PREDICTORS OF SERUM TEQ AND PCDD CONCENTRATIONS IN PEOPLE FROM MICHIGAN, USA

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Introduction and Methods: We studied factors that predict serum concentrations of the TEQ and polychlorinated dibenzo-p-dioxins (PCDDs) for which World Health Organization Toxic Equivalency Factors [1] (TEFs) exist (2378-TCDD, 12378-PeCDD, 123478-HxCDD, 123678-HxCDD, 123789-HxCDD, 1234678HpCDD, and OCDD), using data from 946 participants in the University of Michigan Dioxin Exposure Study (UMDES) [2]. This study was undertaken in an area in which there was widespread contamination of soils and river sediments (in the Tittabawassee River and Saginaw River) 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, lifestyle and reproductive factors. Samples of blood, soil, and household dust were analyzed for PCDDs using HRGC/HRMS. Important factors were identified using procedures for forward stepwise selection. Data were analyzed by linear regression for complex survey data using SAS 9.1 (SAS Institute, Cary, NC), in which the $\log_{10}$(serum TEQ or PCDD) was a linear function of predictors.

Results: The regression models explained between 43 and 68 percent of the variation in serum congener concentration (adjusted R^2) for the TEQ and PCDD congeners (Table 1). Most of the variation was explained by demographic factors (age, sex, body mass index [BMI], BMI loss or gain in the past year), breastfeeding, and smoking. Soil and household dust PCDD concentrations explained no appreciable amount (<0.01%) of the variation in serum dioxin concentrations. Fish consumption, fishing, meat/dairy consumption, and hunting explained small amounts of variation in most serum congener levels.

Table 1. Percent of the variation in serum congener concentration (adjusted R^2) explained by categories of factors for TEQ and each PCDD congener, based on 946 serum samples

	TEQ-WHO_{05}	**2378-TCDD**	**12378-PeCDD**	**123478-HxCDD**	**123678-HxCDD**	**123789-HxCDD**	**1234678-HpCDD**	**OCDD**
% of samples >LOD	-	87	99	93	100	94	100	100
Contribution to Adjusted R^2 (%)								
Overall (Stable only)	**68.38**	**62.35**	**64.48**	**51.13**	**62.00**	**42.56**	**47.12**	**44.57**
Demographic factors*	40.50	30.21	46.83	50.27	35.96	41.91	38.87	38.41
Residence factors**	0.69	4.05	1.42	0.00	0.00	0.00	0.00	0.00
Soil/Household Dust	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Property use factors***	0.83	0.60	0.00	0.40	0.54	0.00	2.31	0.00
Work history factors	0.00	1.49	0.00	0.15	0.21	0.00	0.00	0.04
Water activities factors	0.00	0.38	0.00	0.00	0.68	0.00	0.00	0.29
Fish consumption/fishing	0.88	0.37	0.18	0.09	1.34	0.00	1.39	0.31
Meat/Dairy consumption/hunting	0.00	0.45	0.59	0.00	0.17	1.17	1.64	3.24

* Age, age^2, BMI, BMI gain or loss, smoking, breastfeeding

** Number of years lived in Midland/Saginaw area in different historic periods

*** Lived on a farm, backyard trash burning, used herbicides on the property

In Figures 1-6, the effects of demographic variables (age, age^2, sex, and body mass index, change in BMI) on serum TEQ and PCDDs are shown, indicating that TEQ increases logarithmically with age, and more so among women

Figure 1. Relationship between serum TEQ and age, sex, and BMI.

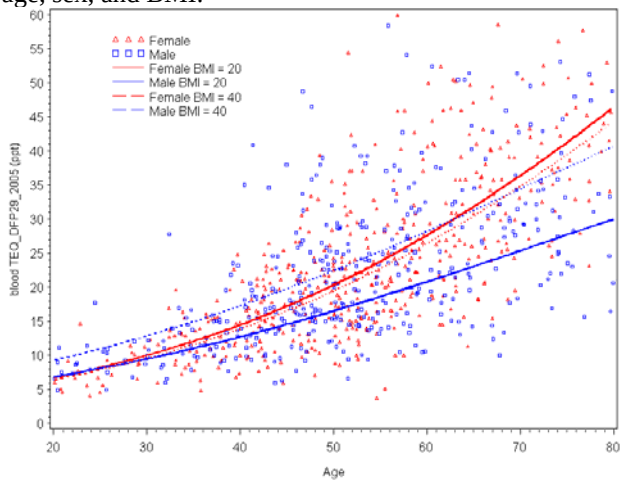


Figure 2. Relationship between serum 2378-TCDD and age and sex.

