FATE OF EXPOSED PCDFS AND PCBS IN PATIENTS WITH YUSHO PCB POISONING

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Introduction

A mass poisoning, patients being counted to about 1860, occurred in western Japan, mainly Fukuoka and Nagasaki prefectures, in 1968. The poisoning is called Yusho, oil disease, as it was caused by ingestion of rice oil that was contaminated with Kanechlor-400, a commercial brand of Japanese polychlorinated biphenyls (PCBs). It was later found that the rice oil had been contaminated with not only PCBs but also polychlorinated dibenzofurans (PCDFs), polychlorinated quaterphenyls (PCQs) and others. Consequently, Yusho was a poisoning by a mixture of PCBs, PCDFs, PCQs and others[1,2]. A very similar poisoning, called Yucheng, occurred in central Taiwan in 1979, 11 years after the Japanese Yusho incident. These two incidents of food poisonings are very valuable as a source of information concerning the behavior of PCBs and PCDFs in human body and the toxic effects of these chemicals on humans.

Materials and Methods

Blood sample

Ten ml of blood was collected from Yusho and Yucheng patients who visited the health center in Fukuoka or Taichung for their health examination. The blood samples were kept frozen at –20° C until analysis.

PCB analysis

Blood sample was added with 5 ng of 2,2',3,4,5,5',6-hepta-CB or four ^{13}C labeled PCBs as internal standards and saponified in 1N NaOH ethanol solution. The mixture was extracted with n-hexane 5 ml twice. The n-hexane extract was washed with 2 ml of water dried over anhydrous sodium sulfate and chromatographed on 1 g of silica gel, eluting with 20 ml of n-hexane. The n-hexane eluate was concentrated to a small volume and analyzed for PCB congeners by gas chromatograph/electron capture detector[3] of gas chromatograph/quadrupole mass spectrometer.[4]

PCDF analysis

To the blood sample added the internal standards consisted of six ^{13}C-PCDDs, seven ^{37}Cl-PCDFs and three ^{13}C-planarPCBs, and then added ethanol, hexane and aqueous saturated

ammonium sulfate. The mixture was homogenized and, after separation, the upper hexane portions were combined, washed with water, and evaporated to dryness for obtaining the extractable lipid. The lipid material was redissolved in hexane and treated with concentrated sulfuric acid. The organic extract passed through multi layer column of cesium hydroxide/silica gel and sulfuric acid/silica gel, separated chromatographically the PCDDs/PCDFs from the major portion of PCBs on Florisil column, and separated the toxic planar components from non planar analyte on a column of Carbopack C carbon dispersed silica. The final extract was added with the recovery standards and injected to high separation gas chromatography / high resolution mass spectrometry (VG Analytical MS or Finnigan MAT 90)[5,6].

Results

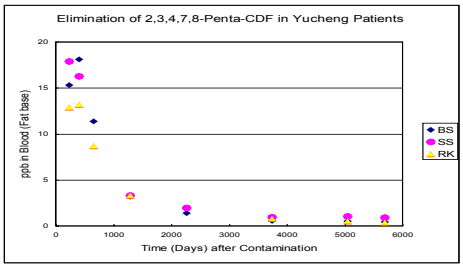
The concentrations (fat base) of three PCDF congeners were determined in the blood of three Yucheng patients from 1980 to 1995 and five Yusho patients from 1982 to 1998. The whole base concentrations of six PCB congeners were also determined in the same blood samples of Yucheng and Yusho patients. The time changes on the concentrations of 2,3,4,7,8-penta-CDF, 2,3,4,4',5-penta-CB and 2,2',4,4',5,5'-hexa-CB are shown graphically in Figure 1.

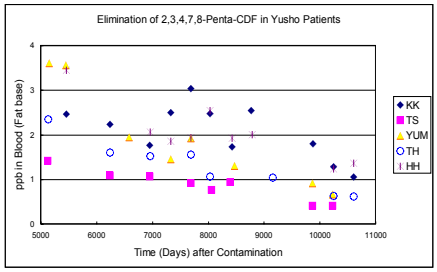
Fig. 1 Time change concentrations of PCDF and PCB congeners in Yusho and Yucheng patients

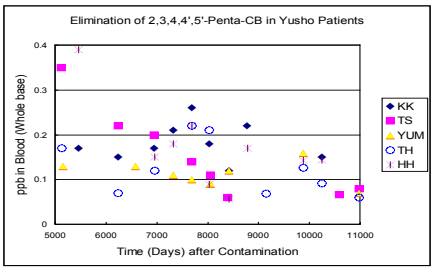
Table 1 lists the biological half-lives of PCDF and PCB congeners in Yucheng and Yusho patients calculated on assuming first order exponential elimination in one compartment model.

