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COPLANAR PCBs AND THE RELATIVE CONTRIBUTION OF COPLANAR PCBs, PCDDs, AND PCDFs TO THE TOTAL 2,3,7,8-TCDD TOXICITY EQUIVALENTS IN HUMAN SERUM

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ABSTRACT

Coplanar PCBs in human serum were measured by high-resolution gas chromatography/isotope-dilution high-resolution mass spectrometry in 46 pulp and paper mill workers and 16 community residents with no specific known source of PCB exposure. The relative contribution of coplanar PCBs, PCDDs, and PCDFs to the total 2,3,7,8-TCDD toxicity equivalents (TEQs) were compared using the toxic equivalency factors proposed by Safe [1] and the factors recently proposed by WHO [2]. The mean concentrations of PCB-126 and PCB-169 were higher in paper mill workers than in community residents. However, these differences were not statistically significant. Serum PCB-126, but not PCB-169, was correlated with body mass index (Spearman's r=0.40, p=0.002). Serum PCB-169, but not PCB-126, was correlated with age (Spearman's r=0.54, p=0.0001). Multiple linear regression analysis for log-transformed combined PCBs showed that age (p=0.008), body mass index (p=0.031), and eating locally caught fish (p=0.019) were statistically significant predictors. The majority of the total TEQ in serum is due to PCDDs (63%), whereas PCDFs account for 21% and coplanar PCBs account for 15% when calculated using the TEFs proposed by Safe. The percent contributions from PCDDs, PCDFs, and coplanar PCBs were 66%, 24%, and 10% respectively when calculated based on the TEFs proposed by WHO. Age, body mass index, and consumption of locally caught fish are significant predictors for coplanar PCB levels in human serum. Serum PCDDs were the major contributors to the total 2,3,7,8-TCDD equivalent toxicity in this study. © 1997 Elsevier Science Ltd

Key words: coplanar PCBs, PCDDs, PCDFs; TEFs, TEQs; human serum

INTRODUCTION

Polychlorinated biphenyls (PCBs) are among the most ubiquitous and persistent environmental contaminants [3]. Non-ortho-chlorine-substituted PCBs (coplanar PCBs) are approximate isostereomers of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and are the most toxic members of all 209 PCB congeners [1, 4]. Although low concentrations of PCBs can be found in outdoor air, in indoor air, on soil surfaces, and in surface water, consumption of fish from polluted waters has been identified as the major environmental source of human exposure to PCBs [3]. Although co-contamination with polychlorinated dibenzofurans (PCDFs) was largely responsible for the overall toxicity in large-scale episodes of PCB poisoning in Japan and Taiwan [5, 6], exposure to coplanar PCBs might be more significant than exposure to PCDFs in the general population [7]. Until recently, a method to measure isomer-specific PCBs has not been available. Patterson et al. [8, 9] developed the first assay for coplanar PCBs and other mono- to tetra-ortho chlorinated PCB congeners by high-resolution gas chromatography/isotope-dilution mass spectrometry. To date, coplanar PCBs have been measured in human serum in only a few studies [12-16].

The toxicities of individual halogenated aromatic compounds, including polychlorinated dibenzo-p-dioxins (PCDDs), PCDFs, and PCBs, have been determined relative to 2,3,7,8-TCDD using toxic equivalency factors (TEFs) [1]. The TEFs were originally based on in vitro and in vivo animal studies. The toxicity equivalents (TEQs), which are derived by multiplying the measured concentration by the TEFs, are particularly useful for hazard and risk assessment. Because of the necessity for more consistent and scientifically based TEF values, the WHO-European Center for Environment and Health (WHO-ECEH) and International Programme on Chemical Safety (IPCS) recently proposed new TEFs for coplanar PCBs [2]. This paper describes the findings from human serum measurement of coplanar PCBs in two selected groups of individuals. These measurements were made incidental to a study of occupational exposure to dioxins and furans. The PCB measurements were made to gain experience with a newly developed analytical technique. The results are reported here to further demonstrate the utility of this technique and to add to a better understanding of the relative contribution of coplanar PCBs to the total body burden of dioxin and related substances in various populations. The relative contribution of the coplanar PCBs, PCDDs, and PCDFs to the total 2,3,7,8-TCDD TEQ was determined using the TEFs proposed by Safe [1] and the values recently proposed by WHO [2].

