Environmental Health Perspectives
Vol. 59, pp. 59-65, 1985

Polychlorinated Biphenyls, Dibenzofurans and Quaterphenyls in Toxic Rice-Bran Oil and in the Blood and Tissues of Patients with PCB Poisoning (Yu-Cheng) in Taiwan

by Paul H. Chen,* Chu-Kwan Wong,† Christoffer Rappe‡ and Martin Nygren‡

A mass outbreak of poisoning occurred in central Taiwan in 1979 due to the ingestion of rice-bran oil contaminated with polychlorinated biphenyls (PCBs), dibenzofurans (PCDFs) and quaterphenyls (PCQs). The incident was called PCB poisoning or Yu-Cheng in Taiwan. The major PCB and PCDF congeners in the toxic oil and in the blood and tissues of the poisoned patients were characterized by gas chromatography and gas chromatography–mass spectrometry using highly efficient glass capillary columns. The levels of toxic agents in the rice oil samples collected from the factory and school cafeterias and the families of the poisoned patients are in the range of 53 to 99 ppm, 0.18 to 0.40 ppm and 25 to 53 ppm for PCBs, PCDFs, and PCQs, respectively. The blood samples of 165 patients collected 9 to 18 months after the onset of poisoning contained 10 to 720 ppb of PCBs, with a mean value of 38 ppb. The blood samples of 10 patients collected 9 to 27 months after poisoning contained 0.02 to 0.20 ppb of PCDFs. Comparative rates of elimination of some PCB congeners from the blood of patients were studied. Various tissues from a patient who died 2 years after poisoning were analyzed for PCBs, PCDFs and PCQs. The intestinal fat contains the highest level of PCBs, while the liver contains the highest concentration of PCDFs. The PCB congeners retained in the tissues either do not have adjacent unsubstituted carbon atoms or have a pair at *ortho-meta* positions of the biphenyl ring. The major PCDF congeners retained in the tissues were 1,2,3,4,7,8-hexachloro-DF, 2,3,4,7,8-pentachloro-DF and 1,2,4,7,8-pentachloro-DF. The former two congeners, especially 2,3,4,7,8-pentachloro-DF, are very toxic PCDFs; they may play important roles in the etiology of Yu-Cheng.

Introduction

The problems of polychlorinated biphenyls (PCBs) and dibenzofurans (PCDFs) have aroused a great deal of concern and interest among scientists and health officials. The first most serious incident of PCB and PCDF poisoning in humans occurred in western Japan in 1968 (*1*). The incident was named Yusho by the Japanese. A similar mass outbreak of poisoning occurred in Taichung and Changhwa in central Taiwan in 1979 due to the ingestion of rice-bran oil contaminated with PCBs, PCDFs and polychlorinated quaterphenyls (PCQs) (*2–5*). This incident was called PCB poisoning or Yu-Cheng (oil disease) in Taiwan. The unfortunate incident provided us a rare opportunity to study the toxic agents (PCBs, PCDFs, and PCQs) present in the contaminated oil and retained in the blood and tissues of Yu-Cheng patients. This paper describes the results of our studies on the toxic agents involved in the incident.

* Department of Biochemistry, National Yang Ming Medical College, Taipei, Taiwan, ROC. Address reprint requests to: LBNT, National Institute of Environmental Health Sciences, P.O. Box 12233, Research Triangle Park, NC 27709 U.S.A.
† Department of Dermatology, Veterans General Hospital, Taipei, Taiwan, ROC.
‡ Department of Organic Chemistry, University of Umea, Umea, Sweden.

Materials and Methods

PCB, PCDF and PCQ Standards

2,4,5,2′,5′-Pentachlorobiphenyl (PnCB), 2,3,4,2′,4′,5′-, 2,4,5,2′,4′5′- and 2,3,4,5,3′,4′-hexachlorobiphenyls (HxCB) were purchased from Ultra Scientific Inc. 2,3,4,5,2′,4′,5′-and 2,3,4,5,2′,3′,4′-heptachlorobiphenyls (HpCB), Kanechlor PCB standards (KC-400 and KC-500), a PCDF mixture, and PCQ standard were gifts from Professor Y. Masuda of Daiichi College of Pharmaceutical Sciences, Japan. Individual PCDF standards

such as 2,3,6,8- and 2,3,7,8-tetrachlorodibenzofuran (TCDF), 2,3,4,7,8- and 1,2,4,7,8-pentachlorodibenzofurans (PnCDF), and 1,2,3,4,7,8-hexachlorodibenzofuran (HxCDF) were synthesized in the laboratory of one of us (CR).

Oil, Blood and Tissue Samples

Five toxic rice-bran oil samples were obtained from the school and factory cafeterias and the families of the poisoned patients in Taichung. One sample was collected from the rice oil retail store in Taichung. The cafeterias and families all bought the toxic oil from this oil retailer. Blood samples of Yu-Cheng patients were collected in the hospital ward and the out-patient clinic of the Department of Dermatology, Veterans General Hospital, Taipei, and in patients' homes or work places during the period December 1979 to September 1980. Tissue samples of a deceased patient were kindly given to us by the Food and Drug Bureau of the Republic of China. The patient died about 2 years after the onset of poisoning.

