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Concentrations of Polychlorinated Biphenyls in Blood Collected from Yusho Patients during Medical Check- ups Performed from 2004 to 2007

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Abstract To elucidate the exposure levels of polychlorinated biphenyls (PCBs) for Yusho patients, we conducted a congener-specific analysis of polychlorinated biphenyls (PCBs) in blood collected from 242, 237, 300, and 96 Yusho patients during medical check-ups performed from 2004 to 2007, respectively, and in samples from 74, 113, 125, and 148 Yusho-suspected persons during those same years, respectively, and compared the individual congener concentrations of PCBs among the groups of Yusho patients, Yusho-suspected persons, and normal controls with the concentrations previously reported. Among the 209 PCB congeners, 8 congeners of mono-*ortho* PCBs and 56 congeners of non-dioxin-like PCBs were identified in the blood of Yusho patients and Yusho-suspected persons. Among the PCB congeners measured in the present study, hexaCB-153, hexaCB-138, heptaCB-180, and heptaCB-182/heptaCB-187 showed high ratios to total concentrations of 64 PCB congeners detected in the blood of Yusho patients and Yusho-suspected persons from 2004 to 2007, and the profiles of the major congeners were the same as those obtained in normal controls. With respect to the minor congeners of PCBs, several differences were observed among the three groups. The sums of the concentrations of 64 PCB congeners in the blood of Yusho patients from 2004 to 2007 were 645, 760, 667, and 510 ng g^{-1} lipid for each year, respectively, and the concentrations were 1.5, 1.8, 1.5, and 1.2 times higher than those of normal controls for each year, respectively. Those of the Yusho-suspected persons were approximately 0.8, 1.1, 0.9, and 1.0 times higher than those of normal controls for each year, respectively. The ratios of heptachlorinated biphenyls (heptaCBs) to the total concentrations of 64 PCB congeners in the blood of Yusho patients and Yusho-suspected persons from 2004 to 2007 tended to be slightly higher than those in the normal controls. From the results comparing the concentrations of 64 PCB congeners in the blood between Yusho patients and normal controls, the concentrations of hexaCB-156, hexaCB-157, heptaCB-181, and heptaCB-189 for Yusho patients were 3.4, 3.8, 3.9, and 3.8 times, respectively, 3.9, 4.1, 3.9, and 4.4 times, respectively, 3.6, 3.9, 5.0, and 4.1 times, respectively, and 2.3, 2.5, 2.7, and 2.9 times higher than those of the normal controls for each year from 2004 to 2007, respectively. These results indicated that Yusho patients still have higher concentrations of hexaCB-156, hexaCB-157, heptaCB-181, and heptaCB-189 in their blood than do unaffected people, even though over 35 years have passed since the outbreak of Yusho. These four congeners can therefore be considered to be the most important congeners for evaluating the PCBs exposure of Yusho patients.

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Introduction

The Yusho poisoning accident, which affected over 1800 people, occurred in 1968 in western Japan, and was caused by the ingestion of rice bran oil that contained the following contaminants : PCBs, polychlorinated dibenzofurans (PCDFs), polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated quarterphenyls, and polychlorinated terphenyls[1]. Since the Yusho outbreak, medical care services and health examinations of the subjects have been carried out by the Yusho study group investigating this disease. From the results of extensive research by the Yusho study group, PCDFs were concluded to be the primary cause of the Yusho disease symptoms[2)~4)]. In order to support the health care of Yusho patients, we measured the concentrations of PCDDs, PCDFs, and non-*ortho* PCBs in blood collected from 279, 269, 242, 237, 300, and 96 Yusho patients during medical check-ups performed from 2002 to 2007, respectively, and in samples from 92, 74, 74, 114, 125, and 148 Yusho-suspected persons during those same years, respectively[5)~11)]. We also measured the concentrations of these dioxin-like compounds in the blood of 127 normal controls unaffected by Yusho whose ages were similar to those of the Yusho patients[8)~10)]. The results showed that PCDFs in the blood of Yusho patients, in particular 2,3,4,7,8-pentachlorinated dibenzofuran (2, 3, 4, 7, 8-pentaCDF), are still present at much higher concentrations than in the blood of unaffected people.

