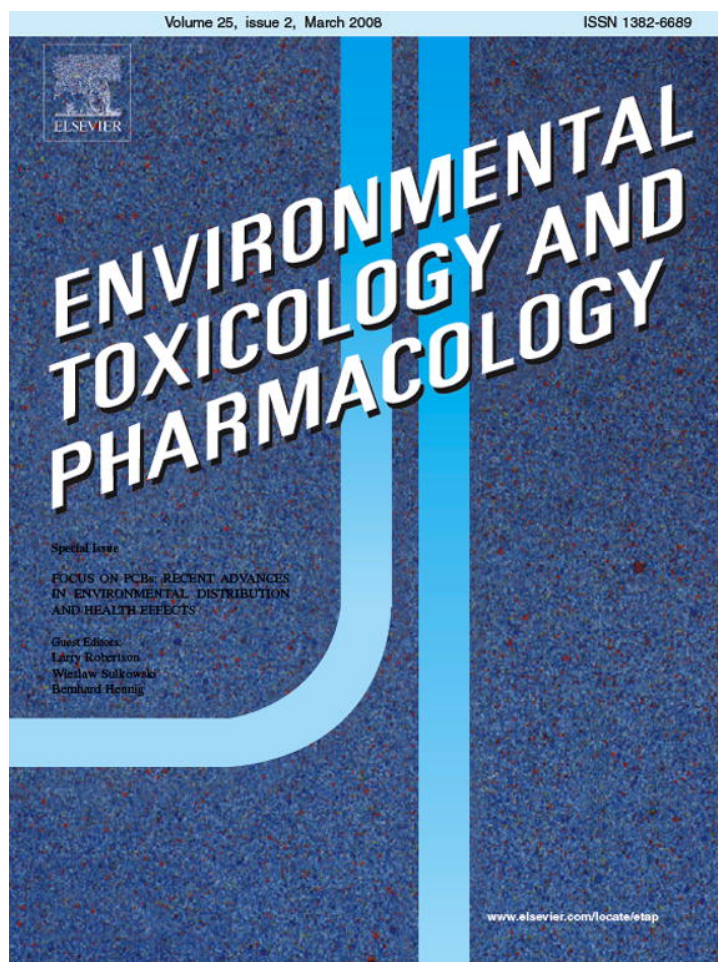


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Dental caries in Faroese children exposed to polychlorinated biphenyls

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Abstract

The effects of exposure to polychlorinated biphenyls (PCBs) on dental caries of first permanent molars in children in the Faroe Islands, where the population is exposed to PCBs in their traditional diet, were evaluated. This study was part of a cohort study aimed at determining developmental risks resulting from the consumption of contaminated seafood. One hundred and fourteen children from a birth cohort of 182 mother–child pairs, aged 9–10 years, were examined. Caries scoring was performed according to WHO criteria; cavitated and noncavitated lesions were included. Exposure assessment was based on the PCB concentrations in maternal milk samples. Data from the project data set provided information on various confounding factors. Mean maternal milk PCB concentration was 2205 (range 70–11,150) ng/g lipids. The number of carious surfaces of first permanent molars correlated with milk PCB concentration ($r=0.26$, $p=0.01$). In multivariate linear regression analysis, PCB exposure was significantly related to caries susceptibility. The findings support an association between children's PCB exposure and caries prevalence.

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Keywords: PCBs; Dental caries; Children; Environmental exposure; Faroe Islands

1. Introduction

Polychlorobiphenyls (PCBs) are lipophilic, persistent, and ubiquitous organochlorine pollutants found in almost every compartment of the global ecosystem including animal and human tissue, where they are associated with a variety of potential health risks (Hays and Aylward, 2003). Humans are exposed to PCBs mainly via diet; they are also transferred to the fetus and infants transplacentally and lactationally (Ahlborg et al., 1992).

Dental caries is one of the most prevalent chronic diseases affecting people worldwide. It forms through a complex interaction over time between acid-producing bacteria and fermentable carbohydrates, and is also affected by many host factors including teeth and saliva (Selwitz et al., 2007).

