Investigation of Indoor Air Pollution by Chlorpyrifos: Determination of Chlorpyrifos in Indoor Air and 3,5,6-Trichloro-2-pyridinol in Residents' Urine as an Exposure Index

Hong DAI¹, Fumiyuki ASAKAWA², Shigeru SUNA¹, Tomohiro HIRAO¹, Tomonori KARITA¹,
Ichiro FUKUNAGA¹ and Fumihiko JITSUNARI¹

¹Department of Hygiene and Public Health, School of Medicine, Kagawa Medical University, Kagawa, Japan

²Human Environmental Science Research Laboratory, College of Liberal Arts and Science for International Studies, Kurashiki University of Science and the Arts, Okayama, Japan

Abstract

Objects: We carried out an investigation to clarify the real state of indoor air pollution by chlorpyrifos (termiticide) and exposure to chlorpyrifos of residents by measuring its urinary metabolite 3,5,6-trichloro-2-pyridinol (TCP) as an exposure index, such as biological monitoring.

Methods: The investigation was conducted in 43 individual houses with termiticide application (whether the termiticide was chlorpyrifos is uncertain) and 3 control houses without any termiticide application in Kagawa, Japan. Urine samples were collected from 46 healthy adult residents of the aforementioned houses.

Results: Chlorpyrifos in indoor air in the control houses was not detected ($ND < 1 \text{ ng/m}^3$, $n=3$), while 41 of 43 houses with termiticide application showed $1\text{--}350 \text{ ng/m}^3$. Although the chlorpyrifos concentrations in these 41 houses did not exceed the indoor air quality guideline of 1000 ng/m^3 , but 3 houses were higher than the guideline 100 ng/m^3 for children in Japan. Urinary TCP concentrations of $0.1\text{--}7.8 \text{ ng/mg-creatinine}$ were detected in 41 residents from the 41 houses where chlorpyrifos had been detected. The chlorpyrifos concentration and the urinary TCP revealed a positive correlation ($r=0.5468$, $p<0.01$, $n=41$).

Conclusions: The immediate health hazard from air born chlorpyrifos in the examined houses was negligible, but the findings suggest that it is necessary to monitor chemicals which may contaminate indoor air and to assess the risk of prolonged exposure to such chemicals. The measuring of urinary metabolite TCP of chlorpyrifos via biological monitoring would be useful, allowing comprehensive evaluation of the exposure to chlorpyrifos in indoor air.

Key words: indoor air pollution, termite control, chlorpyrifos, urinary 3,5,6-trichloro-2-pyridinol, biological monitoring

Introduction

In Europe and the U.S.A., many residents who live in buildings complain of symptoms such as headache, giddiness, irritation of the eyes, etc. This has occurred frequently since the

1980s, and the hazardous health effects are termed "Sick Building Syndrome (SBS)". It may be explained by increases in indoor air contaminants due to reduced ventilation air volume as a result of measures to save energy consumption by air conditioning in buildings (1–3). As the latest Japanese houses are made airtight in order to raise energy efficiency, the use of chemical substances in homes, such as the use of new building materials containing formaldehyde (HCHO), volatile organic compounds (VOCs) etc., and the use of termiticides and insecticides, increases the risk of indoor air pollution. Some residents who live in such houses have begun to complain of similar symptom, and SBS has become known as "Sick House Syndrome" in Japan (4, 5).

Received May 6 2003/Accepted Jul. 28 2003

Reprint requests to: Hong DAI

Department of Hygiene and Public Health, School of Medicine, Kagawa Medical University, 1750-1 Ikenobe, Miki-cho, Kita-gun, Kagawa 761-0893, Japan

TEL: +81(87)891-2133, FAX: +81(87)891-2134

E-mail: dai@kms.ac.jp

Investigations of indoor air pollution by HCHO and VOCs are frequently reported in Japan (6–10). However, there has been almost no investigation of indoor air pollution by chlorpyrifos (termiticide), although investigations on occupational exposures to chlorpyrifos and its urinary metabolite (11) 3,5,6-trichloro-2-pyridinol (TCP) are reported occasionally by ourselves (12, 13) in Japan.

Chlorpyrifos (*O,O*-diethyl-*O*-[3,5,6-trichloro-2-pyridinol] Phosphorothioate) is a broad-spectrum organophosphorus insecticide most widely used for pest and termite control in residential and commercial buildings in Japan. The application of chlorpyrifos as a termiticide increased following the removal of chlordane from the Japanese market in 1986. Following termiticide application such as chlorpyrifos, many residents complain of headache, giddiness, eye irritation, etc., suggesting that chlorpyrifos is becoming an important chemical pollutant of indoor air in Japan.

