

Intracutaneous Tests, Radioallergosorbent Tests, Total Serum IgE Determinations, Total Eosinophil Counts and Nasal Eosinophilia in the Diagnosis of Allergic Diseases*

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During the 12-year period from 1973 to 1984, the prevalence of bronchial asthma in school children in Taipei city increased from 1.34 per cent to 5.80 per cent (unpublished data). In addition, the severity of the disease had also increased as judged from the frequency and duration of attacks and the requirement for medications, including steroids. Therefore, it has become urgent to diagnose and treat patients with allergic diseases as early as possible to prevent the occurrence of irreversible organ damage.

Since the description of the skin test as a diagnostic procedure in clinical allergy by Charles Harrison Blackley in the 1860s,¹ several *in vitro* and *in vivo* tests have been developed for the diagnosis of allergy. They include non-specific tests such as total serum IgE, total eosinophil count (TEC) and nasal smear for eosinophilia and specific tests to detect allergen(s) such as immediate type skin test, radioallergosorbent test (RAST) and bronchial provo-

SUMMARY Intracutaneous skin testing with house-dust and five fungal extracts, total serum IgE concentration (PRIST), radioallergosorbent test (RAST) for house-dust, total eosinophil count (TEC) and nasal eosinophilia were performed in order to evaluate their clinical usefulness on 34 patients with bronchial asthma, 55 with rhinitis, 25 with other allergies, and 61 normal subjects. Their ages ranged from 13 to 19 years. The results showed: 1) The skin test-positive reaction to at least one allergen for the four groups studied was 91.2 per cent, 83.6 per cent, 52.0 per cent and 23.0 per cent, respectively; 2) TEC was $319 \pm 175/\text{mm}^3$, $194 \pm 152/\text{mm}^3$, $143 \pm 106/\text{mm}^3$ and $110 \pm 71/\text{mm}^3$, respectively; 3) total serum IgE level was $1,212 \pm 1,149$ IU/ml for asthma and 260 ± 170 IU/ml for normal subjects; 4) house-dust RAST was positive ($\geq 2+$) in 97 per cent (32/33) of the asthmatic patients but in only 10 per cent (3/30) of the normal subjects and there was a good correlation between skin test and RAST for house-dust; and 5) nasal eosinophilia was positive in 25 per cent of rhinitis patients (especially in skin test-positive individuals), in 35 per cent of asthma patients and in none of the normal subjects. It is concluded that these parameters are useful in making a proper evaluation of allergic patients.

ASIAN PACIFIC J ALLERG IMMUN 1985; 3:43-47.

cation test (BPT).

This project was conducted to study the clinical usefulness of the afore-mentioned tests in the diagno-

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sis of allergy. The results show that these tests are valuable parameters in managing allergic patients, especially when they are used as a panel of tests.

MATERIALS AND METHODS

Study populations

One hundred and seventy-five students aged from 13 to 19 years were included in this study. According to detailed personal and family allergic history and physical examination, they were divided into four groups; 34 with bronchial asthma and/or other allergic diseases, 55 with rhinitis but without asthma, 25 with other allergies such as urticaria, atopic eczema, conjunctivitis and food and drug allergy, and 61 healthy individuals. All of the patients were in remission when studied and none had taken any medication for at least one week. Informed consent was obtained before testing.

Skin testing

A panel of six common local inhalant allergens were used in this study. House-dust extract was prepared in our laboratory and was used at a concentration of 1,000x (W/V), five kinds of mould (*Candida*, *Alternaria*, *Cladosporium*, *Aspergillus* and *Penicillium*) were purchased from Torii & Co. of Japan and were used at a concentration of 10,000x. Four-hundredth of a millilitre of an allergen was injected intracutaneously through a 27-gauge needle and tuberculin syringe into the volar surface of the forearm to raise a wheal 5mm in diameter. The tests were read 15 minutes after administration and the results were recorded according to the following criteria: (-), wheal smaller than 6 mm in diameter; (1+), wheal of 6-9 mm; (2+), wheal of 10-14 mm; (3+), wheal larger than 14 mm; and (4+), wheal with pseudopods. In this study, a skin test of (1+) or greater was considered to be positive.

Radioallergosorbent test (RAST)

Specific IgE antibody to house-dust was determined by using the RAST method. Allergen discs coupled with locally collected house-dust were prepared in our laboratory according to the method of Ceska *et al.*,² other reagents such as ¹²⁵I-labelled antihuman IgE were purchased from Pharmacia Diagnostics of Sweden. A RAST score of (2+) or greater was considered to be positive.

Determination of total serum IgE

Total serum IgE levels were measured utilising commercially available phadebas IgE PRIST kits (Pharmacia Diagnostics, Sweden).