METHODS

Study Subjects

Data from pulp and paper mill employees and residents from the northeastern U.S. community in which the mill was located were analyzed for this study. Detailed information about selection of the study site and study subjects has been previously described [10]. In summary, 46 workers were selected for the study based

on seniority and job title. Each worker who agreed to participate was asked to identify a friend close in age who lived in the community, but never worked in a pulp mill. Sixteen community residents participated. Each study participant was interviewed about personal characteristics known to be related to serum concentrations of PCBs, PCDDs, and PCDFs, such as age, height and weight (used to calculate body mass index), cigarette smoking, and consumption of fish caught in local rivers. Questions also were asked about past work in jobs in waste incineration, reclamation or hazardous waste, work with transformers or capacitors, herbicide manufacturing, military experience in Vietnam, use of herbicides at home, and use of pentachlorophenol to treat wood. All study participants were white males.

Analysis of serum coplanar PCBs

Study participants each provided 250 milliliters of blood. Fasting was not required because of concern about the safety of workers who had to work before or after the blood draw. Serum was analyzed for PCBs using high-resolution gas chromatography/high-resolution mass spectrometry [8, 9]. Each analytical run consisted of a method blank, three unknown samples, and a quality-control pool sample. All measurements reported in this paper were corrected for total serum lipid. PCDD and PCDF levels have been previously reported for each study participants [10]. The numbering system for chlorinated biphenyls, adopted by the International Union of Pure and Applied Chemistry (IUPAC), is used in this paper. PCB-77 is 3,3',4,4'-tetrachlorobiphenyl, PCB-126 is 3,3',4,4',5-pentachlorobiphenyl, and PCB-169 is 3,3',4,4',5,5'-hexachlorobiphenyl.

Statistical analysis

The data were analyzed separately for pulp and paper mill workers and community residents. Although there was no reason to suspect systematic differences between these groups in either absolute or relative levels of PCBs, the original study groups were retained for clarity.

The minimum detectable concentration divided by the square root of two was assigned to nondetectable values [11]. Mean differences in individual PCB congeners between workers and community residents were examined by the Wilcoxon rank-sum test. Because PCB-169 levels, combined results for PCB-126 and PCB-169, and TEQs were log-normally distributed, log-transformed values were used in analyses involving these variables. Based on results from other studies reported in the literature and examination of the bivariate relationships in this study, the effects of age, body mass index, cigarette smoking status (current, former, never), consumption of locally caught fish (ever, never), and consumption of alcoholic beverages (ever, never) were included as independent variables in the regression models for PCBs. The relative amounts of PCBs, PCDDs, and PCDFs were examined by calculating the percent of the total TEQ contributed by each of the congener groups.

RESULTS

Although PCB-77 was not detected, PCB-126 and PCB-169 were detected in most serum samples (94% for PCB-126; 98% for PCB-169). The mean of PCB-126 was higher in serum from pulp and paper mill workers (25 ng/kg) than in community residents (18 ng/kg, Table 1 & Figure 1). However, the difference in the means was not statistically significant (p=0.28). Although the mean of PCB-169 was also higher in serum from pulp and paper mill workers (31 ng/kg) than in community residents (27 ng/kg), the difference in the means was not statistically significant (p=0.71, Table 1 & Figure 2).

Serum PCB-126 (Spearman's r=0.40, p=0.002), but not PCB-169 (Spearman's r=-0.08, p=0.52), was positively correlated with body mass index. Serum PCB-169 (Spearman's r=0.54, p=0.0001), but not PCB-126 (Spearman's r=0.03, p=0.94), was positively correlated with age. There were no mean differences in either PCB-126 or PCB-169 when study participants were grouped by alcohol consumption and local fish consumption. The mean level of serum PCB-126, however, was higher in non- and ex-smokers (26 ng/kg) than in current smokers (13 ng/kg, p=0.0003).

Table 1. Serum PCB-126 and PCB-169 levels in pulp and paper mill workers and community residents

			Paper Mill Workers			Community Residents		
Coplanar PCBs*	TEF(S)†	TEF(W)‡	N§	Mean//	Median (Range)	N§	Mean//	Median (Range)
PCB-126	0.1	0.1	44	25	19(0-106)	14	18	16(0-54)
PCB-169	0.05	0.01	45	31	29(10-70)	16	27	27(10-43)

*PCB-126 = 3,3',4,4',5-pentachlorobiphenyl, PCB-169 = 3,3',4,4',5,5'-hexachlorobiphenyl

†2,3,7,8-TCDD Toxicity Equivalency Factors (TEFs) developed by Safe [1]

‡2,3,7,8-TCDD Toxicity Equivalency Factors (TEFs) proposed by WHO-ECEH [2]

§PCB-126 was non-detectable for four serum samples; PCB-169 was non-detectable for one serum sample. For these samples, the minimum detectable value divided by the square root of two was assigned.

