APPARENT HALF-LIVES OF DIOXINS, FURANS, AND PCBS AS A FUNCTION OF AGE, BODY FAT, BREASTFEEDING, AND SMOKING STATUS

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INTRODUCTION

To account for the effect of historical intake on current serum concentrations of persistent congeners, it is necessary to decay past concentrations over time as a function of their half-lives. Different dioxin, furan, and dioxin-like PCB congeners have different persistence in the human body. This study examines the half-life data for 29 congeners from the literature. Based on the available information, a value for each congener is defined that approximates the half-life in an infant and in an adult. These values can be used as reference half-lives, and further adjusted for individual variation with known modifiers such as age, sex, percent body fat, and smoking status.

METHODS

- An extensive literature search was conducted for studies with half-life or decay values for dioxins, furans, and PCBs in humans.
- Measured and modeled data from over 30 studies were used to examine the relationship between the half-lives of 29 congeners in humans and the factors that affect their length.
- A subset of data representative of a middle -aged adult was selected based on the following criteria:
  - The blood serum concentration was below 700ppt,
  - The subjects were adults,
  - The measurements were not reported as inaccurate in later studies,
  - The values were less than 25 years if they were measured in assumed steady state conditions.
- Reference half-life values for an adult and for an infant were estimated and used to produce a continuous interpolation of the half-life as a function of age, of percent body fat, and of total body fat.
- An equation based on a linear relationship between half-life length and age was developed.

OBJECTIVES

- Examine reported half-life data in literature for 29 dioxin, furan, and PCB congeners
- Define a reference half-life value for each congener
- Provide a method of individual half-life estimation based on individual characteristics

RESULTS

Half-life vs age: We propose a strategy for determining the half-lives of the 29 congeners (in years) in an individual that is based on the relationship of half-life and age.

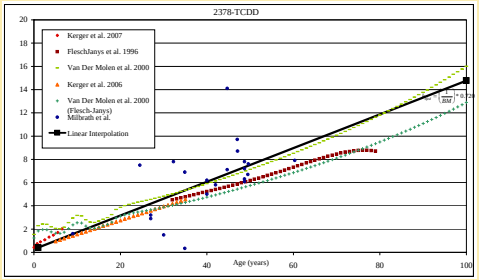

Figure 1 . Half-life (in years) vs. age (in years) for 2378-TCDD

There is a positive nearly linear association between age and half-life (figure 1) . This may indicate a direct relationship between age and half-life, or age may incorporate the effect of other parameters, such as the change in percent body fat with age.

$$t_{1/2}(age_i, smoke_i, pbf_i) = \beta_{0(age)} + \beta_{age} * age_i * smoke_i * \frac{pbf_i}{pbf_{ref(age_i)}} \quad (1)$$

$$k_{bfpd} = \left(\frac{1}{BM}\right) * 0.720 \quad (2)$$

$$t_{1/2(total)} = \frac{\ln(2)}{\frac{\ln(2)}{t_{1/2(age,smoke,pbf)}} + k_{bfpd}} \quad (3)$$

The rate of elimination due to breastfeeding is presented in equation 2, and is based on data collected from a cohort of German women (Wittsiepe *et al.* 2007).

The total half-life is due to elimination both through breastfeeding and other age, smoking, and body fat adjusted processes, and is given in equation 3.

Half-life vs body fat: Half-life increases with percent body fat at older ages, but not at younger ages (shown by the arrow on figure 2). Therefore, this relationship could be useful for correcting the half-life for a given age, but cannot be used to represent every stage of life.

Using absolute body fat rather than percent body fat better accounts for the high percent body fat found in children (figure 3). The two points well below the curve correspond to acute poisoning of two females with high TCDD concentrations.

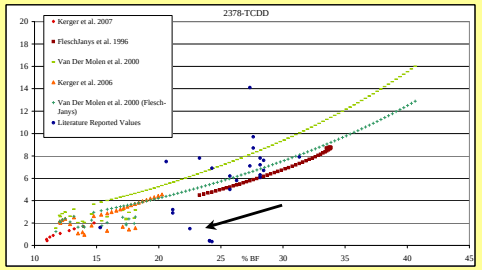

Figure 2. Half-life (in years) vs. percent body fat 2378-TCDD

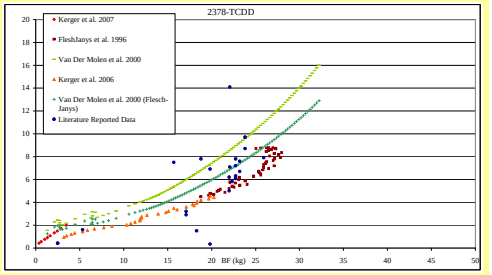

Figure 3. Half-life (in years) vs. body fat (in kg) 2378-TCDD

	2378 TCDD	12378 PeCDD	123478 HxCDD	123678 HxCDD	123789 HxCDD	1234678 HpCDD	OCDD	2378 TCDF	12378 PeCDF	23478 PeCDF	123478 HxCDF	123678 HxCDF	123789 HxCDF	234678 HxCDF	1234678 HpCDF	1234789 HpCDF	OCDF	PCB 77	PCB 81	PCB 126	PCB 169	PCB 105	PCB 114	PCB 118	PCB 123	PCB 156	PCB 157	PCB 167	PCB 189
Infant Reference	**0.4**	**0.32**	0.54	**0.39**	0.28	**0.32**	**0.46**	0.119	0.19	**0.27**	0.36	0.4	0.4	0.16	0.172	0.26	0.08	0	0.04	0.09	0.41	0.13	0.56	0.21	0.41	0.89	1	0.67	1.22
Adult Reference	7.2	11.2	9.76	13.1	5.1	4.92	6.73	2.134	3.5	7	6.42	7.22	7.22	2.79	3.094	4.61	1.4	0.07	0.73	1.6	7.3	2.4	10	3.8	7.4	16	18	12	22
Reference Adult Age	48.7	48.7	48.7	48.7	48.7	48.7	48.7	48.7	48.7	48.7	48.7	48.7	40	48.7	48.7	48.7	48.7	49.5	49.5	42.5	42.5	42.5	42.5	42.5	42.5	42.5	42.5	42.5	42.5
Source	1	2	2	2	2	2	2	3	3	3	2	2	4	3	2	3	3	5	5	6	6	6	6	6	6	6	6	6	6

CONCLUSIONS

- Continued study of the of the kinetics of these compounds in humans, is required, especially for PCBs.
- There is not sufficient data to test the equation based on total body fat, and this approach requires further validation.
- The described equations represent a simple and relatively consistent approach that can be used to determine individual half-lives for numerous dioxin, furan, and PCB congeners.

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0. Infant reference values in bold were taken from Leung *et al* 2006, others are the adult value for that congener multiplied by the ratio of the infant to adult values for 2378-TCDD
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Financial support for this study comes from the Dow Chemical Company through an unrestricted grant to the University of Michigan.