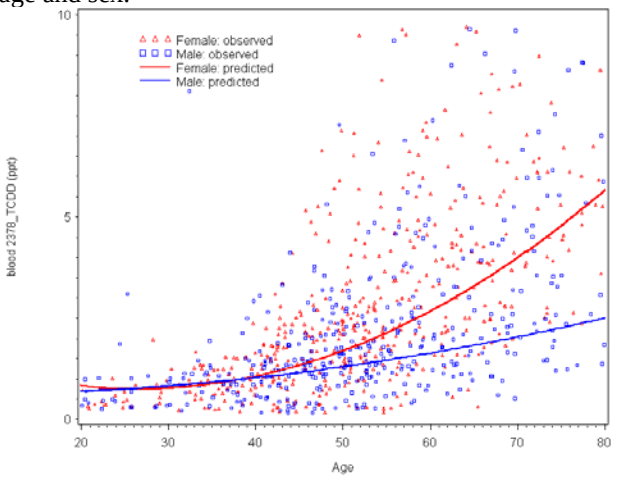


Figure 3. Relationship between serum 12378-PeCDD and age, sex, and BMI.

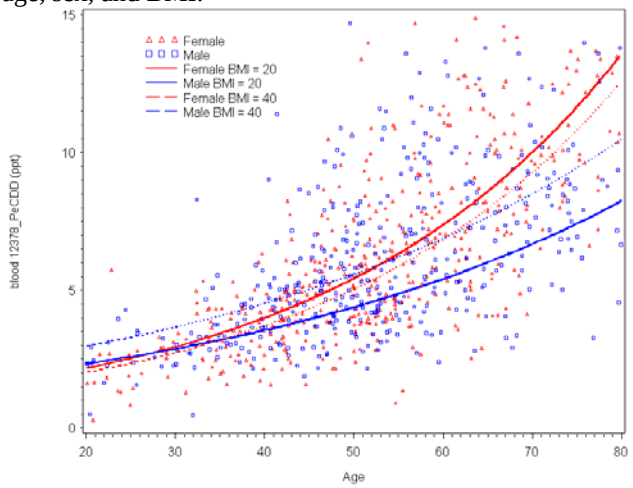


Figure 4. Relationship between serum 123478-HxCDD and age, sex, and BMI.

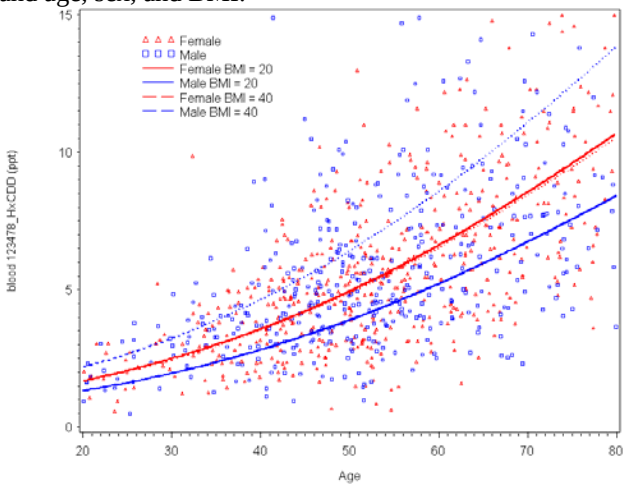


Figure 5. Relationship between serum 123678-HxCDD and age, sex, and BMI.

