

Relationship of Allergen-Specific IgE Antibodies, Skin Prick Tests and Allergic Disorders in Unselected Adolescents

TARI HAAHTELA and ILMARI JAAKONMÄKI

Department of Pulmonary Diseases, Tiuru Hospital, Tiuruniemi, Finland

The relationship between serum levels of allergen-specific IgE (RAST) and skin prick test reactivity and allergic disorders was evaluated in 137 subjects randomly selected from an adolescent population. All subjects were prick tested with six common allergens, interviewed and physically examined. In addition, serum was collected for RAST analysis with three to six allergens. At least one positive RAST result (score 1-4) was observed in 40% and at least two positive RASTs in 22% of the subjects. Boys experienced more RAST reactions and generally with higher scores than girls. For instance, 26% of boys but only 11% of girls were RAST positive to timothy grass pollen.

The correlation between prick test and RAST results was better with pollens than with house dust and animal epithelia. When the test results were discordant, the skin test was usually positive and RAST negative. Many of the small skin reactions (weal diameter 3-4 mm) were accompanied by a negative RAST.

Respiratory allergy was closely connected with both positive skin test and RAST reactivity, while atopic dermatitis was less related. In 17% of the adolescents positive skin tests and in 14% positive RASTs occurred in the absence of any allergic symptom. We conclude that a positive RAST score 3-4 to inhaled allergens is a strong indicator of clinical allergy but low scores 1-2 are frequently found in healthy young people.

Key words: allergic disorders; allergy in adolescents; epidemiology of allergy; RAST; skin prick tests.

Accepted for publication 11 January 1981

CLINICAL ASPECTS

Skin tests producing immediate reactions and radioallergosorbent tests (RAST) for allergen-specific IgE antibodies are used to detect causative factors in allergy, especially respiratory tract allergy. Evaluation of the results in patients seeking care for allergic conditions is not straightforward. Knowledge of the natural history of skin reactivity and occurrence of specific IgE antibodies in unselected populations as well as their correlations to each other and to different allergic symptoms would facilitate interpretation of the test results.

It is well known that a positive skin reaction to any single allergen is frequently, but far from always, related to clinical hypersensitivity. It has been suggested that positive RAST results might have a better clinical relevance. Nevertheless, we found in 137 young people, randomly selected from an adolescent population, nearly as many healthy subjects with positive RASTs as with positive prick tests. Nineteen out of the 55 RAST positive (at least one RAST positive) adolescents were completely symptom-free. As expected, high levels of IgE antibodies were better correlated to the probability of manifest allergy than lower levels. The overall agreement of prick test and RAST results was satisfactory. However, many small prick responses were associated with a negative RAST. The RAST was seldom positive if prick test was negative.

Active treatment should be undertaken cautiously, without undue reliance on skin tests or RAST results.

In a population of young people many positive immediate skin prick test reactions to common allergens are found (9). A positive reaction to any single allergen is frequently, but far from always, related to clinical hypersensitivity to the allergen in question (10). Multiple positive reactions may be taken as an indication of an atopic constitution, whether clinical symptoms are present or not (14). The relationship between skin prick test reactions, specific IgE in serum as measured by the radioallergosorbent test (RAST), and allergic disorders in selected patient groups has been the subject of numerous studies. Knowledge of the correlations between these parameters in unselected populations is scanty. The occurrence of positive RAST results and their clinical relevance in general population samples is not established.

We report RAST results and their correlations to skin prick test reactions and allergic disorders in an unselected group of adolescents.

SUBJECTS AND METHODS

The original population, 708 15–17-year-old unselected students from the town of Imatra in southeast Finland, and the methods of symptom screening as well as skin prick testing have been described before (9, 10). All the subjects were physically examined by two specialists and skin prick tested with 16 extracts of 12 common allergens from two manufacturers (Bencard Ltd. and Dome Laboratories, U.K.). Additionally, 137 of these students (62 boys and 75 girls) were randomly selected for the determination of serum IgE antibodies to three to six allergens using the RAST method (Pharmacia, Uppsala, Sweden). The sera were collected in March and April. All were tested for IgE antibodies to dog and cat epithelia and to house dust. If a positive reaction to a pollen (birch, timothy grass, mugwort) was observed in prick testing, RAST testing with the allergen(s) in question was performed as well. Only those skin prick test results obtained with the six allergens mentioned above were included in the analysis and are presented in this paper.

