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Comparing the Predicted Uptake of TCDD Based on Exposure Calculations With The Actual Uptake: A Case Study of Residents of Times Beach, Missouri

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Abstract

The purpose of this evaluation was to compare the "actual" systemic uptake (absorbed amount) of 2,3,7,8-Tetrachloro-dibenzo-p-dioxin (TCDD) in residents (as estimated by measurements of TCDD in blood) to that "predicted" by standard exposure assessment calculations (using default or scenario specific exposure factors). A few people who lived in Times Beach, Missouri were evaluated. The annual average daily uptake during their residency in this town for five persons was back-calculated from recent blood data using a pharmacokinetic model. For people who were categorized as moderately or highly exposed, the estimated uptake based on site-specific data was within a factor of two of the actual uptake. The uptake estimated using EPA default assumptions tended to significantly overestimate (by a factor of about 5) the actual uptake. The results of the study indicate that scenario specific factors, coupled with standard exposure assessment formulas, much more accurately predict the actual uptake than default approaches. Our results indicate that enough is known about the transfer of TCDD from various media to humans to accurately estimate exposure (respectively or prospectively) and the subsequent uptake if an adequate amount of site-specific data are available.

Introduction

The purpose of this study was to determine whether the "actual" systemic uptake (absorbed amount) of TCDD by residents (as estimated by measurements of TCDD in blood) can be accurately "predicted" using standard exposure assessment calculations (using default or scenario-specific exposure factors). Since TCDD can be measured in blood at parts per quintillion (ppq) concentrations and because it has a long half-life in humans, historic exposures to TCDD can be estimated many years after exposure with reasonable accuracy by simply collecting blood samples.⁽¹⁾ In this evaluation, we "predicted" the uptake of TCDD by those living at Times Beach and compared

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it to their "actual" uptake. The "predicted" body burden was estimated twice; once using scenario-specific parameters and once using EPA's default exposure factors. The actual average daily uptake of TCDD due to contaminated soil for each individual was back-calculated using standard pharmacokinetic equations and blood data collected a few years after exposure.

A number of published papers have discussed how to estimate the human uptake of TCDD when it is present in soil or housedust.⁽²⁻⁶⁾ This study differs from previously published work in that the actual daily uptake is compared against the results of a site-specific exposure assessment.

Methods

Serum (lipid adjusted) concentrations of TCDD in adults and children were obtained from a database of 30 individuals who were measured several years after they lived at Times Beach.⁽⁷⁾ Adults were classified as having relatively "high," "moderate," or "low" exposure based on their serum lipid TCDD levels (47, 32 and 14 ppt, respectively). Likewise two children with relatively "high" (42 ppt) or "low" (15 ppt) serum levels were also analyzed. From these data, peak serum lipid levels of TCDD on the last day they lived in town were estimated using pharmacokinetic methods (back calculated from serum concentrations which were measured several years post-exposure).^(1,8)

The concentration vs. time curve was divided into three parts (time before, during and after exposure). It was constructed based on date of birth, measured serum concentration, date of measurement, date of first exposure, and date of last exposure. The curve was constructed using a three-step process. First, the measured serum lipid level was back calculated to the peak concentration (C_{peak}), which occurred on the last day of residence, using the following equation:

$$C_{peak} = \frac{C_{meas}}{e^{-k \Delta t}} \quad (1)$$

where C_{meas} is the measured serum lipid TCDD concentration (ppt) (which occurred several years after the last date of exposure), k is the first-order rate constant for elimination ($year^{-1}$), and Δt is the time (years) between the date of last exposure and the date of serum measurement. Second, the concentration-time curve over the period of exposure was estimated using equation (1) assuming a constant infusion rate, so that the concentration on the day of last exposure corresponds to the peak concentration. Finally, a constant 10 ppt wet weight serum lipid concentration for TCDD was assumed for adults for the years prior to first exposure in the community since this has been considered a reasonable "background" blood concentrations for Americans who were born 1950-1970.

The validity of this back calculation procedure is predicated on the assumption that uptake is constant during the years of exposure. Although the actual oral, dermal, and inhalation uptake of TCDD may have varied on a day-to-day or week-to-week basis, this variability is essentially irrelevant. The shape of the overall concentration-time curve is virtually insensitive to fluctuations in daily intake levels of

TCDD due to its extremely long half-life and periods of minimal or no intake.

The half-life for TCDD elimination rates have been characterized by a scientist who voluntarily provided values for biologic half-life in a value of 7.5 years was used for actual lipid adjusted serum concentrations presented in Table 1.