Over 35 years have passed since the Yusho outbreak, which occurred because Yusho patients had ingested rice oil contaminated with large amounts of PCBs that were used as a heat-transfer medium in the process of rice oil production[12]. Survey studies of the concentrations of PCB congeners in the blood of Yusho patients are very important when considering the health status of these patients. With respect to the analysis of PCB congeners in the blood of Yusho patients, exposure studies of total PCB levels and the major congeners in the blood were primarily developed beginning 5 years after the outbreak of Yusho[13]. However, a survey study regarding the full congener-specific concentrations of PCBs in the blood of Yusho patients have not been conducted. Recently, advances in the analytic methods used for quantification of PCB congeners have made it much easier to evaluate the exposure levels of PCBs in human[14]. We previously conducted a congener-specific analysis of PCBs in the blood collected from 15 Yusho patients and 43 Yusho-suspected persons in 2006 for a preliminary study[15]. We also measured the 64 PCB congener concentrations in the blood of 127 normal controls unaffected by Yusho[16]. Although our studies have led to reports of the congener concentrates of PCBs in the blood of Yusho patients and Yusho-suspected persons, the studies have suffered from small sample size. To obtain the most useful data for evaluating the exposure levels of PCB congeners in the blood of Yusho patients, it is necessary to measure the concentrations of full PCB congeners in the blood collected from many more Yusho patients. Consequently, the data from congener profiles regarding PCBs in the blood of Yusho patients may provide us with newly important information related to exposure evaluation of patients and with valuable information for future epidemiologic studies.

In this study, we carried out a congener-specific analysis of PCBs in the blood collected from 242, 237, 300, and 96 Yusho patients during medical check-ups performed from 2004 to 2007, respectively, and in samples from 74, 113, 125, and 148 Yusho-suspected persons during those same years, respectively, and compared with the concentrations of PCB congeners among the groups of Yusho patients, Yusho-suspected persons, and normal controls that had been previously reported.

Materials and Methods

1. Sampling

Medical check-ups for Yusho patients have been conducted annually to determine the health status of patients since the outbreak of the Yusho incident. The medical check-ups are available not only to those persons officially registered as Yusho patients but also to Yusho-suspected persons who regard themselves as potential victims. Both officially registered Yusho patients and Yusho-suspected persons are examined based on the "Diagnostic Criteria for Yusho"[1]. The blood samples examined in this study were collected from 316, 351, 425, and 244 participants who received a medical check-up for each year from 2004 to 2007, respectively, from whom informed consent was obtained. The 316 participants included 242 Yusho patients (mean : 65.5 years) and 74 Yusho-suspected persons (mean : 54.7 years) in 2004, the 351 participants included 237 Yusho patients (mean : 67.3 years) and 114 Yusho-suspected persons (mean : 54.7 years) in 2005, the 425 participants included 300 Yusho patients (mean : 66.3 years) and 125 Yusho-suspected persons (mean : 50.7 years) in 2006, and the 244 participants included 96 Yusho patients (mean : 57.8 years) and 148 Yusho-suspected persons (mean : 56.5 years) in 2007. Among 114 Yusho-suspected persons in 2005, the concentrations of PCB congeners in the blood of 113 persons (mean : 56.8 years) were measured in the present study. Blood samples of 10 ml were collected using a vacuum blood-collecting tube containing heparin and were stored at 4℃ until analyses for congener concentrations of PCBs.

2. Materials

Native congeners of mono-*ortho* PCBs and non-dioxin-like PCBs were purchased from Wellington Laboratories (Guelph, Canada). [$^{13}C_{12}$] -congeners of mono-*ortho* PCBs and non-dioxin-like PCBs as internal standards were also purchased from Wellington Laboratories. An active carbon column was prepared as follows: active carbon was purchased from Nacalai Tesque (Kyoto, Japan), refluxed 3 times with toluene for 1 hour, and dried in vacuum, after which 500 mg of the active carbon was mixed with 500 g of anhydrous sodium sulfate (Wako Pure Chemical Industries, Ltd., Tokyo, Japan). A silver nitrate/silica gel was purchased from Wako Pure Chemical Industries, Ltd. An active carbon-dispersed silicagel was purchased from Kanto Chemical Industries, Ltd., Tokyo, Japan. All reagents and solvents used in this experiment were of the analytic grade of dioxin that is commercially available. All glassware instruments used in this experiment were treated in a high-temperature oven (ALP Co. Ltd., Tokyo, Japan) at 450℃ for 6 hours.

3. Analysis of non-dioxin-like PCBs

The extraction and purification of PCB congeners from the blood samples was performed using a previously reported method[15)~17)]. Congener-specific analysis of PCBs was measured using a high resolution gas chromatography/high resolution mass spectrometry (HRGC / HRMS)[15)~17)].