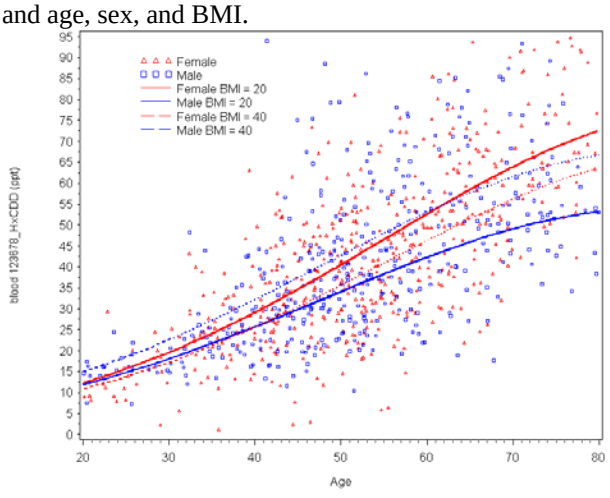
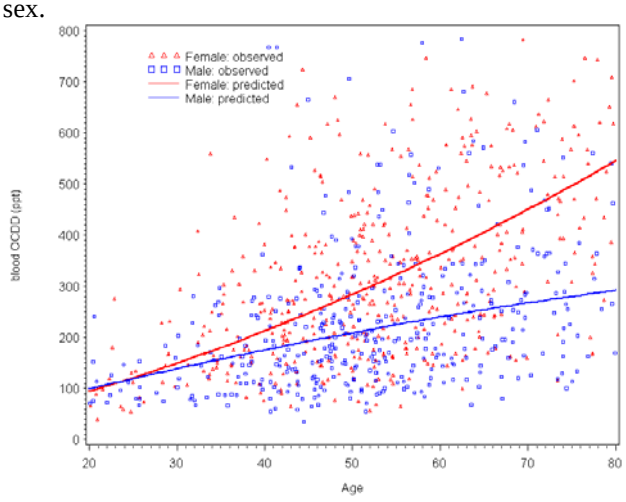


Figure 6. Relationship between serum OCDD and age and sex.



than men for the TEQ and all congeners. Serum levels of TEQ and all PCDD congeners increased with BMI, except for 2378-TCDD. For 2378-TCDD, BMI loss in the past year (rather than BMI itself) was statistically significant. For TEQ, 12378-PeCDD, 123478 HxCDD, and 123678-HxCDD there was an interaction between sex and BMI, such that obese men (for example, BMI=40 shown in the figures) showed a pattern of increasing serum levels with age similar to women. Thin men (for example, BMI=20 shown in the figures) increased much less with age than did obese men or women. The effect of BMI on serum levels in women was small. Breast feeding was inversely associated with serum levels of TEQ, 2378-TCDD, 12378-PeCDD, 123478-HxCDD, and 123678-HxCDD, but not the more highly chlorinated PCDD. Smoking was inversely associated with TEQ, 2378-TCDD, 123478-HxCDD, 123789-HxCDD, 1234678-HpCDD, and OCDD.

Residents had lived in their current homes for an average of 15-20 years. Neither household dust contamination nor living on contaminated soil was associated with increased serum PCDD levels (with the exception of one model that showed a significant association for garden soil due to a single influential observation). There was no significant effect of living currently in any of the Midland/Saginaw regions on TEQ or any PCDD. In contrast, residing in Midland/Saginaw in the 1960s-70s was associated with increased serum TEQ, 2378-TCDD, and 12378-PeCDD. Similarly, working at Dow in the 1940s -1950s was associated with increased serum 2378-TCDD, but there were no positive associations for working at Dow in other time periods or for other serum PCDDs.

Figure 7. Relationship between serum 2378-TCDD levels and years of consumption of fish from any source after 1980.

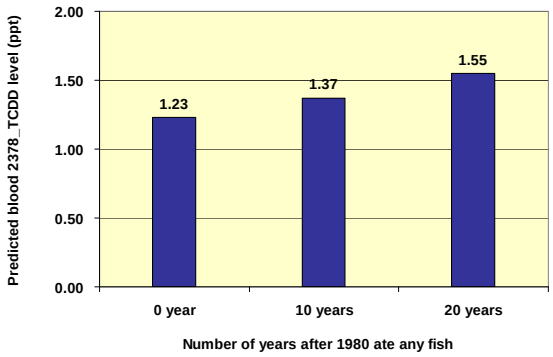
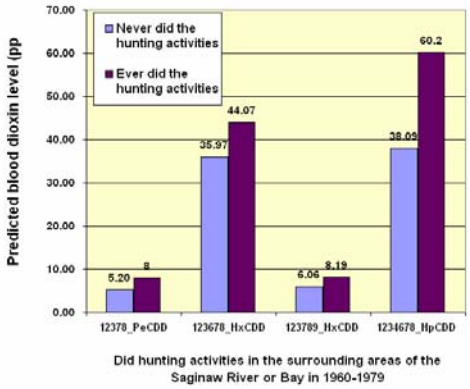


Figure 8. Relationship between serum PCDD levels and years of hunting in the Saginaw River/Bay area in 1960-79.



