EFFECTS OF ORGANOCHLORINE COMPOUNDS SUCH AS PESTICIDES, PCBs AND DIOXINS ON IMMUNE RESPONSE SYSTEM IN JAPANESE MOTHERS

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Introduction

Our environments including food have been polluted with some organochlorine compounds such as dioxins which are polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar polychlorinated biphenyls (Co-PCBs), polychlorinated biphenyls (PCBs) and pesticides [1, 2]. Accordingly, Japanese people have also been contaminated with these chemicals [3, 4]. Some pesticides such as hexachlorocyclohexans (HCHs), 1,1,1-trichloro-2,2-bis-(4-chlorophenyl)-ethane (DDT), dieldrin and heptachlor epoxide (HCE), and PCBs have been determined in Japanese breast milk [5, 6, 7]. Their levels were considered more than 100 to 10,000 times higher than that of dioxins in 2,3,7,8-tetra- chlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) toxic equivalent (TEQ) value [6]. Therefore, we should give due attention to possible health consequences of these organochlorine pesticides and PCBs as well as dioxins in Japanese mothers.

We have already reported effects of the lactational exposure to these compounds on lymphocyte subpopulations in the peripheral blood of Japanese infants [8, 9]. In this study, their effects on immune response system of Japanese mothers who gave us breast milk samples in our former studies were investigated.

Materials and Methods

In our studies, 124 mothers volunteered to participate in all. 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 childbirth, was used to determine concentrations of the organochlorine pesticides and PCBs by ECD gas chromatographic method [6, 10] and dioxins by high resolution GC/MS method [6].

TEQ concentrations of dioxins were calculated by using 1998 WHO toxic equivalent factor (TEF) values [11]. The TEQ-sum of all congeners of dioxins determined in every breast milk sample was summarized as the total 2,3,7,8-TCDD TEQ concentration. Concentrations of pesticides, PCBs and dioxins in the breast milk were used as a measure of their contamination levels in Japanese mothers.

Around 1 year after childbirth, 10 ml of peripheral blood samples were individually obtained from 45 mothers. These blood samples were employed to measure the lymphocyte subpopulations by indirect immunofluorescence using monoclonal mouse anti-human antibodies against CD3, CD4, CD4+8+, CD8, CD16, CD20 and HLA-DR positive lymphocytes, and their relative population densities were calculated [12].

Spearman rank correlation coefficients were computed to examine effects of the organochlorine compounds on the immune response system and statistical significance was evaluated by Student's *t*-test.

Results and Discussion

Concentrations of organochlorine compounds on whole weight basis (median, min.~max.) were as follows : ß-HCH (11.7 ng/g, 0.7~94.1 ng/g), dieldrin (0.14 ng/g, 0.02~1.04 ng/g), DDT, sum of *p*, *p*'-DDE and *p*, *p*'-DDT (11.2 ng/g, 1.0~61.4 ng/g), HCE (0.13 ng/g, 0.02~1.39 ng/g), chlordane, sum of oxychlordane, *trans*-nonachlor and *cis*-nonachlor (2.69 ng/g, 0.33~14.5 ng/g), PCBs (3.84 ng/g, 1.00~20.9 ng/g), and dioxins, sum of PCDDs, PCDFs and Co-PCBs (0.94 TEQ-pg/g, 0.15~2.92 TEQ-pg/g). Contamination level of dioxins as TEQ concentration was 100 to 10,000 times lower than those of the pesticides and PCBs in Japanese breast milk. This was also considered the same in their contamination levels of the Japanese mothers.

Percentages of lymphocyte subpopulations positive to the monochlonal mouse anti-human antibodies examined (median, min.~max.) were as follows: CD3 (73.3 %, 58.6~81.8 %), CD4 (40.4 %, 27.1~53.0 %), CD4+8+ (0.90 %, 0.30~4.6 %), CD8 (28.1 %, 19.1~49.4 %), CD16 (10.6 %, 2.6~22.3 %), CD20 (9.3 %, 1.3~18.4 %) and HLA-DR (16.0 %, 4.4~27.8 %).

In order to get normal distribution, some data were transformed by a natural logarithm both in concentrations of the organochlorine compounds in the breast milk and in percentages of the lymphocyte subpopulation in the blood of mothers. Then, their scatter plots were given like Figs. 1 to 3.