4. Quality control

The limit of detection (LOD) for each congener of PCBs was determined at a signal-to-noise ratio of three on the chromatogram of a standard sample. The limit of quantification for each congener of PCBs was assessed at 0.03 pg g^{-1}. To evaluate the accuracy and reliability in the congener-specific analysis of PCBs, our laboratory in 2007 prepared human blood samples for quality control and attempted to carry out a quality control study for the analysis of these PCB congeners in human blood. Measurements of 64 PCB congeners that were measured in the present study among 209 PCB congeners requested from three different analysis organizations and their results were compared with our results. It was confirmed that the results

obtained by our laboratories were almost identical to those obtained by the three different analysis organizations. The average variation among the total levels of these PCB congeners in human blood samples obtained by four laboratories was within 15% and was considered an acceptable difference. In addition, our laboratory's analytical method for PCB congeners demonstrated high reproducibility based on experiments conducted using the same control blood sample for ten weeks. These findings indicate that our laboratory's analytical method for PCB congeners in human blood provides correct results.

Results and discussion

PCBs form a family of 209 congeners differing in number (mono, di, tri, tetra, penta, hexa, hepta, octa, nona, and deca) and position (2, 2', 3, 3', 4, 4', 5, 5', 6, and 6') of the chlorine atoms on the two basic benzene rings. The 209 PCB congeners consist of 12 dioxin-like PCBs (non-*ortho* PCBs and mono-*ortho* PCBs) and 197 non-dioxin-like PCBs. Among the 209 PCB congeners, 8 congeners of mono-*ortho* PCBs and 56 congeners of non-dioxin-like PCBs were identified in the blood of Yusho patients and Yusho-suspected persons. The concentrations of PCB congeners in the blood of Yusho patients and Yusho-suspected persons from 2004 to 2007, including the dates of the normal controls that had been previously reported, are presented in Table 1-2. We compared the congener patterns of PCBs in normal controls of our studies with those from 24 healthy Japanese volunteers (12 men and 12 women; age range 25-46 years) that had previously been reported in Japan[18]. Among 93 PCB congeners that were measured in the blood, as previously reported, 63 were commonly detected in the blood of normal controls in the present study. The total concentrations of the 63 congeners contributed approximately 96% of the total concentrations of 93 PCB congeners. These 63 PCB congeners measured in the present study may be considered to be the predominant PCB congeners in humans.

Among the 64 PCB congeners that were measured in the present study, hexaCB-138, hexaCB-153, heptaCB-180, and heptaCB-182/heptaCB-187 showed high ratios to the total concentrations of 64 PCB congeners detected in the blood of Yusho patients, Yusho-suspected persons, and normal controls (Table 1-2). Other PCB congeners contributed less than 6% of the total concentrations of these PCB congeners. Although the patterns of the major PCB congeners in the blood of Yusho patients and Yusho-suspected persons from 2004 to 2007 were almost the same as those obtained in normal controls, several differences with respect to the minor PCB congeners were observed among the three groups.

The sums of the concentrations of 64 PCB congeners in the blood of Yusho patients from 2004 to 2007 were 40-3032 (mean : 645, median : 536) ng g^{-1} lipid in 2004, 40-4723 (mean : 760, median : 575) ng g^{-1} lipid in 2005, 74-2432 (mean : 667, median : 553) ng g^{-1} lipid in 2006, and 51-2252 (mean : 510, median : 357) ng g^{-1} lipid in 2007, respectively, and the concentrations were 1.5, 1.8, 1.5, and 1.2 times higher than those of normal controls for each year, respectively (Table 1). In the case of Yusho-suspected persons, the concentrations were 20-1418 (mean : 355, median : 317) ng g^{-1} lipid in 2004, 64-4055 (mean : 490, median : 351) ng g^{-1} lipid in 2005, 18-1850 (mean : 397, median : 257) ng g^{-1} lipid in 2006, and 19-2183 (mean: 440, median : 293) ng g^{-1} lipid in 2007, respectively, which were almost the same or slightly lower than those of normal controls (Table 2).

The arithmetic mean concentrations of triCBs, tetraCBs, pentaCBs, hexaCBs, heptaCBs, octaCBs, nonaCBs, and decaCB-209 in the blood of Yusho patients were 1.9, 16, 45, 292, 228, 57, 4.5, and 1.4 ng g^{-1} lipid in 2004, respectively, 2.5, 21, 53, 331, 268, 78, 5.0, and 1.6 ng g^{-1} lipid in 2005, respectively, 1.7, 19, 49, 305, 240, 46, 5.3, and 1.5 ng g^{-1} lipid in 2006, respectively, and 1.6, 13, 36, 227, 188, 38, 4.4, and 1.4

Table 1 Concentrations of PCB congeners in blood collected fromYusho patients during medical check-ups performed from2004 to 2007

