

Effect of Home Environment Control on Children with Atopic or Non-atopic Asthma

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ABSTRACT

Background: Although allergen avoidance is known to be important for treating atopic diseases, there is a very limited amount of time for clinical education of patients on this topic.

Methods: We compared the effect of the thorough home visit counseling (>60 minutes per visit) for avoiding house dust mites (HDMs) with that of regular guidance in our clinics (10 minutes per patient). We enrolled 36 children with asthma (7 years of age or younger; mean, 3.8) in this study under an informed consent. After enrolling the 24 patients for the home visit, 12 families were enrolled as controls for the regular clinical guidance. Between June 1995 and June 1996, we visited the homes of 24 children with asthma enrolled in this study every month and performed a thorough HDM-avoidance counseling of more than 60 minutes (home visit counsel) at each visit. We compared the effects of this counseling with those of the regular clinical guidance given (10 minutes per patient) to the remaining 12 children with asthma. We also evaluated the effect of home visit counseling on children of two subgroups, *i.e.*, an atopic (with positive IgE antibody against HDM) and a non-atopic (without detectable IgE antibodies against 8 common allergens) subgroup.

Results: Home visit counseling markedly reduced the frequencies of asthma attacks ($p < 0.000001$), the required theophylline dosages ($p < 0.0005$), and the levels of HDM allergens ($p < 0.0005$) in the atopic subgroups, whereas the effect of regular counseling on these 3 items was relatively less ($p < 0.05$ or not significant). Surprisingly, home visit counseling also markedly reduced the asthma attacks ($p < 0.00001$) and theophylline dosages ($p < 0.00001$) of children with non-atopic asthma.

Conclusions: These results suggest that thorough allergen avoidance counseling is effective for children with non-atopic asthma as well as atopic asthma.

KEY WORDS

asthma, Der f 1, Der p 1, environment control, house dust mites

INTRODUCTION

The major risk factors for asthma attacks have been reported to be indoor allergens such as house dust mites (HDMs), virus infections, and passive smoking.¹⁻³ Among them, removal of HDM allergens is the most important strategy for treating asthma patients with specific IgE antibody against HDM.^{4,5} Indeed, some of the methods considered for avoiding HDM have been reported to be effective in preventing asthma exacerbations.⁶⁻⁹ On the other hand, Gotzsche PC *et al.* have reported that the effectiveness of environmental controls for HDM is not really

definitive when the previous reports were reevaluated with meta-analysis.¹⁰ In the discussion, these authors claimed that methods used in some reports did not adequately reduce levels of mite antigen, and also claimed a lack of compliance. According to the recent investigation done by the Ministry of Health and Welfare, the incidences of asthma and atopic individuals are particularly increasing in early childhood in Japan. Thus, examination of whether avoidance of HDM with high compliance is really effective in preventing children with asthma from exacerbation has become an important and urgent issue.^{11,12} Within the present Japanese medical system, however, there

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Received 14 June 2005. Accepted for publication 13 October 2005.

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Table 1 Initial data*

Group †	A	B	C	D
Subjects	11	13	6	6
Gender (male/female)	8/3	8/5	3/3	4/2
Age, yr	3.9 (2–7)	3.5 (2–7)	4.2 (2–7)	3.7 (2–5)
Body weight, kg	16.5 (13–22)	15.8 (12–22)	17.2 (11–24)	16.0 (11–20)
Total IgE, U/ml	326 (31–1924)	31 (5–365)	259 (57–950)	60 (10–423)
Anti-Df IgE, U/ml	59 (8.37–141)	<0.35	37 (7.2–72.8)	<0.35
Der p 1 + Der f 1, µg/g dust				
mattress	22.9 (2.5–105)	14.6 (1.7–95.5)	18.3 (4.3–41.3)	15.7 (5.3–40.2)
bedroom	11.8 (0.8–211)	6.7 (0.5–49.2)	11.5 (3.6–25.1)	9.0 (3.8–28.3)
living room	5.9 (1.3–51.3)	6.9 (0.4–123)	8.0 (2.2–40.7)	6.1 (2.2–15.8)
Number of asthma attacks				
for the past 1 year	6.3 (5–9)	5.5 (5–7)	5.8 (5–7)	6.2 (5–8)
The amount of oral	4.07	3.23	3.59	4.05
theophylline used (mg/kg/day)	(2.10–12.9)	(2.42–4.32)	(2.63–5.11)	(2.74–5.52)

* Values expressed as arithmetical or geometric means (range).

