

Concentrations of Chlorinated Dioxins and Related Compounds in the Blood and Their Genotoxicity in Japanese Young Women

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Objectives

It has been noticed that our human bodies are already contaminated with various chemicals including the highly toxic organochlorine compounds such as polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar polychlorinated biphenyls (Co-PCBs)¹⁾. We have determined the level of PCDDs, PCDFs and Co-PCBs in human breast milk samples obtained from healthy Japanese mothers and daily intakes of these chemicals as 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) toxic equivalent (TEQ) value were estimated to be 93 to 197 pg/kg/day for breast-feeding babies of these mothers²⁾. These TCDD TEQ values are much higher than the acceptable daily intake (ADI) of 1~10 pg/kg/day for TCDD. Therefore, we should give due attention to the possible health effects of sucklings due to these highly toxic chemicals.

We calculate that their concentrations in human milk samples are about 15 times greater than those in human blood samples in terms of TCDD TEQ value on whole weight basis¹⁾²⁾, so it is useful to determine their concentrations in the blood of unmarried Japanese young women in order to estimate their

levels in the breast milk when they will become mothers. We have already reported that these chemicals are also very potent genotoxic compounds and 50% effective concentration for the inductions of sister chromatid exchanges (SCEs) and micronucleated cells (MNs) are 210 to 560 ppt as TCDD TEQ value, which are only about 3 to 8 times higher than the average contamination level in Japanese people, in cultured human lymphocytes^{3,4}. Therefore, we also examined the frequency of SCEs and MNs in cultured human lymphocytes obtained from the same blood samples and statistically analyzed the correlation between the blood level of these chemicals and their frequencies to evaluate whether PCDDs, PCDFs and Co-PCBs in the blood was able to elicit the genotoxicity or not.

Approach and Methods

Sixty to 80 ml of peripheral blood samples were individually obtained from 50 unmarried healthy Japanese women (mean age : ca. 20 years old and range : 18-29 years old). Concentrations of PCDDs, PCDFs and Co-PCBs in the blood samples were determined by ordinary gas chromatography/mass spectrometry (GC-MS) method². Frequencies of SCEs and MNs in the lymphocytes of individual whole-blood cultures were counted and analyzed as described before^{4,5}. Chemicals, experimental procedures and statistical analysis were previously mentioned in detail^{2,4,5}.

Results

1) Concentrations of PCDDs, PCDFs and Co-PCBs in the blood

Respective medians and ranges in concentrations of PCDDs, PCDFs and Co-PCBs in the 50 blood samples are given in Table 1 in terms of TCDD TEQ values on both the whole and fat weight bases. Medians of their total concentrations on the whole and fat weight bases are 0.068 and 23.00 ppt, respectively. The range of the total concentrations is 0.030 to 0.123 ppt on the whole weight basis and

Table 1. Medians and ranges in concentrations of PCDDs, PCDFs and Co-PCBs in the blood of 50 Japanese young women

Organohalogen Compound	Median Concentration (min. ~ max.) in TCDD TEQ Value (ppt)	
	Whole Weight Basis	Fat Weight Basis
PCDDs	0.028 (0.013 ~ 0.051)	13.15 (4.80 ~ 19.30)
PCDFs	0.021 (0.010 ~ 0.035)	7.05 (2.90 ~ 12.20)
Co-PCBs	0.017 (0.004 ~ 0.039)	5.55 (1.40 ~ 11.70)
Total	0.068 (0.030 ~ 0.123)	23.00 (9.10 ~ 38.70)

9.10 to 38.70 ppt on the fat weight basis.

2) Frequencies of SCEs in the lymphocytes of whole-blood cultures

Frequencies in three kinds of SCEs in the blood lymphocytes are summarized in Table 2. Median frequency of SCEs in the absence of 7,8-benzoflavone (ANF), SCE_{baseline} , is 9.52/cell and the range is 7.24~11.32/cell. In the presence of ANF ($8 \times 10^{-5} \text{M}$), SCE_{ANF} , it is 13.82/cell and the range 11.32~16.16/cell. We also calculated ΔSCE , $SCE_{\text{ANF}} - SCE_{\text{baseline}}$, and the range of ΔSCE is 2.72 to 7.04/cell with the median value of 4.70/cell.

Table 2. Frequencies in three kinds of SCEs in the blood lymphocytes of 50 Japanese young women

Category	Median SCEs/Cell (min. ~ max.)
SCE_{baseline} : ANF(-)	9.52 (7.24~11.32)
SCE_{ANF} : ANF(+)	13.82 (11.32~16.16)
ΔSCE : $SCE_{\text{ANF}} - SCE_{\text{baseline}}$	4.70 (2.72~7.04)

ANF : 7,8-benzoflavone

3) Frequencies of MNs in the lymphocytes of whole-blood cultures

Frequencies in two kinds of MNs in the blood lymphocytes are shown in Table 3. Median frequency of MNs in the absence of ANF, MN_{baseline} , is 2.67/500 binucleated lymphocytes and the range is 0.30~4.70. In the presence of ANF ($8 \times 10^{-5} \text{M}$), MN_{ANF} , it is 2.00/500 binucleated cells and the range 1.00~3.70.