The U.S. Environmental Protection Agency (EPA) recently conducted a further "Human Health Risk Assessment" for chlorpyrifos as an active ingredient organophosphate insecticide, and the risk estimation was reported to be much higher than before (14).

Faced with this reality, the Ministry of Health, Labour and Welfare of Japan established indoor air quality guidelines (1000 ng/m³, 100 ng/m³ for children) of chlorpyrifos in 2000 (15).

Accordingly, we carried out an investigation to clarify the real state of indoor air pollution by chlorpyrifos and exposure to chlorpyrifos of residents. In this study, we determined the concentration of chlorpyrifos in residential indoor air and metabolite TCP of chlorpyrifos in residents' urine as an exposure index, such as biological monitoring. This approach by biological monitoring is expected to allow comprehensive evaluation of the exposure to chlorpyrifos by measuring resident's urinary metabolite of chlorpyrifos (16).

Materials and Methods

1. Subjects and procedures of sampling

The investigation was conducted in 43 individual houses with termiticide application (whether the termiticide was chlorpyrifos is uncertain) and 3 control houses without any termiticide application in Kagawa, Japan, in October 2000. Samples of indoor air were collected at a height of 1.5–2.0 m above the floor (the "breathing zone" level) at the center of the living room in each houses for one month continuously (30 days) by passive samplers which we had already prepared and reported (17). The samplers were wrapped in tight fitting aluminum bags, put in a cooling box at once after sampling and delivered to the laboratory.

Details of the passive sampler are as follows: Chlorpyrifos in indoor air is collected with a porous PTFE (poly tetra fluoro ethylene) tube (the maximum size of aperture is 0.2 µm, length 45 mm, inner diameter 10 mm and thickness 1 mm) filled with an adsorbent resins of 0.75 g of the Supelpack^{TM-2} (SUPELCO PA, USA). The sampling rate of the prepared sampler was 0.0859 m³/day. This sampler follows the Fick's first principle of diffusion and collects the gaseous chlorpyrifos.

The urine samples were collected on the 31st morning from one healthy adult resident of each of the aforementioned houses, totaling of 46 residents. On the same day, all urine samples were retrieved from participants, immediately put in a cooling box, and stored at -20°C until analysis.

The following factors were surveyed by questionnaire: construction method, time since construction, time since the termiticide application, and occurrences of symptoms after application. Besides, mean ventilation time and time spent at home, etc. during the sampling period were surveyed by questionnaire.

2. Sample treatment and analysis

2.1. Chlorpyrifos in indoor air

The measurement of chlorpyrifos was based on the previously reported method (18), as follows: the desorption of chlorpyrifos from each passive sampler was carried out with 3 ml of toluene by gently shaking for 1 hour. Next the eluate was analyzed by gas chromatograph-mass spectrometer/selected ion monitoring (GC-MS/SIM, Shimadzu GCMS-QP2000GF Kyoto, Japan). Where necessary, the eluate was condensed to near dryness under a gas current of nitrogen in a Kuderna-Danish evaporative concentrator apparatus with a cooling pump.

The analysis conditions of GC-MS/SIM were as follows: column, DB-5MS (J & W CA, USA) 30 m×0.32 mm i.d., film thickness 0.25 µm; carrier gas He at 10 ml/min; oven, 180°C (2 min) to 260°C at 10°C/min and 260°C (8 min); injection, splitless, 260°C. A strong peak was found at ion mass number (*m/z*) 314 from the mass spectrum's peak retention time of 6.17 minutes in the total ion chromatogram obtained by GC-MS analysis chlorpyrifos as the standard.

