

PREDICTORS OF SERUM PCDF CONCENTRATIONS IN PEOPLE FROM MICHIGAN, USA

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Introduction and Methods:

We studied factors that predict serum concentrations of the polychlorinated dibenzofurans (PCDFs) for which World Health Organization Toxic Equivalency Factors (TEFs) exist (2378-TCDF, 12378-PeCDF, 23478-PeCDF, 123478-HxCDF, 123678-HxCDF, 123789-HxCDF, 234678-HxCDF, 1234678-HpCDF, 1236789-HpCDF, and OCDF)(6), using data from 946 participants in the University of Michigan Dioxin Exposure Study (UMDES)(4, 5). This study was undertaken in an area in which there was widespread contamination of soils and river sediments in Midland and Saginaw, Michigan from the Dow Chemical Company operations in Midland. Participants were interviewed regarding potential exposure pathways (sport caught fish and game, diet, activities in the contaminated area, occupations, residential locations), demographics, smoking, and breast feeding. Samples of blood, soil, and household dust were analyzed for PCDFs using HRGC/HRMS. Important factors were identified using forward stepwise selection. Data were analyzed in SAS 9.1 (SAS Institute, Cary, NC) using linear regression for complex survey data, in which the \log_{10} (serum PCDF) was a linear function of predictors. The Tittabawassee River floodplain was believed to have been contaminated from past chloralkali operations which spilled waste materials into the river. Polychlorinated dibenzofurans predominated in soil and sediment samples from the river downstream of Dow's facilities.

Results:

Serum PCDF concentrations were detectable in at least 95% of subjects for 23478-PeCDF, 123478-HxCDF, 123678-HxCDF, and 1236789-HpCDF. However, some congeners were detectable in only a small proportion of subjects: 2378-TCDF (32%), 12378-PeCDF (25%), 123789-HxCDF (1%), 234678-HxCDF (44%), 1234789-HpCDF (1%), and OCDF (11%), even though the limits of detection for these congeners were below 1 part per trillion. The most important congener was 23478-PeCDF because it is typically associated with wastes from chloralkali operations.

Table 1. Percent of the variation in serum congener concentration (Adjusted R²) explained by categories of factors for PCDF congeners.

Contribution to Adjusted R ² (%)	23478-PeCDF	123478-HxCDF	123678-HxCDF	1234678-HpCDF
Overall (Stable only)	61.59	46.79	34.89	11.01
Demographic factors	41.69	35.51	34.94	6.38
Residence factors	0.00	0.00	0.00	0.00
Soil/Household Dust	0.00	0.00	0.00	0.00
Property use factors	0.87	0.61	0.00	0.00
Work history factors	0.08	0.00	0.00	0.72
Water activities factors	0.00	0.26	0.00	0.00
Fish consumption and fishing	3.44	0.54	0.08	0.15
Meat/Dairy consumption and hunting	0.00	2.56	0.00	4.44

The regression model for 23478-PeCDF explained 62 percent of the variation in the serum concentration (adjusted R²), indicating that the variables we studied included important predictors of the serum level. The regression model

for 123478-HxCDF explained 47% of the variation in serum concentration. In contrast, the models for 123678-HxCDF and 1234678 HxCDF explained substantially less of the variation in serum levels (35% and 11%, respectively), indicating that the factors we studied did not explain a large proportion of variation in serum levels. In all models, most of the variation explained was due to demographic factors (age, age², sex, BMI, and change in BMI in the past year), and breastfeeding. Soil and household dust PCDF contamination explained no appreciable amount (< 0.01%) of the variation in serum PCDF concentrations. Fish consumption and fishing explained 3% of the variation in serum 23478-PeCDF, but meat/dairy consumption and hunting no appreciable amount. In contrast, meat/dairy consumption and hunting explained 3-4% of the variation in 123478-HxCDF and 1234678-HpCDF levels, but far less of the variation in 23478 PeCDF levels. The serum variation in 123678-HxCDF was explained entirely by demographic variables, with almost no contribution from the other categories of variables.

Figure 1. Relationship between serum 23478-PeCDF and age, sex, and BMI.