Table 1: Site-specific Default Values to Predict the Default Value

Exposure Factors
Serum Lipid TCDD Concentration (ppt) in 1982
TCDD Concentration in Soil (ppt)
Exposed Skin Surface Area (cm ²)
Ingestion Rate of soil and housedust (mg/day)
Inhalation Rate (m ³ /day)
Soil Adherence Factor (mg/cm ²)
Soil Bioavailability (unitless)
Dermal:
Ingestion:
Inhalation:
Exposure Frequency (days/year)
Exposure Duration (years)
Body Weight (kg)
Time Since Last Exposure (yr)
Age at Last Exposure (yr)

Estimated Peak Body Burden

The peak lifetime blood concentration of TCDD at Times Beach was estimated from the results of the exposure assessment studies, or see

TCDD due to its extremely slow elimination from humans.⁽⁶⁾ For example, during relatively long periods of minimal or no intake the circulating concentration of TCDD remains unchanged.

The half-life for TCDD elimination in humans is fairly well understood. For example, elimination rates have been characterized for the Ranch Hand cohort,⁽⁹⁾ for industrial workers in Germany,⁽¹⁰⁾ for a scientist who voluntarily ingested TCDD,⁽¹¹⁾ and for the Seveso population.⁽¹²⁾ Mean or median values for biologic half-life in humans from these studies range from 5.2 to 9.7 years. An intermediate value of 7.5 years was used in this analysis and is commonly used in these calculations.^(1, 8, 13) The actual lipid adjusted serum concentrations of TCDD for each adult and child in this study are presented in Table 1.

Table 1: Site-specific and Default Exposure Factors, as well as, Serum Lipid Concentrations Used to Predict the Uptake of TCDD for Adults and Children^(6,6,13) [Bracketed Values Are USEPA Default Values]

Exposure Factors	Children		Adults		
	High	Low	High	Moderate	Low
Serum Lipid TCDD Concentration (ppt) in 1982	42	15	47	32	14
TCDD Concentration in Soil (ppb)	30	1.5	30	12	1.5
Exposed Skin Surface Area (cm ²)	731 [2000]	1000 [2000]	291 [5800]	291 [5800]	230 [5800]
Ingestion Rate of soil and house dose (mg/day)	35 [200]	10 [200]	10 [50]	10 [50]	10 [50]
Inhalation Rate (m ³ /day)	[10]	[10]	[20]	[20]	[20]
Soil Adherence Factor (mg/cm ²)	0.001	0.001	0.001	0.001	0.001
Soil Bioavailability (unitless)					
Dermal:	[0.03]	[0.03]	[0.03]	[0.03]	[0.03]
Ingestion:	0.43 [1.0]	0.43 [1.0]	0.43 [1.0]	0.43 [1]	0.43 [1]
Inhalation:	[1.0]	[1.0]	[1.0]	[1.0]	[1.0]
Exposure Frequency (days/year)	365	365	365	365	365
Exposure Duration (years)	3	6	6	12	15
Body Weight (kg)	17.6 [15]	21.3 [15]	92 [70]	50 [70]	58.4 [70]
Time Since Last Exposure (yr)	8	10	10	4	3
Age at Last Exposure (yr)	5	9	31	23	35

Estimated Peak Body Burden

The peak lifetime blood concentration of TCDD for three adults and two children exposed to TCDD at Times Beach was estimated using either default exposure parameters used in standard exposure assessment studies, or scenario-specific parameters (when data were available).

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Over the past ten years, several papers have addressed how to predict the uptake of dioxin by humans associated with exposure to contaminated soil.^(3,4,5,14,15) Daily TCDD uptake (ng/kg-day) was estimated based on three possible routes of exposure; incidental ingestion of contaminated soil and housedust, inhalation of contaminated particulates, and dermal contact with the soil. Uptake for each of the pathways was estimated using site-specific parameters and standard exposure assessment equations.⁽¹⁷⁾ Site-specific information regarding the soil concentrations of TCDD to which each person was exposed was not available. Thus, for each exposure scenario, "high", "moderate" and "low", correspondingly high (30 ppb), moderate (12 ppb), and low (1.5 ppb) soil concentrations, as measured in Times Beach, were used to estimate the absorbed dose (uptake). The exposure factors used for adults and children are presented in Table 1.

