Birth Weight and Sex of Children and the Correlation to the Body Burden of PCDDs/PCDFs and PCBs of the Mother

Terttu Vartiainen,[1,2] Jouni J. K. Jaakkola,[3,4] Seppo Saarikoski,[5] and Jouko Tuomisto[1]

[1]Division of Environmental Health, National Public Health Institute, Kuopio, Finland; [2]Department of Environmental Sciences, University of Kuopio, Kuopio, Finland; [3]Department of Environmental Health, Harvard School of Public Health, Boston, MA 02115 USA; [4]Environmental Epidemiology Unit, Department of Public Health, University of Helsinki, Helsinki, Finland; [5]Department of Obstetrics and Gynecology, Kuopio University Hospital, Kuopio, Finland

Polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and polychlorinated biphenyls (PCBs) were analyzed in 167 random human milk samples from urban and rural areas in Finland. Dietary habits and background information on each mother and child were gathered by questionnaire. Body mass indexes (BMI) before pregnancy and delivery in the rural area were 5–10% higher than in the urban area, but fat content of mother's milk was about 10% higher in the urban area. The mean weights of children (± standard deviation) were similar in the rural and urban areas among primiparae, 3,500 ± 597 g and 3,505 ± 454 g, respectively, although dioxin international toxic equivalents (I-TEQs) were significantly higher in the urban area. The mother's level of education did not affect the weight of the child, but concentrations of PCDDs/PCDFs (I-TEQ, 2,3,4,7,8-Cl_5 dibenzofuran, 1,2,3,7,8-Cl_5 dibenzodioxin) and PCBs [sum of PCBs (ΣPCB), PCB-TEQ, and most PCB congeners] increased with advanced education. This is considered to be due to differences in the mother's consumption of fish. The birth weight, especially of boys, slightly decreased with increasing concentrations of I-TEQ, 2,3,4,7,8-Cl_5 dibenzofuran, 1,2,3,7,8-Cl_5 dibenzodioxin, and 2,3,7,8-Cl_4 dibenzodioxin; however, when the analysis was restricted to primiparae, there was no statistically significant correlation between birth weight and the concentrations of PCDDs/PCDFs. No correlation was found between the weight of the child and ΣPCBs, PCB-TEQs, or individual PCB congeners in the whole material or among primiparae, or among boys or girls. The concentrations of PCDDs/PCDFs and ΣPCBs in human milk were modeled for primiparae by weighing fish consumption, age of mother, milk fat content, and BMI before pregnancy. The linear regression resulted in values of $R = 0.67$ and 0.30 for the modeled dioxin I-TEQs in the urban and rural areas, respectively, and the corresponding values for ΣPCBs of $R = 0.60$ and 0.11. The increase of PCDD/PCDF body burden was calculated to be on average 0.58 pg I-TEQ/g milk fat/year in the urban area and 0.39 pg I-TEQ/g milk fat/year in the rural area. *Key words*: age, birth weight, BMI, body mass index, diet, dioxins, human milk, modeling, non-*ortho* PCBs, parity, PCDDs/PCDFs. *Environ Health Perspect* 106:61–66 (1998). [Online 15 January 1998]
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One might think that Finland would represent a low-exposure area with respect to dioxins and polychlorinated biphenyls (PCBs). This country of 5 million inhabitants occupies an area of 338,000 km^2, almost the size of Germany, which houses about 80 million inhabitants. About one-half of the exports derive from forestry, but only about 8% of the population work in forestry and agriculture. Sales of pesticides have decreased during recent years, from a total of 5,469 tons in 1989 down to 1,929 tons (843 tons as active ingredients) in 1993 (*1*). 2,4,5-Trichlorophenoxyacetic acid, which contains dioxins, was withdrawn from the market in 1978. Pulp mills chlorinated their products with chlorine and discharged their wastes into the lakes or air until 1993. Currently only chlorine dioxide or nonchlorine bleaching methods are in use. Chlorine production, as well as some chemical processes that use chlorine, are possible dioxin sources. However, a major domestic source of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans (PCDDs/PCDFs) has been uncovered in Finland: chlorophenols and chlorophenol production. Chlorophenol formulations were used as wood preservatives since the 1930s. They were imported from the United States until 1940 when the production of chlorophenols started in Finland under the trade name Ky-5 (Kymi-Kymmene, Kuusankoski, Finland). The production of Ky-5 continued until 1984; this amounted to 23,400 tons of Ky-5 produced between 1940 and 1984, which was mainly used for the preservation of timber. The use of chlorophenols was ultimately banned in 1988. Ky-5 contained dioxins at approximately 0.87 g/ton as international TCDD toxic equivalents (I-TEQs) and 65 g/ton as total PCDDs/PCDFs (*2*). Hence, the total amount of I-TEQs attributable to Ky-5 is about 20 kg as I-TEQ or 1,500 kg as total PCDDs/PCDFs. PCDFs and especially heptachlorinated furans account for the main part of PCDDs/PCDFs; 95% of I-TEQ and 87% of the total PCDDs/PCDFs were polychlorinated dibenzofurans (*2*).

