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Original Article

Isomer pattern and elimination of dioxins in workers exposed at a municipal waste incineration plant

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Abstract: The aim of this study was to clarify patterns of serum concentrations of dioxins in the employees of a waste incineration plant and to estimate elimination rates and half-lives of serum dioxin isomers, and the maximum serum concentrations of dioxin isomers at the time of plant shutdown. Sixteen subjects participating 3 times or more in annual health examinations during an 8-yr period from 2000 to 2007 were recruited for this study. Serum concentrations of dioxins expressed as TEQ/g lipid decreased gradually after plant shutdown with the highest decrease observed in polychlorinated dibenzofurans (PCDFs) followed by polychlorinated deibenzo-p-dioxins (PCDDs) and then coplanar PCBs. The serum toxic equivalency (TEQ) concentrations of PCDF and PCDD congeners in the employees were higher than those in the general population survey by the Ministry of the Environment, Japan, whereas the serum concentrations of coplanar PCBs were similar to those in the general population. The estimated half-lives and elimination rates of PCDDs and PCDFs in the highly exposed workers increased compared with the moderately exposed workers. The estimated geometric mean serum concentrations of PCDDs, PCDFs and total dioxins at the time of plant shutdown were 35, 53 and 107 pg TEQ/g lipid, respectively.

Key words: Dioxin, Polychlorinated dibenzo-p-dioxin, Polychlorinated dibenzofuran, Coplanar PCB, Waste incinerator worker, Elimination rate, Half-life

Introduction

It is of prime importance to examine the dose-response relation between exposure of humans to unintentional by-products, dioxins, and their long-term health status, although exposure to dioxins has tended to decline in the past three decades in response to regulatory actions taken to reduce the generation of dioxins and emission of them into the environment[1, 2]. Episodic exposures of humans to high levels of dioxins and the resulting health outcomes have been reported for residents of Seveso[3], Yusho[4] and Yucheng patients[5], veterans of Operation Ranch Hand in the Vietnam War[6, 7] and herbicide-manufacturing workers[8]. The municipal waste incineration facility has been of great concern as a major source of dioxin emission into the living environment[9–17]. Some studies[9–13] on waste incinerator workers showed that serum concentrations of polychlorinated dibenzofurans (PCDFs) were higher than those of polychlorinated dibenzo-p-dioxins (PCDDs), pre-

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sumably as a result of occupational exposure to fly ash or slags containing higher levels of PCDFs than PCDDs[16, 17]. It is difficult to quantitatively assess occupational exposure of humans to a complex mixture of dioxin isomers that are ubiquitously present in food and the living environment. Examination of time-course changes in patterns and eliminations of serum concentrations of dioxin isomers in the dioxin-exposed incinerator workers is necessary for fingerprint information to distinguish occupational source from nonoccupational sources of PCDDs and PCDFs. A few studies reported the isomer patterns and eliminations of dioxins in waste incinerator workers in comparison with relatively abundant data for the elimination and half-lives of TCDD and dioxins from other sources[18–20].

In 1997, a national survey of dioxins in emission gases from municipal waste incinerators in Japan revealed that some of waste incineration plants emitted high levels of dioxins[21]. In particular, the emission olive for one of the incineration plants in Osaka was reported to be 180 ng TEQ/Nm^3, which far exceeded the national guideline level of 5 ng/Nm^3, and the plant was found to be contaminating the soil near the incineration plant with 8,500 pg TEQ/g of dioxins, which was far higher than the reference value for soil in the same area distant from the plant (0.14 pg TEQ/g)[22]. In addition, there was a close similarity in the isomer patterns of dioxins between the incinerator and the contaminated area outside the plant[22]. The Japan Industrial Safety and Health Association (JISHA) subsequently established the "Research and Investigation Committee on the Assessment of Exposure to Dioxins among Workers in the Waste Incineration Industry" to investigate occupational exposure to dioxins and the health status of workers in municipal and private waste incineration plants in Japan from 1998 to 2007. The survey led by the Committee included investigation of yearly changes in the serum concentrations of dioxins and health status of the ex-employees who had worked for the waste incineration plant in Osaka and left their incineration-related jobs in 1997.

For the purpose of analyzing the data obtained by the aforementioned Committee, the present study aimed to examine the patterns and eliminations of serum concentrations of isomers of PCDDs, PCDFs and coplanar polychlorinated biphenyls (coplanar PCBs) in the incinerator workers in Osaka, whose blood was collected during an 8-yr period of annual medical examinations from 2000 to 2007. We estimated elimination rates and half-lives of serum dioxin isomers, in addition to the estimated maximum serum concentrations of dioxin isomers at the time of plant shutdown in 1997. Two companion papers were published previously, one regarding health effects[23] of the same workers and one regarding occupational exposure[24] to dioxins in the same waste incineration plant in Osaka. All the present data were compiled from the Report of the Research and Investigation Committee on the Assessment of Exposure to Dioxins among Workers in the Waste Incineration Industry[25] and the data compiled and subsequently investigated by the Committee in fiscal years 2006 and 2007.

