THE UNIVERSITY OF MICHIGAN DIOXIN EXPOSURE STUDY: A FOLLOW-UP INVESTIGATION OF CASES WITH HIGH SERUM CONCENTRATIONS OF 2,3,4,7,8-pentaCDF

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Introduction

The 29 congeners of polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and dioxin-like polychlorinated biphenyls (PCBs) that have consensus toxic equivalency factors were measured in serum of 946 subjects who were a representative sample of the general population in five Michigan counties. The study was motivated because of concerns about human exposure to dioxin-contaminated sediments in the Tittabawassee River (TR). Most of the total toxic equivalency (TEQ) in TR sediments is due to two furan congeners, 2,3,7,8-TCDF and 2,3,4,7,8-pentaCDF.[1,2] Only the latter congener has a prolonged serum half life in humans (~7.8-10 years) and thus it can serve as a biomarker of exposure.[3] This report describes results of a follow-up investigation of the 23 subjects with the highest serum levels of 2,3,4,7,8-pentaCDF after adjustment for age, age^2, and body mass index (BMI).

Methods and Materials

The UMDES involved a two-stage clustered random sampling design to recruit subjects from five counties in the State of Michigan, USA. Eligible subjects were required to be at least 18 years old, and to have lived in their homes for at least 5 years. The main study involved an hour-long interview and obtaining blood, house dust and soil samples for chemical analyses from eligible subjects. As noted, 946 subjects provided blood samples (including 251 from Jackson and Calhoun Counties, the control area of the study) that were analyzed for PCDDs, PCDFs and PCBs by Vista Analytical Laboratory (El Dorado Hills, California) using modified United States Environmental Protection Agency methods 8290 and 1668, Revision A.[4,5] Serum results are reported in parts per trillion (ppt) on a lipid adjusted basis and soil results are reported in ppt on a dry weight basis. All TEQ values are calculated with the 29 dioxin-like congeners, using WHO 2005 TEFs.[6]

The 946 subjects in the study were rank ordered with respect to the serum concentration of 2,3,4,7,8-pentaCDF after adjustment for age, age^2, and BMI. The goal was to re-interview the top 15 subjects, i.e., those with the highest studentized residuals above the mean of the control population. Subjects were re-interviewed about diet (in particular, consumption of beef and/or vegetables from the TR flood plain), occupation, residential history, personal habits (e.g., smoking), height, weight and weight change, breast feeding, hobbies, and recreational activities in or near the TR. More limited information was available from the main study interview for all subjects. All subjects provided written consent that had been reviewed and approved by the University of Michigan Health IRB.

Results and Discussion

Sixteen of the 23 subjects with the highest serum concentrations of 2,3,4,7,8-pentaCDF (i.e., 'outliers' after adjustment for age, age^2, and BMI) agreed to be re-interviewed. Among the seven subjects who were not re-interviewed, four could not be relocated, one declined to participate, one was deceased, and one was incarcerated. The serum levels of 2,3,4,7,8-pentaCDF for the 23 subjects ranged from 7.66 ppt to 50 ppt (or, 2.42 to 4.29 studentized residuals above the mean of the control population after correction for age, age^2, and BMI – see Table 1). The mean, median, 95th percentile and maximum for serum 2,3,4,7,8-pentaCDF in the control population of the study were 6.0 ppt, 5.4 ppt, 13.0 ppt, and 26.2 ppt, respectively.

At the time their blood was sampled, ten of the 23 outliers resided in the TR flood plain, nine lived in census blocks adjacent to the TR FP ('NFP'), and three lived elsewhere in Saginaw County ('OMS') (see Table 2). One outlier (case 3) was from the control area of the study and her exposure to 2,3,4,7,8-pentaCDF most likely was not associated with the contamination of the TR (see Table 1). In addition to residing in Jackson/Calhoun Counties, case 3 is also unique for having the highest proportion of TEQ due to PCDFs (48.5%) among the outlier subjects and among all subjects in the UMDES. Unfortunately, Case 3 was one of the subjects who could not be contacted for a follow-up interview.

Nine of 16 outliers who were interviewed reported eating meat, vegetables, wild game, and/or sport caught fish from the TR or flood plain soils from the TR. Case 1 reported a unique history of personally raising beef and vegetables on his property in the flood plain for a number of years – this case is described in more detail elsewhere.[7]

Case 2 had the highest TEQ among all 946 subjects in the study. The elevation of TEQ in her serum appears to be related to a long-standing hobby of making ceramics using ball clay known to be contaminated with PCDDs (not PCDFs or PCBs).[8] She had lived in the flood plain of the TR for almost 30 years, but denied ever eating fish, game, or garden vegetables from the TR flood plain. The source of her elevated serum level of 2,3,4,7,8-pentaCDF is unknown although the total percentage of her serum TEQ due to PCDFs was low.

Two cases (numbers 4 and 20) reported that during summer months they regularly consumed vegetables purchased at local roadside farm stands in or near the TR flood plain. For one farm stand, the farm that supplied the vegetables was known to be in the flood plain of the TR. The source of the vegetables from the other farm stand was unknown.

Aside from case 1, there were four subjects (cases 7, 9, 15 and 19) who reported regular consumption of fish from the TR and/or consumption of wild game taken from the TR flood plain.