Only one small municipal incinerator is functioning in Finland in comparison with the hundreds in Central Europe, but the prevailing winds may carry their emissions toward Finland as well. Because 40% of the total SO_2 deposit in Finland comes via the air from Central Europe, we may assume that a major proportion of the total PCDD/PCDF load is also carried by the wind from other parts of Europe.

Food is the main source of PCDDs/PCDFs and PCBs in humans (*3*). In Finland, meat, milk, and dairy products are virtually devoid of PCDDs/PCDFs, but eggs sometimes contain PCDDs/PCDFs because chicken feed may contain marine products (*4*). The Baltic Sea is badly polluted with PCDDs/PCDFs and PCBs, leading to the contamination of Baltic fish (*5*). PCB concentrations in Finnish food are low except for Baltic fish (*6*). In 1993, the total intake of dioxins as I-TEQs in Finland has been estimated to be about 94 pg/day/person (*7*), with the total PCB intake of 1.64 µg/day/person (*6*).

The World Health Organization Regional Office for Europe (WHO/EURO) has coordinated two rounds of follow-up studies on levels of PCDDs, PCDFs, and PCBs in human milk. Fourteen countries took part in the first follow-up study, with Finland among them (*8*). The detailed, congener-specific analytical results have been published recently (*9*). The objectives of the present study were to correlate the birth weight and sex of a child to PCDD/PCDF and PCB concentrations of its mother's milk and to assess the personal and environmental determinants that correlated with the levels of PCDD/PCDFs and PCBs in human milk in two areas in Finland in 1987.

Methods

Sample collection and survey respondents. This study was part of follow-up studies

Address correspondence to T. Vartiainen, Division of Environmental Health, National Public Health Institute, P.O.Box 95, FIN-70701 Kuopio, Finland.
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into levels of PCDDs, PCDFs, and PCBs in human milk coordinated by WHO/EURO. In Finland, we carried out a larger population-based study in two geographical areas: Helsinki, the capital city, and the province of Kuopio (260,000 inhabitants), located approximately 400 km northeast from Helsinki. All consecutive women giving birth were recruited between January and May 1987 from one of the maternity clinics in Helsinki and from the maternity clinic of Kuopio University Hospital. Four weeks after delivery, milk samples were collected according to WHO's guidelines (for 2 weeks and between 10 and 20 ml breast milk/day) (*8*). Written consent was obtained from all mothers. A questionnaire was distributed to the participating mothers after the delivery, including questions on maternal education, age, parity, height and weight before pregnancy and after delivery, duration of residency in their present home region, smoking, diet including use of milk and milk products, fish consumption, details of possible occupational exposures, use of medicines, and possible complications during pregnancy or delivery. Information on newborns' sex, weight, and height was also included in the questions. The study population who collected and returned the milk samples constituted a total of 167 mothers (56% of those who initially indicated that they would participate), 77 (26% of the total number of childbirths) in Helsinki and 90 (30%) in Kuopio. The study population is described in Table 1.

The levels of education of mothers were divided into five classes: A, high school education (9 years or less; n = 4 and 12 among primiparae and all mothers, respectively); B, senior high school or technical school (n = 44 and 86 among primiparae and all mothers, respectively); C, student in university (n = 5 and 8 among primiparae and all mothers, respectively); D, college degree (n = 19 and 38 among primiparae and all mothers, respectively); E, university or professional degree (n = 11 and 22 among primiparae and all mothers, respectively). Mothers also were divided into two groups: university or college level education (C + D + E; n = 35 and 68 among primiparae and all mothers, respectively) and others (A + B; n = 48 and 98 among primiparae and all mothers, respectively).

Determination of PCDDs, PCDFs, and PCBs. About 40–80 ml of each human milk sample, equivalent to 1.4 g fat, was spiked with 100 pg ^{13}C-labeled PCDD and PCDF standards, with 100 pg ^{13}C-labeled non-*ortho* PCB standards, and with 100 pg ^{13}C-labeled PCB standards. Milk fat was extracted with diethyl ether/hexane, and the fat content was determined and PCDDs/PCDFs and PCBs were analyzed by high resolution mass spectrometry as described previously (*9*). The levels of the 17 most toxic PCDDs/PCDFs were expressed in I-TEQ calculated by using the international equivalency factors (*10*). The toxic equivalents used for PCBs were those recommended by

Table 1. Characteristics of the mothers and the weights of children in urban (n = 77) and rural (n = 90) areas of Finland in 1987

