Occurrence of Tris(4-chlorophenyl)methane, Tris(4-chlorophenyl)methanol, and Some Other Persistent Organochlorines in Japanese Human Adipose Tissue

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Tris(4-chlorophenyl)methane (TCPMe) and tris(4-chlorophenyl)methanol (TCPMOH) are among the most recently identified environmental contaminants. Despite their widespread contamination in the marine environment, human exposure to these compounds remains relatively unknown. We determined the concentrations of TCPMe, TCPMOH, and other persistent organochlorines such as polychlorinated biphenyls (PCBs), DDT and its metabolites, hexachlorocyclohexane isomers, hexachlorobenzene, and chlordane compounds (CHLs) in human adipose tissue from Japan. TCPMe and TCPMOH were detected in all of the adipose samples analyzed; the concentrations ranged from 2.5–21 and 1.1–18 ng/g lipid weight, respectively. Concentrations of TCPMe and TCPMOH in humans were less than those reported in marine mammals, suggesting the possibility of metabolism and elimination of these compounds by humans. Significant correlation between TCPMe and TCPMOH with concentrations of DDT and its metabolites in human adipose tissues suggested that exposure to DDT is the source of TCPMe and TCPMOH in humans. The age- and sex-dependent accumulation of TCPMe and TCPMOH as well as other organochlorines was less pronounced. Results for other organochlorines indicated that recent contamination status of PCBs in human samples from Japan was higher than that in developing countries, whereas DDT contamination is lower. Greater concentrations of CHLs in human adipose tissue from Japan than in those from other countries suggest that continuous monitoring of CHLs in humans in Japan is necessary. To our knowledge, this is the first study on the accumulation of TCPMe and TCPMOH in human adipose tissue. *Key words*: humans, metabolic capacity, organochlorines, tris(4-chlorophenyl)methane, tris(4-chlorophenyl)methanol. *Environ Health Perspect* 108:599–603 (2000). [Online 25 May 2000]
http://ehpnet1.niehs.nih.gov/docs/2000/108p599-603minh/abstract.html

In recent years, in addition to numerous investigations on global pollution and the toxic effects of classic man-made chemicals, the discovery of new environmental contaminants has received considerable attention. Tris(4-chlorophenyl)methane (TCPMe) and tris(4-chlorophenyl)methanol (TCPMOH) are among the most recently detected contaminants in environmental samples. Although the point sources of these compounds are unknown, their environmental contamination is widespread (1). Recent investigations have indicated the high bioaccumulation potential of TCPMe and TCPMOH in the marine food chain comparable to that of DDT, a well known insecticide (2,3).

Because TCPMe and TCPMOH are structurally similar to the pesticides DDT and dicofol, respectively, and because the endocrine-disrupting effects of these chemicals have been well documented, TCPMe and TCPMOH may pose toxic threats to humans and wildlife similar to those observed for DDT. Some toxicologic studies imply that TCPMOH induces hepatic enzymes and poses antiandrogenic effects (4,5). An *in vivo* test in rats revealed that TCPMOH caused increased 4-hydroxylation of estradiol activity in males (6). A more recent study has shown that TCPMOH has a strong binding affinity to androgen receptor; however, the compound did not show any estrogenic or antiestrogenic activity based on the MCF-7 cell proliferation assay (7).

Although a few investigations have been conducted in aquatic mammals, little is known about the exposure of terrestrial animals including humans to TCPMe and TCPMOH. To our knowledge, only one investigation has reported the occurrence of TCPMe and TCPMOH in human milk from Sweden and Italy (8). However, because of the lack of analytical standards in that study, the concentrations of TCPMe and TCPMOH were estimated based on the chromatographic response of 3,3′,4,4′,5,5′-hexachlorobiphenyl (International Union of Pure and Applied Chemistry no. 169) as an internal standard; therefore, the results might be less accurate. For this reason, the actual exposure of humans to TCPMe and TCPMOH is still unknown due to the lack of residue data. Determination of TCPMe and TCPMOH residues in human samples may lead to a further understanding of accumulation features as well as provide a basis for risk assessment to human health posed by these compounds.