	Concentration (pg g^{-1} lipid)									
	Yusho patients								Normal controls	
	2004 (n=242)		2005 (n=237)		2006 (n=300)		2007 (n=96)		2005 (n=127)	
IUPAC#	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
TriCB-28	1818	1191	2420	3808	1715	2184	1582	1358	2571	1658
TriCB-29	34	19	35	61	29	31	18	20	25	18
TetraCB-44	402	202	1139	3063	435	442	296	317	459	175
TetraCBs-47/48	605	348	925	2097	547	482	413	300	607	214
TetraCB-49	282	149	613	1599	248	215	212	177	303	127
TetraCBs-52/69	1192	837	2323	5769	1054	1174	843	748	1292	830
TetraCBs-56/60	712	524	732	956	363	303	255	179	888	704
TetraCB-63	118	69	125	145	130	95	92	62	146	89
TetraCB-66	1718	1431	2049	2208	1935	1613	1483	1051	2349	1823
TetraCB-70	229	116	721	2027	164	124	122	91	260	98
TetraCB-71	189	105	211	550	47	165	58	105	192	73
TetraCB-74	10666	8120	11990	8489	13851	11024	8763	7509	19526	10790
PentaCB-85	236	318	207	307	141	200	120	149	219	142
PentaCB-87	827	580	922	1162	591	510	431	464	693	379
PentaCB-92	707	521	821	923	685	629	588	450	863	662
PentaCBs-93/95/98	774	400	1497	3629	721	986	514	347	836	407
PentaCB-99	15374	12284	17606	14779	18548	14980	13264	17385	12545	6783
PentaCB-101	1787	1305	2349	3119	1914	1828	1394	1119	1902	1235
PentaCB-105[a]	3571	2760	4018	3217	3750	2947	2810	2003	5082	3383
PentaCBs-107/108	718	492	810	647	773	569	561	369	992	757
PentaCB-110	419	364	690	1355	282	225	182	221	412	176
PentaCB-114[a]	2038	1744	2281	1920	2141	1827	1289	1238	1697	826
PentaCB-117	1359	1465	1533	1947	1074	1122	737	1212	926	680
PentaCB-118[a]	17042	12788	19822	15706	18418	14670	14316	10392	24440	14679
PentaCB-123[a]	295	234	311	279	279	258	247	182	468	328
HexaCB-128	826	873	911	693	694	615	527	439	880	505
HexaCB-130	4110	3593	4615	4428	4304	3750	3265	4149	2614	1562
HexaCB-132	294	217	239	371	339	411	257	223	283	170
HexaCB-134	34	35	36	58	31	61	28	39	27	31
HexaCB-135	480	341	517	424	406	418	319	242	477	291
HexaCB-137	5508	5005	6138	6122	6390	6021	4348	5994	2965	1412
HexaCB-138	58147	42072	68094	52006	65917	48236	47976	47789	40924	19598
HexaCB-139	904	971	1000	1091	805	1178	632	797	825	477
HexaCB-141	291	257	334	314	307	325	235	197	325	202
HexaCB-146	20343	12985	24225	17000	20998	13746	16227	14297	13875	6700
HexaCB-147	569	425	614	495	595	459	470	372	484	317
HexaCB-151	1237	955	1356	1170	1044	908	867	677	1260	937
HexaCB-153	126391	86969	148002	109234	132592	89077	102239	91440	89802	40669
HexaCB-156[a]	27074	27229	30671	33787	28793	32309	18496	27136	7945	3720
HexaCB-157[a]	7622	7803	8217	9746	7786	9060	4957	7695	2011	903
HexaCBs-163/164	34429	24083	31623	22719	30325	20793	23396	21654	19286	9784
HexaCB-167[a]	3630	2703	4350	3163	3339	2474	2513	2104	3648	1860
HeptaCB-170	36016	26128	43555	36732	38345	28706	29254	31599	17228	8740
HeptaCB-172	5702	4145	6767	5980	5493	4075	4215	4538	2965	1522
HeptaCB-177	8382	6484	9327	7419	10327	7734	7690	6578	5745	3082
HeptaCB-178	9001	6971	11169	10918	9927	7823	8012	8654	6234	3128
HeptaCB-179	217	185	231	211	306	314	234	179	209	134
HeptaCB-180	109577	87497	127853	121701	110731	87486	89364	102641	59346	30303
HeptaCB-181	276	365	275	452	354	697	191	438	71	45
HeptaCBs-182/187	43472	36974	50928	46733	47492	39917	36728	38985	28073	13989
HeptaCB-183	9470	8265	11224	9513	11455	9285	8033	7807	6155	3047
HeptaCB-189[a]	3931	3418	4607	4451	4243	4223	3035	4030	1046	518
HeptaCB-191	1785	1456	1827	1702	1822	1512	1276	1565	765	371
OctaCB-194	17008	14156	22221	22944	18013	14759	15295	18735	8580	5140
OctaCB-195	3789	2950	4724	3766	4812	3636	3541	3719	1820	946
OctaCBs-196/203	14706	11499	19496	18543	9561	7131	8226	9187	7822	4148
OctaCBs-198/201	17780	15157	25186	29596	8508	7041	7274	8778	10074	5670
OctaCB-200	447	410	669	578	511	504	389	334	652	1394
OctaCB-202	2265	2343	5061	5072	3687	3057	3240	3801	2813	4490
OctaCB-205	622	441	909	709	557	428	428	437	309	139
NonaCB-206	2958	1733	3419	2307	3198	1947	2617	2161	1957	893
NonaCB-207	479	292	459	324	675	437	528	390	340	176
NonaCB-208	1029	585	1100	923	1411	854	1236	1060	775	376
DecaCB-209	1359	648	1646	1046	1522	779	1398	847	1359	543
Total TriCBs	1852	1193	2455	3852	1743	2186	1599	1361	2596	1658
Total TetraCBs	16113	9639	20829	22083	18774	12855	12537	8749	26023	13501
Total PentaCBs	45147	27613	52868	36881	49315	32028	36455	28513	51075	28205
Total HexaCBs	291889	194020	330942	234476	304666	205100	226753	211649	187632	85471
Total HeptaCBs	227829	174468	267761	236075	240496	182066	188032	201281	127837	63542
Total OctaCBs	56618	45696	78265	78912	45649	35380	38393	44263	32068	18677
Total NonaCBs	4467	2551	4978	3450	5285	3125	4380	3545	3072	1409
Total DecaCB	1359	648	1646	1046	1522	779	1398	847	1359	543
Total Mono-*ortho* PCBs	65203	43994	74276	54320	68749	51156	47663	45728	46338	24419
Total PCBs	645274	430699	759745	568301	667449	442851	509548	472748	431662	200299
Age (years)	65.5	11.8	67.3	11.3	66.3	12.0	57.8	14.5	68.1	5.4

