Analysis of NHANES Measured Blood PCBs in the General U.S. Population and Application of SHEDS Model to Identify Key Exposure Factors

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Competing Interests Declaration
All authors declare no potential competing financial interests.

List of Abbreviations and Definitions
A/P/N/M: Asian/Pacific Islander/Native American/Other Multiracial
EPA: U.S. Environmental Protection Agency
FCID: EPA's Food Consumption Intake Database
GLM: general linear model
GM: geometric mean
NHANES: National Health and Nutrition Examination Survey
ORD: Office of Research and Development
PCBs: polychlorinated biphenyls

RAC: raw agricultural commodity
SHEDS: Stochastic Human Exposure and Dose Simulation (model)
U.S.: United States

ABSTRACT

Studies have shown that the U.S. population continues to be exposed to polychlorinated biphenyls (PCBs), despite their ban more than three decades ago, but the reasons are not fully understood. The objectives of this paper are to characterize patterns of PCBs in blood by age, gender, and ethnicity, and identify major exposure factors. EPA's SHEDS-Dietary exposure model was applied, combining fish tissue PCB levels from a NYC Asian Market survey with NHANES dietary consumption data, and then linked with blood biomarkers for the same NHANES study subjects. Results reveal that the mean concentration of total PCBs in blood were higher with increasing age; however, for the same age, gender, and ethnicity, the blood PCB concentrations measured in the later NHANES survey were significantly lower than those in the earlier one. The decrease within an age group between the two survey periods lessened with increasing age. Blood PCBs among different ethnicities ranked differently between the older and younger age groups within each survey. Non-Hispanic Blacks had significantly higher blood PCBs for the >30 year age group. For the 12 to ≤ 30 year age group, the "Asian, Pacific Islander, Native American or multiracial" group had the highest values, with patterns fairly consistent with fish consumption and modeled PCB exposure patterns. We conclude that for younger people, patterns correspond to reduced environmental contamination over time, and are strongly associated with fish consumption and dietary exposures. Higher PCB concentrations in blood of the older population may partially reflect past exposures to higher environmental PCB concentrations, particularly prior to the ban.

Introduction

Polychlorinated biphenyls (PCBs) are synthetic organochlorine compounds representing an important class of anthropogenic xenobiotics. PCBs released into the environment tend to bioaccumulate and persist in ecosystems for a long time (Risebrough, Rieche et al. 1968). As lipophilic compounds, PCBs often bioconcentrate in the food chain and accumulate in the adipose tissues of animals (Pichirallo 1971; Tanabe, Kannan et al. 1987; Picer and Picer 1994; Roose, Cooreman et al. 1998). The exposure to PCBs by the human populations is widespread and has been associated with a variety of health risks (Finkles, Priester et al. 1972; Price and Welch 1972; Yobs 1972; Kimbrough 1995). The United States Environmental Protection Agency (EPA) and the International Agency for Research on Cancer (IARC) classified PCBs as probable carcinogens (U.S.EPA 1997; IARC 1998). Other health risks include adverse effects on neurodevelopment (Needham, Barr et al. 2005), neuropsychological function (Schantz, Widholm et al. 2003; Stewart, Lonky et al. 2008), and contribution to metabolic syndrome (Lee, Lee et al. 2007) and diabetes (Lee 2006) have been reported.

In the U.S., PCBs were manufactured between 1929 and 1977 by Monsanto and distributed under a trade name of Aroclor (Broadhurst 1972). PCBs released from their industrial and residential applications moved into environments via different routes (Nisbet and Sarofim 1972) and resulted in environmental accumulation (Risebrough, Rieche et al. 1968; Risebrough and De Lappe 1972). As early as 1967, PCBs were detected in U.S. human populations (Price and Welch 1972; Yobs 1972). While a ban of open use of PCBs in 1973 and a shut down of PCBs production in 1979 in the U.S. has played a very significant role in curtailing the progression of PCBs contamination (Fensterheim 1993; Hickey, Batterman et al. 2006; Sun, Basu et al. 2007), the persistence of PCBs (Hom, Risebrough et al. 1972; Kuzyk, Macdonald et al. 2010) still presents health problems, and PCBs have been recognized as an important class of persistent organic pollutants (POPs) (Isosaari, Kankaanpaa et al. 2002; Binelli, Ricciardi et al. 2004; Howel 2007; Schuster, Gioia et al. 2010). Studies have shown that much of the U.S. human population is still exposed to PCBs (Kreiss 1985; Robinson, Mack et al. 1990; Fensterheim 1993; He, Stein et al. 2001).

