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The impact of age, lactation and dietary habits on PCB in plasma in Swedish women

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Abstract

The mean concentration of the chlorinated biphenyl 2,2′,4,4′,5,5′-hexachlorobiphenyl (CB-153) in plasma from 192 fishermen's wives from the Swedish east coast was on a fresh weight basis 960 (range 80–4300) pg/g and lipid adjusted 160 (range 20–780) ng/g lipid. The concentration of CB-153 in plasma was significantly influenced by age, total lactation time and place of living during childhood and adolescence (fishing village vs. other place). The residential variable probably reflects early life consumption of fish from the Baltic Sea (at the Swedish east coast) contaminated with persistent organochlorine compounds. © 1997 Elsevier Science B.V.

Keywords: Polychlorinated biphenyls; 2,2′,4,4′,5,5′-hexachlorobiphenyl; Fish consumption; Lactation; Age

1. Introduction

Exposure to persistent organochlorine compounds (POC), such as polychlorinated biphenyls (PCB), has in experimental animal studies as well as in epidemiological studies been associated with health hazards (Tilson et al., 1990; Peterson et al., 1993; Brouwer et al., 1995). In Sweden the main exposure route for POC is through consumption of fatty fish from the Baltic Sea at the Swedish east coast (Svensson et al., 1991, 1995; Asplund et al., 1994). As the biological half-lives of many

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chlorinated biphenyls (CB) are rather long, the body burden will increase during life if the exposure is constant over time (Ahlborg et al., 1992). However, for women it is more complicated, as it has been shown that lactation decreases the body burden (Skaare and Polder, 1990; Hong et al., 1994). Moreover, smoking status and alcohol consumption have in some single reports been associated with high PCB concentrations (Kreiss et al., 1981; Hong et al., 1994).

Evidence for the use of 2,2′,4,4′,5,5′-hexachlorobiphenyl (CB-153, IUPAC number) as a biomarker for 'dioxin like' PCB congeners, and under certain restrictions also for total toxic equivalents (including polychlorinated dibenzo-*p*-dioxins and dibenzofurans) in biotic samples, has been provided (de Boer et al., 1993; Johansen et al., 1994; Brouwer et al., 1995). This suggestion was supported in a study of 50 fishermen's wives from the Swedish east coast (a subset of the present study subjects), where high correlations were observed between the concentration of CB-153, on the one hand, and the sum of 14 CB congeners in plasma ($r = 0.99$) and total PCB toxic equivalency factor in plasma ($r = 0.91$), respectively, on the other hand (Grimvall et al., 1997).

The present study aims to evaluate the impact of different factors on the concentration of CB-153 in plasma in women. In a previous nested case-referent study on birthweight outcome (Rylander et al., in press) fishermen's wives were interviewed and, moreover, blood samples were collected. These women were considered as an appropriate group to study.

2. Materials and methods

2.1. Study population

A cohort of women who were, or had been, married to fishermen from the Swedish east coast was established by linkage of a previously established cohort of fishermen to the national Swedish population register and to registers at the local parish offices (Rylander et al., 1995). These women were linked to the Swedish Medical Birth Register, which includes almost every infant born in Sweden since 1973 (Cnattingius et al., 1990). During the period 1973–1991, 757 women in the cohort had given birth to 1501 infants. Among these women, 192 participated in the present study. They also participated in a nested case-referent study with respect to birthweight (Rylander et al., 1996; Rylander et al., in press). Their median age was 42 years (range 23–62). For 50 of them the concentrations in plasma for 14 different CB congeners have previously been reported (Grimvall et al., 1997).

2.2. Interview

At the time of blood sampling the women were interviewed. The current smokers ($n = 68$), as well as the ex-smokers ($n = 53$) were asked about the year of starting and, if relevant, stopping smoking and their average daily consumption. All, except three, had had at least one lactation period (median three periods, maximum six periods) and the median total lactation time was 11 (range 0–66) months. The women were also asked about their educational level, food frequencies of fish from the Baltic Sea at different time periods, other dietary habits and alcohol consumption. In addition, the women were asked about their place of living during childhood and adolescence (fishing village vs. other place).

2.3. Blood sampling

Venous blood was drawn from a cubital vein and collected in metal-free evacuated tubes (Venoject) with heparin as the anticoagulant. The plasma was stored at 4–8°C for a maximum of 72 h, before it was deep-frozen in ethanol-washed glass bottles and stored at − 70°C until the analyses were performed. All samples were sent coded to the analytical laboratory.

