EXPOSURE ASSESSMENT FOR PCDD/Fs AND COPLANAR PCBs IN JAPAN: FINDINGS OF THE 1999 SURVEY

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Introduction

Since 1998, the Ministry of Environment has conducted a survey to monitor human blood levels of dioxins (PCDDs, PCDFs, and co-planar PCB) as well as exposure analysis of various environmental levels of dioxins in ambient air, ground soil, and water. In 1999, a comprehensive study was designed to cope with a growing concern of health effects caused by dioxins. Dioxin issues drew much attention and people felt anxious about dioxin effects on their health, especially around waste incinerators[1-3]. The objective of this survey is to determine environmental levels of dioxins, estimate exposure levels for humans, and evaluate the relationship among these parameters. In addition, we determined circulatory levels of immunological parameters including CD4, CD8, and NK activity, and those of dioxin-inducible cytochrome P450s, i.e., CYP1A1 and 1B1, to study if blood levels of dioxins affected these parameters.

Materials and Methods

Survey regions, the vicinity of waste incineration facilities (A regions) and reference regions (B regions), were selected based upon the social concern about the dioxin issues during this study period (from Nov., 1999 to Mar., 2000). Those areas were Nose Town in Osaka Prefecture; Cities including Tokorozawa, Sayama, Kawagoe in Saitama Prefecture; and Fuchu City in Hiroshima Prefecture. People who lived in these regions for at least last 10 years, and older than 40 years, and approximately 40 people were requested through local authorities to participate the survey, and those who agreed by a written consent with the objective of the survey were selected as subjects. The total number of people was 121 (49 males and 72 female), the age ranged from 40 to 68. Health examination was arranged for the subjects who were interviewed by questionnaires about health conditions, dietary habits and smoking histories at the time of examination, and asked to provide blood specimens.

Atmospheric sampling was carried out by using high-volume air sampling technique for 24 hours and low-volume method for 7 days. As for analytical protocol, blood sample was spiked with ^{13}C-labeled internal standards, prepared with 10mL ethanol, followed by extraction with n-Hexane. These were treated with sulfuric acid, rinsed with water, and then dehydrated with sodium sulfate. The solution was

purified by a multilayer silica gel and activated charcoal column. Quantification was carried out by isotope/dilution method using HRGC/HRMS (Micromass Ltd., AutoSpec series). Air filters, soil samples, and food were Soxhlet-extracted, polyurethane foams were acetone-extracted, then prepared and quantified as mentioned above.

Immunological measurements in blood specimens were performed by SRL Inc., and gene expression of CYP1A1 and 1B1 were conducted by real-time RT-PCR (ABI Prism 7700) according to the method which will be described elsewhere (C. Suzuki and H. Sone).

Results and Discussion

Dioxin levels in environmental media, food, estimated total exposure and blood are summarized in Table 1. The atmospheric dioxin concentrations of A regions were relatively close to those of B areas, and revealed that the ambient air specimens did not show significant differences between A and B regions with regard to the location of incinerators. The levels varied nearly 10-fold among the areas with a relatively high TCDD concentration in Saitama Prefecture compared to those often reported for cities in industrialized countries as well as background level. The dioxin levels in the soil from the Nose Town area showed that the level in the A region was lower than that in the B region; but in other areas, the A regions tended to show higher levels than the B regions. The mean soil levels differed considerably among areas with a very large standard deviation, but these levels were far below Environmental Standard for Soil (1000 ng/g as standard, and 250 ng/g as a so-called Attention Level). Mean dioxin levels in water was 0.22 pg TEQ/L which was used as reference because this value represented the environmental level and did not account for human exposure. In 1999, the food survey was conducted three times for a three-day period (a total of nine days), compared to three days in 1998, to minimize fluctuation among food specimens.

It is generally accepted that dioxin exposure through food accounts for more than 90% of the total exposure in people who live without excessive exposure to dioxins from particular emission sources or from accidental exposures, and that the contributions through the air and soil were relatively small. Mean values for estimated total exposure to dioxins were below the tolerable daily intake (TDI) of 4 pg-TEQ/kg/day [4]. As might be expected, the results did not show any clear difference between regions in the accumulations of human subjects or between the routes in the estimated total exposures. This observation is an expected consequence since the subjects in the present study purchased food items form local supermarkets where vegetables, meat and fish were not only domestically produced but also imported. The total estimated exposure level to dioxins ranged in average from 1.2 to 2.1 pg TEQ_{DFP}/kg/day. Regarding a blood dioxin concentrations as a biomarker for dioxin exposure, we analyzed PCDD, PCDF and Co-PCB in the blood specimens for all areas, and find the values ranged from 5.3 to 70 pg TEQ_{DFP}/g fat, which fell within the range observed in preceding surveys conducted in Japan[5]. The age-adjusted mean blood dioxin concentrations were similar between in A and B regions in all areas. (Table 1).

Values represent amounts of PCDFs, PCDDs, and Co-planar PCBs (non-ortho and mono-ortho substituted PCB, these compounds have TEF values defined by WHO document, 1998).