2.2. Urinary TCP

The urine samples were analyzed for the presence of the urinary TCP from chlorpyrifos exposure in indoor air. The procedures (18) were as follows: One ml of concentrated sulfuric acid was added to 5 ml of urine in a test tube (20 mm×200 mm). The unsealed tube was heated at 100°C for 1 hour. After cooling, 10 ml of distilled water was added to the residue. Isolation and cleaning of samples were carried out by solid phase extraction. The acid hydrolyzed urine samples were purified by a pretreated Sep-Pak C₁₈ cartridge (Waters MA, USA). The pretreatment involved washing with 5 ml of chloroform, then 5 ml of methanol, and finally two volumes of distilled water through the cartridge. Next, the cartridge was washed with 5 ml of distilled water 4 times to rinse the sample tube. Finally, the cartridge was eluted with 5 ml of chloroform, and the urinary TCP was retrieved in a receiving bottle equipped with a glass funnel lined with a special analysis filter paper (Advantec Tokyo, Japan No. 2s), which allows the elimination of water from the eluate. The eluate was evaporated to near dryness under a gas current of nitrogen in a Kuderna-Danish evaporative concentrator apparatus. One hundred forty µl of benzene was added to the residue of samples, 10 µl of *N,O*-Bis (trimethylsilyl) acetamide (BSA) was added, and the solution was analyzed by GC-MS/SIM within 1 hour. The standard solution of TCP was processed similarly.

The analysis conditions of GC-MS/SIM were as follows:

column, DB-5MS (J & W) 30 m×0.32 mm i.d., film thickness 0.25 µm; carrier gas He at 10 ml/min; oven, 120°C (2 min) to 260°C at 16°C/min and 260°C (4 min); injection, splitless, 200°C. A strong peak was found at m/z 256 from the mass spectrum's highest peak retention time of 5.01 minutes in the total ion chromatogram obtained by GC-MS analysis with the standard TCP.

The creatinine level in the urine was measured with an automatic analyzer (Hitachi 7050 Tokyo, Japan), based on the Jaffe's reaction.

3. Reagents and standard solutions

The chlorpyrifos standard used in this experiment was obtained from Wako Pure Chemical (Osaka, Japan). The TCP standard was supplied by Dow Chemical (MI, USA). Other common reagents (toluene, benzene, concentrated sulfuric acid, chloroform, methanol, acetone, etc.) were purchased from Wako Pure Chemical. The standard solutions of chlorpyrifos were dissolved with toluene. The standard solution of TCP was prepared by a procedure similar to that for urine samples.

Table 1 Outlines of the examined houses and measured data of chlorpyrifos concentrations in indoor air

House No.	Construction method	Time since construction month	Time since application month	Mean ventilation time hour/day	Chlorpyrifos ng/m ³
control-1	conventional	18	no	10.0	ND
control-2	conventional	12	no	10.0	ND
control-3	conventional	13	no	13.0	ND
1	conventional	244	3	0.5	350
2	conventional	88	4	4.5	58
3	conventional	244	5	11.0	21
4	conventional	244	5	11.0	39
5	conventional	380	6	11.8	28
6	conventional	180	6	4.5	33
7	conventional	52	9	6.5	32
8	conventional	344	9	6.0	130
9	conventional	244	10	15.0	1
10	prefab	10	10	5.0	5
11	conventional	220	10	7.0	17
12	conventional	11	11	4.0	ND
13	conventional	280	11	6.0	1
14	conventional	11	11	6.0	2
15	conventional	11	11	8.5	3
16	conventional	11	11	15.0	4
17	conventional	11	11	5.7	9
18	conventional	154	14	23.0	43
19	conventional	185	15	24.0	10
20	prefab	16	16	23.0	ND
21	conventional	244	16	2.8	1
22	prefab	16	16	3.0	1
23	conventional	64	16	1.5	1
24	conventional	16	16	9.5	2
25	conventional	244	16	8.0	2
26	conventional	214	16	9.0	8
27	conventional	208	16	3.5	9
28	conventional	724	16	24.0	10
29	conventional	16	16	20.0	11
30	prefab	16	16	10.5	21
31	conventional	244	16	8.5	64
32	conventional	400	16	6.5	151
33	conventional	292	17	23.5	6
34	conventional	17	17	13.5	9
35	conventional	364	17	4.0	16
36	prefab	18	18	6.5	13
37	conventional	138	19	24.0	16
38	conventional	280	20	16.0	1
39	conventional	280	20	4.5	13
40	prefab	21	21	4.5	48
41	conventional	220	22	5.0	1
42	conventional	76	22	4.0	2
43	conventional	22	22	6.0	25

ND<1 ng/m³, conventional: house of the conventional method in Japan; prefab: prefabricated house.