Extraction and Cleanup

The method for the extraction and cleanup of PCBs and PCDFs from the toxic oil and the tissues was essentially the same as that described previously for the toxic oil (*3*). A similar method was used for the extraction and cleanup of PCBs from the patients' blood (*2*). The method for the extraction of PCQs from the oil and the tissues was the same as that described for the oil (*3*). The condensed extract was cleaned up by Florisil column chromatography similar to the one used by the Japanese scientists to obtain the PCQ fraction (*6*).

Gas Chromatographic (GC) Analysis

The PCB, PCDF and PCQ fractions were analyzed by GC equipped with ^{63}Ni-electron capture detector (ECD).

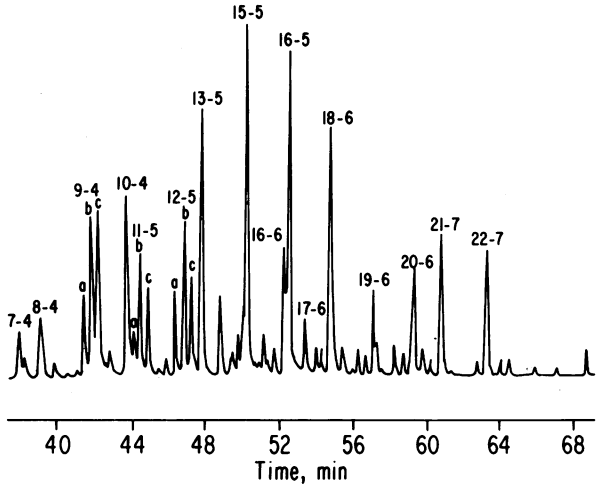

FIGURE 1. Gas chromatogram of PCBs in the toxic rice-bran oil obtained from Taichung using a DB-5 fused silica column. Some of the peaks are identified in Table 3. From Chen et al. (*7*).

The columns and GC conditions used have been described elsewhere (*2–5,7*).

Gas Chromatographic–Mass Spectrometric (GC–MS) Analysis

The PCB, PCDF and PCQ fractions were analyzed by electron impact-GC–MS or negative chemical ionization (NCI)-GC–MS operating in a selected ion-monitoring mode to confirm the identification and to determine the number of chlorine atoms in PCB, PCDF and PCQ. The GC colums and GC–MS conditions used have been described elsewhere (*2–5,7*).

Results and Discussion

PCBs in the Toxic Oil

A gas chromatogram of PCBs in the toxic rice-bran oil obtained from a poisoned patient in Taichung is shown in Figure 1. In Figure 1, the number after a hyphen in each peak is the number of chlorine atoms in each PCB peak as determined by GC–MS. The structural assignments of most of the major peaks as well as the percent distribution of each individual PCB components in the toxic oil have been published elsewhere (*4,5*) (see also Table 3). The percentages of pentachloro-, tetrachloro-, hexachloro-, heptachloro- and trichlorobiphenyls in the toxic oil were calculated as 47.1%, 33.8%, 12.4%, 4.5%, and 2.2%, respectively. A comparison of GC patterns of PCBs in Taiwan and Japan toxic rice oil indicated that the former consisted of a larger percentage of PCB components with longer retention times (*3,8*). This suggests that if the same amounts of PCBs were ingested by both Japanese and Chinese patients, then it would be expected that higher amounts of accumulative PCBs would be retained in the body of Chinese patients because it is difficult to excrete the highly chlorinated PCBs from the human body.

GC patterns of PCBs in the toxic oil obtained with a SE-30 packed column is similar to that of KC-400/KC-500 (1:1) except that in the front portion of the chromatogram peaks are smaller in the rice oil (*3*). This similarity does not mean that the toxic oil was actually contaminated with KC-400 and KC-500, but that it might be contaminated with another PCB preparation that gives a similar GC pattern (*3,5*). The decrease in intensity of early eluting peaks in the rice oil is at least in part due to the evaporative loss of the more volatile PCB components during heating at high temperature. The assumption that PCBs in the toxic oil had been subjected to heating at high temperature is based on the fact that elevated levels of PCQs and, to a lesser extent, PCDFs were found in the toxic oil (see Table 1). The formation of the elevated levels of PCQs and PCDFs in the toxic oil is probably due to the heating of PCBs because it had been demonstrated that PCQs and PCDFs can be produced by heating PCBs at high

temperature (*9,10*). It was generally believed that PCBs in the toxic oil came from accidental leakage of the heat transfer medium during the manufacturing process in which PCB was presumably used as a heat transfer medium.

