH-PCBs in the same people. Although many participants had similar levels of PCBs and OH-PCBs in their blood from one year to the next, a subset of participants had surprisingly different levels, and most participants (82%) had variability in blood concentrations beyond changes due to analytical method differences. Some PCB and OH-PCB congeners had much greater variability than other congeners. This variability could be due to exposure differences, physiological changes such as metabolism and weight, or a combination, and further research to clarify the cause of the observed variability is ongoing.

ASSOCIATED CONTENT

Supporting Information
Method details, quality control results, tables of congener-specific lipid weight and fresh weight PCB and OH-PCB concentrations, and correlation analysis results. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes
The authors declare no competing financial interest.

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