Mother/parity	1	2	3	4	5	8	10
Urban area, Helsinki							
Number of mothers	47	22	7	1	0	0	0
Maternal age (years)							
Mean ± SD	26.9 ± 3.6	28.8 ± 3.8	29.4 ± 2.8	28	–	–	–
Range	20–37	21–36	25–34	–	–	–	–
Body mass index before pregnancy (kg/m^2)							
Mean ± SD	21.3 ± 2.35	23.0 ± 3.35	22.4 ± 4.65	23.9	–	–	–
Range	16.4–28.4	19.3–30.9	17.7–30.5	–	–	–	–
Body mass index before delivery (kg/m^2)							
Mean ± SD	26.2 ± 2.90	27.9 ± 3.45	27.8 ± 5.71	28.2	–	–	–
Range	20.1–34.2	21.0–34.7	22.5–37.0	–	–	–	–
Weight of child (g)							
Mean ± SD	3,500 ± 597	3,846 ± 533	3,623 ± 415	3,720	–	–	–
Range	1,350–4,570	3,190–515	2,880–4,140	–	–	–	–
Weight of child by sex (g)							
Mean ± SD (male)	3,460 ± 739	4,395 ± 464	3,518 ± 447	–	–	–	–
Mean ± SD (female)	3,530 ± 423	3,532 ± 231	3,885 ± 75	3,720	–	–	–
Fat content of human milk (%)							
Mean ± SD	3.58 ± 1.05	3.57 ± 1.02	3.92 ± 0.64	4.01	–	–	–
Range	1.24–6.53	2.18–5.71	2.96–5.18	–	–	–	–
Rural area, Kuopio							
Number of mothers	37	34	12	4	1	1	1
Maternal age (years)							
Mean ± SD	25.4 ± 3.39	28.3 ± 4.20	30.5 ± 2.40	30.3 ± 5.02	35	30	41
Range	19–34	19–35	27–36	24–38	–	–	–
Body mass index before pregnancy (kg/m^2)							
Mean ± SD	22.3 ± 3.15	22.3 ± 4.22	23.1 ± 5.44	27.5 ± 5.22	18.8	25.2	21.2
Range	18.1–32.8	17.4–37.2	13.5–34.9	21.2–35.7	–	–	–
Body mass index before delivery (kg/m^2)							
Mean ± SD	27.4 ± 3.66	26.7 ± 4.87	28.6 ± 4.61	31.6 ± 3.25	24.8	25.2	26.5
Range	22.5–38.1	20.3–43.9	21.1–38.6	26.6–35.7	–	–	–
Weight of child (g)							
Mean ± SD	3,505 ± 454	3,707 ± 485	3,726 ± 403	3,900 ± 241	3,740	3,850	4,500
Range	2,450–4,490	2,460–4,800	3,270–4,800	3,590–4,150	–	–	–
Weight of child by sex (g)							
Mean ± SD (male)	3,730 ± 446	3,775 ± 377	3,733 ± 380	3,900 ± 241	3,740	–	4,500
Mean ± SD (female)	3,370 ± 400	3,620 ± 582	3,723 ± 410	–	–	3,850	–
Fat content of human milk (%)							
Mean ± SD	3.30 ± 0.85	2.88 ± 0.82	3.00 ± 0.92	3.99 ± 0.85	2.16	3.05	2.65
Range	2.10–5.45	1.63–4.36	1.57–4.52	2.74–4.85	–	–	–

SD, standard deviation. Numbers in the panel indicate the number of children that the mother had nursed.

Table 2. Dioxin concentrations in human milk as international TCDD toxic equivalents (I–TEQs) and the sum of polychlorinated biphenyls (∑PCB) concentrations and PCB-TEQs in urban and rural areas in Finland in 1987

Mother/parity	1	2	3	4	5	8	10
Urban area, Helsinki							
Number	47	22	7	1	–	–	–
PCDDs/PCDFS (I–TEQ pg/g fat)							
Mean ± SD	26.3 ± 11.8	16.8 ± 5.8	16.2 ± 8.5	4.46	–	–	–
Range	14.7–96.3	6.0–28.8	6.1–33.1	–	–	–	–
∑PCB (ng/g fat)							
Mean ± SD	496 ± 218	385 ± 132	285 ± 197	68.5	–	–	–
Range	173–1,624	196–615	78–715	–	–	–	–
PCBs (TEQ pg/g fat)							
Mean ± SD	37.0 ± 24.8	27.6 ± 11.8	21.5 ± 18.7	4.01	–	–	–
Range	8.86–162	10.1– 60.6	5.01–65.4	–	–	–	–
Rural area, Kuopio							
Number	37	34	12	4	1	1	1
PCDDs/PCDFS (I–TEQ pg/g fat)							
Mean ± SD	20.1 ± 6.5	18.1 ± 6.2	16.5 ± 6.3	15.8 ± 4.39	10.2	3.86	5.42
Range	10.8–37.4	8.0–33.9	6.92–30.9	8.78–20.2	–	–	–
∑PCB (ng/g fat)							
Mean ± SD	396 ± 164	356 ± 209	258 ± 126	332 ± 47.9	180	60.6	169
Range	140–834	159–1,388	85–570	263–398	–	–	–
PCB (TEQs pg/g fat)							
Mean ± SD	26.5 ± 9.90	26.7 ± 14.8	19.4 ± 12.6	22.0 ± 7.38	16.7	3.71	14.1
Range	10.0–50.9	8.70–95.3	7.48–52.4	13.0–31.3	–	–	–

