Original Contribution

Linking Exposure to Polychlorinated Biphenyls With Fatty Fish Consumption and Reduced Fetal Growth Among Danish Pregnant Women: A Cause for Concern?

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In a selected group of women from the Danish National Birth Cohort, the authors investigated the association between intake of fatty fish and plasma concentrations of polychlorinated biphenyls (PCBs) on the one hand and the association between maternal PCB concentrations and fetal growth on the other. Of 70,183 women who filled in a food frequency questionnaire during 1996–2002, 100 nulliparous women aged 25–35 years with normal pre-pregnancy body mass index were selected according to their intake of fatty fish (low (0 meals/month, \( n = 34 \)), medium (1–3 meals/month, \( n = 33 \)), or high (\( >4 \) meals/month, \( n = 33 \))). Women with a high intake of fatty fish had 50% (95% confidence interval (CI): 31, 72) higher plasma PCB concentrations than women with low intake. Maternal plasma PCB concentrations were inversely associated with birth weight and placental weight. The adjusted mean difference between the 75th and 25th PCB percentiles was \(-155 \) g (95% CI: \(-291, -19 \)) for birth weight and \(-81 \) g (95% CI: \(-135, -26 \)) for placental weight. These results support previous findings from this cohort, where fatty fish intake was inversely associated with fetal growth. Dietary recommendations often encourage weekly consumption of fatty fish. These results suggest that potential exposure to PCBs should be carefully considered before recommending such intakes among women of childbearing age.

Fish is generally considered a healthy dietary choice, being low in saturated fat but rich in proteins and nutrients such as marine n-3 polyunsaturated fatty acids and vitamin D. During pregnancy, intake of marine n-3 fatty acids through regular fish consumption has been associated with increased fetal growth (1–3), prolonged gestation (4, 5), and improved cognitive development in early life (6, 7).

Fish is also a source of industrial contaminants, particularly methyl-mercury and persistent organic pollutants such as polychlorinated biphenyls (PCBs). Prenatal exposures to both methyl-mercury and PCBs have been related to impaired neurodevelopment in infants (8), although the results for PCBs have not been consistent (9). Some studies have also found PCBs to be inversely related to fetal growth (10–12). For pregnant women, however, dietary guidelines have mostly focused on reducing exposure to methyl-mercury through reduced intake of piscivorous species (13).

Because of the lipophilic nature of PCBs, considerably higher tissue concentrations are found in fatty fish than in lean fish (13). Consumption of locally caught fatty fish has been observed to be a dominant route of exposure in areas where environmental levels are high, such as the Baltic Sea (14) and the Great Lakes (15). For the general population, other foods of animal origin are often believed to be more important with respect to exposure (16, 17). Therefore, the general conclusion to date has been that exposure to PCBs from fatty fish is low and is outweighed by the nutritional benefits of fish consumption (13, 18).

However, the fact that levels of PCBs and other pollutants in commercial fish may vary considerably (19) is often ignored. When it comes to the potential benefits of fish...
consumption during pregnancy, observational studies have not been consistent, and inverse associations for both fish consumption (20) and marine n-3 fatty acids (3, 21) with regard to fetal growth have been reported.

In a previous study on 44,824 women from the Danish National Birth Cohort, we observed an inverse association between high consumption of fatty fish and fetal growth (22). No association was observed for lean fish, indicating that persistent organic pollutants might play a role. In the present study, the association between PCBs and fatty fish intake on the one hand and between PCBs and fetal growth on the other was explored in 100 women from the Danish National Birth Cohort. These women were selected according to their intake of fatty fish.

MATERIALS AND METHODS

The Danish National Birth Cohort

The cohort’s structure has been described elsewhere (23). In brief, 101,046 pregnant women from all over Denmark were recruited from 1996 to 2002. Information on parental lifestyle and health was collected through four computer-assisted telephone interviews around gestational weeks 12 and 30 and at months 6 and 18 postpartum. A food frequency questionnaire (FFQ) was sent out to the expecting mothers in midpregnancy. Two maternal blood samples were collected during a routine visit to the general practitioner, in addition to cord blood collected at delivery.

Dietary assessment

Dietary information was collected around week 25 of gestation through an FFQ (24) which has been validated with respect to fish consumption (25). The FFQ solicited information on frequency and type of fish consumed during pregnancy, either as a hot meal or with bread. Information on frequency of fish consumption (but not type) was also available from the two telephone interviews conducted at approximately weeks 12 and 30 of gestation. Consumption of “fatty fish” referred to intakes of salmon, herring, mackerel, trout, and Greenland halibut. Consumption was quantified in terms of number of meals per month and in grams per day (meals and bread combined), using standard portion sizes (26).