† A: atopic children treated with home visit counsel and regular counsel, B: non-atopic children treated with home visit counsel and regular counsel C: atopic children treated with regular counsel, D: non-atopic children treated with regular counsel.

is a limited amount of time for educating patients and their parents on HDM avoidance.

Accordingly, we here examined the effects of HDM-avoidance counseling on a group of 36 children with asthma under 7 years of age. We visited the homes of 24 of these children every month for a year and performed a thorough HDM-avoidance counseling of greater than 60 min (home visit counsel) at each visit. We compared the effects of this counseling on the frequencies of asthma attacks in children with positive anti-mite IgE antibody and on the levels of HDM allergens in their homes with those of guidance usually performed in our clinics for avoiding HDM (<10 minutes per patient). As another control, we investigated the effect of the home visit counsel on asthma attacks in children with undetectable IgE antibody against HDM and found the home visit counsel effective even for these children.

METHODS

SUBJECTS

Thirty-six children with asthma who had been visiting our outpatient clinic since April 1994 and who met the following three criteria in May 1995 were enrolled in this study: (1) An age of 7 years or younger; (2) Five or more asthma attacks between June 1994 and May 1995; and (3) Absence of sensitivity to 7 common allergens (cat, dog, ragweed, *Alternaria*, *Aspergillus*, *Candida* and *Cryptomeria japonica*) as determined by measuring specific serum IgE antibody levels (Pharmacia CAP-assay, Pharmacia Inc., Uppsala, Sweden) and by skin prick testing. The skin prick testing was performed with extracts of each allergen (Torii Pharmaceutical Co., Ltd. Tokyo, Japan) using

Bifurcated needles (Allergy Laboratories of Ohio, Columbus, OH, USA). When the diameter of the wheal induced by the challenge allergens was less than half of that induced by 5 mg/ml histamine phosphate, the result was judged to be negative.

GROUPING

The sensitization to HDM allergens was confirmed by both CAP-assay (class>2) against *Dermatophagoides farinae* (Df) and skin prick testing against Df (1:100wt/vol; Torii Pharmaceutical Co., Ltd.). Seventeen children with asthma were found to be sensitized to HDM allergens, and the remaining 19 children with asthma were found to be sensitized to neither HDM nor 7 common allergens. Eleven HDM-positive (group A) and 13 HDM-negative (group B) children with asthma received home visit counseling for allergen avoidance (see below). After these 24 children were enrolled to receive home visit counseling, the remaining 12 children were chosen to receive regular clinical counseling for allergen avoidance provided with informed consent with their parents. We were able to obtain 6 HDM-positive (group C) and 6 HDM-negative (group D) children for the control group. When this study was performed (1995–1996), the Ethical Review Board did not exist in our hospital. However, we managed the patient information anonymously according to the Ethical Guideline for Medical Research by the Government.