2.4. Determination of CB-153

After adding internal standards, 2,3,3′,5′-tetrachlorobiphenyl (CB-58) and 2,2′,3,3′,4,5,5′,6-octachlorobiphenyl (CB-198), to the plasma samples, formic acid was added as a denaturing agent. The samples were extracted with a mixture of *n*-hexane and methyl-tert-butyl ether and subse-

quently fractionated on silica gel. The final separation and detection was performed by gas chromatography electron capture detection. A more detailed description has been published previously (Rylander et al., in press).

2.5. Determination of lipids by enzymatic methods

Plasma concentrations of triglycerides, cholesterol and phospholipids were determined by enzymatic methods using reagents from Boeringer–Mannheim (Mannheim, Germany) (triglycerides and cholesterol) and Waco Chemicals GmbH (Neuss, Germany) (phospholipids). The total lipid concentration in plasma was calculated by summation of the amounts of triglycerides, cholesterol and phospholipids. In these calculations, the average molecular weights of triglycerides and phospholipids were assumed to be 807 and 714, respectively. For cholesterol, an average molecular weight of 571 was used, postulating that the proportion of free and esterified cholesterol in plasma was 1:2.

2.6. Statistics

Geometric means (GM) were used for summarizing the concentrations of CB-153 in plasma. The influence of different covariates on the concentrations of CB-153 in plasma was examined by linear regression and analysis of variance (ANOVA) techniques. Confidence intervals for different effect estimates were adjusted for multiple comparisons according to Scheffe's method (Kleinbaum et al., 1987). Prediction intervals were calculated for the mean predicted CB-153 concentrations (SPSS for Windows).

3. Results

The mean (GM) concentration of CB-153 in plasma for all 192 women was on a fresh wt. basis 960 (range 80–4300) pg/g and lipid adjusted 160 (range 20–780) ng/g lipid. These two measures were highly correlated (Pearson's correlation coefficient 0.92, Fig. 1).

Univariate analyses indicated that high age, short total lactation time, low educational level,

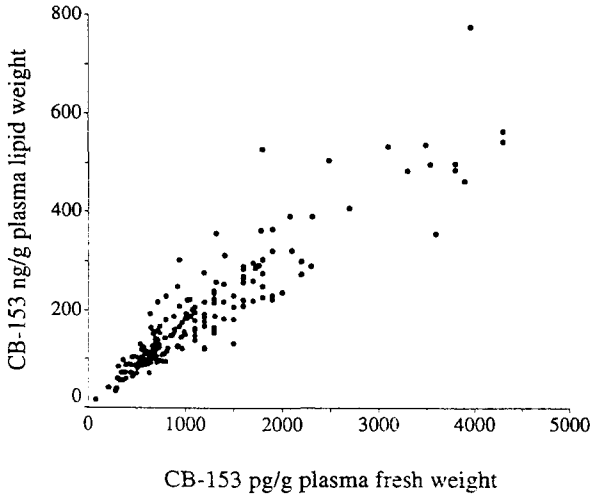


Fig. 1. The concentration of CB-153 in plasma for all 192 women on a fresh wt. basis vs. lipid adjusted (Pearson's correlation coefficient 0.92).

high intake of fish from the Baltic Sea and growing up in a fishing village implied a relatively high lipid adjusted CB-153 concentration in plasma. Consumption on dairy products, alcohol or tobacco was, however, not associated with CB-153 in plasma. When included simultaneously, age and total lactation time contributed significantly to the multivariate ANOVA model (both P-values < 0.001). The GMs for the concentrations of CB-153, stratified by age and total lactation time, are displayed in Table 1. The estimated age effect on the concentration of CB-153 in plasma corresponded to a 38% increase (95% CI: 21, 57) for ≥ 45 vs. ≤ 38 years, whereas the estimated effect of total lactation time was a 24% decrease (95% CI; $-33, -14$) for > 15 vs. < 8 months. With age and total lactation time in the multivariate model, neither present consumption of fish from the Baltic Sea nor the educational level did contribute significantly to any further explanation of the variance for CB-153. However, women who had grown up in a fishing village had increased concentrations of CB-153 in plasma as compared with the other women ($P = 0.03$) (Table 2).

