HUMAN DIOXIN CONTAMINATION IN THE PAST AND PRESENT

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Introduction

2,3,7,8-Tetrachlorodizenzodioxin(TCDD)and related compounds have been known extremely toxic, persistent in the environment, and bio-accumulative. Emission sources and exposure route of these compounds have changed during these 50 years and its contamination level in human body must have reflected by those changes. It is worthy to note the time trend of PCDD/PCDF level in human with consideration of environmental levels and exposure scenarios if we consider the importance of biological effect of these chemicals to the future generation.

Emission Of Dioxin And Related Materials

In recent years, dioxin source is considered mainly of municipal and industrial waste incineration; the total amount of PCDD/PCDF from incineration is estimated roughly 100kg·TEQ for recent 50 years with a maximum emission of 5kg/year in early 1990's. PCDDs/PCDFs from incinerators are emitted to the atmosphere and have given rise to accumulation in human and wildlife through terrestrial and marine contamination.

On the other side, the major source in 1960's and early 1970' was from the production of specific organochlorine chemicals. PCDD is known to occur as an impurity of chlorophenols. For example, the most toxic 2,3,7,8-TCDD is known as a trace impurity of 2,4,5-trichrophenol and its derivates such as 2,4,5-trichlorophenoxy acetic and (2,4,5-T) and its related compounds.

Case reports of TCDD intoxication among the workers in chlorophenol production plant are seen worldwide and also in Japan. The 2,4,5-T formulation in 1960's used for forest herbicide might contain c.a.10 ppm, and 2,3,7,8-TCDD coming from 2,4,5-T in Japan may sum up to 1.5kg. 2,3,7,8-TCDD is also known to occur in hexachlorophene which was used in soaps and other household uses including baby powder and food additive for animal feeding.(WHO1977) The mount of hexachlorophene production and the concentration of TCDD in the product is not reported.

The related herbicide 2,4-D contained a small amount of TCDD but its contribution was small. Another herbicide CNP is known to contain significant amount of PCDDs in the early product (Masunaga et al.) and estimated the total emission of PCDDs from CNP can be 170 kg·TEQ. Our estimation ,however, is much smaller.

Pentachlorophenol (PCP) was one of the high volume production chemicals and was used for a variety of uses including herbicide for rice plantation and fungicide for wood preservation. Major dioxin isomers of PCP are octachlorodioxin and heptachlorodioxins with a lesser extent of hexachlorodioxins. There is a possibility that fire of PCP stock factory produced significant amount of octachlorodioxin because Na salt of PCP is known to combert to OCDD quantitatively at 360 ℃ (Langer et al. 1973). The total amount of dioxins from PCP source is estimated to be 100-150kg·TEQ which are now retained mainly in soil and in part in sediment.

An important human intoxication by PCDF may be the case of Yusho which happened in 1968 by the ingestion of PCB contaminated food oil (Nagayama et al. 1976). PCDFs were known as a toxic impurity in commercial PCB preparations (Vos et al. 1974) and the case of Yusho was

intoxication of PCDF produced from PCB during long-term heating giving rise to markedly elevated toxicity (Morita et al. 1978). Apparently PCB itself is one of the major sources of PCDFs and may count up to 3kg·TEQ for PCDF and 100kg TEQ for co-planer PCBs if we assume that 5000 ton of PCB entered into the environment. There is other minor sources including chlorine breaching. Although emission from chlorine beaching in paper and pulp industry is considered small compared to other sources, its direct introduction to aquatic system contributes to the contamination of marine fish and crabs which are subjected to diet.
Information on other TCDD-like compounds such as brominated dioxins and furans, and 3,4,3',4'-tetrachloroazobenzene is limited and further study is necessary.

PCDD/PCDFs In Human Milk

Determination of PCDDs/PCDFs in human milk sample by high resolution mass spectrometry started in 1990 in Japan giving a preliminary data of 2,3,7,8-TCDD and OCDD as 5.7 pg/g fat and 1890 pg/g fat, respectively. Monitoring program started under MHW scientific program since 1994, and the program was expanded to cover nationwide since 1997. Samples were collected from mothers who were nursing her first child. The result is given in Table 1.

Dioxin isomer that appears dominantly in human milk is OCDD. The large use of PCP in 1960's and the stopped use in the 1970's may be reflected to high concentration of OCDD in the past Japanese population .