//ppt = part per trillion, lipid-adjusted

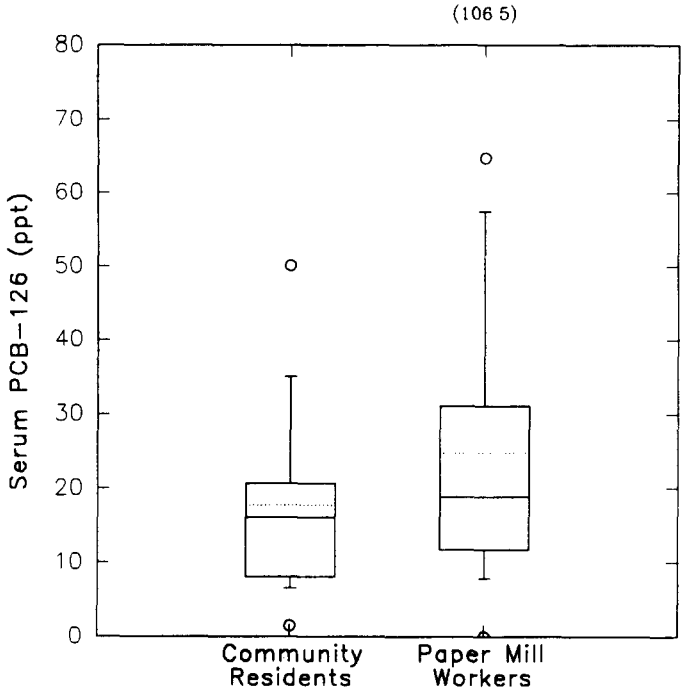

Figure 1. Box and whisker plot of serum PCB-126 in paper mill workers and community residents. (Lowest whisker: 10 percentile, lower edge of box: 25 percentile, middle line of the box: 50 percentile, dotted line: mean, upper edge of box: 75 percentile, highest whisker: 90 percentile of the data)

Multiple linear regression analysis for the log-transformed TEQ for combined PCB-126 and PCB-169 showed that age, body mass index, and eating locally caught fish were statistically significant predictors, whereas working at the pulp and paper mill and cigarette smoking were not (Table 2). Overall, 32% of the variation in TEQ for combined PCBs was explained by variables in the model.

In all study participants, the majority of the total TEQ in serum was due to PCDDs (63%), whereas PCDFs accounted for 21% and coplanar PCBs accounted for 15% when calculated using the TEFs proposed by Safe. The percent contributions from PCDDs, PCDFs, and coplanar PCBs were 66%, 24%, and 10%, respectively, when calculated based on the TEFs proposed by WHO. There were no significant differences in the percent contribution of coplanar PCBs, PCDDs, and PCDFs between workers and community residents (Figure 3).

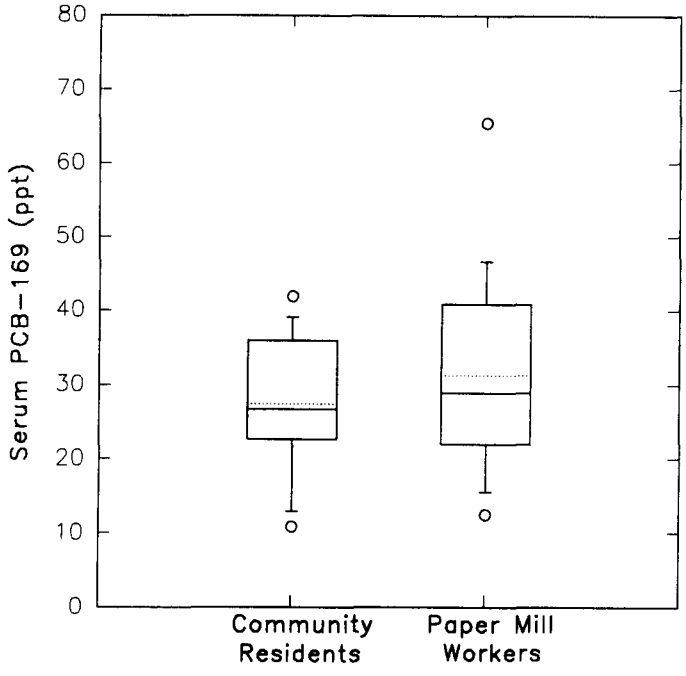

Figure 2. Box and whisker plot of serum PCB-169 in paper mill workers and community residents. (Lowest whisker: 10 percentile, lower edge of box: 25 percentile, middle line of the box: 50 percentile, dotted line: mean, upper edge of box: 75 percentile, highest whisker: 90 percentile of the data)

DISCUSSION

Knowledge of congener-specific PCB levels in human tissues is important for understanding the toxicity of PCBs since coplanar PCBs are more toxic than other PCB congeners. Although coplanar PCBs have been measured in human adipose tissue in several studies, coplanar PCBs have been measured in human serum in only a few studies [12, 13, 14, 15, 16]. Because the study groups described in this paper are not a representative general population sample, the extent to which these findings are generalizable to other populations is unknown. No known sources of PCBs, beyond backgound environmental exposures, however, were identified in either study group.

