PCDD/PCDF Indoor Exposure in Day-Care Centers and PCDD/PCDF Blood Concentrations of Female Employees

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We determined blood concentrations of polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) in 41 female employees with previous exposure to pentachlorophenol-based wood preservatives from 10 day-care centers in the Hamburg, Germany, area. We compared the blood concentrations with estimated age-dependent reference values and analyzed the correlation between PCDD/PCDF indoor air exposure and blood concentrations. The analyses based on the PCDD congeners 1,2,3,4,7,8-, 1,2,3,6,7,8- and 1,2,3,7,8,9-hexaCDD (hexaCDD), 1,2,3,4,6,7,8-heptaCDD (heptaCDD), octaCDD, and the 2,3,7,8-tetrachlorodibenzo-p-dioxin toxicity equivalents calculated according to the international NATO-CCMS model (I-TEQ). In comparison to the estimated reference values, the blood concentrations of hexaCDD and I-TEQ spread around the mean estimate. Data for octaCDD scattered in some cases distinctly above the upper confidence limit. Reference values for heptaCDD could not be estimated. The correlation between PCDD/PCDF indoor air exposure and PCDD/PCDF blood concentrations was examined by linear multiple regression analysis considering different exposure variables and taking confounders into account. Analyses were carried out with the total study group and with a restricted subgroup. Associations were shown between the PCDD/PCDF indoor air concentrations and blood concentrations for heptaCDD and for the I-TEQ, whereas hexaCDD showed no association. OctaCDD showed a negative association in the total study group and no association in the subgroup analysis. In summary, the analyses showed no clear association between PCDD/PCDF indoor air exposure in day-care centers and PCDD/PCDF blood levels of female employees previously exposed to wood preservatives. By contrast, the results consistently indicated a positive association between PCDD/PCDF blood concentrations and exposure to wood preservatives in private homes. — Environ Health Perspect 106(Suppl 2):707–714 (1998).

http://ehpnet1.niehs.nih.gov/docs/1998/Suppl-2707-714manikowsky/abstract.html

Key words: polychlorinated dibenzo-p-dioxins, PCDD, polychlorinated dibenzofurans, PCDF, pentachlorophenol, PCP, blood, indoor air, exposure assessment, wood preservatives

Objectives

In the 1960s and 1970s paneling and wooden building materials in private homes and public buildings in Germany were frequently treated with pentachlorophenol (PCP)-based wood preservatives. PCP was usually contaminated by polychlorinated dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs). The major contaminants of higher chlorinated congeners such as hexachlorodibenzo-p-dioxins, heptachlorodibenzo-p-dioxins, and octachlorodibenzo-p-dioxin (octaCDD) were found in indoor air of several day-care centers treated with PCP-based wood preservatives (1,2).

Between 1987 and 1990 the Hamburg State Department of Labor, Health, and Social Affairs carried out the Hamburger Kindergartenstudie to investigate health effects on children exposed to PCP-based wood preservatives (3). At the same time a second study dealt with employees working in the day-care centers (4). Both studies had some shortcomings concerning their exposure assessment because methods of determination of low-dose PCDD/PCDF blood concentrations were not available in 1986. In 1993 the parents of the exposed children demanded a follow-up study. To evaluate the feasibility of such a study, the relationship between exposure to PCDD/PCDF in indoor air and PCDD/PCDF blood levels was examined in the investigation reported here.

The potential impact of exposure was assessed by studying the correlation between PCDD/PCDF indoor air concentrations of 10 day-care centers and the PCDD/PCDF blood concentrations of female employees working in those day-care centers. For this purpose we analyzed blood samples collected in 1987 from female employees with previous exposure to PCP-based wood preservatives. The analysis was based on the findings of the congeners 1,2,3,4,7,8-, 1,2,3,6,7,8- and 1,2,3,7,8,9-hexaCDD, 1,2,3,4,6,7,8-heptaCDD, and octaCDD in indoor air (1). Because the health risk assessment of PCDD/PCDFs usually referred to all 2,3,7,8-substituted congeners, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) toxicity equivalents calculated as international toxicity equivalents calculated according to the international NATO–CCMS model (I-TEQ) were also used.

