CURRENT ESTIMATES OF BACKGROUND SERUM TCDD LEVELS IN THE UNITED STATES

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Abstract
Three recent studies of chlorinated dioxin-like compounds in the serum of residents in the United States were compared to capture the current body burden of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD). The three studies, two at a local level, one at a national level, showed that serum TCDD levels in the general population are somewhere in the range of 1 - 2 pg/g lipid. Age stratification indicated that adults under the age of 45 years often have serum TCDD levels falling below 1 pg/g lipid. With decreasing ambient exposure to chlorinated dioxin-like compounds, the general population in the United States is continuing to see a concurrent decrease in TCDD and total body burden of chlorinated dioxin-like compounds.

Introduction
With the exception of accidental incidents of point-source contamination, levels of polychlorinated dibenzo-*p*-dioxins, polychlorinated dibenzofurans and dioxin-like polychlorinated biphenyls (PCBs) have been decreasing in the environment. Mirroring this trend, levels in the foodchain and the general population have been decreasing over the past few decades.[1] For example, a recently analyzed pooled human serum sample from 1973 yielded a total TEQ-WHO_{98} of 150 pg/g lipid and a TCDD level of 13.8 pg/g lipid; pooled serum taken from subjects in 2003 yielded a total TEQ-WHO_{98} of 26.8 and TCDD level of 1.77 pg/g lipid.[2] Likewise, individual studies with referent populations have yielded a smattering of background human serum data to follow this decreasing trend. One of the first studies to measure TCDD in serum found a mean level of 5.7 and a median level of 4.6 pg/g lipid from 17 subjects in 1986.[3] A mean serum TCDD level of 7 pg/g lipid was measured from 79 reference subjects in 1988.[4] Studies from the 1990s put the mean serum TCDD level in the general population at approximately 4 pg/g lipid.[5]

Over the past decade a push has been made to monitor the serum levels of dioxins in the general population - this has been fueled by concerns that body burdens due to background exposures are still sufficient to cause adverse health effects. The aim of this paper is to compare the serum TCDD levels from three recent studies of the general population in the United States. Data is taken from the 2004-2005 University of Michigan Dioxin Exposure Study (UMDES) which measured dioxin-like compounds in the serum of 946 Michigan subjects including 251 control subjects; the Agency for Toxic Substances and Disease Registry's (ATSDR) 2001 study of 415 subjects from two parishes in Louisiana; and the 2001-2002 National Health and Nutrition Examination Survey (NHANES) of the United States which included 1228 serum dioxin measurements from the general population.[6,7,8] While each study has strengths and weaknesses, the overall comparison allows for a more complete picture of the current human body burden of TCDD in the United States.

Materials and Methods
The entire protocol for the University of Michigan Dioxin Exposure Study can be found elsewhere.[6] Briefly, adults age 18 and over who had lived in their current residence for five or more years were eligible to participate. Eligible subjects were randomly selected from one of five counties in Michigan and invited to donate an 80 milliliter whole blood sample for analysis. Data from two counties used as a reference population (Jackson and Calhoun Counties, MI) are included in this paper. For this population, serum samples were obtained and analyzed in 2005. Isolated serum was analyzed for the 29 congeners recognized by the World Health Organization as having dioxin-like activity, including TCDD. Samples that fell below the limit of detection were estimated using LOD/$\sqrt{2}$. All results shown are lipid adjusted and population weighted to reflect the entire referent population

region

The protocol and results from the 2001 exposure study of residents in Louisiana can be downloaded through ATSDR.[7] Residents 15 years of age and older from two parishes in Louisiana were randomly selected to participate; Calcasieu Parish was chosen because of its proximity to industrial sources of dioxins and Lafayette Parish was chosen as a reference population. Analyses showed no significant differences in serum total TEQ or congener pattern between the two parishes. The serum TCDD levels cited in this report were obtained from a subsequent publication of the combined parish data using single imputation and multiple imputation methods to more precisely estimate serum levels of TCDD that fell below the limit of detection.[9] This data is lipid adjusted, but is not population weighted.

The 2001-2002 serum dioxin dataset from NHANES is freely available through the NHANES website.[8] NHANES serum analyses for dioxins are limited to a sub-sample of adults age 20 years and over who reside in the United States. Data from pregnant women were omitted for this comparison, resulting in a final N = 1145 individuals. Samples that fell below the limit of detection were estimated using LOD/√2. Results shown are lipid adjusted and survey weighted to reflect the United States population.