Subjects and Methods

Subjects

The incinerator workers in this facility were divided into four different groups (group I to IV), depending on exposure to dioxins, as previously described by Takata[24]. Among a total of 28 male ex-employees who had worked inside the incineration facility (group III or IV), we recruited 16 subjects who participated three times or more in the annual health examinations during the 8-yr period from 2000 to 2007, and 11 of the 16 subjects participated every year. Nine of the 16 subjects were engaged in operation and maintenance of a furnace, electric dust collector and wet scrubber in the incineration plant (group IV), while the other 7 subjects termed group III helped with incineration-related jobs inside the incineration facility but did not take part in jobs assigned to group IV. Workers in group I did not engage in the jobs inside the incineration facility, while workers in group II engaged only in handling of solidified fly ash and nonflammable residues. We did not recruit any subjects engaged in group I or II because they did not participate in annual health examinations three times or more. It was confirmed that none of the incinerator workers who participated in this study were occupationally exposed to dioxins after they left the incineration plant in 1997. After the purpose and methods of the present survey were explained to all the subjects, written informed consent was obtained from them. The Ethics Review Committee of JISHA approved the protocol of the present study.

Clinical examination

A questionnaire on lifestyle, present and past illness and medical history was handed out to all the subjects in advance and was collected on the day of medical examination. We first conducted blood cell counts and physical examinations for all subjects to exclude anemic subjects, because we had to take a 180 ml-blood sample. Physical examinations were performed by physicians, and diagnosis of skin conditions such as chloracne was performed by dermatologists; blood tests and interviews concerning job history, lifestyle factors and self-reported present and past illnesses were conducted by occupational physicians, who also distributed and collected a self-administered questionnaire.

Blood dioxin measurements

Analysis of serum concentrations of dioxins was carried out according to the analytical method described in the interim report issued by the Ministry of Welfare (MOW), Japan[26]. Blood samples were collected into transfusion bags containing heparin sodium solution and divided into two portions: one for a blood test for examination of health effects and another for analysis of dioxins by Otsuka Assay Laboratory (Tokushima, Japan) after centrifugation. The analytical method for dioxins was as follow: Lipids were extracted from plasma with a solution of saturated ammonium sulfate and ethanol:hexane solution after addition of an internal standard of ^{13}C-labeled mixed dioxin isomer solution containing 10 pg each of PCDDs and PCDFs and 20 pg each of coplanar PCBs as clean-up spike. Extracted hexane layer was washed with distilled water, and treated with anhydrous sodium sulfate and evaporated to dryness, and the lipid weight was then measured. After elution with hexane again, sulfate acid was added and the layer was removed repeatedly until it became transparent. The hexane layer was washed with distilled water again, treated with anhydrous sodium sulfate and evaporated until a small volume of residues was obtained. The residue was applied to a multilayer silica column and silica gel column. Analysis of PCDDs, PCDFs and coplanar PCBs was carried out by gas chromatography-high resolution mass spectrometry (GC-MS) after addition of an internal standard of ^{13}C-labeled mixed dioxin isomer solution containing 10 pg each of PCDDs and PCDFs and 20 pg each of coplanar PCBs as a syringe spike. The quantitation limit for TCDD, TCDF, penta-CDDs (PeCDDs) and PeCDFs was set as 1 pg/g lipid, that for hexa-CDDs (HxCDDs), HxCDFs, hepta-CDDs (HpCDDs) and HpCDFs as 2 pg/g lipid, that for octa-CDD (OCDD) and OCDF as 4 pg/g lipid and that for coplanar PCBs as 10 pg/g lipid, respectively. If the measured value was less than the quantitation limit, a half of the limit was used for calculation.

Statistical analysis

Patterns of serum concentrations of dioxin isomers

The serum concentrations of dioxin isomers in the subjects who had worked for the waste incineration plant in Osaka were compared with those in the general population living in the farming areas of Japan in a survey by the Ministry of Environment, Japan (MOEJ)[27], which were arithmetically averaged over an 8-yr period from 2002 to 2009. We transformed our data into the toxic equivalency (TEQ) values expressed as pg TEQ/g lipid according to the WHO TEF method[28].