Materials and Methods

Study Group and Blood Samples

A total of 41 female employees working between 1970 and 1987 in 10 day-care centers in the Hamburg area participated in the study. Blood had been sampled in 1987 by the attending physician in expectation of a future analysis. About 60 to 80
ml blood was drawn and kept frozen below −20°C until analysis in 1996. Informed consent was obtained from all participants.

The determination of PCDDs and PCDFs in blood was carried out by ERGO Forschungsgesellschaft (Hamburg, Germany). The analytical method used for the blood samples was nearly identical to that used for the successful participation in World Health Organization interlaboratory validation studies (rounds II and III) on human blood and is described elsewhere (5–7). The blood concentrations of hexaCDD, octaCDD, and 1-TEQ were compared to age-dependent reference values we assessed before chemical analyses of the blood samples were provided by ERGO Forschungsgesellschaft (8). The assessment of the reference values was performed by regression estimation and extrapolation of background data from Germany in 1994 (9).

The attending physician collected information on age, weight, height, nursing, smoking, kind of work in the day-care centers, time of exposure, time after exposure, and exposure to wood preservatives in private homes for the 41 female employees. Most of the information is summarized in Tables 1 and 2. The average working time of the employees in the day-care centers was 9 years. Most (n = 32) of the employees worked the whole time in one day-care center with the same daily working hours. Some of the employees (n = 4) changed working hours over their time of employment; some of them (n = 4) changed day-care centers. The average daily working time amounted to 7 hr (median) (4 hr, 14 employees; > 4 to < 8 hr, 9 employees; 8 hr, 18 employees) (Table 1).

Time after exposure (Table 1) ranged from less than 1 week up to 10 years (< 4 weeks, 12 employees; 4 weeks–1 year, 22 employees; > 1 year, 7 employees). The average time after exposure amounted to 9 weeks (median). In two cases time after exposure was more than 7 years. Because of the long half-life of the PCDD/PCDF congeners used in the statistical analysis, the decline after exposure could be disregarded. Possible bias resulting from the two cases with time after exposure of more than 7 years has been checked and found to be irrelevant.

Three of the employees smoked at the time of blood sampling and 14 were ex-smokers (Table 2). Nine of the 41 employees were additionally exposed to wood preservatives at home (yes or no from subject’s information). Nine of the 41 employees worked as cleaning staff and were considered because they may have had a more intensive exposure to PCDD/PCDF-contaminated dust.

### Table 1. Age, body-mass index, nursing, exposure time, and time after exposure of 41 female employees.

| Age in 1987 | Min | Max | Median | Mean | SD | Cases, no. |
|-------------|-----|-----|--------|------|----|------------|
| 20°C        | 23  | 55  | 40     | 40   | 8  | 41         |
| Body-mass index in 1987 | 18  | 34  | 24     | 24   | 3  | 41         |
| Duration of nursing period, weeks | 1   | 60  | 16     | 17   | 12 | 27*        |
| Years working in day-care centers | 0.3 | 19  | 9      | 9    | 5  | 41         |
| (one or two centers) |     |     |        |      |    |            |
| Average daily working time, hr | 4   | 8   | 7      | 6    | 2  | 41         |
| Time after exposure, weeks | 0   | 546 | 9      | 52   | 119| 41         |

Abbreviations: Max, maximum; Min, minimum; SD, standard deviation. *21 women nursed before exposure time (four women nursed during exposure, three after).

### Table 2. Smoking habits of female day-care center employees.

| Cigarettes/day | ≤10 | 11 ≤20 | >20 |
|----------------|-----|--------|-----|
| Smoker (n = 3)* | 2   | –      | –   |
| Ex-smoker (n = 14)* | 6   | 7     | 1   |
| Nonsmoker (n = 24) | –   | –     | –   |

*Missing information for one case. Smoking at time of blood sampling. Smoking before time of blood sampling.