In the present study, we report for the first time the quantitative data of TCPMe and TCPMOH residues in Japanese human adipose tissue. Bioaccumulation features of these compounds in humans is discussed in comparison to other classic persistent organochlorines (OCs) such as DDT and its metabolites (DDTs), polychlorinated biphenyls (PCBs), hexachlorocyclohexane isomers (HCHs), hexachlorobenzene (HCB), and chlordane compounds (CHLs). Existing data were compiled from our recent investigations on TCPMe and TCPMOH residues in fish and marine mammals collected from Japanese coastal waters and interpreted to understand the bioaccumulation potential and metabolic capacity in marine and terrestrial animals. In addition, we examined the accumulation of other classic OCs and attempted to compare OC residues of Japanese human adipose tissue with those from other countries in the world to understand the status of contamination.

Materials and Methods

Samples. We obtained human adipose tissue samples from patients autopsied in Keio University Hospital (Tokyo, Japan) during the period of May–August 1998. We obtained informed consent from bereaved family members for all of the samples analyzed in this study. The adipose tissues were wrapped in aluminum foil and stored at -80°C until analysis. These samples were taken from randomly selected patients in several cities from Japan. The details of cases are shown in Table 1.

Chemical analysis. Chemical analyses of TCPMe, TCPMOH, and other OCs followed the method previously described (3).

Briefly, approximately 2 g adipose tissue samples were homogenized with anhydrous Na_2SO_4 and extracted using a Soxhlet apparatus with a mixture of hexane and diethyl ether. We gravimetrically determined fat content from an aliquot of the extract. The extract was then added into a dry Florisil column to remove fat. Organochlorines were eluted with 150 mL 20% water in acetonitrile to a separatory funnel containing hexane and water. After partitioning, the hexane layer was concentrated and then passed through an 8-g activated Florisil column for fractionation. The first fraction eluted with hexane contained PCBs, p,p'-DDE, *trans*-nonachlor, and HCB; the second fraction eluted with 20% dichloromethane in hexane contained other OC pesticides and TCPMe. The third fraction eluted with 50% dichloromethane in hexane contained TCPMOH. Each fraction was concentrated and injected into a gas chromatograph with electron capture detector (GC-ECD) and a gas chromatograph with a mass selective detector (GC-MSD) for quantification.

OCs (except TCPMe and TCPMOH) were quantified by a Hewlett Packard 5890 Series II GC-ECD (Wilmington, DE) equipped with a moving needle-type injection port. The GC column used was a DB-1 fused silica capillary column (0.25 mm × 30 m; J & W Scientific Inc., Folsom, CA) coated with 100% dimethylpolysiloxane at 0.25 µm film thickness. The column oven temperature was programmed from 60 to 160°C, held for 10 min, then increased to 260°C at a rate of 20°C/min and held for 20 min. Injector and detector temperatures were set at 260 and 280°C, respectively. Helium and nitrogen were used as carrier and makeup gases, respectively. We calculated OC concentrations from the peak area of the sample to the corresponding external standard. The PCB standard used for quantification was an equivalent mixture of Kanechlor preparations (KC-300, KC-400, KC-500, and KC-600) with known PCB composition and content. Concentrations of individually resolved peaks of PCBs isomers and congeners were summed to obtain total PCB concentrations. A Hewlett-Packard 5890 series II GC-MSD coupled with a 5972 mass selective detector was used for the quantification of TCPMe and TCPMOH. Data acquisition was performed by a Hewlett-Packard 5972C data system, in which the cluster ions were monitored at *m/z* 311, 313, 346, and 348 for TCPMe and 139, 251, 253, 362, and 364 for TCPMOH. Recoveries of target analytes through this analytical method were 95 ± 1.1% for TCPMe, 100 ± 2.1% for TCPMOH, 99 ± 2.0% for PCBs, 95 ± 7.5% for DDTs, 96 ± 7.7% for HCH, 100 ± 4.7% for CHLs, and 94 ± 5.9% for

HCB. Concentrations were not corrected for recovery rates. A procedural blank was analyzed with every set of six samples to check for interfering compounds and to correct samples values, if necessary. DDTs are the sum of p,p'-DDT, p,p'-DDD, and p,p'-DDE; CHLs include *cis*-chlordane, *trans*-chlordane, *cis*-nonachlor, *trans*-nonachlor, and oxychlordane. HCHs include α-, β-, and γ-isomers. The concentration of OCs was expressed as nanogram per gram on a lipid weight basis unless otherwise specified. We calculated concentration on lipid weight basis based on concentration in wet weight basis and lipid content, which was gravimetrically measured as mentioned previously. Thus, we obtained values in lipid weight basis from the following calculation: concentration in lipid weight = concentration in wet weight ÷ lipid content (as a percentage).

