Evaluation of Risk Factors for Asthma in Taipei City

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Background: Asthma has rarely been studied by evaluating all of its trigger factors in a single patient population. Thus, correlations between the concentration of allergen immunoglobulin (Ig) E antibodies and airway limitation or asthma severity remain unclear.

Methods: Five hundred and seventy-nine asthmatic patients were enrolled, and serum specific IgE antibodies to allergens were analyzed. All suspected trigger factors were assessed by questionnaire, case histories over a 4-year period, and diary card recordings; possible trigger factors were then re-evaluated.

Results: Antibodies to the following allergens were found: Dermatophagoides pteronyssinus (59.8% of patients), D. microceras (58.8%), D. farinae (56.8%), cockroach (38.3%), dog dander (26.3%), Candida albicans (13.3%), cat dander (10%), and Cladosporium herbarum (6.6%). A greater prevalence of allergy to dog and cat dander was found than previously. Younger patients were more often positive for mite allergens, and had higher titers of antibodies against such allergens, than older patients. Further, females had a lower concentration of mite allergen antibodies than males. No correlation between the concentration of allergen antibodies and forced expiratory volume in 1 second (FEV1), or the ratio of FEV1:forced vital capacity (FEV1:FVC), was found. In addition, there was no significant change in antibody titers with varying asthma severity. Non-allergenic trigger factors were irritant air inhalants (94.6% of patients), respiratory infection (92.2%), exercise (75.2%), emotional factors (58.8%), drugs and chemical substances (16%).

Conclusion: There are multiple trigger factors in asthma. Allergic trigger factors are more common in younger than older patients, whereas non-allergic trigger factors are more common in older patients. There was no linear correlation between the concentration of specific IgE antibodies and asthma severity or airway limitation; therefore, to prevent asthma attacks in individual asthmatic patients, greater attention should be paid to avoiding all potential trigger factors, and not just house dust mite allergens. [J Chin Med Assoc 2005;68(5):204–209]

Key Words: asthma, cockroach, exercise, house dust mite, trigger factor

Introduction

Bronchial asthma is a chronic inflammatory disorder of the airways that causes hyper-responsiveness of the bronchial tree to various stimuli. Among the many factors capable of triggering asthmatic symptoms, specific allergen-immunoglobulin (Ig) E antibody reactions still play one of the most important roles.1–3 Aside from allergens, other non-allergic trigger factors, such as respiratory infection, airborne particles, emotional factors, and exercise, are also important in inducing asthma attacks.4 Pharmacologic intervention to treat established asthma is highly effective in controlling symptoms and improving quality of life. In addition, the most important aspect of asthma management is to avoid exposure to trigger factors and, thus, prevent asthma attacks; subsequently, the control of asthma can be improved and medication needs reduced.

In Taiwan, there has been no survey of allergenic

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Trigger factors for asthma in a large population of patients, and previous studies have focused more on allergenic trigger factors, especially house dust mite allergens, than non-allergenic factors. Thus, information about non-allergenic trigger factors is limited. Further, as no study has evaluated all trigger factors for asthma in 1 population, correlations between the concentrations of specific allergen IgE antibodies and airway limitation or asthma severity remain unclear.

In this study, we attempted to analyze the prevalence of various trigger factors for asthma, related or unrelated to allergens, in patients living in Taipei city, and to determine whether correlations exist between the concentrations of specific allergen antibodies and airway limitation or asthma severity.

Methods

Study population

Five hundred and seventy-nine asthmatic patients, who had been followed up regularly at the Asthmatic Clinic of the Pulmonary Division of Tri-Service General Hospital from January 1997 to December 2001, were included in this investigation. The hospital review board for human studies approved the protocols used, and informed consent was obtained from each patient before participation.

Study protocols

Bronchial asthma was diagnosed using Global Initiative for Asthma (GINA) criteria:4 namely, a history of recurrent, paroxysmal attacks (at least 3) of reversible obstructive airway disease, which resolved either spontaneously or after treatment with bronchodilators. Pulmonary function tests, bronchodilation tests, and methacholine bronchial provocation tests were performed to confirm airway obstruction, reversibility of obstruction, and hyper-responsiveness, respectively.

After pulmonary function tests, each patient underwent serum assay for specific IgE antibodies to the following common allergens: Dermatophagoides pteronyssinus, D. farinae, D. microceras, cockroach, cat dander, dog dander, Alternaria tenuis, Cladosporium herbarum, and Candida albicans. Antibody analysis was performed with the Pharmacia CAP System™ (Pharmacia Diagnostics, Uppsala, Sweden).

