Environmental Health Perspectives Supplements
Vol. 102 Suppl 1:149–158 1994

Polychlorinated Biphenyl Levels in the Tissues of Exposed and Nonexposed Humans

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Polychlorinated biphenyls (PCBs) are synthetic chemicals, manufactured in volume from about 1929 to the 1970s. Environmental contamination by PCBs has been documented in various substances, including human tissue. PCBs have been measured in human tissue by a variety of analytical methods. PCB levels have been reported as an approximation of total PCB content expressed in terms of a commercial mixture, by identification and quantification of chromatographic peaks, or by qualitative and quantitative characterization of specific congeners. Until recently, the coplanar mono-*ortho*- and di-*ortho* substituted PCBs, which are especially toxic and present in significant concentration in humans from industrial countries, had not been measured in human tissues. Examples of various types of commonly used analyses are presented in general population subjects and in persons who experienced special exposure. In this paper, the usefulness of PCB blood determinations following potential exposure is demonstrated, and their application in health studies is illustrated from a number of case studies. Coplanar PCB, mono-*ortho*-substituted and di-*ortho*-substituted PCB levels in human blood are presented and compared with polychlorinated dioxin (PCDD) and polychlorinated dibenzofuran (PCDF) levels in the U.S. population. Dioxin toxic equivalents for the two groups of chemicals are calculated and compared. It is found that mono-*ortho*-substituted and, to a lesser extent, coplaner PCBs, contribute substantially to dioxin toxic equivalents (TEq) in blood from U.S. adults. Because of substantial PCB contribution to dioxin toxic equivalents, total dioxinlike toxicity can only be determined if dioxins, dibenzofurans, and dioxinlike PCBs are measured. At the present time, PCBs may contribute more dioxinlike toxicity in human tissues than do dioxins and furans in human tissues from the general population in the United States, and probably for other industrialized countries as well.

Introduction

PCBs are persistent, synthetic, lipophilic, toxic chemicals that are currently ubiquitous environmental contaminants (*1*). Their manufacture and distribution increased markedly beginning about 1929. Based on laboratory, wildlife, and some human studies, their toxicity was later appreciated, and PCBs were banned from production and new use in the United States and in other countries (*2*). Human health studies have been hampered by difficulty in estimating actual intake as distinguished from potential exposure and in characterization and quantification of isomers. Levels of the toxic coplanar, mono-*ortho*-substituted, and di-*ortho*-substituted PCB congeners have not been reported in human tissues from the general population or exposed persons from the United States until recently.

In the United States, packed column chromatography of blood or fat, followed by matching of peaks containing several PCB isomers, with patterns reported as commercial PCB mixtures, such as Aroclor 1242 or Aroclor 1260, was the usual approach used for measurement and reporting of PCBs in human tissue. Frequently, the detection limits even for this total value were quite high, for example, 5–15 ppb in human serum at some laboratories, which may be above the mean level for the general population.

Packed-column approaches common in the United States are being replaced by capillary-column methods with the use of PCB

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standards, which have recently become widely available, to aid in identification of peaks. It is only recently that values for individual congeners have been reported by a small number of laboratories, very few of which are in the United States.

Since the 209 possible PCB congeners vary considerably in toxicity and in persistence in humans, failure to report individual congeners presents at least two problems. In some cases, total levels found in a potentially exposed person after an incident may be within the "normal" range for a given population, but because levels before exposure were not known, it is impossible to determine whether exposure and increase in body burden did occur. This problem might be avoided if congeners with longer half-lives were reported and found to be elevated. Further, it is now known that certain PCB mixtures and specific PCB congeners exert a neurotoxic action (*3–9*). If the individual congeners are not identified and quantified, it is not possible to determine if there is an increase in body burden of those PCBs that may be of concern for a given health outcome.

In health studies, whether epidemiological or clinical, determination of dose from exposure to PCBs in cases as well as in controls is essential. If all or most of the toxic PCBs present are not measured, the exposure estimates are far less accurate than would otherwise be the case. If one measures dioxins and dibenzofurans in human tissues, but not the dioxinlike coplanar PCBs and mono-*ortho*-substituted PCBs, then only a portion of the dioxinlike toxic chemicals are being measured. With measurement only of the dioxins and dibenzofurans in human tissue, clinical and epidemiological studies may well misclassify exposure in cases and controls. This may, in part, explain the conflicting human health studies regarding these chemicals. We recently began to measure coplanar, mono-*ortho* and di-*ortho*-substituted PCBs when it was suggested that measurement of dioxins and dibenzofurans alone resulted in a misclassification of total dioxin toxicity; this in turn could lead to errors in epidemiology studies.

In this paper, we review selected case histories from our recent work measuring human tissue PCB levels, on occasion in conjunction with dioxin measurements, as it has evolved over the past decade. The studies were performed either to attempt to determine whether intake occurred after potential exposure to PCBs, polychlorinated dibenzodioxins, or polychlorinated dibenzofurans or to determine baseline levels for a population.

Table 1. Concentration of PCB (ppb, whole blood) in the blood of 11 Yusho patients and 30 controls taken 21 years after exposure (*14–16*).

	Yusho patients (n=11)		Controls (n=30)[b]	
PCB no.[a]	Average	SD	Average	SD
A 66=2,4,3′,4′-tetra-CB	0.20	0.17	0.07	0.07
B 118=2,4,5,3′,4′-penta-CB	0.14	0.07	0.11	0.02
C 153=2,4,5,2′,4′,5′-hexa-CB	2.36	1.34	0.65	0.14
D 138=2,3,4,2′,4′5′-hexa-CB	1.48	0.94	0.28	0.06
E 156=2,3,4,5,3′,4′-hexa-CB	1.20	1.02	0.10	0.02
F 180=2,3,4,5,2′,4′,5′-hepta-CB	0.93	0.70	0.27	0.04
G 170=2,3,4,5,2′,3′4′-hepta-CB	0.57	0.48	0.11	0.01
Sum of PCBs	6.9	4.7	1.6	.30
B/C % ratio	5.8	5.1	16.4	16.8
E/C % ratio	50.9	76.4	15.2	11.8

[a]Ballschmiter and Zell IUPAC numbers (*30*).
[b]Controls are the mean of three samples of pooled blood from 10 persons from Fukuoka, Japan.

Despite the now preferred congener-specific methods, the older packed-column separation and measurement of PCBs has proved useful in some cases for documenting actual intake following a potential exposure. For historical reasons, this will be illustrated also.

Methods

Human blood, plasma, or tissue was placed in chemically clean containers and frozen at temperatures of at least -20 °C until analyzed. The analytic techniques are referenced and will not be repeated here (*10–14*).