Selection of study participants

Of the 44,824 participants from our previous study on fish and fetal growth (22) who gave birth to singleton full-term infants, only nulliparous women aged 25–35 years with normal (18.5–25) prepregnancy body mass index (weight (kg)/height (m)²) were made eligible for selection (n = 9,815). We imposed these restrictions to minimize confounding by these factors in our study of PCBs and fetal growth. For these women, three intake strata were defined according to frequency of fatty fish intake (low (0 meals/month), medium (1–3 meals/month), or high (≥4 meals/month)), as reported on the FFQ. To minimize misclassification due to changes in fish consumption, we selected subjects whose reported frequences of fish intake in the 2 prenatal telephone interviews (weeks 12 and 30) were in the same strata as those assigned by the FFQ. On the basis of these restrictions, 34, 33, and 33 women were randomly selected from the low, medium, and high intake strata, respectively. By chance, these women were recruited between 1998 and 2002 (relatively few women entered the cohort in 1996 and 1997).

Fetal outcome assessment

Birth weight, birth length, head circumference, and placental weight were measured by the midwives who attended the children’s births. Date of birth was extracted from the Danish Civil Registration System. Gestational age was assessed from the date of the last menstrual period. In the absence of that information (n = 50), we used the expected date of delivery as reported in the telephone interview in gestation week 30, which should in most cases have been based on ultrasound scanning.

Blood sample collection

The blood samples were collected by the general practitioner at approximately weeks 8 and 25 of gestation. The blood was centrifuged, and the plasma was stored at −30°C. Because of low available sample volumes, plasma from the 2 blood samples was pooled so that each woman would have the total of 1.5 mL required for the analyses.

Chemical analyses

The plasma samples were analyzed for major PCB congeners (PCB-101, PCB-105, PCB-118, PCB-138, PCB-153, PCB-156, and PCB-180), as well as for p,p’-dichlorodiphenyltrichloroethane (DDT), p,p’-dichlorodiphenyldichloroethylene (DDE), hexachlorobenzene, and β-hexachlorocyclohexane, by gas chromatography with electron-capture detection as described previously (27). The concentrations of PCB-101, DDT, and β-hexachlorocyclohexane were below the detection limit of the method. The median limit of detection for the PCB congeners was 0.03 parts per billion. The lipid content of the plasma samples was determined as “total lipids” by means of the “total lipids” kit (HB018) from Cypress Diagnostics (Langdorp, Belgium). The coefficient of variation for within-day repeatability was lower than 9% for the PCBs and lower than 11% for DDE. The between-day reproducibility (coefficient of variation) was lower than 10% for the PCBs and lower than 13% for DDE.

Statistical analyses

The sum of PCB congeners 105, 118, 138, 153, 156, and 180 was used as a measure of exposure. PCB-101 was excluded because its levels were below the limit of detection in all participants. We used absolute concentrations (μg/L) rather than lipid-standardized levels, which have been observed to be prone to bias (28). Instead, plasma lipid concentration was included as a covariate where appropriate. Data for the PCB variable were transformed using the natural logarithm.
Institute Inc., Cary, North Carolina). All analyses were performed using SAS, version 9.1 (SAS body mass index, and total plasma lipid concentrations. Age (in days), maternal smoking (yes/no), prepregnancy identified and included as covariates infant sex, gestational the association between obstetric outcomes and PCBs, we that were associated with PCBs in univariate analyses. For of covariate adjustment was explored for those host factors test (type III) for categorical variables and test (type III) to compare the linear model with curvature, (P-curvature, F test) to compare the linear model with a model fit that was based on restricted cubic splines (29). For the association between PCBs and fatty fish, the effect of covariate adjustment was explored for those host factors that were associated with PCBs in univariate analyses. For the association between obstetric outcomes and PCBs, we identified and included as covariates infant sex, gestational age (in days), maternal smoking (yes/no), prepregnancy body mass index, and total plasma lipid concentrations. All analyses were performed using SAS, version 9.1 (SAS Institute Inc., Cary, North Carolina).

RESULTS

The median value and the 5th, 25th, 75th, and 95th percentiles for the sum of 6 PCB congeners were 1.15 µg/L, 0.64 µg/L, 0.91 µg/L, 1.45 µg/L, and 1.88 µg/L, respectively. The median values for PCB-153, DDE, and hexachlorobenzene were 0.43 µg/L, 0.42 µg/L, and 0.14 µg/L, respectively.