Fish consumption and fishing were considered in detail. Eating fish from any source (store bought, sport caught, or restaurant) was associated with increased serum TEQ and 2378-TCDD, but not clearly with other PCDD congeners. Consumption of fish for 20 years after 1980 was predicted to be associated with an increase in serum 2378-TCDD of 0.32 ppt (from 1.23 ppt to 1.55 ppt, based on the parameter estimate of a 1.011-fold increase in serum level per year eaten, p=0.003) (Figure 7). Consumption of fish from the Saginaw River/Bay in the past 5 years showed inconsistent results. Consumption of walleye or perch from the Saginaw River/Bay was associated with **decreased** 12378-PeCDD and 1234678-HpCDD, but walleye or perch from the Tittabawassee River were associated with **increased** 1234678-HpCDD. Walleye and perch do not reside in the Tittabawassee River or Saginaw River, (coming into the rivers in the spring only to spawn) and typically have low concentrations of dioxins in their tissues. Consumption of other fish besides walleye and perch from the contaminated waters were associated with **decreased** PCDDs. Fishing in the Saginaw River/Bay after 1980 was associated with **increased** serum 12378-PeCDD, but not TEQ or other PCDD congeners. Fishing in the Saginaw River/Bay prior to 1980 was not associated with TEQ or PCDD congeners. Somewhat contradictory was the finding that fishing in the Tittabawassee River in 1960-79 was associated with **increased** serum 123678-HxCDD, but not with other congeners, and fishing in this river after 1980 was not associated with TEQ or any PCDD. The lack of consistency among these findings with respect to the species of fish, the locations where caught, and the dates of activities is inconsistent with their interpretation as important exposure sources and is consistent with the modest contributions of fish consumption to the model R^2.

Consumption of game meat from the contaminated areas was not associated with TEQ or any serum PCDD congener. However, hunting in the areas around the Saginaw River/Saginaw Bay in 1960-1979 was associated with **in-**

creased serum 12378-PeCDD, 123678-HxCDD, 123789-HxCDD, and 12234678-HpCDD (Figure 8). Hunting in the areas around the Tittabawassee River in 1960-1979 was associated with **increased** serum 2378-TCDD. In contrast, hunting in the areas around the Tittabawassee River/Saginaw River/Saginaw Bay after 1980 was not associated with serum TEQ or any PCDD congener. Consumption of home raised eggs or dairy products in the Tittabawassee River flood plain in the past five years was associated with **increased** serum 123789-HxCDD but not TEQ or any other PCDD. Water activities more than once per month near the Tittabawassee River after 1980 were associated with increased serum 2378-TCDD, but not TEQ or any other PCDD.

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 PCDD levels for almost all subjects. Few other studies have achieved these levels and, as a result, have been limited by large numbers of non-detectable serum levels. These results indicate that demographic factors, especially age, sex, and BMI, are important predictors of serum TEQ and PCDD levels, and comparisons across populations must be made after controlling for these factors. Other studies also show the importance of age on serum PCDD levels [3-6]

These results suggest that historic exposures to PCDDs contributed to current serum PCDD levels, but that current sources of contamination contribute little to current serum concentrations. A study of the Czech general population living in the vicinity of a chemical factory producing chlorinated herbicides and pesticides showed that ambient exposures to PCDDs were not important contributors to serum PCDDs, but that consumption of home produced eggs was associated with increased serum PCDDs, PCDFs, and PCBs [7]. A study of residents near an industrial corridor in Calcasieu Parish, Louisiana, USA found no contribution to serum PCDD levels from consumption of locally caught fish or other current exposure sources [3]. These results may be relevant to other populations exposed to low-moderate levels of soil contamination with dioxins. Future studies should focus on fishing and hunting and consumption of fish and game 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 PCDDs 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, the effect of influential data points (e.g.., outliers), 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 TEQ and PCDDs among the population.

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