THE UNIVERSITY OF MICHIGAN DIOXIN EXPOSURE STUDY: A FOLLOW-UP INVESTIGATION OF A CASE WITH HIGH SERUM CONCENTRATION OF 2,3,4,7,8-PentaCDF

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Overview

- As part of the UMDES Outlier Investigations, we followed-up on participants with extreme concentrations of serum 2,3,4,7,8-PentaCDF
- 2,3,4,7,8-PentaCDF is of interest because of the increased concentrations of furans in residential soils and sediments surrounding the Tittabawassee River
- The individual with the highest (age-adjusted) concentration of serum 2,3,4,7,8-PentaCDF reported a history of raising and consuming beef cattle from the Floodplain
- This consumption resulted in a 21% increase to his serum concentration (as compared to a similarly aged person in the referent community).
- This participant and his history represent a 'worst case' scenario of exposures to Tittabawassee River soils

Background

As part of the University of Michigan Dioxin Exposure Study (UMDES) the 29 congeners of polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and dioxin-like polychlorinated biphenyls (PCBs) that have consensus toxic equivalency factors (TEFs) 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 possible human exposure to dioxin-contaminated sediments in the Tittabawassee River (TR).

Background

- Approximately 80% 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
- The half life of 2,3,7,8-TCDF is short and it does not accumulate in humans
- The 2,3,4,7,8-PentaCDF congener has a prolonged serum half life in humans (~7.8-10 years) and therefore can serve as a biomarker of exposure to contaminated sediment

Background

- The UMDES involved a two-stage clustered random sampling design to recruit a representative sample of subjects from five counties in the State of Michigan
- Eligible subjects were at least 18 years old, and lived in their homes $\geq$ 5 years
- The main study involved an hour-long interview and obtaining blood, house dust and soil samples for chemical analyses
- 946 subjects provided blood samples that were analyzed for PCDDs, PCDFs and PCBs (reported in parts per trillion (ppt) on a lipid adjusted basis)

Background

- The individual with the highest adjusted serum level of 2,3,4,7,8-PentaCDF in the UMDES reported a unique history involving consumption of beef and vegetables raised in the floodplain (FP) of the TR.
  - 42.5 parts per trillion 2,3,4,7,8-PentaCDF, or 4.29 studentized residuals above the log-normalized mean of the control population after adjustment for age, age^2, and body mass index
- This report describes his results and results of a follow-up investigation of friends and family members who also reported eating the beef and/or vegetables.

Outlier Investigation

- The index case reported a unique dietary history of consuming beef and vegetables from the TR FP
- He identified 15 friends and family members who were most likely to have consumed beef and/or vegetables from the TR FP; all 15 were invited and agreed to participate in the follow-up investigation
- Participants were interviewed about diet (particularly consumption of beef and/or vegetables from the TR FP), occupation, residential history, personal habits (e.g., smoking), height, weight, hobbies and recreational activities in or near the TR
- Participants were also invited to donate blood for measurement of PCDDs, PCDFs and PCBs in serum

Exposure/Diet History - Beef

- From 1984/1985 to 1996 the index case raised cows on his land in the TR FP.
- Each year in the spring he bought 2-3 calves from local farms outside the TR FP and raised them for ~18 months.
- The cows routinely roamed and grazed in areas that regularly flooded. They ate FP grass, grain not grown in the FP, and hay from a nearby field that was near the FP but did not flood.
- The cattle were slaughtered at a local commercial abattoir. The meat passed federal inspection, but the livers did not, and no organ meats were consumed.
- The meat was distributed to friends and family members. At the time of this follow-up investigation (2008) no meat samples were available for chemical analyses.

Exposure/Diet History - Vegetables

- Beginning in the early 1980's the index case started a vegetable garden in the TR FP. Vegetables included: asparagus, tomatoes, cucumbers, green beans, corn, radishes, potatoes, beets, green peppers, onions, Swiss chard, watermelon and pumpkins.

