

Allergic Profile of Chinese Children in Hong Kong: A Skin Prick Test and ELISA Comparative Study

CHRISTOPHER C. CHANG, M.D., Ph.D.,¹ GEORGES M. HALPERN, M.D.,¹
ALFRED Y. TAM, M.B., B.S.,² YU-LUNG LAU, M.D.,² and
CHAP-YUNG YEUNG, M.B., B.S.²

ABSTRACT

Forty-four Chinese children were recruited from the Allergy Clinic, University of Hong Kong, and scored for respiratory symptoms with or without associated skin symptoms, with a score of 8 (maximum 16) for inclusion. They were skin tested with Stallerpoint, using mite, cat, dog, *Cladosporium*, *Alternaria*, cockroach, cow's milk, egg white, peanut, shrimp, soybean, codfish, and positive and negative controls. Sera were tested with the IVT test for total IgE, mite mix, grass pollen mix, short ragweed, mulberry tree pollen, mold mix, cow's milk, egg white, fish/shrimp, rice, soybean, and positive and negative controls. Children tested positive to *Dermatophagoides pteronyssinus* (34/44), cat (8/44), cockroach (5/44), fish (3/44), and dog (3/44). The IVT ELISA detected specific IgE to *Dermatophagoides pteronyssinus* (42/44), rice (1/44), and fish/shrimp mix (1/44). A limited number of allergens could screen Chinese allergic children in Hong Kong.

INTRODUCTION

IN MOST COUNTRIES, there has been a significant increase in children with respiratory problems, including allergic rhinitis and asthma. The most disturbing trend is an increase in asthma in young children under 3 years of age. This trend has been reported in Hong Kong. The increase may be due to changes in the recent two decades, including rapid modernization and urbanization, with resultant augmentation of air pollution due to increasing traffic, construction, and industrial wastes. Overcrowding and its associated problems, such as infection, is another prominent factor. In Hong Kong, public housing in large skyscrapers with limited individual space is the rule. Cockroaches thrive in the ventilation shafts and garbage disposal pipes. The ambient humidity ranges from 62% to 99%, and the temperature is subtropical most of the year. Natural fibers (cotton, wool, kapok, jute) generally are used for traditional, cultural, and economic reasons, and house dust

¹Division of Rheumatology, Allergy and Clinical Immunology, Department of Internal Medicine, University of California Davis School of Medicine, Davis, California.

²Department of Paediatrics, Queen Mary Hospital, University of Hong Kong, Hong Kong.

mites thrive in such a favorable environment. Airborne pollens, being hygroscopic, generally fall on the ground or other surfaces and usually are not involved in respiratory allergic manifestations.

The psychosocial environment also has changed dramatically. In Asia, there is mounting pressure for children to be high achievers in a more competitive society. This same society keeps parents away from home and at work longer, depriving children of their proper emotional fulfillment. A tentative substitute is the acquisition of a pet, mostly cats, as a surrogate affection and care giver.

Another recent factor in Asia is the campaign of American, Western European, and Japanese tobacco companies to induce smoking in children, adolescents, and young adults, with young women of childbearing age as major targets. Food, with its incredible variety in Chinese cuisine, has changed recently, with the ubiquitous presence of monosodium glutamate, artificial colorings, and preservatives and aggressive promotion of sugar-salt-fat-laden fast foods. Chronic or recurrent gastrointestinal inflammatory ailments pave the way to food allergies. Chinese children, with their mucosal immaturity, are experiencing an increase in food-induced sensitivities.

Eighty percent of allergic Asian children have a history of allergic disease within families (immediate family and distant relatives),⁽¹⁻⁴⁾ and skin tests to grass pollens give larger reactions in American-born Chinese (ABCs). ABCs were 2.3 times more likely to be allergic to grass than were Caucasians, and those allergic to grass were 10.8 times more likely than Caucasians to be allergic to at least one Californian tree pollen.⁽⁵⁾

Previous studies indicated that Chinese allergic and asthmatic children in Hong Kong were most sensitized to house dust mites (*Dermatophagoides*).^(3,4) Given the cited changes, however we organized a study of 44 children and 1 adult using a battery of relevant allergens for prick skin testing and a new compact in vitro assay for determination of total and allergen-specific IgE in order to evaluate and identify the major actual allergens affecting a Chinese population in Hong Kong.