A total of 485 RASTs were carried out. The RAST results were scored from 0 to 4 according to the scale given by the manufacturer. Score 1 was regarded as a positive RAST result in this investigation, although this may not be suitable for routine clinical purposes.

RESULTS

At least one positive RAST reaction (score 1–4) was observed in 44% of the boys and in 37% of the girls. The figures for at least one positive prick reaction (weal diameter 3 mm or larger) were 48% and 47% respectively. The cumulative incidence of positive skin and RAST reactions are shown in Fig. 1. Boys had significantly more positive RAST reactions than girls. For instance, 26% of boys but only 11% of girls were found to be positive to timothy grass pollen (Table 1). Boys also exhibited higher RAST scores than girls (Fig. 2). A positive prick reaction to pollen was followed by a positive RAST

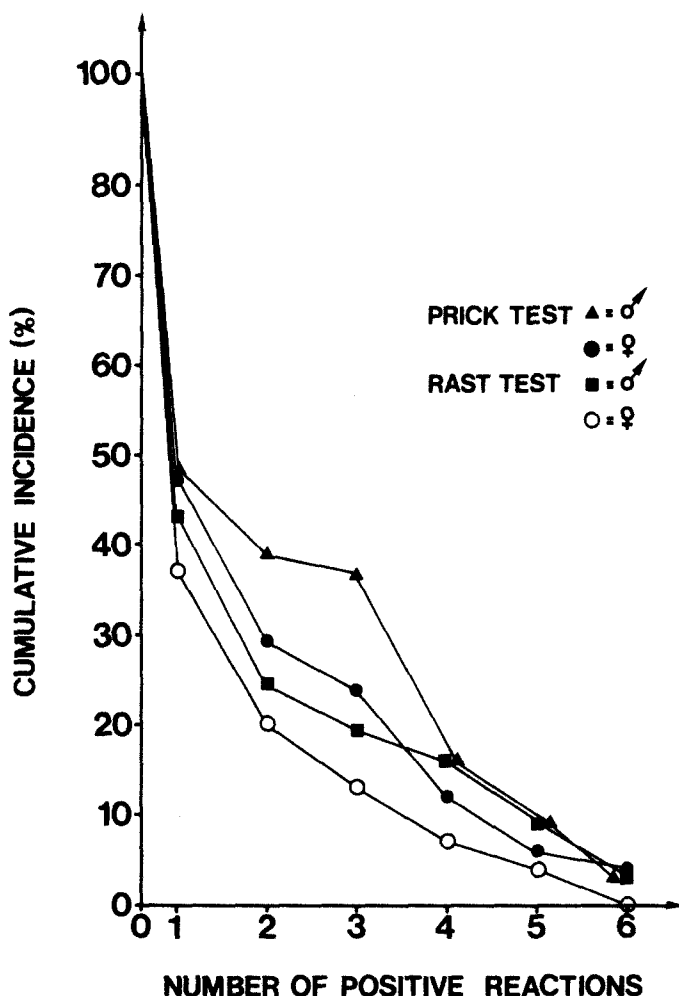


Fig. 1. Cumulative incidences of positive skin test and RAST results for six common allergens in boys and girls.

Table 1

Occurrence of positive skin prick test and RAST results in a random sample of 137 adolescents. RAST tests with pollens were performed only when the prick test was positive. Also given are the HEP values for the allergen preparations employed in prick testing as calculated from weals of a diameter ≥ 3 mm (positive reaction) (9). The HEP units are expressed in terms of a histamine reference of 1 mg/ml

Allergen	Supplier for prick testing	HEP	Percentage of positive reactions			
			Prick		RAST	
			Boys	Girls	Boys	Girls
Birch	Dome	18.9	15	17	13	15
Timothy grass	Dome	7.5	29	15	26	11
Mugwort	Dome	3.6	18	17	15	15
Dog epithelium	Bencard	0.9	19	11	18	8
Cat epithelium	Bencard	1.8	32	27	21	20
House dust	Bencard	1.3	40	36	24	15

