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TEMPORAL TRENDS OF PCDD/FS AND PCBS IN MOTHER´S MILK IN SWEDEN – ARE THE CURRENT MATERNAL BODY BURDENS SAFE FOR THE FETUS?

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Introduction

Human exposure to PCDD/Fs and PCBs has decreased considerably in Sweden since emission controls commenced in the 1970s. This has resulted in a more than 10-fold decrease in maternal PCDD/F and PCB body burdens during pregnancy, as determined by mother´s milk concentrations of the compounds (1). However, at the same time knowledge about toxicity of the compounds have improved, resulting in a more restrictive view regarding the level of exposure that is safe for the consumers. Between 1990 and 2002 WHO lowered the health-based tolerable intake of PCDD/Fs and dioxin-like PCBs from around 300 pg TEQ/kg body weight/month to 70 pg TEQ/kg bw/month (2). In 2012 US EPA published a non-cancer reference dose (Rfd)for TCDD of 0.7 pg/kg bw/day, corresponding to 20 pg/kg bw/month, being more than 10-fold lower than the WHO tolerable intake from 1990 (3). This Rfd is based on two studies from Seveso, one of them dealing with associations between maternal body burdens of TCDD during pregnancy and levels of thyroid hormones in neonates. Here we report temporal trends of PCDD/F and dl-PCBs in mother´s milk in Sweden 1996-2014. We investigate if there are non-linear trends during the study period. Current body burdens of PCDD/F/PCB TEQs among pregnant women in Sweden are used in risk assessment of fetal exposure to these pollutants in Sweden.

Materials and methods

Mothers were randomly recruited among primiparous women born in Sweden and delivered at Uppsala University Hospital from January to November each year of sampling. The participating rate was 42-63% and mothers sampled milk at home day 14-21 post partum. Milk was sampled during nursing using a manual mother's milk pump and/or a passive mother's milk sampler. The women were instructed to sample milk both at the beginning and at the end of the breast-feeding sessions. During the sampling week, milk was stored in the home freezer in acetone-washed bottles. Newly sampled milk was poured on top of the frozen milk. At the end of the sampling week, a midwife visited the mother to collect the bottles. Data on maternal characteristics were obtained from interviews and questionnaires.

Altogether 8 mono-ortho substituted PCBs (PCB 105, 114, 118, 123, 156, 157, 167, 189), 4 non-ortho PCBs (PCB 77, 81, 126, 169) and 17 tetra- to octa-chlorinated PCDD/F congeners were measured by gas chromatography coupled to high resolution mass spectrometry as described in Aune et al. (4). The concentrations of the compounds were summed into toxicity equivalent (TEQ) concentrations using the WHO-2005 toxicity equivalent factors (5).

Multiple linear regressions were used to analyze associations between concentrations of PCDD/F/PCB TEQs in mother's milk and sampling year. Logarithmically transformed contaminant concentrations were used, since the distribution of data closely followed a log-normal distribution. Independent variables (life-style factors) that have been shown to influence TEQ levels in mother's milk were included as explanatory variables in the models, i.e. age of the mother (years), pre-pregnancy body mass index (BMI) (kg/m2), body weight gain during pregnancy (%), and body weight change during the period from delivery to sampling (%). As a consequence of the logarithmic transformation, the associations between sampling year and POP concentrations are presented as percent change of concentrations per year, and not as change in absolute levels.

Non-linearity of trends was investigated by a Change-Point detection method suggested by Sturludottir et al. (6). The method iteratively search for a combination of two log-linear regression lines that explains significantly more of the total variance explained by a single regression line for the whole study period. Also a simple 3-point running mean smoother was fitted to the annual geometric mean values. The significance of this line is tested by means of an Analysis of Variance, where the variance is explained

by the smoother line, and the regression line is compared with the total variance. This procedure has been used in assessments at ICES and is described by Nicholson et al. (7).

The lowest adverse effect maternal body burden of 235 pg/g lipid in the Seveso thyroid hormone study was modelled by the US EPA to correspond to a long-term average maternal oral daily intake of 20 pg/kg body weight/day before pregnancy. An uncertainty factor of 30 was used ending up with a Rfd of 0.7 pg/kg bw/d (3). An uncertainty factor of 30 on the LOAEL maternal body burden of 235 pg/g lipid results in a Rfd body burden of 7.8 pg/g lipid. This Rfd body burden was used in the risk assessment of maternal body burdens of TEQs in pregnant women from Sweden. The 95 % confidence interval band around the log-linear regression line for changes in total TEq concentrations 1996-2014 was used to determine which year the upper limit of the confidence limit band crossed a TEQ concentration the was half of the Rfd body burden, i.e. 3.9 pg TEQ/g lipid. This conservative approach was used in order to account for possible regional differences in total TEQ exposure among young women in Sweden. With the same rate of decline of total TEQ concentrations in body lipids (6% per year) but a general exposure that is twice as high as in the Uppsala population the upper 95% confidence band would cross 7.8 pg/g lipid the same year as the Uppsala population.