MATERIALS AND METHODS

Patients

Forty-four children were recruited from the Allergy Clinic, Sai Ying Pun Specialist Clinic, Department of Pediatrics, University of Hong Kong. Selection was based on a questionnaire scoring the atopic symptoms 0-3. All patients had a significant history of atopy. These diagnoses were categorized into (1) allergic rhinitis, (2) allergic bronchitis, (3) allergic conjunctivitis, (4) asthma, and (5) eczema. An atopy score was determined based on the following symptoms: runny nose, congestion, cough, eye itching, wheezing, eczema, and hives. A score of 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, and 3 = severe symptoms was assigned for each symptom, and the score was totaled to yield the overall atopy score. All questionnaires were completed by a single investigator to diminish intersubject variation and differences in interpretation of symptoms. To be included in this study, each patient had a score of 8 or more. Patients with other illnesses have been excluded. Short-acting antihistamines had to be held for 7 days and long-acting ones for 30 days before skin testing. The protocol was approved by the University of Hong Kong Ethics Committee, and all parents signed an informed consent form in English or Chinese. In addition, we have included one adult, the wife of a Hong Kong University immunologist, who has been suffering from allergic rhinitis to grass pollen for over 30 years. She was included as a positive control and tested exclusively positive to grass pollen by skin test and IVT allergy in vitro test. We could not include a negative control group (nonallergic in children) in this study.

Skin prick testing

The device used was the Stallerpoint (SP), a kind gift from Stallergenes, Fresnes, France. SP is a Morrow-Brown type needle made of polymethacrylate. It has a 1 mm conical point with four microgrooves designed to introduce a precise amount of antigen into the skin.⁽⁶⁾

ALLERGIC CHINESE CHILDREN IN HONG KONG

Before testing, the skin was cleansed with isopropyl alcohol. A drop of control solution or allergenic extract was placed on the skin. The SP was directed through a drop of test solution into the skin at a 90-degree angle, with moderate pressure. One device was used for each test and then discarded. Tests were performed on the volar side of the forearm between 11:00 and 13:00.⁽⁷⁾ Excess antigen was blotted from the skin surface within several minutes. A negative control of 50% glycerosaline and a positive control of histamine 1 mg/ml (Stallergenes, France; Hollister-Stier, West Haven, CT) were used. This dosage of histamine has been considered as low, but the Ethics Committee of the University of Hong Kong refused higher dosage in children.

Extracts of *Dermatophagoides pteronyssinus*, cat dander, dog dander, *Cladosporium*, *Alternaria*, cockroach, cow's milk, egg white, peanut, shrimp, soybean, and codfish in glycerosaline (Stallergenes; Hollister-Stier) comprised the allergenic extract panel.

Reactions were measured at 15 minutes and 30 minutes after application. Maximum diameters of wheal and erythema were measured and recorded. The measurements were translated into degrees of reactivity from class 0 to class 3 based on the classification shown in Table 1.

All testing and measurements were performed by either a trained registered nurse or the authors, all being experienced in skin test procedures.

The IVT allergy screen

The IVT allergy screen (IVT, Arlington, TX) is a solid-phase, enzyme-linked immunosorbent assay (ELISA) designed to detect simultaneously but separately in a single test the presence of IgE specific for inhalants and food allergens and to provide an estimate of total IgE levels in patient samples.⁽⁸⁾

Blood (3–5 ml) is collected using a 23G butterfly connected to a 10 ml syringe and transferred to a red-top tube. It is allowed to clot and is centrifuged, and serum is collected and frozen (–70°C) until assayed.

IgE immunoglobulin or antibody in the sample is allowed to react for 1 hour in the allergy screen device (PVC). After rinsing, the device is filled with an anti-IgE–urease conjugate and incubated for 1 hour. The device is then rinsed again and filled with substrate/indicator. IgE bound to a particular segment will bind conjugate, which triggers a visually detectable yellow to purple color change about that segment, permitting the positive identification of IgE to one or more of the specific allergen categories in the test. Color change was read at 25 minutes by one investigator who was blinded to the results of history and skin tests. Using a color scale provided with the kits, the color intensity was graded 0–3.

The anti-IgE was calibrated for 30 IU/ml. The segments comprised control, positive control, total IgE, cow's milk, egg white, codfish and shrimp, rice, soybean, mold mix (*Cladosporium*, *Aspergillus*, *Candida*), mulberry tree pollen, short ragweed, mite mix (*Dermatophagoides pteronyssinus*, *D. farinae*), and grass pollen mix (*Cynodon*, *Lolium*, *Phleum*, *Poa*). This specific IVT allergy screen was specially designed for Southeast Asian children.

Graphs were generated using Cricketgraph on a MacIntosh IICI computer with 5MB RAM.

TABLE 1. CLASSIFICATION OF SKIN TEST RESULTS

Erythema		Wheal	
Class ^a	Dimensions (mm)	Class	Dimensions (mm)
0	0–9	0	0–4
1	10–19	1	Not used
2	20–29	2	5–9
3	>29	3	9–14
		4	>15

^aClass 1 or above was considered positive.