For quality assurance and quality control, our laboratory participated in the Intercomparison Exercise for Persistent Organochlorine Contaminants in Marine Mammal Blubber, organized by the National Institute of Standards and Technology (Gaithersburg, MD) and the Marine Mammal Health and Stranding Response Program of the National Oceanic and Atmospheric Administration's National Marine Fisheries Service (Silver Spring, MD). Standard reference material (SRM 1945) was analyzed for selected PCB congeners and persistent OCs. Reliable results were obtained by comparison of generated data from our laboratory with those from material reference values.

Results and Discussion

Bioaccumulation characteristics of TCPMe and TCPMOH in humans. Mean, range, median, and geometric mean of concentrations of TCPMe, TCPMOH, and other OCs are given in Table 2. The residue pattern order was PCBs > DDTs > HCHs > CHLs > HCB > TCPMe > TCPMOH. This observation was somewhat similar to that revealed in our recent investigations on the occurrence of TCPMe and TCPMOH in

Table 1. Information on the Japanese human adipose tissue samples analyzed in this study.

Sample no.	Sex	Age (years)	Residence	Occupation	Cause of death
1	M	50	Kawasaki	Pharmacist	Brain tumor
2	M	55	Tokyo	Officer	Hepatocellular carcinoma
3	M	63	Yokohama	Shopkeeper	Myocardial infarction
4	M	65	Chiba	Officer	Pulmonary fibrosis
5	M	68	Tokyo	Officer	Bronchopneumonia
6	M	73	Yokohama	Officer	Lung cancer
7	M	79	Tokyo	Officer	Urinary bladder carcinoma
8	M	87	Tokyo	Without occupation	Bronchopneumonia
9	F	29	Tokyo	Without occupation	Acute myelocytic leukemia
10	F	33	Tokyo	Housewife	Spinal cord tumor
11	F	53	Tokyo	Housewife	Takayasu's arteritis
12	F	75	Tokyo	Housewife	Cerebral hemorrhage
13	F	76	Tokyo	Without occupation	Acute myelocytic leukemia
14	F	85	Tokyo	Housewife	Ovarian carcinoma

Abbreviations: F, female; M, male.

Table 2. Concentrations (ng/g lipid weight) of TCPMe, TCPMOH, and other OCs in human adipose tissue from Japan.

Sample no.	Sex	Age[a]	Fat (%)	TCPMe	TCPMOH	PCBs	DDTs[b]	HCHs[c]	CHLs[d]	HCB
1	M	50	80	11	5.5	1,800	350	140	280	30
2	M	55	80	8.9	7.5	1,800	1,300	150	180	31
3	M	63	74	11	8.1	2,600	950	360	260	64
4	M	65	86	6.2	5.8	1,300	600	600	110	22
5	M	68	85	3.1	1.1	520	110	60	65	22
6	M	73	66	15	8.5	3,200	710	260	710	44
7	M	79	57	11	4.7	1,700	660	160	210	30
8	M	87	63	17	16	2,500	1,900	320	220	27
9	F	29	57	2.5	2.8	560	400	210	110	33
10	F	33	56	3.0	2.9	930	820	430	96	38
11	F	53	57	21	18	2,300	820	540	250	68
12	F	75	66	6.7	4.5	2,300	1,300	560	270	68
13	F	76	78	8.5	8.2	1,700	420	510	210	60
14	F	85	74	4.9	2.4	720	620	300	260	38
Mean			70	9.3	6.9	1,700	780	330	230	41
Range			56–86	2.5–21	1.1–18	520–3,200	110–1,900	60–600	65–710	22–68
Median				8.9	5.6	1,800	690	310	220	35
Geometric mean				8.3	5.4	1,500	650	280	200	38