The CB-153 concentration in blood plasma differed only slightly with respect to different regions of the Swedish east coast. Fig. 2 shows the predicted CB-153 values obtained from a multi-

Table 1
Lipid-adjusted plasma concentration of CB-153 (ng/g) in 192 women who were, or had been, married to fishermen from Swedish east coast, stratified by age and lactation time

Age (years)	Total lactation time (months)											
	< 8			8–15			> 15			All		
	n	GM[a]	(Range)	*n*	GM[a]	(Range)	*n*	GM[a]	(Range)	*n*	GM[a]	(Range)
≤ 38	17	120	(40–290)	32	140	(60–360)	18	100	(30–320)	67	120	(30–360)
39–44	22	210	(90–530)	16	190	(100–310)	28	110	(20–570)	66	160	(20–570)
≥ 45	25	240	(120–780)	16	270	(80–540)	18	180	(100–500)	59	230	(80–780)
All	64	190	(40–780)	64	180	(60–540)	64	120	(20–570)	192	160	(20–780)

[a] Geometric mean.

Table 2
Lipid-adjusted plasma concentration of CB-153 (ng/g) in 192 women who were, or had been, married to fishermen from Swedish east coast, stratified by age, lactation time and place of living during childhood and adolescence

Age (years) Grown up in a fishing village	Total lactation time (months)								
	≤ 15			> 15			All		
	n	GM[a]	(Range)	*n*	GM[a]	(Range)	*n*	GM[a]	(Range)
≤ 44									
No	71	160	(60–510)	39	100	(20–570)	110	140	(20–570)
Yes	16	160	(40–530)	7	160	(90–320)	23	160	(40–530)
≥ 45									
No	31	230	(80–540)	14	180	(100–500)	45	210	(80–540)
Yes	10	330	(150–780)	4	200	(140–230)	14	290	(140–780)
All									
No	102	180	(60–540)	53	120	(20–570)	155	150	(20–570)
Yes	26	210	(40–780)	11	170	(90–320)	37	200	(40–780)

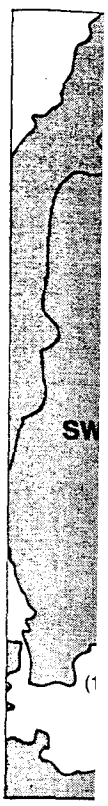
[a] Geometric mean.

variate regression model (including age, total lactation time and place of living during childhood and adolescence) for a 40-year-old woman who had not grown up in a fishing village and with a total lactation time of 10 months.

4. Discussion

The main finding of the present study was the importance of age, lactation and place of living during childhood and adolescence on the concentration of CB-153 in plasma in fishermen's wives from the Swedish east coast. The residential variable probably reflects early life consumption of fish from the Baltic Sea contaminated with POC. In contrast to results from some previous single reports there were, however, no associations between the concentration of CB-153 in plasma and smoking habits or alcohol consumption (Kreiss et al., 1981; Hong et al., 1994).

The GM of CB-153 in plasma in the present study was approx. 30% higher as compared with that based on 136 women from the Swedish inland with a relatively low dietary intake of fish from the Baltic Sea (Annika Hanberg, personal communication). The mean concentration of CB-153 in plasma in the present study was, however, similar to the mean blood plasma concentration of CB-153 in samples collected from a consecutive series of delivering women from the Nether-



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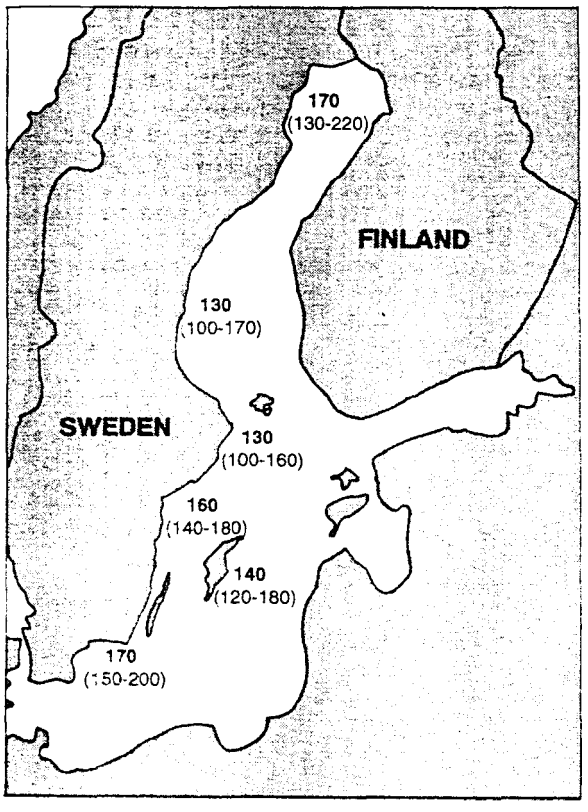