Results and Discussion

A total of five residents exposed to TCDD at Times Beach were evaluated (values presented in Table 2). Figure 1 compares the estimated uptake (absorbed amount) and the actual uptake of TCDD for these people. The results indicate that default exposure factors recommended by most regulatory agencies will often overestimate an individual's actual uptake of TCDD, while scenario-specific calculations can provide a more accurate estimate.

Table 2: Estimated Average Daily Uptake of TCDD Using Exposure Assessment Methods Compared to the Actual Uptake for Select Residents at Times Beach (Children and Adults)

Uptake	Children		Adults		
	High	Low	High	Moderate	Low
Actual (ng/kg-day)	0.024	0.004	0.019	0.005	0.001
Estimated (ng/kg-day)	0.065 [0.52]	0.003 [0.026]	0.021 [0.097]	0.013 [0.039]	0.002 [0.005]

The total uptake for each individual was estimated by summing the amount taken up via dermal contact with soil, inhalation of particulates, and ingestion of soil. For adults, of the absorbed amount, the majority was attributed to dermal absorption (88% using site-specific factors and 77% using USEPA default factors). For children, the majority of that absorbed was due to ingestion (76%) when it was calculated using USEPA default values. This difference is due to the much higher default value for soil ingestion by children (100 mg/day for children versus 20 mg/day for adults), as well as children's relatively small body weight (15 kg for children versus 70 kg for adults). In contrast, when uptake for children was estimated using the scenario-specific factors, most was due to dermal absorption.

The accuracy of the predicted uptakes was similar between adults and children. Using the scenario-specific approach, "predicted" uptake by adults was within a factor of 2-fold of the actual uptake for the high and low exposure scenarios and less than a 2.5-fold difference for the moderate exposure scenarios (Figure 1). However, the "predicted" uptake, using USEPA default exposure factors for the adult overestimated the actual uptake by at least five-fold.

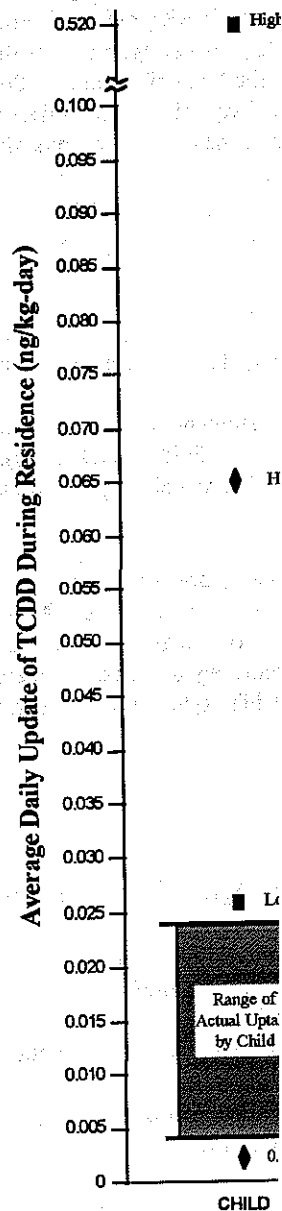


Figure 1: The estimated uptake by select residents of Times Beach, Indiana, using default exposure factors or site-specific exposure factors. ■ Denotes use of default exposure factors. ◆ Denotes estimates based on scenario-specific exposure factors.