RESULTS

There were 27 male and 17 female children in this study. The ages ranged from 1 year plus 10 months to 16 years. The allergy scores of the patients are shown in Figure 1 and ranged from 8 to 16. The majority of patients had moderate to severe symptoms (8–12); nine patients had a combination of severe symptoms (≥ 13). The frequency of positive skin tests for each of the allergens tested is shown in Figure 2. Thirty-four of forty-four patients had a strongly positive skin test to *D. pteronyssinus*, 8/44 to cat dander, 5/44 to cockroach, 3/44 to fish, 3/44 to dog, 2/44 to *Cladosporium*, 2/44 to cow's milk, and 1/44 to soybean, shrimp, peanut, egg white, and *Alternaria*, respectively. The distribution of dimensions of erythema and wheal of skin reactions to each of the 12 allergens tested with the Stallerpoint is shown in Figure 3. The reactions to *D. pteronyssinus* were the strongest by far. The relatively high number of negative (<9 mm erythema, <4 mm papula) skin reactions to histamine was probably due to the weak concentration of histamine we had to use. The IVT allergy tests positive results are shown in Figure 4. Forty-two of forty-four tested strongly positive to *D. pteronyssinus*, 1/44 to the combination fish/shrimp, and 1/44 to rice. Distribution of total IgE by IVT is shown in Figure 5: 2/44 had levels <30 IU/ml, 18/44 had levels 30–90 IU/ml, and 25/44 had elevated levels ≥ 90 IU/ml (most >200 IU/ml according to the speed and intensity of the color reaction). The correlation between allergy score and IgE as measured by the IVT allergy test is shown in Figure 6.

DISCUSSION

Information on the allergic aspects of asthma and respiratory allergic diseases in Hong Kong is still incomplete. The ultimate appropriate diagnosis is made only in selected groups of populations who have been

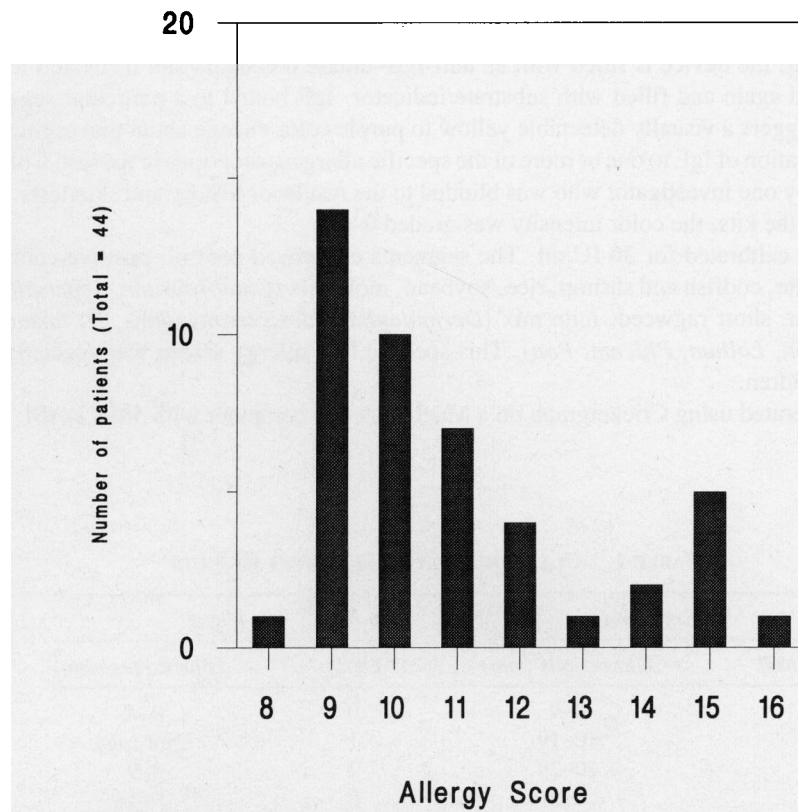


FIG. 1. The frequency of allergy scores based on our criteria. Only those patients with atopy scores greater than or equal to 8 were included in our study.