4. The statistical treatment of chlorpyrifos and TCP' data

Because the distribution of chlorpyrifos and TCP' data showed a logarithmic normal distribution, geometric mean value was used. The relationship between the pollution level of chlorpyrifos in indoor air and the concentrations of TCP was assessed by logarithm value. They are not introduced to calculate the geometric mean concentration, while data of chlorpyrifos and TCP were lower than 1 ng/m³ and 0.1 ng/ml respectively (it was written to ND).

Results

Outlines of the examined houses and measured data of chlorpyrifos concentrations in indoor air are shown in Table 1. During sampling, temperature and relative humidity in the houses ranged from 21.1 to 26.4°C and 52 to 72%, respectively.

Chlorpyrifos was not detected in indoor air in the control houses (ND<1 ng/m³, n=3). Concentrations of chlorpyrifos in indoor air ranging from 1 to 350 ng/m³ were detected in 41 of the 43 houses with termiticide application (95% detection rate), and the geometric mean level of chlorpyrifos was approximately 10 ng/m³ in the 41 houses. This shows that termite control by chlorpyrifos is frequent. Although the concentrations of chlorpyrifos in indoor air in these 41 houses did not exceed the indoor air quality guideline of 1000 ng/m³, but it was found that three houses (house Nos. 1, 8, 32) were higher than the guideline of 100 ng/m³ for children, in Japan (15). They were 350, 130 and 151 ng/m³ respectively. The highest level of 350 ng/m³ was measured just 3 months after the termiticide application.

Moreover, the authors have examined the relationship between time course and concentrations of chlorpyrifos in indoor air after the termiticide application. The geometric mean concentration of chlorpyrifos in houses within 6 months after application was approximately 50 ng/m³, 7–12 months after application was approximately 6 ng/m³, 13–18 months after application was 8 ng/m³ and over 19 months after the application was approximately 6 ng/m³. Thus, there is a general tendency for the concentration of chlorpyrifos in indoor air to

rise in houses within 6 months after application.

The relationship between the time course (x) and the concentrations of chlorpyrifos in indoor air (y) after application is shown in Figure 1. The chlorpyrifos level in indoor air tended to lower gradually with time after application. The exponential function formula $y=43.016e^{-0.108x}$ (n=41) was obtained, giving a half-life of chlorpyrifos concentration in indoor air of 6 months.

Table 2 shows the concentration of metabolite TCP of chlorpyrifos in urine of residents from the examined houses. All measured data of urinary TCP were corrected with the respective urinary creatinine concentration. The TCP levels were 0.1–7.8 ng/mg-creatinine in 41 of the 43 residents from examined houses with termiticide application and the geometric mean concentration was 1.4 ng/mg-creatinine (95% detection rate). The urinary TCP of 3 control residents and 2 residents from 2 houses (house Nos. 12, 20) whose chlorpyrifos in indoor air was not detected (ND<0.1 ng/ml, as urinary TCP concentration without the correction with urinary creatinine).

The highest concentration of urinary TCP was 7.8 ng/mg-creatinine in the resident who came from the house with the highest level of chlorpyrifos in indoor air (350 ng/m³, house Nos. 1). Similarly, in the houses (house Nos. 8, 32) where levels of chlorpyrifos in indoor air were 130 and 151 ng/m³ respectively, higher concentrations of urinary TCP in the residents also were found (6.0, 5.3 ng/mg-creatinine, respectively).

The relationship between the concentration of chlorpyrifos in indoor air and the concentration of metabolite TCP in residents' urine is shown in Figure 2. Although it must be considered that many examined houses were low levels of chlorpyrifos in indoor air, a positive correlation is seen ($r=0.5468$, $p<0.01$, $n=41$).

Moreover, the symptoms of sick house syndrome after the termiticide application were surveyed by a simple questionnaire. But only 3 residents (house Nos. 2, 7, 42) of 43 residents with a urine sample were collected who jotted down some symptoms, such as the headache, eye irritation, dry and irritation of throat, skin irritation, and fatigue, etc.

Fig. 1 Relationship between chlorpyrifos concentration in indoor air and the time since application. The chlorpyrifos level in indoor air tended to lower gradually with time after application.