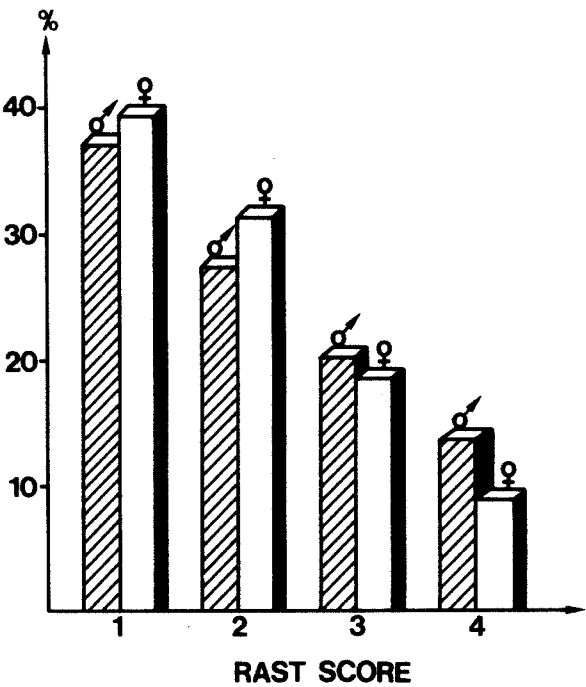


Fig. 2. Distribution of the positive RAST scores (1–4) in boys and girls.

in 63/75 tests (Fig. 3). The figure for dog and cat epithelia and house dust was 69/111 respectively (Fig. 4). The likelihood of a positive RAST was clearly increased with increasing size of the prick weal. Only 9/299 negative prick reactions to epithelia or dust were followed by a positive RAST.

Sixty-five per cent (36/55) of the RAST-positive subjects had experienced during the last year at least one of the following symptoms: recurrent bronchial wheezing, asthma, perennial allergic rhinitis, hay fever, atopic dermatitis or allergic urticaria. The definitions used for

these disorders have been described in our previous paper (10). Thus 19 adolescents (35%) with one or more positive RAST results were completely asymptomatic. On the other hand, symptoms mentioned above were present in 16 subjects (19%) belonging to the RAST-negative group. It should be noted that only three to six RASTs per subject were performed.

In subjects with bronchial wheezing including asthma, RAST was positive in 78%, with allergic rhinitis in 74% and with atopic dermatitis in 69%. The distribution of allergic disorders and wheezing among RAST-negative and -positive

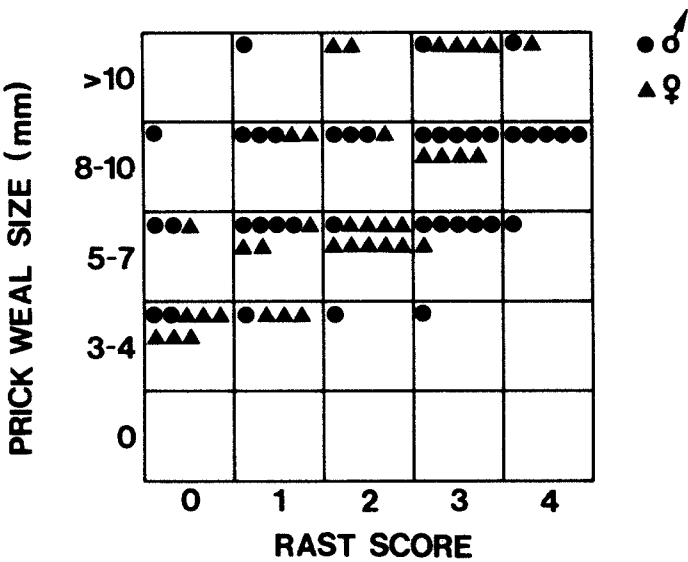


Fig. 3. Correlation between results of skin prick tests with birch, timothy grass and mugwort pollen extracts from Dome Laboratories, and Phadebas RAST allergosorbents with these pollens. RAST was not performed if skin prick test was negative.