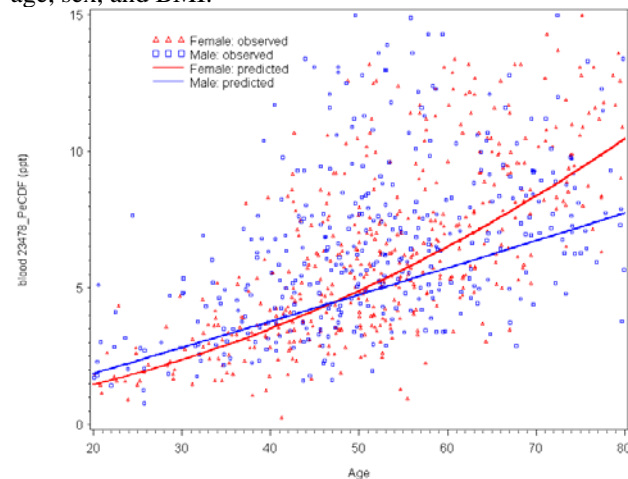


Figure 2. Relationship between serum 123478-HxCDF and age and sex.

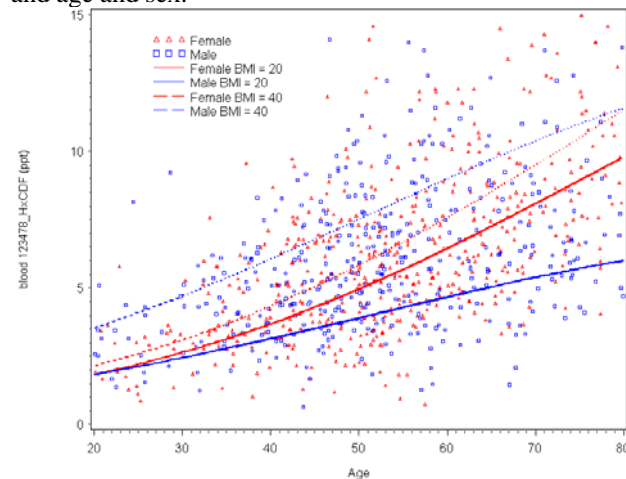
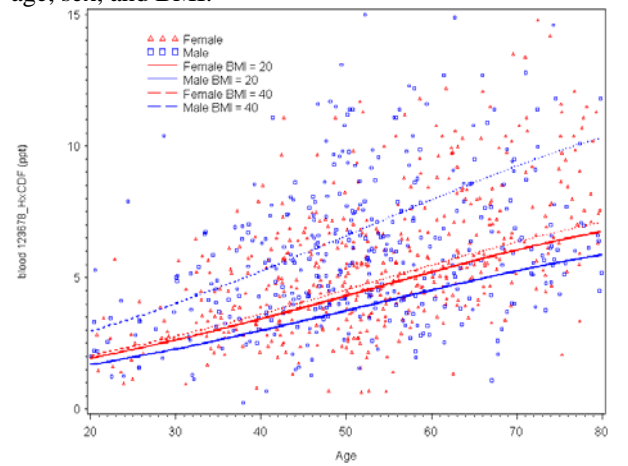


Figure 3. Relationship between serum 123678-HxCDF and age, sex, and BMI.



Age was positively associated with serum 23478-PeCDF (Figure 1), 123478-HxCDF (Figure 2), and 123478-HxCDF (Figure 3) levels, but not 1234678-HpCDF. There were significant interaction terms between age and sex for 12478-PeCDF and 123478-HxCDF, such that serum levels increased with age more so among females than among males. There were significant interaction terms between BMI and sex for 123478-HxCDF and 123678-HxCDF, such that obese males had higher levels of these congeners at all ages than did females or thin males. BMI was positively associated with 123478-HxCDF, and 123478-HxCDF, and 1234678-HpCDF, but not 23478-PeCDF. In addition, BMI loss in the past 12 months was positively associate with all four PCDF congeners. These results suggest that total body fat and loss of body fat are both important predictors of PCDF concentrations in serum.

Breast feeding was inversely associated with serum levels of 23478-PeCDF, but not other congeners. Smoking was inversely associated with 123478-HxCDF and 1234678-HpCDF

Neither living on contaminated soil, contaminated household dust, living in or near the Tittabawassee River flood plain, nor living downwind of the Dow facilities was associated with increased serum levels for any PCDF congener. Working at Dow Chemical Company was not associated with serum levels of any PCDF congener.

