ESTIMATION OF HALF-LIVES OF 2,3,7,8-CHLORINE SUBSTITUTED DIOXINS AND FURANS, AND DIOXIN-LIKE PCBS IN HUMANS

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Introduction

The health effects of dioxins are a public concern. Dioxin toxicity in animals is severe, and their half-lives are long. Investigation of health effects and risk evaluation are important for the health risk management of dioxins. Important factors for risk evaluation are the body burdens of dioxins and the strength of toxicity. Body burdens are calculated from longitudinal exposure levels and half-lives of dioxins. The half-lives of only a few congeners are known. However, the contribution of 2,3,7,8-TCDD for total TEQ is not so large among Japanese, while that of coplanar PCBs (Co-PCBs) is more than 50%. Therefore, it is necessary to investigate the health effects and risks of many congeners other than 2,3,7,8-TCDD which have toxicity (TEF>0). In this study, the half-life of several dioxin congeners in humans was estimated using a single compartment model for a health risk study.

Methods and Materials

Half-lives of 17 PCDD/F congeners with 2,3,7,8-chlorine substitution and 12 Co-PCBs (non-*ortho* and mono-*ortho* PCBs) were estimated. Dioxins mostly enter the human body via food; therefore only dioxins from food are included in our model. It was assumed that all dioxins in the body were dissolved in the lipid. It was also assumed that dioxins are eliminated from the body through two routes, feces without metabolism and metabolites from the liver (clearance). Half-lives only through the latter route were estimated in this model.

Half-lives were determined as follows. For each congener, the estimated body burden calculated with an assumed half-life was compared with an observed value for the congener. If the difference between the two distributions was small enough, we accepted the assumed half-life as the correct, model-based half-life. If the difference was large, we recalculated the burden until the difference became small enough.

Observed values of the body burden were necessary for our calculations. The concentration of dioxins in breast milk was used as an estimate of the body burden. The levels of dioxins were investigated for about 230 women (25-29 years old) sampled from Japan by the Ministry of Health and Welfare in 1998[1]; therefore, the target population of our study was women who were age 27 in 1998.

The model used in this study was based on a model developed by van den Molen[2] and then improved by Kreutzer[3]. Kreutzer *et al*. assumed that elimination of dioxin as feces is proportional to the product of the concentration of dioxin in the body and total fat volume. The ratio of dioxins distributed between feces and the intestines was considered constant for this

model.

The model was constructed to estimate the body burden from birth to 27 years old. Therefore, we chose to use a non-stationary state model, because metabolic ability is dependent on sex, age and other factors. Fat volume and liver weight are the most important factors for determining metabolic ability. Fat volume was estimated from height and weight, and liver weight was determined based on the assumption that liver weight was proportional to body weight. Height and weight values for each sex and age category were taken mainly from the data of the 1996 National Nutrition Survey[4].

Concentrations of dioxins in foods were used to estimate exposure levels. Exposure data were derived from the surveys conducted by the Ministry of Health and Welfare in 1996, 1997, and 1998[5]. The survey was conducted at 10 areas in Japan using a market basket method, and the concentrations of dioxins in food were measured. Before 1996, the survey was conducted at only one area. According to the concentration measurements, Japanese are exposed to dioxins mostly (more than 90%) through fish, meat, dairy products, and colored vegetables. Only these four food groups are considered in our model. Dioxin data in food before 1977 do not exist in Japan, and then it was necessary to estimate the exposure levels from 1971 to 1976. We assumed dioxin concentrations before 1977 (1971-1976) were equal to the levels in 1977. In this study, we considered the longitudinal variation of the concentrations in the food, but we did not consider the difference of food intake among persons due to their tastes.

An initial half-life value was arbitrarily set for each congener. Then body burden at 27 years old, considering exposure from birth until 27 years old, was estimated using the model. The model accounted for exposure levels at each sex and age, body fat rate, and other body indices. Exposure level calculated monthly in the model. The simulation was repeated 10000 times. These parameters were given as values with distributions, and the estimated values of body burdens were described as distributions. If the distribution of estimated body burden was well-fit to the observed distribution of body burdens, the initial half-life was considered as the estimate of the half-life. If both distributions were different, another half-life was set and the body burden would be recalculated until the estimated distribution would be almost consistent with the observed.