Abbreviations: SD, standard deviation; PCDDs/PCDFs, polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans.

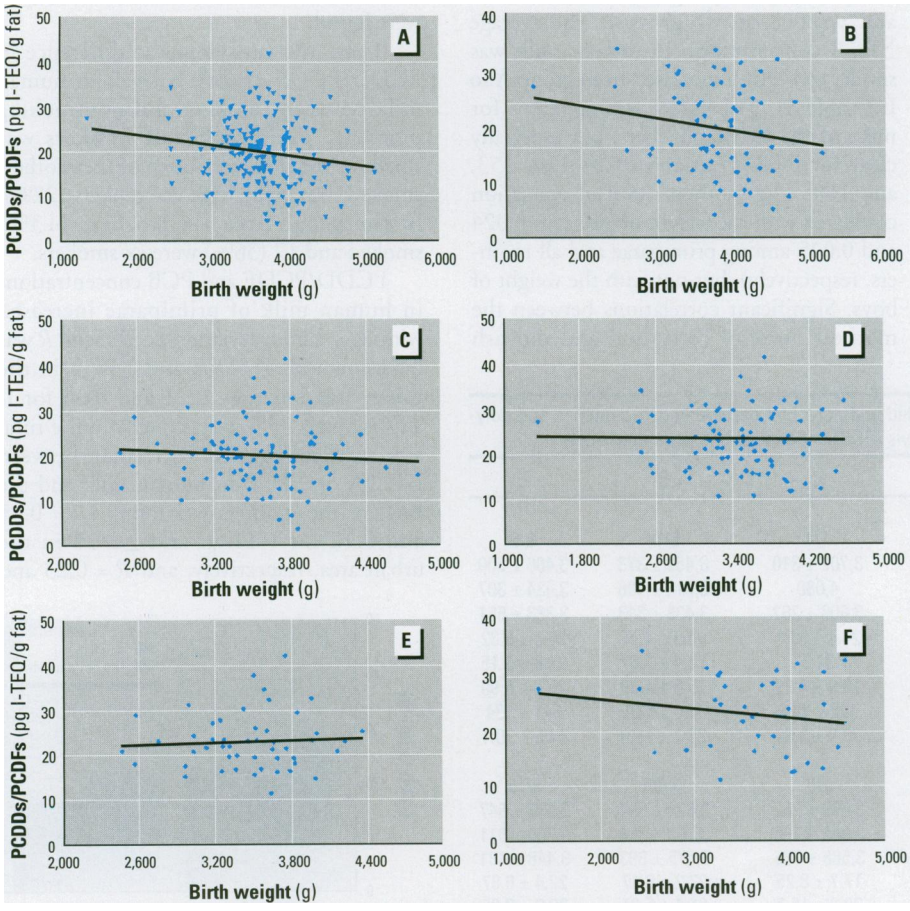

Figure 1. Correlation of newborn children's birth weights with dioxin levels of mother's milk. (A) Among all children (regression intercept = 28.4 and slope = -0.00228). (B) Among all boys (regression intercept = 30.8 and slope = -0.00302). (C) Among all girls (regression intercept = 24.0 and slope = -0.00107). (D) Among all primiparae (regression intercept = 24.3 and slope = -0.00021). (E) Among primiparae girls (regression intercept = 20.3 and slope = 0.00065). (F) Among primiparae boys (regression intercept = 28.7 and slope = -0.00106). Abbreviations: PCDDs/PCDFs, polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans; I-TEQ, international-TCDD toxic equivalents.

WHO, i.e., 0.1 for PCB 126; 0.01 for PCB 169; 0.0005 for PCBs 77, 114, 156, and 157; 0.0001 for PCBs 105, 118, 123, 170, and 189; and 0.00001 for PCB 180 (*11*). This laboratory has participated successfully in international quality control studies for the analysis of PCDDs and PCDFs in cow milk samples organized by the European Community Bureau of Reference (EU/BCR) project in 1993 (*12,13*) and is an accredited testing laboratory (No. T77) in Finland (SFS-EN 4500 and ISO/IEC Guide 25). The scope of accreditation includes PCDDs/PCDFs, PCBs, and non-*ortho* PCBs from milk. Regression analysis was carried out using Lotus 1-2-3 (release 2.01; Lotus, Cambridge, MA). Student's *t*-test, Pearsson's, and analysis of variance (ANOVA) in SPSS (SPSSPC+, Chicago, IL) were used to test the statistical significance of results.