Calculation of the half-lives of dioxins and their maximum serum levels at the time of plant shutdown

We assumed that the one-compartment, first-order kinetic model holds for the elimination rate of dioxins that had accumulated in the body:

$$C_{t,occup} - C_{non\text{-}occup} = (C_{0,occup} - C_{non\text{-}occup}) \exp(-\lambda t) \quad \cdots\cdots\cdots\cdots(1)$$

where $C_{0,occup}$ is the serum concentration of dioxins at the time (0; 1997) when the incineration plant was shut down in 1997 and the subjects left their jobs at the plant. $C_{t,occup}$ is the serum concentrations of dioxins in the *t*th year after having left their incineration-related jobs and $C_{non\text{-}occup}$ is the serum concentration of each dioxin isomers in the general population living in the farming areas of Japan. These data were obtained from the MOEJ report[27], and were averaged over an 8-yr period from 2002 to 2009. The general population is exposed to dioxins from the air, water and soil in the living environment as well as food, but is not occupationally exposed in the workplace. In the above equation, λ is an elimination rate constant.

Equation (1) is converted as follows.

$$\ln (C_{t,occup} - C_{non\text{-}occup}) = -\lambda t + \ln (C_{0,occup} - C_{non\text{-}ocup}) \quad \cdots\cdots\cdots\cdots(2)$$

For this equation, λ was calculated by a linear mixed model of ln $C_{t,occup}$ vs. t function adjusted for age and percent body fat, since Leung *et al.*[29] suggested a positive association between age and the half-lives of the serum concentrations of some PCDF isomers, and since Emond *et al.*[30] revealed that the half-life of serum concentration of TCDD was influenced by body fat mass in an animal study using rats exposed to TCDD. The half-life value was derived as follows: $T_{1/2}=\ln 2/\lambda$. For calculation of $C_{0,occup}$, we excluded the subjects whose ($C_{2000,occup} - C_{non\text{-}occup}$) resulted in a negative value. Statistical analysis was conducted with SPSS Statistics, ver.19.0 (IBM Corp., Armonk, NY, USA).

Table 1. Demographic characteristics of the study population in the year 2000

	Total	Job categories	
		III	IV
Number of subjects	16	7	9
Working duration (yr)[1]	4.4 ± 2.8	2.9 ± 1.6	5.6 ± 2.9
Age (yr)[1]	58.0 ± 11.3	60.4 ± 10.1	56.1 ± 12.5
Percent body fat (%)[1]	20.8 ± 4.4	20.4 ± 3.2	21.1 ± 5.3
Body mass index[1]	24.3 ± 4.1	23.9 ± 2.1	24.6 ± 5.2
Personal protective equipment			
Respirators	13	7	6
Goggles	4	3	1
Gloves	8	3	5
Smoking habit			
Nonsmoker	4	2	2
Smoker	12	5	7
Ex-smoker	3	1	2
Current smoker	9	4	5
Alcohol consumption			
Nondrinker	2	0	2
Drinker	14	7	7

The job categories are described in Subjects and Methods. [1]The values represent arithmetic means ± SD.

Results

Subjects

Table 1 shows demographic characteristics of the 16 subjects observed in the health examination of the year 2000. The study population consisted entirely of male workers with the age of 58.0 ± 11.3 yr, body mass index (BMI) as 24.3 ± 4.1% and percent body fat as 20.8 ± 4.4% (mean ± SD). There was no difference in these parameters between group III and group IV workers except for the working duration. Notably, the subjects of group IV worked at the incineration plant twice as long as those in group III.

Patterns of serum concentrations of dioxin isomers

Table 2 shows isomer patterns of the serum concentrations of dioxins in the 16 subjects measured in 2000, expressed as both pg/g lipid and the value converted into pg TEQ/g lipid. The serum concentrations of the same dioxin isomers in the general population in the farming areas of Japan averaged over an 8-yr period from 2002 to 2009 were used as reference values and were obtained from the survey by the MOEJ[27)]. Since the serum levels in the MOEJ's general population were expressed as arithmetic means, we added the arithmetic means for comparison with our subjects. Notably, the serum concentrations of coplanar PCB congener expressed as pg/g lipid were far higher than those of PCDD and PCDF congeners. However, this relationship was reversed after the conversion into pg TEQ/g lipid. The arithmetic mean serum concentration of PCDF congener expressed as pg TEQ/g lipid increased over that of PCDD in the incinerator workers, whereas this increased relation was reversed in the general population. The arithmetic mean of the serum concentration of total dioxins in the 16 subjects in 2000 was 114.4 pg TEQ/g lipid, which was higher than the arithmetic mean (18.6 pg TEQ/g lipid) of the MOEJ's general population. The arithmetic means of the serum concentrations of PCDD and PCDF congeners in the subjects were 37.2 and 68.8 pg TEQ/g lipid, respectively, both of which were higher than those in the Japanese general population. The arithmetic mean of the serum TEQ concentration of coplanar PCB congener in the subjects was similar to that in the general population. Closer examination of the isomer patterns of dioxins revealed notable increases (>4-fold) in the serum concentrations of penta-, hexa- and hepta-forms of PCDDs and PCDFs in the incinerator workers compared with those in the Japanese general population. The highest increase was in 2,3,4,7,8-PeCDF, followed by 1,2,3,7,8-PeCDD, 1,2,3,6,7,8-HxCDF, 2,3,4,6,7,8-HxCDF, 1,2,3,4,7,8-HxCDF, 1,2,3,6,7,8-HxCDD, 1,2,3,4,6,7,8-HpCDF, 1,2,3,7,8,9-HxCDD,