To better characterize the impact of PCBs in the general U.S. human population, U.S. Centers for Disease Control and Prevention (CDC) began to include measurements of PCBs in serum samples of human subjects participating the National Health and Nutrition Examination Survey (NHANES) since 1999 (Centers for Disease Control and Prevention 2005). Analyses of NHANES data have yielded some interesting observations (Centers for Disease Control and Prevention 2005; Needham, Barr et al. 2005; Nichols, Hentz et al. 2007; Axelrad, Goodman et al. 2009; Cave, Appana et al. 2010; Jain and Wang 2010). For example, PCBs detected in the blood of the general U.S. population exhibit an age-related trend, with older individuals displaying higher concentrations (Nichols, Hentz et al. 2007). Higher total PCBs levels were associated with older age and non-Hispanic black race (Cave, Appana et al. 2010). Regression models were used for estimating total PCBs and confirmed the pattern of increasing blood PCBs with increasing age as well as some ethnicity difference in the blood levels of PCBs (Jain and Wang 2010).

However, it has not been well addressed what exposure route(s) and vehicle(s) have played major roles in shaping the observed levels and patterns of the PCBs in the general U.S.

population at the post-ban era of PCBs. Human exposure to PCBs can happen from inhalation of polluted air, dermal exposure to dusts, and ingestion of contaminated food. Because the pollution of PCBs in the air in the post ban era of PCBs is limited to certain specific situations and general population is more likely exposed to PCBs via dietary consumption of foods contaminated by PCBs (WHO 2003), we focused our study in understanding the patterns of PCBs in participants of NHANES by analyzing the food consumption patterns of the U.S population and assessing their likely contribution to the patterns of PCBs in blood. We also used the EPA's Stochastic Human Exposure and Dose Simulation (SHEDS) model (Xue, Zartarian et al. 2006; Zartarian, Xue et al. 2006; Zartarian, Xue et al., 2012) to predict dietary PCBs exposures from fish consumption. Our study helps to identify major exposure routes and vehicles in the post-ban era of PCBs that contribute significantly to the observed biomonitoring pattern of PCBs in the blood of general U.S population.

Materials and Methods

Collection and analysis of blood PCB data. We obtained blood PCBs concentration data from the National Health and Nutrition Examination Survey (NHANES) (http://www.cdc.gov/nchs/nhanes.htm) and performed our analyses by taking into the account of the varying sampling weight for the respective NHANES data sets. Four-year subsample weights were used in the analyses; we tried both 2-year and 4-year subsample weights and results were very similar. We used all congeners (30 congeners supplementary table 3) measured in each survey and combined their concentrations into the total or sum PCBs. Our initial analyses explored the total concentrations of blood serum PCBs in the general U.S. population between the 2001-02 and 2003-04 survey times and between two major age groups considered, i.e. >30 years old and 12 to ≤30 years old at the time of the survey. The selection of 30 years as a time division was based on the assumption that the ban on open PCBs use in the U.S. approximately 30 years before the first survey might exert some impact on the release of PCBs into the environment, and thus exposure to PCBs by the U.S. population.

Because the big difference in the limit of detection (LOD) between the 2001-2002 and the 2003-2004 NHANES measurements of blood PCBs (Supplementary table 3) may artificially impact the study of the changes in blood levels of PCBs over the two survey period we adopted an approach of reducing the impact of LOD difference on the change of levels of PCBs between the two surveys. We hypothesize that, if we use the same sets of LOD for both surveys, the calculated concentrations of PCBs would be influenced by other factors other than a difference in LODs. Then we used the maximum LOD for each congener of 30 congeners in the 2001-2002 survey as reference values for selecting all the data of PCBs whose 2003-2004 levels are below the reference values and calculating their mean values as "new adjusted LODs" for each congener. These new adjusted LODs are used for filling in all the 2001-2002 and 2003-2004 values reported as below their respective maximum LODs from 2001-2002. In this way we "artificially increased" LODs of the 2003-2004 survey, which will be consistent with LODs in 2001-2002 survey. New adjusted LODs were used to fill values below Detection Limits (see supp. Table 3).

To examine the effect of ethnicity, we analyzed the blood total PCBs within the two major age groups by combining the two NHANES survey data sets. Regression and Tukey Kramer

analyses were conducted to explore the upward age-related trend, ethnicity patterns in the blood levels for the two age groups, and the degree of ethnicity-related differences within each age group.