All CAP System assays were performed at the same time, and in the same laboratory, according to previously detailed techniques that employed an immunoenzymatic method.5 Briefly, test sera were incubated with the solid phase, consisting of a flexible hydrophilic allergen carrier (polymer) encased in a capsule (ImmunoCAP™, Pharmacia Diagnostics). This carrier comprises a cyanogen bromide-activated cellulose derivative, which can bind at least 3 times more antigen than the corresponding paper disk used in the radioallergosorbent test (RAST), and up to 50 times more allergen than the amount adsorbed on a coated tube. An anti-human IgE (polyclonal and monoclonal) antibody mixture labeled with β-galactosidase (generating fluorescence) was then added. This reagent has high immunoreactivity and low background, allowing a wider range of measurement than in the RAST. Finally, the intensity of the resulting color was measured in a spectrophotometer. The entire procedure is automated. Results, expressed in kilounits per liter (kU/L), were obtained by reference to a standard curve derived from serial dilution of human IgE calibrated against the World Health Organization standard for IgE. One kU/L corresponds to 2.4 ng of IgE per mL. A value ≥ 0.35 kU/L is defined as a positive CAP System result.

Asthma severity was assessed in terms of symptoms, amounts of β2-agonist used to treat symptoms, and lung function, and was subdivided into 4 categories according to GINA criteria: mild intermittent, mild persistent, moderate persistent, and severe persistent.6

The study questionnaire contained many items, such as detailed general data, history of respiratory symptoms and treatment of asthma, history of allergies (e.g. allergic rhinitis, urticaria, and asthma), smoking habit, genetic background in relatives, occupation history, and a detailed checklist of previous exposure to trigger factors (e.g. air stimulants, respiratory infection, exercise, emotional factors, drugs, chemical substances, etc.) and which ones had induced asthmatic attacks in the past. The questionnaire was completed at the Asthma Clinic by a nurse, with responses subsequently confirmed by a doctor. In the following years, patients were regularly followed-up in the outpatient department.

Suspected previous trigger factors were confirmed from diary card records, since these records may reveal the factors responsible for a drop in peak expiratory flow rate. Only 294 asthmatic patients agreed to record daily asthma cards (i.e. symptom scores, expiratory peak flow rate, and adverse effects of antiasthmatic drugs).

Statistical analysis

Values for study parameters were expressed as mean ± standard deviation, or percent. Comparisons among all groups for a given variable were performed using 1-
way analysis of variance and Dunnett’s methods. A p value < 0.05 was considered statistically significant. Simple linear regression between forced expiratory volume in 1 second (FEV₁), or the ratio of FEV₁:forced vital capacity (FEV₁:FVC), and concentration of mite allergen antibodies was performed.

Results

Among the 579 patients enrolled, 294 agreed to complete the questionnaire study: 139 males (43.7%) and 155 females (52.7%); mean age, 42.7 years (range, 10–85 years). In these 294 asthmatic patients, 69.4% had allergic rhinitis, 67.7% had a history of bronchial asthma in relatives, 22.4% had atop dermatitis, and 18% were smokers. The severity of bronchial asthma was classified as mild intermittent in 37.1% of patients, mild persistent in 11.9%, moderate persistent in 28.6%, and severe persistent in 19.4% (Table 1).

Case histories for the 294 asthmatic patients revealed the following non-allergic trigger factors: stimulant inhalation (94.6% of patients); respiratory tract infection (92.2%); exercise (75.2%); emotional factors (58.8%); and chemical agents and drugs (18.0%) (Table 2).

Serum specific IgE antibodies to allergens in 579 asthmatic patients were analyzed, and the following allergens were confirmed in the following proportions of patients: D. pteronyssinus (59.8%), D. microceras (58.8%), D. farinae (56.8%), cockroach (38.3%), dog dander (26.3%), C. albicans (13.3%), cat dander (10%), and C. herbarum (6.6%) (Table 3).

Increasing asthma severity was not significantly related to IgE concentrations, or to the proportions of patients positive for antibodies to mite allergens (Table 4). There were also no correlations between antibody titers to mite allergens and FEV₁ or FEV₁:FVC. The findings were also similar for other allergens (cockroach, dog dander, cat dander, C. albicans, and C. herbarum). Thus, no allergenic trigger factors independently influenced asthma severity. However, rates of antibody positivity and antibody titers correlated with age and gender. In all age groups, the rate of antibody positivity to D. pteronyssinus was greater in males than females (Figure 1).