The paticipants of the medical check-up for Yusho during 2004 to 2007 were 316 351, 425, and 244 for each years, respectively.
[a] Mono-*ortho* PCBs; CB: chlorinated biphenyls; S.D.: standard deviation.

Table 2 Concentrations of PCB congeners in blood collected fromYusho-suspected persons during medical check-ups performed from2004 to 2007

	Concentration (pg^{-1}glipid)									
	Yusho suspected persons								Normal controls	
	2004 (n=74)		2005 (n=113)		2006 (n=125)		2007 (n=148)		2005 (n=127)	
IUPAC#	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
TriCB-28	1819	1025	3320	3653	1636	2114	2010	2488	2571	1658
TriCB-29	34	22	43	64	25	46	28	25	25	18
TetraCB-44	394	155	1656	3167	348	242	345	279	459	175
TetraCBs-47/48	539	257	1237	2208	429	296	421	261	607	214
TetraCB-49	269	142	907	1707	212	172	211	164	303	127
TetraCBs-52/69	1242	1023	3391	6159	947	1198	941	855	1292	830
TetraCBs-56/60	578	441	1161	1090	382	550	410	521	888	704
TetraCB-63	105	77	162	161	120	114	115	90	146	89
TetraCB-66	1575	1205	2354	2191	1909	1973	1961	1900	2349	1823
TetraCB-70	230	105	1124	2143	111	82	155	114	260	98
TetraCB-71	180	106	361	682	38	59	91	145	192	73
TetraCB-74	11737	9797	13839	11460	14243	16616	14448	15962	19526	10790
PentaCB-85	193	203	231	307	119	118	111	85	219	142
PentaCB-87	542	288	881	1194	373	324	400	310	693	379
PentaCB-92	639	674	883	1041	646	717	583	536	863	662
PentaCBs-93/95/98	722	380	2061	3733	605	473	601	382	836	407
PentaCB-99	8985	6289	10419	7321	10970	10233	11433	9464	12545	6783
PentaCB-101	1464	1102	2520	3147	1537	1342	1531	1182	1902	1235
PentaCB-105[a]	3364	2733	4224	3566	3626	3655	3945	3867	5082	3383
PentaCBs-107/108	648	507	840	740	723	667	703	624	992	757
PentaCB-110	373	297	904	1472	251	209	205	234	412	176
PentaCB-114[a]	1091	837	1397	1105	1153	1080	1253	1107	1697	826
PentaCB-117	633	513	976	922	562	555	560	468	926	680
PentaCB-118[a]	16544	13835	20545	16861	17950	18522	19488	19310	24440	14679
PentaCB-123[a]	308	269	395	357	309	365	353	366	468	328
HexaCB-128	654	535	810	603	571	490	571	429	880	505
HexaCB-130	1858	1561	2594	2565	2145	2233	2421	2110	2614	1562
HexaCB-132	238	169	254	329	281	248	271	236	283	170
HexaCB-134	34	28	34	58	24	40	31	45	27	31
HexaCB-135	391	282	442	389	344	294	369	248	477	291
HexaCB-137	2122	1574	2695	2427	2625	2445	2740	2351	2965	1412
HexaCB-138	31378	23233	38959	31084	36864	36524	39862	36242	40924	19598
HexaCB-139	685	736	890	1001	543	538	593	492	825	477
HexaCB-141	239	171	297	297	260	234	259	240	325	202
HexaCB-146	11517	8429	15591	16878	12719	13093	14023	13151	13875	6700
