LEVELS OF PERSISTENT ORGANIC POLLUTANTS (POP) IN HUMAN MILK FROM FIRST-TIME MOTHERS IN UPPSALA, SWEDEN: TEMPORAL TRENDS FOR THE TIME PERIOD 1996-2016

Fridén U[1], Aune M[1], Bignert A[2], Cantillana T[1], Glynn A[3], Gyllenhammar I[1], Lignell S[1]

[1]National Food Agency, Uppsala, Sweden, SE-751 26, ulrika.friden@slv.se; [2]Swedish Museum of Natural History, Stockholm, Sweden; [3]Swedish University of Agricultural Sciences, Uppsala, Sweden

Introduction

Recurrent measurements of persistent organic pollutants (POPs) in mother's milk from primiparous women in Uppsala, Sweden have been performed since 1996 [1-3].The aim of the cohort is to estimate the body burdens of persistent organic pollutants (POPs) among pregnant and nursing women and to estimate temporal trends of the exposure of fetuses and breast-fed infants. Results of the analysis of polychlorinated biphenyls (PCBs), polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), polybrominated diphenyl ethers (PBDEs), and hexabromocyclododecane (HBCD) in human milk sampled in 2015 and 2016 and updated temporal trends for the period 1996-2016 are presented.

Materials and methods

Mothers were randomly recruited among primiparous who were Swedish by birth and delivered at Uppsala University Hospital from February 2015 to December 2016 (n=30). The participating mothers sampled milk at home during the third week after delivery (day 14-21 post partum)[1]. The recruitment during the period 1996-2014 (n=426) has been described earlier [1,2].

Analyses was performed at NFA using accredited methods described in detail in Lignell *et al* (2009)[1] for PBDEs and HBCD and in Aune *et al* (2012)[4] for PCBs and PCDD/Fs.

Multiple linear regressions (MINITAB 15® Statistical Software for Windows) were used to analyse the associations between concentrations of POPs in mother's milk and sampling year[1]. Data on age, weight, length, lifestyle, medical history, food habits etc. were obtained from questionnaries and independent variables that have been shown to influence POP levels in human milk[5,6] were included in the model[1,3,5]. To estimate a possible change-point (CP) in the temporal trends we used a technique similar to that suggested by Sturlurdottir *et al* (2015)[7] and the technique is described in detail in Gyllenhammar *et al* (2017)[3].

Results and discussion:

Mean age and BMI of the participating women was 30.5 years (range 25-38) and 22.9 kg/m^2 (range 17-37). The levels of POPs in human milk from 2015 and 2016 are shown in Table 1. Among the PCBs, the di-*ortho* congener CB-153 showed the highest mean concentration (27 ng/g lipid, Table 1). CB-126 was the highest non-*ortho* congener and contributed the most to the non-*ortho* PCB TEQ. Among the PCDD/Fs, 1,2,3,7,8-PeCDD and 2,3,4,7,8,-PeCDF contributed the most to the total PCDD/F TEQ (33 % each). The mean total-TEQ level was 6.0 pg TEQ/g lipid and non-*ortho* PCBs contributed most to this level (mean 2.3 pg TEQ/g lipid). Among the PBDEs, BDE-47 and BDE-153 showed the highest mean levels (0.75 and 0.46 ng/g lipid, respectively, Table 1). Estimated PBDE-levels <LOQ are presented in brackets in Table 1 and were used in the analyses of temporal trends.

The results from this cohort showed decreasing trends (-3.2 to -6.7 % per year) for PCBs and PCDD/Fs (Table 2 and Figure 1). A faster declining rate was showed for PCDD TEQ (6.7 %) than for PCDF TEQ (3.5 %). Levels have been decreasing faster during the first part of the study for CB-153, di-*ortho*, mono-*ortho* PCB and PCDD/F TEQ and significant CPs were observed (Table 3) with a slower decreasing trend after that year. The levels of BDE-47, -99, -100, and sumPBDEs decreased with similar rates as previously reported for the period 1996-2014[8] (-5.6 to -12 %, Table 2 and Figure 1). BDE-47, -153, and HBCD had observed significant CPs (Table 3 and Figure 1) with increasing trends before and declining trends after the CPs.

Table 1. Concentrations of POPs in milk sampled from primiparous women in Uppsala in 2015-2016 (n=30). TEQ concentrations based on 2005 WHO TEFs[9].Values <LOQ were set to ½LOQ in calculations of mean, medians, sum of PBDEs and sum of TEQs. Levels <LOQ were also reported and results using these levels (adjusted for blank samples) are presented in brackets ([]).

