Serum Levels of PBDEs, PCB and DDE in Middle-aged and Older California Women: Temporal Trends, 2011-2015

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Introduction

In response to health concerns and widespread human exposures, the Penta- and Octa- formulations of polybrominated diphenyl ethers (PBDEs) were banned in California in 2006 [1]. Initial biomonitoring data have provided indications of reduced human exposures since these bans took effect. Our objective was to evaluate temporal trends in PBDE serum levels among a population of older California women during a four-year period (2011-2015), beginning approximately five years after these formulations were banned. For comparison, time trends were also evaluated for polychlorinated biphenyl-153 (PCB-153) and 4,4'-dichlorodiphenyldichloroethylene (DDE), two persistent organic pollutants (POPs) that were banned in the U.S. many decades earlier.

Materials and methods

Blood was collected in a 10 mL BD® tube (catalog#367985, Becton Dickinson) from 1,253 women, 40 to 94 years of age, who were participating as controls in a breast cancer case control study nested within the California Teachers Study, an on-going prospective cohort study of female California professional public school employees. Participants included in the present analysis included those who had provided a blood sample between May 2011 and August 2015; each completed a questionnaire at the time of blood collection. Serum was separated using a portable centrifuge in the field, frozen and shipped to the laboratory where samples were stored at -20 ºC until analysis. Samples were analysed for PBDEs, PCBs, and organochlorine pesticides using automated solid phase extraction (Biotage) and gas chromatography/high resolution mass spectrometry (DFS, ThermoFisher)[2]. Briefly, samples (2 mL) were fortified with ^{12}C labelled standards before formic acid and water were added. Oasis HLB cartridges (3 cc, 500 mg, Waters Co.) and acidified silica were used for sample extraction and clean-up. The final eluates were concentrated and spiked with recovery standards. Bovine serum pre-spiked with target analytes and NIST SRM 1958 were used for QA/QC.

Only the three PBDE congeners with detection frequencies $\geq$ 75% were included in the present analysis: 2,2',4,4'-tetrabromodiphenyl ether (BDE-47); 2,2',4,4',6-pentabromodiphenyl ether (BDE-100); and 2,2',4,4',5,5'-hexabromodiphenyl ether (BDE-153). PCB-153 and 4,4'-DDE (DDE) were chosen to represent their respective classes. Linear models were used to regress the $\log_{10}$-transformed lipid-normalized serum concentration of each compound on serum collection date, adjusting appropriately for age and/or race (covariate selection based on backwards stepwise regressions). Regression coefficients (β) for collection date were converted to average annual percent increases (APIs) where $API=100*(10^{\beta}-1)$.

Results and discussion

The distributions of serum concentrations are presented in Table 1. In comparison to other California populations, serum concentrations of PBDEs in our study were marginally lower, while PCB-153 and DDE were slightly higher[3]. Bivariate scatterplots of serum concentration versus blood collection date are depicted in Figure 1. As expected, serum levels of PCB-153 and DDE demonstrated slight declines over the four years of specimen collection. In contrast, all three PBDEs displayed a modest upward temporal trend over the same time period. After adjusting for age and/or race, these temporal patterns persisted. Table 2 summarizes the results from adjusted linear regression models, expressed as the estimated average annual percent increase (API) in serum concentrations. All three PBDE congeners exhibited statistically significant increases in serum concentrations (API for BDE-47=5.6% (p=0.017); API for BDE-100 = 12.0% (p<0.001); API for BDE-153 = 7.1% (p = 0.005)). PCB-153 and DDE, on the other hand, exhibited slight, but not statistically significant, declines: API for PCB-153 = -1.6% (p = 0.22); API for DDE = - 2.4% (p = 0.23).

The downward trend in serum levels of PCB-153 and DDE observed in our study mirror the temporal patterns that have been reported for general populations in the U.S. and California [3-5]. The increasing levels we observed for PBDEs, however, stand in contrast to other biomonitoring data that have indicated some initial declines in body burden levels shortly after these compounds were banned [6-8,4]. Our results, in the context of these other biomonitoring data, suggest that initial declines in PBDE levels reported shortly after the PBDE phase-outs may have plateaued and levels may be starting to increase, indicating a possible shifting in exposure pathways. Alternatively, it is possible that the upward trend in PBDE levels is due to some characteristic or exposure unique to our study population. Regression models, which included adjustment only for age or race, explained very little of the overall variability in serum PBDE levels (ranging from 1.1% to 2.1%, depending on the congener). We therefore cannot dismiss the possibility that this trend is due to residual confounding by unmeasured factors. Further biomonitoring to ascertain current trends and determinants of PBDE exposures in other populations is warranted.

Figure 1. Serum concentrations versus date of sample collection among 1,253 study participants, 2011-2015.