Table 2. Patterns of serum concentrations of dioxin isomers of the 16 subjects whose blood was collected in 2000 after the incineration plant was shutdown in 1997

Substances	Measured value (pg/g lipid)			TEQ value (pg TEQ/g lipid)				MOEJ[1] (pg TEQ/g lipid)	A/B[2]
	Geometric mean	95% CIs		Geometric mean	95% CIs		Arithmetic mean (A)	Arithmetic mean (B)	
		Lower	Upper		Lower	Upper			
Congeners									
PCDDs	403.0	279.9	580.1	28.0	18.2	42.9	37.18	7.88	4.7
PCDFs	437.6	228.1	839.5	41.1	22.9	74.0	68.82	3.25	21.2
Coplanar PCBs	20,254.8	14,593.0	28,113.3	7.1	5.1	9.9	8.40	7.44	1.1
Total dioxins	22,152.4	16,708.3	29,370.5	81.2	51.0	129.4	114.40	18.58	6.2
Isomers									
2,3,7,8-TCDD	2.6	1.9	3.5	2.6	1.9	3.5	2.94	0.86	3.4
1,2,3,7,8-PeCDD	15.4	9.4	25.2	15.4	9.4	25.2	21.89	4.84	4.5
1,2,3,4,7,8-HxCDD	12.5	7.0	22.4	1.3	0.7	2.2	2.16	0.12	18.0
1,2,3,6,7,8-HxCDD	54.5	39.6	74.9	5.4	4.0	7.5	6.41	1.59	4.0
1,2,3,7,8,9-HxCDD	20.1	12.0	33.6	2.0	1.2	3.4	3.05	0.26	11.7
1,2,3,4,6,7,8-HpCDD	40.6	24.3	67.8	0.4	0.2	0.7	0.63	0.15	4.2
OCDD	242.5	171.6	342.6	<0.1	<0.1	<0.1	0.09	0.06	1.5
2,3,7,8-TCDF	0.5	0.5	0.5	<0.1	<0.1	<0.1	0.05	0.09	0.6
1,2,3,7,8-PeCDF	1.1	0.6	1.9	<0.1	<0.1	<0.1	0.06	<0.01	11.3
2,3,4,7,8-PeCDF	63.8	37.4	108.9	19.1	11.2	32.7	29.11	2.49	11.7
1,2,3,4,7,8-HxCDF	50.0	27.0	92.6	5.0	2.7	9.3	8.67	0.23	37.7
1,2,3,6,7,8-HxCDF	94.2	48.9	181.3	9.4	4.9	18.1	17.31	0.33	52.5
1,2,3,7,8,9-HxCDF	2.0	1.2	3.5	0.2	0.1	0.4	0.38	<0.01	76.2
2,3,4,6,7,8-HxCDF	45.2	22.4	91.3	4.5	2.2	9.1	9.84	0.07	140.6
1,2,3,4,6,7,8-HpCDF	156.5	73.8	331.9	1.6	0.7	3.3	3.22	0.02	161.1
1,2,3,4,7,8,9-HpCDF	6.1	2.4	15.4	<0.1	<0.1	0.2	0.18	<0.01	36.9
OCDF	2.0	2.0	2.0	<0.1	<0.1	<0.1	0.00	<0.01	0.1
Non-ortho PCBs									
PCB77	6.5	5.0	8.4	<0.1	<0.1	<0.1	0.00	<0.01	0.1
PCB81	5.3	4.7	5.8	<0.1	<0.1	<0.1	0.00	<0.01	0.3
PCB126	48.7	31.3	75.6	4.9	3.1	7.6	6.31	5.72	1.1
PCB169	41.2	31.6	53.8	1.2	0.9	1.6	1.37	1.16	1.2
Mono-ortho PCBs									
PCB105	1,766.6	1,216.4	2,565.7	<0.1	<0.1	<0.1	0.07	0.05	1.3
PCB114	668.2	461.4	967.6	<0.1	<0.1	<0.1	0.02	0.02	1.2
PCB118	8,887.9	6,049.0	13,059.0	0.3	0.2	0.4	0.34	0.30	1.1
PCB123	121.6	79.7	185.4	<0.1	<0.1	<0.1	0.00	<0.01	1.0
PCB156	4,927.5	3,602.0	6,740.8	0.1	0.1	0.2	0.17	0.10	1.7
PCB157	1,238.8	931.5	1,647.7	<0.1	<0.1	<0.1	0.04	0.03	1.4
PCB167	1,445.1	1,003.5	2,080.9	<0.1	<0.1	<0.1	0.05	0.05	1.1
PCB189	541.9	434.3	676.2	<0.1	<0.1	<0.1	0.02	0.01	1.7