We next examined immunological parameters and gene expression of CYP1A1 and 1B1 in the subjects of the three areas as summarized in Table 2. As a group, no abnormal findings were detected for immunological parameters and no positive relationship was so far found between

Table 1 Concentrations of PCDD+PCDF+Co-PCB in Various Media and Estimated Total Exposure

	Osaka Prefecture Nose Town		Saitama Prefecture			Hiroshima Prefecture Fuchu City	
	A Region	B Region	A1 Region	A2 Region	B Region	A Region	B Region
Blood Concentration adjusted for age [p g-TEQ/g-fat]	29±14 (2 2)	30±15 (15)	27±10 (12)	27±9.0 (24)	24±8.5 (13)	26±10 (16)	27±15 (19)
Air Ambient [p g-TEQ/m^3]	0.077 ±0.0094 (6)	0.076 ±0.013 (7)	0.42 ±0.36 (8)	0.30± 0.067 (6)	0.76 ±0.032 (5)	0.11 ±0.047 (5)	0.044 ±0.0034 (5)
Air Indoor [p g-TEQ/m^3]	0.092 ±0.062 (7)	0.64 ±1.6 (7)	0.21 ±0.16 (8)	0.16± 0.079 (6)	0.37 ±0.067 (5)	0.072 ±0.039 (5)	0.029 ±0.0086 (5)
Soil [p g-TEQ/g]	13 ±16 (8)	20 ±37 (8)	42 ±30 (8)	44 ±43 (5)	8.5 ±8.8 (6)	2.7 ±3.5 (5)	0.10 ±0.038 (5)
Food [p g-TEQ/g]	0.045 ±0.027 (2 2)	0.044 ±0.022 (15)	0.047 ±0.031 (14)	0.039 ±0.020 (22)	0.033 ±0.013 (13)	0.030 ±0.020 (16)	0.038 ±0.018 (19)
Total Exposure Estimate [p g-TEQ/kg/day]	1.8±1.3 (2 2)	2.1±1.0 (15)	1.7±0.81 (14)	1.8±0.83 (21)	1.4±0.56 (13)	1.2±0.77 (16)	1.7±0.80 (19)

[mean value ± s. d. (number of samples)]

blood dioxin and the gene expression of the two CYP genes. We also failed to find an apparent difference among residential areas.

In summary, it is thought that from the dioxin levels in the blood, environmental media and food, as well as immunological parameters and gene expression of CYP 1A1 and 1B1, no significant effects directly linked to the location of incinerators were found. Since dioxin concentrations in the environmental media may exceed the Environment Standard under yet-unidentified conditions, emission of dioxin to the environment should be regulated based up on precautious measures. Furthermore, it is desirable to develop a more specific and sensitive bioindicator to reflect the current exposure level of dioxin and related compounds from the environment.

Table 2 Immunological Parameters and Inducible Enzymes in Subjects in three areas in Japan

	Osaka Prefecture Nose Town		Saitama Prefecture			Hiroshima Prefecture Fuchu City	
	A Region	B Region	A1 Region	A2 Region	B Region	A Region	B Region
CD4 [%]	45±9.4 (22)	47±9.3 (15)	46±7.6 (13)	44±9.5 (22)	42±11 (13)	45±11 (15)	43±7.4 (18)
CD8 [%]	28±7.2 (22)	26±8.1 (15)	25±9.9 (13)	24±7.6 (22)	27±6 (13)	26±8.9 (15)	29±8.6 (18)
CD56 [%]	18±7.5 (22)	18±9.1 (15)	19±6.9 (13)	19±6.8 (22)	20±6.8 (13)	21±9.7 (15)	24±9.3 (18)
NK cell activation [%]	53±17 (22)	54±16 (15)	44±15 (13)	31±12 (22)	33±15 (13)	59±9.5 (16)	51±17 (18)
PHA [cpm]	42,000 ±7,600 (22)	42,000 ±11,000 (15)	34,000 ±13,000 (13)	49,000 ±9,300 (22)	41,000 ±7,600 (13)	37,000 ±11,000 (15)	38,000± 9,500 (18)
Con-A [cpm]	33,000 ±8,600 (22)	37,000 ±9,000 (15)	25,000 ±7,000 (13)	43,000 ±11,000 (22)	36,000 ±11,000 (13)	32,000 ±9,600 (15)	32,000± 8,800 (18)
CONTROL [cpm]	530 ±180 (22)	620 ±260 (15)	220 ±78 (13)	440 ±240 (22)	780 ±360 (13)	420 ±240 (15)	450 ±190 (18)
CYP1A1 [copies/ng total RNA]	4,900 ±5,100 (16)	6,300 ±3,500 (14)	8,200 ±4,200 (8)	17,000 ±37,000 (22)	21,000 ±37,000 (6)	13,000 ±11,000 (15)	5,400 ±3,600 (11)
CYP1B1 [copies/ng total RNA]	12,000 ±7,200 (16)	7,700 ±7,800 (14)	6,600 ±3,700 (8)	9,000 ±7,600 (22)	6,700 ±3,100 (6)	19,000 ±21,000 (15)	9,700 ±5,400 (11)

[mean value±s. d. (number of samples)]

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