Major contribution to total toxicity equivalency (TEQ) is from 1,2,3,7,8-pentachlorodioxin, 1,2,3,6,7,8-hexachlorodioxin and 2,3,4,7,8-pentachlorodibenzodibenzofuran and the sum of these three isomers occupies more than 80% of total TEQ of PCDD/PCDFs. Isomer pattern of PCDD/PCDF in the diet is a bit more complex by reflecting the pattern of emission source especially from incinerators. However that of human samples is simplified indicating that 2,3,7,8-isomers are selectively retained in human body.

Table 1. PCDD/PCDF/Co-PCB in Japanese human milk (WHO 1998-TEF)

	Sample Size	Sites(prefecture)	PCDD/PCDF (pg-TEQ/g fat)	Co-PCB (pg-TEQ/g fat)	Total
1994FY	n=26	5	43.6	13	56.6
1995FY	n=26	5	18.1	4.8	22.9
1996FY	n=26	5	19.6	8.8	28.4
1997FY	n=78	4	14.9	9.9	24.8
1998FY	n=415	20	12.2	6.2	18.4
1999FY	n=111	6	15.2	8.8	24.0

Although it is not conclusive because of the difference of sampling sites, it seems that slow decline of PCDD/PCDF is occurring during these observation period. In another project of MHW, Dr. Hori reported a clear decline of PCDD/PCDF and PCB in a pooled human milk sample collected at Osaka prefecture.

Human Adipose Tissue

PCDD/PCDFs in human adipose tissue currently analysed for autopsy samples gives the average values of 11.9 pgTEQ/g fat (Choi et al. 2001) and 23 pgTEQ/g fat (MOE1999)。 PCDD/PCDFs level in the adipose seems higher in the past :31.6 pgTEQ/g fat for 1970-71 samples and 31.5 pgTEQ/g fat for 1994-96 samples. It is also worthy to note that OCCD level, HpCDD as well, was quite high in 1970-71 sample. Since the time that PCP stopped of its use for herbicide in 1970, the level of OCDD in adipose tissue fell down to 1/30 during these 30 years. The overall decline rate appears to be half in every 6 years. Another point one may notice is that the level of

1,2,3,6,7,8-HxCDDs is coming up between 1970 and 2000. 1,2,3,6,7,8-HxCDD is considered as an impurity of early CNP product. Expanded production of CNP in 1970's and early 1980's might contribute in part to the elevated concentration in adipose tissue.
PCB including co-planer PCB level in human adipose level also declined in response to the stopped production and use since 1973.

Human Blood
PCDD/PCDFs and Co-PCBs have been analyzed in human blood in recent five years. Reported average value for general population lies in the range of 10-50 pg TEQ/g fat for total blood. Isomer patterns are quite similar to those of human milk or adipose tissue. Because of limited number of reliable data, it is hard at this moment to see the time trend of PCDD/PCDF.
Analysis of cordial blood gave the result of 0.007 pgTEQ/g wet weight. The value is significantly lower than the frequently observed value of 0.1 pg TEQ/g wet weight in general population. It may indicate the limited transfer through placental barrier.

Dietary Exposure
Major pathway that PCDD/PCDFs and PCB to human body is food intake. Analysis of food samples in the past will give information of exposure of the past. Analysis of reserved diet samples of 1990 gave an average value of 170 pg TEQ/day (Sakurai et al. 2001). This value seems higher than currently reported value 90-120 pg TEQ/day indicating that the exposure in the past was bigger than now. In another study of MHW using archived market-basket samples have shown a trend of decline :58% reduction from 1975 to 1998.

Conclusion
Emission of PCDD/PCDF to the environment has changed during recent fifty years, major source being from agriculture chemicals until 1970 to waste incineration later on. Information on other Dioxin-like compounds including bromodioxins and tetrachloroazobenzenes is limited and further study is necessary. PCDD/PCDF and PCB contamination of food changed even slowly because of their bioaccumulation and cycling in the environment. Although intake from food is likely declining, its level is still exceeding than 1 pg TEQ/kg b.w./day.
PCDD/PCDFs and co-PCB level in human body is approximately 20 pg TEQ/g fat for general population. The level seems declining during these 25 years reflecting the change of emission.
The meaning of the concentration of PCDD/PCDFs and co-PCB should be understood especially for the past high contamination and workplace exposure in relation to several endpoints such as sperm quality deterioration and endometritis which have been demonstrated in animal experiments at very low doses of the compounds.

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