Collection and analysis of food consumption data. Because dietary exposure from fish, meat, milk, and fat consumption is a major route for PCBs exposure by the general human population in the post PCBs-ban era (Tee et al. 2003, Weintraub and Birnbaum 2008), we conducted an analysis to assess whether food consumption differences may explain the varied blood PCBs among different ethnicities and age groups. For dietary consumption inputs, we used 1999-2006 NHANES data, containing instantly recorded consumption of food and water by each survey participant. Recipe files in the U.S. EPA's Food Consumption Intake Database (FCID) were used for breaking down consumed foods reported in NHANES into raw agricultural commodities (RACs), following methodologies detailed in previous publications (Xue, Zartarian et al. 2010; Xue, Zartarian et al. 2012; Zartarian, Xue et al., 2012). Because the food consumption surveys in NHANES are only snapshots of food consumption in a short time window but the blood levels of PCBs should reflect the end results of some long-term exposure we used food consumption data from all participants over a wider time window (1999-2006) than that shown for the data on blood PCBs (2001-2004) to compensate the lack of long-term observation of food consumption of the same survey participants. More importantly, with a larger set of data used in the analysis, the results are more stable and reliable.

Exposure modeling. Because the fish consumption appeared to be a significant factor affecting the blood PCBs in the studied U.S. population, and we were able to use available residue data, we applied the SHEDS dietary exposure model to explore dietary contributions and patterns related to the observed blood levels. SHEDS-Dietary is a probabilistic, population-based dietary exposure assessment model that can simulate individual exposures to chemicals in food and drinking water over different time periods (http://www.epa.gov/heasd/products/sheds_multimedia/sheds_mm.html). Model inputs were NHANES consumption data, FCID recipe files, and PCBs concentration data in fish from a New York City Asian market survey (McKelvey, Chang et al. 2010). Detailed descriptions of the SHEDS model methodology for estimating dietary exposure can be obtained from previous publications (Xue, Zartarian et al. 2010; Xue, Zartarian et al. 2012; Zartarian, Xue et al., 2012). SHEDS modeled results were compared against NHANES measurements of total PCBs in blood. This model has undergone extensive review by expert panels, and has been evaluated with comparison to both measured and modeled data for various chemical classes.

Results

Age and Ethnicity Patterns for Blood Levels in Different Time Periods

While age and the ethnicity composition were similar between the two NHANES survey time periods (see Table 1), the mean total blood concentrations of PCBs (30 common congeners in two surveys) in the study population decreased statistically significantly from the earlier time period to the later one for a given age group (Figure 1A; Supplementary Figure 1). Total blood PCBs of the 2003-04 survey decreased by 18% and 19% (mean) and 10% and 20% (geometric mean, GM) for the 12 to <=30 years and 30+ year age groups, respectively, in comparison with the 2001-2002 survey (Figure 1A).

Total blood PCBs for the 2003-04 survey decreased by 8%, 26%, 25% and 20% (mean) and 5%, 16%, 23% and 22% (GM) for the 12-19, 20-30, 31-49 and 50+ age groups, respectively, in comparison to the 2001-02 survey levels. Figure 1B shows that blood PCBs concentrations increased as age increased in the both surveys. For these 4 age groups, the absolute reductions of total blood PCBs between the two surveys are 0.03, 0.16, 0.29 and 0.46 ng/g.

To further confirm the above pattern of decreasing blood PCBs over time for the same age groups, we analyzed the blood PCBs of two specific PCB congeners (138 and 153) whose detection rates were the highest and which were comparable between the two surveys (79% and 100% for PCB138 and 84% and 100% for PCB 153 for NHANES survey 2001 and 2003, respectively). We observed the similar level of decreasing blood PCBs for PCB153 (Figure 1C and 1D) and PCB138 (Supplementary Figure 3).

Ethnicity Patterns for Blood Concentrations

The patterns of ethnicity rankings of total blood PCBs were different between the two major age groups. For the older age group (> 30 years at the survey time), Non-Hispanic Black had the highest blood total PCBs, followed by Non-Hispanic White, Other Hispanic, Asian/Pacific Islander/Native American/Other Multiracial (A/P/N/M), and then Mexican American (Figure 2). For the younger age group (12 to ≤30 years at the survey time), the ranking of total blood PCBs from high to low concentration was: A/P/N/M, Non-Hispanic White, Other Hispanic, Non-Hispanic Black, and Mexican American.