COUNSELING FOR ALLERGEN AVOIDANCE

The HDM-avoidance counseling consisted of the following recommendations. First, the bedding encasement of the child with asthma, as well as that of other

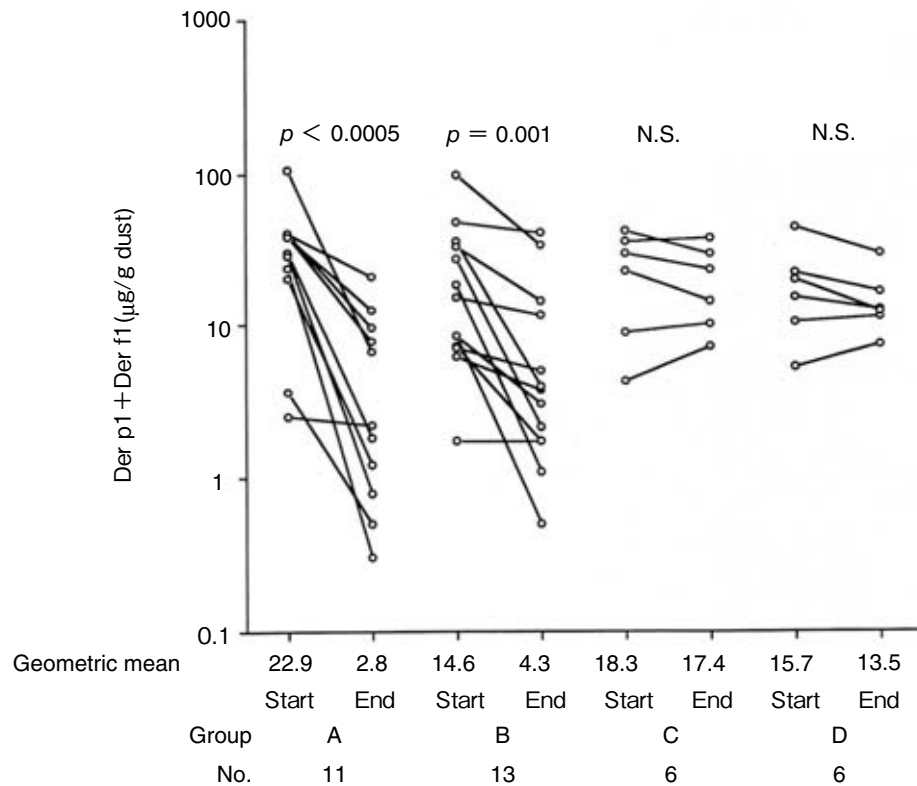


Fig. 1 Der p 1 + Der f 1 concentrations were measured as µg/gm dust in mattresses of four groups at the beginning and end of this study. The levels of Der p 1 + Der f 1 obtained at the end of this study were significantly lower than those at the beginning in groups A (atopic children treated with home visit counseling) and B (non-atopic children treated with home visit counseling), but not in groups C (atopic children treated with regular counseling) or D (non-atopic children treated with regular counseling).

Table 2 Der p 1 + Der f 1 in dust from mattresses, bedrooms, and living rooms at the end of this study.*

Group †	A	B	C	D
No.	11	13	6	6
Der p 1 + Der f 1, µg/g dust				
mattress	2.8 (0.3–20.9) ‡	4.3 (2.0–39.8) ‡	17.4 (7.2–37.2)	13.5 (7.4–29.5)
bedroom	2.6 (0.4–16.2) ‡	1.8 (0.3–20.0) ‡	10.5 (5.2–23.4)	8.3 (2.7–16.2)
living room	1.3 (0.3–5.0) ‡	1.3 (0.2–11.0) ‡	6.5 (3.7–17.0)	7.1 (3.0–25.7)

*Values expressed as geometric means (range).

† A: atopic children treated with home visit counsel and regular counsel, B: non-atopic children treated with home visit counsel and regular counsel, C: atopic children treated with regular counsel, D: non-atopic children treated with regular counsel.

‡ $p < 0.01$ for comparison with the value at start of this study.

family members, should be washed at room temperature more than once a week. All of the mattress and pillow covers were regular Japanese bedding encasings, which consists of polyester and cotton that is permeable to mites. Second, the children's mattresses and quilts, as well as the bedroom and living room of the home, should be cleaned with a powerful (>900 watts) vacuum cleaner more than once a week.