Abbreviations: F, female; M, male.
[a]In years. [b]DDTs = sum of p,p'-DDE; p,p'-DDD; and p,p'-DDT. [c]HCHs = sum of α-HCH; β-HCH; and γ-HCH. [d]CHLs = sum of oxychlordane; *trans*-chlordane; *cis*-chlordane; *trans*-nonachlor; and *cis*-nonachlor.

marine mammals (*3,9*). TCPMe and TCP-MOH have to date been considered impurities in technical DDT and dicofol (*10,11*) as well as high polymers and agrochemical products (*1*). The environmental exposure as impurities from other materials may explain the relatively lower concentrations of TCPMe and TCPMOH as compared to other persistent OCs. Concentrations of TCPMe and TCPMOH ranged between 2.5–21 and 1.1–18 (nanogram per gram lipid weight), respectively, which were approximately 2 orders of magnitude lower than those of DDTs (ranging between 110 and 1,900 ng/g lipid weight). The rather high concentrations of TCPMe and TCPMOH were found in an 87-year-old male patient (sample no. 8) and a 53-year-old female patient (sample no. 11) (Table 2). In these male and female patients, relatively higher levels of DDTs and PCBs were also recorded.

TCPMe and TCPMOH concentrations found in Japanese human adipose tissue were approximately 6 and 3 times greater than those estimated in human milk from Sweden and Italy, respectively (*8*). However, residue levels in human samples were much lower than those reported in various marine mammals and sea birds from several locations such as Canada, United States, Japan, Hong Kong, and European regions (*1–3,9,12*).

To understand the metabolic capacity to TCPMe and TCPMOH in humans, data on these compounds in humans were compared with those in fish and marine mammals (seals and cetaceans) that we collected from Japanese coastal waters. As shown in Figure 1, TCPMe concentrations in human adipose tissues were higher than those reported in fish and comparable to those in the larga seal, harbor porpoise, Dall's porpoise, and striped dolphin, but significantly lower than those in

Fraser's dolphin. However, TCPMOH residue levels in humans were approximately 10 times lower than those in most marine mammals examined. This result implies that contamination and bioaccumulation of TCPMe and TCPMOH extends over a wide range of higher trophic animals, not only in the marine ecosystem, but also in the terrestrial environment. In general, residues in humans were comparable or apparently lower than those in marine mammals. This may be due to the differences in the capacity to metabolize xenobiotics between humans and marine mammals. Our earlier studies pointed out that terrestrial mammals have higher drug metabolizing enzyme activities as compared to marine mammals (*14–17*). Moreover, Kannan et al. (*16*) found lower concentrations of toxic chemicals such as PCBs, including coplanar congeners, in terrestrial mammals including humans than in marine mammals. This finding may suggest higher ability to degrade toxic contaminants in humans.

In this study, there was no age- and sex-dependent accumulation of TCPMe, TCPMOH, or other OCs (Table 2). We did not find any significant trend of OC concentrations with age. This result differed from that reported in human adipose tissues from Spain (*18*), The Netherlands (*19*), Italy (*20*), and Korea (*21*), which showed increased OC concentrations with age. The less pronounced age- and sex-dependent accumulation in the present study might be due to the small number of samples analyzed, which makes it difficult to conclusively verify the age trend in humans.

Based on our results, the occurrence of TCPMe and TCPMOH in human adipose tissues suggest possible widespread contamination by these compounds in terrestrial environment. To date, the point sources of TCPMe and TCPMOH are still unknown. Jarman et al. (*1*) suggested that these compounds may be derived from synthetic polymers and acrylic fibers. On the other hand, Buser (*10*) and de Boer (*11*) suggested that TCPMe and TCPMOH are impurities in technical DDT and dicofol, respectively. However, no investigation has reported on the residues of TCPMe and/or TCPMOH in synthetic polymers and agrochemicals.