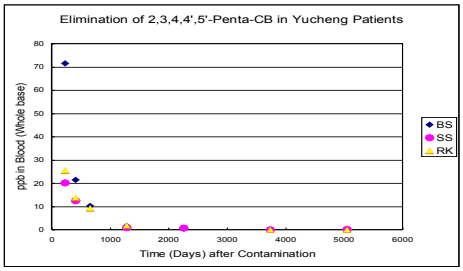
Table 1 Biological Half-life of PCDF and PCB Congeners in Yusho and Yucheng Patients

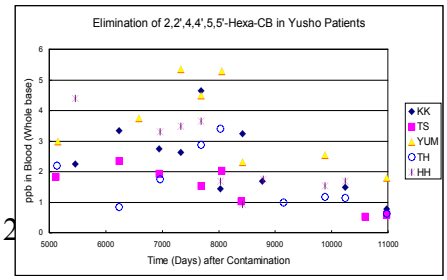
	Half-life (Years)									
	Yucheng patient				Yusho patient					
	BS	SS	RK	Median	KK	TS	YUM	TH	HH	Median
2,3,4,7,8-Penta-CDF	2.7	3.6	2.9	2.9	14.3	7.7	6.1	5.2	11.4	7.7
1,2,3,4,7,8-Hexa-CDF	2.7	3.6	3.5	3.5	6.5	4.5	3.9	5.1	6.9	5.1
1,2,3,4,6,7,8-Hepta-CDF	2.6	2.5	2.2	2.5	6.6	2.6	3.5	3.5	3.4	3.5
Average	2.7	3.2	2.9	3.0	9.1	4.9	4.5	4.6	7.2	5.4
2,3',4,4',5-Penta-CB	1.6	1.9	1.5	1.6	19.5	6.9	33.7	17.6	10.4	17.6
2,2',4,4',5,5'-Hexa-CB	3.4	4.2	4.2	4.2	9.1	7.4	16.0	12.9	7.4	9.1
2,2',3,4,4',5'-Hexa-CB	4.4	4.5	5.5	4.5	12.8	8.9	13.7	31.0	9.5	12.8
2,3,3',4,4',5-Hexa-CB	3.8	5.6	5.3	5.3	9.4	8.5	21.5	13.2	14.4	13.2
2,2',3,3',4,4',5-Hepta-CB	4.7	6.0	5.9	5.9	18.4	12.3	-237.5	13.3	443.7	18.4
2,2',3,4,4',5,5'-Hepta-CB	4.3	6.0	6.0	6.0	16.7	12.2	20.4	10.3	224.6	16.7
Average	3.7	4.7	4.7	4.6	14.3	9.4	21.1 except -237.5	16.4	118.3	14.6

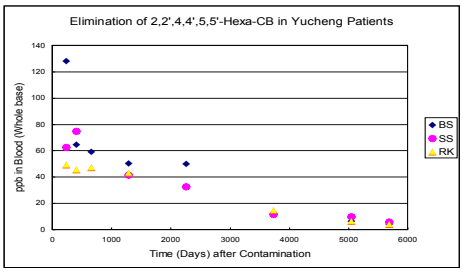

Elimination of 2,3,4,7,8-Penta-CDF in Yucheng Patients
ppb in Blood (Fat base)
Time (Days) after Contamination
BS
SS
RK


Elimination of 2,3,4,7,8-Penta-CDF in Yusho Patients
ppb in Blood (Fat base)
Time (Days) after Contamination
KK
TS
YUM
TH
HH


Elimination of 2,3,4,4',5'-Penta-CB in Yusho Patients
ppb in Blood (Whole base)
Time (Days) after Contamination
KK
TS
YUM
TH
HH