Total lipid concentration (Table 1) was positively associated with plasma PCBs, while prepregnancy body mass in- dex was inversely associated. Plasma PCB concentrations decreased by 9.0% per year (95% confidence interval (CI): 3.3, 14.4) for recruitment year but increased by 7.3% per year (95% CI: 5.2, 9.4) for maternal age. When both variables were included simultaneously in the regression model, the absolute changes in plasma PCB concentrations per year were almost identical: a 6.9% increase for maternal age (95% CI: 4.9, 9.0) and a 6.6% decrease for recruitment year (95% CI: 1.7, 11.1). Maternal smoking, alcohol consumption, socioeconomic status, gestational age, and infant sex were not associated with plasma PCBs.

Figure 1 shows the association between plasma PCB concentrations and fatty fish consumption quantified in grams per day (Spearman’s r = 0.54, P < 0.0001). The restricted cubic spline fitted to the data shows a clear deviation from linearity (P-curvature = 0.02). Despite large between-person variation in plasma PCBs, the lower bound for exposure increases steadily with increased fatty fish intake. When fatty fish was categorized into meals per month (Table 2), plasma PCB concentrations were 50% (95% CI: 31, 72) higher in women consuming 4 or more meals per month than in those with no intake. After adjustment for age, recruitment year, and prepregnancy body mass index, the parameter estimate was reduced to 37% (95% CI: 22, 52), which was mostly attributable to the age adjustment. Additional adjustment for plasma lipids reduced the parameter estimate further to 18% (95% CI: 5, 34). The average lipid concentrations for the low, medium, and high intake strata

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median or %</th>
<th>Association with Plasma PCBs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β^b</td>
<td>95% Confidence Interval</td>
</tr>
<tr>
<td>Median age at recruitment, years</td>
<td>29 (25–35)^c</td>
<td>7.3</td>
</tr>
<tr>
<td>Median year of recruitment</td>
<td>2000 (1998–2002)</td>
<td>−9.0</td>
</tr>
<tr>
<td>Median prepregnancy body mass index e</td>
<td>21.3 (18.5–25.0)</td>
<td>−4.4</td>
</tr>
<tr>
<td>Median total plasma lipid concentration, g/L</td>
<td>6.4 (3.5–9.7)</td>
<td>12.2</td>
</tr>
<tr>
<td>Median gestational age, days</td>
<td>282 (259–293)</td>
<td>−0.2</td>
</tr>
<tr>
<td>Male infant sex, %</td>
<td>53</td>
<td>−0.7</td>
</tr>
<tr>
<td>Alcohol consumption during pregnancy, %</td>
<td>35</td>
<td>−0.4</td>
</tr>
<tr>
<td>Smoking during pregnancy, %</td>
<td>20</td>
<td>−5.5</td>
</tr>
<tr>
<td>Socioeconomic status, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>45</td>
<td>0</td>
</tr>
<tr>
<td>Intermediate</td>
<td>19</td>
<td>−13.7</td>
</tr>
<tr>
<td>Worker</td>
<td>12</td>
<td>−5.2</td>
</tr>
<tr>
<td>Not working</td>
<td>24</td>
<td>−8.4</td>
</tr>
</tbody>
</table>

Abbreviation: PCB(s), polychlorinated biphenyl(s). ^a Sum of PCB congeners 105, 118, 138, 153, 156, and 180, in µg/L. ^b Percent change in plasma PCB concentration for a 1-unit change in the dependent variable. ^c Numbers in parentheses, range. ^d Two-sided P value from Student’s t test. ^e Weight (kg)/height (m)^2. ^f Two-sided P value from F test (type III).
were 5.3 g/L, 6.7 g/L, and 7.2 g/L, respectively (P for trend < 0.0001), and this increase explained the reduction in the parameter estimate after lipid adjustment.

For the obstetric outcomes, the mean value was 3,580 g (standard deviation (SD), 435; range, 2,600–4,580) for birth weight, 52.5 cm (SD, 2.0; range, 49–57) for birth length, 35.2 cm (SD, 1.7; range, 31–39) for head circumference, and 666 g (SD, 166; range, 400–1,380) for placental weight. In the unadjusted analysis (Table 3), placental weight was inversely associated with plasma PCB concentrations, while a nonsignificant decrease was observed for birth weight, length, and head circumference. After covariate adjustment, an inverse association was observed for birth weight and placental weight, with parameter estimates of −334 g (95% CI: −628, −40) and −174 g (95% CI: −291, −57), respectively. The parameter estimate reflects a 1-unit increase in log-transformed PCB concentrations, corresponding approximately to the change from the 5th PCB percentile (0.64 µg/L) to the 95th PCB percentile (1.88 µg/L). Table 3 also shows the more modest change between the 25th (0.91 µg/L) and 75th (1.45 µg/L) percentiles. For the associations in Table 3, a test for deviation from linearity was nonsignificant (P-curvature >0.80 in all cases).