The only available evidence of the source of these compounds was technical DDT, in which TCPMe was detected at trace levels (*10*). In the present study, we examined the relationship of concentrations of TCPMe/TCPMOH and DDTs to understand the possible source of these compounds detected in human samples. Significant correlation was found between concentrations of TCPMe/TCPMOH and DDTs (Figure 2). Significant correlations
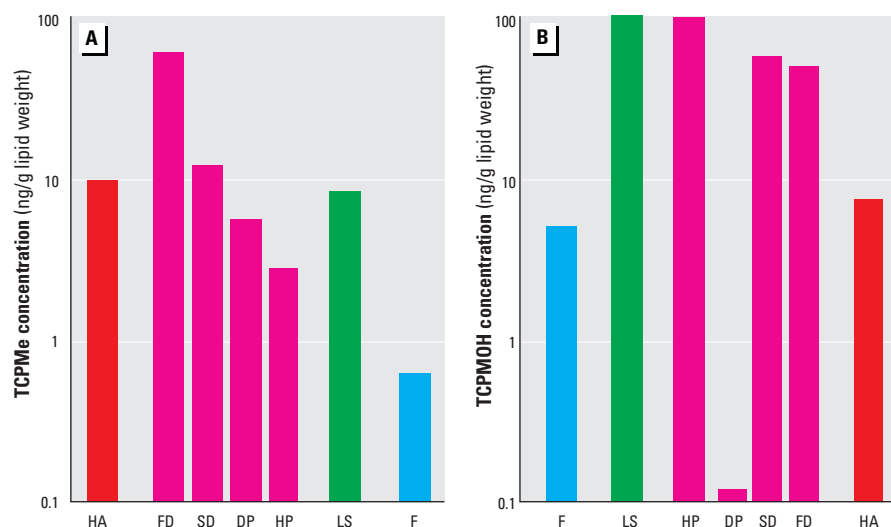
Figure 1. Comparison of (*A*) TCPMe and (*B*) TCPMOH residue levels in fish, marine mammals, and humans from Japan. Abbreviations: DP, Dall's porpoise; F, fish; FD, Fraser's dolphin; HA, human adipose tissue; HP, harbor porpoise; LS, larga seal; SD, striped dolphin. Data on F and LS from Watanabe et al. (*3*); data on cetaceans from Minh et al. (*13*). F and LS from northwestern Japan; HP from Hokkaido; DP from the Japan Sea; SD from off Sanriku; FD from off Kii Peninsula; and HA from Japan.
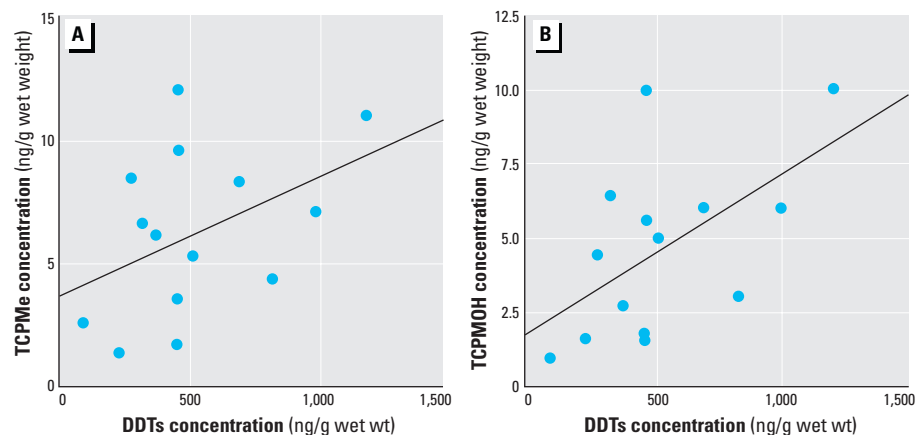
Figure 2. Correlation between (*A*) TCPMe and (*B*) TCPMOH and DDTs concentrations in Japanese human adipose tissue. (*A*) $y = 0.005x + 3.7$; $r = 0.44$ ($p < 0.01$; $n = 14$). (*B*) $y = 0.005x + 1.8$; $r = 0.60$ ($p < 0.01$; $n = 14$).

were also observed in other biologic samples previously reported, which includes harbor seals from Puget Sound in Washington State (*22*); eggs of birds and marine mammals from the Canadian Arctic and the United States (*1*); Caspian seals from Russia (*3*); coastal cetacean species from Hong Kong (*9*); and various fish species, harbor porpoises, and white-tailed sea eagles from the Baltic Sea (*2*). Considering such links between environmental occurrence of TCPMe, TCPMOH, and DDTs in various marine and terrestrial biota, it seems likely that technical DDT may be a plausible source for the presence of TCPMe and TCPMOH in humans.