[1]Arithmetic means of the serum concentrations of dioxin isomers in the general population living in the farming areas of Japan were averaged over an 8-yr period from 2002 to 2009. [2]The arithmetic means less than 0.01 in the MOEJ data were substituted with half the quantitation limit (0.005). CIs: confidence intervals

1,2,3,4,7,8-HxCDD, 1,2,3,4,6,7,8-HpCDD, 1,2,3,7,8,9-HxCDF, 1,2,3,4,7,8,9-HpCDF, and 1,2,3,7,8-PeCDF. On the other hand, there was no difference in the serum TEQ concentrations of coplanar PCBs between our subjects and the MOEJ's general population.

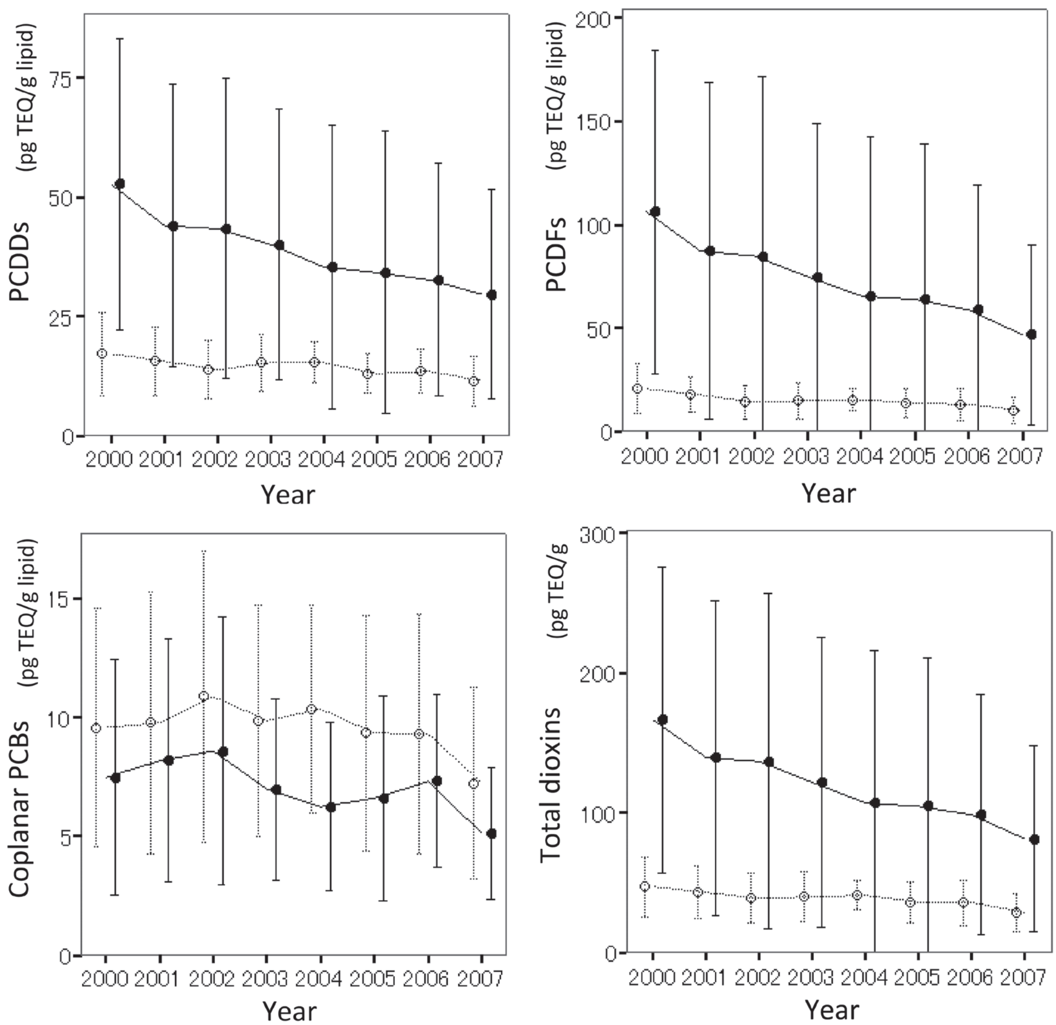

Fig. 1. Yearly changes in serum concentrations (geometric means and SDs) of PCDDs, PCDFs, coplanar PCBs and total dioxins for the highly exposed workers classified as group IV (with means indicated by a solid line with closed circles and SDs indicated by vertical bars) and for the moderately exposed workers classified as group III (with means indicated by a dotted line with open circles and SDs indicated by vertical bars).