The relatively large change in the parameter estimate for PCBs after covariate adjustment was attributable to the lipid adjustment. Taking birth weight as an example, the parameter estimate for PCBs changed from −203 g (95% CI: −467, 61) in the unadjusted analysis to −319 g (95% CI: −621, −17) after lipid adjustment. Adding the remaining four covariates then resulted in the fully adjusted estimate of −334 g (95% CI: −628, −40). In this fully adjusted model, plasma lipid concentrations had a marginally significant positive association with birth weight, with a parameter estimate of 63 g (95% CI: −3, 130).

Fish intake and DDE exposure are also potentially confounding factors with respect to PCBs and birth weight (30). However, the effect of adjusting for these variables was small. When total fish consumption was added as a covariate to the adjusted analysis in Table 3, the parameter estimate for PCBs changed to −350 g (95% CI: −659, −42), and when DDE was also added, the parameter estimate changed to −346 g (95%: CI: −681, −12).

Initially, we suspected that the results for placental weight were confounded by birth weight, but when we substituted birth weight for gestational age in the adjusted analysis for placental weight, the association was still significant, with a parameter estimate of −103 g (95% CI: −198, −8).

**DISCUSSION**

In this study, intake of fatty fish was positively associated with concentrations of PCBs in maternal plasma. Maternal

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**Table 2.** Association between intake of fatty fish and concentrations of polychlorinated biphenyls in maternal plasma (n = 100), Danish National Birth Cohort, 1998–2002

<table>
<thead>
<tr>
<th>Fatty Fish Intake, meals/month</th>
<th>% of Subjects</th>
<th>Unadjusted</th>
<th>Adjustment A</th>
<th>Adjustment B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>β</td>
<td>95% CI</td>
<td>β</td>
</tr>
<tr>
<td>0</td>
<td>34</td>
<td>0 Referent</td>
<td>0 Referent</td>
<td>0 Referent</td>
</tr>
<tr>
<td>1–3</td>
<td>33</td>
<td>29 13, 49</td>
<td>14 2, 28</td>
<td>3 −9, 15</td>
</tr>
<tr>
<td>≥4</td>
<td>33</td>
<td>50 31, 72</td>
<td>37 22, 52</td>
<td>18 5, 34</td>
</tr>
<tr>
<td>P for trendd</td>
<td></td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.005</td>
</tr>
<tr>
<td>R²</td>
<td></td>
<td>0.25</td>
<td>0.56</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; PCB(s), polychlorinated biphenyl(s).

* Adjusted for maternal age, prepregnancy body mass index, and recruitment year.

*b Same covariates as in adjustment A, with the addition of total plasma lipid concentration.

c Percent change in PCB concentration as compared with nonconsumers of fatty fish (sum of PCB congeners 105, 118, 138, 153, 156, and 180, in µg/L).

* Two-sided P value from Student’s t test.

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**Figure 1.** Association between intake of fatty fish (g/day) and plasma concentrations of polychlorinated biphenyls (PCBs), Danish National Birth Cohort, 1998–2002. PCB concentration is the sum of PCB congeners 105, 118, 138, 153, 156, and 180 in µg/L, log-transformed (n = 100).
exposure to PCBs was also inversely related to birth weight and placental weight. Note that these results were observed in a population with relatively moderate exposure. The lipid-standardized median concentration of PCB-153 was 70 ng/g lipid in our study, which is below the overall median of 110 ng/g lipid previously reported from a comparison of 10 studies on neurodevelopment (31).

Other investigators have found a correlation between fish intake and plasma PCB concentrations, but their focus has often been on communities where fish from contaminated waters (14, 15) or marine mammals (21) have been a part of the seafood diet. Our results should be more general, since consumption in our study population was based on commercial fish commonly sold in supermarkets in Northern Europe.

In market-basket studies from both Northern Europe (16) and the United States (17), researchers have concluded that the proportion of PCB exposure originating from fish is low (<26%) compared with other foods of animal origin. These assessments are derived from contamination data on foods commonly found in supermarkets combined with population intake estimates. One interpretation of these studies has been that PCB exposure from fish is marginal and should not be taken into account in dietary recommendations (13).