Results and Discussion

Yusho Rice Oil Poisoning, Japan, 1968

To illustrate current findings from the Yusho rice oil poisoning incident of Fukuoka, Japan, where PCBs, PCDFs, and PCDDs were ingested, Table 1 reports a total of 6.9 ppb on a wet-weight basis for the Yusho patients blood in this series as compared with 1.6 for the controls (*15–17*). These samples were from sick Yusho patients, where the rice oil contamination with PCBs, PCDFs and, to a lesser extent PCDDs, had previously been documented by chemical measurement. The samples were obtained 21 years after exposure occurred. The B/C ratio (PCB 118 = 2,4,5,3′,4′/PCB 153 = 2,4,5,2′,4′,5′) of 5.8 in the Yusho patients is characteristically lower than the controls, at 16.4, even two decades after their exposure. It was found that the total amount of PCBs did not always have to be high for illness to occur. This was previously reported by Masuda and colleagues soon after the exposure. It is currently felt that the PCDFs in the rice oil contributed far more to illness than did the PCBs. A typical PCB pattern, ratio, and level was found to be characteristic of this first reported major PCB environmental poisoning.

Figure 1 graphically depicts mean PCB serum levels for the selected tetra through heptachlorinated PCBs in blood of 11 patients as compared to the control blood from the general population. The levels vary by congener, although the total PCB level is 6.9 ppb for the Yusho patients and 1.6 for the Japanese controls, by the method used. For specific isomers, such as 2,4,5,3′,4′-PeCB, levels are similar at this time period, at 0.11 and 0.14 ppb. As previously noted, the blood specimens from these Yusho victims were collected 21 years after exposure which occurred in 1968, documenting the persistence in human tissue of certain PCB congeners following high exposures.

Guam PCB Transformer Incident, 1987

Table 2 compares whole-blood PCB congeners and ratios from nine Guam workers who were potentially exposed to PCBs after a PCB transformer incident and subsequent cleanup that occurred in 1987 (*17*). Blood was obtained 2 years after the incident. Worker number 7 clearly has elevated congener levels compared to other workers, and his total PCB level, obtained by adding the measured congeners, is 14.01 ppb, whereas the average for this group is 4.02. Moreover, a characteristic Yusho-like B/C congener ratio, a low 7.2 is noted, where the

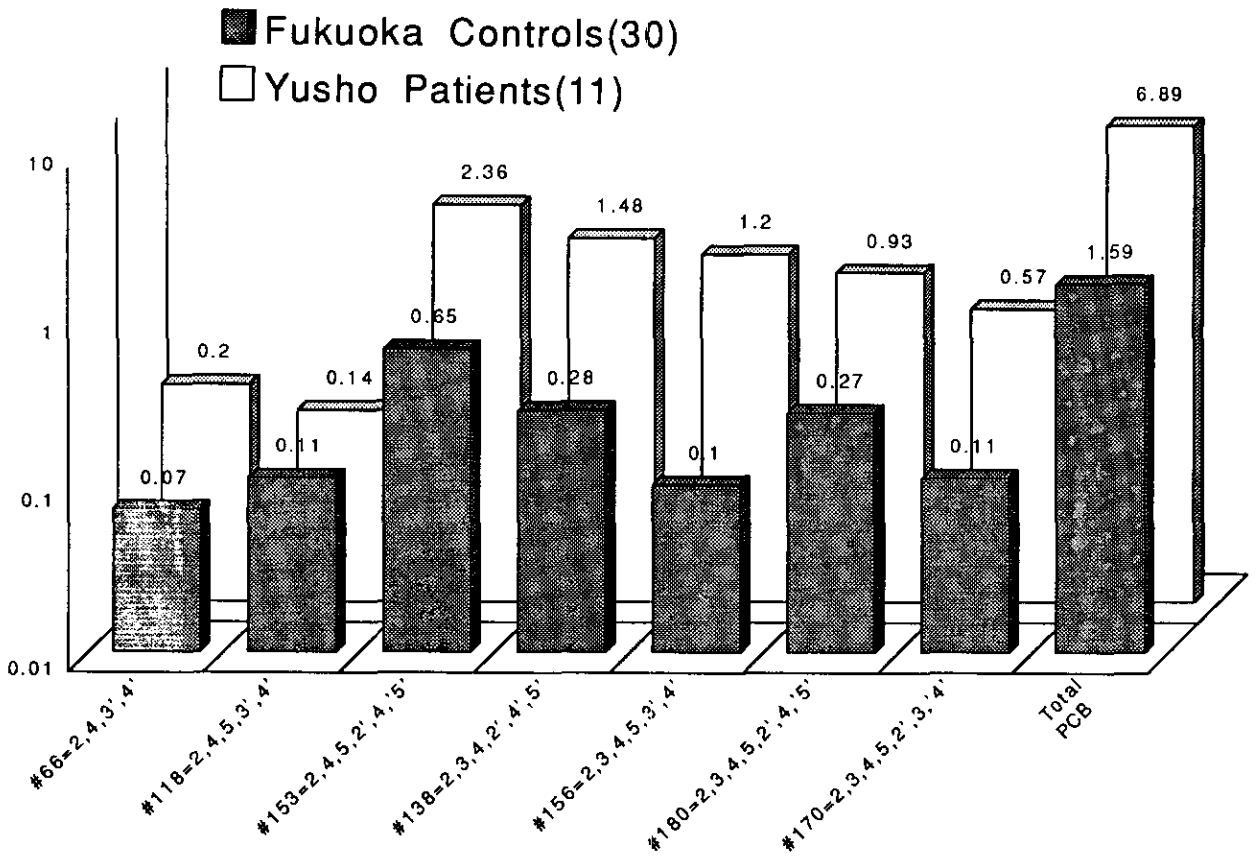

FIGURE 1. Mean PCB levels in Yusho patients and Fukuoka controls, wet weight, ppb.

Table 2. Concentration of PCB in blood of Guam workers (wet weight pbb [*14*]).

PCB no.[a]	1	2	3	4	5	6	7	8	9	Average	SD
A 66=2,4,3',4'-tetra-CB	0.14	0.09	0.14	0.12	0.27	0.93	1.33	0.09	0.21	0.37	0.42
B 188=2,4,5,3',4'-penta-CB	0.19	0.11	0.13	0.19	0.11	0.15	0.42	0.14	0.17	0.18	0.09
C 153=2,4,5,2',4',5'-hexa-CB	1.49	0.88	1.06	1.40	0.61	0.57	5.78	0.96	1.59	1.59	1.52
D 138=2,3,4,2',4',5'-hexa-CB	0.58	0.36	0.40	0.64	0.27	0.26	1.95	0.41	0.69	0.62	0.49
E 156=2,3,4,5,3',4,-hexta-CB	0.20	0.20	0.19	0.28	0.04	0.18	0.87	0.26	0.32	0.28	0.22
F 180=2,3,4,5,2',4',5'-hepta-CB	0.54	0.30	0.41	0.81	0.28	0.20	2.73	0.43	0.77	0.72	0.74
G 170=2,3,4,5,2',3',4'-hepta-CB	0.21	0.11	0.15	0.31	0.09	0.06	0.93	0.15	0.30	0.26	0.25
Sum of PCBs	3.35	2.05	2.48	3.74	1.67	2.35	14.01	2.44	4.05	4.02	3.61
B/C % ratio	12.8	12.5	12.3	13.5	18.0	26.3	7.2	14.7	10.7	11.2	5.9
E/C % ratio	13.4	22.7	17.9	20.0	6.6	31.6		27.4	20.1	17.7	14.5

[a]Ballschmiter and Zell's IUPAC numbers (*30*).

average value is 11.2 for the potentially exposed workers in this series. This lower B/C ratio is believed to be due to induction of hepatic enzymes capable of metabolizing the B congener, 2,4,5,3',4'-penta-CB, more readily than the C congener, 2,4,5,2',4',5'-hexa-CB.