Concentrations of PCBs in the toxic oil samples were determined by GC equipped with ECD using a SE-30 packed column (*3*). The calculation method described by Ugawa et al. (*11*) was used for quantification of PCBs. The results are shown in Table 1. This table shows that, with the exception of sample A, which had a high PCB level of 405 ppm, the other five samples contain PCB in the range of 53 to 99 ppm. Sample A was given to us by the Food and Drug Bureau (FDB) of the National Health Administration of the Republic of China. According to the FDB's report, this sample contained the highest level of PCB among the 39 samples collected by them at the rice oil retail store from which the patients in Taichung bought the toxic rice oil. The other five oil samples obtained from the factory and school cafeterias and the families of PCB-poisoned patients in Taichung contained much lower levels of PCBs than sample A.

If PCB levels of the five samples (B to F) in Table 1 are representative of the toxic oil ingested by the patients in Taichung, then PCB levels in the toxic oil consumed by the patients in Taichung was only about one-tenth to one-twentieth of that in the Japanese toxic oil (*5,12*). This does not necessarily mean that the Chinese patients in Taichung ingested less PCBs than the Japanese Yusho patients because the former consumed about 15 to 20 times more toxic oil than the latter (*13,14*). A more detailed discussion of the total oil consumption will be described later. The level of PCBs in the toxic oil consumed by the patients in Changhwa is not known, because no toxic oil sample has ever been available for analysis. However, based on the severity of clinical symptoms for the patients in Changhwa and the blood PCB analysis which showed that the patients in Changhwa had in general higher PCB levels than those in Taichung, one can presume that the toxic oil ingested by the patients in Changhwa contained higher levels of PCB than that consumed by the patients in Taichung (*3,5*).

PCDFs in the Toxic Oil

A gas chromatogram of PCDFs in the toxic oil obtained from Taichung is shown in Figure 2. In this figure, all of the major peaks except peaks A and B are due to PCDFs. GC–MS analysis indicated that peaks 1 to 3 were tetrachlorodibenzofurans, peaks 4 to 9 were pentachlorodibenzofurans, and peaks 10 and 11 were PCDFs with 6 and 7 chlorine atoms, respectively. The structural assignments of most of these peaks have been published elsewhere (*5,7*). Using a DB-5 fused silica column for analysis, peak 3 is coincidental in retention time with that of the authentic standard of a very toxic PCDF, namely, 2,3,7,8-TCDF. However, when a fused silica column coated with Supelco 2330 was used for analysis, we found that 2,3,7,8-TCDF was only a minor component in this peak. The major components of this peak are 2,3,4,8-TCDF and another unidentified TCDF. It should be noted that another very toxic PCDF, i.e., 2,3,4,7,8-PnCDF (peak 8 of Fig. 2), is one of the major PCDFs in the toxic oil.

Quantification of PCDFs in the toxic oil was made by GC–MS operating in selected ion monitoring node (*3*). The results are shown in Table 1. It is noted that with the exception of sample A, the PCDF levels in the samples B to F in Table 1 are about 10 times lower than that of the Japanese toxic oil (*5*).

Table 1. Concentrations of PCBs, PCDFs and PCOs in the toxic rice-bran oil obtained in Taichung.[a]

Sample	PCBs, ppm	PCDFs, ppm	PCOs, ppm
A	405	1.68	–
B	53	0.18	25
C	99	0.40	40
D	78	0.25	–
E	77	0.21	43
F	65	0.30	53

[a]Data from Chen et al. (*5*).

PCQs in the Toxic Oil

A gas chromatogram of PCQs in the toxic oil that caused Yu-Cheng has been published elsewhere (*5*). This chromatogram is similar to the chromatogram of PCQs in the Japanese toxic oil (*6*). GC–MS analysis of the PCQ fraction indicated that PCQs in the toxic oil contained 6 to 10 chlorine atoms.

The concentrations of PCQs in the toxic oil samples were determined by comparing the area of the broad PCQ peak in the gas chromatogram of the sample with

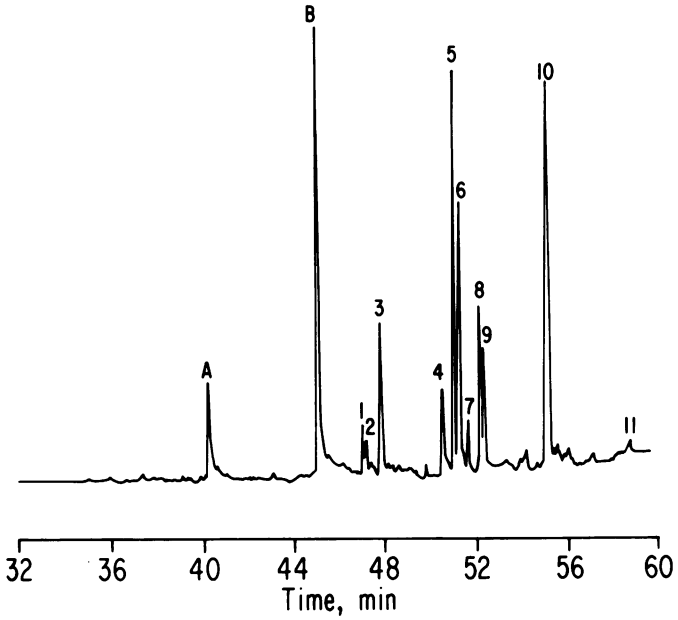

FIGURE 2. Gas chromatogram of PCDFs in the toxic rice-bran oil obtained from Taichung using a DB-5 fused silica column. From Chen et al. (*7*).

that of PCQ standard isolated from the Japanese toxic oil. The results of quantification of PCQs in the toxic oil samples are shown in Table 1. The levels of PCQs shown in this table are only about one-twentieth of that of the Japanese toxic oil.