Fig. 2. Predicted lipid adjusted concentrations of CB-153 in plasma (ng/g) with 95% prediction intervals, for a 40-year-old woman who had not grown up in a fishing village and with a total lactation time of 10 months, with respect to different coastal stretches from the Swedish east coast.

lands (Koopman-Esseboom et al., 1994). The Netherland study indicated an association between prenatal exposure to POC and subtle signs of neurological dysfunctioning and a small delay in psychomotor development in the infants (Koopman-Esseboom, 1995). The concentration of CB-153 in plasma was not measured in the studies from the Lake Michigan area in the United States in which prenatal exposure to PCB indicated a negative long-term impact on intellectual functions (Jacobson and Jacobson, 1996). The mean fresh-wt. concentration of total PCB in maternal serum samples was 5.5 ng/ml in the Lake Michigan studies (Fein et al., 1984). For 50 of the fishermen's wives in the present study, concentrations of 14 specific PCB congeners in plasma were assessed (Grimvall et al., 1997). The range of the sum of these CBs (1.0–10.7 ng/ml) was very similar to those from the Lake Michigan area. This comparison is, however, hampered by differences in the analytical methods.

There seems to be no obvious discrepancies in concentration of CB-153 in plasma between women from different parts of the Swedish east coast. This is not a surprising finding as no such discrepancies have been observed for PCB in fish from the Baltic Sea (Bergqvist et al., 1989).

In the present study both age and total lactation time affected the concentration of CB-153 in plasma. Negative associations between total lactation time and PCB concentrations in mothers milk have been shown previously (Rogan et al., 1986; Skaare and Polder, 1990; Hong et al., 1994). Moreover, in previous studies age has been found to be correlated with the PCB concentrations in mothers milk (Rogan et al., 1986; Drijver et al., 1988; Skaare and Polder, 1990; Hong et al., 1994).

Consumption of fish from the Baltic Sea did not contribute significantly to explain the variance of CB-153 in plasma in the employed regression model. This may be due to the positive association between calendar-year of birth and consumption of fish from the Baltic Sea. The percentage of women with a high intake of fish from the Baltic Sea (> six meals per month) in the oldest age group (≥ 45 years) was 49%, as compared with only 30% in the youngest age group (≤ 38 years). In addition, the PCB concentrations in the Baltic Sea fish have decreased since the early 1970s (Bignert et al., 1993), which means that the older women in the present study have consumed fish with higher PCB concentrations than the younger ones. The correlation between calendar-year of birth and fish consumption is supported by a comparison made with data from 136 women from the Swedish inland with a modest fish intake. The difference in GM for CB-153 in plasma between those women ≤ 38 years and those ≥ 45 years of age was in the present study 110 ng/g lipid whereas the corresponding difference in the 'inland study' was only 50 ng/g lipid (Annika Hanberg, personal communication).

As compared with consumption of fish from the Baltic Sea, the variable 'grown up in a fishing village' explained a greater degree of the variance for CB-153 in plasma. This residential variable may be interpreted as an indirect measure of the women's accumulated consumption of fish from the Baltic Sea during childhood and adolescence. A greater fraction of the women grown up in a fishing village had, at the time of investigation, a higher intake of fish from the Baltic Sea (57%), as compared with the other women (32%). Thus, a woman's dietary habit may, to some extent, have been indirectly influenced by her place of growing up.

In the case-referent analysis with respect to low birthweight, kinetic modelling of CB-153 in plasma resulted in decreasing concentrations with increasing age (Rylander et al., in press). In the present cross-sectional analysis age was, however, positively correlated with the concentration of CB-153 in plasma. This seems to be a paradox, but can be explained when we consider the influence of calendar-year. In the kinetic modelling a yearly constant intake of fish from the Baltic Sea was assumed, whereas the concentration of PCB in fish was assumed to decrease over the calendar-years. Hence, for a given calendar year of birth, CB-153 in plasma decreased with age, at least when steady-state was reached. Thus, in a longitudinal study design, the plasma concentration of CB-153 decreases with age, but in a cross-sectional approach, older women have higher concentrations than younger ones.

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