Results

The characteristics of the mothers and the weights of children, all together as well as boys and girls separately, in urban and rural areas of Finland in 1987 are shown in Table 1. Altogether, 47 of 77 mothers from the urban area and 37 of 90 mothers from the rural area were primiparae. A mother in the rural area nursing her tenth child and a mother in the urban area nursing her fourth child were included in this study. The ages of the mothers ranged between 20 and 37 years (both first-time mothers) in the urban area and between 19 (first child) and 41 years (tenth child) in the rural area. Body mass indexes (BMI) before pregnancy and delivery were 5–10% higher in the rural area than in the urban area, but the fat content of milk was about 10% higher in the urban area than in the rural area. The average weight of all children was 3,630 g, the median was 3,625 g, and the standard deviation (SD) was 527 g.

Dioxin I-TEQ and PCB concentrations of the milk are shown in Table 2. The average dioxin and ∑PCB concentrations of all primiparae were 26.3 pg I-TEQ/g and 496 ng/g fat, respectively, in the urban area and 20.1 pg I-TEQ/g and 396 ng/g fat, respectively, in the rural area. The differences were statistically significant ($p<0.001$ for dioxin I-TEQs and $p<0.01$ for ∑PCB). Dioxin (as TEQs) and ∑PCB levels in human milk decreased with the number of children. In the urban area, the mean decrease was on average 20% per one breast-fed child; in the rural area, the decrease was about 10% for both PCDD/PCDF and ∑PCB concentrations.

Correlation of weight and sex of the child with PCDD/PCDF and PCB concentrations in milk. The mean weights of

children were similar in both areas, 3,500 g in primiparae with an increasing trend in multiparae (Table 1). The second child was heavier than the first child, 10% in the urban area and 6% in rural area. Using Pearsson's correlation 2-tailed test, the weight of the child correlated negatively with I-TEQs in mother's milk in the whole group of children (-0.1779; p = 0.022; n = 166; Fig. 1A) and more so in boys (-0.239; p = 0.038; n = 76; Fig. 1B), but not in girls (-0.0806; p = 0.450; n = 90; Fig. 1C). If the analysis was restricted only to primiparae, no correlations were detected in all firstborn children (-0.075; p = 0.502; n = 83; Fig. 1D), either in girls (Fig. 1E) or in boys (-0.179; p = 0.310; n = 34; Fig. 1F). The slight decrease in weight of children did slightly correlate with the concentrations of 2,3,4,7,8-Cl_5 dibenzofuran (-0.159; p = 0.041; n = 166), 1,2,3,7,8-Cl_5 dibenzodioxin (-0.156; p = 0.045), and 2,3,7,8-Cl_4 dibenzodioxin (-0.130; p = 0.095; n = 166). No correlation was found between the weight of children and ΣPCBs in all the children (-0.0953; p = 0.222; n = 166), in boys (-0.0551; p = 0.636, n = 76), in girls (-0.1439; p = 0.176; n = 90), among all primiparae (-0.0003; p = 0.998; n = 83), or in primiparae girls or boys (-0.0096; p = 0.957; n = 34). There was also no correlation between the weight of the child and PCB-TEQs (-0.0229; p = 0.769; n = 166) or individual PCB congeners.

Influence of education of mother on the weight of newborns and on PCDD/PCDF and PCB concentrations in milk. The education of the mother had no effect on the weight of the children either among primiparae (F = 0.308 and p = 0.872 in the analysis of variance in five groups and F = 0.099 and p = 0.754 in two groups) or among all mothers (F = 0.084 and p = 0.987 in five groups and F = 0.099 and p = 0.754 in two groups). Also, no effect was found on the weight of the child when boys and girls were analyzed separately (Table 3). However, a highly significant effect was detected with respect to I-TEQ in primiparae (F = 3.63 and p = 0.009 in five groups and F = 11.6 and p = 0.001 in two groups) and in all mothers (F = 3.52 and p = 0.009 in five groups and F = 9.53 and p = 0.002 in two groups). The average dioxin and PCB concentration in human milk increased with the education of the mothers from group A to E (Table 3). This correlation was particularly clear with I-TEQ, 2,3,4,7,8-Cl_5 dibenzofuran, 1,2,3,7,8-Cl_5 dibenzodioxin, and octochloro dibenzo-p-dioxin (OCDD) congeners, and even more significant for ΣPCB in primiparae (F = 4.69 and p = 0.002 in five groups and F = 14.99 and p<0.001 in two groups) and with all mothers (F = 6.14 and p<0.001 in five groups and F = 15.3 and p<0.001 in two groups). The average ΣPCB concentration in human milk was similar to I-TEQ, increased from group A to E (Table 3). This effect was apparent for most of the PCB congeners, but especially clear for PCB-TEQ and PCBs 126, 153, and 169. The mothers' level of education correlated with the weight of girls (p = 0.024 and 0.025 among primiparae and all mothers, respectively), but not with the weight of boys. Significant correlations between the mothers' level of education and the fish consumption and BMI before delivery were also found.