HexaCB-147	405	334	460	449	466	453	493	391	484	317
HexaCB-151	969	782	1253	1150	922	865	954	853	1260	937
HexaCB-153	75410	58818	96651	91057	83566	86696	91192	88541	89802	40669
HexaCB-156[a]	5887	4326	8869	9380	6900	6094	7802	6869	7945	3720
HexaCB-157[a]	2166	2222	2174	2097	1785	1679	1942	1704	2011	903
HexaCBs-163/164	16999	13390	19007	21801	16910	17510	18590	17661	19286	9784
HexaCB-167[a]	2712	2405	3769	3289	2687	2825	3024	3104	3648	1860
HeptaCB-170	14794	13515	22610	29747	17887	19341	20739	22864	17228	8740
HeptaCB-172	2608	2426	3928	6411	2828	3096	3276	3624	2965	1522
HeptaCB-177	4777	4048	6358	6967	6601	7273	7445	7408	5745	3082
HeptaCB-178	5177	4610	7857	11852	6493	7073	7157	7781	6234	3128
HeptaCB-179	170	114	198	163	254	233	259	196	209	134
HeptaCB-180	55302	53045	78372	114192	63109	72895	72408	85344	59346	30303
HeptaCB-181	57	52	58	70	150	882	81	87	71	45
HeptaCBs-182/187	25597	21831	35459	47747	31520	36851	35742	40465	28073	13989
HeptaCB-183	5476	4956	7059	7060	7084	8231	7859	8806	6155	3047
HeptaCB-189[a]	857	785	1433	2034	1120	1152	1274	1394	1046	518
HeptaCB-191	653	574	781	843	748	820	845	877	765	371
OctaCB-194	7892	8116	13424	24994	9785	11465	11573	14976	8580	5140
OctaCB-195	1674	1400	2576	3354	2479	2710	2892	3360	1820	946
OctaCBs-196/203	7202	6295	12104	18641	5299	6007	6697	7843	7822	4148
OctaCBs-198/201	9456	9330	17503	31026	5226	5988	6128	7475	10074	5670
OctaCB-200	285	232	445	412	372	424	414	440	652	1394
OctaCB-202	1530	1239	3517	5375	2504	2691	2776	3092	2813	4490
OctaCB-205	264	215	509	813	270	315	314	350	309	139
NonaCB-206	1519	1026	2243	3576	1787	1598	1962	1908	1957	893
NonaCB-207	270	179	302	282	398	378	453	407	340	176
NonaCB-208	612	462	788	1279	855	754	972	860	775	376
DecaCB-209	966	567	1399	2130	1053	781	1152	823	1359	543
Total TrCBs	1853	1026	3362	3698	1661	2116	2038	2488	2596	1658
Total TeCBs	16848	11984	26191	22475	18739	19489	19097	18351	26023	13501
Total PeCBs	35506	26017	46276	33755	38823	36269	41167	35744	51075	28205
Total HxCBs	153666	114958	194751	177719	169610	169682	185138	172086	187632	85471
Total HpCBs	115468	104054	164114	224475	137794	155300	157085	176803	127837	63542
Total OcCBs	28303	26319	50077	83787	25936	29185	30796	37186	32068	18677
Total NoCBs	2401	1639	3333	5074	3040	2663	3388	3139	3072	1409
Total DecaCB	966	567	1399	2130	1053	781	1152	823	1359	543
Total Mono-*ortho*PCBs	32930	25581	42805	34002	35529	34102	39082	35572	46338	24419
Total PCBs	355011	274465	489503	516382	396656	402035	439860	426872	431662	200299
Age (years)	54.7	17.0	56.8	16.7	50.7	20.4	56.5	17.7	68.1	5.4

