PREDICTORS OF SERUM 23478-PentaCDF CONCENTRATION IN A BACKGROUND POPULATION IN MICHIGAN, USA AND IN A REPRESENTATIVE USA SAMPLE

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Abstract: Background U.S. levels of 2,3,4,7,8-PentaCDF were estimated for a 2-county area of Michigan (the University of Michigan Dioxin Exposure Study), and for the entire U.S. using a population-based sample (National Health and Nutrition Examination Survey). Mean levels by age and gender are presented. The additional effects of weight loss or gain, smoking, breastfeeding, and other variables were investigated using regression models. In general, the majority of background values are less than 20 ppt. Larger values tend to occur with older age and female gender. Weight loss tends to increase serum concentrations, and weight gain, smoking, and breastfeeding tend to reduce serum concentrations. Hispanics have significantly lower concentrations than other ethnic groups.

Introduction: Serum dioxin concentrations in heavily exposed populations are often compared to populations exposed only to background levels. Modeling dioxin as a function of demographic and lifestyle variables in a background population can allow prediction of background values in different populations, and can aid in understanding the mechanism of dioxin elimination.

This investigation was carried out using data from two sources: (1) the University of Michigan Dioxin Exposure Study (UMDES), and (2) the National Health and Nutrition Examination Survey (NHANES). The UMDES collected samples of serum, house dust, soil, and vegetation from subjects (and their homes and property) living in Michigan, USA in areas potentially exposed to dioxin-like compounds as well as areas presumably exposed only to background levels of these compounds. The NHANES collected data from non-institutionalized residents of the U.S., and measured serum dioxin levels in 1230 of these subjects. This study presents prediction models for serum 2,3,4,7,8-PentaCDF levels in both the UMDES background region and the NHANES study.

Materials and Methods: The UMDES was carried out in Michigan, USA, in Midland, Saginaw and parts of Bay County (all potentially exposed areas) and in Jackson and Calhoun Counties (control areas, and the focus of this analysis). A two-stage probability household sampling design was used.[1] Eligible subjects were at least 18 years of age, lived in their current residence for at least 5 years, and provided written informed consent. A detailed exposure questionnaire asked several hundred questions including demographics, smoking history, pregnancy history, occupational exposure, food consumption, and other questions possibly related to human body burden. In addition, serum samples were collected from subjects who consented and were medically eligible to give blood as defined by the American Red Cross. Chemical analyses were performed by Vista Analytical Laboratory, Inc. (El Dorado Hills, California, USA) for the World Health Organization designated 29 PCDD, PCDF, and dioxin-like PCB congeners using US Environmental Protection Agency (EPA) methods 8290 and 1668. [4,5,6] Values below the limit of detection (LOD) were identified, and the LOD was given in each case.

The National Health and Nutrition Examination Survey (NHANES) is a publicly available dataset of national health and vitality information for a sample of the United States population, with over-sampling of younger individuals and ethnic minorities. The NHANES data were taken from the 2001-2002 sample release. All individuals answered a general questionnaire covering health, diet and social-demographics; medically eligible persons were asked to donate a blood specimen, and a sub-sample of 1230 persons aged 20 years and older was selected for additional analysis of serum dioxins and furans. Individuals 85 years and older were assigned the age of 85 to protect identity. Pregnant women (n=85) were excluded from this analysis. Chemical analyses and lipid measurements were performed by the Centers for Disease Control and Prevention laboratories. Results below the LOD were identified, and reported as LOD/√2.

Statistical Methods: For the UMDES data, the $\log_{10}$ serum dioxin level was the outcome variable in a linear regression model with demographic, lifestyle, food, and other variables as potential predictors. Values below the LOD were replaced with the LOD/√2. Covariates included age, sex, BMI, BMI loss in the past year, pack-years of smoking, months of breastfeeding the first child, and number of incomplete pregnancies. Selected interactions were tested. Residual plots were examined to confirm that model assumptions of normality and homoscedasticity were met. Backward selection was used to remove non-significant variables. The regression models used survey weights to adjust for the probability of sample selection and allow inference to the entire two-county population (SAS proc surveyreg). SAS® version 9.1 was used for all analyses.