ALLERGIC CHINESE CHILDREN IN HONG KONG

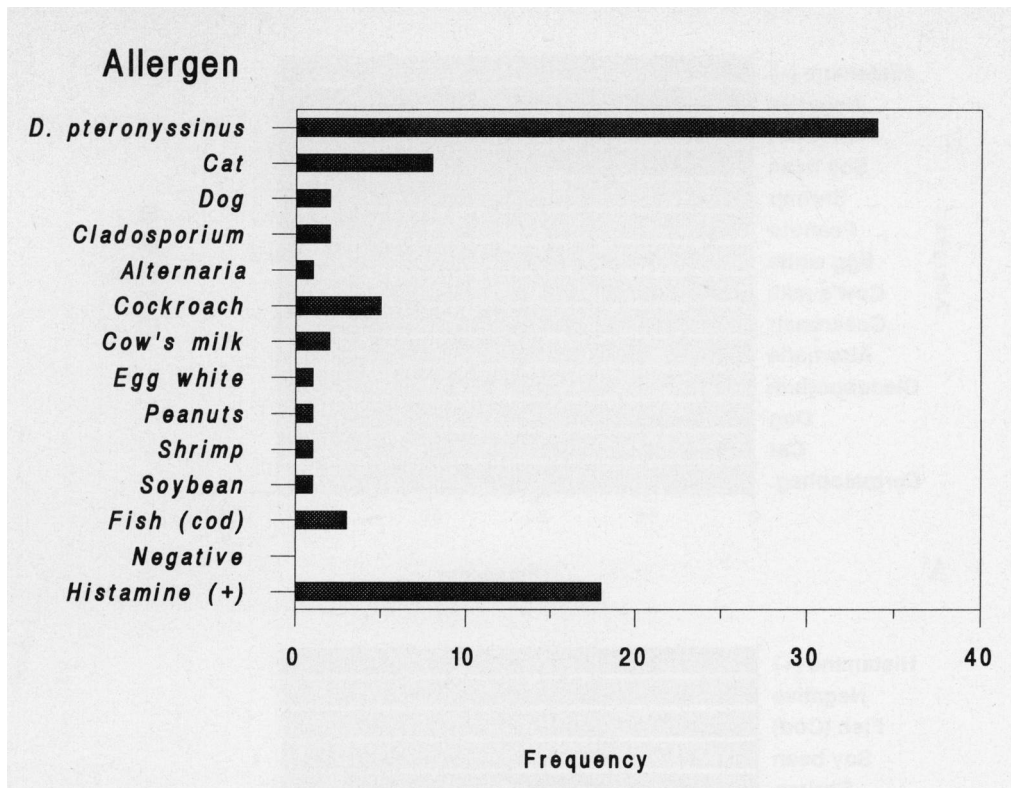


FIG. 2. The number of patients with positive skin tests to each of the 12 allergens tested. *Dermatophagoides* is the predominant allergen in Hong Kong, followed by cat and cockroach.

influenced by westernized education and medicine or by failure of the inexpensive traditional Chinese approach. However, HLA studies suggest that Chinese and Caucasian populations differ in both types and frequency of HLA-associated gene(s) that predispose to atopic disease.^(5,9) Racial differences in immunoglobulin development have been reported.⁽⁹⁻¹²⁾ Incidence and severity of atopic diseases have been reported in Asians.⁽¹³⁾ The mean total serum IgE levels for Chinese asthmatic children in Taiwan were 1643 ± 1231 IU/ml compared to 67 ± 86 IU/ml in control children ($p < 0.001$).⁽¹⁴⁾ In Japan, the median values and range of serum IgE were 1050 IU/ml and 20–10,000 IU/ml respectively in 308 children with bronchial asthma.⁽¹⁵⁾ In Thailand, serum IgE, measured in 120 children, revealed that 87.5% had serum IgE above 400 IU/ml, whereas 78% of 50 normal children as control had serum IgE below 400 IU/ml.⁽²⁾ A study in Hong Kong showed that the IgE was 963 ± 475 IU/ml (range 2–1857).⁽⁴⁾

We decided to screen a population of children with a limited number of allergens. Previous studies had demonstrated that the prevalent allergens in Hong Kong were house dust mites, pets, molds, and some foods. These data were correlated with similar results published in Taiwan,^(14,16) the People's Republic of China,^(17,18) Thailand,⁽²⁾ Japan,⁽¹⁵⁾ Singapore,⁽¹⁹⁾ The Philippines, and even Korea.⁽²⁰⁾ The major allergen in Hong Kong is the house dust mite, either *D. pteronyssinus* or *D. farinae*.^(3,4) We found a very high incidence of both skin sensitivity and specific IgE to house dust mites. It has been reported that samples of house dust and the filling of Chinese quilts contain very large numbers of both *D. farinae* and *D. pteronyssinus*. A finding of importance was made in examination of the cotton filling of a quilt, where over 500 mites were counted in an area of about 6 square inches. These quilts are used by all patients, being normally the only form of bed covering during the winter months from October until March or April. This time interval coincides with the season of asthma in Hong Kong. The climate of Hong Kong is ideal for the growth of house dust mites, with high humidity and moderate temperatures throughout most of the year.⁽³⁾ Animals, which are present in 40% of homes, appeared to be potentially of importance, but this was demonstrated in our study only by skin testing. Changes in the home and microenvironment caused by stirring up of dormant particles by heaters at