The toxicologic impacts of TCPMe and TCPMOH residues on humans are currently unknown. Proliferation of the MFM-223 human breast cancer cell was induced after exposure to TCPMOH at the concentration of 5 μmol/L (approximately 1.8 ppm) *in vitro* (*5*). Concentrations of TCPMe and TCPMOH measured in fat-rich tissue such as human adipose and milk were, however, approximately 2 orders of magnitude lower than those representing an antiandrogenic effect. A recent study on the possible endocrine-disrupting effect of TCPMOH has revealed that this compound showed high affinity for androgen receptor binding, comparable to that of *p,p′*-DDE, a major breakdown product of insecticide DDT (*7*). Considering these toxicologic observations, the high bioaccumulation potential of TCPMe and TCPMOH in the food chain, widespread contamination in marine environment, and their occurrence in human samples, further studies are necessary to obtain a better understanding of possible risk for wildlife and human health.

Contamination by other persistent OCs. PCBs are the most abundant contaminants in human adipose tissues from Japan. Concentrations of PCBs ranged from 520 to 3,200 ng/g lipid weight (mean 1,700 ng/g lipid weight) (Table 2). The sex- and age-dependent accumulation was less pronounced in these samples. The highest concentration of PCBs was found in a 73-year-old male patient who suffered from lung cancer. In general, mean concentrations of PCBs in males (1,900 ng/g lipid weight) were higher than those in females (1,400 ng/g lipid weight); however, no significant difference was noted. Our earlier survey on the temporal trend of OCs in human adipose tissue from Japan indicated that the decline of PCBs during the period 1975–1985 was extremely slow (*23*). Because it was also observed that spatial variation in the OC residues in human adipose tissue samples in Japan was not large, it is possible to compare PCB concentrations reported during the period 1975–1985 with those from the present study to understand the temporal

change (*23*). As a result, PCB concentrations were comparable to those reported in 1985. This implies that the exposure to PCBs in humans from Japan is still occurring.

DDT levels found in human adipose tissue samples were in the range of 110–1,900 ng/g lipid weight (mean 780 ng/g lipid weight). *p,p′*-DDE was the most predominant metabolite (accounting for 96% of the total DDTs), indicating that humans have a high capacity to metabolize DDT compounds. Similar to PCBs, concentrations in males were higher than those in females, but no age trend was observed. This study provides some of the most recent data on the contamination status of DDTs in human adipose tissue from Japan. These results indicate that DDT residues have declined substantially as compared to those reported in 1985 (*23*). However, it should be noted that humans have a long life span, leading to a long-term accumulation of persistent OCs with high lipophilicity and less biodegradability, like PCBs and DDTs.

We detected concentrations of HCHs in human adipose tissues ranging from 60 to 600 ng/g lipid weight. β-HCH was the most abundant isomer, accounting for 99% of total HCHs. Chlordane compounds were detected at relatively high concentrations ranging from 65 to 710 ng/g lipid weight. The composition of the chlordane compounds (in order of concentration) was *trans*-nonachlor (64%), oxychlordane (23%), *cis*-nonachlor (11%), *trans*-chlordane (1.4%), and *cis*-chlordane (0.6%). The lowest levels among the classic OCs was HCB, which ranged from 22 to 68 ng/g lipid weight.