Other Polychlorinated Aromatic Compounds

In addition to PCBs, PCDFs and PCQs, GC–MS analysis indicated the presence of polychlorinated quaterphenyl ethers, diphenyl ethers, and terphenyls in the toxic oil.

Estimate of Amounts of the Toxic Agents Ingested by the Patients

The amount of toxic oil consumption by 98 patients from four patient groups was estimated on average as 1.02 to 1.55 kg/month for adults (*13*). The period of toxic oil ingestion was about 9 months (*13*). From these data, the total amount of toxic oil consumption by an adult for these patient groups is estimated on average as 9 to 14 kg. This is about 15 to 20 times the average total oil consumption by the Japanese Yusho patients which was estimated at 688 mL (*14*).

An accurate estimation of total PCBs, PCDFs and PCQs intake by Yu-Cheng patients is difficult. However, it could be estimated roughly by the assumption that the concentrations of these toxic agents in the oil (see Table 1) which was collected for analysis at the end of a 9-month period of toxic oil taken represent the concentrations of these toxic agents in the oil taken in the whole 9-month period. Based on this assumption, the average toxic agents intake for these patient groups was estimated at 973 mg, 3.8 mg and 586 mg for PBs, PCDFs and PCQs, respectively. These values are comparable to 633 mg, 3.3 mg and 596 mg estimated for the Japanese Yusho patients for PCBs, PCDFs and PCQs, respectively (*14*).

PCBs in the Blood of Yu-Cheng Patients

The blood PCB levels of 165 Yu-Cheng patients sampled about 9 to 18 months after the onset of poisoning were in the range of 10 to 720 ppb with a mean value of 38 ppb (*5*). The distribution of blood PCB levels of these patients is shown in Table 2. The blood PCB levels of these Yu-Cheng patients are much higher than those of the Japanese Yusho patients, which had a mean PCB level of 5.9 ppb for 72 patients 5 years after poisoning (*15*). This great difference is largely due to the difference in time lags between PCB ingestion and sampling of blood for PCB analysis (*2*). Another factor which is attributable to the difference is that the Taiwanese toxic oil contains a larger percentage of highly chlorinated PCBs which would be retained in the human body for a longer time (*2*).

Table 2. Distribution of blood PCB levels for 165 Yu-Cheng patients.[a]

	PCB levels					
	10–19 ppb	20–29 ppb	30–39 ppb	40–49 ppb	50–100 ppb	100–800 ppb
No. of patients	29	57	39	14	22	4
Percentage	17.6	34.6	23.6	8.5	13.3	2.4

[a]Blood samples were collected about 9 to 18 months after poisoning.

A few laboratories in Taiwan have been engaged in blood PCB analysis since the outbreak of Yu-Cheng. A large range of variation in the blood PCB levels has been reported by these laboratories. Factors that contribute to the difference or discrepancy include analytical techniques involved, difference in patient groups (for instance, in the early stage of poisoning patients from Changhwa generally had much higher blood PCB levels than those from Taichung), and time of sampling blood for analysis.

Rates of Elimination of PCBs from Blood

The toxic oil ingested by the patients contained PCBs with three to eight chlorine atoms. These PCBs components are metabolized and eliminated from the patient's body at different rates, depending on the number and position of chlorine substitutions. We studied the changes in the concentration of individual PCB isomers and congeners in the blood of a given patient at different times during the post-poisoning period. This had enabled us to investigate the comparative rates of elimination of some individual PCBs from the blood of patients. The results of this study were published recently (*4*) and are reproduced in Table 3. The results indicate that most of the hexa- and heptachlorobiphenyls

Table 3. Comparative rates of elimination of some major PCBs from the blood of PCB-poisoned patients.[a]

Peak no.[b]	Substitution pattern	Elimination rate[c]	Adjacent unsubstd. carbon
9-4-a	2,4,5,4′(?)	+ + +	2′,3′; 5′,6′
9-4-b	2,5,3′,4′	+ + + + +	3,4; 5′,6′
9-4-c	2,4,3′,4′	+ + + +	5,6; 5′,6′
10-4	2,3,3′,4′(?)	+ + + + +	4,5,6; 5′,6′
11-5-a	2,5,2′,3′,5′	+ + + +	3,4
11-5-b	2,5,2′,4′,5′	+ + + +	3,4
11-5-c	2,4,2′,4′,5′	+ +	5,6
12-5-a	2,3,2′,4′,5′	+ + + + +	4,5,6
12-5-b	2,5,2′,3′,4′	+ + + + +	3,4; 5′,6′
12-5-c	2,4,2′,3′,4′	+ + + + (?)	5,6; 5′,6′
13-5	2,3,6,3′,4′	+ + + + +	4,5; 5′,6′
15-5	2,4,5,3′,4′	+ + +	5′,6′
16-5	2,3,4,3′,4′	+ + +	5,6; 5′,6′
16-6	2,4,5,2′,4′,5′	+	none
18-6	2,3,4,2′,4′,5′	+	5,6
19-6	2,3,4,2′,3′,4′	+ +	5,6; 5′,6′
20-6	2,3,4,5,3′,4′	+	5′,6′
21-7	2,3,4,5,2′,4′,5′	+	none
22-7	2,3,4,5,2′,3′,4′	+	5′,6′

[a]Data from Chen et al. (*4*).