- The vegetables also were shared with the same friends and family members. Vegetables were canned and consumed year-round. The vegetable garden was largely discontinued in about 1997, but some limited vegetable consumption continued through 2008 (only asparagus and occasionally tomatoes).

Table 1: Summary of Reported Consumption of Beef/Vegetables

	Floodplain Beef Consumption			Floodplain Vegetable Consumption		
Case Number	Years Consumed	Avg Meals per Year	Approx. Total Beef Meals	Years Consumed	Avg Meals per Year	Approx Total Veg. Meals
1 (index)	1985-1996	48-96	792	1982-2008	40	1040
2	1985-1996	144-192	1848	1987-2007	46	920
3	1985-1996	144-180	1848	1988-2008	6	120
4	1985-1996	104-280	1559	1988-2008	26	520
5	1985-1996	2	22	1997-2007	4	40
6	1985-1996	156-20	2002	1985-1993	46	368
7	1985-1996	144	1584	1985-2004	59	1121
8	1985-1996	208	2288	1985-1995	26	260
9	None	0	0	1998-2008	52	520
10	1985-1996	52	572	7yrs	13	91
11	1985-1996	52	572	1975-1990	33	495
12	1986-1990	96	384	1980-2007	90	2430
13	1990-1996	240-300	1656	1998-2008	91	910
14	1985-1996	52	572	10 yrs	3	30
15	2 yrs	360	720	2000-2006	unsure	-
16	1985-1996	120	1320	1986-2006	6	120

Table 2: Summary of Serum Results

Case Number	TEQ_{DFP05}, ppt	TEQ Studentized Residuals*	2,3,4,7,8-PentaCDF, ppt	PentaCDF Studentized Residuals*	Predicted PentaCDF, ppt**	Percent Contribut'n of Excess to TEQ
1 (index)	52.4	2.2	42.5	4.3	6.8	20.4
2	17.6	1.2	14.7	3.5	3.5	19.1
3	18.1	1.0	9.5	2.3	3.8	9.4
4	44	0.3	21.4	1.8	9.9	7.9
5	69.4	1.5	20.1	1.6	10.2	4.3
6	33.1	0.8	12.9	1.5	7.2	5.1
7	24.1	0.5	8.84	1.0	6.0	3.5
8	24.3	0.2	8.42	0.6	6.7	2.1
9	13.7	-0.4	6.34	0.7	4.9	3.1
10	31	1.0	7.11	0.4	6.4	0.7
11	19.6	0.0	6.72	0.5	5.9	1.3
12	22.5	-0.3	8.45	0.5	7.3	1.5
13	14.8	-0.5	6.03	0.4	5.4	1.4
14	20.4	0.1	6.29	0.2	6.0	0.5
15	19.3	-0.7	6.94	-0.0	7.3	-0.6
16	19.2	-0.3	5.34	-0.4	6.4	-1.7

*Based on lognormal mean of Jackson/Calhoun population after adjustment for age, age^2 and BMI