PCDD/PCDF Indoor Air Data

PCDD/PCDF indoor air concentrations in the day-care centers were measured in 1986 and 1987 by ERGO Forschungsgesellschaft (seven centers and eight measurements) and by the Institut für Hygiene an der Ruhr-Universität Bochum (two centers) using different methods. At that time there was no consensus about the best analytical method for determining PCDD/PCDF indoor concentrations. The actual German guideline VDI 4300-2 (10) for the measurement of PCDD/PCDF had not yet become available. ERGO Forschungsgesellschaft performed a long-term measurement (3 days at the end of the week with a combination of polyurethane-foam/glass fiber filter); the Institut für Hygiene carried out a short-term measurement with a high-volume sampler (impregnated glass fiber filter). For one of the 10 day-care centers PCDD/PCDF indoor air measurements were not available; therefore, the PCDD/PCDF indoor air concentration (1-TEQ) was approximated based on the PCP concentration measured in wooden building materials in the day-care center (11). This affects two employees working in this day-care center the whole time and three employees working in this center for a time.

Table 3 shows the PCDD/PCDF indoor air concentration (picograms/standard (std) meter³) and information about the indoor temperature and humidity of the day-care centers. The results of the measurements for the PCDD congeners and the 1-TEQ are in a wide range. The largest range existed for octaCDD. The PCDD/PCDF indoor air concentration given as 1-TEQ ranged between 0.01 and 1.74 pg/std m³, with an average of 0.57 pg/std m³. Thus a part of the results showed values above the average outdoor air pollution in Hamburg 1985 and 1986 (0.005–0.2 pg/m³) (12) and above the 1986 preliminary action level of 0.5 pg/m³ TCDD toxicity equivalents calculated according to the German Federal Health Office (Berlin, Germany) model (TEQ–FHO) the Hamburg State Department of Health (J), but below the guidance value of 5 pg/m³ 1-TEQ suggested 1992 by the German Federal Health Office (13).

### Table 3. PCDD/PCDF indoor air concentration (pg/std m³) and indoor air temperature and humidity in 10 day-care centers.

| Min | Max | Median | Mean | SD | Cases, no. |
|-----|-----|--------|------|----|------------|
| HexaCDD | 0.05 | 2.90 | 0.69 | 0.87 | 0.83 | 10 |
| HeptaCDD | 0.53 | 57.00 | 16.49 | 20.31 | 19.89 | 10 |
| OctaCDD | 0.52 | 94.60 | 13.80 | 32.25 | 34.75 | 9 |
| 1-TEQ | 0.01 | 1.74 | 0.42 | 0.57 | 0.54 | 11 |
| Indoor air humidity, % | 15.00 | 49.00 | 27.00 | 28.00 | 11.00 | 8 |
| Indoor air temperature, °C | 21.20 | 28.20 | 23.00 | 23.90 | 3.20 | 9 |

*Original data, pg/m³, were converted into pg/std m³ if necessary (pg/std m³ = 1.1 pg/m³). One day-care center was considered with two measurements (different parts of the day-care center). For one day-care center 1-TEQ was assessed roughly by PCF wood concentration.
PCDD/PCDF indoor air concentrations are influenced by the room temperature, indoor air dust concentration, and indoor ventilation (14, 15). We controlled for the influence of temperature and humidity by calculating standardized data for the original PCDD/PCDF indoor air concentration (TEQ=F-HO) of the day-care centers based on standard temperature of 20°C and indoor air humidity of 50% derived from Selkena et al. (15) by regression analysis. We compared these standardized data with the PCDD/PCDF concentrations of the day-care centers (expressed as TEQ=F-HO).

The impact of the ventilation could not be evaluated because only data without ventilation were available and the measurements were conducted during weekends, when the centers were not in use. The house dust concentration was not controlled.

Exposure Assessment

Difficulties in exposure assessment for the female employees arose from activity in different day-care centers over the time and varying working times in the day-care centers. To take these circumstances into account we used different exposure variables for the statistical analyses described in Table 4 (models 1–6). For analyses based on the total study group we calculated an exposure index (model 1) that included the total of exposure days (model 2), the average of daily working time (model 3), and the measured indoor air PCDD/PCDF concentration related to all day-care centers where the employees had worked. The fourth exposure variable was the weighted indoor air concentration (model 4) related to all day-care centers where the employees had worked (weighted by time of exposure because of the different work places of the female employees). For a subgroup analysis with a modified regression model, unweighted indoor air concentrations were used (model 5) and additionally divided into three categories (model 6).