Figure 3 shows more detailed regression analyses than Figure 2 to emphasize that concentrations of total blood PCBs exhibited an upward age-related trend, the differences in ethnicity-related patterns for the two age groups, and the degree of ethnicity-related differences within each age group. A/P/N/M had significantly higher blood PCBs for the younger age group (12 to ≤30 years at the time of the surveys) (Figure 3A), and had the highest rate of change in total PCBs with age. Non-Hispanic Blacks had significantly higher blood PCBs for the >30 year age group (see Figure 3B), and the highest rate of change by age within that group. GLM analyses revealed that age group, survey year (2001-02 vs. 2003-04), ethnicity, and interaction of age group with ethnicity are statistically significant factors for total blood PCBs, while gender is not (Supplementary Tables 1 and 2).

Food and Fish Consumption Patterns, and Dietary Exposures by Ethnicity and Age Group

While the consumption of meat and of skin and fat were similar among different ethnicities, the consumption of fish and milk varied significantly (Figure 4). The greatest variation among ethnicities occurred with the fish consumption. A/P/N/M showed the highest fish consumption in both age groups, and the older people (>30 years) consumed larger amounts of fish than the younger people (12 to <= 30 years).

The distribution of mean (Figure 5A) and 95th percentile (Fig. 5B) SHEDS modeled PCBs exposures from fish consumption, generated by 100 simulations for variability analyses, displayed a predicted ethnicity ranking (from high to low) as: A/P/N/M, Non-Hispanic Black, Other Hispanic, Non-Hispanic White, and Mexican American for the older age group; and A/P/N/M, Other Hispanic, Non-Hispanic Black, Mexican American, and Non-Hispanic White

for the younger age group. For the younger age group (12 to <=30), the ethnicity-specific PCBs blood concentration patterns in NHANES (Figure 2) are fairly consistent with patterns for NHANES fish consumption (Figure 4) and SHEDS modeled exposure estimates (Figure 5), but not for the older age group.

Using the SHEDS model, we further analyzed the exposures of total PCBs within each ethnicity (Table 2). The highest level of fish consumption-contributed PCBs exposure was 0.015 ug/kg/day for A/P/N/M females and 0.017 ug//kg/day for A/P/N/M males in the >50 year age group. The averaged PCBs exposures of males are higher than those of females, and as age increased, the exposures increased: A/P/N/M averaged exposures were 0.006, 0.009, 0.11, 0.015 ug/kg/day (female) and 0.011, 0.012, 0.016, 0.017 ug/kg/day (male) for the 12-20, 21-30, 31-49, and 50+ year age groups, respectively.

Correlation analyses between food consumption and concentrations of total blood PCBs at participant level show a correlation coefficient of 0.07 (p-value < 0.01), and no positive correlation with meat and milk.

Discussion

Our analyses confirmed previous analyses of NHANES biomonitoring data for PCBs, and revealed important new findings on how age, ethnicity, and diet influence PCBs exposures and blood concentrations. Within each of the two NHANES survey periods considered, a trend of increased average total blood PCBs with increased age group was observed; however, for the same age, gender, and ethnicity, the blood PCBs measured in the later NHANES survey were significantly lower than those measured in the earlier one. Variations of PCB concentrations in blood among different ethnicities ranked differently between the older and younger age groups within each survey. Analyses of available food and fish consumption data, and SHEDS dietary exposure modeling helped explain these differences and patterns for the younger age group (12 to <=30 years).

Age and Ethnicity Patterns for Blood Concentrations

Our analyses (Figure 1and Supplementary Figure 3) confirmed previous findings of apparent increased of PCBs in blood with increasing age, and longitudinal studies that have shown decreasing blood PCBs over time for given individuals (e.g., Tee, Sweeney et al. 2003). The analyses on PCB congeners 138 and 153, whose detection rates are very close between two NHANES surveys, indicate that the observed trend of decreasing total blood PCBs over time for the same age groups is not a measurement bias but a true reflection of a decline, especially in the over 30 years old groups. This trend may be explained by one or several of the following possibilities: a) bioaccumulation naturally leads to higher body burden with age, i.e. persistence of higher concentrations of blood PCBs in the older subjects might be a reflection of continued mobilization of some internally stored PCBs (Goncharov, Haase et al. 2008); b) people are eating more fish as they get older, as shown in Figure 4; and c) fish PCB concentrations have declined in recent years, so older individuals have higher blood levels because of higher exposures in the past or disappearance of some exposure pathways.

While the blood PCBs decreased from the earlier to the later NHANES survey period, the decrease between the survey times for 12-19 year-olds is the smallest (8% for mean and 5% for

GM; Figure 1b). This implies that the body burden of PCBs is a key contributor to the blood concentrations, especially for older people. The relatively small change of absolute total blood PCBs between the two surveys indicates long half-life of PCBs in human body. Mobilization of internal PCBs may be accelerated with the aging process (Liu 2005).