Figure 2 summarizes PCB findings from the same incident, using different analytic techniques (*14*). Because Guam is a remote South Pacific island, no previous data were available on general population levels of PCBs, so the highest and lowest PCB levels from potentially exposed workers are compared. As noted in the previous Guam series in Table 2, one worker in a series of nine showed elevation of specific PCB congeners and total PCBs. Here, the ten highest PCB levels are compared with the ten lowest levels found in a second series of 200 potentially exposed Guam workers. The total levels were obtained by summing the individual congener values. Clearly, even without having previous general population PCB levels on Guam, the 10 high levels are markedly above that of others potentially exposed, which is consistent with exposure to and intake of PCBs in some of the potentially exposed workers.

Binghamton, New York, PCB Transformer Fire Incident, 1981

Figure 3 shows a different approach to the use of blood serum PCB measurement to establish actual exposure or increased body

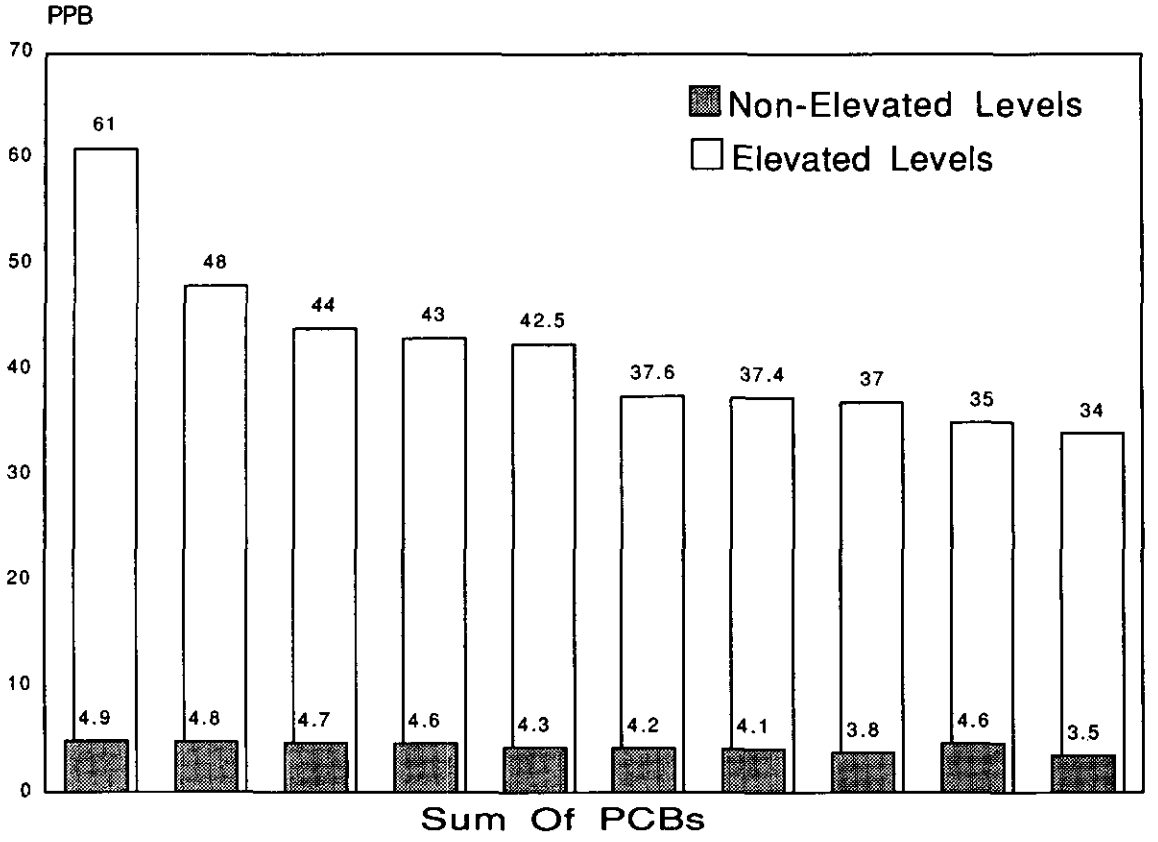

FIGURE 2. PCB blood levels of 20 workers after a PCB transformer incident in Guam (wet weight).

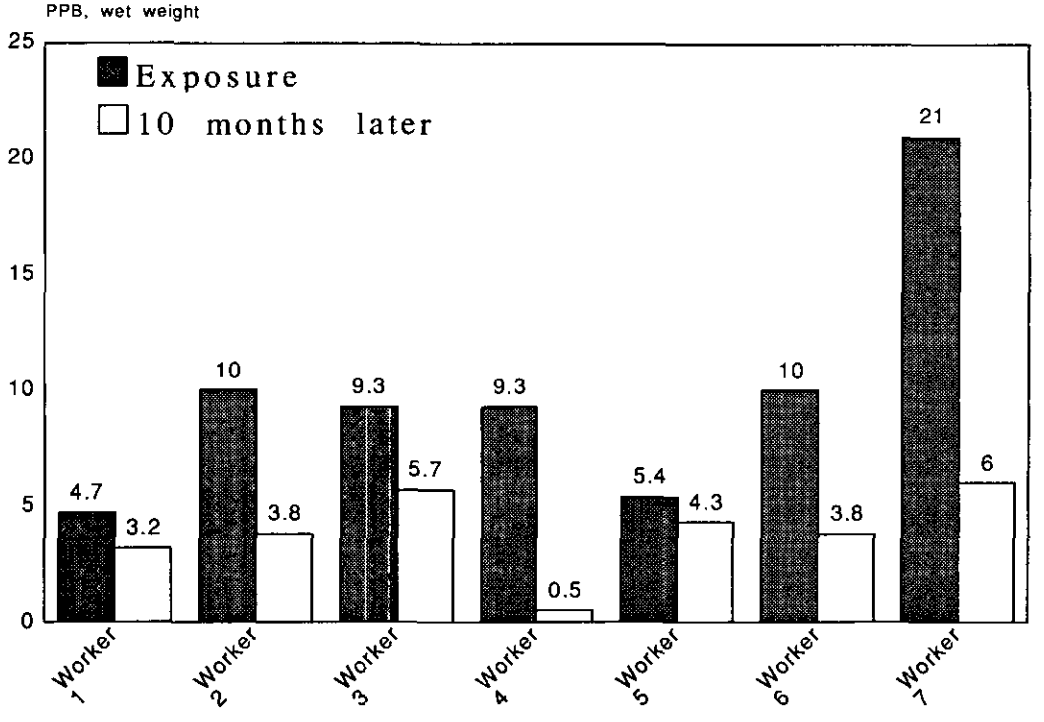

FIGURE 3. Serial serum PCB levels in exposed firefighter. PCBs reported as Aroclor 1254. PCB fire in 1981, in Binghamton, New York, State Office Building.