Statistical Analysis

The bivariate associations between the PCDD/PCDF blood levels and some potential confounding factors (age, body-mass index, smoking, duration of nursing period, kind of work, time after exposure, and exposure to wood preservatives in private homes) were checked. We expected a positive association between PCDD/PCDF blood concentrations and age (16, 17) and a weak negative correlation with body-mass index (18). According to the decreasing effect of nursing on PCDD/PCDF body burden (19), a negative correlation between duration of nursing period and PCDD/PCDF concentrations in blood fat was expected. For smoking we assumed a weak positive association (20) with PCDD/PCDF blood concentrations.

Correlations between dioxin indoor air exposure and PCDD/PCDF blood levels were examined by multiple regression analysis. According to the results from the bivariate analyses we controlled for age, body-mass index, duration of nursing period, and exposure to wood preservatives in private homes (0/1-variable). Because of the log-normal distribution of the PCDD/PCDF blood levels, we used the natural logarithm of these data in the multiple regression analysis. Collinearity was checked. The relationship between the independent variables should not be correlated above r = 0.40. Statistical analyses were performed with the statistical program SPSS Windows (SPSS, Inc., Chicago, IL).

We used six regression models according to the exposure assessment (Table 4, models 1–6). In the preliminary analysis the total study group was considered in the regression (models 1–4). Further examinations should reduce a possible bias by differences in the analytical methods to determine the indoor air concentration of PCDD/PCDFs, a possible bias by individual measurement errors, and a possible bias by exposure in different day-care centers. Therefore subgroup analyses of the present material with a modified regression model were conducted. In this subgroup analysis, the study group was restricted by the method of exposure measurement from ERGO Forschungsgesellschaft because the analytical method used from 1986 to 1987 followed more closely the German guideline VDI 4300-2 (10) established in 1995.

PCDD/PCDF indoor air concentrations were used unweighted by time of exposure; cases with multiple exposure in different day-care centers were excluded (model 5). Furthermore, one outlier with a long nursing period was excluded. The subgroup analysis based on the mentioned restrictions was also performed with categorized exposure data (low, medium, high) (Table 4, model 6).

Results

PCDD/PCDF Blood Levels

Table 5 illustrates the PCDD/PCDF blood concentrations (picograms/gram blood fat) of the study group for hexaCDD, octaCDD, and the I-TEQ (descriptive analysis). Because of the age dependence of PCDD/PCDF blood concentrations, the descriptive statistics gave only a rough estimation. OctaCDD showed a noticeably wide range. A scatterplot of the PCDD/PCDF blood concentrations (picograms/gram blood-fat) for the different variables (age, smoking, duration of nursing period, kind of work, time after exposure, and exposure to wood preservatives in private homes) was created.

Table 4. Exposure assessment for the indoor air concentration in 10 day-care centers (center 1 and center 2)*, (six models).

| Model no. | Exposure assessment                                      | Calculation                                                                 |
|----------|----------------------------------------------------------|------------------------------------------------------------------------------|
| 1        | Exposure index                                           | Indoor air concentration center 1 × exposure-hr³ center 1  + indoor air concentration center 2 × exposure-hr 2 |
| 2        | Total days of exposure                                    | Days of exposure center 1 + days of exposure center 2                        |
| 3        | Average daily exposure time                              | (Exposure-hr center 1 + exposure-hr center 2) / (days of exposure center 1 + days of exposure center 2) |
| 4        | Indoor air concentration, weighted                       | (Indoor air concentration center 1 × exposure-hr center 1 + indoor air concentration center 2 × exposure-hr center 2) / (exposure-hr center 1 + exposure-hr center 2) |
| 5        | Indoor air concentration, unweighted                     | Indoor air concentration, unweighted center 1 ³ |
| 6        | Categorized indoor air concentration, unweighted         | Three categories of indoor air concentration center 1, unweighted³ (low, medium, high) |

*Center 2 refers to a different daily working time in a second time period in center 1 or activity in a different day-care center in a second time period. Exposure-hr at center = days of exposure at the center × daily hr at the center.

Subgroup analysis: employees with exposure in a second day-care center were excluded.