Total eosinophil count

Total eosinophil counts (TEC) were performed by the method of Horn *et al.*³

Nasal secretion smear

Nasal secretions were collected by the method of Bryan *et al.*⁴ A swab was passed along the floor of the nose and the surface of the inferior turbinate in each nostril with a twisting motion. The nasal secretion was painted on a slide and stained. Nasal eosinophilia was considered positive if the eosinophils accounted for more than 25 per cent of the cells present in one microscopic field at 400x magnification.

Statistics

The student's t test was used for statistical analysis throughout the study.

RESULTS

The results of skin tests are shown in Table 1. The percentage of patients skin test-positive to at least one of the allergens was 91.2 per cent for bronchial asthma, 83.6 per cent for rhinitis, 52.0 per cent for other allergies and 23.0 per cent for normal subjects. The positive reaction in patients with respiratory

allergy was much higher than that in normal subjects ($P < 0.001$). Sex had no bearing on skin reactivity. In all four groups, the positive reaction to house-dust was twice that to fungal extracts (Table 2).

The mean total serum IgE concentrations and house-dust RAST in 33 asthmatics and 30 age-matched normal subjects are shown in Table 3. The mean total serum IgE concentration of patients was much higher than that of normal subjects ($1,212 \pm 1,149$ vs 260 ± 270 , $P < 0.001$). Eighty-nine per cent of the patients had serum IgE higher than mean +1 SD. While 97 per cent (32/33) of the patients showed positive RAST (score $\geq 2+$), only 10 per cent (3/30) of the normal subjects gave a positive result. Furthermore, there was a very good correlation between skin test and RAST (Fig. 1 and Table 4).

Table 1 The results of intracutaneous tests with fungal allergens and house-dust extract

Subjects	No. tested	No. positive #
Normal		
M	43	10 (23.3%)
F	18	4 (22.2%)
	61	14 (23.0%)†@
Rhinitis		
M	43	35 (81.4%)
F	12	11 (91.7%)
	55	46 (83.6%)@**
Asthma		
M	30	28 (93.3%)
F	4	3 (75.0%)
	34	31 (91.2%)
Other allergies		
M	20	9 (45.0%)
F	5	4 (80.0%)
	25	13 (52.0%)†**

positive to at least one of the allergens used.
† $P < 0.01$; @ $P < 0.001$; ** $P < 0.02$

Table 2 Comparison of the intracutaneous test with fungal allergens and with house-dust extract

Subjects	No. tested	House-dust no. +ve (%)	Fungal extracts# no. +ve(%)
Normal	61	13 (21.3)	5 (8.2)
Other allergies	25	12 (28.0)	6 (24.0)
Rhinitis	55	42 (76.4)	24 (43.4)
Asthma	34	31 (91.2)	12 (35.0)

#positive to at least one allergen.

Table 3 The mean total serum IgE concentrations and house-dust RAST in asthmatics and age-matched controls

Subjects	Total serum IgE (mean \pm SD)	IgE \geq mean \pm 1SD No. of cases	RAST \geq 2+ No. of cases
Normal (n = 30)	260 \pm 170*	5 (16.6%)	3 (10.0%)#
Asthma (n = 33)	1 212 \pm 1 149*	29 (89.0%)	32 (97.0%)#

*P < 0.001; #P < 0.001.

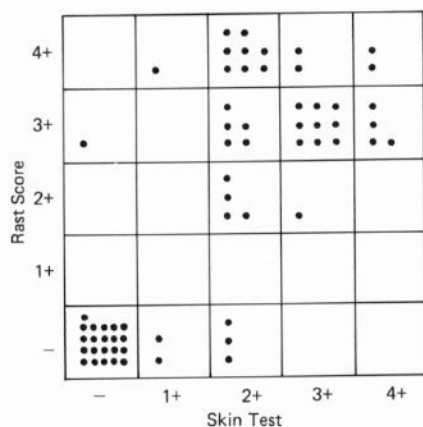


Fig. 1 Correlation between skin test and RAST for house-dust

The total eosinophil counts (TEC) in the four groups studied are presented in Table 5. The mean TEC of both the asthma and rhinitis groups was much higher than that of the normal group (319 ± 175 vs 110 ± 71 , $P < 0.001$ and 194 ± 152 vs 110 ± 71 , $P < 0.001$).

Table 6 shows that about one third of each of the three allergy groups had nasal eosinophilia, but none of normal subjects had such a phenomenon.

neous reaction. Subsequent studies by many investigators have now firmly established the clinical usefulness of skin testing in the diagnosis of allergy, especially after a good correlation has been found between skin testing and newly developed diagnostic procedures, such as total serum IgE,⁵ specific IgE antibody⁶ and bronchial provocation test.^{7,8}

