

Concentration of PCBs, PCDFs and PCDDs in the blood of Yusho patients and their Toxic Equivalent Contribution

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Introduction

A mass poisoning, called Yusho, occurred in Western Japan in 1968. Yusho was caused by ingestion of rice oil which was contaminated with polychlorinated biphenyls (PCB), polychlorinated dibenzofurans (PCDF), polychlorinated quaterphenyls, and a small amount of polychlorinated dibenzo-p-dioxin (PCDD)¹⁾. PCBs and PCDFs have been separately analyzed in the adipose tissue and blood of Yusho patients after the incidents. This time, we quantified various congeners of PCBs, PCDFs and PCDDs in the blood of Yusho patients which were collected in 1990 and 1991, more than 20 years after the incident. TEQ, toxic equivalent quantity estimated to 2,3,7,8-tetrachlorodibenzo-p-dioxin, in the blood was calculated using the International toxic equivalent factors (TEF) for PCDDs and PCDFs²⁾ and the TEFs by WHO European Centre for Environment and Health for PCBs³⁾.

Materials and Methods

Blood samples were collected from 4 Yusho patients in 1990 and 1991. Pooled sera were obtained from 2 clinical laboratories in Fukuoka in 1991 and 1992. Other blood samples were collected from 11 Yusho patients and 3 x 10 control persons in 1995 for the analysis of PCB congeners. The samples were kept frozen until analyses. The analytical method used for PCDDs, PCDFs and PCBs was previously reported^{4,5)}, involving chemical cleanup and extraction followed by gas chromatography/mass spectrometry analysis.

Results and Discussion

Analysis of PCDD, PCDF and PCB congeners

Concentrations of PCDD, PCDF and PCB congeners in Yusho blood and control blood and serum were measured by high-resolution gas chromatography/mass spectrometry. Table 1 shows the TEQ concentrations calculated from their concentrations and the TEFs. Concentrations of 2,3,4,7,8-penta-CDF, 1,2,3,4,7,8-hexa-CDF and 1,2,3,6,7,8-hexa-CDF in