Results and discussion:
Multiple linear regressions showed that concentrations of mono-ortho PCB TEQ and non-ortho PCB TEQ decreased with about 6% per year between 1996 and 2014, whereas PCDD TEQs and PCDF TEQs decreased 7.1 and 3.9% per year, respectively (Table 1).

Between 2008 and 2014 22% of the study participants had body burdens of 7.8 pg TEQ/g lipid or higher (Fig. 1), showing that efforts to lower PCDD/F/PCB TEQ exposures in Sweden should continue. Using the results of the regression analysis, and assuming a continuous decline in total TEQ concentrations with 6% per year, we estimated the year when the upper 95% confidence band limit of the regression line crosses a body burden of 3.9 pg TEQ/g lipid, which is half the Rfd body burden. This body burden in the population of first-time mothers is reached in 2028 (Fig. 2).

No significant non-linear change point was observed for trends of PCDD and PCDF TEQ concentrations. However, two log-linear regression lines better explained the total variance of the PCDD/F TEQ, DL-PCB TEQ and PCDD/F + DL TEQ concentrations than a single regression line (Fig. 3). The estimated change-point was 2008, with a slower decline in concentrations after the change-point. This suggests that the previous decline in human exposure in Sweden is levelling off. If the current decline in total TEQ concentrations is slower than before 2008, a safe body burden for pregnant women in Sweden will not be reached around 2030.

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References:
1. Fång, J., Nyberg, E., Bignert, A., Bergman, Å. (2011) Environ Int 60, 224-231.
2. WHO. (2002) WHO Food Additive Series 48, 1-212.
3. US EPA. (2012) Epa´s reanalysis of key issues related to dioxin toxicity and response to NAS comments, Volume 1.
4. Aune, M., Fridén, U., Lignell, S., (2012). Analysis of polychlorinated dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) in human milk – a calibration study. Report to the Swedish EPA.
5. Van den Berg, M., Birnbaum, L.S., Denison, M., et al. (2006). Toxicol Sci 93, 223-241.
6. Sturludottir, E., Gunnlaugsdottir, H., Nielsen, O.K., Stefansson, G. (2016) Communications in Statistics - Simulation and Computation. In press.
7. Nicholson, M.D., Fryer, R., Larsen, J.R. (1998) ICES Techniques in Marine Environmental Sciences 20, 1-29.

Table 1. Temporal trends of PCDD/F and dioxin-like (DL-) PCB concentrations in mother´s milk from primiparous mothers living in Uppsala County, Sweden, between 1996 and 2014.

Compounds	% change/year[a]	Half-time (year)[b]	P
PCDD TEQ	-7.1 (-7.6,-6.6)	9	<0.001
PCDF TEQ	-3.9 (-4.6,-3.3)	17	<0.001
PCB TEQ	-6.2 (-6.9,-5.5)	11	<0.001
Total TEQ	-6.0 (-6.5,-5.4)	11	<0.001

[a]Percent change (decrease (-)) of concentrations per year determined from multiple regression of log-normally transformed concentrations. Covariates in regression models were maternal age, pre-pregnancy BMI, weight change during pregnancy and between delivery and sampling. [b]The estimated time it takes for the concentrations to be *halved* in the population.

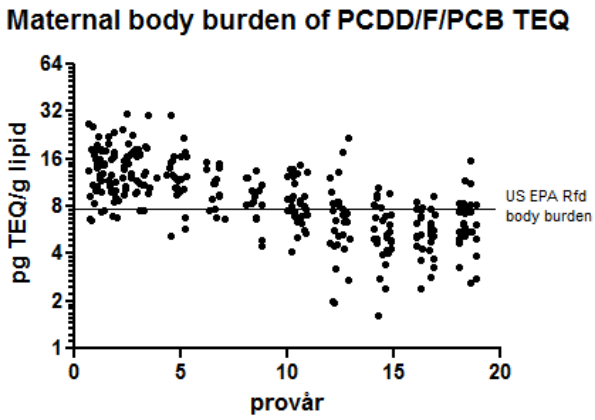

Figure 1. Maternal body burdens of PCDD/F/PCB TEQs during pregnancy, determined from mother´s milk lipid TEQ concentrations, between 1996 and 2014. Body burdens are compared with the maternal body burden during pregnancy (7.9 pg TEQ/g lipid) corresponding to the US EPA Rfd of 0.7 pg/kg body weight/day.