Results and Discussion

Lipid adjusted serum TCDD levels for the three studies are listed in Table 1. A range of upper percentiles is provided to display the right-handed side of the distribution. Lower percentiles were not provided because they rely more heavily on estimated concentrations (see column "Fraction Below LOD"). Table 1 indicates that the overall median serum TCDD level in adults in the United States is somewhere in the range of 1 - 2 pg/g lipid. The three studies referenced suggest that ten percent or less of the general adult population has a body burden of TCDD over 5 pg/g lipid – this is in contrast to the median levels of 4 -5 pg/g reported in earlier decades.

Table 1: Serum TCDD Levels from Three Recent Studies in the United States

	Year of Sample	N	Fraction < LOD	Percentile of Serum TCDD (pg/g lipid)			
				50^{th}	75^{th}	90^{th}	95^{th}
UMDES Referent	2005	251	0.207	1.4	2.3	3.6	4.7
Louisiana	2002	415	0.615	0.6-1.2	2.8-3.1	5.1-5.3	7.2
NHANES	2001-2002	1145	0.866	2.1	2.8	3.8	5.3

Table 2 presents the same data broken down by age group. It is of note that, for the Michigan and Louisiana studies, estimates of the median levels fall at or below 1 pg/g for adults under the age of 45 years. Median levels for persons 45 years and over are around 2 - 3 pg/g. Over the next decade human levels of TCDD may fall below detection limits despite improving technology; larger volumes of serum may be necessary for detection of some congeners.

Table 2 also suggests that the 95^{th} percentile serum TCDD level for the oldest age group is somewhere in the range of 10 pg/g lipid. This is a large increase from the 4 - 5 pg/g serum levels in the 95^{th} percentiles of the younger age brackets. Across the three studies and all the percentiles, there is a larger increase in serum levels between the final two age brackets (from 45 – 59 years to the 60 and over) than there are between any other age bracket. This is partially due to larger range of ages grouped into the highest age bracket, but also an indication that the oldest age bracket experienced a greater environmental exposure over their lifetime.

With the decreasing serum TCDD levels in the general population, the percent contribution to the total TEQ provided by TCDD is also decreasing. Pooled serum analyses from Dallas, Texas, USA by Schecter et al from 1973 and 2003 show the percent contribution of TCDD to the TEQ-WHO_{98} decreasing from 9% to 7%, respectively, even as the total TEQ is decreasing.[2] Likewise, the percent contribution to the TEQ-WHO_{98}

calculated from the medians in the UMDES referent population put TCDD levels at 6% of the total TEQ.

The three studies referenced in Tables 1 and 2 all point to a continued decreasing exposure to TCDD by the general population as compared to previously published serum data. Though limited to a select region in the United States, the Michigan and Louisiana studies show reasonably similar distributions. One caveat is that the racial make-up of both study populations is primarily white. On the other hand, NHANES samples multiple different ethnicities from multiple locations. Though the detection limits are poor due to the small serum aliquot, NHANES is able to offer a good estimate of the upper bounds of dioxin levels in the general population.

Table 2: Serum TCDD Levels by Age Group

Age Group (years)	Study	N	Fraction < LOD	Percentile of Serum TCDD (pg/g lipid)			
				50^{th}	75^{th}	90^{th}	95^{th}
18 – 29	UMDES	16	0.75	0.4	0.5	1	3.1
	Louisiana	102	0.941	0.5 – 0.7	0.6 – 1.3	0.8 – 2.1	1.9-3.3
	NHANES	167	0.982	2.3	2.7	3.6	3.9
30 – 44	UMDES	66	0.318	0.9	1.4	1.8	1.9
	Louisiana	101	0.693	0.6 – 1.1	1.7 – 2.3	3.2 – 3.3	4.0 – 4.4
	NHANES	323	0.954	2	2.7	3.3	3.8
45 – 59	UMDES	98	0.173	1.5	2.3	2.8	3.5
	Louisiana	110	0.518	0.9 – 1.7	3.2 – 3.4	4.3 – 4.4	5.6 – 5.9
	NHANES	256	0.898	2.1	2.7	3.5	5.2
60 and over	UMDES	71	0.028	2.6	3.9	5.3	7.7
	Louisiana	102	0.314	3.5 – 3.6	5.9	8.3	11.7
	NHANES	399	0.727	2.4	3.8	7.9	9.9

As serum TCDD and total TEQ levels in the general population continue to fall, emphasis will likely shift from monitoring individual congeners to monitoring total dioxin-like activity. As long as there is the concern of health effects due to background exposure there will need to be a method for monitoring population trends.

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