Elimination of 2,3,4,4',5'-Penta-CB in Yucheng Patients
ppb in Blood (Whole base)
Time (Days) after Contamination
BS
SS
RK


Elimination of 2,2',4,4',5,5'-Hexa-CB in Yusho Patients
ppb in Blood (Whole base)
Time (Days) after Contamination
KK
TS
YUM
TH
HH



The three PCDF congeners eliminated in Yucheng patients at about 3 years of biological half-life for 5700 days (15.5 years) after the contamination. As observed in Yusho patients, from 5000 days after the contamination, half-lives of these PCDF congeners were prolonged to 3.5-7.7 years. Half-lives of the five PCB congeners (4.2-6.0 years), except for 2,3',4,4',5-penta-CB, were longer than those of PCDF congeners in the same Yucheng patients. When the concentrations of the PCB congeners decreased to 1-5 ppb (whole base), the PCB congeners eliminated more slowly from the human body as observed in Yusho patients from the time of 5000 days after the contamination. Among the PCBs determined, 2,3',4,4',5-penta-CB was an unique PCB. Its half-life was shorter than those of PCBs and PCDFs in the Yucheng patients, and its concentration decreased to lower than the control level at 4000 days after the contamination.

Discussion

Estimating from the elimination curve of 2,3,4,7,8-penta-CDF in the Yucheng patients, the fat base concentration in Yusho patients would be 30-45 ppb just after the ingestion of the contaminated rice oil. As the 2,3,7,8-tetra-CDD toxic equivalent (TEQ) factor for 2,3,4,7,8-penta-CDF is 0.5 and about 70 % of the dioxin like toxicity was contributed by 2,3,4,7,8-penta-CDF in Yusho rice oil and adipose tissue of Yusho patients[7], TEQ concentrations (fat base) in the Yusho patients would be 20-30 ppb just after the contamination. Typical Yusho symptoms such as chloracne, pigmentation, cheesy secretions from the meibomian glands of eyes and others were observed in Yusho patients at the time of poisoning occurred and the fat base TEQ level was high as 20-30 ppb. These Yusho symptoms diminished with time when the PCDF concentrations gradually decreased down to 1-3 ppb. However, disorder of enzyme and hormonal conditions adhered in Yusho patients for 20-30 years, showing abnormally high levels of serum triglycerides and thyroxins and higher activity of aromatic hydrocarbon hydroxylase in lymphocyte.

The concentrations of TEQ and observed symptoms in human[8] is graphically shown in Fig. 2. When normal persons exposed tenfold more to dioxin like compounds, human TEQ levels will elevated to about 500 ppt in fat base which level shows subtle dioxin toxicities such as abnormal thyroxin levels, small penis length and low intelligence quotients levels.

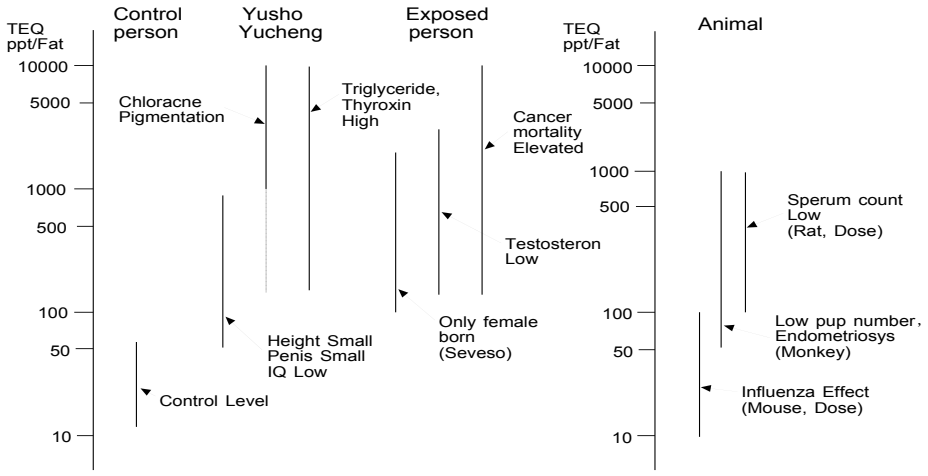


Fig.2 TEQ Level and Symptom or Sign

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