The paticipants of the medical check-up for Yusho during 2004 to 2007 were 316 351, 425, and 244 for each years, respectively.
[a] Mono-*ortho* PCBs; CB: chlorinated biphenyls; S.D.: standard deviation.

ng g^{-1} lipid in 2007, respectively (Table 1). In the case of Yusho-suspected persons, these concentrations were 1.9, 17, 36, 154, 115, 28, 2.4, and 1.0 ng g^{-1} lipid in 2004, respectively, 3.4, 26, 46, 195, 164, 50, 3.3, and 1.4 ng g^{-1} lipid in 2005, respectively, 1.7, 19, 39, 170, 138, 26, 3.0, and 1.1 ng g^{-1} lipid in 2006, respectively, and 2.0, 19, 41, 185, 157, 31, 3.4, and 1.2 ng g^{-1} lipid in 2007, respectively (Table 2). On the other hand, these concentrations in the blood of normal controls were 2.6, 26, 51, 188, 128, 32, 3.1, and 1.4 ng g^{-1} lipid, respectively. The concentrations of hexaCBs, heptaCBs, octaCBs, and nonaCBs in the blood of Yusho patients were slightly higher than those of the normal controls.

The relative contribution ratios of the concentrations of triCBs, tetraCBs, pentaCBs, hexaCBs, heptaCBs, octaCBs, nonaCBs, and decaCB-209 to the total concentrations of the 64 PCB congeners compared the ratios among the groups of Yusho patients, Yusho-suspected persons, and normal controls. The ratios of the mono-*ortho* PCBs concentrations to the total concentrations of 64 PCB congeners for Yusho patients and Yusho-suspected persons were almost the same as those of normal controls. The ratios of the triCBs, tetraCBs, pentaCBs, hexaCBs, heptaCBs, octaCBs, nonaCBs, and decaCB-209 concentrations to the total concentrations of 64 PCB congeners for normal controls were 0.6, 6.0, 11.8, 43.5, 29.6, 7.4, 0.7, and 0.3%, respectively. In the case of Yusho-suspected persons, the contribution ratios of these eight concentrations were 0.5, 4.7, 10.0, 43.3, 32.5, 8.0, 0.7, and 0.3% in 2004, respectively, 0.7, 5.4, 9.5, 39.8, 33.5, 10.2, 0.7, and 0.3 % in 2005, respectively, 0.4, 4.7, 9.8, 42.8, 34.7, 6.5, 0.8, and 0.3% in 2006, respectively, and 0.5, 4.3, 9.4, 42.1, 35.7, 7.0, 0.8, and 0.3% in 2007, respectively (Table 2). Finally, the ratios of these concentrations in Yusho patients were 0.3, 2.5, 7.0, 45.2, 35.3, 8.8, 0.7, and 0.2% in 2004, respectively, 0.3, 2.7, 7.0, 43.6, 35.2, 10.3, 0.7, and 0.2% in 2005, respectively, 0.3, 2.8, 7.4, 45.6, 36.0, 6.8, 0.8, and 0.2% in 2006, respectively, and 0.3, 2.5, 7.2, 44.5, 36.9, 7.5, 0.9, and 0.3% in 2007, respectively (Table 1) ; it was confirmed that the ratios of triCBs, tetraCBs, and pentaCBs to the total concentrations of the 64 PCB congeners for Yusho patients and Yusho-suspected persons were slightly lower than those of the normal controls, and the ratios of hexaCBs, octaCBs, nonaCBs, and decaCB-209 concentrations to the total PCB concentrations for Yusho patients and Yusho-suspected persons were nearly the same as those of the normal controls. However, the ratios of the concentrations of heptaCBs to the total concentrations of 64 PCB congeners in the blood for Yusho patients and Yusho-suspected persons tended to be slightly higher compared to those of the normal controls.