[b]Peak no. corresponds to that shown in Fig. 1.

[c]The symbols +, + +, + + +, + + + +, + + + + + denote extremely slow, very slow, slow, less rapid and rapid, respectively.

with adjacent unsubstituted carbon atoms at the *ortho–meta* positions of the biphenyl ring are eliminated very slowly and would be expected to remain in the patient's body for a long time. The results also indicate that tetra- and pentachlorobiphenyls with adjacent unsubstituted carbon atoms at *meta–para* positions are rapidly eliminated from the blood of patients, while PCB with the same degree of chlorination but with adjacent unsubstituted carbon atoms at *ortho–meta* positions are eliminated more slowly. Peaks 15-5 and 16-5 are two major components in the toxic oil (*5*). They are eliminated slowly from the patient's body, and the rates of elimination vary greatly among the patients (*4*).

PCBs Retained in the Tissues

Various tissues from a Yu-Cheng patient who died about 2 years after the onset of poisoning were available to us for the toxic agents analysis (*7*). A gas chromatogram of PCBs retained in the bronchus of the deceased patient is shown in Figure 3. GC patterns of PCBs in other tissues of this patient (see Table 4) are very similar to that in the bronchus shown here. A comparison of Figures 1 and 3 indicates that with the exception of 11-5-c, and to much lesser extents, 9-4-a and 15-5,

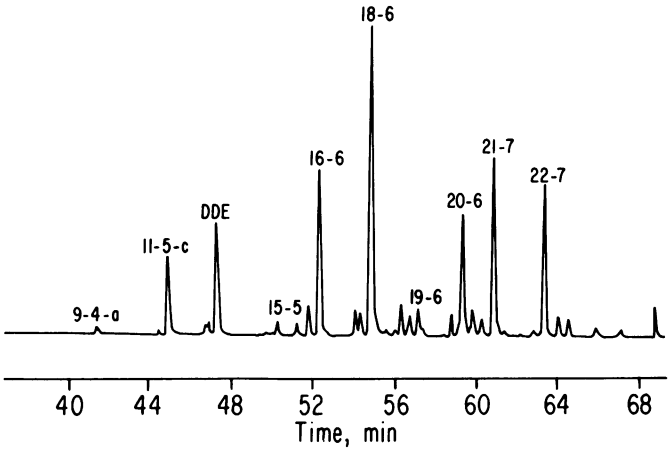

FIGURE 3. Gas chromatogram of PCBs retained in the bronchus of the deceased patient. From Chen et al. (*7*).

PCBs with five or fewer chlorine atoms were almost completely excreted from the patient's tissue about 2 years after the ingestion of the toxic agents. In contrast, most of the PCB congeners with six or more chlorine atoms were still retained in the tissue. The concentrations of major individual PCB congeners retained in various tissues are shown in Table 4. As reported in our study on the blood of Yu-Cheng patients (*4*) and described above in this paper, these very slowly eliminated PCB congeners either do not have adjacent unsubstituted carbon atoms in the biphenyl ring or have a pair of adjacent unsubstituted carbon atoms at *ortho–meta* positions but not at *meta–para* positions.

Relationship Between the Severity of Dermatological Signs and the Blood PCB Levels

The severity of dermatological manifestations of 79 Yu-Cheng patients was graded from I to IV according to the method described by Goto and Higuchi (*16*). The concentrations of total PCBs and 2,3,4,5,2′,4′,5′-heptachlorobiphenyl (peak 21-7 in Fig. 1) in the blood of these patients were determined and used to correlate with the severity of skin signs. A significant positive correlation ($r = 0.553$, $p<0.01$) was observed between the severity of skin signs and the concentration of the heptachlorobiphenyl. A smaller correlation coefficient was obtained ($r = 0.407$, $p < 0.01$) when the levels of total PCBs in the blood were used for correlation.

