THE RELATIONSHIP BETWEEN DIOXIN CONCENTRATIONS (TEQ) IN BLOOD AND BREAST FEEDING

Knutson Kristine[1], Hong Biling[1], Chen Qixuan[1], Chang Chiung-Wen[1], Jiang, Xiaohui[1], Hedgeman Elizabeth[1], Towey Timothy[2], Gillespie Brenda W[1], Franzblau Alfred[1], Lepkowski James[3], Adriaens Peter[4], Demond Avery[4], Garabrant David H[1]

[1]School of Public Health, University of Michigan, Ann Arbor, Michigan 48109, USA; [2]LimnoTech, Ann Arbor, Michigan 48108, USA; [3]Institute for Social Research, University of Michigan, Ann Arbor, Michigan 48104, USA; [4]College of Engineering, University of Michigan, Ann Arbor, Michigan 48109, USA

Introduction

Studies of blood and breast milk from mothers have demonstrated that dioxins are eliminated from the body during breast feeding[1-5]. The purpose of this paper is to explore the relationship between dioxin toxic equivalency (TEQ) levels in blood and breast feeding for participants in a large population-based exposure study in Michigan, USA. The focus is on exploring 1) the overall effect of lifetime duration of breast feeding and 2) the effects of duration of breast feeding the first time compared to duration of breast feeding additional children.

Materials and Methods

The data come from the University of Michigan Dioxin Exposure Study (UMDES), which was conducted to identify exposure pathways by which dioxin contamination in the environment contribute to dioxin concentrations in blood. Study participants were selected from five populations in Midland, Saginaw, Bay, Jackson, and Calhoun counties in Michigan in 2004-2005 using a multi-stage sampling procedure. In order to be eligible to participate in the UMDES, subjects had to be at least 18 years old and had to have lived in their residence for at least five years.

Serum analyses for dioxins were performed by Vista Analytical Laboratory (El Dorado Hills, California, USA) for the 29 polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and dioxin-like polychlorinated biphenyls (PCBs) for which the consensus toxic equivalency factors (TEF) have been published[6, 7], using modified US EPA protocols 8290[8] and 1668[9]. Results for concentrations that fell below the analytical limit of detection (LOD) were estimated by LOD/√2 for analysis[10]. Toxic equivalencies (TEQs) were calculated based on the World Health Organization 2005 toxic equivalency factors (TEFs)[7]. All blood sample results were lipid adjusted and survey weighted to characterize the populations of the regions.

Information on pregnancy and breast feeding were obtained during an hour-long interview of each study participant. The interview was administered by trained interviewers and included questions grouped into the following eight categories: health, residential history, property use, work history, recreational activities, food consumption, current diet, and demographics. The full UMDES protocol[11] is available online at www.umdioxin.org.

SAS version 9.1 statistical software was utilized to complete all analyses[12]. All analyses for this part of the UMDES were performed using only the female UMDES participants. Linear regression models were run for the $\log_{10}$ of the serum TEQ, adjusting for all other covariates in the UMDES model, including age, body mass index, smoking status, food consumption, and recreational activities. Regression models were run twice with different breast feeding variables included in each model. In the first model, the breast feeding variable accounts for the total lifetime months of breast feeding. In the second model, two breast feeding variables were included in the model to account for months of breast feeding for the first time and months of breast feeding additional children.

Influence diagnostics were performed on each model to investigate the effects of potentially influential observations. For each model, the top three influential observations were identified by calculating DFBETAs

which are a normalized measure of the effect of observations on the estimated regression coefficients[12]. Regression models were then rerun after dropping the single most influential observation determined by the DFBETAs. If the regression coefficients did not change in terms of its significance, the model was considered to be stable. If the regression coefficients did change in terms of its significance, the second and third influential observations were subsequently dropped from the models until the model was considered to be stable.

Results and Discussion

Descriptive Statistics

Serum samples and interviews were collected from 946 UMDES study participants. Five hundred and thirty-two of the study participants were women, 442 of the women had at least one child, and 241 of the women with at least one child breast fed for at least one month. The mean and median duration of lifetime breast feeding for women who breast fed at least one month were 14.1 months and 6 months, respectively. The mean number of children for women in the study was 2.2. The mean length of breast feeding for the first breast fed child and additional children was 5.72 months and 14.1 months, respectively (Table 1).

Table 1: Survey weighted descriptive statistics for female UMDES study participants

		Breast Feeding (months)						
Variable	**N**	**Mean**	**S.E.**	**Min**	**Median**	**75th%ile**	**95th%ile**	**Max**
First breast fed child*	241	5.72	0.63	1	3	6	18	45
Additional breast fed children	157	14.1	3.18	1	7	18	42	120
Total lifetime breast feeding	241	14.1	2.09	1	6	16	54	120

*Note: The first breast fed child is not necessarily the first born child

Regression Results for the TEQ

The two sets of regression models, exploring the overall effect of lifetime duration of breast feeding and the duration of breast feeding the first time compared to breast feeding additional children, are displayed in Table 2 and Table 3.