To understand the extent of recent OC contamination in human adipose tissue from

Japan, we compared OC residues reported for several countries worldwide. The cited data are not fully representative of nationwide contamination status (Table 3). In general, PCB concentrations in Japanese human adipose tissue were comparable to those reported in developed nations in North America and somewhat lower than those from the Netherlands and Spain. However, these levels were significantly greater than those found in some Asian countries such as South Vietnam and Korea. This trend implies that the extent of PCB contamination in humans was more serious in developed nations, where the production and usage of PCBs for industrial purposes are deemed heavier than those in developing countries. However, for DDT compounds, recent residue levels in Japan were apparently lower than those reported in other countries, particularly in Poland and developing countries such as Vietnam, Turkey, Jordan, Iran, and Mexico. The use of DDT was banned in most developed nations in the early 1970s, whereas DDT is still used for vector control in some tropical developing countries (*37*). HCH concentrations were in the range of those reported in the Netherlands and Poland, but lower than those in Spain and the United States. HCHs were banned in Japan in 1971 (*23*). HCB concentrations in humans from Japan were lower than in many other countries. It is interesting to consider that CHLs were relatively scarcely reported in human adipose tissue samples. Greater CHL residues were found in humans from Japan as compared to those from Canada, the United States, and Poland. Relatively high concentrations of CHLs were also reported in human breast milk from Japan (*38*). In

Table 3. Comparison of recent organochlorine residue levels (ng/g lipid weight) in human adipose tissue from various countries.

Country	Survey year	PCBs	DDTs	HCHs	HCB	CHLs	Reference
Canada	1984	2,000	3,400	80[a]	80	160[b]	(*24*)
Canada	1992	ND	600[c]	25[d]	25	56	(*25*)
United States	1984	1,200	4,100	620[a]	ND	ND	(*26*)
United States	1997	196	72[e]	34[a]	36	72	(*27*)
Mexico	1997–1998	ND	5,660[f]	156	58	ND	(*28*)
Poland	1989–1992	860	6,300[e]	320	310	ND	(*29*)
Poland	1990	1,500	15,000	250	260	70	(*30*)
Navarra, Spain	1991	2,400	4,300[e]	1,530[a]	3,400	ND	(*31*)
Zaragoza, Spain	1988–1989	1,500	2,960[g]	530[a]	2,950	ND	(*18*)
Netherlands	1986	3,400	2,500	280	380	ND	(*19*)
Italy	1984	1,800	8,200[e]	130[h]	2,300	ND	(*20*)
Sweden	–	1,180	788[g]	ND	56	ND	(*32*)
Turkey	1995–1996	ND	2,130[e]	520	33	ND	(*33*)
Iran	1991–1992	ND	2,900[e]	770	55	ND	(*34*)
Jordan	1996	ND	3,900[i]	1,550	120	ND	(*35*)
South Vietnam	1991	300	4,900	30	ND	ND	(*36*)
Korea	1994–1995	400	1,100	190	20	ND	(*21*)
Japan	1998	1,700	780	330	41	230	Present study

ND, not determined.
[a]β-HCH only. [b]Oxychlordane + *trans*-nonachlor + *cis*-nonachlor. [c]*p,p′*-DDE + *o,p′*-DDT + *p,p′*-DDT. [d]α-HCH + β-HCH. [e]*p,p′*-DDE + *p,p′*-DDT. [f]*p,p′*-DDE + *p,p′*-DDD + *p,p′*-DDT + *o,p′*-DDT. [g]*p,p′*-DDE only. [h]γ-HCH only. [i]*p,p′*-DDE + *p,p′*-DDD + *p,p′*-DDT + *o,p′*-DDE + *o,p′*-DDD + *o,p′*-DDT.

Japan, CHLs were mainly used for termite control (*39*), and the use of these compounds was banned in 1986. Time-trend monitoring revealed that CHL residues exhibited increasing trend until 1985 (*23*). The late restriction or ban of CHLs in Japan may account for the high levels found in human adipose tissues. In view of these facts, continuous monitoring of CHLs in humans from Japan is necessary.

Conclusions

This study presents current residue levels of two newly detected contaminants, TCPMe and TCPMOH, as well as other classic persistent OCs in human adipose tissue from Japan. To our knowledge, this is the first report showing the occurrence of TCPMe and TCPMOH in human adipose tissue samples. Our results provide a basis for human exposure to TCPMe and TCPMOH and subsequently for risk assessment. Widespread occurrence of TCPMe and TCPMOH in various kinds of marine mammals and their presence in human samples imply the expansion of contamination by these compounds in wide range of animals including humans. In view of these observations, further comprehensive information regarding contamination status, sources of exposure, and toxicokinetics of TCPMe and TCPMOH is necessary to understand bioaccumulation and to evaluate possible risks of these compounds to humans and wildlife.

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