Effect of fish consumption, smoking habits, age, and body mass index of mother on PCDD/PCDF and PCB concentrations in human milk. Fish consumption was categorized into five classes: more than once a week (I; 2.6% and 1% of mothers in urban and rural areas, respectively); once a week (II; 38% and 38%); once in 2 weeks (III; 36% and 32%); once or less than once a month (IV; 21% and 24%); and never (V; 2.6% and 2.2%). Primiparae who ate fish (classes I, II, and III) in the rural area showed significantly higher concentrations of PCDD/ PCDFs than primiparae who ate little or no fish (classes IV and V; p<0.01; Fig. 2). In the urban area, higher I-TEQs were found in primiparae who ate fish than in those who did not eat fish, but the difference was not statistically significant (Fig. 2). Statistically nonsignificantly higher ΣPCB concentrations were found among primiparae in the urban area who ate fish than in those primiparae who did not regularly consume fish; in the rural area, no differences were found.

There was no systematic difference in PCDD/PCDF or ΣPCB levels in human milk between smoking and nonsmoking mothers. The number of smokers was small: in the rural area none of the mothers smoked, but eight were ex-smokers (22%), in the urban area six mothers (13%) smoked and 17 (36%) were ex-smokers.

PCDD/PCDF and PCB concentrations in human milk of primiparae increased with age. The correlation coefficient R was 0.51 for both I-TEQs and ΣPCB in the urban area but only 0.21 and 0.06 for I-TEQs and ΣPCB, respectively, in the rural area. A slight negative correlation between I-TEQs or ΣPCB in human milk and the BMI of the mothers was found (R = 0.05 and 0.12 for I-TEQs and ΣPCB in the urban area, respectively, and R = 0.23 and

Table 3. Effect of education of mother on weight of child and polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans and polychlorinated biphenyls (PCB) concentrations in mother's milk.

Mother/education	A[a]	B	C	D	E
Primiparae					
Number boys/girls	1/3	22/22	1/4	5/14	5/6
Weight of child (g)	3,428 ± 428	3,523 ± 646	3,702 ± 310	3,459 ± 373	3,406 ± 500
Boys	4,030	3,556 ± 802	4,080	3,518 ± 486	3,434 ± 307
Girls	3,227 ± 181	3,490 ± 459	3,608 ± 262	3,438 ± 343	3,383 ± 651
I–TEQ (pg/g fat)	18.7 ± 4.95	20.9 ± 6.92	21.4 ± 6.81	25.9 ± 4.41	26.3 ± 5.32
Boys	12.1	21.5 ± 7.36	31.7	26.4 ± 3.07	25.8 ± 5.15
Girls	20.9 ± 2.71	20.4 ± 6.56	18.9 ± 4.29	25.8 ± 4.89	26.7 ± 5.90
ΣPCB (ng/g fat)	339 ± 109	389 ± 160	405 ± 74.9	520 ± 130	541 ± 134
PCB–TEQ (pg/g fat)	23.0 ± 7.30	26.0 ± 11.4	28.9 ± 3.94	36.1 ± 15.0	44.5 ± 20.1
All mothers					
Number boys/girls	5/7	46/40	2/6	14/24	9/13
Weight of child (g)	3,638 ± 481	3,641 ± 600	3,676 ± 262	3,624 ± 394	3,576 ± 547
Boys	4,022 ± 335	3,709 ± 682	3,940 ± 198	3,709 ± 394	3,760 ± 611
Girls	3,360 ± 372	3,563 ± 488	3,588 ± 226	3,575 ± 393	3,448 ± 481
I–TEQ (pg/g fat)	16.0 ± 4.66	18.6 ± 7.46	17.7 ± 8.25	22.2 ± 6.47	22.4 ± 6.87
Boys	14.8 ± 4.43	18.5 ± 8.05	20.2 ± 16.2	21.4 ± 5.31	20.9 ± 8.05
Girls	16.8 ± 5.00	18.7 ± 6.81	16.9 ± 6.29	22.6 ± 7.14	23.5 ± 6.09
ΣPCB (ng/g fat)	305 ± 115	346 ± 159	327 ± 136	432 ± 149	516 ± 249
PCB–TEQ (pg/g fat)	24.8 ± 11.8	24.3 ± 12.6	22.3 ± 10.3	30.2 ± 13.2	39.4 ± 21.4

Abbreviations: I-TEQ, international TCDD toxic equivalents; ΣPCBs, sum of PCBs. Values shown are mean ± standard deviation.