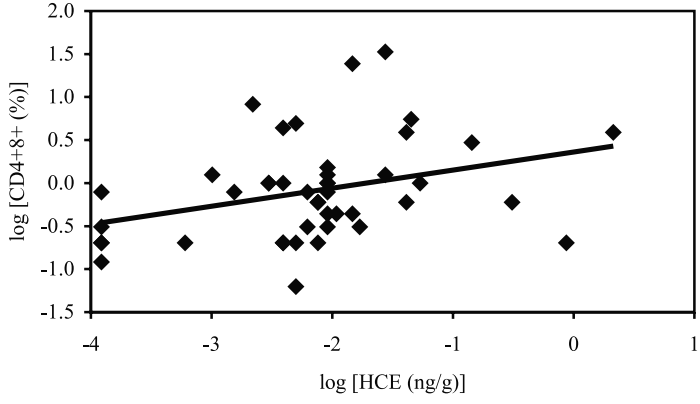

Figure 1. Correlation of percentages of CD4and CD8 both positive (CD4+8+) lymphocyte in the blood with concentrations of HCE in the breast milk of 44 Japanese mothers (rank correlation coefficient = 0.323, p = 0.026)

Significant correlations were observed between CD3 and dieldrin, between CD4 and dieldrin or HCE, between CD4+8+ and HCE, between CD4/CD8 and dieldrin, between CD16 and dieldrin, and

between CD20 and DDT or PCBs. Figs. 1, 2 and 3 show relationships between CD4+8+ and HCE, between CD4/CD8 and dieldrin, and between CD20 and PCBs, respectively.

Accordingly, the organochlorine compounds such as dieldrin, HCE, DDT and PCBs which have already been contaminating Japanese mothers seem to cause some adverse effects on the immune response system not only in Japanese infants [8, 9] but also in Japanese mothers.

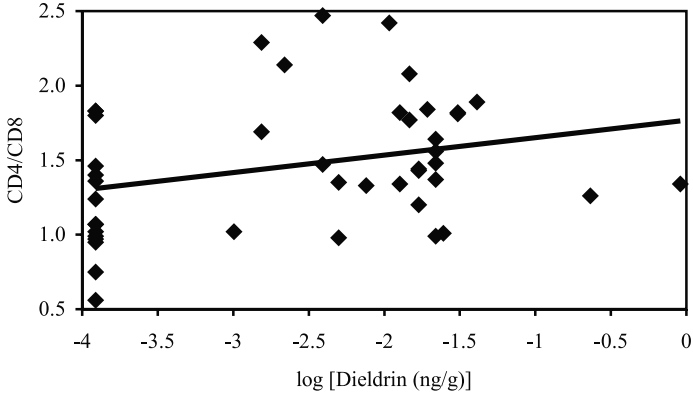

Figure 2. Correlation of ratios of percentages of CD4 positive to CD8 positive lymphocyte in the blood with concentrations of dieldrin in the breast milk of 44 Japanese mothers (rank correlation coefficient = 0.298, p = 0.095)

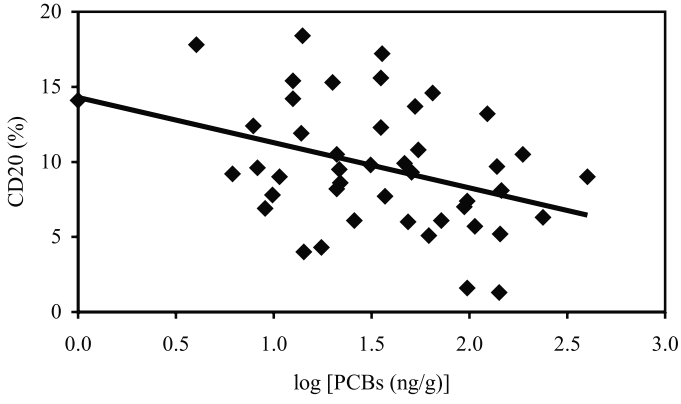

Figure 3. Correlation of percentages of CD20 positive lymphocyte in the blood with concentrations of PCBs in the breast milk of 45 Japanese mothers (rank correlation coefficient = 0.356, p = 0.022)

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