Compound	Mean	Median	Min	Max	N<LOQ[a][n=0][b]
BDE-47 (ng/g lipid)	0.75 [0.76]	0.23 [0.34]	<0.24 [0.04]	6.3	16 [0]
BDE-99 (ng/g lipid)	0.22 [0.16]	0.14 [0.06]	<0.16 [0]	1.7	26 [5]
BDE-100 (ng/g lipid)	0.14 [0.14]	0.09 [0.09]	<0.04 [0.01]	0.65	9 [0]
BDE-153 (ng/g lipid)	0.46 [0.42]	0.46 [0.42]	<0.09 [0.05]	1.3	3 [0]
BDE-209 (ng/g lipid)	0.13 [0.12]	0.08 [0.10]	<0.10 [0.003]	0.30	20 [0]
sumPBDE[c] (ng/g lipid)	1.6 [1.5]	1.1 [1.1]	0.27 [0.27]	9.3	-
HBCD (ng/g lipid)	0.18 [0.19]	0.15 [0.15]	<0.09 [0.07]	0.72	3 [0]
CB-28 (ng/g lipid)	1.6	1.1	0.28	7.1	0
CB-153(ng/g lipid)	27	24	8.0	52	0
di-*ortho* PCB[d] (ng/g lipid)	54	50	17	108	-
mono-*ortho* PCB TEQ[e] (pg/g lipid)	0.23	0.21	0.09	0.47	-
non-*ortho* PCB TEQ[f] (pg/g lipid)	2.3	2.1	1.1	5.0	-
PCDD TEQ (pg/g lipid)	2.0	1.9	0.75	4.1	-
PCDF TEQ (pg/g lipid)	1.5	1.4	0.73	3.0	-
PCDD/F TEQ[g] (pg/g lipid)	3.5	3.1	1.6	6.0	-
Total-TEQ[h] (pg/g lipid)	6.0	5.5	2.8	11	-

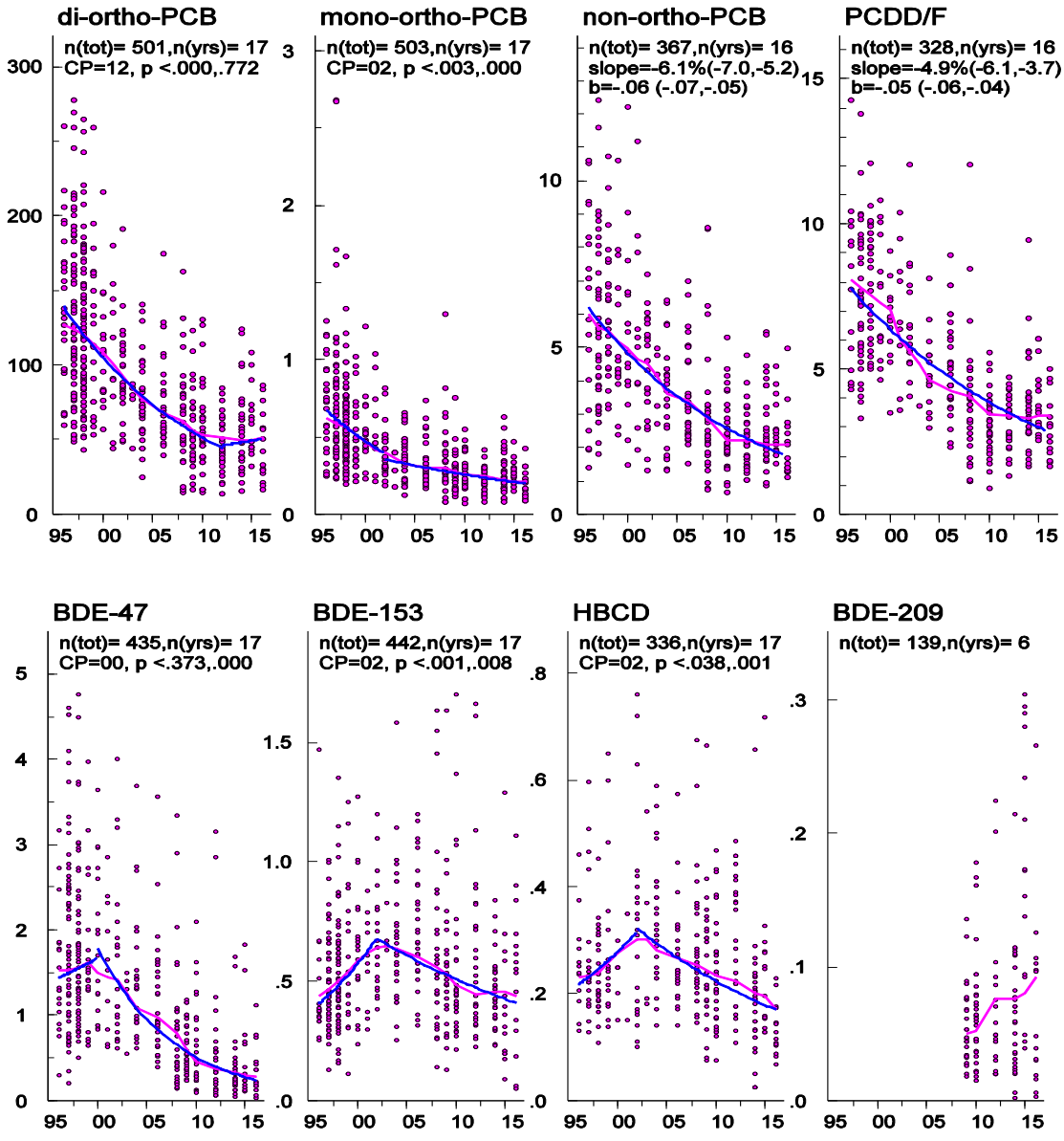
[a]number of samples with levels below LOQ. [b]number of samples with levels estimated to be zero or negative after adjustment for blank levels. [c]sum of BDE-47, -99, -100 and -153. [d]sum of CB-153, -138, and -180. [e]sum of CB-105, -118, -156, and -167. [f]sum of CB-77, -126, -169 TEQs. [g]sum of PCDD TEQ and PCDF TEQ. [h]sum of mono-*ortho* PCB TEQ, non-*ortho* PCB TEQ, PCDD TEQ, and PCDF TEQ.