burden in workers who are potentially exposed. Levels reported here in serum are from seven firefighters who were involved in putting out a PCB transformer fire in Binghamton, New York, in 1981. The capillary-column technique was not available to us then, nor were the firefighters' PCB levels available before the incident. Blood samples were obtained immediately after exposure in these firefighters (within days after they put out the PCB fire). Serum PCB levels were also obtained approximately 10 months later. These serial values document a decrease in PCB levels in that 10-month period for these 7 firefighters. It is also of interest to note that some of the initial values are within the usual range found in adults in New York, which is 5 – 10 ppb, wet weight, in serum. If serial measurements had not been obtained, it would have been difficult to document intake of these chemicals from the incident. Also, if the blood had been collected only 10 months after the incident, serum PCB levels would have provided no information documenting the intake of PCBs that occurred. These serial values illustrate the possibility of error in concluding a lack of exposure from one tissue PCB level when not taken immediately after exposure. Depending on the congeners, half-lives may vary from months to years (*18,19*).

U. S. Capacitor Explosion and Exposure of Children

Tissue PCB levels from another incident are shown in Figure 4. This incident involved a PCB capacitor explosion in the United States after which metal and insulator wrapping, impregnated with PCBs, fell to the ground (*11*). A group of children played with these attractive wrappings and some experienced various acute health effects. One developed an allergic reaction and was treated for respiratory distress and ocular discharge at a hospital emergency room. Several others developed rashes and pruritus. Because the incident involved a capacitor rather than a transformer, lower chlorinated biphenyls predominated in the mixture. In Figure 4, data are presented for three groups of children; those with direct exposure (skin contact), those with indirect exposure (contact with direct-contact children at time of exposure), and those with no exposure (i.e., siblings living in the same household or friends). The PCBs are categorized as higher chlorinated and lower chlorinated depending on their retention compared to DDT. Children with no exposure were tested once and found to have 1.9 ppb of lower chlorinated PCBs (LPCBs) and 2.4 ppb of higher chlorinated PCBs (HPCBs). For four children with direct exposure, the LPCBs averaged 12.9 in August, 9 in January, and 6.3 ppb in July, whereas the HPCBs were found initially to be only 2.6 ppb, 2.1 in January, and finally 1.5 ppb in July. The different levels and response over time to the LPCBs is striking in the directly exposed group of children.

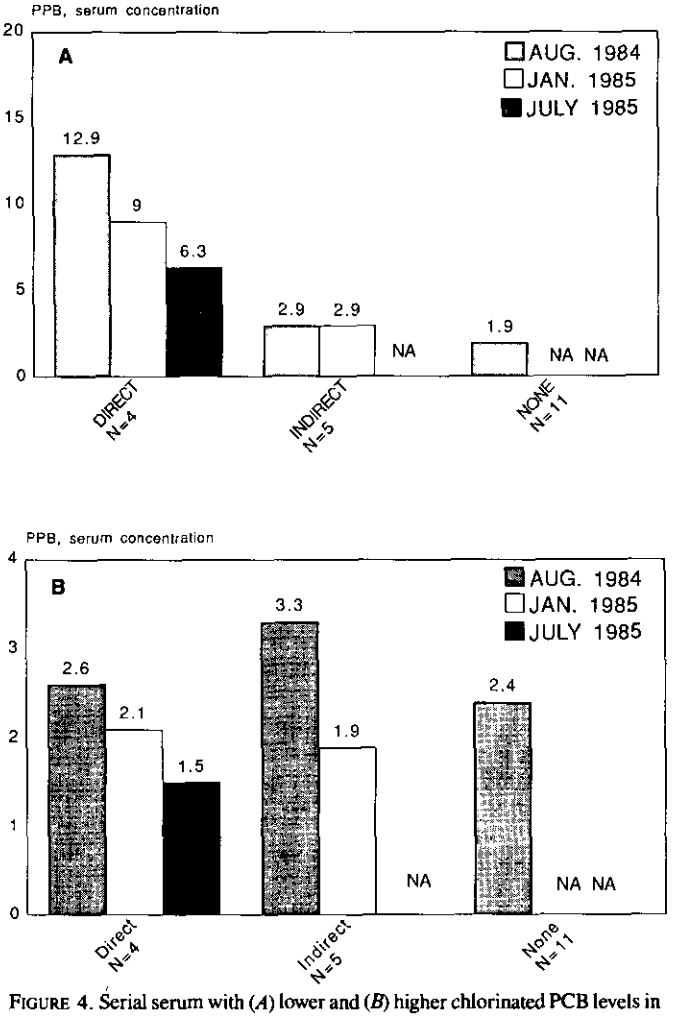

FIGURE 4. Serial serum with (*A*) lower and (*B*) higher chlorinated PCB levels in three groups of varying degrees of exposure. (Direct) had direct exposure, skin contact; (indirect) had contact with direct-contact children; (none) had no contact.

PCB Congeners in Human Tissues

PCB levels are usually reported from fat tissue or blood specimens. It is useful to recognize that these levels reflect body burden and are related to levels in various target organs of concern, but are not necessarily identical in level to these organs on either a wet weight or lipid basis. Table 3 summarizes autopsy data from two patients for various organs reported on both a wet weight and lipid basis (*10*). Certain organs have greater amounts of PCBs, and, as expected, adipose tissue, followed by liver, has the highest levels of these lipophilic compounds, which are metabolized to a large extent by the liver. Certain congeners such as 180 and 153 are typically at higher levels. In our experience to date, different organs appear to present different patterns and levels not based exclusively on their lipid content. Because few autopsies have been performed with PCB measurements, it is not yet possible to generalize as to which congeners are found in specific organs and how the levels and patterns compare with blood and fat.

PCB Congeners in Human Milk from Various Geographical Regions

Figure 5 presents samples from our recent human milk PCB congener data from various countries: the United States and Germany (North-Rhine Westphalia) are typical heavily industrialized western countries; Novosibirsk and Kachug, two cities in Siberia, represent remote cities in a country that is being rapidly industrialized; Vietnam is composed of both the less-

Table 3. Mean PCB isomer levels in human autopsy tissue from two patients from North America, 1980s (ppb, wet weight and lipid) (*10*).