Third, stuffed dolls or soft toys should not be kept in the house. Fourth, furred pets, such as cats, dogs or birds, should not be kept in the house. Fifth, all carpets should be removed or, where this is not possible, carpets should be cleaned with a powerful vacuum cleaner more than once a week. Nevertheless, all the carpets at least in the children's bedrooms were removed. The carpets firmly installed in the liv-

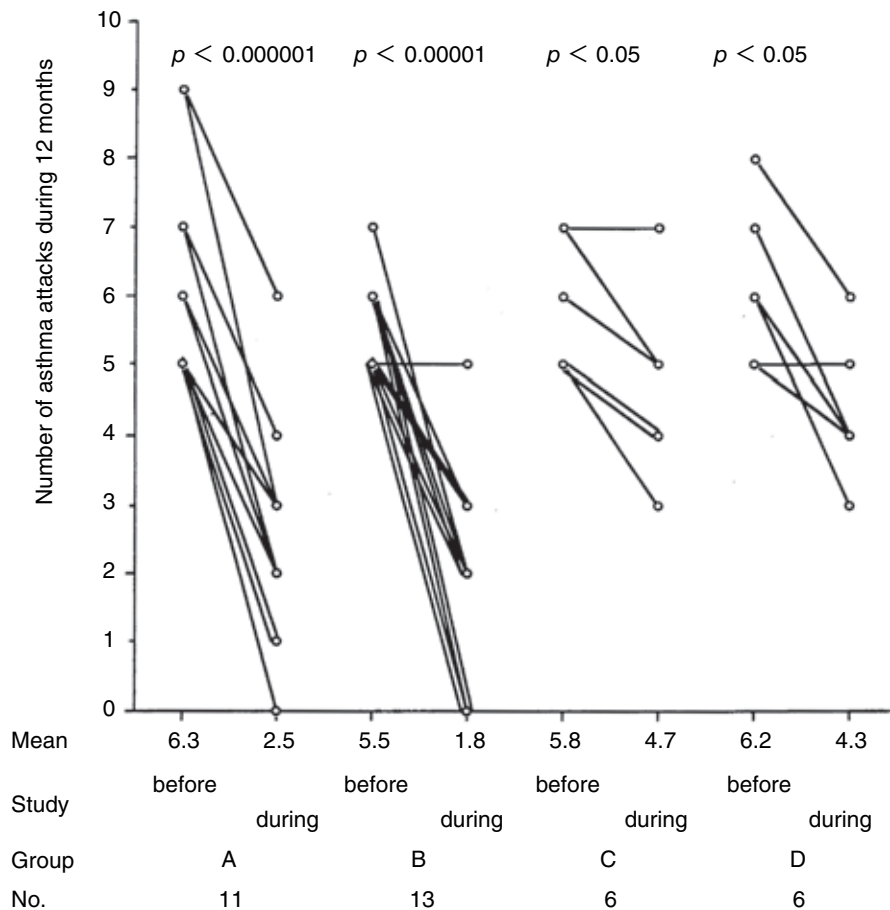


Fig. 2 Comparison between the number of asthma attacks in the 12 months before and during the 12 months of the study period. The numbers of asthma attacks during the study period were markedly lower than those in the year prior to study in groups A (atopic children treated with home visit counseling) and B (non-atopic children treated with home visit counseling), and significantly lower than those in groups C (atopic children treated with regular counseling) and D (non-atopic children treated with regular counseling).

ing rooms were not removed in 1 of group A, 2 of B, 1 of C, and 1 of D. All groups were equally instructed with the above counseling.