Table 2. Percent change in concentrations of POPs per year in milk sampled from primiparous women in Uppsala in 1996-2016. Adjusted for age of mother, pre-pregnancy BMI, weight gain during pregnancy and weight loss after delivery. Concentrations <LOQ was recalculated to ½LOQ. TEQs based on 2005 WHO TEFs[9].

Compound	Period	Change/year (%)[a]		Half-time[b]	R^{2c}	n	P
		Mean	95% CI	(years)			
BDE-47	1996-2016	-9.0	-10/-7.9	7	37	443	<0.001
BDE-99	1996-2016	-12	-14/-11	5	39	443	<0.001
BDE-100	1996-2016	-5.6	-6.7/-4.4	12	19	443	<0.001
BDE-153	1996-2016	-0.1	-0.9/+0.7	-	12	443	0.81
BDE-209	2009-2016	+4.8	-2.2/+12	-	0	149	0.19
sumPBDE[d]	1996-2016	-5.7	-6.6/-4.9	12	30	443	<0.001
HBCD	1996-2016	-2.0	-3.1/-0.9	35	4.4	349	0.001
CB-28	1996-2016	-3.2	-4.3/-2.1	21	10	488	<0.001
CB-153	1996-2016	-6.4	-6.9/-5.9	11	67	488	<0.001
di-*ortho* PCB[e]	1996-2016	-6.1	-6.6/-5.7	11	68	488	<0.001
mono-*ortho* PCB TEQ[f]	1996-2016	-6.1	-6.6/-5.6	11	64	488	<0.001
non-*ortho* PCB TEQ[g]	1996-2016	-5.6	-6.2/-5.0	12	58	359	<0.001
PCDD TEQ	1996-2016	-6.7	-7.2/-6.2	10	75	325	<0.001
PCDF TEQ	1996-2016	-3.5	-4.1/-2.9	19	44	325	<0.001
PCDD/F TEQ[h]	1996-2016	-5.5	-6.0/-5.0	12	66	325	<0.001
Total-TEQ[i]	1996-2016	-5.6	-6.1/-5.1	12	68	324	<0.001

[a]Percent change (decrease (-) or increase (+)) of the concentrations per year. [b]The estimated time it takes for the concentrations to be halved in the population. [c]Coefficient of determination for the regression model. [d]sum of BDE-47, -99, -100, and -153. [e]sum of CB-153, -138, and -180. [f]sum of CB-105, -118, -156, and -167. [g]sum of CB-77, -126, and -169 TEQs. [h]sum of PCDD and PCDF TEQs. [i]sum of mono-*ortho* PCB TEQs, non-*ortho* PCB TEQs, PCDD TEQs, and PCDF TEQs.