Table 3. Associations between obstetric outcomes and log-transformed concentrations of polychlorinated biphenyls* in maternal plasma (n = 100), Danish National Birth Cohort, 1998–2002

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted</th>
<th>Adjusted</th>
<th>75th Percentile of PCB Concentration vs. 25th Percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β^</td>
<td>95% CI</td>
<td>P Value^</td>
</tr>
<tr>
<td>Birth weight, g</td>
<td>−203</td>
<td>−467, 61</td>
<td>0.13</td>
</tr>
<tr>
<td>Birth length, cm</td>
<td>−0.8</td>
<td>−2.0, 0.4</td>
<td>0.20</td>
</tr>
<tr>
<td>Head circumference, cm</td>
<td>−1.0</td>
<td>−2.0, 0.02</td>
<td>0.06</td>
</tr>
<tr>
<td>Placental weight^d, g</td>
<td>−128</td>
<td>−228, −28</td>
<td>0.01</td>
</tr>
<tr>
<td>Birth weight, g</td>
<td>−334</td>
<td>−628, −40</td>
<td>0.03</td>
</tr>
<tr>
<td>Birth length, cm</td>
<td>−1.2</td>
<td>−2.5, 0.2</td>
<td>0.08</td>
</tr>
<tr>
<td>Head circumference, cm</td>
<td>−0.8</td>
<td>−1.9, 0.4</td>
<td>0.20</td>
</tr>
<tr>
<td>Placental weight^d, g</td>
<td>−174</td>
<td>−291, −57</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; PCB(s), polychlorinated biphenyl(s).
* Sum of PCB congeners 105, 118, 138, 153, 156, and 180, in µg/L.
^ Change in growth measure for a 1-unit increase in log-transformed PCB concentration.
^ Two-sided P value from Student's t test.
^ Data on placental weight were missing for 3 women (n = 97).
^ Adjusted for gestational age, infant's sex, maternal smoking, prepregnancy body mass index, and plasma lipid concentration.

Plasma PCB concentrations was low, corresponding to an approximately 10% increase in comparison with no intake. Still, increasing consumption to 4 meals per month resulted in a 50% increase in plasma PCB concentrations. One meal of fatty fish per week is comparable to what many dietary recommendations encourage (13, 32). Note, however, that the large between-person variation in plasma PCB concentrations in Figure 1 suggests that PCB exposure is often related to sources other than fish as well.

With respect to PCBs and plasma lipid concentrations, two things are worth noting. Firstly, the increase in plasma lipid concentrations with fatty fish intake weakened the association between PCBs and fatty fish after lipid adjustment. As in our study, a positive association between blood lipids and PCBs is often observed (33, 34). Therefore, the positive correlation between plasma lipids and fatty fish in our study is more likely to be related to a higher PCB body burden among fatty-fish consumers than to nutrient components in the fish. A similar increase in blood lipids with contaminated fish intake has also been observed among Great Lakes fish consumers (35, 36). Secondly, a relatively large change in the parameter estimate for PCBs with respect to birth weight was observed after lipid adjustment. In the covariate-adjusted analysis, the change in the parameter estimate for PCBs was mostly attributable to a marginally significant positive association between plasma lipids and birth weight (P = 0.06). Similar results for serum lipids were reported in a recent study on PCBs and birth weight from Slovakia (37), although no association was observed between PCBs and birth weight.
To our knowledge, results on PCBs and placental weight have been reported in only one other study, a study from the Faroe Islands, in which a nonsignificant decrease was observed (21). The association was adjusted only for parity, and an effect of other potential confounders (38), such as smoking, was not reported. In a study on the effect of PCBs on mink placenta, Backlin et al. (39) reported an increase in vascular and trophoblastic lesions among exposed animals, but the dose used was not comparable to current environmental levels. In a study of 30 Canadian women, Hamel et al. (40) observed altered calcium uptake in syncytiotrophoblast cells in the placenta related to DDE exposure, and small but nonsignificant changes were also observed for PCB-153. In contrast to our study, the DDE levels were much higher than the PCB-153 levels, and the level of PCB-153 was one-fourth of what we observed in our study. The authors concluded that altered calcium uptake was most likely due to placental damage. Our findings of an inverse association between PCBs and placental weight are compatible with such a deleterious effect on placental function. However, more detailed studies are needed to confirm or reject that hypothesis.