The mean and range of PCB-126 and PCB-169 in this study were similar to previous results in pooled serum from the general U. S. population [8, 13] and were similar to the values in pooled serum from 10 spouses of fishermen living in Quebec [14]. However, the values observed in this study were higher than values measured in nine patients undergoing appendectomy and one capacitor manufacturer [15] and lower than the values measured from thirty-seven men with no known occupational PCB exposure including fourteen

Table 2. Multiple linear regression model for log-transformed total coplanar PCBs in human serum (n=60, overall model r^2=0.32)

Variable	Parameter estimate	Standard error	p value
Intercept	-0.921	0.578	0.116
Age (years)	0.017	0.006	0.008
Body Mass Index	24.473	11.043	0.031
Work at pulp and paper mill (yes, no)	0.197	0.171	0.256
Current smoking	0.333	0.180	0.070
Local fish consumption (ever, never)	0.430	0.179	0.019

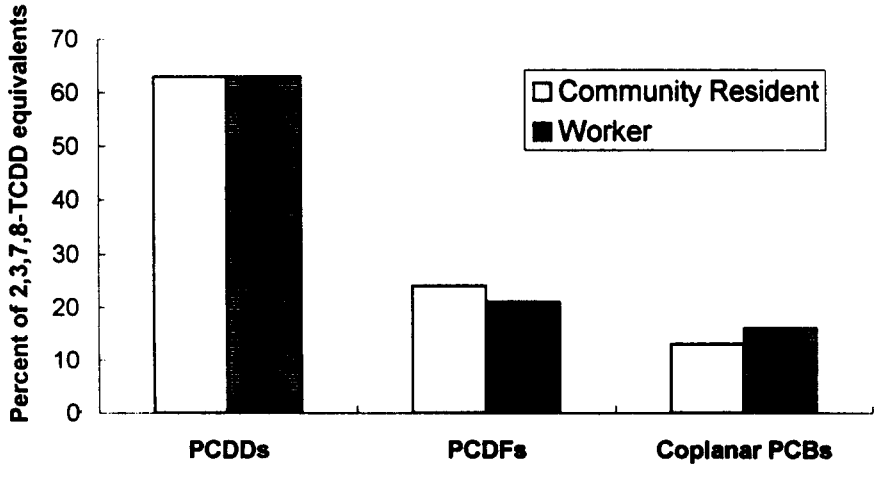

Figure 3. Relative contribution of coplanar PCBs, PCDDs, and PCDFs to the total 2,3,7,8-TCDD toxicity equivalents in human serum calculated using the TEFs proposed by Safe.

fishermen in Sweden [16]. These differences may be due to differences in i) interlaboratory calibration standards and assay conditions (e.g., sample clean-up, detectors), ii) PCB exposure, iii) sample collection years, and iv) demographic characteristics of study subjects (e.g., age, sex).

Measurable amounts of PCBs have been found in some virgin paper and paperboard; environmental contamination (e.g., air, water) is the likely source of these PCBs [17]. Although there was a slight increase in both PCB-126 and PCB-169 in pulp and paper mill workers compared to community residents in this study, working at the pulp and paper mill was not a significant predictor of coplanar PCB levels when covariates were considered. This study found that age, body mass index, and consumption of locally caught fish are significant predictors for the total coplanar PCB levels in serum.

In the present study, coplanar PCBs accounted for less than 20% of the 2,3,7,8-TCDD TEQs. This confirms the results found in adipose tissue in the U.S. population [13], in breastmilk samples of Caucasian and Inuit women in Canada [14], and in serum of Ontario residents (18). In contrast, a number of investigators indicated that PCBs play a major role in the total TEQs especially when the TEFs of other ortho-substituted PCBs are included [13, 14, 16, 19]. In our study, only coplanar PCBs were measured, while Asplund et al. [16] measured ten PCBs, Dewailly et al. [14] measured eight, and Schecter [19] measured seventeen.

In conclusion, this study found that age, body mass index, and consumption of locally caught fish are significant predictors for two important coplanar PCB levels in serum. The TEFs of these two congeners indicate that they are among the most toxic of all PCB congeners. Among the PCDDs, PCDFs, and coplanar PCBs, the serum PCDDs were the major contributors to the total 2,3,7,8-TCDD equivalent toxicity in this study.

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