![Figure 1](image_url) Rates of immunoglobulin E (IgE) antibody positivity against Dermatophagoides pteronyssinus according to age and gender.

| Table 1. Demographic data for the 294 asthmatic patients who completed the questionnaire study |
|-------------------|-------------------|-------------------|-------------------|
| **Age distribution, yr** | 10–19 | 20–29 | 30–39 | 40–49 | 50–59 | 60–69 | ≥ 70 |
| Number of patients (%) | 30 (10.2) | 61 (20.7) | 36 (12.2) | 65 (22.1) | 35 (11.9) | 37 (12.6) | 30 (10.2) |
| **Gender** | Male | Female | | | | | |
| Number of patients (%) | 139 (47.3) | 155 (52.7) | | | | | |
| **Heredity** | Yes | No | | | | | |
| Number of patients (%) | 199 (67.7) | 95 (32.3) | | | | | |
| **Smoking** | Yes | No | | | | | |
| Number of patients (%) | 53 (18.0) | 241 (82.0) | | | | | |
| **Allergic history** | | | | | | | |
| Number of patients (%) | 204 (69.4) | 66 (22.4) | 22 (7.5) | | | | |
| **Asthma severity** | | | | | | | |
| Number of patients (%) | 109 (37.1) | 35 (11.9) | 84 (28.6) | 57 (19.4) | 9 (3.1) | | |
### Discussion

Our results indicate that the house dust mite is the most common allergen in asthmatic patients in Taiwan. Younger versus older patients have higher rates of antibody positivity, and higher titers of antibodies, against mite allergens; indeed, the rate of antibody positivity against *D. pteronyssinus* was 93.2% in patients aged < 20 years, compared with a rate of only 45.9% in patients aged 60–70 years. Further, rates of antibody positivity against mite allergens were lower in females than males.

Since the report of Voorhorst et al. in 1967, *D. pteronyssinus* and *D. farinae* have proved to be among the most important allergens causing bronchial asthma worldwide. The prevalence of these allergens among subjects with asthma varies from 45% to 85%, and sensitivity to mites is a risk factor for asthma. In 1984,
the first RAST study in asthmatic children in Taiwan was conducted by Hsieh, who showed that *D. farinae* (90.2% of patients) was one of the most common allergens in asthmatic children aged <16 years. This is similar to our finding (93.2% of asthmatic patients aged <20 years had antibodies against *D. pteronyssinus*), and indicates that house dust mites are very common aeroallergens in young asthmatic patients. In contrast, the prevalence of antibodies to mite allergens in adult and elderly asthmatic patients has not yet been well explored. In our studies, the sensitivity to mites was comparatively weak in aged patients, for unknown reasons. Nor can we explain why male rather than female asthmatic patients had higher rates of antibody positivity, although sex hormones may play some role in allergic conditions.

Custovic et al showed that the clinical activity and severity of asthma in mite-sensitive patients are related to exposure to mite allergens in the dust reservoir, with levels in beds being an important indicator of disease activity. However, no study has found an association between specific antibody concentrations against mites and asthma severity or airway obstruction. Our study found no significant difference in antibody levels against mites in 4 groups of patients with different severities of asthma; nor did we find any correlation between airway obstruction (FEV₁) and an increase in IgE antibody levels against mites. The findings were similar for other allergenic trigger factors. Although mites are a very common allergenic trigger factor, asthma severity is affected not by a single factor, but by the sum of effects due to both allergenic and non-allergenic trigger factors.

Cockroaches have been identified and recognized as a major cause of asthma. In 1988, Lan et al documented that 39.2% of 79 atopic patients in the Taichung area of Taiwan had IgE antibodies against cockroach. In 1984, Hsieh found antibodies to cockroach in 17.9% of asthmatic children aged <16 years in the Taipei area. Our finding of antibodies to cockroach in 38.3% of asthmatic patients in the Taipei area is similar to that of Tsai et al in 1998, who reported that 36.4% of asthmatic patients were hypersensitive to German cockroach in the same area.

Our study also found sensitivity to dog dander (26.3% of patients) and cat dander (10%) across asthmatic patients of all ages, whereas Hsieh reported sensitivity to dog and cat dander in 8.2% and 7.4%, respectively, of asthmatic children aged <16 years. The greater rates of antibody positivity against dog and cat dander in our study, compared with the rates in the Hsieh study, can be attributed to the presence of more pets in Taipei City than previously.

Various fungal spores have been implicated as trigger factors in asthmatic patients. Indeed, our study found antibodies to the following microbes in such patients: *C. albicans* (13.3% of patients), *C. herbarum* (6.6%), and *A. tenuis* (3.5%). In Germany, sensitization to *C. albicans* was found in 25% of asthmatics, whereas that to molds was found in 36%. The prevalence of allergy to fungi in asthmatic patients in Taiwan seems to be lower than that in Western countries.