EVALUATION OF EXPOSURE TO HDM ALLERGENS

The sum of the concentrations of *Dermatophagoides pteronissynus* group 1 allergen (Der p 1) and *Dermatophagoides farinae* group 1 allergen (Der f 1) in dust was determined as the HDM allergen level. Dust samples of 1 m² were collected from the upper surface of the children's mattress encasements and floors of bedroom and living room. All dust samples were collected by application of HC-V15 hand-held vacuum cleaner (198 W, 0.60 m³/min airflow rates, National, Osaka, Japan) for 2 minutes by the one of the authors (KN). We thought that the allergen levels might be reduced by the act of sampling in the experimental group but not for the less frequently sam-

pled control group. Thus, this investigator carefully took samples with the same vacuum cleaner, for example, he collected dust samples from an alternate half (1 m²) of the bedding (2 m²) every month. Dust samples were weighed and extracted with 1:100 wt/vol phosphate-buffered saline containing 0.2% Tween 20, 0.2% bovine serum albumin, and 0.05% sodium azide overnight at 4°C. Concentrations of Der p 1 and Der f 1 were measured by means of a monoclonal antibody-based enzyme-linked immunosorbent assay, and the values for Der p 1 and Der f 1 were added together (Der p 1+Der f 1 level)¹³ and expressed in µg/g dust. In groups A and B, dust samples were collected every month during the study period and in groups C and D they were collected only twice, in June 1995 and June 1996.