Table 3. Frequencies in two kinds of micronucleated cells (MNs) in the blood lymphocytes of 50 Japanese young women

Category	Median MNs (min. ~ max.) [*]
MN_{baseline} : ANF(-)	2.67 (0.30~4.70)
MN_{ANF} : ANF(+)	2.00 (1.00~3.70)

* : per 500 binucleated lymphocytes

ANF : 7,8-benzoflavone

4) Correlation between the concentrations of PCDDs, PCDFs and Co-PCBs and the frequency of SCEs

We examined the correlation between the concentrations of PCDDs, PCDFs and Co-PCBs and the frequencies of SCE_{baseline} , SCE_{ANF} and ΔSCE . At this point, respective concentrations of PCDDs, PCDFs and Co-PCBs and their total concentration on the whole and fat weight bases in the blood were divided into three groups, namely, low, middle and high groups. In the low group, their concentrations belong to the first quartile including minimum ones and in the high group, their concentrations are in the last quartile including maximum ones. The middle group comprises the rest of them, that is, the second and third quartiles.

We did not find any significant correlation between these groups and the frequency of SCE_{baseline} . However, the frequencies of SCE_{ANF} and ΔSCE significantly decreased in inverse proportion to the concentration of Co-PCBs, indicating that the frequencies of SCE_{ANF} and ΔSCE in the low group were meaningfully higher than those in the high group. These results are indicated in Fig. 1.

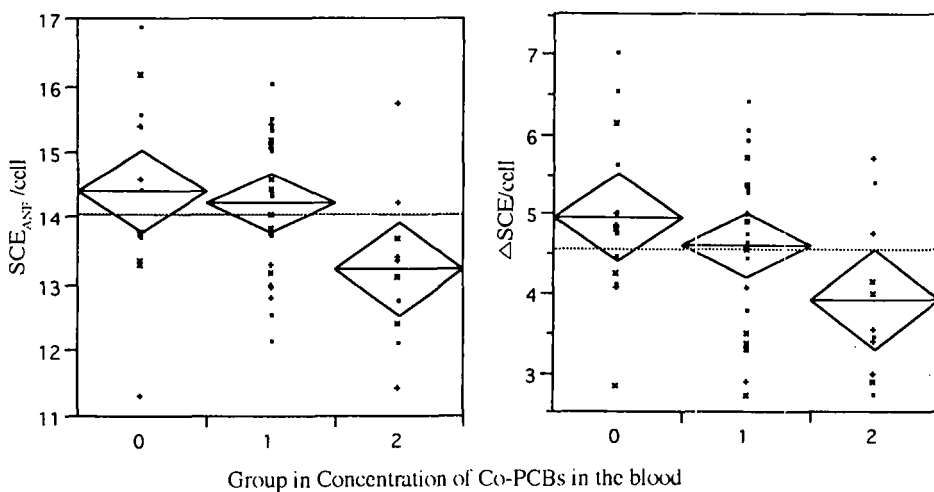


Fig. 1. Frequencies of SCE_{ANF} (left) and ΔSCE (right) in the blood lymphocytes plotted in relation to the three groups in concentration of Co-PCBs on whole weight basis
0 : Low group, 1 : Middle group, 2 : High group

5) Correlation between the concentrations of PCDDs, PCDFs and Co-PCBs and the frequency of MNs

We also investigated the correlation between the three groups in their concentrations and the frequencies of MN_{baseline} and MN_{ANF} . In this study, PCDDs in the blood seemed not to elicit any effect on the

frequencies of MN_{baseline} and MN_{ANF} in the lymphocytes of whole-blood cultures. We, however, observed that the frequency of MN_{baseline} in the low group was significantly lower than that in the middle group, but not in the high group and that the frequency of MN_{ANF} was significantly higher in the low group than in the high group. These results are shown in Fig. 2.

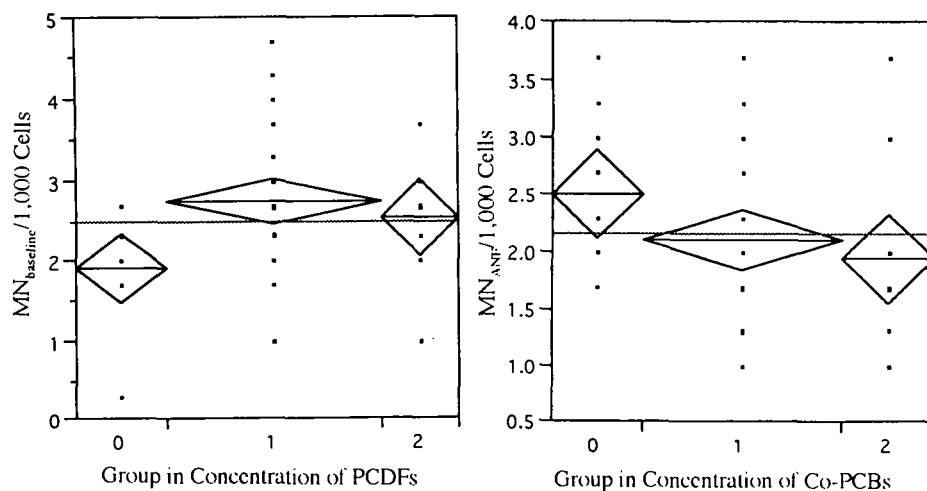


Fig. 2. Frequencies of MN_{baseline} (left) and MN_{ANF} (right) in the blood lymphocytes plotted in relation to the three groups in respective concentrations of PCDFs and Co-PCBs on fat weight basis

0 : Low group, 1 : Middle group, 2 : High group

Conclusions

- 1) Total level of PCDDs, PCDFs and Co-PCBs as TCDD TEQ value in the blood of Japanese young women (mean age : ca. 20 years old) is about a half of that in Japanese people aged ca. 40 years on the whole weight basis.
- 2) PCDDs in the blood did not induce any significant effects on the frequencies of SCEs and MNs.
- 3) PCDFs and Co-PCBs in the blood significantly enhanced and/or decreased the frequencies in some kinds of SCEs and MNs.
- 4) Consequently, present contamination of these chemicals in the blood may cause some genotoxic influences for Japanese young women.

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