Elimination rates, half-lives and estimated maximum serum concentrations of major serum dioxin isomers

Figure 1 shows yearly changes in the serum concentrations of dioxin congeners during the entire 8-yr examination period. The serum concentrations of dioxins were found to decrease clearly year by year except for coplanar PCBs. Notably, the group IV workers were exposed to higher levels of PCDDs, PCDFs and total dioxins than the group III workers. This finding can be attributed to differences in the incineration-related job and in the working duration, since the group IV workers engaged in operation and maintenance of the furnace, electric dust collector and wet scrubber, and since their working duration was 2-fold longer than that of the group III workers.

Table 3 shows changes in serum concentrations of dioxin congeners and major isomers of the 16 subjects (7 for group III and 9 for group IV). Geometric mean of the serum concentration of total dioxins decreased from 90.5 pg TEQ/g lipid in 2000 to 41.1 pg TEQ/g lipid in 2007. The elimination rates and half-lives of dioxin congeners and major isomers were calculated by the one-compartment, first-order kinetic model. Since the results with the linear mixed model showed no significant association with age and percent body fat, we excluded these parameters as covariates from our analysis. For all 16 subjects, the estimated half-lives for the serum concentrations of PCDDs, PCDFs and total dioxins were 11.1 yr (95% CI: 9.3–13.9), 7.3 yr (95% CI: 6.5–8.4) and 9.1 yr (95% CI: 7.9–10.7), respectively. The half-lives of PCDDs tended to be shorter and the elimination rates of PCDDs also tended

Table 3. Elimination rates, half–lives and serum concentrations of principal dioxin isomers measured in 2000 and 2007 as well as the estimated serum concentrations at the time of plant shutdown in 1997

Substances	Geometric mean of serum concentration				Total (n=16)						Job categories: Group III (n=7)						Group IV(n=9)					
		1997[a]	2000	2007	Elimination	95% CI		Half-life	95% CI		'Elimination	95% CI		'Half-life	95% CI		'Elimination	95% CI		'Half-life	95% CI	
	n[†]	(pg TEQ/g lipid)			rate (yr^{-1})	Lower	Upper	(yr)	Lower	Upper	rate (yr^{-1})'	Lower	Upper	(yr)'	Lower	Upper	rate (yr^{-1})'	Lower	Upper	(yr)'	Lower	Upper
Congeners																						
PCDDs	15	34.8	30.6	16.1	–0.06	–0.07	–0.05	11.1	9.3	13.9	–0.06	–0.07	–0.04	12.30	9.49	17.48	–0.07	–0.09	–0.05	9.9	7.8	13.5
PCDFs	16	52.8	41.1	17.5	–0.09	–0.11	–0.08	7.3	6.5	8.4	–0.09	–0.11	–0.08	7.39	6.31	8.91	–0.10	–0.12	–0.08	7.2	6.0	9.1
Coplanar PCBs	6	13.2	12.6	7.7	–0.04	–0.06	–0.03	17.0	12.4	27.3	–0.04	–0.06	–0.02	15.57	10.78	28.01	–0.04	–0.06	–0.01	19.4	11.4	64.9
Total dioxins	15	107.4	90.5	41.1	–0.08	–0.09	–0.06	9.1	7.9	10.7	–0.07	–0.09	–0.06	9.81	8.15	12.33	–0.08	–0.10	–0.06	8.3	6.7	10.7
Isomers																						
2,3,7,8-TCDD	15	3.6	2.9	1.3	–0.11	–0.14	–0.07	6.6	4.9	9.7	–0.09	–0.14	–0.05	7.60	5.08	15.03	–0.12	–0.18	–0.07	5.6	3.9	9.9
1,2,3,7,8-PeCDD	14	21.2	17.4	9.7	–0.05	–0.06	–0.04	13.8	10.9	18.9	–0.04	–0.06	–0.02	16.69	11.24	32.36	–0.06	–0.08	–0.04	11.2	8.8	15.6
1,2,3,4,7,8-HxCDD	16	1.5	1.3	0.6	–0.07	–0.09	–0.05	10.0	7.8	13.8	–0.06	–0.09	–0.03	11.10	7.65	20.23	–0.08	–0.10	–0.05	8.8	6.7	13.0
1,2,3,6,7,8-HxCDD	16	6.1	5.4	3.3	–0.06	–0.07	–0.04	12.5	10.2	16.2	–0.06	–0.07	–0.04	12.56	9.74	17.69	–0.06	–0.08	–0.03	12.5	9.1	20.2
1,2,3,7,8,9-HxCDD	16	2.8	2.0	0.6	–0.14	–0.16	–0.12	4.8	4.3	5.6	–0.14	–0.17	–0.12	4.87	4.17	5.84	–0.14	–0.18	–0.11	4.8	3.9	6.2
1,2,3,4,6,7,8-HpCDD	12	0.7	0.6	0.2	–0.10	–0.12	–0.08	6.7	5.7	8.3	–0.09	–0.12	–0.07	7.50	5.95	10.11	–0.12	–0.15	–0.08	5.9	4.6	8.4
2,3,4,7,8-PeCDF	15	26.1	19.1	9.9	–0.07	–0.08	–0.06	10.3	8.7	12.6	–0.07	–0.09	–0.05	9.99	8.01	13.27	–0.06	–0.08	–0.05	10.7	8.3	14.9
1,2,3,4,7,8-HxCDF	16	6.9	5.0	1.8	–0.11	–0.13	–0.10	6.2	5.5	7.1	–0.11	–0.13	–0.09	6.10	5.23	7.31	–0.11	–0.13	–0.09	6.4	5.2	8.1
1,2,3,6,7,8-HxCDF	16	12.5	9.4	4.0	–0.10	–0.11	–0.09	7.0	6.2	8.0	–0.10	–0.11	–0.08	7.08	6.07	8.49	–0.10	–0.12	–0.08	6.9	5.7	8.7
2,3,4,6,7,8-HxCDF	16	8.1	4.5	0.9	–0.20	–0.23	–0.18	3.4	3.0	3.9	–0.20	–0.24	–0.17	3.38	2.93	4.01	–0.20	–0.24	–0.16	3.4	2.8	4.4
1,2,3,4,6,7,8-HpCDF	16	3.1	1.6	0.3	–0.23	–0.25	–0.21	3.0	2.8	3.3	–0.23	–0.25	–0.20	3.07	2.78	3.44	–0.24	–0.27	–0.21	2.9	2.6	3.3
PCB126	6	11.0	10.1	4.9	–0.07	–0.09	–0.05	9.6	7.4	13.8	–0.07	–0.09	–0.04	10.60	7.53	17.89	–0.08	–0.12	–0.04	8.5	5.8	15.7