Table 5. PCDD/PCDF blood concentrations (pg/g blood fat).*

|                | Min   | Max    | Median | Mean  | SD    | Cases, no. |
|----------------|-------|--------|--------|-------|-------|------------|
| HexaCDD        | 38.80 | 138.87 | 82.88  | 85.64 | 21.27 | 41         |
| HeptaCDD       | 44.58 | 282.49 | 130.20 | 133.21| 56.85 | 41         |
| OctaCDD        | 366.94| 3121.50| 914.91 | 1040.76| 539.43| 41         |
| I-TEQ          | 15.38 | 65.22  | 37.59  | 38.51 | 11.17 | 41         |

*Study group (blood sampled in 1987 and analyzed in 1996).
blood fat) along with the estimated age-dependent reference values (estimated for 1987) is shown in Figure 1. Cases with exposure to wood preservatives in private homes are marked as rhombus. The estimated reference values are demonstrated in two lines (lower line, mean estimate; upper line, upper confidence limit, 95%, one tailed). Estimation of the 1987 reference values for hepta CDD was not possible using the available data. The PCDD/PCDF blood concentration, given as I-TEQ, spread around the mean estimate, and no point was observed above the confidence limit. The blood levels of hexaCDD ranged between the mean estimate and the confidence limit; two points above the confidence limit were observed. Blood data for octaCDD scattered in some cases distinctly above the confidence limit. Cases with exposure to wood preservatives in private homes often showed elevated PCDD/PCDF blood concentrations.

**Bivariate Regression**

Figure 2 illustrates the PCDD/PCDF blood levels (picograms/gram blood fat) plotted against age stratified by exposure to wood preservatives in private homes. Except for octaCDD, the determined PCDD/PCDF blood levels were clearly correlated with age. For octaCDD (the group with no exposure to wood preservatives in private homes) the correlation was weaker than for the other congeners. The cases with exposure to wood preservatives in private homes showed a correlation with age for octaCDD contrary to the expectations (Figure 2). Between body-mass index and PCDD/PCDF blood levels, no consistent correlations could be found. PCDD/PCDF blood concentrations of the cleaning staff were not elevated compared with the other employees.

No association was shown between smoking (number of cigarettes/day) and octaCDD blood concentrations. The blood levels for hexaCDD, heptaCDD, and I-TEQ were—contrary to hypothesis—negatively associated with smoking (number of cigarettes/day). Further examinations showed a negative correlation between age and smoking and confirmed a false correlation between smoking and PCDD/PCDF blood levels; smoking (number of cigarettes/day) decreased with age.

Figure 3 shows the PCDD/PCDF blood levels and the duration of nursing period for women who nursed \( n = 27 \) for the PCDD congeners and the I-TEQ with the line of a bivariate regression. One case has been identified as an outlier (difference between individual nursing period and mean nursing period amounted to 3.6 standard deviations) and has been excluded from regression. The bivariate regression excluding the outlier showed a significant negative correlation for hexaCDD (Pearson \( r = 0.42, p = 0.032 \)) and I-TEQ (Pearson \( r = -0.46, p = 0.016 \)). For heptaCDD a weak negative and non-significant correlation (Pearson \( r = -0.23, p = 0.258 \)) was shown. Contrary to expectations octaCDD showed no association with nursing period.

Collinearity has been checked by analyzing the correlation between the independent variables age and body-mass index (Pearson \( r = 0.1497, p = 0.350 \)), age and duration of nursing (Pearson \( r = 0.3326, p = 0.034 \)), body-mass index and duration of nursing (Pearson \( r = -0.0653, p = 0.685 \)), as well as age and total days of exposure (Pearson \( r = 0.5055, p = 0.001 \)).
The correlation between age and duration of nursing (Pearson $r = 0.3326$, $p = 0.034$) showed a decrease in the duration of nursing over the years. The correlation did not cross the defined limit for Pearson $r = 0.40$, so age and duration of nursing simultaneously entered the regression model. The correlation between age and total days of exposure was expected and must be considered in the interpretation of the respective regression models. Correlation between age and exposure index for the analyzed congeners was irrelevant.