Table 1 Concentrations of TEQ in Yusho blood and control blood and serum

Sample amount (g)	TEQ Factor	Lipid basis, ppt						
		Cont 1	Cont 2	Cont TS	Yusho1	Yusho2	YushoTAK	YushoKEY
		Serum 1991	Serum 1992	Blood 1992	Blood 1990	Blood 1991	Blood 1990/91	Blood 1990/91
Lipid amount (g)		0.202	0.214	0.102	0.052	0.052	0.044	0.036
2,3,7,8-Tetra-CDD	1	3.30	2.90	1.65	2.30	2.20	2.35	2.40
1,2,3,7,8-Penta-CDD	0.5	4.70	4.45	3.80	3.70	3.50	5.80	9.90
1,2,3,4,7,8-Hexa-CDD	0.1	0.50	0.35	0.30	0.24	0.34	0.00	0.00
1,2,3,6,7,8-Hexa-CDD	0.1	3.80	3.96	4.21	3.40	3.73	7.27	13.40
1,2,3,7,8,9-Hexa-CDD	0.1	0.79	0.87	0.94	0.59	0.49	0.27	0.50
1,2,3,4,6,7,8-Hepta-CDD	0.01	0.49	0.43	0.40	0.17	0.17	0.32	0.37
Octa-CDD	0.001	1.22	1.05	0.43	0.54	0.52	0.19	0.29
Total PCDDs		14.80	14.02	11.73	10.94	10.95	16.19	26.86
2,3,7,8-Tetra-CDF	0.1	0.44	0.50	0.71	0.25	0.25	0.41	0.70
2,3,4,7,8-Penta-CDF	0.5	8.70	8.70	4.45	121.50	120.00	76.50	247.50
1,2,3,7,8-Penta-CDF	0.05	0.04	0.08	0.62	0.09	0.08	0.06	0.13
1,2,3,4,7,8-Hexa-CDF	0.1	1.21	1.17	0.90	15.70	14.80	19.40	36.70
1,2,3,6,7,8-Hexa-CDF	0.1	0.87	0.78	0.66	3.45	3.43	4.27	9.88
2,3,4,6,7,8-Hexa-CDF	0.1	0.04	0.05	0.00	0.06	0.07	0.00	0.00
1,2,3,7,8,9-Hexa-CDF	0.1	0.33	0.34	0.58	0.40	0.44	0.61	0.74
1,2,3,4,6,7,8-Hepta-CDF	0.01	0.10	0.07	0.08	0.17	0.17	0.10	0.17
1,2,3,4,7,8,9-Hepta-CDF	0.01	0.01	0.01	0.00	0.03	0.04	0.00	0.00
Octa-CDF	0.001	0.00	0.00	0.00	0.00	0.00	0.01	0.01
Total PCDFs		11.74	11.69	8.00	141.64	139.27	101.35	295.83
3,3',4,4'-Tetra-CB	0.0005	0.01	0.01	0.01	0.01	0.01	0.00	0.00
3,3',4,4',5-Penta-CB	0.1	14.90	13.40	2.90	4.60	4.40	2.64	2.86
3,3',4,4',5,5'-Hexa-CB	0.01	0.84	0.99	0.32	1.27	1.25	2.81	3.62
Total Coplanar PCBs		15.75	14.40	3.23	5.88	5.66	5.45	6.48
2,4,4'-Tri-CB	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3,3',4,4'-Penta-CB	0.0001	1.13	0.86	0.36	0.33	0.37	0.79	0.94
2,3,4,4',5-Penta-CB	0.0005	1.37	1.38	1.00	1.64	1.48	3.05	5.25
2,3',4,4',5-Penta-CB	0.0001	4.36	4.10	1.71	1.50	1.31	1.76	1.52
2',3,4,4',5-Penta-CB	0.0001	0.07	0.08	0.00	0.00	0.00	0.00	0.00
2,3,3',4,4',5-Hexa-CB	0.0005	6.98	9.11	2.70	15.99	17.40	76.50	65.00
2,3,3',4,4',5'-Hexa-CB	0.0005	1.57	2.05	0.85	4.27	4.50	24.90	19.80
2,3',4,4',5,5'-Hexa-CB	0.00001	0.08	0.08	0.03	0.05	0.05	0.09	0.07
2,3,3',4,4',5,5'-Hepta-CB	0.0001	0.09	0.09	0.13	0.21	0.27	1.60	1.97
Total Mono-ortho PCBs		15.65	17.75	6.78	23.98	25.37	108.69	94.55
2,2',5,5'-Tetra-CB	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,2',4,5,5'-Penta-CB	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,2',3,4,4',5'-Hexa-CB	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,2',4,4',5,5'-Hexa-CB	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,2',3,3',4,4',5-Hepta-CB	0.0001	1.75	2.08	1.54	2.27	2.71	16.10	14.90
2,2',3,4,4',5,5'-Hepta-CB	0.00001	0.84	0.80	0.31	0.52	0.61	2.00	1.97
2,2',3,3',4,4',5,5'-Octa-CB	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Total Di-ortho PCBs		2.59	2.88	1.85	2.79	3.32	18.10	16.87
2,2',3,3',4,4',5,5',6,6'-Deca-CB		0.00	0.00	0.00	0.00	0.00	0.00	0.00
Total PCBs		33.99	35.03	11.86	32.65	34.35	132.24	117.89
Total TEQ		60.53	60.74	31.58	185.22	184.57	249.78	440.58

HUM (po)