The reason that a higher correlation was obtained for 2,3,4,5,2′,4′,5′-heptachlorobiphenyl can be explained as follows. The heptachlorobiphenyl is a nonmetabolized PCB; its concentration in a patient's blood is less likely to be affected by the time of sampling the blood and the patient's capability to excrete certain PCB components in his body, hence it can reflect more accurately the total amount of PCB ingested by the patient. On the other hand, the concentration of total PCBs in the blood is affected by the time of sampling and the patient's capability to excrete 2,4,5,3′,4′- and 2,3,4,3′,4′-pentachlorobiphenyls (peaks 15-5 and 16-5, respectively, in

Table 4. Concentrations of PCB congeners in the tissues of the deceased patient with Yu-Cheng in Taiwan.[a]

Tissue	Level of PCB congener, ppm[b]						Total major PCB, ppm[c]
	11-5-c	16-6	18-6	20-6	21-7	22-7	
Intestinal fat	1.84	1.47	3.44	1.57	1.28	1.21	10.81
Bronchus	0.92	0.75	1.79	0.86	0.63	0.61	5.56
Large intestine	0.56	0.45	1.04	0.47	0.40	0.36	3.28
Heart	0.41	0.32	0.80	0.38	0.29	0.28	2.48
Stomach	0.12	0.09	0.21	0.09	0.08	0.07	0.66
Liver	0.11	0.08	0.21	0.10	0.08	0.07	0.65
Small intestine	0.04	0.04	0.08	0.04	0.04	0.03	0.27
Kidney	0.04	0.03	0.08	0.04	0.03	0.03	0.25
Lung	0.03	0.02	0.06	0.03	0.02	0.02	0.18
Brain	0.01	0.01	0.03	0.01	0.01	0.01	0.08
Spleen	0.01	0.01	0.02	0.01	0.01	0.01	0.07

[a]Data from Chen et al. (*7*).
[b]See Table 3 for the chemical structure of each individual PCB congener.
[c]Total major PCBs are the sum of six congeners listed in the table which are about 74% of total PCBs retained in the tissues.

Fig. 1) and other PCB components in the body that are metabolized in the intermediate rates. These two pentachlorobiphenyls are two of the most abundant PCB components in the toxic oil taken by the patients (*5*), and their rates of elimination from patient's blood differed greatly among the patients (*4*).

The fact that the blood PCB level can correlate with the clinical severity does not necessarily mean that PCBs are causal agents for Yu-Cheng in Taiwan. Causal agents for Yu-Cheng are likely PCDFs, PCBs and PCQs with PCDFs probably playing major roles. Our finding of a positive correlation suggests that the concentration of causal agents in the toxic oil is directly proportional to that of PCBs in the toxic oil. This can be substantiated by the results of our analysis of oil samples obtained from Taichung (see Table 1).

PCDFs Retained in the Tissues

PCDFs retained in the tissues of a patient who died 2 years after poisoning was published recently (*7*). Figure 4 shows a gas chromatogram of PCDFs retained in the liver of the deceased patient. This figure shows that the major PCDFs retained in the liver of the patient are 1,2,3,4,7,8-HxCDF, 2,3,4,7,8-PnCDF and 1,2,4,7,8-PnCDF. Minor amounts of 1,2,3,4,6,7,8-HpCDF, 2,3,6,8-TCDF and 2,3,7,8-TCDF were also found in the liver. The PCDF congeners retained in other tissues are essentially the same as those retained in the liver. However, the relative amounts of each individual PCDF congeners are somewhat different between the liver and other tissues (see Table 5).

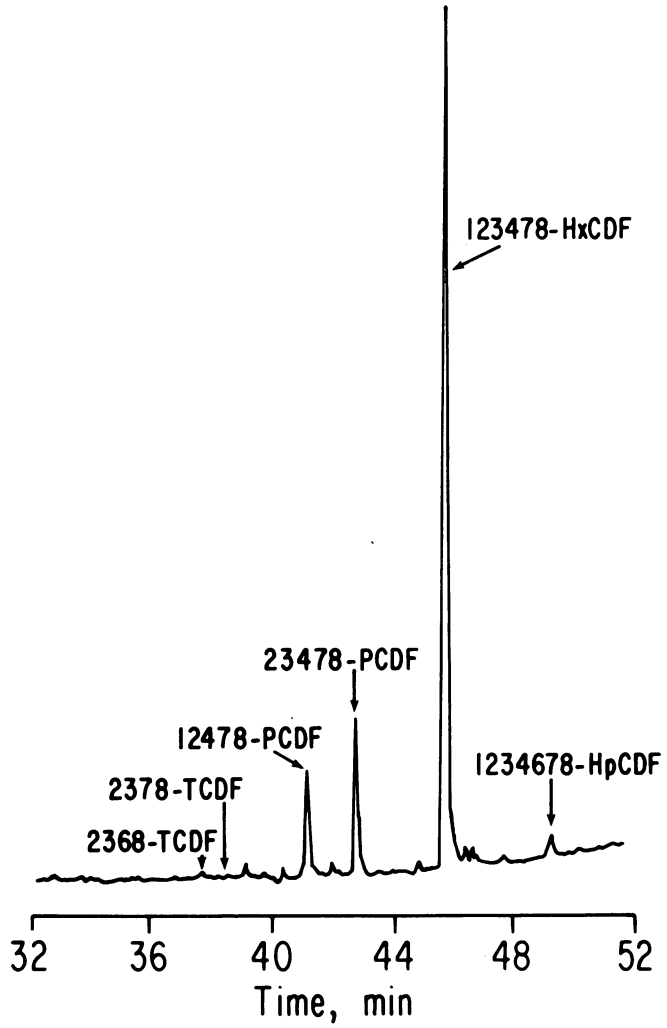

FIGURE 4. Gas chromatogram of PCDFs retained in the liver of the deceased patient. From Chen et al. (*7*).