**Multiple Regression**

The results of the multiple regression for PCDD/PCDF blood concentrations based on the six models are shown in Table 6. Standardized regression coefficients ($\beta$), corresponding $p$ values for each predictor, number of cases entered the prevailing model, and the coefficient of determination ($R^2$) are represented. The results of the analysis of the total study group entering the weighted indoor air concentration (model 4) showed an association between the PCDD/PCDF blood levels and the weighted indoor air concentration for...
Table 6. Multiple regression models predicting n-transformed PCDD/PCDF blood concentrations, models 1 to 6.

| Exposure assessment (model) | n | R² | Age, 1987 | BMI, 1987 | Wood pres | Nursing, weeks | Exposure (1–6) |
|-----------------------------|---|----|-----------|-----------|-----------|----------------|----------------|
| HexaCDD (ln) (pg/g blood fat)/exposure variable/hexaCDD (pg/std m² indoor air) | 35 | 0.64 | 0.7825 | 0.0000 | -0.2433 | 0.0696 | 0.2333 | 0.0673 | -0.1663 | 0.1857 | -0.0315 | 0.6000 |
| Exposure index (1) | 35 | 0.41 | 0.4368 | 0.0129 | 0.2256 | 0.1695 | 0.3075 | 0.0564 | -0.1102 | 0.4850 | 0.1998 | 0.1839 |
| Total days of exposure (2) | 35 | 0.40 | 0.4415 | 0.0107 | 0.3090 | 0.0054 | 0.3171 | 0.0278 | -0.0718 | 0.6133 | -0.0181 | 0.9086 |
| Average daily exposure time (3) | 35 | 0.41 | 0.4078 | 0.0088 | 0.3063 | 0.0330 | 0.3089 | 0.0394 | -0.0943 | 0.5105 | 0.0982 | 0.4902 |
| Indoor air concentration | | | | | | | | | | | | |
| Weighted (4) | 35 | 0.45 | 0.4515 | 0.0082 | 0.1958 | 0.2229 | 0.3279 | 0.0348 | -0.0981 | 0.5220 | 0.2770 | 0.0653 |
| Unweighted (5) | 24 | 0.38 | 0.4452 | 0.0430 | 0.2230 | 0.3029 | 0.2096 | 0.3308 | -0.1935 | 0.3969 | 0.1947 | 0.3983 |
| Indoor air concentration categorized (6) | | | | | | | | | | | | |
| Medium | 24 | 0.42 | 0.5469 | 0.0248 | 0.2476 | 0.2571 | 0.1514 | 0.4982 | -0.1964 | 0.3415 | -0.2156 | 0.3931 |
| High | | | | | | | | | | | | |
| OctaCDD (ln) (pg/g blood fat)/exposure variable/octaCDD (pg/std m² indoor air) | 31 | 0.35 | 0.0150 | 0.9398 | -0.0612 | 0.7550 | 0.4268 | 0.0325 | 0.0671 | 0.7003 | -0.2245 | 0.2258 |
| Exposure index (1) | 31 | 0.35 | 0.1030 | 0.6193 | 0.0495 | 0.7454 | 0.5148 | 0.0017 | 0.3847 | 0.2428 | 0.1452 | 0.3546 |
| Total days of exposure (2) | 41 | 0.28 | -0.0417 | 0.1810 | 0.0554 | 0.7233 | 0.5041 | 0.0021 | 0.1449 | 0.3565 | 0.0843 | 0.6262 |
| Average daily exposure time (3) | 41 | 0.29 | 0.0370 | 0.1913 | 0.0496 | 0.7454 | 0.5148 | 0.0017 | 0.3847 | 0.2428 | 0.1452 | 0.3546 |
| Indoor air concentration | | | | | | | | | | | | |
| Weighted (4) | 31 | 0.42 | -0.1569 | 0.4289 | 0.0224 | 0.9065 | 0.3743 | 0.0450 | 0.0636 | 0.5676 | -0.4081 | 0.0357 |
| Unweighted (5) | 20 | 0.30 | -0.4334 | 0.1382 | 0.2061 | 0.4737 | 0.4453 | 0.0935 | 0.0572 | 0.8081 | -0.0870 | 0.7215 |
| Indoor air concentration categorized (6) | | | | | | | | | | | | |
| Medium | 20 | 0.34 | -0.3596 | 0.2478 | 0.2002 | 0.4988 | 0.3894 | 0.1546 | -0.0444 | 0.8525 | -0.1318 | 0.6479 |
| High | | | | | | | | | | | | |
| I-TEQ (ln) (pg/g blood fat)/exposure variable/I-TEQ (pg/std m² indoor air) | 40 | 0.67 | 0.7793 | 0.0000 | -0.0519 | 0.6260 | 0.2468 | 0.0277 | -0.1822 | 0.0939 | -0.0379 | 0.7162 |
| Exposure index (1) | 40 | 0.65 | 0.7740 | 0.0000 | -0.0619 | 0.5734 | 0.2718 | 0.0152 | -0.2013 | 0.0721 | 0.0376 | 0.7586 |
| Total days of exposure (2) | 41 | 0.64 | 0.7571 | 0.0000 | -0.0986 | 0.5201 | 0.2661 | 0.0178 | -0.2018 | 0.0753 | -0.0235 | 0.8326 |
| Average daily exposure time (3) | 41 | 0.64 | 0.7571 | 0.0000 | -0.0986 | 0.5201 | 0.2661 | 0.0178 | -0.2018 | 0.0753 | -0.0235 | 0.8326 |
| Indoor air concentration | | | | | | | | | | | | |
| Weighted (4) | 40 | 0.67 | 0.7553 | 0.0000 | -0.0409 | 0.7017 | 0.2345 | 0.0354 | -0.1831 | 0.0900 | -0.0969 | 0.4275 |
| Unweighted (5) | 24 | 0.61 | 0.7604 | 0.0002 | -0.1881 | 0.3029 | 0.2549 | 0.1458 | -0.3468 | 0.0434 | 0.2123 | 0.2496 |
| Indoor air concentration categorized (6) | | | | | | | | | | | | |
| Medium | 24 | 0.61 | 0.7447 | 0.0008 | -0.1552 | 0.3819 | 0.2761 | 0.1415 | -0.3283 | 0.0619 | 0.1221 | 0.5525 |
| High | | | | | | | | | | | | |