Yusho blood were 9-56, 12-41 and 4-15 times, respectively, higher than corresponding concentrations in control blood and serum. Concentrations of 2,3,3',4,4',5-hexa-CB and 2,3,3',4,4',5-hexa-CB were also 2-8 and 2-29 times, respectively, higher in Yusho blood. The high concentrations have persisted for 23 years after the incident. Contrary to these levels, concentrations of some planar PCB congeners such as 3,3',4,4',5-penta-CB and 2,3',4,4',5-penta-CB were lower up to 5.6 and 3.3 times, respectively, in Yusho blood than those in control blood and serum. The lower concentrations of 2,3',4,4',5-penta-CB in Yusho blood were already observed in 1977⁶⁾ and 1992⁵⁾. The decrease of the congeners in the blood of Yusho patients was probably caused by enzyme induction of long-retaining strong enzyme inducers such as 2,3,4,7,8-penta-CDF. In Yusho blood, 2,3,4,7,8-penta-CDF contributed the highest toxicity (TEQ 77-248 ppt in lipid) among the congeners determined and 1,2,3,4,7,8-hexa-CDF and 2,3,3',4,4',5-hexa-CB contributed the following toxicity (TEQ 15-37 and 16-77 ppt in lipid, respectively). TEQ levels of 1,2,3,6,7,8-hexa-CDF, 2,3,4,4',5-penta-CB, 2,3,3',4,4',5-hexa-CB and 2,2',3,3',4,4',5-hepta-CB in Yusho blood (TEQ 3.4-9.9, 1.5-5.3, 4.3-25 and 2.3-16 ppt) were slightly higher than those in the control persons. Contrary to these congeners, 3,3',4,4',5-penta-CB and 2,3',4,4',5-penta-CB (TEQ 2.6-4.4 and 1.3-1.8 ppt) contributed a little less toxicity in some of Yusho patients than did in the control persons. Total TEQ concentrations in Yusho blood were only 3-14 times higher than those of control blood. Figure 1 illustrates the TEQ levels of PCDDs, PCDFs, coplanar PCBs, mono-ortho PCBs and di-ortho PCBs in the Yusho patients and control persons. Percent TEQs of PCDDs, PCDFs and PCBs were calculated in Yusho patients and control persons. The greater part of the total TEQ was contributed by PCDFs (41-77%) and the following part of TEQ was by PCBs (18-53%) in Yusho patients. In control persons, contrasting to Yusho, the greater part of the TEQ was contributed by PCBs (38-59%) and PCDDs (23-37%) and less part was by PCDFs (19-25%).