[a] The estimated geometric mean serum concentrations at the time of plant shutdown in 1997. [†]The subjects whose (C2000,occup − Cnon–occup) was negative were excluded.

to be increased in the group IV workers, compared with those in the group III workers. The estimated maximum serum concentrations of PCDDs, PCDFs and total dioxins at $C_{0,occup}$ were 34.8, 52.8 and 107.4 pg TEQ/g lipid, respectively. Ten subjects exposed to coplanar PCB126, 4 subjects exposed to 1,2,3,4,6,7,8-HpCDD, 2 subjects exposed to 1,2,3,7,8-PeCDD and 1 subject exposed to 2,3,7,8-TCDD and 2,3,4,7,8-PeCDF were excluded from the calculation of $C_{0,occup}$, since their values for ($C_{2000,occup} - C_{non\text{-}occup}$) were negative for these compounds.

Discussion

In the present study, we analyzed longitudinal data of serum concentrations of dioxin isomers in 16 subjects who were engaged in incineration-related jobs (group III) but did not take part in the jobs assigned to group IV or were assigned to operation and maintenance of the furnace, electric dust collector and wet scrubber (group IV) in the municipal waste incineration plant in Osaka. These two groups of workers were exposed to relatively high levels of dioxins in comparison to the other two groups of workers, that is, groups I and II. The patterns of the serum concentrations of dioxin isomers in the incinerator workers were characterized by a marked increase in PCDFs compared with PCDDs and by high levels of PCDDs, PCDFs and total dioxins compared with those in the general population. In particular, penta-, hexa- and hepta-forms of PCDDs and PCDFs were more abundant in the incinerator workers than in the general population. There was no difference in the serum concentrations of coplanar PCBs between the incinerator workers and the general population. The present findings were essentially consistent with those of Schecter *et al.*[9], Päpke *et al.*[10] and Kumagai *et al.*[11–13] with respect to the abundance of PCDFs compared with PCDDs in the incinerator workers. Our findings showing that the incinerator workers were exposed to high levels of penta-forms of PCDDs and PCDFs are in contrast with the results reported by Schecter *et al.*[9] and Kumagai *et al*[11, 12]. They[9, 11, 12] reported that there was no significant difference in penta-form of PCDDs or PCDFs between waste incinerator workers and their control. This difference might be attributable to the operating conditions[16] of the waste incinerators such as the furnace temperature and structure of the incinerator[23, 24]. The fluidized-bed incinerator with an open-type cooling tower for alkaline-water recycling employed in the Osaka incineration plant might result in highly concentrated dioxins cosmpared with the stoker type incinerator[13].