Table 2 TCP concentration in urine of residents from the examined houses and outlines of the residents

House No.	Sex	Age year	Time of spent at home hour/day	TCP ng/mg-creatinine
control-1	female	29	19	ND
control-2	female	66	15	ND
control-3	male	31	14	ND
1	male	40	14	7.8
2	female	33	16	1.0
3	female	49	16	4.2
4	male	26	14	3.4
5	female	30	11	1.6
6	female	53	14	2.7
7	female	24	14	4.5
8	male	28	7	6.0
9	female	39	20	0.9
10	male	30	14	1.2
11	female	47	15	0.5
12	female	31	22	ND
13	female	45	24	0.9
14	male	35	10	3.3
15	female	47	14	0.8
16	female	51	10	0.6
17	female	34	10	0.6
18	male	21	18	2.3
19	female	58	24	3.7
20	female	26	22	ND
21	female	50	20	2.1
22	female	31	13	0.3
23	female	44	18	1.0
24	female	39	18	0.9
25	female	49	14	1.1
26	male	22	12	2.3
27	female	40	24	2.4
28	female	46	13	1.3
29	male	39	11	0.5
30	male	33	14	1.5
31	male	26	12	2.9
32	male	49	12	5.3
33	female	47	14	3.2
34	female	29	22	3.0
35	male	48	10	0.4
36	female	28	19	1.4
37	male	48	13	0.8
38	male	38	10	0.1
39	male	61	12	1.2
40	female	39	15	4.0
41	female	47	13	0.3
42	male	32	12	3.9
43	female	38	12	0.5

ND<0.1 ng/ml (urinary TCP concentration without the correction with urinary creatinine).

Discussion

Chlorpyrifos is a broad-spectrum organophosphorus insecticide. It affects the nervous system by reversibly inhibiting the activity of cholinesterase (ChE), an enzyme necessary for the proper functioning of the nervous system. Inhibition of ChE is the most sensitive effect in animals and in humans. Excessive exposure to chlorpyrifos can produce typical symptoms of acute organophosphorus poisoning (19).

In Japan, chlorpyrifos has been widely used to control

termite in residential and commercial buildings since the prohibition of chlordane in 1986. Thus, after termiticide application such as chlorpyrifos, many residents living in the treated houses complain of headache, giddiness, eye irritation, etc. Chlorpyrifos is becoming an important chemical pollutant of the indoor air in Japan.

Meanwhile, the US-EPA recently conducted a further "Human Health Risk Assessment" for chlorpyrifos as an active ingredient organophosphate insecticide, in which the risk estimation was reported to be much higher than before (14).

Fig. 2 Relationship between chlorpyrifos concentration in indoor air and urinary TCP level. The x-axis values and the y-axis values were used with logarithmic distribution. A positive correlation has been accepted ($r=0.5468$, $p<0.01$, $n=41$).

The Ministry of Health, Labour and Welfare of Japan established indoor air quality guideline for chlorpyrifos in 2000 (15). The guideline values for indoor air concentration imply that, given the current available scientific knowledge, no adverse health effects would be caused in humans by lifetime exposure to the chemical at any level less than the value. These values may be revised in the future, as necessary, depending on further available knowledge and/or progress in international assessment works based on such scientific knowledge. The guideline in Japan specifies a maximum concentration of chlorpyrifos in indoor air of 1000 ng/m³. However, because chlorpyrifos may cause changes to the brain's morphological structure and deficit of cognitive function, resulting in delayed behavioral effects in newborn infants, from the results of some animal tests (20, 21), a level of 100 ng/m³ was applied for children in Japan.

Chlorpyrifos levels in indoor air of 1–350 ng/m³ were detected in 41 of the 43 houses in this study. The geometric mean level of chlorpyrifos was approximately 10 ng/m³. Although these results could not be compared with other studies in the scientific literature as strictly as the guideline because of different measuring methods, the concentration of chlorpyrifos in indoor air was within the guideline for children in all except 3 residences; the others were considerably less than the guideline as a 100 ng/m³. However the concentrations of chlorpyrifos in these 3 houses were 350, 151, 130 ng/m³ respectively, which may have some effects on children.

Hanai et al. (22) observed that the chlorpyrifos concentration in living room air was 100–120 ng/m³ in the early stages after application for termite control. Katsura et al. (23) reported 258 ng/m³ of chlorpyrifos concentration in living room air with 2 months after application.

In our study, the house with the highest concentration of chlorpyrifos in indoor air (350 ng/m³) was examined just three months after application and the geometric mean concentration of chlorpyrifos in the examined houses within 6 months after application was approximately 50 ng/m³. Accordingly, we examined the relationship between the concentration of chlorpyrifos in indoor air and time after termiticide application and found an inverse correlation. As the time since application

increases, the pollution level of chlorpyrifos in indoor air gradually lowers. The result suggests that a house in the early stages after chlorpyrifos application may have a remarkably high pollution level of chlorpyrifos in indoor air. The half-life of chlorpyrifos concentrations in indoor air was calculated to be 6 months.