The NHANES regression analyses required a different strategy because a substantial proportion of values (35%) were below the LOD. We used likelihood-based regression methods for left-censored data, assuming a lognormal distribution (SAS proc lifereg). We used the generalized R^2 to estimate explained variation, although it may yield an underestimate with censored data. Unfortunately, this method did not permit the inclusion of survey weights, which would have allowed inference to the entire U.S. population. We used the same covariates as in the UMDES model, with two exceptions. The NHANES data did not collect the months of breastfeeding the first child, but instead collected the number of children breastfed. We also added race/ethnicity as a covariate.

Results and Discussion: The UMDES interviewed over 1300 subjects, of whom 946 provided serum samples, 251 from Jackson/Calhoun. Of the Jackson/Calhoun samples, 1.2% fell below the LOD. The median LOD was 1.1 ppt. In the NHANES study, 1145 subjects had serum 2,3,4,7,8-PentaCDF levels measured, although 33% were below the LOD. The median LOD was 2.8 ppt [mean(s.d.)=2.9(0.9)], and the range of LOD was 1.1 to 5.4 ppt. Figure 1 shows similar overall effects of age and gender in UMDES and NHANES.

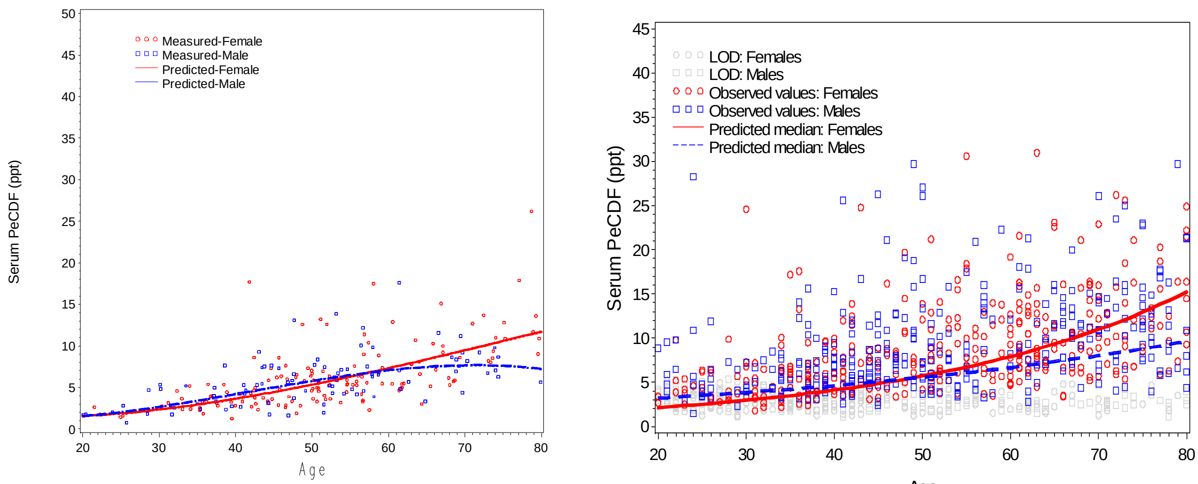

Figure 1. Plots of serum 2,3,4,7,8-PentaCDF data and model predicted means by age and gender for both (a) UMDES (n=251) and (b) NHANES (n=1145). In (b), for values below the LOD, the LOD itself is plotted (grey circles), and the predicted curves are for non-Hispanics without weight loss or gain in the past year.

Characteristics of subjects from the two groups are given in Table 1 below. The two groups are reasonably similar with respect to demographic characteristics.

Table 1. Characteristics of subjects from two background population groups.

	UMDES (n=251): Two Michigan Counties	**NHANES (n=1230):** U.S. Population
	Mean (s.d.) or %	**Mean (s.d.) or %**
Age (years)	52.3 (15.2)	49.1 (18.7)
Sex: Female	63%	54%
Body Mass Index (BMI)	28.8 (6.3)	28.2 (6.1)
BMI loss in past year	1.0 (1.7)	0.7 (1.8)
Smoking (packyears)	13.0 (18.6)	23.4 (28.3)
Breastfeeding (% of women)	53%	43%
# Incomplete Pregnancies	0.5 (1.5)	0.8 (1.2)

Table 2 below shows the final models for the two groups. Both models show effects of age, sex, and BMI loss, but several other effects are different between models. The R^2 for the UMDES model (60%) increases somewhat after adding diet and occupational variables (65%).

Table 2. Regression results predicting serum 2,3,4,7,8-PentaCDF levels from two background populations.