In agreement with the findings by other workers in the study of Japanese Yusho patients (*17*), we found that all PCDF congeners that were retained in the patient's tissues had no vicinal hydrogens in the dibenzofuran ring (*7*). In contrast, all PCDF congeners that were excreted from the patient's body had at least two vicinal hydrogens in the ring (*7*). These excreted PCDF congeners include 2,3,4,8-TCDF, 1,2,3,4,8-PnCDF, 1,2,6,7,8-PnCDF, 2,3,4,6,7-PnCDF and 1,2,3,4,6,7-HxCDF which correspond to peaks 3, 6, 7, 9, and part of 10 in Figure 2, respectively.

The levels of three major PCDF congeners in the tissues were given in Table 5. This table shows that the concentration of PCDFs in the liver is about three times as much as in the intestinal fat, whereas the levels of PCBs in the liver is only about 1/17 of that in the intestinal fat (see Table 4). This high accumulation of PCDFs in the liver has been reported by other workers in an animal study (*18*) as well as for Japanese Yusho patients (*19*).

The most toxic PCDF congeners retained in the patient's tissues are 2,3,7,8,-TCDF and 2,3,4,7,8-PnCDF. Since 2,3,4,7,8-PnCDF is one of the major PCDFs retained in the tissues while 2,3,7,8-TCDF is only a very minor PCDF retained in the tissues and a minor PCDF present in the toxic oil, the former probably plays a much more important role in the etiology of Yu-Cheng in Taiwan (*7*). 1,2,3,4,7,8-HxDF is the most abundant PCDF component retained in the tissues; it is also a toxic PCDF (*20*). This PCDF, along with 2,3,4,7,8-PnCDF (*8*), could play important roles in the etiology of Yu-Cheng.

Table 5. Concentrations of PCDF congeners in the tissues of the deceased patient with Yu-Cheng in Taiwan.[a]

	Level of PCDF congener, ppb		
Tissue	12478	23478	123478
Liver	3.4	6.3	25.4
Intestinal fat	0.9	4.0	7.8
Bronchus	0.4	1.8	3.2
Large intestine	0.3	1.2	2.3
Heart	0.2	0.8	1.4
Stomach	0.05	0.23	0.40
Small intestine	0.05	0.21	0.34
Kidney	0.04	0.18	0.32
Lung	0.01	0.06	0.15
Brain	0.01	0.06	0.15
Spleen	0.01	0.08	0.10

[a]Data from Chen et al. (*7*).

PCDFs in the Blood

PCDFs in the blood of 10 patients were analyzed by NCI-GC–MS. The blood samples were collected 9 to 27 months after the onset of poisoning. The total PCDFs in the blood of 10 patients ranged from 0.02 to 0.20 ppb. The major PCDFs found in the blood were 1,2,3,4,7,8-HxCDF and 2,3,4,7,8-PnCDF. Minor amounts of 1,2,3,4,6,7,8-HpCDF and 1,2,4,7,8-PnCDF were also found in the blood.

PCQs in the Tissues

The tissues from the deceased patients were also analyzed for PCQs. The bronchus and the intestinal fat were found to contain high levels of PCQs, amounting to 4.3 ppm and 3.8 ppm, respectively. The large intestine and the heart also contained high levels of PCQs.

3,4,3′,4′-Tetrachlorobiphenyl

3,4,3′,4′-Tetrachlorobiphenyl is considered to be the most toxic PCB present in commercial PCB preparations (*21*). This tetrachlorobiphenyl was found in the toxic oil in the amount of about 1.0% of total PCBs in the oil (*5*). This toxic PCB component was also found in both blood and an adipose tissue (biopsy) of a patient sampled about 10 months after the onset of poisoning or 1 to 2 months after stop taking the toxic oil. However, this toxic PCB was not detected in the blood of most of the patients nor was it found in the intestinal fat of a patient who died about two years after the poisoning (*5*). This suggests that 3,4,3′,4′-tetrachlorobiphenyl can be metabolized and excreted from the body. This is in agreement with the result of an animal study (*21*).

The authors wish to express their sincere thanks to Professor R. A. Hites of Indiana University for his support in providing his laboratory facilities for part of this study. The authors also would like to thank Professor Y. Masuda of Daiichi College of Pharmaceutical Sciences, Japan, for the gift of PCB, PCDF and PCQ standards. The authors are also grateful to the Food and Drug Bureau of the Republic of China for the donation of a rice oil sample and tissue samples, and also to the National Science Council of the Republic of China for the financial support for part of this work.