PCB isomer no.[a]	Tissue													
	Intra-abdominal		Subcutaneous[b]		Adrenal		Liver		Kidney		Muscle		Spleen	
	Wet	Lipid	Wet	Lipid	Wet	Lipid	Wet	Lipid	Wet	Lipid	Wet	Lipid	Wet	Lipid
28	2.25	3	4.3	5.3	2.2	7.3	0.55	3.5	0.25	6.9	0.85	11.0	1.55	63.9
52	1.3	1.7	1.55	1.9	0.7	2.1	0.9	4.4	0.35	9.2	0.35	4.0	0.4	17.8
74	0.9	1.1	1.0	1.2	0.2	0.8	8.2	31.1	0.6	17.1	0.1	0.9	0.3	14.4
66	2.5	3.3	2.15	2.6	0.65	2.2	0.75	4.0	0.3	7.1	0.25	3.2	0.3	13.4
101	0.75	1.0	1.15	1.5	0.8	2.5	9.2	2.7	1.0	2.5	0.25	0.9	0.15	5.0
151	0.8	1.0	0.75	0.9	0.3	1.1	0.23	0.9	0.1	2.1	0.08	1.0	0.13	5.5
118	5.95	7.3	2.15	2.6	0.8	2.6	9.2	34.8	1.0	29.4	0.25	2.7	0.15	6.1
153	88.3	118.6	21.45	26.1	6.15	20.5	4.85	24.6	2.15	61.4	2.4	27.7	0.3	13.4
105	7.35	8.8	79.5	98.1	20.05	67	16.2	57.1	0.13	2.9	4.5	57.8	0.63	9.3
138	46.1	61.8	39.9	49.3	2.85	9.2	14.05	50.1	0.75	21.3	0.5	5.9	0.45	16.9
187	4.15	5.6	5.5	6.4	1.2	4.0	0.5	3.5	0.5	14.5	0.35	3.9	0.1	3.5
183	10.15	13.7	14.2	17.7	3.45	11.7	2.98	10.5	0.23	6.1	1.53	19.6	0.4	8.6
156	4.55	5.8	7.3	8.9	1.55	5.1	1.05	5.1	0.08	2.4	0.3	3.4	0.1	1.2
180	79.45	104.5	99.8	121.7	22.45	74.7	17.55	70.8	1.35	37.1	6.25	37.2	0.7	7.6
Sum of PCBs	254.5	337.2	280.7	344.2	63.35	210.8	86.21	303.1	8.79	220	17.96	179.2	5.66	186.6

[a]Numbering systems according to Ballschmiter and Zell (*30*) and in order of gas chromatographic elution. 28=2,4,4′; 52=2,2′,5,5′; 74=2,4,4′,5; 66=2,3′,4,4′; 101=2,2′,4,5,5′; 151=2,2′3,5,5′,6; 118=2,3′,4,4′,5; 153= 2,2′4,4′,5,5′; 105=2,3,3′,4,4′; 138=2,2′,3,4,4′5′; 187=2,2′,3,4′5,5′,6; 183=2,2′,3,4,4′,5′,6; 156=2,3,3′,4,4′,5; 180=2,2′,3,4,4′,5,5′.

[b]Subcutaneous adipose or fat tissue.

Table 4. Dioxin, dibenzofuran, and coplanar PCB levels in selected Vietnam veterans from the Michigan Agent Orange study and in five controls from a Kansas City, Missouri, blood bank (ppt, lipid).

Congener	TEF	Patient								Controls
		#1109	#1111	#1117	#1107	#0493	#0500	#1102	#1103	
2,3,7,8-TCDD	1	ND (14.1)	3.58	ND (2.59)	131	22.9	54.5	8.21	4.4	3.3
1,2,3,7,8-PeCDD	0.5	7.93	8.68	3.98	9.61	35.5	10.5	9.62	6.05	7.1
1,2,3,4,7,8-HxCDD	0.1	0[a]	0[a]	0[a]	0[a]		10.9	0[a]	5.75	0[a]
1,2,3,6,7,8-HxCDD	0.1	94.4	84.8	38.4	52.6	168	120	89.8	38.2	70.7
1,2,3,7,8,9-HxCDD	0.1	13.6	10.4	5.68	9.12	35.9	23.8	10.9	7.78	14.3
1,2,3,4,6,7,8-HpCDD	0.01	179	122	44.1	63.6	333	128	146	70.3	156
OCDD	0.001	1410	829	316	368	1740	465	631	553	1180
2,3,7,8-TCDF	0.1	6.65	0.865	7.32	2.88	7.27	3.71	ND 2.30	ND 1.37	NA
2,3,4,7,8-PeCDF	0.5	17.75	6.72	ND 4.52	7.81	26.6	9.75	6.18	4.68	6.9
1,2,3,7,8-PeCDF	0.05	8.6	0.945	2.72	ND 1.82	4.91	ND 2.21	ND 3.14	ND 1.66	NA
1,2,3,4,7,8-HxCDF	0.1	15.75	9.35	5.5	12.1	21.5	13.7	9.5	5.89	9.6
1,2,3,6,7,8-HxCDF	0.1	19.25	6.74	ND 4.97	11.2	0[b]	0[b]	9.5	4.76	NC[b]
2,3,4,6,7,8-HxCDF	0.1	19.25	2.37	5.41	6.56	7.38	7.86	7.90	3.77	NA
1,2,3,7,8,9-HxCDF	0.1	18.45	2.48	ND 6.09	ND 6.82	ND 6.8	ND 7.94	ND 6.92	ND 4.05	NA
1,2,3,4,6,7,8-HpCDF	0.01	22.4	18	17.1	15.7	29.9	25.8	18.2	15.5	20.9
1,2,3,4,7,8,9-HpCDF1	0.01	20.75	2.85	ND 7.98	ND 8.85	ND 7.2	ND 8.45	ND 4.8	ND 4.72	NA
OCDF	0.001	54.5	6.1	ND 19.9	ND 20.1	ND 17.5	ND 19.5	ND 10.7	ND 10.6	0
Non-*ortho* coplanar PCBs										
77=3,4,3′,4′-TCB	0.01	160	22.1	209	51.4	82.7	168	44.6	28.1	28.6
126=3,4,5,3′,4′-PeCB	0.1	54.1	38	33.8	77.9	432	39.8	38	47.3	42
169=3,4,5,3′,4′,5′-HxCB	0.05	46.4	41.3	31.2	34.3	98.6	48.6	52.9	38.7	30.7
Mono-*ortho* PCBs										
28=2,4,4′-Tri	0.001	1650	6650	1440	4060	6460	2100	9140	3060	7860
74=2,4,4′,5-Tetra	0.001	14900	10100	8580	29200	47000	9280	14400	4770	10800
105=2,3,3′,4,4′-Penta	0.001	3860	3850	3920	7600	30000	3000	3000	3340	1500
118=2,3′,4,4′,5-Penta	0.001	10100	9230	6890	31200	125000	9180	10600	7610	12700
156=2,3,3′,4,4′,5-Hexa	0.001	5050	3430	4720	16100	24200	8700	10100	5760	7020
Di-*ortho* PCBs										
99=2,2′,4,4′,5-Penta	0.00002	3710	8460	5680	33200	54300	8050	5640	6120	6990
128=2,2′3,3′,4,4′-Hexa	0.00002	3330	2900	3100	5100	12000	3000	3000	2220	1500
138=2,2′,3,4,4′,5′-Hexa	0.00002	12500	22000	17400	56000	102000	20800	20400	16900	16100
153=2,2′,4,4′,5,5′-Hexa	0.00002	24100	34300	29900	71400	123000	30000	32800	26900	25400
170=2,2′,3,3′,4,4′,5-Hexa	0.00002	7450	12200	14600	11600	20600	9240	12600	10300	7840
180=2,2′,3,4,4′,5,5′-Hepta	0.00002	21300	28000	40400	22400	48400	21200	24400	24600	19000
183=2,2′,3,4,4′,5′,6-Hepta	0.00002	1650	1010	2800	4560	8940	3000	3000	900	1500
185=2,2′,3,4,5,5′,6-Hepta	0.00002	1650	2400	2800	3520	7360	3000	3000	2120	1500
187=2,2′,3,4′,5,5′,6-Hepta	0.00002	3410	8050	13000	9080	18100	4820	6240	5400	3500