Two cases in addition to case 1 (cases 14 and 21) reported growing vegetables on their personal property. For case 21, the soil from the garden had a TEQ of 39.2 ppt, with a congener distribution that was dominated by furans (89% of the TEQ from PCDFs) and matched the profile of contamination from the flood plain.[2] For case 14, the garden soil had a TEQ of only 10.5 ppt, though the congener pattern was dominated by furans (63% of the TEQ from PCDFs).

Living in the flood plain of the TR, or in nearby areas of Midland and Saginaw counties, appears to be associated with elevated levels of 2,3,4,7,8-pentaCDF in serum for these outlier cases, although the exact pathway of exposure is unclear in many cases. It is possible that foods from the flood plain were consumed, but that subjects were unaware of the origin of foods they ate (e.g., foods purchased in local grocery stores may have been grown in the TR flood plain). Case 3 suggests that there are other important sources of exposure to furans, particularly 2,3,4,7,8-pentaCDF, aside from the contamination in the TR flood plain. Overall, even among cases with outlier concetrations of 2,3,4,7,8-pentaCDF in serum, the contribution of PCDFs to the total serum TEQ in this population is modest.

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Table 1. Summary of TEQ and 2,3,4,7,8-pentaCDF Concentrations (in ppt on a lipid adjusted basis) in Serum Rank Ordered by Studentized Residuals of 2,3,4,7,8-PentaCDF

Case No.	Serum TEQ	Serum TEQ S.R.*	Serum 2,3,4,7,8-PentaCDF	Serum PentaCDF S.R.*	Percent of TEQ from PCDDs	Percent of TEQ from PCDFs	Percent of TEQ from PCBs
1	52.5	2.22	42.5	4.29	56.9	31.8	11.3
2	211	4.47	50.0	3.76	72.2	9.9	17.9
3	20.3	1.03	17.7	3.58	40.0	48.5	11.5
4	19.7	1.79	12.3	3.35	62.0	26.7	11.3
5	112	2.54	43.5	3.24	71.9	14.7	13.4
6	38.0	2.29	16.9	2.96	67.6	19.4	13.0
7	39.0	2.33	17.0	2.95	60.2	20.0	19.9
8	76.3	2.86	25.7	2.94	65.2	16.7	18.1
9	89.9	3.46	23.9	2.88	44.4	13.2	42.4
10	17.8	2.07	7.66	2.88	51.2	26.3	22.5
11	23.9	0.79	17.2	2.84	47.2	32.7	20.1
12	42.8	1.85	20.6	2.82	63.4	22.5	14.1
13	63.8	3.98	13.4	2.73	27.7	9.1	63.2
14	95.6	3.38	23.7	2.69	44.8	10.6	44.7
15	141	3.12	34.1	2.69	59.6	11.3	29.1
16	69.5	1.84	28.9	2.67	64.6	17.3	18.1
17	35.1	2.69	11.7	2.66	63.5	19.6	16.9
18	38.0	2.50	13.1	2.58	59.1	23.5	17.3
19	68.0	3.67	15.0	2.58	55.8	13.2	31.1
20	71.4	2.94	20.5	2.56	36.8	11.6	51.6
21	50.5	1.74	21.2	2.48	58.3	22.4	19.3
22	107	2.5	29.8	2.44	80.3	11.9	7.9
23	154.4	2.93	33.9	2.42	54.4	10.6	35.0
Jackson/ Calhoun Median	18.5	-	5.4	-	64.8	16.3	17.4
Jackson/ Calhoun 95th Percentile	46.5	-	13.0	-	73.9	24.1	35.8

*S.R., Studentized Residuals: Distance from the lognormal mean of the referent population after adjustment for age, age^2 and BMI

Table 2. Demographic and Behavioral Characteristics of 2,3,4,7,8-pentaCDF Outliers

Case No	Follow-up Status	Age at Blood Draw	Gender	Location of Residence	Reported Flood Plain Food Consumption
1	Yes	≥60	male	TR FP	Meat, Vegetables, Game
2	Yes	≥60	female	TR FP	None Reported
3	No	30-44	female	J/C	No Contact
4	Yes	30-44	female	TR FP	Flood plain vegetable stand
5	Yes	≥60	female	TR FP	None Reported
6	No	45-59	male	OMS	No Contact
7	Yes	45-59	male	NFP	Sport fish
8	Yes	≥60	male	NFP	None Reported
9	Yes	≥60	male	TR FP	Sport fish
10	No	18-29	male	NFP	No Contact
11	Yes	45-59	male	TR FP	None Reported
12	No	45-59	male	TR FP	No Contact
13	No	30-44	male	NFP	No Contact
14	Yes	≥60	male	NFP	Personal vegetable garden
15	Yes	≥60	female	TR FP	Sport Fish, Game
16	Yes	≥60	female	NFP	None Reported
17	Yes	30-44	male	NFP	None Reported
18	No	30-44	male	TR FP	No Contact
19	Yes	45-59	male	NFP	Sport Fish, Game
20	Yes	≥60	female	OMS	Flood plain vegetable stand
21	Yes	≥60	male	TR FP	Personal vegetable garden
22	No	≥60	female	OMS	No Contact
23	Yes	≥60	male	NFP	None Reported

TR FP: Tittabawassee River flood plain
NFP: Near Flood plain
OMS: Other Midland/Saginaw Counties
J/C: Jackson or Calhoun Counties

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