Aspirin allergy has been found in 7.1% of a population of asthmatic patients, and in 3–8% of asthmatic patients, ingestion of aspirin or other non-steroidal anti-inflammatory drugs caused profound, sometimes life-threatening, bronchoconstriction, and naso-ocular, dermal, and gastrointestinal responses. This prevalence of aspirin sensitivity is similar to that found in a study conducted in Finland which showed that 8.8% of asthmatic patients had aspirin intolerance.

About 50% of children worldwide are exposed to environmental tobacco smoke, which in turn exacerbates asthma in 20% of children with the condition. Our study showed that 18% of asthmatic patients are smokers, and clearly, major efforts are

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**Table 4. Asthma severity in relation to the proportions of patients positive for antibodies to specific mite allergens, and mean (± standard deviation [SD]) antibody titers; data for 111 asthmatic patients**

<table>
<thead>
<tr>
<th>Asthma severity</th>
<th>Dermatophagoides pteronyssinus</th>
<th>Dermatophagoides farinae</th>
<th>Dermatophagoides microceras</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of</strong></td>
<td><strong>Mean (± SD)</strong></td>
<td><strong>Mean (± SD)</strong></td>
<td><strong>Mean (± SD)</strong></td>
</tr>
<tr>
<td><strong>antibody-positive</strong></td>
<td><strong>antibody titer (kU/L)</strong></td>
<td><strong>antibody titer (kU/L)</strong></td>
<td><strong>antibody titer (kU/L)</strong></td>
</tr>
<tr>
<td><strong>patients (%)</strong></td>
<td><strong>kU/L</strong></td>
<td><strong>kU/L</strong></td>
<td><strong>kU/L</strong></td>
</tr>
<tr>
<td>Mild intermittent</td>
<td>28/38 (73.7)</td>
<td>27/38 (71.1)</td>
<td>26/34 (76.5)</td>
</tr>
<tr>
<td></td>
<td>31.0 ± 32.7</td>
<td>25.2 ± 28.9</td>
<td>24.1 ± 28.5</td>
</tr>
<tr>
<td></td>
<td>5/10 (50)</td>
<td>5/10 (50)</td>
<td>5/10 (50)</td>
</tr>
<tr>
<td>Mild persistent</td>
<td>30/42 (71.4)</td>
<td>29/42 (69.0)</td>
<td>27/39 (69.2)</td>
</tr>
<tr>
<td></td>
<td>34.4 ± 34.5</td>
<td>32.4 ± 33.5</td>
<td>32.2 ± 33.5</td>
</tr>
<tr>
<td>Moderate persistent</td>
<td>15/21 (71.4)</td>
<td>13/21 (61.9)</td>
<td>14/21 (66.7)</td>
</tr>
<tr>
<td></td>
<td>24.0 ± 33.6</td>
<td>24.5 ± 32.0</td>
<td>22.3 ± 29.1</td>
</tr>
<tr>
<td>Severe persistent</td>
<td></td>
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needed to educate asthmatic patients to stop smoking. Approximately 2-thirds of asthmatic patients revealed that some of their relatives also have asthma; hence, this finding supports previous data that genetic factors play a key role in asthma.18

Non-allergic trigger factors are difficult to evaluate with scientific clinical tests. Thus, in this trial, a detailed questionnaire was completed and diary card records from a 4-year period were evaluated to identify the most likely trigger factors. Our findings show that inhalation of allergens in the air (94.6% of patients), respiratory tract infection (92.2%), exercise (75.2%), and emotional factors (58.8%), are very common non-allergic trigger factors for asthma. Exacerbation of asthma in adults is frequently associated with a respiratory tract viral infection (RTVI).19 Our results showed that 92.2% of asthmatic patients had previously had an asthma attack induced by a respiratory tract infection, and earlier studies showed that 55–89% of asthma exacerbations were associated with an RTVI.20,21 In addition, exercise appeared to cause bronchoconstriction in 70–80% of asthmatic patients,22 which is similar to our finding of 75.2%.

In conclusion, the common inhaled allergens causing asthma in Taipei City were, in descending order, mites, cockroach, dog dander, C. albicans, cat dander, C. herbarum, and A. tenuis. Non-allergic trigger factors were, in descending order, airborne stimulant inhalation, respiratory tract infection, exercise, emotional factors, and chemical agents and drugs. Exposure to mites is an important allergenic trigger factor in young, particularly male, asthmatic patients, whereas non-allergic factors are important in adult asthmatics, especially the elderly. In the absence of a correlation between antibody titers against specific allergens and asthma severity, we suggest that all trigger factors can contribute to asthma severity. Efforts should, therefore, be made to identify all possible trigger factors so that exposure to them can be avoided and asthma exacerbations reduced.

Acknowledgments

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References