[a]Letters indicate the mother's level of education; A = high school education or less, B = senior high school or technical school, C = student in university, D = college degree, E = university or professional degree.

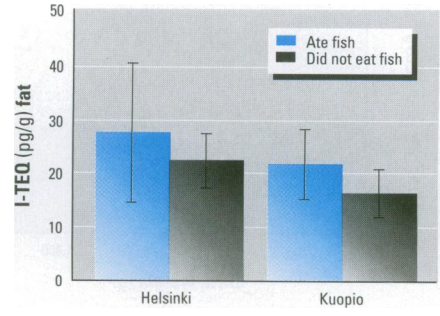

Figure 2. Effect of fish consumption on the levels of polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans in human milk in the urban (Helsinki) and rural (Kuopio) areas of Finland. Only primiparae are included. I-TEQ, international TCDD toxic equivalents.

0.20 for I-TEQs and ∑PCB in the rural area, respectively).

Modeling of PCDD/PCDF and PCB concentrations in human milk. The dioxin and furan I-TEQs were modeled by an equation where slight effects, such as fat content of milk and BMI, in addition to the stronger effects such as age of the mother and use of fish, were taken into account. The model was used only for primiparae. The equation is as follows:

$$\text{Modeled I-TEQ for PCDD/PCDF} = k_1/\text{Fat} \times (A\text{-}19) \times F_{\text{fish}}/\text{BMI} + k_2$$

where k_1 = constant (80 and 135 for I-TEQs for urban and rural areas, respectively); k_2 = constant [I-TEQ-concentration of a 19-year-old mother (I-TEQs of 13 for urban and 7 for rural areas, respectively)]; Fat = fat content of human milk (%); A = age of mother (years); F_{fish} = 0.1 for mothers who never eat fish, 0.25 for mothers who eat fish less than once in 2 weeks, 1 for mothers who eat fish once in 2 weeks, 2 for mothers who eat fish once a week, and 4 for mothers who eat fish more frequently than once a week; and BMI = body mass index before pregnancy [weight (kg)/height^2 (m)].

The linear regression resulted in a correlation between modeled and measured I-TEQs in Helsinki (R = 0.67) and in Kuopio (R = 0.30), and for both together (R = 0.60). After a mother with exceptionally high I-TEQ (96 pg/g fat; 37 years old; F_{fish} = 4) was excluded, R decreased to 0.60 in Helsinki (Fig. 3). The increase of PCDD/ PCDF body burden was calculated to be on average 0.58 pg I-TEQ/g milk fat/year in the urban area and 0.39 pg I-TEQ/g milk fat/year in the rural area. Adding the education of mother to the model slightly worsened the model.

The same model could be used for modeling PCB concentrations of human milk. The linear regressions obtained for ∑PCB were R = 0.60 in Helsinki and R = 0.11 in Kuopio; for both together, R = 0.42. Adding smoking habits to the model did not alter the outcome.

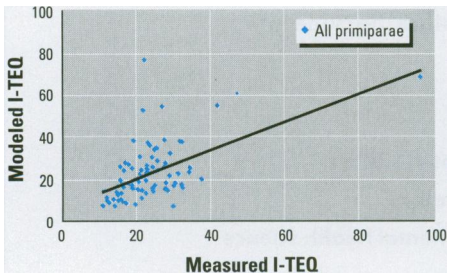

Figure 3. Correlation between measured and modeled polychlorinated dibenzo-*p*-dioxin and polychlorinated dibenzofuran concentrations in human milk. Only primiparae from Helsinki were included. I-TEQ, international TCDD toxic equivalents. Regression intercept = 6.34 and slope = 0.765.

Discussion

The levels of dioxins and furans have been analyzed in several countries under the auspices of WHO/EURO. WHO organized the first sampling of human milk samples in 1986–1987, and Finland was one of several participating countries (*8*). Due to the high costs of analyses, only two pooled samples were analyzed; in these, only PCDDs/PCDFs were analyzed in Finland in 1987, but milk samples were collected using a population-based sampling frame that allowed generalization of the results. Fat from the milk samples was extracted into hexane soon after the collection of the samples, and these extracts were analyzed after the quality assurance of the methods used to analyze PCDDs/PCDFs and individual PCB congeners. The mothers also completed extensive questionnaires. The detailed, congener-specific analytical results have been published separately (*9*); the present study attempted to model PCDD/PCDF and PCB concentrations on the basis of the individual dietary and living habits and aimed to determine if an elevated concentration of PCDDs/PCDFs or PCBs in mother's milk and in the body of the mother could influence the birth weight or sex of the newborn baby.