Among the PCB congeners measured in the present study, the concentrations of 64 PCB congeners in the blood for Yusho patients and Yusho-suspected persons were compared with those of the normal controls. The concentrations of hexaCB-156, hexaCB-157, heptaCB-181, and heptaCB-189 in the blood samples for Yusho patients were 27, 7.6, 0.3, and 3.9 ng g^{-1} lipid in 2004, respectively, 31, 8.2, 0.3, and 4.6 ng g^{-1} lipid in 2005, respectively, 29, 7.8, 0.4, and 4.2 ng g^{-1} lipid in 2006, respectively, and 18, 5.0, 0.2, and 3.0 ng g^{-1} lipid in 2007, respectively. These levels were 3.4, 3.8, 3.9, and 3.8 times, respectively, 3.9, 4.1, 3.9, and 4.4 times, respectively, 3.6, 3.9, 5.0, and 4.1 times, respectively, and 2.3, 2.5, 2.7, and 2.9 times higher than those of the normal controls for each year from 2004 to 2007, respectively (Table 1). In the case of Yusho-suspected persons, the concentrations were 0.7, 1.1, 0.8, and 0.8 times, respectively, 1.1, 1.1, 0.8, and 1.4 times, respectively, 0.9, 0.9, 2.1, and 1.1 times, respectively, and 1.0, 1.0, 1.1, and 1.2 times higher than those of the normal controls for each year from 2004 to 2007, respectively (Table 2). These findings indicated that Yusho patients still have higher concentrations of hexaCB-156, hexaCB-157, heptaCB-181, and heptaCB-189 in their blood than do unaffected persons more than 35 years after the Yusho incident. These four congeners can be considered the characteristic

congeners of PCBs in the blood of Yusho patients.

We have previously reported that the concentrations of 2,3,4,7,8-pentaCDF, which were the highest among the PCDF congeners for Yusho patients, were approximately 10 times higher than those of the normal controls[5)~11)]. From the results obtained by the present study, the concentrations of hexaCB-156, hexaCB-157, heptaCB-181, and heptaCB-189, which were the highest among the PCB congeners in the blood samples for Yusho patients, were 3.4, 3.8, 3.9, and 3.8 times, respectively, 3.9, 4.1, 3.9, and 4.4 times, respectively, 3.6, 3.9, 5.0, and 4.1 times, respectively, and 2.3, 2.5, 2.7, and 2.9 times higher than those of the normal controls for each year from 2004 to 2007, respectively. These finding indicate that the ratios of 2,3,4,7,8-pentaCDF in the blood of Yusho patients for the more than 35 years since the outbreak of Yusho remain higher than those of PCB congeners.

In conclusion, the exposure levels of PCB congeners for Yusho patients and Yusho-suspected persons were able to be determined in the present study. The results indicated that Yusho patients still have higher concentrations of hexaCB-156, hexaCB-157, heptaCB-181, and heptaCB-189 in their blood than do unaffected people more than 35 years after the Yusho incident. These four congeners can be considered the most important congeners for evaluating the PCBs exposure of Yusho patients. We provide newly important information regarding the exposure evaluation of PCB congeners for Yusho patients and hope that these data can be used in future epidemiological investigations of Yusho patients.

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（和文抄録）

平成 16 年から 19 年度におけるカネミ油症検診者の血液中ポリ塩化ビフェニール濃度

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平成 16 年から平成 19 年度に，それぞれ 242,237,300 および 96 名の油症患者およびそれぞれ 74, 113，125 および 148 名の未認定者から採取した血液中 PCB の異性体濃度を測定し，一般健常人の結果と比較した．油症患者と未認定者の血液中において，PCB 64 異性体を分離・定量した．油症患者の血液中，hexaCB-153，hexaCB-138，heptaCB-180 および heptaCB-182/187 は他と比較して高い濃度を示したが，この結果は一般健常人と同じであった．平成 16 年から 19 年度に受診した油症患者血液中 PCB の 64 異性体総濃度は，それぞれ 645,760,667 および 510 ng g^{-1} lipid で，その濃度は一般健常人のそれぞれ 1.5,1.8,1.5 および 1.2 倍であった．未認定者の場合，総 PCB 濃度はほぼ健常人と同レベルであった．PCB 総濃度に対する各異性体の割合を比較した結果，油症患者と未認定者の heptaCBs 濃度は一般健常人より高かった．油症患者の血液中 64 PCB 異性体濃度を健常人と比較した場合，hexaCB-156，hexaCB-157，heptaCB-181 および heptaCB-189 の濃度は，一般健常人のそれぞれ 2.3-3.9，2.5-4.1，2.7-5.0 および 2.9-4.4 倍高い値を示した．以上の結果から，油症発症から 35 年以上が経過した現在も患者の血液中 PCB 濃度，特に hexaCB-156，hexaCB-157，heptaCB-181 および heptaCB-189 濃度は以前高いレベルにあり，油症患者の PCB 暴露を評価する上で最も重要な異性体であると言える．