

## Effects of Perinatal Exposure to Dieldrin and Heptachlor Epoxide on Lymphocyte Subsets in Japanese Infants

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### Introduction

Our environment including food has been contaminated with some organochlorine pesticides<sup>1)</sup> and Japanese people have also been polluted with these pesticides<sup>3)</sup>. Consequently, some pesticides such as hexachlorocyclohexans (HCHs), 1,1,1-trichloro-2,2-bis-(4-chlorophenyl)-ethane (DDT) and its metabolites, dieldrin and heptachlor epoxide (HCE) have been determined in Japanese breast milk<sup>4)5)</sup> and their mean concentrations on fat weight basis were about 420, 345, 3 and 4, respectively<sup>5)</sup>. Their levels are more than 100 to 10,000 times higher than those of polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar polychlorinated biphenyls (Co-PCBs) as a whole in 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) toxic equivalent (TEQ) value<sup>5)</sup>. Therefore, we should give due attention to possible health consequences of these organochlorine pesticides in Japanese infants.

We have already reported the perinatal exposure to  $\beta$ -HCH, DDT and chlordane on lymphocyte subsets in the peripheral blood of Japanese infants<sup>6)</sup>, so in this study, effects of dieldrin and HCE on them were investigated in the same infants.

### Materials and Methods

One hundred and twenty four mothers volunteered to participate in all in this study. Pregnancy and delivery were completed without overt signs of serious illness or complications. Only babies

born at term (37 to 42 weeks of gestation) without congenital anomalies or diseases were included. Breast milk (50~100 ml), sampled 2 to 4 months after the childbirth, was used to determine concentrations of dieldrin and HCE by ECD gas chromatography method <sup>2)</sup>.

About 1 year after birth, 5 to 10 ml of peripheral blood samples were individually obtained from 93 infants. These blood samples were used to measure the lymphocyte subsets by indirect immunofluorescence using monoclonal mouse anti-human antibodies against CD3, CD4, CD8, CD4+CD8, CD16, CD20 and HLA-DR, and their relative population densities were calculated <sup>7)</sup>.

The contamination levels of dieldrin and HCE in the breast milk were truncated at the detection limits and also censored. So, in order to conduct more reliable statistical analysis, the concentrations of dieldrin and HCE determined in the breast milk were categorized into three classes according to the levels of the pesticide, denoted by 0 (low level), 1 (medium level) and 2 (high level). More specifically, the ranges of categories for dieldrin are 0 (~2.0 ng/g), 1 (2.0~3.0 ng/g) and 2 (3.0 ng/g~) and for HCE 0 (~2.0 ng/g), 1 (2.0~6.0 ng/g) and 2 (6.0 ng/g~).

Statistical significance was evaluated by the analysis of variance or Wilcoxon/Kruskal-Wallis test.

## Results

### 1) Concentrations of the organochlorine pesticides in the breast milk

Analytical results on fat weight basis of dieldrin and HCE in 124 breast milk samples are indicated in Fig.1. About 61% and 37% in 124 samples of the breast milk were less than the detection limit in dieldrin and HCE, respectively. Median and maximum levels on fat weight basis of dieldrin were 3 and 27 ng/g, and those of HCE 3 and 23 ng/g.

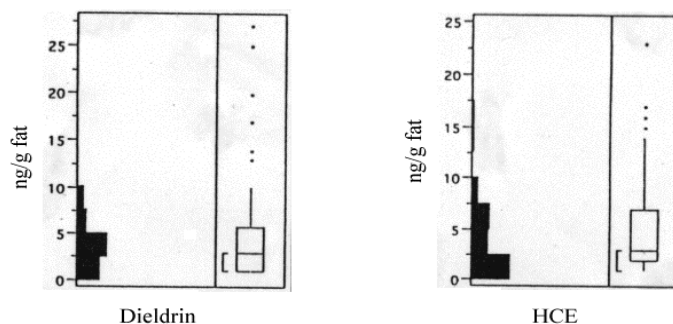


Fig.1. Distributions in concentrations of dieldrin and HCE (ng/g) in the Japanese breast milk of 124 mothers

### 2) Percentages of lymphocyte subsets in the peripheral blood of Japanese infants

Results of lymphocyte subsets in the Japanese infants have already been reported <sup>8)</sup>, so the main

results are summarized in Table 1.

Table 1. Percentages of lymphocyte subsets in the peripheral blood of 93 Japanese infants

Lymphocyte Subsets (Positive Cells)	Median (min.~max.), %
CD3	60.4 (31.2~76.6)
CD4	39.6 (15.7~61.7)
CD8	19.1 (10.6~41.2)
CD4+CD8	0.5 (0.1~2.1)
CD16	8.6 (1.7~25.4)
CD20	21.7 (5.5~56.2)
HLA-DR	25.6 (8.2~62.1)
CD4/CD8	2.08 (0.62~4.52)

### 3) Relationship between levels of the organochlorine pesticides and peripheral lymphocyte subsets in the infants

Special attention was paid to the percentages of helper/inducer (CD4+) and suppressor/cyto-toxic (CD8+) T lymphocytes, and their ratio, because the balance of these two types of lymphocytes are considered to very important to maintain the normal or healthy condition of immune response. The percentages of CD4+ and CD8+T lymphocytes showed decreasing and increasing tendencies with the group of low to high level of dieldrin ( $p=0.006$ ) and HCE ( $p=0.055$ ) in the breast milk, respectively. Consequently, the ratios of both cell types seemed to be decreased with the groups of higher levels of the two pesticides, as indicated in Fig.2.

### Discussion

Effects of  $\beta$ -HCH, DDT and chlordane in the breast milk on the lymphocyte subsets in the same infants have already been reported and higher level of DDT only was considered to decrease the percentage of CD4+T lymphocytes<sup>6)</sup>. In this study, despite of the levels of dieldrin and HCE were two orders of magnitude lower than that of DDT, they seemed to show stronger effects on the immune response of CD4+ and CD8+T lymphocyte systems.

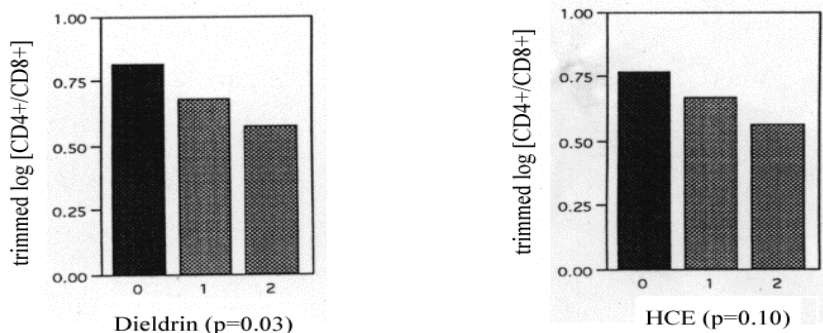


Fig.2. Relationship between the ratios of the percentages of CD4+ and CD8+ T lymphocytes and the levels of dieldrin and HCE in the breast milk

Patients with severe atopic dermatitis showed a decreased CD4+CD29+: CD4+CD45RA+Ratio ( $p < 0.01$ )<sup>9</sup>. They also found a decreased absolute number of CD4+CD29+lymphocytes ( $p < 0.05$ ) and an increased absolute number of CD4+CD45 RA+ lymphocytes ( $p < 0.05$ ) in the peripheral blood of the patients. Therefore, attention should be paid to some pesticides such as DDT, dieldrin and HCE, which have been contaminating the maternal body and breast milk, as possible etiological factors of atopic dermatitis.

#### References

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