Figure 1. Levels of BDE-47 (n=435), BDE-153 (n=442), HBCD (n=336), and BDE-209 (n=139) di-*ortho* PCBs (n=501), mono-*ortho* PCB TEQs (n=503), non-*ortho* PCB TEQs (n=367) and PCDD/F TEQs (n=328) in mother's milk from first-time mothers in Uppsala, Sweden. TEQs based on 2005 WHO TEFs[9]. Each point corresponds to the concentration in a milk sample from an individual woman. The blue lines represent regression lines obtained from the CP-analyses or in cases where the CP analysis is not significant a regression line for the whole period. Purple lines display a three-year unweighted moving average smoother. Possible outliers are excluded.



An increasing trend is observed for BDE-209 (+4.8 per year) but more data points are needed to draw further conclusions. The continuous decline in human milk levels of PBDEs, HBCD, PCBs, and PCDD/Fs are in

Table 3. Change point (CP) analyses for temporal trends of POPs in milk sampled from primiparous women in Uppsala in 1996-2016. Possible outliers are included. TEQs based on 2005 WHO TEFs[9].

Compound	Period	Change point (CP, year)	n	p
BDE-47	1996-2016	2000	454	0.294
BDE-153	1996-2016	2002	454	0.01
BDE-209	2009-2016	-	149	ns
HBCD	1996-2016	2003	355	0.008
CB-28	1996-2016	-	503	ns
CB-153	1996-2016	2012	503	<0.001
di-*ortho* PCB[a]	1996-2016	2012	503	<0.001
mono-*ortho* PCB TEQ[b]	1996-2016	2002	503	0.003
non-*ortho* PCB TEQ[c]	1996-2016	-	369	ns
PCDD TEQ	1996-2016	-	332	ns
PCDF TEQ	1996-2016	-	332	ns
PCDD/F TEQ[d]	1996-2016	2002	332	0.022
Total-TEQ[e]	1996-2016	-	331	ns

[a]sum of CB-153, -138, and -180. [b]sum of CB-105, 118,156, and 167. [c]sum of CB-77, -126, and -169 TEQs. [d]sum of PCDD and PCDF TEQs. [e]sum of mono-ortho PCB TEQs, non-ortho PCB TEQs, PCDD TEQs, and PCDF TEQs.

agreement with results from Swedish market basket studies performed in 1999, 2005, 2010 and 2015 showing declining exposure to these substances from food[10,11].

It is important to continue following concentrations of POPs in human milk from Swedish mothers in order to further investigate the temporal trends of PBDEs and HBCD and if the concentrations of PCBs and PCDD/Fs are stabilizing at current levels or continue to decrease.

Acknowledgements:
The Swedish EPA (Environmental Protection Agency) is acknowledged for financial support. Appreciation is also expressed to the participating women, to the midwifes Marie Walterzon, Monica Rudin, Marianne Leimar, and Johanna Elwinger and to Ellen Edgren, Jane Karlsdotter, Apri Bergh, Maria Haglund, Matilda Näslund, Anders Eriksson, and Andreas Gulde for technical assistance.

References:

1. Lignell S, Aune M, Darnerud PO, Cnattingius S, Glynn A. (2009); *Environ Res* 109: 760-7
2. Lignell S, Aune M, Glynn A, Cantillana T, Fridén U. (2014); Report to the Swedish Environmental Protection Agency, 2014-05-06
3. Gyllenhammar I, Glynn A, Fridén U, Cantillana T, Aune M, Lignell S. (2017); Report to Swedish Environmental Protection Agency, 2017-11-01
4. Aune, M, Fridén, U, Lignell, S. (2012); Report to Swedish Environmental Protection Agency, 2012-01-10
5. Lignell s, Aune M, Darnerud, PO, Soeria-Atmadja D, Hanberg A, Larsson S, Glynn A. (2011); *J Environ Monit* 13:1607
6. Glynn A, Aune M, Darnerud PO, Cnattingius S, Bjerselius R, Becker W, Lignell S. (2007); *Environ Health*, 6:2
7. Sturlurdottir E, Gunnlaugsdottir H, Nielsen OK, Stefansson G. (2015); *PhD thesis,* School of Engineering and Natural Sciences, Reykjavik
8. Lignell S, Aune M, Glynn A, Cantillana T, Fridén U. (2015); Report to Swedish Environmental Protection Agency, 2015-11-20
9. van der Bergh M, Birnbaum LS, Dension M, De Vito M, Farland W, Feeley M et al. (2006); *Toxicol Sci* 93: 223-241
10. National Food Agency. (2012); Report 7 (2012)
11. National Food Agency. (2017); Report 26 (2017)