Abbreviations: CDD, chlorinated dibenzodioxin; CDF, chlorinated dibenzofuran; T, tetra; Pe, penta; Hx, hexa; Hp, hepta; O, octa; ND, not detected; NA, not available; NC, not calculated (half of the detection limit used for calculations).

[a]1,2,3,4,7,8- and 1,2,3,6,7,8-HxCDD, reported as 1,2,3,6,7,8-HxCDD.

[b]1,2,3,6,7,8 and 2,3,4,6,7,8-HxCDF reported as 2,3,4,6,7,8-HxCDF.

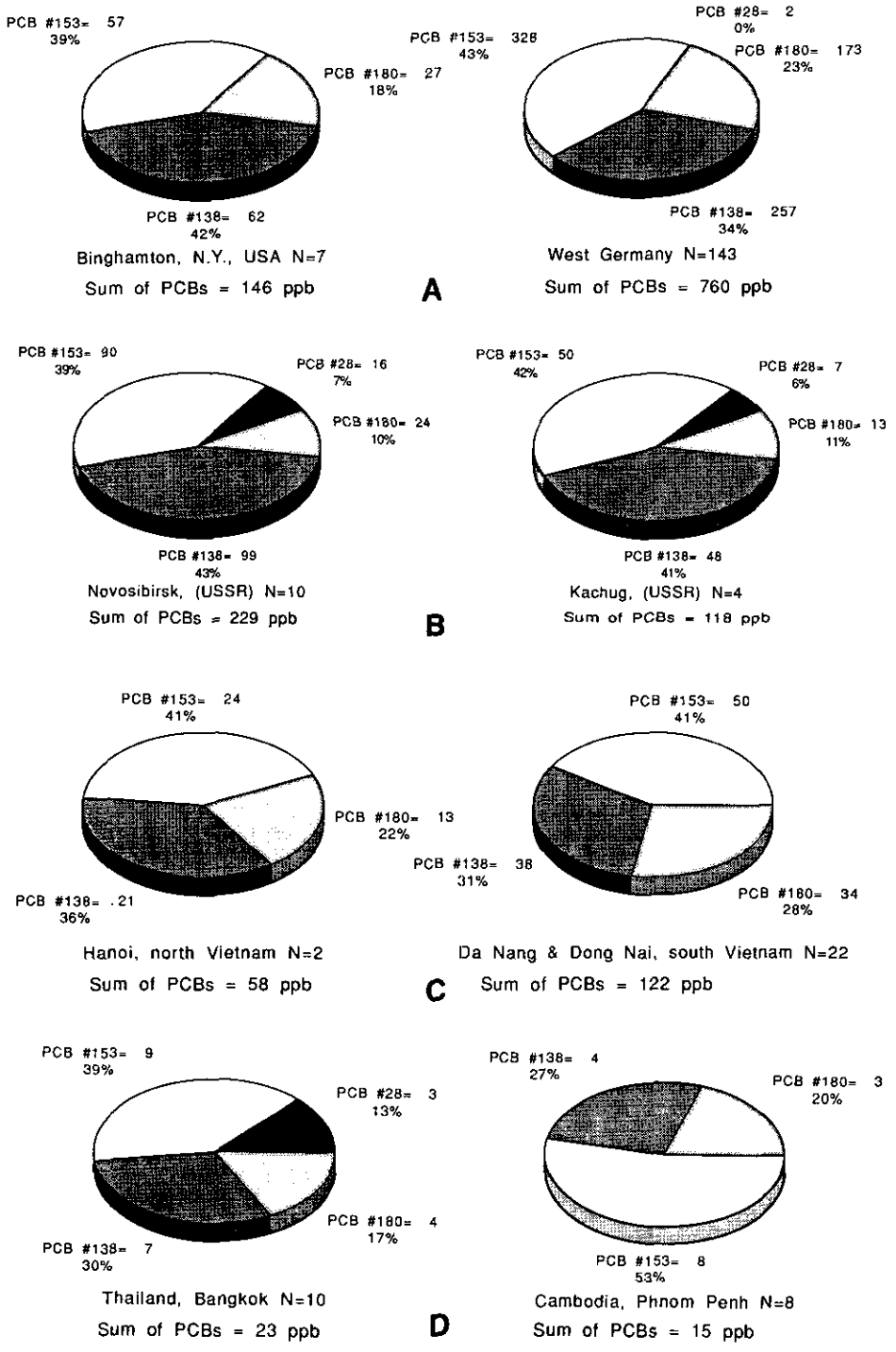

FIGURE 5. PCBs in human milk from the general population (ppb, lipid). (*A*) Binghamton, New York, and West Germany; PCB 52 and 101 are not detected. (*B*) Novosibirsk and Kachug in Siberia; PCB 52 and 101 are < 2 ppb. (*C*) Hanoi, in North Vietnam, and Da Nang and Dong Nai, in South Vietnam; PCB 28, 52, and 101 are not detected. (*D*) Bangkok, Thailand (PCB 52 and 101 are not detected) and Phnom Penh, Cambodia (PCB-28, 52, and 101 are not detected).

industrialized north and the more-industrialized south; Cambodia is a nonindustrial country; and Thailand is a rural, developing country beginning the process of industrialization (*20–22*). The congeners measured are those we recently selectively measured and reported in the World Health Organization interlaboratory and field studies of human milk and blood (*23*). Although total levels are higher in industrial and lower in less industrial countries, PCB 153 and 138 are seen to contribute substantially in most locations. Because the possibility exists that PCBs can decrease neurobehavioral and cognitive ability in

developing children, it seems appropriate to measure individual congeners in milk and blood, especially when effects on the fetus and newborn are of concern (*3–7*). These patterns and levels may change markedly over time because PCBs are no longer produced, and their disposal is being regulated in many countries. The values presented here should be considered only illustrative of the current values in these countries.