Fish consumption and fishing were considered in detail. Eating fish in general (from any source - store bought, sport caught, or restaurant) was not associated with increased serum levels of any PCDF congener, nor was eating walleye or perch caught from the Tittabawassee River, Saginaw River, or Saginaw Bay. Eating any fish other than walleye or perch (including benthic fish and water column fish) from Saginaw River or Bay in the last 5 years was inversely associated with serum levels of 123478-HxCDF, and 123478-HxCDF, and 1234678-HpCDF, and 23478-PeCDF. There were no positive associations for eating fish from the contaminated areas. Fishing in the Saginaw River or Saginaw Bay more than once per month after 1980 was associated with increased serum 23478-PeCDF, but not other PCDF congeners. The lack of a consistent pattern among these findings with respect to the species of fish (particularly the benthic fish which are of greatest concern regarding contamination), the locations where caught, and the dates of activities does not indicate that these are important sources of PCDF exposure and is consistent with the modest contributions of fish consumption to the model R^2 .

There were no significant associations between any PCDF congener and consumption of meat or game from the contaminated areas. Consumption of eggs or dairy products from cows that were home raised in the Tittabawassee River flood plain during the last 5 years was significantly associated with increased serum levels of 123478-HxCDF, but not other PCDF congeners.

Discussion:

Because this is a population-based study, the results apply to the general population of Midland and Saginaw Counties. Few other studies have concurrent measurements of serum, soil, and household dust PCDDs, PCDFs, and PCBs, nor do they include as many subjects. Our serum analyses were based on large samples (80 ml of blood, yielding >25 ml serum for analyses) which allowed us to achieve limits of detection that were below 1.0 parts per trillion for all congeners, such that we had measurable levels of 23478-PeCDF, 123478-HxCDF, 123678-HxCDF, and 1236789-HpCDF for over 95% of subjects. Few other studies have achieved these levels and, as a result, have been limited by large numbers of non-detectable serum levels. However, even with our low detection limits, we had detectable serum levels for less than half of our study subjects for the other PCDF congeners (2378-TCDF, 12378-PeCDF, 123789-HxCDF, 234678-HxCDF, 1234789-HpCDF, and OCDF). We did not perform linear regression analyses for these congeners.

This large body of data allowed us to examine the contributions of many potential exposure pathways to serum PCDF levels. These results indicate that demographic factors, especially age and BMI, are important predictors of serum PCDF levels. Other studies also show the importance of age on serum PCDF levels (1, 3).

These results show little evidence that current contamination in the Midland/ Saginaw area contributes appreciably to current serum concentrations. Fishing in the Saginaw River or Saginaw Bay after 1980 was associated with increased serum 23478-PeCDF, and this result is of particular interest because of the high concentrations of 23478-PeCDF in the river sediments and the plausibility of serum 23478-PeCDF levels as a marker of exposure. The association with fishing activities, but not with fish consumption from the contaminated areas, provides equivocal evidence that these activities contribute to serum levels, based on population estimates of their frequency. These findings do not provide assurance that high consumption of contaminated fish will have no influence of serum levels, and studies of serum 23478-PeCDF among high consumers of bottom feeding fish from the contaminated waterways would be informative.

Second, consumption of eggs or dairy products from cows that were home raised in the Tittabawassee River flood plain during the last 5 years was significantly associated with increased serum levels of 123478-HxCDF, suggesting a possible exposure pathway. However, there is no clear explanation for why this congener but not others is associated with egg and dairy consumption. Although the regression analyses did not find a significant association for meat and game taken from the contaminated areas, a related investigation of a family that consumed beef raised

in the flood plain suggests that heavy consumption of such meat can contribute substantially to serum 23478-PeCDF levels (Franzblau A. Personal communication).

There are few other studies that have examined congener-specific exposure pathways for dioxin like compounds, especially PCDFs. Most have reported only results for TEQ without reporting specific congeners (1-3, 7) A study of the Czech general population living in the vicinity of a chemical factory producing chlorinated herbicides and pesticides showed that consumption of home produced eggs was associated with increased serum PCDDs, PCDFs, and PCBs (2). Future studies should focus on consumption of fish, meat, game, dairy products and eggs from the contaminated areas to further investigate the contributions of these sources to serum concentrations. Recent data on fish and game contamination will allow more precise estimates of the intake of PCDFs from these sources and will allow more precise modeling to be completed.

This study was large and was capable of finding small associations that are statistically significant. Inferences regarding these associations should include consideration of the magnitude of the effect, the statistical significance of the parameter estimate, and the amount of variance in serum dioxin explained by the factor. A number of the significant findings are small in magnitude and explain little variation in serum PCDFs among the population.

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