HEALTH EFFECTS OF LOW DOSE EXPOSURE OF POLYCHLORINATED DIBENZO-p-DIOXINS, DIBENZOFURANS AND COPLANAR PCB AMONG JAPANESE RESEDENTS

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Introduction

A national survey of polychlorinated dibenzo-p-dioxins (PCDD) and dibenzofurans (PCDF) in emission gases from municipal waste incinerators in 1997 revealed that the several factories emitted excess amount of PCDD/PCDF. We reported the results of 92 incinerator workers in DIOXIN'99, in which blood dioxin levels ranged from 13.3 to 805.8 pg TEQ/g lipid. It caused serious social problems among residents around the incinerators, so the Ministry of Health, Labour and Welfare started health screening program for the residents in 4 areas around the incinerators and 4 control areas. As the results showed no highly exposed residents in these areas, background exposure level and their health effects of Japanese were requested to be clarified. This report is the summary of blood dioxin levels and their health effects from 17 areas in Japan.

Subjects and Methods

Japanese residents in 17 different areas participated the study on health and dioxin exposure between 1998-2002. Participants were all volunteers aged from 40s' to 60s'. They received detailed explanation of the study and gave us the written informed consent.

Life habits and dietary habits were collected by questionnaire and checked by trained dieticians. The questionnaire included dietary habits, smoking and drinking habits, residential and work environment, physical activity, past history of diseases and treatments, reproductive history, etc.

About 30 ml of blood was divided to tubes to perform peripheral blood tests, such as RBC, WBC, and platelet counts, and hematocrit, and blood chemistry studies, such as determination of AST(GOT), ALT(GPT), gamma-GTP, LDH, ALP, LAP, CPK, amylase, total cholesterol, HDL-cholesterol, triacylglycerol, total protein, albumin, total bilirubin, blood urea nitrogen, creatinine, uric acid, glucose, creatine phosphokinase, sodium, potassium, calcium, iron, and inorganic phosphate. These tests were performed by the Serum Research Laboratory (Tokyo).

As immunologic markers, T lymphocytes subsets determined by surface antigens, such as CD3, CD4, CD8, and CD4/CD8 ratio, were also measured. NK activity was measured by surface antigen (CD56), and natural killer cell activity was determined against K562 cells. Stimulation by PHA and Con A was also applied.

Blood PCDD/PCDF/Co-PCB was measured by a modification of Patterson's method.

Lipids were extracted from 70-80 g of whole blood with a solution of 30 ml saturated ammonium sulfate and 80 ml of ethanol:hexane (1:3) solution after the addition of an internal standard of ^{13}C-

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labeled mixed dioxin congener solution (Wellington Isotope Laboratories, Massachusetts, USA)). Clean up was achieved by a multilayer silica column. Analysis of PCDD/PCDF/Co-PCB was carried out by gas chromatography-high resolution mass spectrometry (GC-MS). The column used was a DB-dioxin fused silica capillary column (J&W Scientific, Folsom, California). Details are described in the previous paper[1].

The toxicity of the dioxins was calculated by the WHO TEF method (1997) and is expressed as TEQ/g lipid and body burden. Statistical analysis. SPSS version 10 was used for the statistical analyses. Correlation analysis was performed between PCDD/PCDF/Co-PCB and various variables. Linear regression analysis and logistic analysis were used for evaluating the effects of dioxins, if a significant correlation ($p < 0.05$) was obtained, and Odds Ratio was calculated if necessary.

Results

Dioxin levels of so far 585 out of 757 participants were measured. Blood dioxin level of PCDDs and PCDFs was 17.5+/-12.0 (median 14.4) pgTEQ/g lipid, that of PCBs was 4.8+/-5.6 (median 2.9) pgTEQ/g lipid, and the total was 22.3+/-14.5 (median 18.6) pgTEQ/g lipid. Maximum concentrations were 84.3, 42.4, and 109.1 pg TEQ/g lipid, respectively. Concentration of congeners,TEQ and body burden were shown in Table 1.