We also determined the concentration of metabolite TCP (11) of chlorpyrifos in residents' urine as an exposure index. Such an approach by biological monitoring is expected to allow comprehensive evaluation of the exposure to chlorpyrifos. In this study, the TCP levels were 0.1–7.8 ng/mg-creatinine in 41 of 43 residents from object houses with termiticide application and the geometric mean concentration was 1.4 ng/mg-creatinine. However no urinary TCP was detected in 3 control residents and 2 residents from 2 houses where chlorpyrifos in indoor air was undetectable.

Hill et al. (24) measured TCP in 900 adults (20–59 years old) selected from a broad spectrum of the U.S. population and reported that the mean urinary TCP concentration was 3.1 ng/mg-creatinine (in 82% of adults), and they considered that this high frequency of exposure is consistent with the reported frequent use of chlorpyrifos as a common household insecticide, particularly as a replacement for the termiticide chlordane. Furthermore, Buckley et al. (25) reported that urinary TCP was correlated with chlorpyrifos concentration in indoor air and dust.

Accordingly, we examined the relationship between the concentration of chlorpyrifos in indoor air and the concentration of metabolite TCP in residents' urine. Although it must be considered that many examined houses were low levels of chlorpyrifos in indoor air, a positive correlation was found ($r=0.5468$, $p<0.01$, $n=41$), implying that the concentration of urinary TCP would change depending on the pollution level of chlorpyrifos in indoor air.

Anyway, for the urinary TCP to have been detectable in 41 of the 43 residents in houses where termiticide was applied, it could be said that many residents were exposed to a low concentration of chlorpyrifos via indoor air of houses indicating that a quantitative relationship exists between exposure level of chlorpyrifos in indoor air and concentration of urinary TCP.

In this study, we applied biological monitoring approach in which urinary TCP was used as an exposure index to study non-occupational exposure to chlorpyrifos among residents. Measurement of urinary TCP would be useful for directly checking whether the residents are exposed to chlorpyrifos and it is absorbed, and is expected to allow comprehensive evaluation of the exposure to chlorpyrifos via indoor air.

Consequently, the authors think that it is important to further clarify the quantitative relationship between chlorpyrifos exposure and urinary TCP.