It was found in the present study that the half-lives of the serum concentrations of dioxin congeners were 11.1 yr for PCDDs, 7.3 yr for PCDFs, 17.0 yr for coplanar PCBs and 9.1 yr for total dioxins. These half-life values were derived from the one-compartment, first-order kinetic model and were essentially consistent with those reported by Aylward *et al.*[18] for former chlorophenol workers, those reported by Flesch-Janys *et al.*[19] for herbicide-factory workers and those reported by Ryan *et al.*[20] for Yusho and Yucheng patients. However, an exception was the long half-life of 2,3,4,7,8-PeCDF, which was 19.6 yr[19], for the herbicide-factory workers based on 5 paired samples. Aylward *et al.*[31] reported that the dependence of TCDD elimination on body burden in the first-order kinetic model was improved by alternate toxicokinetic modeling using increased hepatic elimination of TCDD by CYP1A2 induction. Lorber[32] argued validity of use of a single elimination rate for the complex mixture of chemicals that comprised a TEQ concentration. It was also found in the present study that the half-lives of PCDDs, PCDFs and total dioxins, except for coplanar PCBs tended to be shorter in the group IV workers than in the group III workers, suggesting a dose-dependent trend in the half-lives. Geusau *et al.*[33] and Emond *et al.*[34] reported shorter half-lives of TCDD in two TCDD-intoxicated women depending on the amount accumulated in the body and the body burden-dependent elimination rate in selected veterans of Operation Ranch Hand, respectively. Our results showing an increased elimination rate of dioxins in the group IV workers provides additional evidence for the increased elimination of PCDDs and PCDFs, which is similar to TCDD. Leung *et al.*[29] also showed dose- and age-dependent increases in the elimination rate of PCDFs in Yusho and Yucheng patients.

No difference in the serum concentrations of coplanar PCBs between the incinerator workers and the general population in the farming area of Japan or between group III and IV workers can be taken as indicating that the occupational route of exposure to coplanar PCBs contributes little to the total body burden of dioxins accumulated in the human body. Accordingly, although we obtained a statistically significant half-life for PCB126, it may be explained by a decrease of intake by routes other than the occupational settings.

It was noteworthy that the estimated serum concentrations of PCDDs, PCDFs and total dioxins at the time of plant shutdown in 1997 were 34.8, 52.8 and 107.4 pg TEQ/g lipid, respectively, and that they subsequently decreased gradually. The present estimates for the serum concentrations of PCDDs, PCDFs and total dioxins in 1997, which were obtained using the one-compartment, first kinetic model, might be low given the inference of Aylward *et al.*[31]regarding the limitation of this model. These estimated values suggest that our subjects were occupationally exposed to dioxins in the waste incineration plant. Using 92 incinerator workers in Osaka, including the 16 subjects in the present study, Kitamura *et al.*[23] reported that the levels of gamma-glutamyltransferase (GGT), total protein, uric acid, calcium and ferrum (Fe) in serum were significantly correlated with serum dioxin levels but that these significant correlations disappeared in a the multivariate analysis adjusted for age, smoking status and alcohol drinking. Takata[24] concluded that there were no signs or findings correlated with blood level of dioxins among the incinerator workers, although the concentrations of dioxins among the blood of the incinerator workers who had engaged in maintenance of the furnace, the electric dust collector and the wet scrubber of the incinerator were higher than those of residents in the surrounding area.

Our study has following limitations. We did not adopt the lifestyle factor of dietary intake of dioxins as a confounder. Kitamura *et al.*[23] found a close association of intake of fatty food such as butter, cheese and lard with the serum concentrations of PCDDs, PCDFs and total dioxins. Although we tried to adjust for the factor of percent body fat in the present study, no significant association was observed between percent body fat rate and elimination rate. Further studies will be needed in order to identify lifestyle factors that are covariates for the elimination rate of dioxins.

Conclusion

We provided additional evidence indicating that the incinerator workers in Osaka were occupationally exposed to high concentrations of PCDDs, PCDFs and total dioxins, although the serum concentrations of these compounds decreased year by year. High levels of penta- and hexa-forms of PCDD and PCDF were formed in the fluidized-bed incinerator as compared with other types of incinerators. In the present study, we showed that estimated half-lives of PCDDs and PCDFs depended on the amount accumulated in the body, and we estimated the maximum serum concentrations of dioxin isomers at the time of plant shutdown.

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