**Predicted serum 2,3,4,7,8-PentaCDF based on Jackson/Calhoun population with adjustment for age, age^2 and BMI

Figure 1: Serum $TEQ_{DFP-2005}$ Results by Age with Quantile Curves

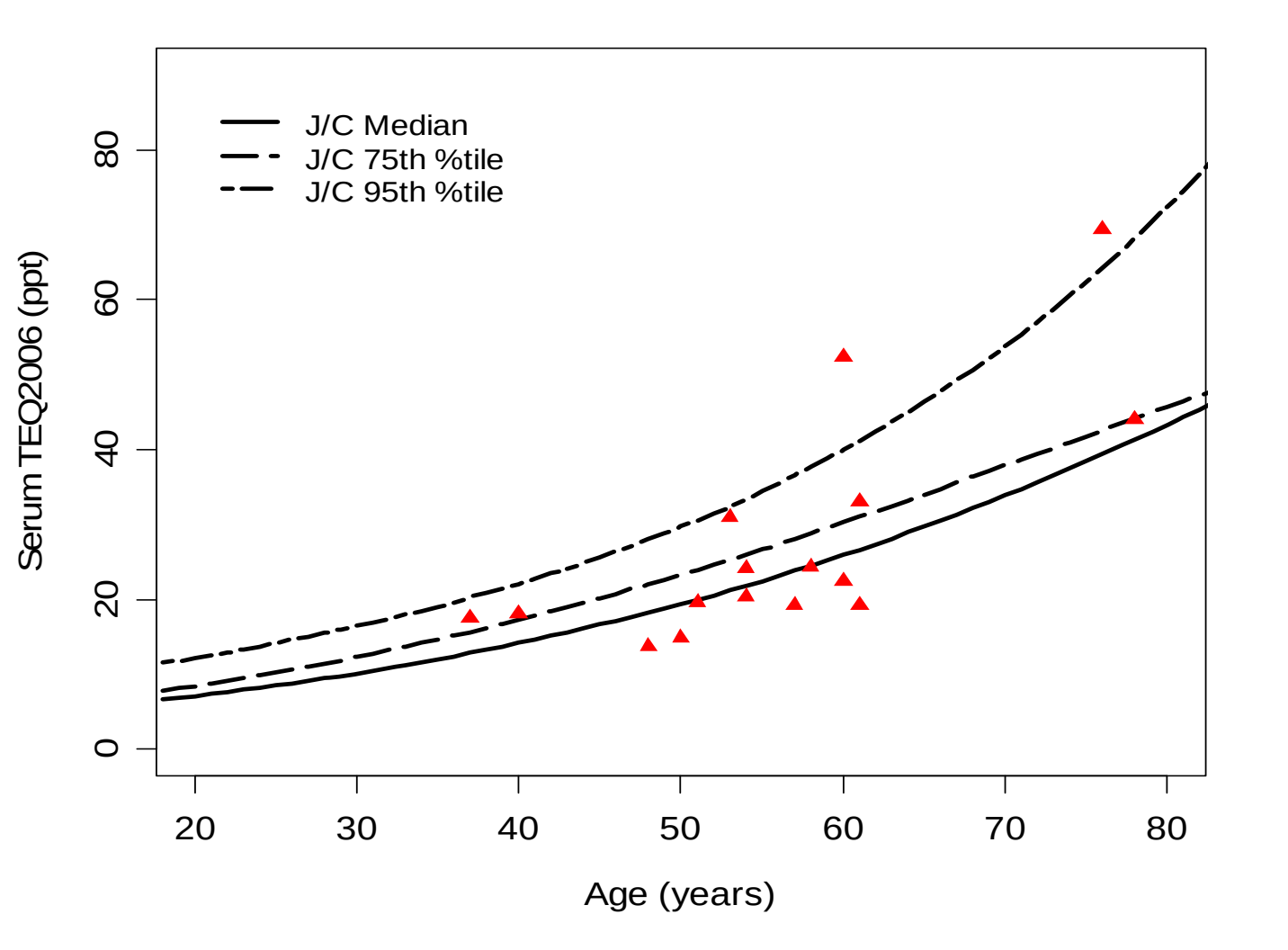
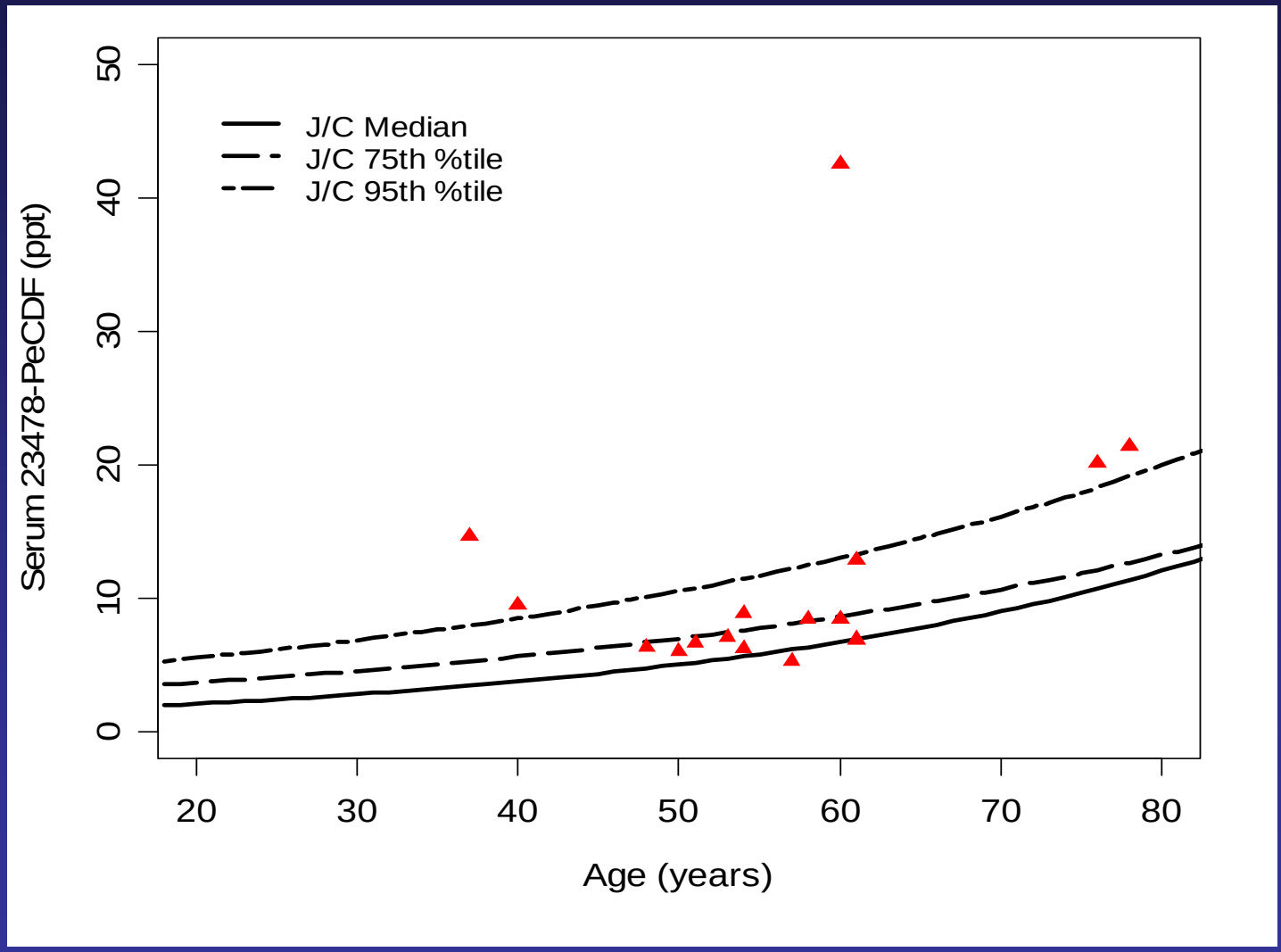


Figure 2: Serum 2,3,4,7,8-PeCDF Results by Age with Quantile Curves



Conclusions

- Most cases included in this follow-up investigation had higher adjusted serum concentrations of 2,3,4,7,8-PentaCDF than the mean of the control population.
- With two exceptions, all cases were less than 2.5 studentized residuals above the mean.
- The mean extra or excess contribution of 2,3,4,7,8-PentaCDF to the TEQ was 4.9%, and was less than 21% in all cases. This contribution may have been higher in the past during the period of active beef consumption.

Conclusions

- The current cases reported a unique dietary history, one that appears to represent a ‘worst case’ scenario of exposure to contamination in TR sediments within our representative sample of the population

- Prolonged and regular consumption of beef and/or vegetables raised in the FP of the TR can be an important route of exposure to dioxin contamination, but the contribution of such exposure to serum TEQ above the control population mean is modest (less than 21%).

Please see the related poster on display during the Poster Session:

Poster 361 - 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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