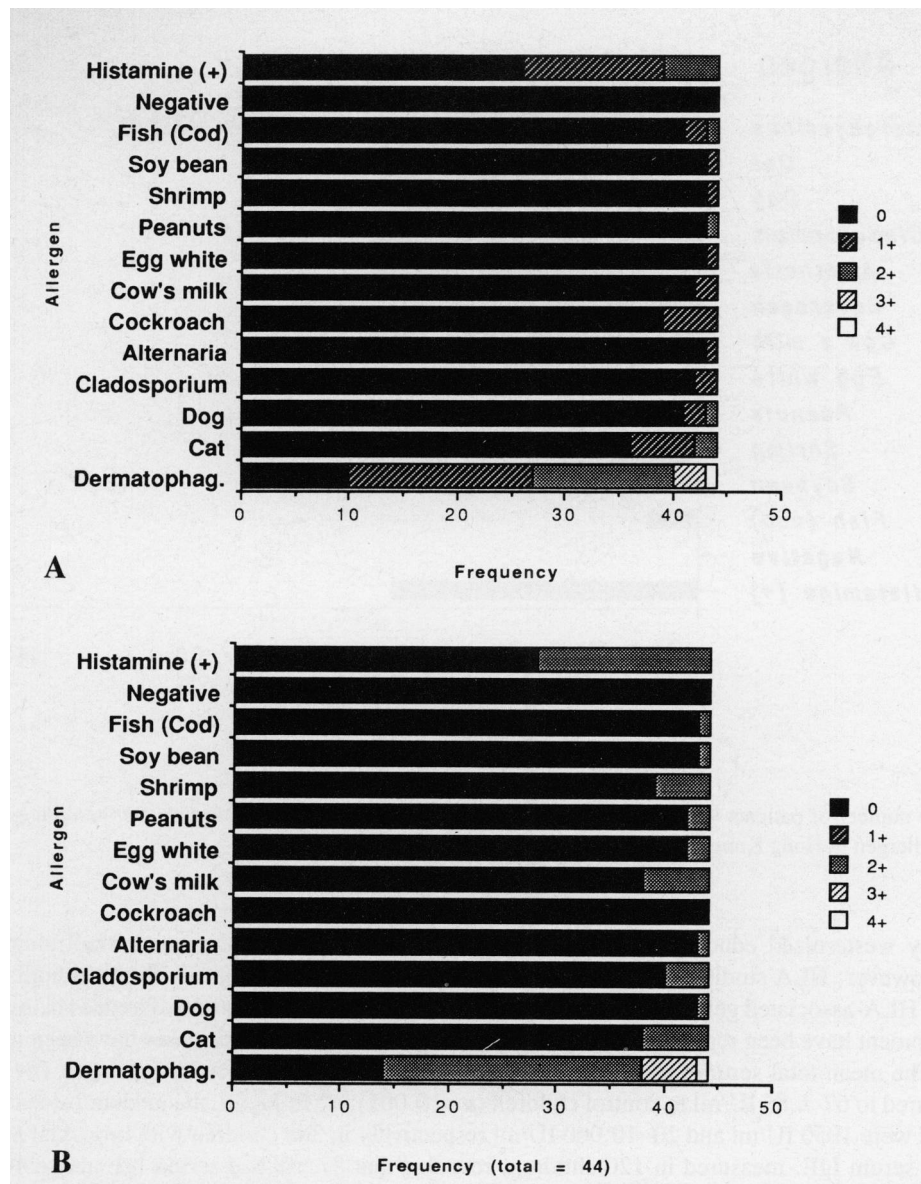


FIG. 3. Distribution of skin test dimensions of erythema (Fig. 3a) and wheal (Fig. 3b) for each of the allergens tested. There were a total of 44 patients tested. The class of allergic response was defined as follows:

<i>Erythema</i>		<i>Wheal</i>	
<i>Class</i>	<i>Dimension</i>	<i>Class</i>	<i>Dimension</i>
0	0–9 mm	0	0–4 mm
1	10–19 mm	1	not used
2	20–29 mm	2	5–9 mm
3	21–29 mm	3	10–14 mm
4	> 29 mm	4	> 14 mm

the beginning of winter or air conditioners at the start of summer also might contribute, an indirect association with seasonal changes. There are two peaks of asthmatic admissions in Hong Kong, a major one in November and a smaller peak 6 months apart in May.⁽¹¹⁾