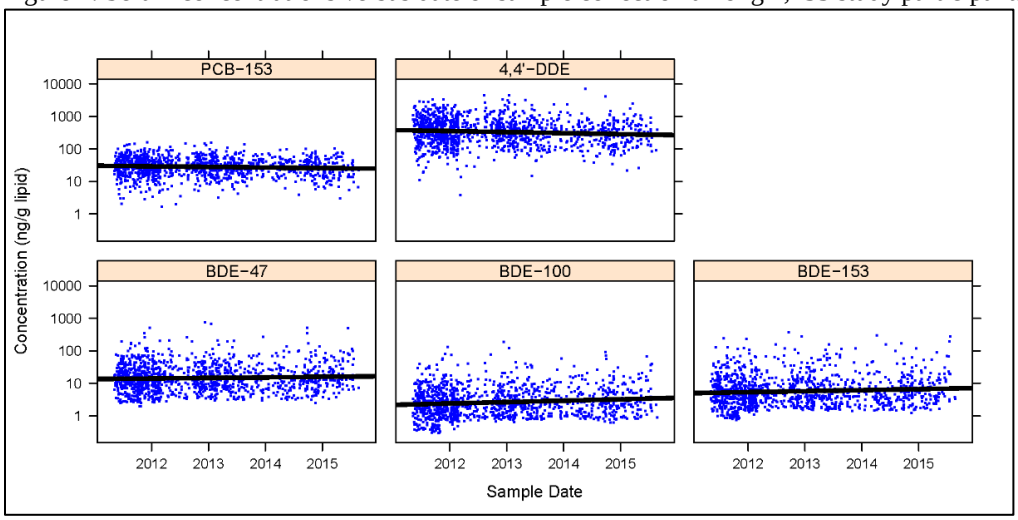

Table 1. Distribution of serum concentrations among 1,253 study participants.

Compound	N*	Detection Frequency	Serum Concentration (ng/g lipid)** Mean	Median	Minimum	Maximum
BDE-47	1,253	88%	25.56	13.34	1.94	749.67
BDE-100	1,253	78%	5.08	2.31	0.30	186.31
BDE-153	1,253	80%	12.03	4.89	0.74	379.31
PCB-153	1,240	100%	34.39	29.72	1.66	163.19
4,4'-DDE	1,240	100%	506.01	345.27	3.80	6981.78

** If below the minimum detection level (MDL), the value was imputed as the MDL divided by the square root of 2.

Table 2. Annual Percent Increase (API) in serum concentrations of PBDEs, PCB-153 and DDE: results from linear models.

	Unadjusted			Adjusted [a]		
Compound	API [b]	95% CI[c]	p-value	API[b]	95% CI[c]	p-value
BDE-47	4.0	−0.42, 8.6	0.0770	5.6	0.99, 10	0.0170
BDE-100	10.0	5.5, 16	<0.0001	12.0	6.8, 17	<0.0001
BDE-153	7.4	2.4, 13	0.0036	7.1	2.1, 12	0.0047
PCB-153	−4.1	−7, −1.2	0.0061	−1.6	−4.1, 0.96	0.2200
4,4'-DDE	−7.0	−11, −3	0.0007	−2.4	−6.2, 1.6	0.2300

[a] BDE-47, BDE-100 were adjusted for race/ethnicity; BDE-153 was adjusted for age at blood draw; PCB-153 and DDE were adjusted for both race/ethnicity and age at blood draw.

[b] Annual Percent Increase (API) converted from time trend coefficients (β) obtained from regressing $\log_{10}$ serum concentration (ng/g lipid) on date of sample collection, expressed as year and fraction of a year, where API = $100*(10^{\beta} - 1)$.

[c] CI = 95% confidence interval.

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References

1. Linares V, Belles M, Domingo JL (2015) Human exposure to PBDE and critical evaluation of health hazards. *Arch Toxicol* 89 (3):335-356. doi:10.1007/s00204-015-1457-1
2. Park JS, Voss RW, McNeel S, Wu N, Guo T, Wang Y, Israel L, Das R, Petreas M (2015) High exposure of California firefighters to polybrominated diphenyl ethers. *Environ Sci Technol* 49 (5):2948-2958. doi:10.1021/es5055918
3. California Department of Public Health Department of Toxic Substances Control Office of Health Hazard Assessment. (2012-2016) Biomonitoring California. http://www.biomonitoring.ca.gov/. 2016
4. Centers for Disease Control and Prevention (2015) *Fourth Report on Human Exposure to Environmental Chemicals*, Updated Tables, (February, 2015). Atlanta, GA
5. Sjodin A, Jones RS, Focant JF, Lapeza C, Wang RY, McGahee EE, 3rd, Zhang Y, Turner WE, Slazyk B, Needham LL, Patterson DG, Jr. (2004) Retrospective time-trend study of polybrominated diphenyl ether and polybrominated and polychlorinated biphenyl levels in human serum from the United States. *Environ Health Perspect* 112 (6):654-658
6. Guo W, Holden A, Smith SC, Gephart R, Petreas M, Park JS (2016) PBDE levels in breast milk are decreasing in California. *Chemosphere* 150:505-513. doi:10.1016/j.chemosphere.2015.11.032
7. Ma WL, Yun S, Bell EM, Druschel CM, Caggana M, Aldous KM, Buck Louis GM, Kannan K (2013) Temporal trends of polybrominated diphenyl ethers (PBDEs) in the blood of newborns from New York State during 1997 through 2011: analysis of dried blood spots from the newborn screening program. *Environ Sci Technol* 47 (14):8015-8021. doi:10.1021/es401857v
8. Zota AR, Linderholm L, Park JS, Petreas M, Guo T, Privalsky ML, Zoeller RT, Woodruff TJ (2013) Temporal comparison of PBDEs, OH-PBDEs, PCBs, and OH-PCBs in the serum of second trimester pregnant women recruited from San Francisco General Hospital, California. *Environ Sci Technol* 47 (20):11776-11784. doi:10.1021/es402204y