	UMDES: Two Michigan Counties		***NHANES: U.S. Population***	
	Coefficient	p-value	Coefficient*	p-value
Age	0.0357	<.0001	0.0080	<.0001
Age*age	-0.0003	0.0001	--	--
Sex (female)	0.4540	0.0041	-0.2926	<.0001
BMI	0.0094	0.0257	--	--
BMI loss (past yr)	0.0158	<.0001	-0.0271	0.1429
Breastfed	-0.0092	0.0001	--	--
Pack-years	-0.0119	0.0017	--	--
Age*sex	-0.0105	0.0897	0.0062	<.0001
BMI*sex	--	--	--	--
Age*age*sex	0.0001	0.0175	--	--
Age*pack-years	0.0002	0.0024	--	--
BMI*sex	-0.0110	0.0238	--	--
Age*BMI loss	--	--	0.0008	0.0357
BMI gain (past yr)	--	--	-0.0191	0.0006
Hispanic	--	--	-0.1559	<.0001
R^2 (*100%)	Adjusted R^2 = 60%		Generalized R^2 = 33%	
R^2 after addition of diet and occupational variables (*100%)	Adjusted R^2 = 65%		---	

*Coefficients were divided by 2.303 (=ln(10)) to make comparable to coefficients from UMDES model.

Figure 2 illustrates (a) an interactions in the UMDES model between gender and BMI, with BMI having a larger effect in men than in women; and (b) the NHANES effects of a past-year BMI loss or gain or 5 units, by age.

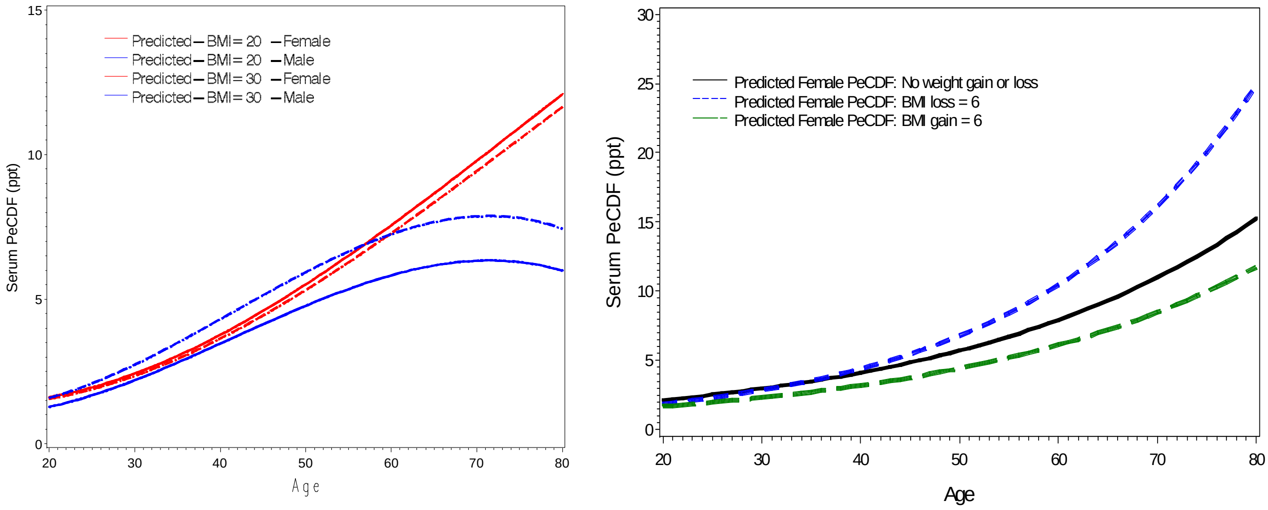

Figure 2. Illustrations of (a) BMI by gender interaction in UMDES, and (b) the effects of past-year BMI loss and gain by age on serum PeCDF in NHANES.

In conclusion, the Jackson/Calhoun sample had similar serum levels as the NHANES sample. In both groups, the strongest predictors of higher background serum 2,3,4,7,8-PentaCDF levels were older age, female gender, and recent weight loss. However, several predictors of serum concentration were different in the two populations. In Jackson/Calhoun, decreased serum levels were significantly associated with breastfeeding and smoking, whereas in NHANES, decreased serum levels were associated with weight gain and Hispanic ethnicity. These effects are consistent with previously reported effects.

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