Predictors of Serum 2378-TCDD Concentration in a Background Population in Michigan, USA and in a Representative USA Sample

Brenda Gillespie[1], Chiung-Wen Chang[1], Elizabeth Hedgeman[1], Biling Hong[1], Qixuan Chen[1], Olivier Jolliet[1], Kristine Knutson[1], Shih-Yuan Lee[1], James Lepkowski[1], Kristen Olsen[1], Peter Adriaens[1], Avery Demond[1], Timothy Towey[1], Lynn Zwica[1], Kathy LaDronka[1], Barbara Ward[1], William Luksemburg[2], Martha Maier[2], Alfred Franzblau[1], and David Garabrant[1].

[1]University of Michigan, Ann Arbor, Michigan, USA; [2] Vista Analytical Lab, El Dorado Hills, California, USA.

INTRODUCTION & OBJECTIVES

Serum dioxin concentrations were measured in two U.S. samples thought only to be exposed to background dioxin levels. Both were population-based samples: one of a 2-county area of Michigan, U.S. (the University of Michigan Dioxin Exposure Study, UMDES), and the other of the entire U.S. (the National Health and Nutrition Examination Survey, NHANES). Here we examined predictors of serum **2378-TCDD** within both populations using regression models, accounting for complex sample design and values below the limit of detection (LOD). In addition to age and gender, the effects of body mass index (BMI), weight loss or gain, smoking, breastfeeding, race and food intake were also investigated.

METHODS

UMDES Sample

- Data collected in Jackson and Calhoun Counties of Michigan, USA, using a two-stage probability household sampling design.
- Eligible subjects were at least 18 years of age, lived in their current residence for at least 5 years, and provided written informed consent.
- An exposure questionnaire collected demographics, smoking and pregnancy history, occupational exposure, and food consumption.
- Serum samples were collected from subjects medically eligible to give blood as defined by the American Red Cross.
- Chemical analyses, reporting lipid-adjusted concentrations, were performed by Vista Analytical Laboratory, Inc. (El Dorado Hills, California, USA).

NHANES Sample

- The NHANES database of national health and vitality information for a sample of the U.S. population are publicly available through the U.S. National Center for Health Statistics. The NHANES data were taken from the 2001-2002 sample release.
- Serum samples were collected from medically eligible persons; a sub-sample aged ≥20 was selected for analysis of serum dioxins and furans.
- Chemical analyses, reporting lipid-adjusted concentrations, were performed by the Centers for Disease Control and Prevention laboratories.

Statistical Methods

- For both samples, interval-censored regression methods were used to handle left censoring in cases where dioxin levels fell below the LOD. In addition, the analyses incorporated the complex sample design within the model specification.
- Covariates considered included age, gender, race, BMI, BMI gain or loss in the previous year, smoking (current, former, never), number of incomplete pregnancies, duration of breastfeeding, and selected interactions. In addition, food indicators and quantities (gm) were explored for beef, pork, poultry, game, and dairy. Lifetime consumption data were available in UMDES, but only past 24-hour data in NHANES.
- Backward elimination was used to arrive at the final models. All analysis was performed using STATA 9.2. Regression analyses used the intreg procedure.

RESULTS

Subjects from UMDES (n=251) were slightly older than those from NHANES (n=1228) (mean (s.d.) age: UMDES 52.3 (15.2), NHANES 49.1 (18.7)). UMDES was 96% Caucasian while NHANES was 44% Caucasian, 29% Hispanic, 23% African American and 4% Other/Multi-racial. Other characteristics were similar between UMDES and NHANES.

Figure 1 shows the values with model estimates by age and gender for UMDES and NHANES. UMDES had larger sample volumes, which led to smaller LOD values (below LOD: UMDES 21%, NHANES 87%).

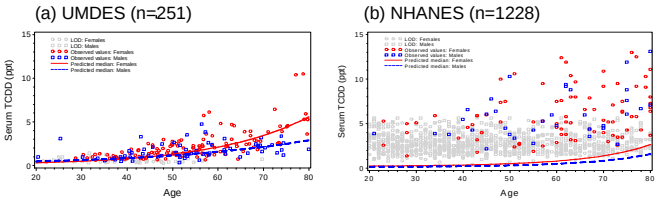

Figure 1. Plots of TCDD data and model predicted medians by age and gender for both (a) UMDES and (b) NHANES. For values below the LOD, the LOD itself is plotted (grey circles/squares). One value of 42.7 ppt for a 65-year-old male (BMI=39.9, BMI loss in past year=1.1) was omitted from the NHANES plot to show more detail for the other values.

Model estimates are given in Table 1.

- UMDES model: higher TCDD was associated with increasing age, female gender, BMI, and BMI loss (especially with increasing age), whereas breastfeeding and smoking were associated with decreasing TCDD.
- NHANES model: higher TCDD was associated with increasing age, female gender, BMI loss (especially among males), African American and Other multi-racial versus Caucasian & Hispanic, whereas smoking was associated with lower TCDD at older ages.
- The interactions between age and gender are illustrated in Fig. 1a and b.
- The UMDES interaction between age and BMI loss is shown in Fig. 2a.
- The NHANES interaction between age and smoking is shown in Fig. 2b.

Table 1. Regression results predicting serum TCDD concentration.

	UMDES	NHANES
	Estimate (s.e.)	Estimate (s.e.)
Age	.0117 (.0023)	-.0026 (.0104)
Age^2	-----	.0002 (.0001)
Sex (female)	-.3091 (.1732)	.2533 (.0791)
BMI	.0071 (.0034)	----
BMI loss (past yr)	-.0575 (.0302)	.0314 (.0134)
Breastfeeding (month)	-.0133 (.0043)	----
Pack Years	-.0029 (.0011)	.0178 (.0045)
Race (African American) †	-----	.2584 (.0857)
Race (Other or Multi-racial) †	-----	.2947 (.1209)
Age*Sex	.0077 (.0030)	-----
Sex*BMI loss	-----	-.0562 (.0209)
Age*BMI loss	.0017 (.0006)	-----
Age*Pack Years	-----	-.0003 (.0001)

†Reference group for race is Caucasian & Hispanic combined

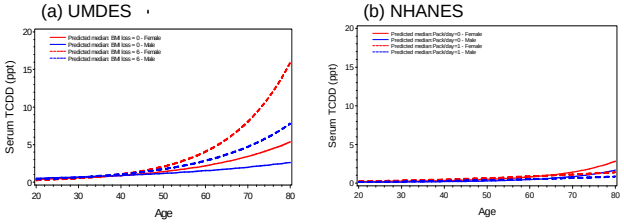

Figure 2. Plots of TCDD model interactions for a) UMDES (gender by BMI loss) and b) NHANES (gender by pack years).

CONCLUSIONS

These results showed generally low levels of serum TCDD in background U.S. populations, but higher concentrations with older age particularly among women. Breastfeeding was associated with lower TCDD levels in UMDES. Both samples showed higher TCDD with BMI loss, particularly at older ages in UMDES, suggesting that TCDD is concentrated as body fat is lost. Smoking was associated with lower TCDD in both samples. Race effects could only be investigated in NHANES data: African American and Other/Multi-racial had higher TCDD levels than Caucasians or Hispanics. There was no evidence that specific foods consumed had an impact on serum TCDD levels.

Serum dioxin concentrations in exposed populations are often compared to background populations. Modeling dioxin as a function of demographic and lifestyle variables in a background population can allow background prediction in different populations.

Financial support for this study comes from the Dow Chemical Company through an unrestricted grant to the University of Michigan.