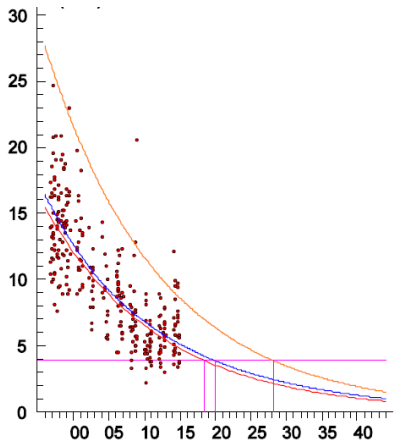

Figure 2. Temporal trend of total TEQ concentrations in mothers´s milk 1996-2014 (pg TEQ/g lipid). The lines represent the log-linear regression line, the upper 95% confidence interval band of the regression line and the upper population 95% confidence band limit. This line crosses a body burden of 3.9 pg TEQ/g lipid, which is half of the Rfd body burden of 7.9 pg TEQ/g lipid, in 2028. This conservative approach was used in order to account for possible regional differences in total TEQ exposure among young women in Sweden. With the same rate of decline of total TEQ concentrations in body lipids (6% per year) but a general exposure that is twice as high as in the Uppsala population the upper 95% confidence band would cross 7.9 pg/g lipid the same year as the Uppsala population.

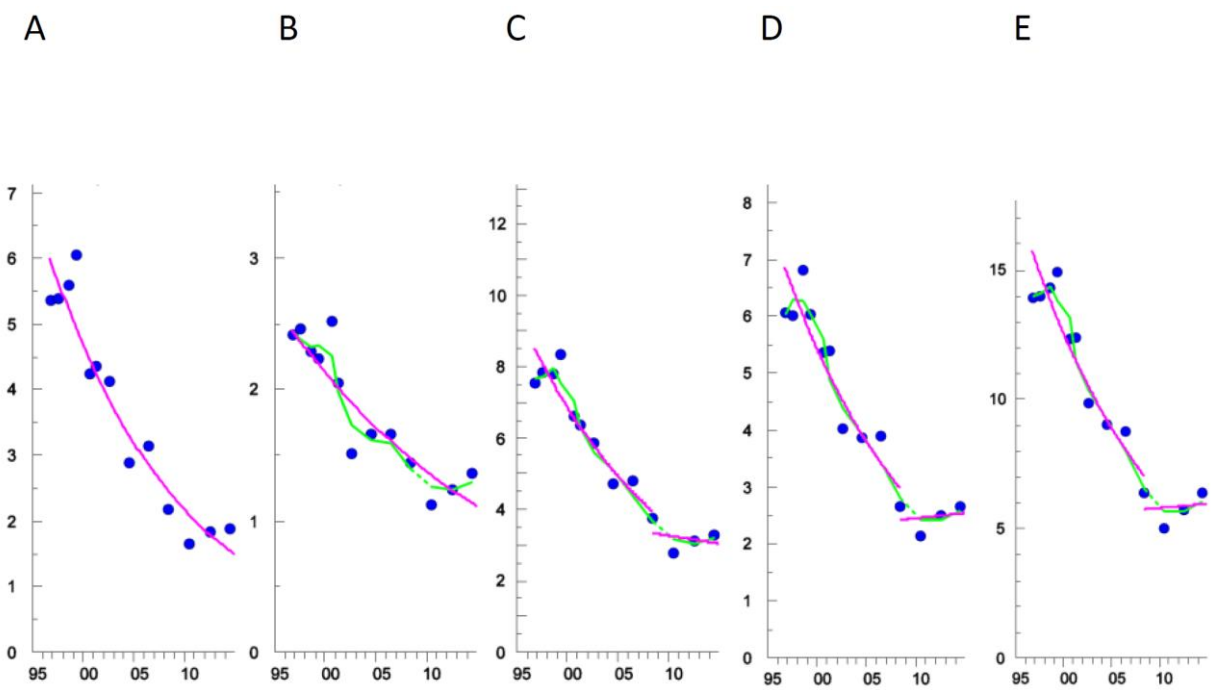

Figure 3. Temporal trends of PCDD TEQ (A), PCDF TEQ (B), PCDD/F TEQ (C), PCB TEQ (D) and total TEQ (E) concentrations in mother´s milk. Purple lines represents temporal trends analyzed by linear regression using log-normal concentration data. In these analyses it was possible to find statistically significant change-points in trends represented in Figure C, D and E by two regression lines. The green lines represent non-linear trends using a simple 3-point running mean smoother that was fitted to the annual geometric mean values.