Our age-stratified analysis of the ethnicity variation in NHANES blood PCBs showed different rankings between the older age group considered (> 30 years at the survey time) and the younger age group (12 to ≤30 years at the survey time) (Figure 2). This suggests that some exposure pathway(s) changed after the ban of PCBs. For the younger age group, A/P/N/M had the highest levels: this new finding warrants follow-up investigation to determine approaches for reducing exposures in this group.

For the older age group, Non-Hispanic Black had the highest blood total PCBs; this has been seen in previous studies that have also reported ethnic/racial differences for PCBs body burden (Cave, Appana et al. 2010). Another study on two separate data sets of blood PCBs in the NHANES also showed a consistent pattern of ethnicity ranking between two survey times when all ages were combined (Jain and Wang 2010).

Food and Fish Consumption Patterns and Dietary Exposures by Ethnicity and Age Group

Our analyses confirm that fish consumption is a key factor in PCBs body burden, and reveal new findings on ethnicity- and age-related patterns. Ethnicity-related fish consumption patterns were fairly consistent with fish dietary exposure levels for both age groups. For the younger age group, both the fish consumption and modeled exposure patterns matched reasonably well the pattern and rankings of blood PCBs among the studied ethnicities.

Detailed analysis of PCBs exposure from specific fish species would be useful as follow up research, but challenging due to limited data. We did find that the distribution of PCBs concentrations in fish tissue for various fish species is different than for methyl mercury. Also, PCBs concentrations in bottom-dweller fish are higher than predator fish, but the opposite is seen for methyl mercury.

The SHEDS modeling predictions are consistent with other studies showing that fish eaters usually have higher serum PCBs than non fish eaters in the same region (He, Stein et al. 2001). Our study reveals that A/P/N/M generally had higher PCBs exposures than other ethnicities because of the dietary exposure route via fish consumption. Similar findings were reported in Xue et al., 2012, which reported a SHEDS exposure modeling analysis for methyl mercury and NHANES blood concentrations.

The fish PCBs concentrations used in our exposure model came from a 2007 Asian market survey in New York City (McKelvey, Chang et al. 2010). This may introduce some bias, as the types of fish consumed by other ethnicities may be different (Weintraub and Birnbaum 2008). Due to lack of available PCBs residue data in meat, skin, fat, and milk, we were not able to model contributions to dietary PCBs exposures from these foods.

Dynamic Model Evaluation, Considering Trends of PCBs in Fish over Time

A WHO report has disclosed the decreasing trend of PCBs exposure over time via dietary intake (WHO 2003). Studies have shown that overall, PCBs levels decreased in fish tissues over time from 1980 to 2004 (El-Shaarawi et al., 2011; Hickey et al., 2006). Because SHEDS inputs for fish PCBs levels and consumption data were from fixed time periods, we conducted additional dynamic model evaluation analyses, using fish PCBs data from EPA's National Lake Fish Tissue study collected at different years as exposure model inputs.

The additional SHEDS simulations for dynamic evaluation confirmed the decline in exposures due to lower levels of PCBs in fish, and indicated that an accelerated decline starting in 1996. The mean modeled dietary PCBs exposures using residue data from the National Lake Fish Tissue study was 0.0087 ug/kg/day, which is 1.3 times higher than the modeled mean exposure using the 2007 NYC Asian market survey data; the 95th and 99th percentiles were 1.2 times higher (see Supplemental Figure 2).

Conclusions

The reduction in total blood PCB concentrations in each NHANES age group over two survey periods (2001-02 and 2003-04) is evidence of the effectiveness of U.S. control measures on PCB release and production. Currently, the major route of PCBs exposure is dietary via consumption of fish and other foods with that tend to bioaccumulate PCBs present in the environment. This is particularly evident in A/P/N/M populations. Analysis of food consumption explained the blood concentrations of PCBs for the younger (12 to <=30 years) age group and the A/P/N/M ethnicity group within that younger subpopulation. Dietary ingestion, particularly via fish consumption, remains a major route of exposure to environmental PCBs for the general human population.

Additional research is also needed to consider cumulative exposures of fish consumption (i.e. from multiple exposure routes and chemicals including PCBs, methyl mercury, and other persistent pollutants), vulnerable groups such as tribes and children, and other PCBs sources (e.g., old schools, other food types such as meat and dairy).

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