### ORIGINAL ARTICLE

# **Evaluation of Risk Factors for Asthma in Taipei City**

Chi-Huei Chiang<sup>1,2\*</sup>, Kuen-Ming Wu<sup>1</sup>, Chin-Pyng Wu<sup>3</sup>, Horng-Chin Yan<sup>3</sup>, Wann-Cherng Perng<sup>3</sup>

<sup>1</sup>Division of Pulmonary Immunology and Infectious Diseases, Chest Department, Taipei Veterans General Hospital,

<sup>2</sup>National Yang-Ming University School of Medicine, and <sup>3</sup>Pulmonary Division, Tri-Service General Hospital,

National Defense Medical Center, Taipei, Taiwan, R.O.C.

**Background:** Asthma has rarely been studied by evaluating all of its trigger factors in 1 study 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 (FEV $_1$ ), or the ratio of FEV $_1$ :forced vital capacity (FEV $_1$ :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. Allergenic trigger factors are more common in younger than older patients, whereas non-allergenic 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. <sup>1-3</sup> Aside from allergens, other non-allergenic trigger factors, such as respiratory infection, airborne particles,

emotional factors, and exercise, are also important in inducing asthma attacks.<sup>4</sup> 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

\*Correspondence to: Dr. Chi-Huei Chiang, Division of Pulmonary Immunology and Infectious Diseases, Chest Department, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, R.O.C. E-mail: chiang01@vghtpe.gov.tw • Received: April 14, 2004 • Accepted: January 13, 2005

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: <sup>4</sup> 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<sup>TM</sup> (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.<sup>5</sup> Briefly, test sera were

incubated with the solid phase, consisting of a flexible hydrophilic allergen carrier (polymer) encased in a capsule (ImmunoCAP<sup>TM</sup>; 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 βgalactosidase (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  $\geq 0.35 \text{ kU/L}$  is defined as a positive CAP System result.

Asthma severity was assessed in terms of symptoms, amounts of  $\beta_2$ -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.<sup>4</sup>

The study questionnaire<sup>6</sup> 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-

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