ALLERGIC CHINESE CHILDREN IN HONG KONG

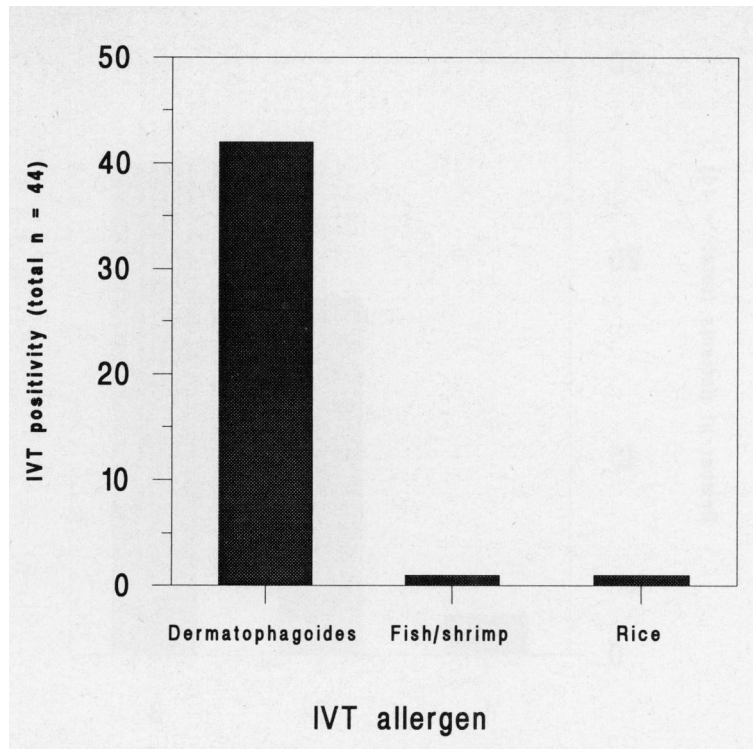


FIG. 4. The number of patients with positive in vitro allergen-specific IgE tests. Twelve allergens were tested. *Dermatophagoides* was the predominant allergen, and only two other tests were positive to fish/shrimp in 1 patient and rice in another.

Food may be an underestimated factor for allergies in Chinese children in Hong Kong. In Thailand, 10% of children showed positive reactions to food materials, with shrimp being the most common, whereas egg white, cow's milk, and fish were found to be less common, in that order.⁽²⁾

The selection of allergens for skin testing and the choice of Stallerpoint were motivated by practical and economic considerations. Chinese patients have limited resources, and the system of health coverage in the territory of Hong Kong is different from those in Western Europe and the United States. The use of a Stallerpoint is very simple and easy, and its reliability has been confirmed by different studies.^(6,21) We included in the skin testing the mites and animal allergens, as well as some molds, but restricted the foods. Conversely, the IVT allergy tests, which was especially designed for Southeast Asia, comprised several food allergens that were not included in skin testing, since the RAST-type determination has been demonstrated in several studies to be more reliable than skin tests.^(22, 23) The size of the IVT allergy test device limited the number of allergens to 13, and we are currently considering two IVT allergy tests for screening populations in Southeast Asia—one that will be very similar to the one used in this study, and another that will address a more extensive number of airborne allergens.

Laboratory measurements of total serum IgE and eosinophil levels correlate insufficiently with the diagnosis of allergy to be used alone as confirmatory tests.^(24,25) Although diagnostic skin tests remain the benchmark for identifying relevant IgE antibodies,⁽⁵⁾ the applicability of skin tests for nonspecialist physicians who treat the bulk of the affected population is limited. More readily accessible serologic tests of specific IgE antibodies done in commercial laboratories are based on the radioallergosorbent test (RAST). These in vitro tests have decreased sensitivity, cost effectiveness, and timeliness compared with the skin tests.⁽²⁶⁾ An ideal screening test for allergy would detect IgE antibodies for 6–15 representative allergens,⁽²⁷⁾ be as sensitive and specific as the skin tests and as cost effective and time effective, and be designed for use

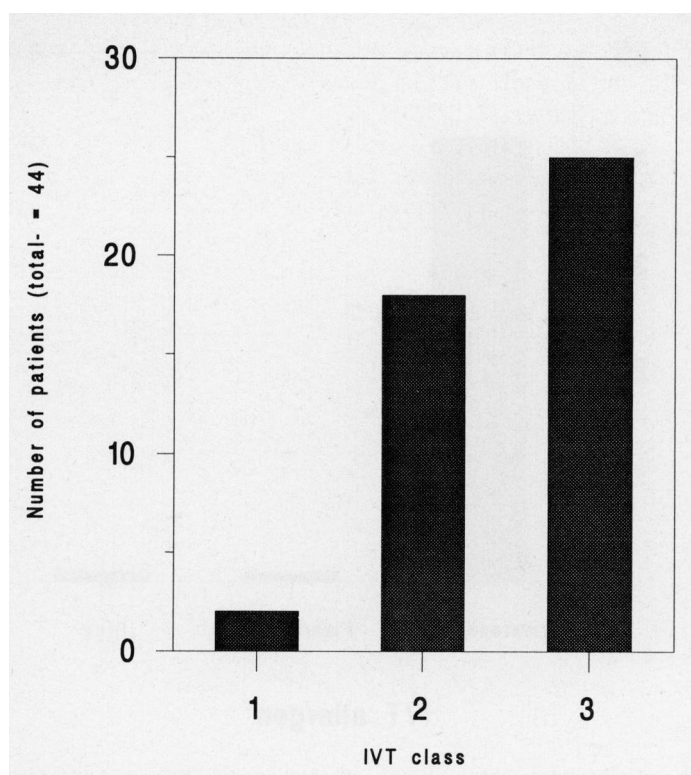


FIG. 5. A breakdown of the total IgE levels obtained from the IVT. All patients had at least 1+ IgE.