Table 1. Congener Distribution of Dioxins among Japanese Residents by sex

	males n=294				females n=291			
	mean	s.d.	median	max	mean	s.d.	median	max
2,3,7,8-TCDD	1.8	1.9	1.1	14.3	1.7	1.9	1.1	10
1,2,3,7,8-PeCDD	4.9	4.2	4	28.6	4.6	4.5	3.5	33.3
1,2,3,4,7,8-HxCDD	4	6.7	2.4	49	3.6	6.6	2.3	63.7
1,2,3,6,7,8-HxCDD	25.8	22	19.1	170	22.6	20	17.1	180
1,2,3,7,8,9-HxCDD	5.7	7.7	3.3	53.4	5.4	6.6	3.6	54.1
1,2,3,4,6,7,8-HpCDD	21.2	14.2	17.3	104.9	22.4	15.8	18.4	104.9
OCDD	324.3	464.4	194.6	3981	406.6	432	240.2	3152.1
2,3,7,8-TCDF	2.6	3.5	1.4	23.6	2.3	2.6	1.6	19.7
1,2,3,7,8-PeCDF	2	3.7	0.8	28.6	1.6	2.8	0.7	28.6
2,3,4,7,8-PeCDF	10.8	7.1	9.6	45.7	9.3	6.7	8.3	51
1,2,3,4,7,8-HxCDF	5.5	5.5	3.7	38.3	5.1	4.5	3.7	38.3
1,2,3,6,7,8-HxCDF	6.3	6.5	4.3	38.6	5.3	4.4	4.1	38.3
1,2,3,7,8,9-HxCDF	1.9	3.8	0.5	28.3	1.7	2.9	0.5	25.6
2,3,4,6,7,8-HxCDF	4.9	8.8	2	68.4	3.8	5.1	2.1	38.5
1,2,3,4,6,7,8-HpCDF	6.7	8.4	4.4	71.5	6	5.4	4.2	31.9
1,2,3,4,7,8,9-HpCDF	1.7	2.5	1	15.7	1.5	1.9	1	15.7
OCDF	6	6.9	5	54.3	6	8.7	5	105
PCB77	81	118.7	27.6	1015.8	76.4	98.7	36.9	604.6
PCB126	46.9	58.8	25.2	390.1	36.5	40.9	24.4	298.3
PCB169	63.1	93.9	43	938	51.9	94.9	29.4	917
DF_TEQ	18.5	12.7	15	84.3	16.6	11.2	14.2	83.6
PCB_TEQ	5.3	6.4	3	42.4	4.2	4.5	2.8	31
TOTAL_TEQ	23.8	15.8	19.2	109.1	20.8	13	17.3	89.4
BODY_BURDEN	5.4	3.9	4.4	23.7	5.7	3.7	5	28.9

Dioxin and PCB levels were not correlated with age, but correlated with profession. The blood concentration of farmers showed higher blood level of dioxins, so these may be derived from the remnant of herbicides for cultivating rice.

GOT, GPT, triacylglycerol, total bilirubin, CPK, and albumin were positively correlated with body burden in males, and total protein, alkaline phosphatase, triacylglycerol and calcium in females. Amylase was negatively correlated in both sexes. CD56 (NK cell marker) and NK activity showed reverse correlation with body burden in both sexes. In females, testosterone and androstendion showed negative association with dioxin level.

Congener distribution of residents in 15 areas showed different pattern. Median body burden ranged from 2.2 to 6.9 ng/kg body weight. Simultaneously performed questionnaires about working history, dietary habits, drinking and smoking habits, family history and past history, history of gestation and number of children, etc. were analyzed in relation to the blood dioxin levels (results are not shown here).

Past history or hypertension, diabetes mellitus and hyperlipidemia showed significantly higher level of body burden (Table 2). Body burden more than 5 ng/kg body weight seemed to cause any chronic effects.

Table 2. Past history and median body burden (ng/kg body weight)

		Hypertension	Diabetes	Hyperlipemia	Peptic ulcer	Allergy
Male	+	5.2	5.3	5.1	4.2	5.4
	-	4.2	4.4	4.3	4.6	4.1
Female	+	6.5	3.2	6.3	4	4.1
	-	4.8	4.9	4.9	4.9	4.9

Discussion

In Japan, 90 % of the daily intake of PCDDs, PCDFs, and other dioxin-like compounds is estimated to come from food. However, congener pattern of fish and other foods were different from those accumulated in the body. The effect of herbicide remnant is considered to be still present. Dioxin accumulation in the body showed significant increase by age due to very long half-life of dioxins. The low dose chronic accumulation should give adverse health effects.

A history of hypertension and hyperlipidemia had significantly increased odds ratios. Although the history was self-reported, it was well correlated with laboratory data. Diabetes mellitus showed marginal association. Lipid soluble dioxins may present in the lipid membrane, which could modify cellular function through impaired surface receptor functions. Prediction of future health effects in the subjects with low-level exposure is difficult. Body burden of 5 ng/kg b.wt. may be at risk level. Very long half-life of dioxins inside the body, however, may cause various effects at the lipid membrane of lipoprotein and cells. Follow-up of the chronically exposed people should be important.

References

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