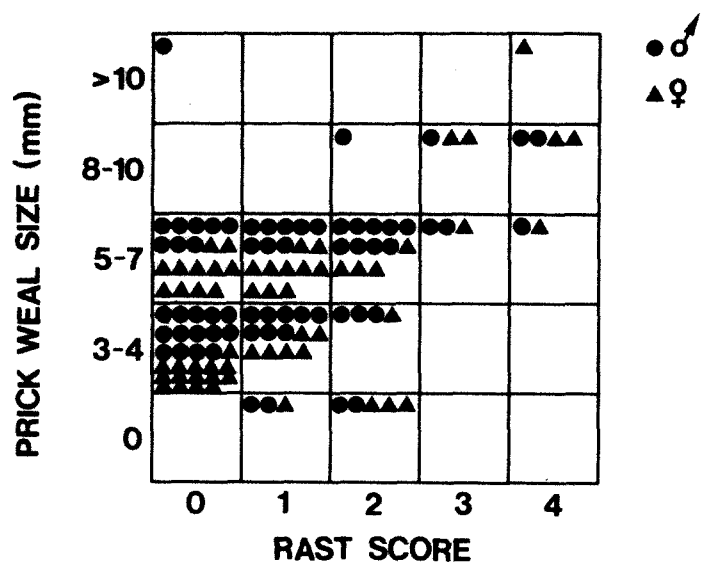


Fig. 4. Correlation between results of skin prick tests with dog and cat epithelia and house dust allergen extracts from Bencard, and Phadebas RAST allergosorbents with these allergens. RAST was performed with the three allergens regardless of the results in prick testing. Both prick test and RAST were negative in 290 tests (not shown).

subjects is indicated in Table 2. Twenty adolescents (15%) gave a history of clinical pollen allergy. All had a positive prick test to one or more of the pollens, and all except one a positive RAST result as well.

Forty-four per cent of the RAST-positive subjects had a positive history of respiratory or dermal allergy in parents or siblings. The figure in RAST-negative subjects was 30%.

When a general population is surveyed, a

great number of asymptomatic subjects with positive immediate skin reactions are found. There were 23 such individuals in the present population. In them many of the small prick test reactions (3–4 mm) were accompanied by a negative RAST result and no RAST score larger than 2 was observed (Fig. 5). However, there were 19 subjects (14%) with one or more RAST results in the range 1–2 and no symptoms.

DISCUSSION

In this unselected population of Finnish adolescents a high number of positive (score 1–4) RAST reactions to common allergens were observed. At least one positive RAST was found in 40% and at least two positive RASTs in 22% of the subjects, when three to six allergens were tested. Positive reactions were most prevalent with cat epithelium (20%) and house dust (19%). It should be noted that the sera were collected in the spring, when the level of pollen specific IgE is lower than after the season (3, 4). The British Thoracic and Tuberculosis Association (5) screened healthy non-allergic blood donors with five common allergens using the RAST technique. Specific IgE was detected in 11–17% of those 24–65 individuals tested for the allergen in question.

Table 2

Occurrence of active allergic disease and bronchial wheezing (symptoms present during the last year) in the RAST-negative and -positive adolescents. The percentages given indicate the distribution of symptomatic boys/girls between the RAST-negative and -positive groups and the total prevalences of the symptoms. Three to six RASTs per adolescent were performed

Symptom	RAST negative				RAST positive				Total			
	Boys		Girls		Boys		Girls		Boys		Girls	
	(n = 35,		(n = 47,		(n = 27,		(n = 28,		(n = 62,		(n = 75,	
	N	%	N	%	N	%	N	%	N	%	N	%
Bronchial wheezing including asthma	1	10	3	37	9	90	5	63	10	16	8	11
Allergic rhinitis including hay fever and perennial allergic rhinitis	3	18	7	33	14	82	14	67	17	27	21	28
Atopic dermatitis including allergic urticaria	3	27	6	33	8	73	12	67	11	18	18	24
One or more of the symptoms	6	24	10	38	19	76	17	62	25	40	27	37