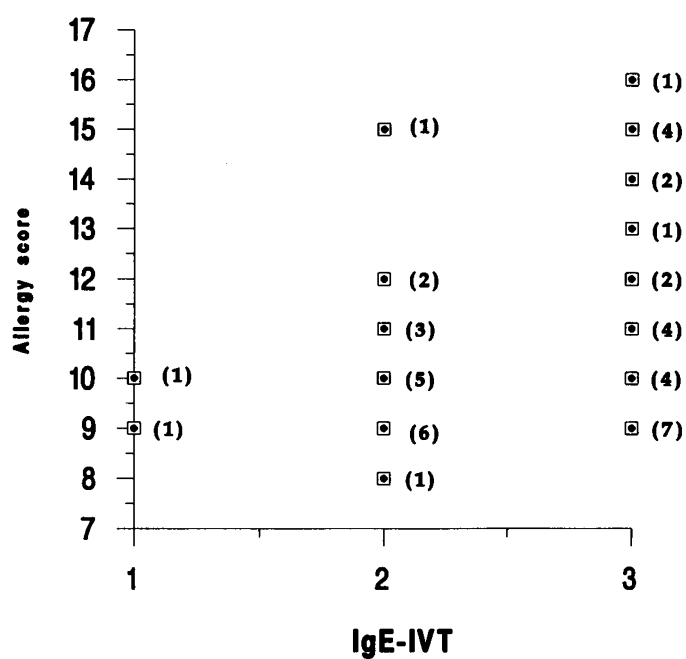


FIG. 6. The correlation between allergy score and the total IgE as obtained by IVT is shown. The number of patients corresponding to each datapoint is shown in parenthesis.

ALLERGIC CHINESE CHILDREN IN HONG KONG

in a primary care setting without complex equipment or highly specialized personnel. New methods for measuring allergen-specific IgE antibodies in the serum use a multiallergen device in an ELISA designed for visual detection by color intensity in less than 3 hours.^(6,28)

The purpose of these screens is to provide easy, rapid, and cost-effective means of screening for allergic disorders in primary care settings. These tests are proposed as an allergy screen and not as a diagnostic tool for initiating a comprehensive, specific treatment program that includes avoidance measures, environmental controls, and so on.

However, we believe that further research is needed before selecting either a limited panel of skin prick tests, or an in vitro screen (e.g., IVT). Our present study confirms that some allergens can be identified more precisely by one and not the other assay. Until such problems are resolved, the complemented use of screens by skin prick tests and user-friendly IgE in vitro assay can be recommended in Hong Kong.

ACKNOWLEDGMENTS

We want to express our gratitude to Professor Faith C.S. Ho, Chairperson, Department of Pathology, University of Hong Kong, and John W. Lawton, M.D., Brian Jones, Ph.D., David Higgins, D.V.M., Ph.D., who helped us for this study. Michel Garcelon, M.D. (Stallergenes, Fresnes, France), Kenneth A. Kelly, Ph.D. (IVT, Arlington, TX), Brian Hewitt, Ph.D. (3M Diagnostic Systems, Santa Clara, CA) kindly supplied the material and reagents. Joseph Silva, Jr., M.D., Chairman, Department of Internal Medicine and M. Eric Gershwin, M.D., Chief, Division of Rheumatology, Allergy and Clinical Immunology, University of California Davis School of Medicine, gave invaluable support to one of us (G.M.H.), allowing for the realization of this study. Nikki Rojo superbly typed the manuscript.