Although inverse associations between PCB concentrations and birth weight have been reported in a few studies (10–12, 41), a lack of association is often reported as well (21, 30, 42–44). Two studies had exposure levels comparable to ours. In a study of Dutch infants born between 1990 and 1992, Patandin et al. (11) observed an inverse association between PCBs in umbilical cord plasma and birth weight. Similar results were obtained for maternal plasma at average concentrations 2 times higher than those in our study. However, the inverse association was not confined to the higher end of exposure and a decrease of 86 g in birth weight was observed between the 10th and 50th PCB percentiles, which is within the exposure range of our study. In a large study of infants born in Massachusetts during 1993–1998, Sagiv et al. (42) also observed a similar inverse trend for birth weight at a relatively low concentration in cord plasma. The decrease in birth weight leveled off at the higher end of exposure. Although the inverse trend was not statistically significant, a consistent decrease was observed for birth weight, length, and head circumference.

Inconsistent results among observational studies might be partly related to changes in congener profiles over time, such as the relative decrease of PCB-118 with respect to PCB-153 (31). Some of the more prevalent PCB congeners such as 138, 153, and 180 have been observed to elicit antiestrogenic activity (45), while the less persistent lower-chlorinated congeners elicit estrogenic activity (46). Because estrogen levels in pregnancy have been linked to increased birth weight (47), an overall antiestrogenic activity might be one mechanism by which PCBs would decrease birth weight. The toxicity of the hydroxylated PCB metabolites might also be important, since they have been shown to transfer more efficiently through the placenta than the parent compounds (48).

Inconsistent results for birth weight might also be due to the complex pharmacokinetics of PCBs with respect to fetal uptake, changes in maternal body mass index, and previous breastfeeding (49). Restriction of our data to normal-weight nulliparous women helped us to partly avoid this problem and is one of the strength of this study.

Our results should be interpreted with some care, however, since the association between PCBs and birth weight could have resulted from the influence of unadjusted or unmeasured confounders, such as other chemical exposures that might be associated with PCBs. It is also possible that our results for birth weight might reflect reverse causality due to higher uptake of maternal PCBs in larger fetuses (50). For each woman, half of the plasma sample was obtained during gestational week 25, when variation in fetal uptake might have affected the maternal concentration. However, this potential effect should have been negligible for the other half of the sample, which originated from gestational week 8.

Our use of gestational age estimated on the basis of ultrasound scanning could, in some cases, have led to underestimation of gestational age if PCBs are inversely associated with early fetal growth. In our adjusted analyses on PCBs and birth weight, a slightly weaker association was observed for women with gestational age estimates based on ultrasound scanning ($n = 50$) as compared with those based on the last menstrual period ($n = 50$). Therefore, potential distortions in the gestational age estimate due to reliance on ultrasound scanning should not have led to overestimation of our results.

Despite divergent findings, the current evidence to date suggests that background levels of PCBs are, at most, weakly associated with birth weight (42). It is in that context that our results should be interpreted, since the inverse association in our study applies to infants whose birth weights were in all cases above the definition of low birth weight ($<2.500$ g).

Although several observational studies have indicated that a high intake of fish or marine fats might be detrimental for fetal growth (20–22), the results have perhaps not been given much weight in dietary recommendations, since these findings have not been consistent (1–3). However, regional differences in environmental contaminants might be important. Hites et al. (19) showed that levels of PCBs and other persistent organic pollutants in farmed and wild salmon varied by more than 1 order of magnitude, depending on the origin of the fish. The same is likely to hold for other species as well. Unfortunately, labeling of fish with respect to region of origin is often poor, which limits consumer options for choosing less-contaminated fish. Likewise, consumers’ access to contaminant data on different fish species is limited.

We have shown that regular consumption of fatty fish commonly found in Danish supermarkets is associated with a substantial increase in plasma PCB concentrations. Although our exposure levels were low in comparison with most previous reports of background exposed populations, plasma PCB concentrations in our population were inversely associated with birth weight and placental weight. These results support our previous findings from this cohort (22), where fatty fish consumption was inversely related to fetal growth while no association was observed for lean fish. It is our conclusion that the potential benefits of fish for pregnant women should not be ignored, and regular
consumption of various types of fish should generally be encouraged. Attention should be given to the fact that contaminant levels in commercial fish can vary considerably. Furthermore, potential exposures to persistent organic pollutants should be considered carefully before high intakes of fatty fish are recommended to women of childbearing age.

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Conflict of interest: none declared.

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