Occupational PCB exposure of mothers has been linked to carious and mottled primary teeth in children (Hara, 1985), and excessive ectodermal defects (Ahlborg et al., 1992), including carious teeth (Rogan et al., 1988), have been reported in epidemic PCB poisoning. Children born to exposed mothers would have had both transplacental exposure and exposure through maternal milk, but co-contamination with polychlorinated dibenzofurans (PCDFs) was largely responsible for

the overall toxicity (Safe, 1994; Masuda, 1996). However, no correlation has been found between PCB/PCDF or tetra-chloro-dibenzo-*p*-dioxin (TCDD) exposure and caries in the Yucheng children (Wang et al., 2003), subjects accidentally exposed to dioxin in Seveso (Alaluusua et al., 2004), nor in long-term PCB-exposed children in polluted regions of Slovenia (Jan and Vrbič, 2000) and Slovakia (Jan et al., 2007).

Experimental studies have confirmed that cells forming the teeth are sensitive to polychlorinated aromatics, which lead to permanent changes in dental hard tissues (Alaluusua and Lukinmaa, 2006). Rhesus macaques exposed to PCDDs and dioxin-like compounds, including PCBs via food, showed metaplasia of ameloblasts (McNulty, 1985). Studies conducted on continuously growing rat incisors reported the selective toxic effects on ameloblasts in adult rats treated with PCB mixture KC-400 (Hashiguchi et al., 1985). In rats, TCDD impairs enamel and dentin mineralization (Gao et al., 2004), and even low perinatal TCDD exposure enhances dental caries susceptibility (Miettinen et al., 2006), which could not be explained by altered mineral composition only.

PCB exposure produces histopathological changes in the major parotid salivary gland in mice (Kawasaki et al., 1995), suggesting a decrease in salivary function and a concomitant increase in dental caries risk.

Organochlorines are present in dental tissues (Jan et al., 2006) as well as in saliva (Ogawa et al., 2003), although

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their possible local effect on the caries process is yet unknown.

The aim of this study was to evaluate the effects of PCB exposure on dental caries in 9–10-year-old children from a Faroese birth cohort. This part of the cohort study was part of the EU funded project “ANEMONE”, with the objectives to improve methods for assessment of hazardous exposures and determining developmental risks resulting from the consumption of contaminated seafood (<http://www.anemone-project.dk>). The population in the Faroe Islands is exposed to PCBs present in their traditional diet, which may include pilot whale blubber (Weihe et al., 1996). Although the Faroe Islands are located far from conventional pollution sources, there are high concentrations of polychlorinated aromatic hydrocarbons, particularly PCBs, in maternal milk (Fångström et al., 2005). The concentrations of chlorinated dibenzo-*p*-dioxins and furans are within the normal ranges from other countries (Grandjean et al., 1995). In the study, exposure was assessed by PCB levels in maternal milk. First permanent molars develop in utero, their crowns calcify during the first 3 years of life, and erupt around age six (Nancy, 2003). We analyzed caries on first permanent molars, as PCB concentrations in maternal milk indicate exposure at the time of their development.

2. Materials and methods

A birth cohort of 182 mother–child pairs was established in the Faroe Islands in 1994–1995 (Steuerwald et al., 2000; Grandjean et al., 2001). The cohort was based on the primary catchment area, in the central and northwestern villages where access to fish and whales is the easiest, i.e. away from the capital area of Tórshavn. At age 9–10, 114 children (58 boys and 56 girls), with all four first permanent molars present, were examined at the Department of Occupational Medicine and Public Health in Tórshavn. Children rotated between stations staffed by health professionals, where physical examination, neurophysiological and neuropsychological tests, and dental examination were covered. Table 1 provides descriptive characteristics of the study sample population divided into low, medium, and high exposure groups according to their maternal milk PCB concentration, with other plausible predictors of caries occurrence included. A detailed description has previously been published (Steuerwald et al., 2000; Grandjean et al., 2001).

The exposure of the children to PCBs was assessed by measuring PCB concentrations in maternal milk collected on days 3–5 post partum for major PCB congeners, as presented previously (Steuerwald et al., 2000). Analyses were performed by the Department of Environmental Health, State Agency for Health and Occupational Safety of Schleswig-Holstein, Germany (Schade and Heinzow, 1998). Total PCB concentration was calculated as the sum of congeners PCB-138, PCB-153, and PCB-180 multiplied by 2.0 (Grandjean et al., 1995). Because of the relevance of dioxin-like effects at increased PCB exposures, the weighted sum of the three main mono-*ortho* substituted congeners PCB-105, PCB-118, and PCB-156 was also calculated using toxicity equivalency factors to obtain the dioxin equivalent concentration PCB_{TEQ} (Van den Berg et al., 1998).