*Abbreviations: BMI, body-mass index; ln, transformed to base e; Wood pres, wood preservatives in private homes. *n and R², predictor variables; standardized regression coefficient β, p value. Models 1–4, total study group; models 5 and 6, restricted study group. Exposure in private homes (with 0/1 variable).

heptaCDD (β = 0.2770; p = 0.0653). HexaCDD showed no association. For octaCDD a significant negative association was observed between PCDD/PCDF blood levels and weighted PCDD/PCDF indoor air concentration. Association for I-TEQ was nearly 0. The results of the regression model with exposure index (model 1) corresponded with the analysis of the weighted indoor air concentration (model 4) but were still reduced.

In the first subgroup analysis with the modified regression model (model 5, indoor air concentration unweighted), the borderline significant positive association between heptaCDD indoor concentrations and blood levels shifted to a nonsignificant positive association. The significant negative association for octaCDD (model 4) was noticeably decreased. The association for I-TEQ of nearly 0 shifted to a weak positive but nonsignificant association. The categorized analysis (model 6, measuring the high indoor air concentration) confirmed the results for I-TEQ and for heptaCDD with a noticeably decreased β-coefficient. For octaCDD the categorized analysis confirmed the negative associations found in the analysis of the total study group using weighted indoor air concentrations (model 4). For heptaCDD the results were not clear.

No associations between PCDD/PCDF blood levels and the total of exposure days (model 2) and the average of daily working time (model 3) were observed for one of the three PCDD congeners or the I-TEQ.

With regard to the control variables—except for octaCDD—a significant age dependence was confirmed in the multiple regression. For the body-mass index a negative association with blood levels was shown for hexaCDD (borderline significant in the models 1 and 4) and for I-TEQ. In contrast a significant positive association existed for heptaCDD (models 2 and 3). In the analysis of the total study group, duration of nursing period showed a negative but nonsignificant association with blood levels for the analyzed congeners and the I-TEQ except for octaCDD. These associations improved in the subgroup analyses, which excluded the one outlier with a long duration of nursing. For I-TEQ the influence shifted from a borderline significant association in the analysis
of the total study group (models 1–4) to a significant association in the subgroup analysis (model 5; Pearson 4 = −0.3468, p = 0.0434).