EVALUATION OF ASTHMATIC SYMPTOMS

The parents kept diaries to describe asthma symp-

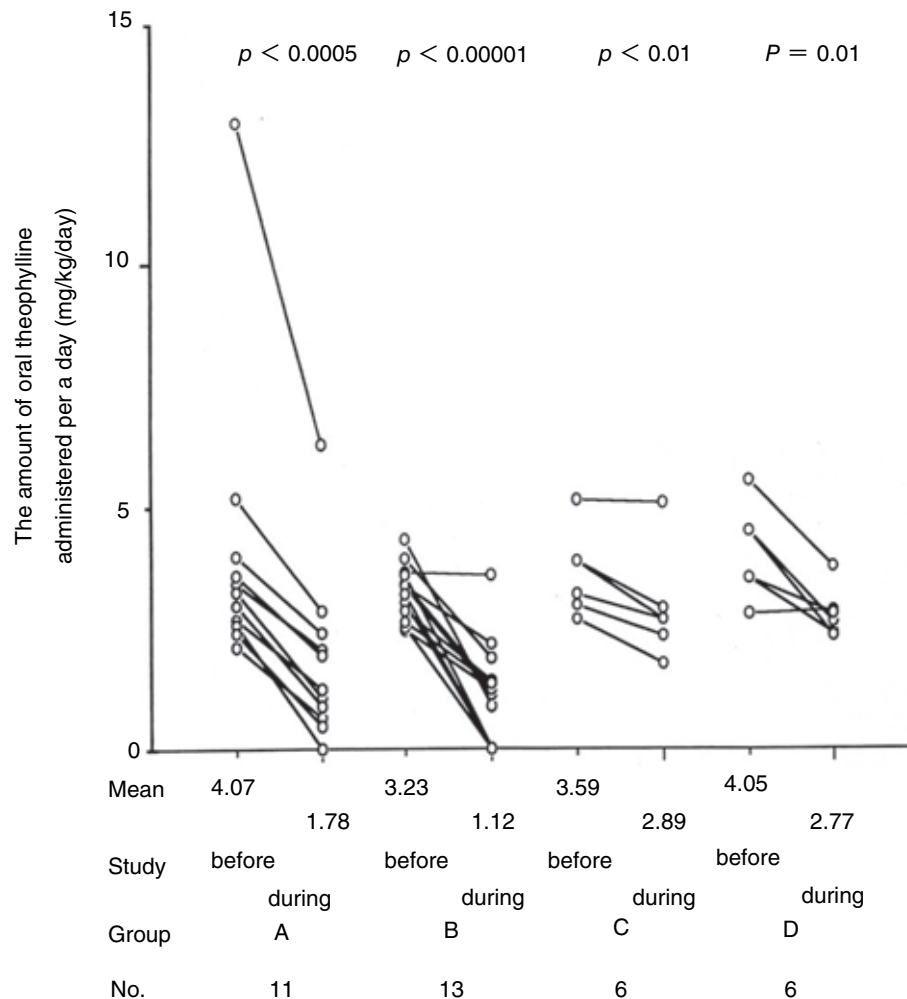


Fig. 3 Comparison between the amounts of oral theophylline per day used in the 12 months before and during the 12 months of the study period. The amounts used during the study period were markedly lower than those in the year prior to study in groups A (atopic children treated with home visit counseling) and B (non-atopic children treated with home visit counseling). Those during the study period were significantly lower than those in the year prior to study in groups C (atopic children treated with regular counseling) and D (non-atopic children treated with regular counseling).

toms. All children were recommended to visit our clinic when they developed frequent coughing or wheezing. Asthma attacks were then confirmed by physical examination. A single asthma attack in the present study usually lasted for several days, and a single episode of transient wheezing was excluded from asthma attacks.

MEDICATION

All children were judged to have mild to moderate asthma according to the Global Guidelines.¹⁴ About 70% of children with asthma who visited our clinics had ≥ 5 asthma attacks in the previous 12-month period. They were primarily treated with oral theophylline from June 1994 to June 1996. Theophylline was

given to maintain serum theophylline levels at 10–20 $\mu\text{g}/\text{ml}$ for at least a few weeks after an asthma attack. Oral and nebulized β_2 -agonists (procaterol hydrochloride or clenbuterol hydrochloride) were given thereafter as needed. None of the children studied had received inhaled corticosteroids for at least one year prior to the study period except one child in group A, who received intravenous administration of corticosteroid (100 mg of hydrocortisone) once prior to the study. The compliance for the medication seemed to be good in group C and D. The children in these groups actually still needed medication at the end of this study as shown in Figure 3.

STATISTICAL METHODS

Paired Student's *t*-test was used to compare the patient characteristics, Der p 1 + Der f 1 levels, number of wheezing episodes, and required dosages of oral theophylline among the four groups. The values of Der 1 were converted to logarithms before statistics were applied. We also performed the two-by-two analysis of variance to separate the variance attributable to clinical and home education from variance to atopy and non-atopy.

RESULTS

INITIAL DATA

The arithmetical mean ages of children with atopic asthma who received home visit counseling and regular counseling (group A), of those with non-atopic asthma who received home visit counseling and regular counseling (group B), of those with atopic asthma who received regular counseling only (group C), and of those with non-atopic asthma who received regular counseling only (group D) at the beginning of this study were 3.9, 3.5, 4.2, and 3.7 years, respectively. The arithmetical mean body weights were 16.5, 15.8, 17.2, and 16.0 kg for groups A, B, C, and D, respectively. The geometric mean levels of Der p 1 + Der f 1 in mattress-dust samples were 22.9, 14.6, 18.3 and 15.7 µg/g dust in groups A, B, C, and D, respectively, and were not significantly different among groups. These Der p 1 + Der f 1 levels were about half of those in the bedding of general Japanese homes.¹⁵ The frequencies of asthma attacks and the dosages of oral theophylline for a year prior to the study were also not significantly different among the four groups (Table 1).

The geometric mean total serum IgE concentrations were 326, 31, 259, and 60 U/ml in groups A, B, C, and D, respectively. The geometric mean levels of serum anti-Df IgE were 59, <0.35, 37, and <0.35 U/ml in groups A, B, C, and D, respectively. No significant differences were found between groups A and C or between groups B and D (Table 1).

HDM ALLERGENS EXPOSURE

HDM allergens exposure levels (Der p 1 + Der f 1) in mattress-dust samples were calculated in µg/g dust (Fig. 1). The average Der p 1 + Der f 1 levels at the end of the study were 2.8, 4.3, 17.4 and 13.5 in groups A, B, C, and D, respectively. The levels were markedly reduced in groups A ($p < 0.0005$) and B ($p = 0.001$), but significant differences were not found in groups C and D. The average Der p 1 + Der f 1 levels from bedroom and living room samples at the end of the study are shown in Table 2 for each group. The changes in Der p 1 + Der f 1 levels in the rooms were very similar to those in the mattresses.