REFERENCES

1. Kuratsune, M., Yoshimura, T., Matsuzaka, J., and Yamaguchi, A. Epidemiologic study on Yusho, a poisoning caused by ingestion of rice oil contaminated with a commercial brand of polychlorinated biphenyls. Environ. Health Perspect. 1: 119–128 (1972).
2. Chen, P. H., Gaw, J. M., Wong, C. K., and Chen, C. J. Levels and gas chromatographic patterns of polychlorinated biphenyls in the blood of patients after PCB poisoning in Taiwan. Bull. Environ. Contam. Toxicol. 25: 325–329 (1980).
3. Chen, P. H., Chang, K. T., and Lu, Y. D. Polychlorinated biphenyls and polychlorinated dibenzofurans in the toxic rice-bran oil that caused PCB poisoning in Taichung. Bull. Environ. Contam. Toxicol. 26: 489–495 (1981).
4. Chen, P. H., Luo, M. L., Wong, C. K., and Chen, C. J. Comparative rates of elimination of some individual polychlorinated biphenyls from the blood of PCB-poisoned patients in Taiwan. Food Chem. Toxicol. 20: 417–425 (1982).
5. Chen, P. H., Luo, M. L., Wong, C. K., and Chen, C. J. Polychlorinated biphenyls, dibenzofurans, and quaterphenyls in the toxic rice-bran oil and PCBs in the blood of patients with PCB-poisoning in Taiwan. Am. J. Ind. Med. 5: 133–145 (1984).
6. Kashimoto, T., Miyata, H., and Kunita, N. The presence of polychlorinated quaterphenyls in the tissues of Yusho victims. Food Cosmet. Toxicol. 19: 335–340 (1981).
7. Chen, P. H., and Hites, R. A. Polychlorinated biphenyls and dibenzofurans retained in the tissues of a deceased patient with Yucheng in Taiwan. Chemosphere 12: 1507–1516 (1983).
8. Masuda, Y., Kuroki, H., Yamaryo, T., Haraguchi, K., Kuratsune, M., and Hsu, S. T. Comparison of causal agents in Taiwan and Fukuoka PCB poisonings. Chemosphere 11: 199–206 (1982).
9. Morita, M., Nakagawa, J., and Rappe, C. Polychlorinated dibenzofuran (PCDF) formation from PCB mixture by heat and oxygen. Bull. Environ. Contam. Toxicol. 19: 665–670 (1978).
10. Yamaryo, T., Miyazaki, T., Masuda, Y., and Nagayama, J. Formation of polychlorinated quaterphenyls by heating polychlorinated biphenyls. Fukuoka Acta Med. 70: 88–92 (1979).
11. Ugawa, M., Nakamura, A., and Kashimoto, T. Studies on a calculation method for polychlorinated biphenyl isomers. In: New Methods in Environmental Chemistry and Toxicology (F. Coulston, F. Karte and M. Goto, Eds.), International Academic Printing Co., Tokyo, 1973, pp. 253–267.
12. Nagayama, J., Masuda, Y., and Kuratsune, M. Chlorinated dibenzofurans in Kanechlors and rice oils used by patients with Yusho. Fukuoka Acta Med. 66: 593–599 (1975).
13. Lan, C. F., Chen, P. H., Shieh, L. L., and Chen, Y. H. An epidemiological study on polychlorinated biphenyls poisoning in Taichung area. Clin. Med. (Taipei) 7: 96–100 (1981).
14. Hayabuchi, H., Yoshimura, T., and Kuratsune, M. Consumption of toxic rice oil by Yusho patients and its relation to the clinical response and latent period. Food Cosmet. Toxicol. 17: 455–461 (1979).
15. Koda, H., and Masuda Y. Relation between PCB level in the blood and clinical symptoms of Yusho patients. Fukuoka Acta Med. 66: 624–628 (1975).
16. Goto, M., and Higuchi, K. The symptomatology of Yusho (chlorobiphenyls poisoning) in dermatology. Fukuoka Acta Med. 60: 409–431 (1969).
17. Rappe, C., Buser, H. R., Kuroki, H., and Masuda, Y. Identification of polychlorinated dibenzofurans (PCDFs) retained in patient with Yusho. Chemosphere 8: 259–266 (1979).
18. Kuroki, H., Masuda, Y., Yoshihara, S., and Yoshimura, H. Accumulation of polychlorinated dibenzofurans in the livers of monkeys and rats. Food Cosmet. Toxicol. 18: 387–392 (1980).
19. Kuroki, H., and Masuda, Y. Determination of polychlorinated dibenbofuran isomers retained in patients with Yusho. Chemosphere 7: 771–777 (1978).
20. Yoshihara, S., Nagata, K., Yoshimura, H., Huroki, H., and Masuda, Y. Inductive effect on hepatic enzymes and acute toxicity of individual polychlorinated congeners in rats. Toxicol. Appl. Pharmacol. 59: 580–588 (1981).
21. Abdel-Hamid, F. M., Moore, J. A., and Matthews, H. B. Comparative study of 3,4,3′,4′-tetrachlorobiphenyl in male and female rats and female monkeys. J. Toxicol. Environ. Health 7: 181–191 (1981).