Results and Discussion

The results of the estimations are shown in Table 1. We estimated half-lives of 24 congeners. We could not estimate the half-lives of 5 congeners, since their concentrations in food were very low. In these cases, the body burden became zero, which may be due to the model characteristics. According to our model, half-lives of most dioxins were less than 10 years. The estimated half-life of 2,3,7,8 TCDD is 6.0 years (range: 5.5-7.0 years). This value is similar to values calculated in other studies. The half-lives of furans in our study were also relatively consistent with other studies.

The longest half-life value is 11 years for 1,2,3,6,7,8-PCDD. Half-lives of only a few Co-PCBs have been reported. The half-lives of non-*ortho* PCBs are very short. The shortest is 0.5 years for 3,3', 4,4'-T4CB (#77), and the longest is 4.5 years for 3,3,'4,4', 5-P5CB (#114). The range for the half-lives of PCBs, including non-*ortho* and mono-*ortho* PCBs, is 0.5 to 17.5 years.

In order to check our model, we conducted a simulation using our model with another population data set. This population consisted of 50-years old men in Japan in 1998. The exposure period was from 25 to 50 years old. The body burdens of dioxins at 25 years old was calculated based on the concentrations of dioxins in breast milk in 1973. Our model did not

make good fit for some PCDF congeners. This inconsistency may be due to the setting error of the distribution coefficient between feces and lipid. However, the estimated body burdens are fairly consistent with the observed values for many congeners. We consider our model and results to be relatively valid and reliable, although it is still necessary to improve our model.

Table 1. Estimated half-lives of dioxins

	Congener	*Abbr.*	Half-life (years) Estimate	Range
PCDD	2,3,7,8-T4CDD	TCDD	**6.0**	5.5 - 7
	1,2,3,7,8-P5CDD	PCDD	**6.5**	5.5 - 7
	1,2,3,4,7,8-H6CDD	HxCDDa	**3.0**	3 - 4
	1,2,3,6,7,8-H6CDD	HxCDDb	**11.0**	10 - 13
	1,2,3,7,8,9-H6CDD	HxCDDc	**---**	
	1,2,3,4,6,7,8-H7CDD	HpCDD	**4.5**	- 5
	O8CDD	OCDD	**3.7**	3.2 - 4.2
PCDF	2,3,7,8-T4CDF	TCDF	**0.5**	0.5 - 0.7
	1,2,3,7,8-P5CDF	PCDFa	**0.8**	0.7 - 1
	2,3,4,7,8-P5CDF	PCDFb	**7.5**	7 - 8
	1,2,3,4,7,8-H6CDF	HxCDFa	**5.0**	4.5 - 5
	1,2,36,7,8-H6CDF	HxCDFb	**5.0**	4 - 5
	1,2,3,7,8,9-H6CDF	HxCDFc	**---**	
	2,3,4,6,7,8-H6CDF	HxCDFd	**3.0**	2.5 - 3
	1,2,3,4,6,7,8-H7CDF	HpCDFa	**2.0**	1 - 2
	1,2,3,4,7,8,9-H7CDF	HpCDFb	**---**	
	O8CDF	OCDF	**---**	
Non-*ortho* PCB	3,4,4',5-T4CB	#81	**1.3**	1 - 1.3
	3,3',4,4'-T4CB	#77	**0.5**	0.5 - 0.8
	3,3',4,4',5-P5CB	#126	**4.5**	3 - 4.5
	3,3',4,4',5,5'-H6CB	#169	**1.5**	1 - 1.8
Mono-*ortho* PCB	2',3,4,4',5-P5CB	#123	**---**	
	2,3',4,4',5-P5CB	#114	**17.5**	15 - 18.5
	2,3,4,4',5-P5CB	#118	**5.0**	4 - 5.5
	2,3,3',4,4'-P5CB	#105	**5.0**	4 - 5.5
	2,3',4,4',5,5'-H6CB	#167	**6.0**	5 - 6
	2,3,3',4,4',5-H6CB	#156	**17.0**	15 - 18
	2,3,3',4,4',5'-H6CB	#157	**9.0**	7 - 9
	2,3,3',4,4',5,5'-H7CB	#189	**11**	10 - 12

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