Dioxins and furans induce a number of serious effects in experimental animals (*14*). Humans have been thought to be less sensitive than other animals, but there is little direct information for such a claim. Rylander et al. (*15*) studied infants born to fishermen's wives on the eastern Swedish coast of the Baltic Sea and on the western Swedish coast of the North Sea in a cohort study and reported an increased risk of low birth weight without any dose–response relationship. The effect was more conspicuous for the boys [odds ratio (OR) = 2.1] than for the girls (OR = 1.1). The exposure estimate was based simply on interview only. In a study in Michigan (*16*), a lower birth weight was reported to be in association with higher fish (and PCB) intake, although this result is not generally accepted and severe criticisms have been raised (*17–21*). In contrast, in North Carolina, no such effect was observed (*22*). In our study, the mean weights of children increased with the numbers of children and the I-TEQs decreased. However, first-born infants usually weigh less than second- or third-born infants, a phenomenon that was recognized long before PCDDs/PCDFs were released into the environment (*23*). When one wishes to study the PCDD/PCDF concentrations in human milk, controlling for parity is essential, especially in Nordic countries where breast-feeding may last several months, resulting in a decrease of PCDD/ PCDF body concentrations (*24–28*). This decrease was clearly apparent in this study. Despite the fact that the average PCDD/ PCDF concentrations of human milk among primiparae in Helsinki were 33% higher than in Kuopio, the average weights of children were equal. Also no correlations were found between the weight of the newborn and the dioxin concentrations of primiparae mothers. Hence, the present results do not confirm the theory proposed by Rylander et al. (*15*). However, the power of the present study is not sufficiently great to completely rule out the existence of some relationship. It is possible that the congeners 2,3,4,7,8-Cl_5 dibenzofuran, 1,2,3,7,8-Cl_5 dibenzodioxin, and 2,3,7,8,-Cl_4 dibenzodioxin might correlate with the weight in children. It is somewhat surprising that the mother's level of education had no effect on the weight of child. The health care for Finnish mothers is extremely well organized and is free of charge throughout the nation. On the other hand, a linear relationship was detected between dioxin and PCB concentrations in mother's milk and the mother's level of education. PCB concentrations in mother's milk correlated even better than dioxins or furans with the mother's educational degree. One explanation is fish consumption in Finland: the better educated the mother, the more likely she is to eat fish. The mother's education positively correlated in this study with fish consumption and negatively with BMIs.

Because analyses of dioxin are difficult and expensive, an approximate model for PCDD/PCDF body burden would be very useful both for purposes of control as well as for epidemiological studies. It is possible to calculate the daily intake of PCDDs/PCDFs from food if levels and amounts of different food items are known. This has been performed in many countries, and the intake values vary between 49.5 pg/day in Norway (*29*) to 18–192 pg/day in the United States (*30*). However, other factors also influence the concentrations of dioxins in humans, e.g., age of the person. In our study, the most important factors affecting the model of PCDDs/PCDFs in human milk were the frequency of fish consumption and the age of the mother; minor factors were BMI and fat concentration of human milk. The model would probably have been better if the species of fish had also been determined along with the frequency of fish consumption. The concentrations of PCDDs/PCDFs in different fish species are well known in Finland; mature Baltic fish contains high levels of PCDDs/PCDFs and lake fish have low

levels; fish from the Atlantic Ocean are almost devoid of PCDD/PCDFs as are cultivated fish (*5*). This is a reasonable explanation for the better fit of the model in Helsinki than in Kuopio because in Kuopio mainly lake fish with low levels of PCDDs/PCDFs are used. The model also revealed that the I-TEQ concentrations of 19-year-old primiparae mothers were almost the same in urban and rural areas, 9.4 and 9.9 pg/g fat, respectively. Addition of the education of the mother to the model did not improve the fit, probably because fish consumption and BMI were already included. The model developed in this study to evaluate the concentrations of PCDDs/ PCDFs and PCBs in human milk is valid only for primiparae. For second children, we should have known at least the duration of breast feeding of the previous children and the time period between the first and subsequent children. Beck et al. (*31*) calculated the decrease of PCDDs/PCDFs during a 12-week breast-feeding period to be 15–25%. With respect to the dependence on the age of the mothers, they found the increase of the PCDD/PCDF body burden to be 0.71 pg I-TEQ/g fat/year. In our study, the increase was 0.58 pg I-TEQ/g fat/year in the urban area and 0.39 pg I-TEQ/g milk fat/year in the rural area. Beck et al. (*31*) did not find any dependence of PCDD/PCDF levels on BMI or smoking, but we did detect a slight negative correlation with BMI.

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