Table 1

Characteristics of the study population with plausible predictors of caries occurrence by tertiles of their maternal milk PCB concentration

Child PCB exposure	Low (<i>n</i> = 37)	Medium (<i>n</i> = 38)	High (<i>n</i> = 39)
Maternal milk PCB concentration, mean (S.D.) [range] (ng/g lipids)	690 (230) [70–1050]	1640 (300) [1060–2180]	4060 (2240) [2200–11,150]
Cord blood mercury concentration, mean (S.D.) [range] (μmol/L)	16.37 (10.87) [2.28–45.79]	31.22 (20.03) [7.23–83.26]	27.56 (17.95) [6.72–82.94]
Cord blood lead concentration, mean (SD) [range] (μmol/L)	0.05 (0.02) [0.01–0.10]	0.06 (0.02) [0.02–0.10]	0.06 (0.03) [0.03–0.2]
Duration of exclusive breast-feeding, mean (S.D.) [range] (month)	3.8 (1.6) [0.0–6.0]	3.5 (1.7) [1.0–6.0]	3.2 (2.4) [0.0–8.0]
Gestational age, mean (S.D.) [range] (week)	39.5 (1.1) [37.0–42.0]	39.6 (1.4) [36.0–42.0]	39.5 (1.3) [37.0–42.0]

Table 2

Multiple regression analysis, with the number of carious surfaces of first permanent molars as dependent variable

Source	<i>B</i>	95% CI	Beta	<i>p</i> -Value
Constant	15.65	–1.97–33.28		0.08
Mercury concentration in cord blood	0.03	0.00–0.05	0.19	0.08
PCB concentration in maternal milk	0.29	0.03–0.56	0.25	0.02
Lead concentration in cord blood	–6.49	–26.42–13.43	–0.07	0.52
Duration of breast-feeding	0.13	–0.14–0.41	0.10	0.34
Gestational age	–0.40	–0.84–0.03	–0.21	0.07

$R^2 = 0.16$.

Dental examinations were conducted under artificial light, using a clinical mirror and a dental probe, with drying of the surface using gauze. For each child we defined caries as the number of decayed, missing, or filled surfaces (DMFS) according to WHO criteria (WHO, 1997). Both cavitated and noncavitated decayed lesions were included. No radiographs were used. Developmental enamel defects on first permanent molars were assessed by the modified FDI index (FDI, 1992).

Data from the ANEMONE project data set provided information on various confounding factors (i.e. parity, duration of breastfeeding, alcohol consumption by the mother, smoking during pregnancy, diabetes, gestational age, mercury and lead exposure) (Grandjean et al., 2001).

All the data were analysed using the SPSS 12.0 statistical software package.

3. Results

Of the 114 children examined, 53.5% had at least one first permanent molar affected with caries. The mean number of decayed and/or filled or extracted first permanent molars per child was 1.36 (± 1.63); the mean number of affected surfaces was 2.23 (± 3.24). The percentage of first permanent molars affected by developmental enamel defects of non-fluoride origin was 16.1. Mean PCB concentration in maternal milk was 2205 (range 70–11,150) ng/g lipids.

Statistically significant positive correlations were observed between the number of carious surfaces of first permanent molar teeth and PCB concentrations in maternal milk (Spearman $r = 0.26$, $p = 0.01$), but not between the number of carious surfaces and milk PCB_{TEQ} (Spearman $r = 0.16$, $p = 0.07$). No association between PCB exposure and developmental defects of enamel was observed.

To assess the influence of potential confounding variables on the results, we utilized standard multiple regression analysis (Table 2). Variables with *p*-values < 0.20 in bivariate analysis were selected for inclusion in a multivariate model, as well as variables that previous studies had suggested were plausible pre-

dictors of caries occurrence. The best model, based on statistical significance for the number of carious surfaces of first permanent molars as the dependent variable, was the model with predictors: mercury levels in umbilical blood, gestational age, lead levels in umbilical blood, duration of breast-feeding, and maternal milk PCB concentrations. Only PCB concentration in maternal milk proved to be statistically significant in the model, even though bivariate results showed there was a positive correlation between both caries and mercury exposure (Spearman $r = 0.23$, $p = 0.02$), and caries and gestational age (Spearman $r = -0.22$, $p = 0.02$). In the model, the positive association with concomitant exposure to methylmercury was borderline ($p < 0.10$), and not much different from PCBs ($p < 0.05$). Gestational age seemed to be “protective” (Table 2). When milk PCB_{TEQ} concentrations were included in separate multivariate linear regression analysis (data not shown), they were not significantly related to caries susceptibility ($p = 0.28$).