Mono-*ortho*-, Di-*ortho*-, and Coplanar PCBs in Human Tissue: Michigan Vietnam Veterans Study

Of considerable interest are recent reports of the toxic coplanar PCB congeners in human tissue at relatively high levels compared to dioxins and dibenzofurans (*24–27*). We were concerned that by reporting dioxin and dibenzofuran congeners and PCBs other than coplanar and mono-*ortho*-substituted PCBs in human tissue, we might be underestimating total dioxinlike chemicals and their toxicity in humans from industrial countries. We were also concerned that this lack of information might be producing misleading estimates of such toxicity, thus causing major methodological problems in human health studies concerning dioxin, or, for that matter, PCB exposure. Therefore, we included all measurable PCBs in a Michigan Agent Orange Blood Dioxin Pilot Study in addition to the dioxins and dibenzofurans. There is no reason to suppose that the 50 U.S. Vietnam veterans in this study would have any special exposure to PCBs or would differ from other Michigan residents or a laboratory pooled blood control sample from Kansas City, Missouri, residents. Of concern for the Vietnam veterans was elevated 2,3,7,8-TCDD from Agent Orange exposure (20 years previously) and total dioxin toxicity. Our findings are presented in Table 4. We measured the dioxins, dibenzofurans, non-*ortho*- coplanar PCBs,3,4,3′,4′-TCB (PCB 77), 3,4,5,3′,4′-PCB (PCB 126), 3,4,5,3′4′5′-HCB (PCB 169), and mono-*ortho*-substituted and di-*ortho*-substituted PCBs.

Table 4 shows the actual levels for each congener measured. TCDD levels ranged from not detected to 131 ppt, suggesting elevation of TCDD from Agent Orange in some of these Vietnam veterans. Blood TCDD for the general U.S. population ranges from 3 to 6 ppt. Patients 1107, 0493, and 0500 are clearly above the average, with TCDD levels of 131, 22.9, and 54.5 ppt, respectively. For the PCBs, the di-*ortho*- congeners were present in the largest amount, with levels ranging from 900 to 123,00 ppt.

Table 5 presents total levels, toxic equivalents (TEq), and percent contribution for each type of compound. Total dioxins ranged from 409 to 1712 ppt, the furans from 44 to 203 ppt. The total coplanar non-*ortho* PCBs ranged from 101 to 613 ppt, the total mono-*ortho* PCBs 24,540 to 232,660 ppt and the total di-*ortho* PCBs from 79,100 to 394,700 ppt. There is a ratio of 1:143 for total dioxins and dibenzofurans to total measured PCBS. Using the estimated PCB toxic equivalency factors proposed by Safe (*18*) and the current international dioxin toxic equivalency factors (TEF) (*28,29*), we found mono-*ortho*-substituted PCBs in whole blood of adult Michigan males to contribute a significant portion of the total dioxin toxic equivalents. The total TEq for the mono-*ortho* PCBs ranges from 24.5 to 232.7 and contributes 25–62% of the total PCDD/Fs plus PCBs TEq in this group of eight male Vietnam veterans and five controls. The dioxins contribute total levels from 409 to 2335 ppt and total TEq ranging from 8.5 to 143. The percent contribution to the total TEq was between 18 and 61%, with TCDD alone contributing

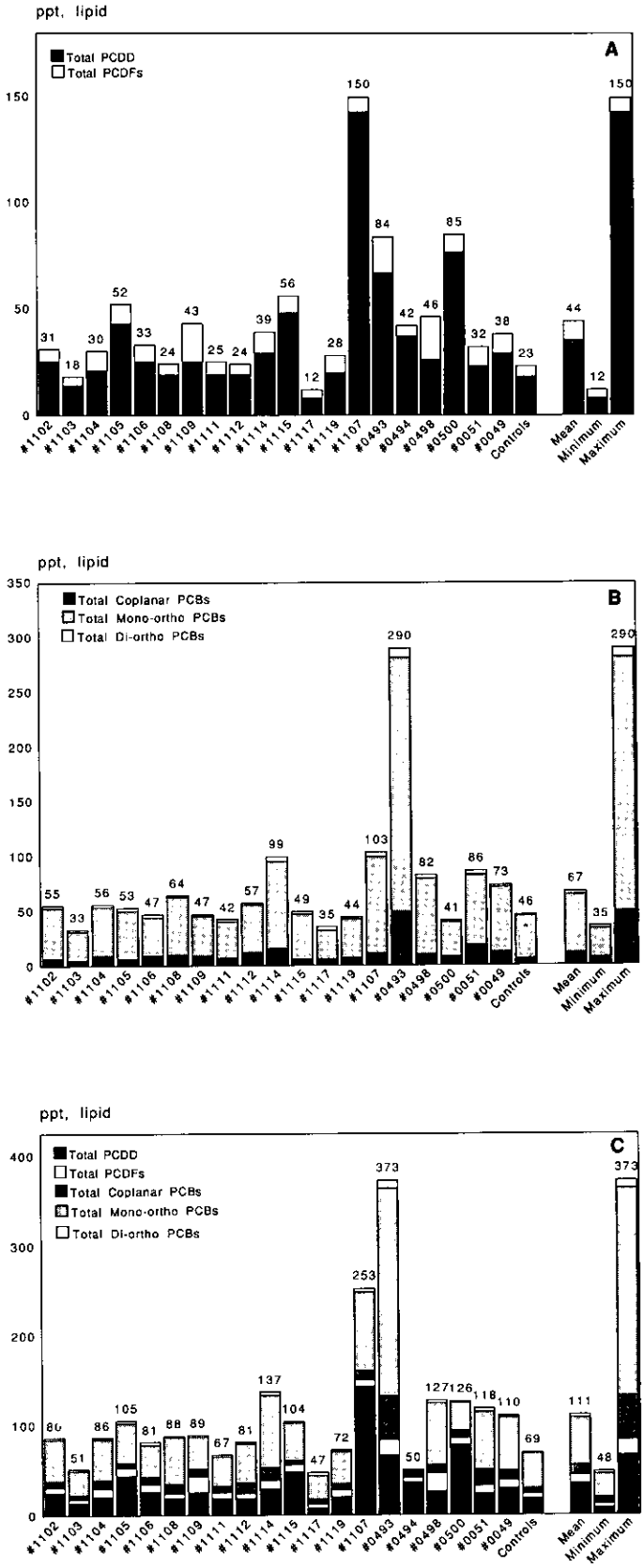

FIGURE 6. PCBs and dioxins in the blood of Michigan Vietnam veterans. (*A*) Dioxin and dibenzofuran dioxin toxic equivalents, (*B*) PCB dioxin toxic equivalents, (*C*) PCDD/F and PCB dioxin toxic equivalents.