References

- (1) WHO Regional Office for Europe. Indoor Air Pollutants: Exposure and Health Effects, Report on a WHO Meeting. 1982.
- (2) Sterling E, Sterling T, McIntyer D. New health hazards in sealed buildings. *AIA. J. April.* 1983; 72: 64–67.
- (3) Godish T. Sick Buildings Definition, Diagnosis and Mitigation. Florida: CRC Press. Inc., Boca Raton, Florida, USA. 1996.
- (4) Matsumura T. The indoor air contamination by chemicals: VOC and formaldehyde. *Jpn. J. Soc. Atmos. Environ.* 1996; 31: A154–A164. (in Japanese)
- (5) Ikeda K. Sick house syndrome. *Seikatsu to Kankyo.* 1998; 43: 24–33. (in Japanese)
- (6) Matsumura T, Kametani K, Muramatsu S. Studies on indoor air pollution (III): The concentration of formaldehyde in indoor air. *Jpn. J. Public Health.* 1983; 30: 303–308. (in Japanese)
- (7) Kumagai K, Ikeda K, Hori M, Matsumura T, Nozaki A, Kimura H, Iikura K, Yoshizawa S. Field study on volatile organic compounds in residences. *Indoor Environ.* 1999; 2: 130–133. (in Japanese)
- (8) Dai H, Asakawa F, Suna S, You S, Hirao T, Tadokoro S, Kitamado T, Jitsunari F. The VOCs concentration in the living environment and individual exposure in university. *J. Shikoku Public Health Soc.* 2000; 45: 75–78. (in Japanese)
- (9) Hara K, Ito A, Harada K, Miyakita T, Wei CN, Ueda A. Time series of indoor concentrations of formaldehyde and volatile organic compounds in a newly-built brick house. *Indoor Environ.* 2000; 3: 45–50. (in Japanese)
- (10) Asakawa F, Dai H, Suna S, Manabe Y, Jitsunari F. Change of formaldehyde, volatile organic compounds concentrations in indoor air of new school building/exposure levels to these compounds, and health conditions of the staff. *Indoor Environ.* 2001; 4: 188–191. (in Japanese)
- (11) Nolan RJ, Rick DL, Freshour NL, Saunders JH. Chlorpyrifos: Pharmacokinetics in human volunteers. *Toxicol. Appl. Pharmacol.* 1984; 73: 8–15.
- (12) Asakawa F, Jitsunari F, Suna S, Shiraishi H, Manabe Y, Gotoh A, Nakajima T. The actual state of occupational exposure to chlorpyrifos of termite control workers. *Jpn. J. Hygiene.* 1989; 44: 921–928. (in Japanese)
- (13) Jitsunari F, Asakawa F, Nakajima T, Shimada J. Determination of 3,5,6-trichloro-2-pyridinol levels in the urine of termite control workers using chlorpyrifos. *Acta Med. Okayama.* 1989; 43: 299–306.
- (14) USA Environmental Protection Agency, Office of Pesticide Programs, Health Effects Division (7509C). Human Health Risk Assessment: Chlorpyrifos. 2000.
- (15) Ministry of Health, Labour and Welfare of Japan. Environmental Health Committee on Sick House Syndrome: Indoor Air Pollution Progress Report No. 2, Summary on the Discussions at the 4 and 5 Meetings. 2000.
- (16) Asakawa F, Jitsunari F, Dai H, Kitamado T. Monitoring of indoor air contamination by chemicals: Chlorpyrifos, permethrin, HCHO, VOCs. *Bull. Kurashiki Univ. Sci. Arts.* 2002; 7: 45–55. (in Japanese)
- (17) Asakawa F, Jitsunari F, Dai H, SUNA S, Hirao T, Kitamado T, Fukunaga I. Research on monitoring of indoor air contamination by chemicals: Preparation and trial use of passive sampler for measuring chlorpyrifos, permethrin in ambient air. *District Environ. Health Welfare Res.* 2000; 4: 10–13. (in Japanese)
- (18) Asakawa F, Jitsunari F, SUNA S, Hirao T, Dai H. Research on monitoring of indoor air contamination by chemicals: Measuring methods of chlorpyrifos, permethrin in air and their urinary metabolite. *District Environ. Health Welfare Res.* 1999; 3: 22–25. (in Japanese)
- (19) WHO. Environmental Health Criteria 63, Organophosphorus Insecticides; a General Introduction. Geneva. WHO. 1986.
- (20) Johnson DE, Seidler FJ, Slotkin TA. Early biochemical detection of delayed neurotoxicity resulting from developmental exposure to chlorpyrifos. *Brain. Res. Bull.* 1998; 45: 143–147.
- (21) David AJ, Ryman VN, Rondell AB, Gabrielle LM. Cognitive function and cholinergic neurochemistry in weanling rats exposed to chlorpyrifos. *Toxicol. Appl. Pharmacol.* 2001; 174: 89–98.
- (22) Hanai Y, Chen YH, Naganishi J. Indoor air pollution from construction materials. *Bull. Institute Environ. Sci. Tech. Yokohama Univ.* 1996; 22: 1–10. (in Japanese)
- (23) Katsura E, Ogawa H, Kojima H, Fukushima A. Indoor air pollution by chlorpyrifos and s-421 after application for termite control. *Jpn. J. Toxicol. Environ. Health.* 1996; 42: 354–359. (in Japanese)
- (24) Hill RH, Head SL, Baker S, Gregg M, Shealy DB, Bailey SL, Williams CC, Sampson EJ, Needham LL. Pesticide residues in urine of adults living in the united states: Reference range concentrations. *Environ. Res.* 1995; 71: 99–108.
- (25) Buckley TJ, Liddle J, Ashley DL, Paschal DC, Burse VW, Needham LL, Akland G. Environmental and biomarker measurements in nine homes in the lower Rio Grande Valley: Multimedia results for pesticides, Metals, PAHs and VOCs. *Environ. Int.* 1997; 23: 705–732.

Conclusions

In this study, the immediate health hazard due to chlorpyrifos in house air was negligible. However, the findings suggest that it is necessary to monitor chemicals such as chlorpyrifos contaminating indoor air and to assess the risk of prolonged exposure to these chemicals. The measuring of urinary metabolite TCP of chlorpyrifos via biological monitoring would be useful, allowing comprehensive evaluation of the exposure to chlorpyrifos in indoor air.