ASTHMA ATTACKS

The arithmetical mean of frequency of asthma attacks

during 1 year of the study period were 2.5, 1.8, 4.7 and 4.3 in groups A, B, C, and D, respectively. Those in groups A ($p < 0.000001$) and B ($p < 0.00001$) were markedly decreased in comparison to the corresponding levels at one year prior to the study. Those in groups C ($p < 0.05$) and D ($p < 0.05$) were significantly but relatively less decreased (Fig. 2). The frequency of asthma attacks in group A were markedly ($p < 0.0005$) decreased as compared with those in group C. Surprisingly, those in group B were significantly ($p < 0.05$) decreased as compared with those in group D.

ORAL THEOPHYLLINE DOSAGES

All children were primarily treated with oral theophylline during the study period. Nebulized and oral β₂-agonists (procaterol hydrochloride or clenbuterol hydrochloride) were given as needed. The dosages of oral and nebulized β₂-agonists in all groups were decreased as compared with those at 1 year prior to the study. But, these were not significantly decreased. No oral or inhaled corticosteroids were given to any of the subjects throughout the study period. The arithmetical mean of dosages of oral theophylline used during study period were 1.78, 1.12, 2.89 and 2.77 mg per kg (body weight) per day for groups A, B, C, and D, respectively. The amounts in groups A ($p < 0.0005$) and B ($p < 0.00001$) were significantly less than the corresponding levels at 1 year prior to the study. Those in groups C ($p < 0.01$) and D ($p = 0.01$) were also significantly decreased as compared with those at 1 year prior to the study (Fig. 3).

DISCUSSION

We demonstrated here that thorough counseling for allergen avoidance markedly reduced the number of asthma attacks and theophylline dosage of children with asthma. Although environmental control of indoor allergen levels is the most important strategy for treating atopic asthma, the time available for educating patients is limited in clinics, particularly within the Japanese medical system, where more than 50 children with allergic or non-allergic disease should be treated every day. Therefore, thorough counseling for environmental control of allergens should be increasingly considered as a primary treatment for atopic asthma. We¹⁶ and others⁶⁻⁹ have previously described a decrease in the number of asthma attacks in children by the use of bedding encasements or chemicals for reducing HDM allergens. Here, we demonstrated that home visit counseling without recourse to these useful but expensive tools can also markedly reduce both HDM allergens and the frequency of asthma attacks.

We enrolled 36 children with asthma in the present study. All parents of 36 children were cooperative in performing indoor allergen avoidance and asked us to visit their home. However, we serially chose 24

families for home visit counsel (groups A and B) and then chose 12 families as control groups under informed consents. The characteristics of the patients such as severity were not biased in these groups except for IgE levels between A+C and B+D. All the children were equally taught how to avoid HDM allergen by the same doctor. All the children had been treated with oral theophylline as a primary medication. The patients requiring inhaled corticosteroids for treatment were excluded in this study, since the effect of the corticosteroid (beclomethasone dipropionate is the only drug available for children use in Japan) may not be correctly inhaled, and that may not be evaluated in early childhood.¹⁷ One may consider that the thorough counseling group and the control group were treated differently, and thereby influencing the factors other than HDM such as compliance for medication or smoking. However, as commonly seen in Japan, the parents are equally educated and none of the mothers in this study were smoking. In this study, we have successfully modified the behavior of families who smoked tobacco products. They gave up smoke or smoked outdoors away from children. There were twelve fathers (4, 5, 2, and 1 father in groups A, B, C, and D) and no mothers who were smoking out of the 36 families at the beginning. However, there were eight smoking fathers (3, 3, 1, and 1 father in groups A, B, C, and D, respectively) at the end of the period. The decrease of asthma exacerbation in groups C and D without the decrease in Der 1 levels may result from the avoidance of the environmental tobacco smoke exposure. Moreover, since home visit counseling reduced the required dosage of oral theophylline, the usual primary medication for controlling children with asthma, the children in the control groups received more medications.