Six common inhalant allergens, including house-dust and five moulds, were used for skin testing. The fact that the patients with respiratory allergy (asthma and rhinitis) had a much higher incidence and greater intensity of positive skin test than did the normal subjects (Table 1) clearly shows that skin testing can be used not only to detect allergen(s) but also to differentiate between allergic patients and normal subjects. The results obtained in this study, i.e. that more than 90 per cent of the childhood asthmatics were sensitive to house-dust but only one third of them were sensitive to moulds (Table 2), were in agreement with other previous studies made in Taiwan.⁹⁻¹³ It is worth noting that 20 per cent of the normal subjects also showed positive skin test, although less intensely and less frequently than did allergic individuals. This phenomenon had also been reported by other investigators although the incidence ranged widely from 1.5 per cent to 33.7 per cent.¹⁴⁻¹⁶ However, the skin reaction revealed allergen

DISCUSSION

The use of skin testing as a diagnostic test in clinical allergy dates back to the studies on hay fever by Charles Harrison Blackley in the 1860s. In his book describing his researches on the causes and nature of summer catarrh, he described scarifying a large area of the skin of his forearm and applying moist pollen. The first attempt produced a wheal $2\frac{1}{2}$ by $1\frac{1}{2}$ inches in diameter and was followed by a late cuta-

Table 4 Correlation between skin tests and RAST for house-dust

RAST (n = 63)*	Skin test score				
	-	1+	2+	3+	4+
Positive (\geq 2+) (N = 37)	1	1	17	12	6
Negative (\leq 1+) (N = 26)	21	2	3	0	0
Correlation	95%	66%	85%	100%	100%

*Including 33 asthmatics and 30 normal subjects

Table 5 Total eosinophil counts (TEC)

Subjects	TEC (mean \pm SD)	TEC > mean + 1 SD for normals No. of cases
Normal	110 \pm 71*†	10 (16.7%)
Other allergies (n = 25)	143 \pm 106	5 (20.0%)
Rhinitis (n = 55)	194 \pm 152*@	22 (40.0%)
Asthma (n = 34)	319 \pm 175†@	27 (79.4%)

*P < 0.001, † P < 0.001, @ P < 0.001

Table 6 Nasal eosinophilia

Subjects	No. tested	No. positive		
		skin test +	skin test -	Total
Normal	13	0	0	0 (0%)
Other allergies	3	1	0	1 (33%)
Rhinitis	44	10	1	11 (25%)
Asthma	20	6	1	7 (35%)

specificity because such hypersensitivity could be passively transferred to other healthy subjects.¹⁷

The significance of determination of total serum IgE and specific IgE antibody in clinical allergy has been reviewed extensively.^{18,19} Due to racial differences, socio-economic status and criteria in selecting a "normal" population, the IgE concentration reported for healthy individuals varied widely. In developed western countries, 100 IU/ml is usually chosen as the cut-off point to separate allergic patients from normal subjects.^{18,20,21} However, studies undertaken in Singapore²² and India²³ reported a value as high as 1,000 IU/ml. The results obtained in this study, i.e. that the mean total serum IgE level for normal subjects was 260 \pm 170 IU/ml and a value of 400 IU/ml could separate allergic patients from normal subjects (Table 3), were comparable to those obtained in our study reported two years ago,²⁴ but was lower than that published eight years ago.²⁵ Again, the discrepancy might be due to the country's socio-economic progress on the one

hand and differences in the population studied on the other. The mean total serum IgE level for asthmatic children was 1,212 \pm 1,149 IU/ml which was similar to the levels reported in our previous studies. In this study, a very good correlation was found between skin test and RAST (Fig. 1 and Table 4) and this result is in agreement with those reported by many investigators,¹⁹ including our own previous studies.^{8,11}

Allergy is one of the diseases characterised by eosinophilia and the measurement of total eosinophil count (TEC) is one of the essential laboratory examinations for the proper evaluation of asthmatic patients.³ The mean TEC of 110 \pm 71/mm³ found in this study was within the ranges reported by many investigators, including our own (138 \pm 117/mm³).²⁵ TEC was increased (> mean +2 SD) in 60 per cent of the asthmatic children; this figure was similar to that reported by Hsieh²⁵ but was lower than that reported by Foucard (89%).²⁰ Horn *et al*³ described that the enumeration of TEC could be used to moni-

tor the dose of steroids in the treatment of bronchial asthma.

Nasal eosinophilia has been used for years as a diagnostic test in both adults and children with symptoms suggesting allergic rhinitis,^{30,31} although marked eosinophilia in nasal secretion and sputum may also be observed in non-allergic rhinitis and in intrinsic asthma.^{32,33} Although no nasal eosinophilia was found in normal subjects, the positive rate for nasal eosinophilia was rather low in patients with rhinitis (25%) and asthma (35%). The result that the positive rate for nasal eosinophilia was much higher in the skin test-positive patients (especially in the rhinitis group) is in agreement with that reported by Robert *et al*.³⁴

The low incidence of nasal eosinophilia in this study, in face of the high positive rate of skin test and frequent association with allergic bronchial asthma,³⁵ may be due to the methodology used for collecting nasal secretions (by nasal scraping instead of nasal blowing) and severity of disease (all of the patients were symptom-free when studied).

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