After adjusting for covariates, the total duration of breast feeding in a woman's lifetime was significantly associated with a lower TEQ in blood (Table 2). The parameter estimates indicate that each six month increase in breast feeding was associated with a 3.7% decrease in blood TEQ. This is a stable model, there are no influential observations.

Table 2: The effect of lifetime breast feeding

	All Breast Feeding Females (n=241)	
Variable	Estimate	p-value
Total lifetime breast feeding*	-0.0028	0.0004

*measured in months of breast feeding

In a model with all breast feeding females, months of breast feeding the first time was not significantly associated with blood TEQ while breast feeding additional children was significantly associated with a lower TEQ in blood (Table 3). However, the influence diagnostics showed that the first breast fed child and additional

breast fed children variables were each influenced by one single observation. If this influential observation is excluded from the analyses, the effect of breast feeding the first child becomes significantly associated with a lower TEQ in blood while breast feeding additional children becomes marginally significantly associated with a lower TEQ in blood. Overall, the effect of breast feeding the first breast fed child was still larger than the effect of breast feeding additional children. The parameter estimates indicate that each six month increase in breast feeding of the first breast fed child was associated with a 7.6% decrease in blood TEQ and each six month increase in breast feeding additional children was associated with a 2.5% decrease in blood TEQ.

Table 3: The effect of breast feeding for the first time compared to breast feeding additional children

	All Breast Feeding Females (n=241)		Without the Most Influential Observation (n=240)	
Variable	Estimate	p-value	Estimate	p-value
First breast fed child*	-0.0031	0.2586	-0.0057	0.0011
Additional breast fed children*	-0.0025	0.0217	-0.0018	0.0721

*measured in months of breast feeding

Future Directions

Future investigations will look at the impact of environmental contamination on the relationship between breast feeding and dioxin concentrations.

Of the 29 dioxin, furan, and PCB congeners analyzed, the five congeners in the UMDES that provide the greatest contribution to the blood TEQ are 2378-TCDD, 123678-HxCDD, 23478-PeCDF, 12378-PeCDD, and PCB 126[13]. Regression analyses will also be performed on these additional dioxin congeners to determine if the effects of breast feeding vary by congener.

Acknowledgements

Financial support for this study comes from the Dow Chemical Company through an unrestricted grant to the University of Michigan. The sponsor did not participate in the design of the study or in the collection, analysis or interpretation of the data. The authors acknowledge Drs. Linda Birnbaum, Ronald A. Hites, Paolo Boffetta, and Marie Haring Sweeney for their guidance as members of the UMDES Scientific Advisory Board (SAB).

References

1. Abraham K., Papke O., Gross A., Kordonouri S., Wiegand S., Wahn U. and Helge H. *Chemosphere* 1998; 37: 1731.
2. Furst P., Kruger C., Meemken H-A., and Groebel W. *Chemoshpere* 1989; 18: 439.
3. Schecter A., Papke O., Lis A., Ball M., Ryan J.J., Olson J.R., Li L. and Kessler H. *Chemosphere* 1996; 32: 543.
4. Schecter A., Ryan J.J. and Papke O. *Chemosphere* 1998; 37: 1807.
5. Uehara R., Peng G., Nakamura Y., Matsuura N., Kondo N., and Tada H. *Chemoshpere* 2006; 62: 1135.
6. Van den Berg M., Birnbaum L., Bosveld A.T.C., Brunstrom B., Cook P., Feeley M., Geisy J.P., Hanberg A., Hasegawa R., Kennedy S.W., Kubiak T., Larsen J.C., Rolaf van Leeuwen F.X.., Djien Liem A.K., Nolt C., Peterson R.E., Poellinger L., Safe S., Schrenk D., Tillitt D., Tysklind M., Younes M., Waern F., and Zacharewski T. *Environ Health Perspect* 1998; 106: 775.
7. Van den Berg M., Birnbaum L.S., Denison M., DeVito M., Farland W., Feeley M., Fiedler H., Hakansson H, Hanberg A., Haws L., Rose M., Safe S., Schrenk D., Tohyama C., Tritscher A., Tuomisto J., Tysklind M., Walker N. and Peterson R.E. *Toxicol Sci* 2006*;* 93: 223.

8. United States Environmental Protection Agency (US EPA). Washington, DC: Office of Solid Waste and Emergency Response, 1994.
9. United States Environmental Protection Agency. Washington, DC: Office of Water, 1999.
10. Finkelstein MM, Verma DK. *AIHAJ* 2001;62: 195-198.
11. Garabrant, D.H., Franzblau, A., Lepkowski J., Gillespie B.W., Adriaens P., Demond A., Ward B., LaDronka K., Hedgeman E., Knutson K., Zwica., Olson K., Towey T., Chen Q. and Hong B. *In Progress.*
12. SAS Institute. Cary, NC: SAS Institute Inc., 1999.
13. Hedgeman E., Chen Q., Hong B., Chang C-W., Olson K., LaDronka K., Ward B., Adriaens P., Demond A., Gillespie B.W., Lepkowski J., Franzblau, A. and Garabrant, D.H. *In Progress.*