Table 5. Dioxin, dibenzofuran, and PCB levels, TEqs, and percent contribution in selected Vietnam veterans from the Michigan Agent Orange study and controls from a Kansas City, Missouri, blood bank donor pool (ppt, lipid).[a]

	Patient no.								
Congener	1109	1111	1117	1107	0493	0500	1102	1103	Controls
Total PCDDs	1712	1058	409	634	2335	833	896	685	1431
Total PCDFs	203	56	56	72	110	76	61	44	37
Total PCDD/Fs	1915	1115	465	706	2445	909	956	729	1468
Total non-*ortho* coplanar PCBs	261	101	274	164	613	256	136	114	101
Total mono-*ortho* PCBs	35560	33260	25550	88160	232660	30760	47240	24540	39880
Total di-*ortho* PCBs	79100	119320	126880	216860	394700	98610	106580	95460	83330
Total PCBs	114921	152681	152704	305184	627973	12926	153956	120114	123311
Total PCDD/Fs and PCBs	116836	153796	153169	305889	630418	130535	154912	120844	124780
Total PCDDs TEq	25	19.5	8.5	143	66.1	77	25.2	13.9	18.1
Total PCDFs TEq	17.7	5.8	3.5	7.4	17.4	7.7	6.1	4.1	4.6
Total PCDD/Fs TEq	42.7	25.3	11.9	150.4	83.5	84.7	31.3	18	22.7
Total non-*ortho* PCBs TEq	9.3	6.1	7.03	10	49	8.1	6.9	7	6
Total mono-*ortho* PCBs TEq	35.6	33.36	25.6	88.2	232.7	30.8	45.7	24.5	38.8
Total di-*ortho* PCBs TEq	1.6	2.4	2.5	4.3	7.9	2	2.1	1.9	1.7
Total PCBs TEq	46.5	41.7	35.1	102.5	289.5	40.8	54.8	33.4	46.3
Total PCDD/Fs and PCBs TEq	89.2	67	47	253	373	125.6	86.1	51.3	69.2
TCDD % contribution to total PCDD/Fs and PCBs TEq	8	5	3	52	6	43	10	9	5
Total PCDD % contribution to total PCDD/Fs and PCBs TEq	28	29	18	57	18	61	30	27	26
Total PCDF % contribution to total PCDD/Fs and PCBs TEq	20	9	7	3	5	6	7	8	7
Non-*ortho* PCBs % contribution to total PCDD/Fs and PCBs TEq	10	9	15	4	13	6	8	14	9
Mono-*ortho* % contribution to PCDD/Fs and PCBs TEq	40	50	54	35	62	25	53	48	56
Di-*ortho* % contribution to PCDD/Fs and PCBs TEq	2	4	5	2	2	2	2	4	2
Total PCBs % contribution to total PCDD/Fs and PCBs TEq	52	62	75	41	78	32	64	65	68

TEq, toxicity equivalents.

[a]Controls and means of n = percent contributions and totals are rounded.

3–52%, among this group where some persons had elevated TCDD and others did not. The dibenzofurans' percent contribution ranges from 3–20%, and non-*ortho* PCBs contribute between 4 and 15%, but the di-*ortho*-substituted PCBs, which contributed the most to the measured levels, contributed only 2–5% to the total TEq.

Figure 6 summarizes and graphically presents the total TEq values for nineteen of the Michigan veterans and also the Kansas City, Missouri, pooled blood bank (n=5) whole-blood laboratory controls, as well as the mean, minimum, and maximum levels. Figure 6*A* shows the total PCDD/F TEq levels ranging from 12 to 150, with a mean of 44. Figure 6*B* presents the levels for the PCBs dioxin toxic equivalents (TEq). The Missouri controls have a mean level of 46, and the values for the veterans (mean, 67) range from 35 to 290, the latter value documenting an exposure from an unknown source. From Figure 6*C* it is possible to visualize a ratio of almost 1:2 for PCDD/Fs to PCBs in the total TEq. With these findings, it is probable that human health studies concerning these previously unmeasured, highly toxic PCBs may be making serious misclassification errors as to exposure of cases and controls. Clearly, using current estimates of dioxin TEqs, total dioxin toxicity is considerably higher in the tissues of persons from the general population than was previously thought to be the case.

Conclusion

In the 60 years since large-scale PCB production began, PCBs have become of concern because of their toxicity and the amount synthesized. Several analytic approaches have been used to measure PCBs in human tissue. Each has its uses and its drawbacks. Analysis by packed column for total PCBs, presented as an Aroclor mixture approximation, is relatively inexpensive, at $75–$125 per analysis, and only 5–10 mL of whole blood or serum is required. Measurement of individual congeners usually costs $300–$600 per analysis. If coplanar PCBs, *ortho*-substituted PCBs, and dioxins and dibenzofurans are measured, cost is usually between $1,500 and $3,000 per analysis. PCDD/F analysis in human tissues usually costs $1,500–$2,500 per analysis, and only about one dozen laboratories qualified in a recent WHO interlaboratory PCDD/F and PCB blood and milk validation study. Several other highly competent laboratories exist, but worldwide capacity is quite limited at present. Health insurance usually does not pay for such monitoring because it is currently considered experimental or a research tool. Workers' compensation programs also usually do not pay for PCB blood, fat or milk analyses, even when exposure at work and subsequent illness is in question.

It is apparent that PCB human tissue measurement is not a

standard medical tool at the present time. There is no consensus as to how to analyze blood for PCBs; which congeners are of importance for documentation of intake and for health concerns or whether to report values on a wet weight or lipid basis for these lipid-soluble compounds. Whether whole blood, serum, or plasma is best for PCB measurement is an active topic of discussion and to a large extent is still an open question based on the lack of data regarding correlation with body burden or target tissue dose.

PCB human tissue analysis offers the promise of providing a useful tool in the practice of medicine (and possibly of law as well) in such areas as clinical and epidemiological estimates of exposure, which is essential for scientifically valid studies and conclusions. Although the approaches we have described here have been very useful, a substantial amount of work remains before PCB human tissue measurement will be routine. Surprisingly, although PCB measurement in human tissue began earlier than dioxin measurement, the field has not advanced as rapidly, or as far, until recently.

Some of the studies here have been made possible by the generous assistance of the Christopher Reynolds Foundation, the Samuel Rubin Foundation, the CS Fund, Church World Service, the territory of Guam, and the State of Michigan. The expert technical assistance in preparation of this manuscript is due to Ruth Stento, Karan Charles, Deborah Suess, and Diann Yannantuono. Most of all, we thank the patients whose blood and other tissues were used in these studies.

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