Nearly all analyses of the total study group showed a positive association between PCDD/PCDF blood levels and exposure to wood preservatives in private homes. In the subgroup analysis these results lost significance.

**Discussion**

With the exception of octaCDD, the determined PCDD/PCDF blood levels were clearly correlated with age, as was expected. For the body-mass index, a weak negative association was observed for hexaCDD and I-TEQ. Also with the exception of octaCDD, the duration of nursing period was negatively associated with the PCDD/PCDF blood concentrations, as was expected. This relationship shifted in the subgroup analysis to a more powerful and, for I-TEQ, to a significant association—despite a decreasing number of cases entering the regression model in the subgroup analysis. The failed correlations of age and duration of nursing period with octaCDD could be explained by some cases with increased octaCDD blood levels.

An association between PCDD/PCDF indoor exposure and PCDD/PCDF blood concentrations was shown in the analysis of the total study group with the weighted indoor air concentration for heptaCDD. In this analysis a significant negative association was observed for octaCDD and an association of nearly 0 for the I-TEQ. HexaCDD showed no association. The analysis of the subgroup (unweighted indoor air concentration) lost significance in the association for heptaCDD because fewer cases were entered in the regression model. In summary, this modified regression model showed a still better consistency for the results: the inexplicable significant negative correlation for octaCDD shifted to a weak negative correlation of nearly 0, the correlation for I-TEQ nearly 0 shifted—according to hypothesis—to a positive but still nonsignificant association.

The subgroup analysis based on categorized data could not confirm the results for all analyzed congeners. This could be because of our classification scheme: Because of the small number of cases in the subgroup, analysis dividing into unequivocal exposure groups with the same number of cases was not always exactly possible. In additional, several cases were related to the same PCDD/PCDF indoor air concentration.

No associations were shown between PCDD/PCDF blood levels and the total of exposure days and the average of daily working time. In terms of total exposure days, the correlation with age (collinearity in regression model 2) must be considered. Average of daily working time may be not representative for assessment of long-term exposure. Uncertainties also arose from equating the daily working time with daily exposure time. Because day-care teachers spend much of their working time outside the buildings (playground, trips, etc.), the daily working time gives only a rough estimation of daily exposure.

In summary, the subgroup analyses with the modified regression models (models 5 and 6) reduced inaccuracies from the first models (different methods to determine the PCDD/PCDF indoor air concentration, estimating the PCDD/PCDF indoor air concentration [I-TEQ] on the basis of PCP concentration in the wooden building materials for one day-care center, inaccuracies from estimating the time of exposure, and inaccuracies from calculating the indoor air concentration considering working activity in two different day-care centers). Because of the decreased number of cases, the results of the subgroup analyses lost significance; however, the results showed more consistency. The results showed a weak association between PCDD/PCDF indoor air concentration and PCDD/PCDF blood levels for heptaCDD and I-TEQ. In summary, the analyses showed no clear association between PCDD/PCDF indoor exposure in day-care centers and PCDD/PCDF blood levels of female employees previously exposed to wood preservatives.

These inconsistent findings may be explained by general inaccuracies resulting in exposure assessment: Single indoor air measurements may be not representative for valid quantitative assessment of long-term exposure. Inaccuracies resulted from differences between conditions during the measurement and those during the normal activities in the day-care centers. The measuring period does not reflect a regular indoor ventilation situation (14). Because a worst-case approach for the measurements of PCDD/PCDF indoor air concentration was used, we cannot exclude the possibility that the true exposure was lower.

Altogether the number of PCDD/PCDF indoor air measurements and the respective number of cases considered in the multiple regression was rather small and reduced the probability of a significant association. In contrast, the results consistently indicated an association between PCDD/PCDF blood concentrations and exposure to wood preservatives in private homes, which can be indicative of a possible association between exposure to wood preservatives and increased PCDD/PCDF blood concentrations. However, it must be considered that the PCDD/PCDF indoor air concentration of the private homes is unknown.

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