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Interruption of Chronic Chlordane Exposure and Plasma Residue Levels in Occupational Workers

Koji Takamiya

Division of System Biology, Center for Neurobiology and Molecular Immunology, School of Medicine, Chiba University, Chiba, Inohana 1-8-1, Japan

Chlordane, which had been exclusively used for termite control, was completely prohibited in September 1986 in Japan, not only with respect to use but also with respect to import and manufacture.

Some findings were reported previously (Takamiya 1987) regarding the accumulative characteristics of trans-nonachlor and oxychlordane in the plasma of spraymen following chlordane exposure. However, there has been no report on the residual disposition of these chlordane-related compounds in humans. Therefore, the levels of these residual compounds in the plasma of occupational workers were monitored after they ceased use of the insecticide. The present paper describes the time course of the changes in the levels of these lipophilic organochloride compounds after termination of the use of chlordane.

MATERIALS AND METHODS

The subjects were four pest control operators belonging to two firms. One of them had been engaged in the work for about eight years and the others for about six years. The time course of changes in the plasma levels of the components or metabolites of chlordane, i.e. cis, trans-nonachlor, oxychlordane, heptachlor epoxide, as well as those of pp'-DDE as a lipophilic control compound was made from February 1986 (when the termiticide was in use) to October or November 1986 (when occupational use was suspended) and for several months thereafter. Analysis of these compounds in plasma was performed as described previously (Takamiya 1987).

RESULTS AND DISCUSSION

Time course changes of plasma levels of the compounds monitored are shown in Figure 1 for each of the four subjects.