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0.013	0.002
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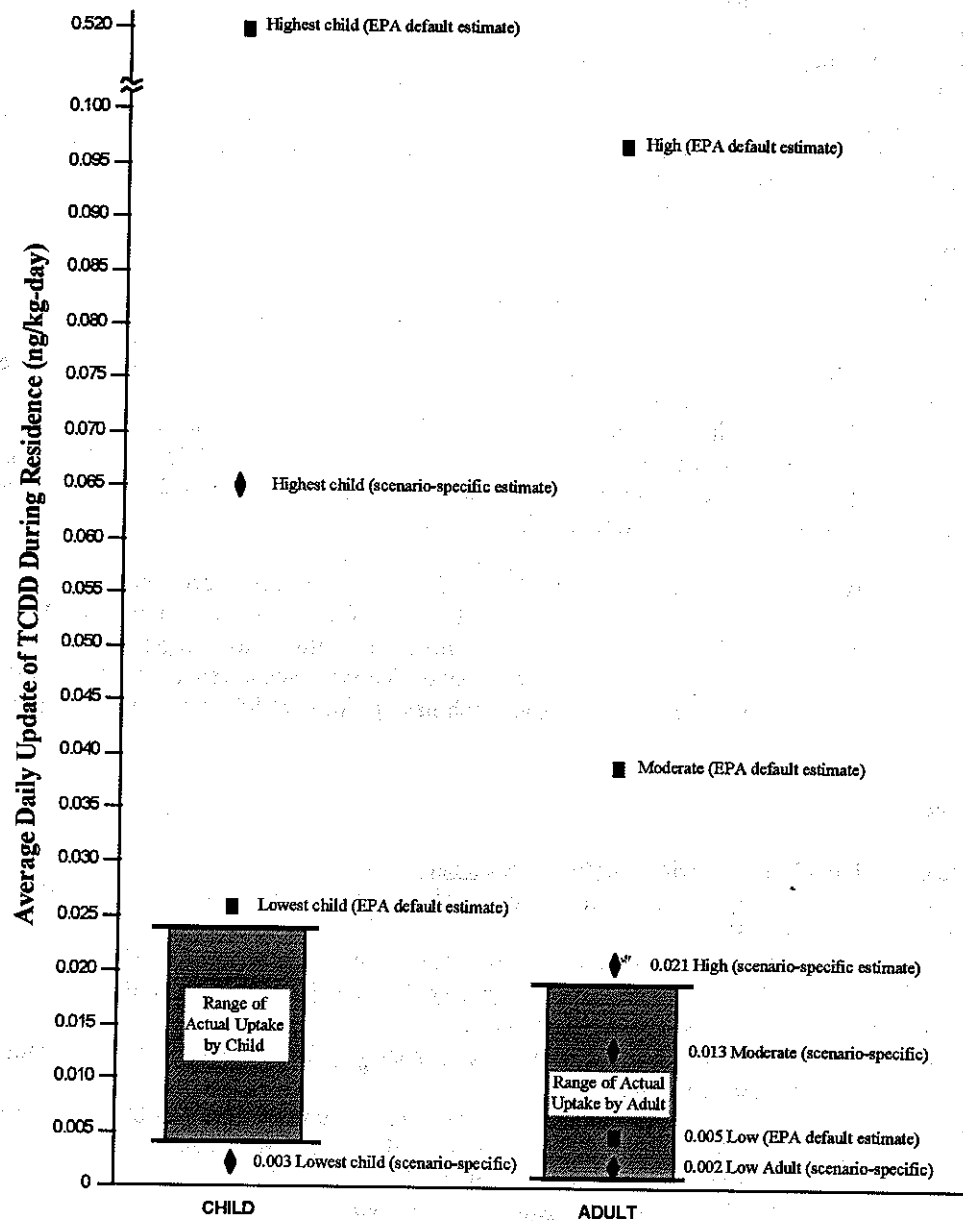


Figure 1: The estimated and actual average daily absorbed amounts (ng/kg-day) of 2,3,7,8-TCDD for select residents of Times Beach, Missouri. The figures for estimated uptake are based on either EPA's default exposure factors or site-specific exposure factors.

- Denotes use of default values.
- ◆ Denotes estimates based on site-specific values.

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For the children, there was less than a 3-fold difference between the scenario-specific estimates compared to the "actual" uptake for the "high" exposure scenario. There was less than a 2-fold difference for the "low" exposure scenario. The uptake calculated using USEPA default factors overestimated the "high" and "low" exposure scenarios by about 5-fold. It is noteworthy that the site-specific estimate for the "low" exposure scenario underestimated the "actual" intake (0.003 ng/kg-day versus 0.004 ng/kg-day). This result may be due to interindividual variation in the different soil ingestion rates, or more probably, differences in the amount of dioxin in the diet (meat, milk and fish) and the amount of various foods ingested.

Conclusions

Based on these results, we concluded the following:

- Children's uptake of TCDD due to contaminated soil will usually be dominated by exposure via ingestion and dermal absorption.
- Use of USEPA default parameters generally results in an overstatement of the uptake of TCDD compared to the actual uptake (as back-calculated from serum lipid TCDD levels).
- When properly used, scenario-specific exposure factors appear to yield excellent predictions of the actual uptake of TCDD due to soil exposure.

These conclusions support the general paradigm that default exposure factors are conservative and that site-specific exposure factors can better predict the uptake of dioxin by humans. More importantly, it appears that the art of exposure assessment has matured to a degree that we can accurately predict human uptake of soil-bound contaminants. To more accurately describe the likely breath of exposures for a large group of people (each having different life styles) a monte carlo approach would be needed.

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