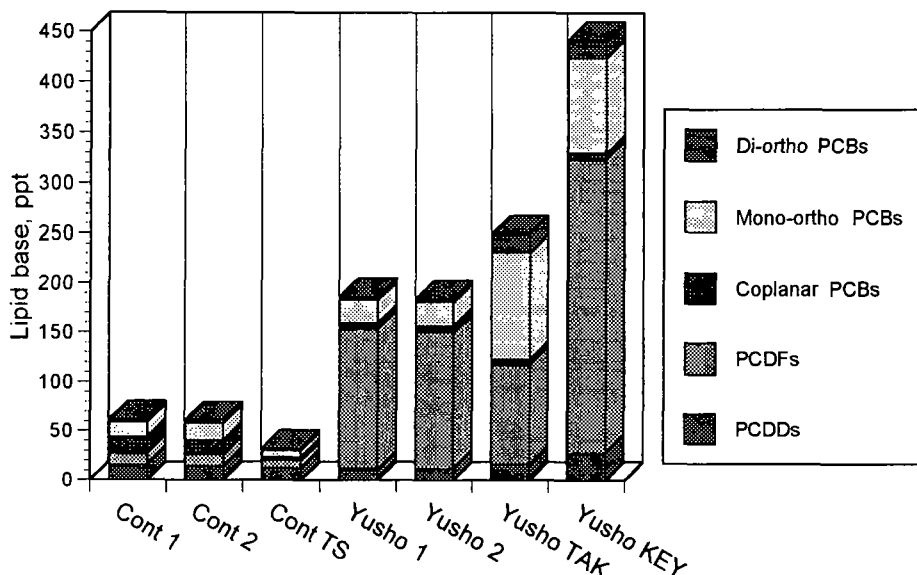


Figure 1 TEQ levels in Yusho and control blood

Table 2 Concentration and ratio of PCB in the blood of Yusho and Control

IUPAC	PCB	PCB concentration in blood, ppb					Yusho Control Ratio
		Yusho patients				Control Average	
		Minimum	Maximum	Average	S.D.		
74	2,4,4',5-tetra-CB	0.058	0.423	0.141	0.113	0.079	1.8
99	2,2',4,4',5-penta-CB	0.097	0.973	0.303	0.237	0.040	7.5
118	2,3',4,4',5-penta-CB	0.063	0.207	0.120	0.039	0.077	1.6
114	2,3,4,4',5-penta-CB	0.021	0.106	0.044	0.024	nd	--
133	2,2',3,3',5,5'-hexa-CB	0.080	0.576	0.193	0.130	0.041	4.7
153	2,2',4,4',5,5'-hexa-CB	0.455	2.551	1.042	0.571	0.220	4.7
105	2,3,3',4,4'-penta-CB	0.021	0.061	0.035	0.012	0.023	1.5
138	2,2',3,4,4',5'-hexa-CB	0.331	2.487	0.859	0.578	0.120	7.2
187	2,2',3,4',5,5',6-hepta-CB	0.123	0.593	0.286	0.155	0.078	3.7
183	2,2',3,4,4',5',6-hepta-CB	0.055	0.227	0.111	0.054	0.026	4.2
128	2,2',3,3',4,4'-hexa-CB	0.024	0.102	0.060	0.021	0.022	2.7
167	2,3',4,4',5,5'-hexa-CB	0.084	0.322	0.120	0.065	0.065	1.8
177	2,2',3,3',4',5,6-hepta-CB	0.021	0.208	0.091	0.058	0.012	7.6
156	2,3,3',4,4',5-hexa-CB	0.119	1.917	0.567	0.478	0.036	15.9
157	2,3,3',4,4',5-hexa-CB	0.046	0.703	0.214	0.178	nd	--
180	2,2',3,4,4',5'-hepta-CB	0.259	1.975	0.822	0.487	0.164	5.0
170	2,2',3,3',4,4',5-hepta-CB	0.169	1.959	0.642	0.475	0.068	9.4
203	2,2',3,4,4',5,5',6-octa-CB	0.090	0.590	0.218	0.139	0.013	16.4
189	2,3,3',4,4',5,5'-hepta-CB	0.014	0.295	0.088	0.076	nd	--
194	2,2',3,3',4,4',5,5'-octa-CB	0.115	0.443	0.226	0.099	0.052	4.3
Total PCBs		2.396	16.540	6.181	3.774	1.138	5.4

Analysis of PCB congeners

Concentrations of PCB congeners in Yusho and control blood sampled in 1995 were measured by low-resolution gas chromatography/mass spectrometry. Table 2 displays the concentrations of 20 PCB congeners. Average total PCB concentrations in Yusho blood was 5.4 times higher than those of controls. Characteristic PCB congeners in Yusho patients were 2,3,3',4,4',5-hexa-CB, 2,2',3,3',4,4',5-hepta-CB and 2,2',3,4,4',5,5',6-octa-CB and their concentration ratios to the corresponding controls were 15.9, 9.4 and 16.4, respectively. In contrast, the concentration ratios of 2,4,4',5-tetra-CB, 2,3',4,4',5-penta-CB, 2,3,3',4,4'-penta-CB and 2,3',4,4',5,5'-hexa-CB were less than 2. These concentrations in blood lipid were similar levels in both Yusho patients and control persons, although the Yusho patients had total PCBs at 5 times higher concentrations than the control persons did.

4. References

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