4. Discussion

The study demonstrated a dose–response relationship between PCB exposure and dental caries of first permanent molars in Faroese children.

In first permanent molars, hard dental tissues formation begins in utero and is completed at the end of the third year of life (Nancy, 2003). PCB levels in maternal milk were significantly related to caries susceptibility of first permanent molars in both bivariate analysis and the multivariate model (Table 2). However, no association between the duration of breast-feeding and caries susceptibility was found. PCB concentrations in maternal milk reflect the mother’s exposure, and transfer of PCBs from the mother’s body burdens occurs via milk as well as via placenta (Ahlborg et al., 1992). First permanent molars were thus exposed to PCBs not only during the breast-feeding period, at the time of their mineralization, but also earlier in their development. It should also be noted that the duration of breast-feeding was only around 7 months.

Dioxins and PCBs have previously been shown to cause aberrant tooth development (Alaluusua and Lukinmaa, 2006), but these earlier studies have not clarified which PCBs may account for dental defects and caries. The active congeners could well include non-planar and dioxin-like co-planar PCBs. In this study, milk PCB_{TEQ} concentrations reached near-significant correlations in bivariate analysis; however, in multivariate analysis, the relation was not significant.

Some human studies are in line with our results and suggest that PCBs might have cariogenic effect (Hara, 1985; Rogan et al., 1988), but not all studies have found a correlation (Jan and Vrbič, 2000; Wang et al., 2003). In the study in eastern Slovakia (Trnovec et al., 2004), where PCBs from a chemical plant contaminated the surrounding district (Kočan et al., 2001) and very high levels of PCBs were detected in breast milk (Petrik et al., 2001) and serum (Kočan et al., 2004), detrimental effects of PCB exposure on dental development were reported (Jan et al., 2007). However, no associations between caries susceptibility and PCB exposure were observed. One of the possible explanations for this controversy is the methods used to measure the

prevalence of caries. There is a possibility of underreporting because only frank cavitation was recorded, and the outcome measure was not caries lesion on each tooth surface, but on a whole tooth. Another factor to consider is the stage of tooth development at the time of exposure. As teeth are vulnerable to the toxic effects of organochlorines mostly during the early morphogenesis (Miettinen et al., 2002), exposure afterwards might not result in higher caries susceptibility. Also, the PCB congener mixtures were different from those occurring in seafood (Weihe et al., 1996), and foremost, levels of exposure were different. Differences in exposure assessment would additionally hamper comparisons between the prospective study in the Faroe Islands and other studies.

Caries is regarded as an infectious disease, the result of a multifactorial process. There are several possible mechanisms through which PCBs could enhance susceptibility to caries. For example, their effect on adequate salivary flow and structurally sound enamel and composition are clearly important.

As shown by experimental studies in the mouse (Kawasaki et al., 1995), PCB exposure adversely affects the function of the major salivary glands, suggesting that the causal mechanism of PCBs’ cariogenicity could be a PCB-related decrease in salivary flow. A decrease in salivary flow impairs the buffering function of saliva in protecting the tooth against bacterial acids and leads to an increase in the prevalence of caries (Bowen et al., 1988).

PCB cariogenicity could reflect the effect of PCBs on hard dental tissues formation rather than a secondary effect mediated by reduced salivary flow, thereby rendering dental tissues more susceptible to caries. In humans, broken and chipped teeth were reported after PCB/PCDF exposure (Rogan et al., 1988; Guo et al., 1999), and in experimental studies, adverse effects of PCBs on enamel-forming cells have been demonstrated (Hashiguchi et al., 1985; McNulty, 1985).

As caries is an infectious disease, and PCBs have been shown to impair humoral as well as cell-mediated immune response (Levin et al., 2005; Heilmann et al., 2006) that may be another possible mechanism for enhanced caries susceptibility.

This study demonstrated a dose–response relationship between PCB exposure and caries susceptibility of first permanent molars in Faroese children. These findings add to the evidence supporting an association between children’s PCB exposure and caries prevalence. Further evaluation of the biologic mechanism of PCB cariogenicity is needed.

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