REFERENCES

1. Yeung CY. Childhood asthma—Some local viewpoints. *HK J Paediatr* 1988;5:95–104.
2. Tuchinda M, Habanananda S, Vareenit J, et al. Asthma in Thai children: A study of 2000 cases. *Ann Allergy* 1987;59:207–211.
3. Pickering CAC, Gabriel M. The pattern of atopy and asthma in the Chinese of Hong Kong. *Bull HK Med Assoc* 1973;25:95–100.
4. Tseng RYM, Lam CYK, Pang JCK. Allergy testing in asthmatic children: Further information or further confusion? *HK J Paediatr* 1989;6:91–97.
5. Kaufman HS, Kelly PT, Modin GW. Antigen recognition in Chinese and Caucasians. *Ann Allergy* 1984;53:135–137.
6. Guerin B, Watson RD. Skin tests. *Clin Rev Allergy* 1988;6:211–227.
7. Paquet F, Boulet LP, Bedard G, et al. Influence of time of administration on allergic skin prick tests response. *Ann Allergy* 1991;67:163–166.
8. Errigo E. New perspectives in serological tests for the diagnosis of allergic disorders. *Proceedings of the XV World Congress of Anatomic and Clinical Pathology* 1989;387–391.
9. Schwartz BD, Shreffler DC. Genetic influences on the immune response. In: Parker CW, ed. *Clinical immunology*. Philadelphia: WB Saunders Co., 1980;1:49–85.
10. Kaufman HS, Kvitash VI. Racial differences in antigen recognition among allergic Japanese, Chinese and Caucasians. *Immunol Allergy Pract* 1985;7:458–461.
11. Wong KW, Davies DP. Seasonal variations in asthmatic admissions. *HK J Paediatr* 1985;2:19–23.
12. Orgel HA, Lenoir MA, Bazara M, et al. Serum IgG, IgA, IgM and IgE levels and allergy in Filipino children in the United States. *J Allergy Clin Immunol* 1974;53:213–218.
13. Kaufman HS, Ranek K. Antigen recognition in Filipinos, Japanese, Chinese and Caucasians. *Ann Allergy* 1988;60:53–56.

14. Tsai LC, Tang RB, Hung MW, et al. Correlation between serum IgE and specific IgE antibody titer to house dust mite in children with asthma. *J Asthma* 1988;25:7–13.
15. Kuno-Sakai H. Total serum IgE and specific IgE antibodies in children with bronchial asthma. *Ann Allergy* 1986;56:488–491.
16. Tang RB, Tsai L, Hwong HM, et al. The prevalence of allergic disease and IgE antibodies to house dust mite in school children in Taiwan. *Clin Exp Allergy* 1990;20:33–38.
17. Chien YK, Yang WP, Xue ZL, et al. House dust mite asthma in China: A review. *Ann Allergy* 1987;59:147–148.
18. Chen KE, Liao YF, Zhang J. The major aeroallergens in Guangxi, China. *Clin Allergy* 1988;18:589–596.
19. Tan WC, Teoh PC. An analysis of skin prick test reactions in asthmatics in Singapore. *Ann Allergy* 1973;43:44–46.
20. Halpern GM, Lau YL. Comparing asthmatic Asian and American children. *Clin Adv Asthma* 1990;1(6):11–16.
21. Ryhal BT, Halpern GM, Davis P, et al. A comparison of four prick skin test devices in patients with allergic rhinitis. *Immunol Allergy Pract* 1991;13:355–358.
22. Johansson SGO, Yman L. In vitro assays for immunoglobulin E. Methodology, indications and interpretations. *Clin Rev Allergy* 1988;6:93–139.
23. Bahna SL. Diagnostic tests for food allergy. *Clin Rev Allergy* 1988;6:259–284.
24. Geha RS. Human IgE. *J Allergy Clin Immunol* 1985;74:109–120.
25. Kajosaari M, Saarinen UM. Evaluation of laboratory tests in childhood allergy—Total serum IgE, blood eosinophilia and eosinophils and mast cells in nasal mucosa of 178 children aged 3 years. *Allergy* 1981;36:329–335.
26. Adkinson NF Jr. The radioallergosorbent test in 1981—Limitations and refinements. *J Allergy Clin Immunol* 1981;67:87–89.
27. Friedhoff LR, Marsh DG, Meyers DA, et al. The structuring of an allergy index based on IgE-mediated skin sensitivity to common environmental allergens. *J Allergy Clin Immunol* 1983;72:274–287.
28. Iman AA, Novey HS, Orgel HA, et al. A simplified screening test for the diagnosis of allergy. *West J Med* 1990;152:313–316.

Address reprint requests to:
Georges M. Halpern, M.D.
Division of Rheumatology, Allergy
and Clinical Immunology
University of California
TB 192, School of Medicine
Davis, CA 95616

This article has been cited by:

1. Moira CHAN-YEUNG, Christopher K.W. LAI, Kin-Sang CHAN, Amy H.K. CHEUNG, Tzy-Jyun YAO, Alice S.S. HO, Fanny W. KO, Loretta Y. YAM, Poon-Chuen WONG, Kenneth W. TSANG, Wah-Kit LAM, James C. HO, Chung-Ming CHU, Wai-Cho YU, Hok-Sum CHAN, Mary S.M. IP, David S. HUI, Cheuk-Yin TAM. 2008. The burden of lung disease in Hong Kong: A report from the Hong Kong Thoracic Society. *Respirology* **13**, S133-S165. [[CrossRef](#)]