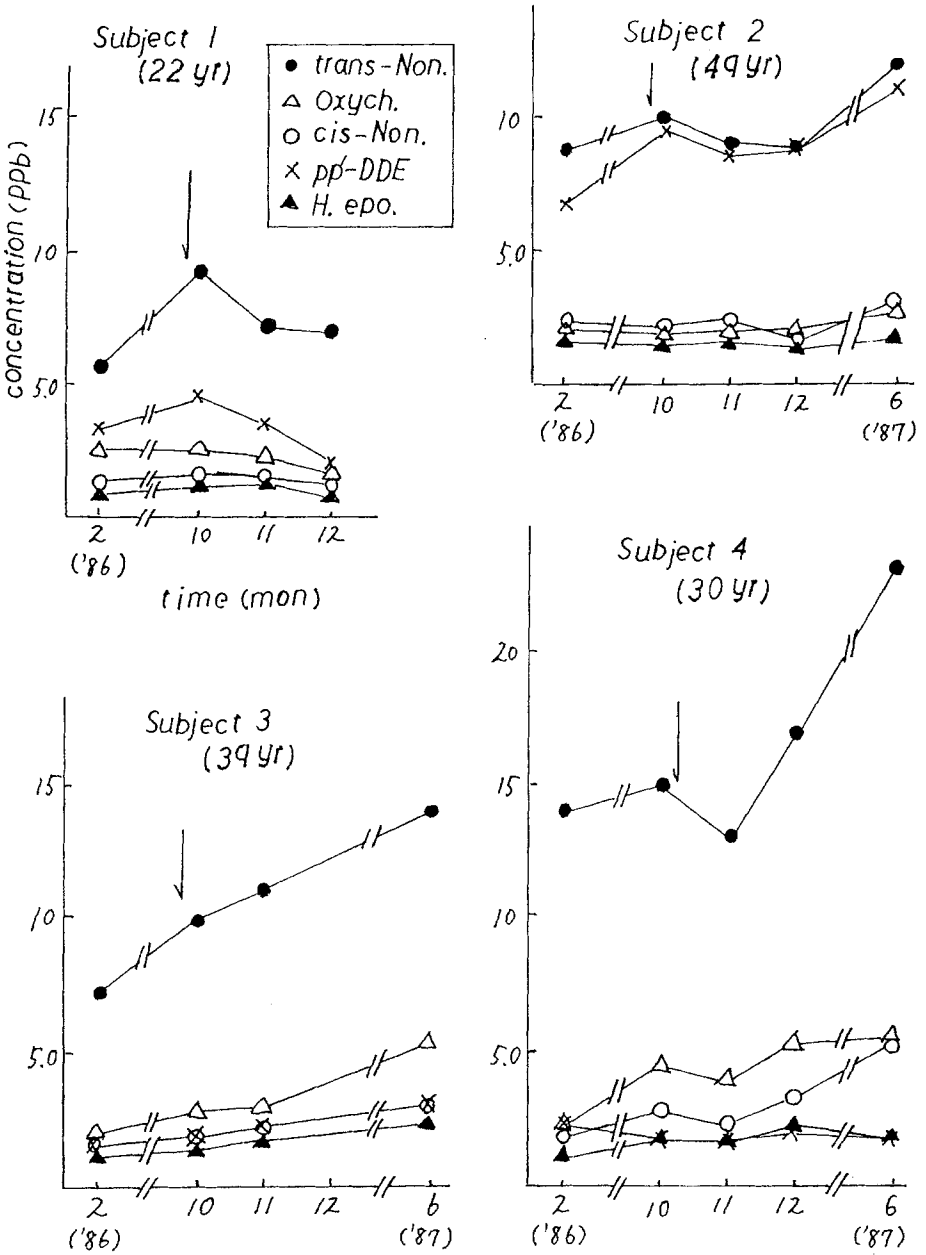

Figure 1. Time course changes of plasma chlordane levels following interruption of its use. The arrows indicate the time of interruption. The age of each subject in Oct. '86 is shown in parenthesis.

In the first subject, the trans-nonachlor residue level was the highest among the compounds derived from chlordane and showed a slow decline roughly in proportion to the changes of the pp'-DDE level in the two months following termination of exposure. The time course changes of the others compounds also showed similar trends.

The second subject, also demonstrated a similar slow decline in the levels of trans-nonachlor and pp'-DDE during the two months from the end of the exposure period. Thereafter, the levels of these two compounds rose until in June 1987 they were again similar to at the end of the exposure period. It is noteworthy that a close parallel relationship between trans-nonachlor and pp'-DDE levels was observed both in this case and in the first subject.

The plasma levels of these chlordane-related compounds and of pp'-DDE increased slightly one month after the last exposure in the third subject. Furthermore, an increase was also observed uniformly eight months after the end of exposure (Subject No. 3).

The fourth subject showed a transient decrease in the level of trans-nonachlor one month after the termination of exposure, and then an increase beyond the level during exposure by eight months after the end of chlordane use. In this subject, a parallel relationship was observed between both the trans and cis-isomers of nonachlor, and also between oxychlordane and heptachlor epoxide, for the changes of these residue levels.

From these results, it is obvious that no chlordane-related compound monitored definitely declined in the plasma except in the first subject despite interruption of chlordane use for over eight months. Quantitatively, the following order of concentrations was seen both before and after the use of chlordane for the four chlordane-related compounds: trans-Nonachlor > Oxychlordane ≧ cis-Nonachlor > Heptachlor epoxide. Trans-nonachlor is scarcely metabolized in the human liver in vitro (Tashiro and Matsumura 1978) and probably the same is true of its cis isomer, because the time course changes of both isomers corresponded in two subjects (Nos. 3 and 4). On the other hand, the time course changes of oxychlordane residue were different from the pattern predicted by Tashiro and Matsumura (1978) and the previous report of Takamiya (1987). The oxychlordane residue levels were almost the same as those of cis-nonachlor and heptachlor epoxide in all subjects, and the time course changes of oxychlordane corresponded with heptachlor epoxide in all subjects. In addi-

tion, the variations in level of the metabolite were small throughout the monitoring period in all subjects. These facts suggest that oxychlordane, as well as heptachlor epoxide, may be a stable and terminal metabolite of chlordane in humans. A study of Morgan and Cifford (1971) on the dynamics of pp'-DDT in human volunteers showed that pp'-DDE (the terminal metabolite of pp'-DDT) did not show a significant decrease in the serum level during eight months after dosing stopped, despite a prompt decline in the pp'-DDT level. The low level of oxychlordane observed in all the subjects suggests that synthesis of this metabolite in vivo from both cis and trans-chlordane (Tashiro and Matsumura 1978), which are major components of technical chlordane, may be extremely low. The case of heptachlor epoxide may be also similar, because the content of heptachlor in technical chlordane is about 7% which is almost the same as that of trans-nonachlor (Sovocool et al. 1979).

In this survey, a nearly parallel relationship between the two isomers of nonachlor and pp'-DDE was demonstrated which was accompanied by some fluctuations. These fluctuations in the time course changes are suggested to be mainly due to the influence of plasma lipids. This was also suggested regarding lipophilic PBBs (Eyster and Humphrey 1983) and was demonstrated for PCBs in humans (Brown and Lawton 1984).

As regards the plasma pp'-DDE level, the time course changes in the fourth subject were different from the other subjects regarding the correlation between isomers of nonachlor and pp'-DDE, and remained in a narrow range slightly over the detection limit (approx. 0.5 ppb) of the compound during the monitoring period. It was suggested that the amount of daily intake in the diet might have affected the levels in the subjects. According to the survey by Matsumoto et al. (1987) concerning the average daily intake of lipophilic xenobiotics, the intakes of pp'-DDE and trans-nonachlor were 1.7 μg and 0.56 μg, respectively, in 1985 in urban districts of Japan. Consequently, it is considered that the dietary intake of chlordane-related compounds would have had no significant effect on the plasma levels of the subjects.

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