Home visit counseling also markedly reduced the asthma attacks and theophylline dosages of children with non-atopic asthma. Nineteen children with asthma who had no detectable anti-IgE against HDM were enrolled in the non-atopic group (groups B and D). In 18 of these 19 cases, Der p 1 + Der f 1 levels of greater than 2 µg/g dust — a sufficient level for sensitization¹⁸ — were detectable in the home. Furthermore, we were unable to detect any specific IgE antibodies against 8 common allergens, *i.e.*, Df, cat, dog, ragweed, *Alternaria*, *Aspergillus*, *Candida* and *Cryptomeria japonica*. Therefore, the children were judged to be non-atopic children. We could find a difference between clinical and home education for Der p 1 + Der f 1 ($p = 0.001$), asthma attack ($p < 0.001$), and theophylline dosage ($p = 0.003$), but not between atopy and non-atopy by using the 2 by 2 analysis of variance. Most of them had symptoms of a common cold when they had asthma attacks, suggesting that the attacks may have been triggered by viral infections. In addition to the possibility that HDMs act as a

T cell antigen to induce non-IgE-mediated allergic inflammation through IL-5 production,¹⁹ HDMs have also been reported to act as a protease to cleave T cell IL-2 receptors and viral hemagglutinin, and thereby diminish interferon γ secretion^{20,21} and enhance the virus incorporation.²² Thus, HDMs may enhance the clinical symptoms induced by viral infection.

We also evaluated the number of asthma attacks in all patients. A single asthma attack was defined as a certain number of wheezing symptoms in the course of a single month. A single attack usually included wheezing symptom that lasted for several days, and we did not encounter any case in which only one transient wheezing was heard in one month. We did not evaluate asthma symptoms by assessing such objective respiratory functions as peak expiratory flow rate, because most of the children were under 5 years of age and could not correctly operate the meter. It will therefore be necessary to perform a similar study in older children with asthma.

Although this study was not blinded, the patients were serially allocated into 4 groups. All of the parents understood the significance of this study and were quite cooperative. We also could not completely rule out that some biases remained in dust samples, *i.e.*, allergen levels might be reduced by the act of sampling in the experimental group but not for the less frequently sampled control group. Thus, this investigator carefully took samples with the same vacuum cleaner, for example, he collected dust samples from an alternate half (1 m²) of the bedding (2 m²) every month.

The relationship between exposure to indoor allergens and symptoms of asthma is complex. Other researchers have stated the ineffectiveness of HDM avoidance for asthma control.^{23,24} Although patients in these studies were sensitized to multiple indoor allergens, clinical trials of remediation interventions have targeted only one allergen. In contrast, thirty-six children in our study were not sensitized to indoor allergens except house dust mite. Recently, Morgan WJ *et al.* demonstrate that an individualized, home-based, comprehensive environmental intervention decreases exposure to indoor allergens, including cockroach and dust-mite allergens, resulting in reduced asthma-associated morbidity.²⁵ Halken S *et al.* also conclude that house dust mite allergen avoidance is significantly effective in children with asthma.²⁶

In conclusion, our results may indicate that thorough counseling and education on avoidance of HDM allergens is beneficial for children with asthma with, as well as without, detectable specific anti-HDM IgE antibodies. Although it is difficult to compare the effects of counseling methods on the clinical symptoms, the thorough counseling was clearly effective for reducing HDM allergens. The decrease of asthma attacks could have resulted from producing enthusiastic compliance with all forms of treatment by home

visits. Yet, it is clear that more time is needed for effective HDM-allergen avoidance counseling. Individualized intervention is considered to be one of reasons why home visit counseling is so effective.

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