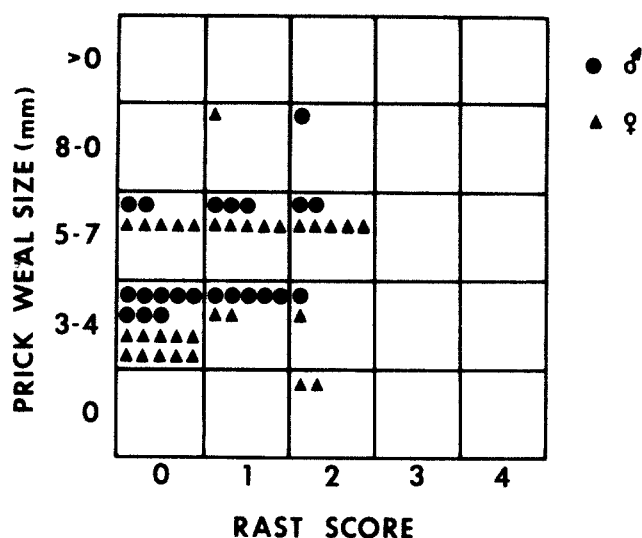


Fig. 5. Comparison of skin prick test and RAST results in nine boys and 14 girls who were asymptomatic, but showed at least one positive reaction in prick testing. Both prick test and RAST were negative in 34 tests (not shown).

We found boys to have more positive RAST results and higher RAST scores than girls. This fits our previous observations of higher skin test reactivity in boys (9). The higher atopic status, as judged by skin test and RAST results, is reflected in the higher frequency of hay fever and asthma observed in boys (10). The reason for the sex-difference, established in several studies, has not been satisfactorily explained.

Skin tests, especially when performed as an end-point titration procedure, correlate reasonably well with RASTs (12). When the skin prick test and RAST results have been discordant the skin test has been usually positive and the RAST negative, while negative RAST results have corresponded with negative provocation tests (16). Generally, the correlations have been better with pollen allergens than with house dust, mite and animal epithelia (13, 15). The overall agreement between RAST results and provocation tests has been reported to be about 85% (11). However, the correlation between results of different allergy tests is largely dependent on the quality of allergen extracts used. For instance, Aas & Lundkvist (2) found a 100% correlation between RASTs and provocation tests in 112 allergic children when the same highly purified allergen from cod-fish was employed in both tests.

In the present study, the correlations between prick tests and RASTs were similar to those

observed previously. (We employed allergens derived from different sources and manufacturers for the skin prick tests on one hand and for the RASTs on the other. This should be kept in mind, when the comparison of these two tests in our study is judged.) The correspondence was better with pollens (84% prick-positive subjects had a positive RAST) than with house dust and animal epithelia (62%), and the positive prick reaction accompanied by a negative RAST was generally a small one (Figs. 3, 4). Only a very few negative prick results to house dust or animal epithelia were followed by a positive RAST, and the scores were low. RASTs with pollens were not performed if prick tests were negative. Brown et al. (6) employed Bermuda grass allergen for prick tests and RASTs in their population study, and observed that 97.5% of the prick-negative subjects had a negative RAST. Of prick-positive subjects 78.5% had a positive RAST score. They stated: "when there was disagreement between tests, the reason was usually a small prick response associated with a negative RAST". Our observations agree with that.

Although positive skin tests do correlate with clinical symptoms of immediate hypersensitivity, it is well-established that skin test reactions are far from always accompanied by symptoms in the individual case and that a negative skin test does not exclude clinical hypersensitivity (8, 10). It has been suggested that unspecific positive reactions, including many small (2–4 mm) skin prick test reactions, are due to low-molecular weight impurities (irritants) in allergen extracts (1). However, this can only be part of the explanation. The RAST is not affected by the difficulty with the irritants, but we still observed that 19 out of the 55 RAST-positive adolescents were completely symptom-free. Further, 53% of the positive skin test reactions in asymptomatic individuals were accompanied by a positive RAST result to the allergen in question (Fig. 5). This suggests that at least half of the skin test reactions were IgE-mediated and immunologically specific also in asymptomatic subjects. On the other hand, a number of the small positive skin test reactions were accompanied by negative RASTs and no RAST score larger than 2 was observed in an asymp-

tomatic subject. Foucard & Johansson (7) have stated: "a positive RAST to inhaled allergens is a strong indicator of clinically relevant allergy as it is very rarely seen in healthy adults or in atopsics without symptoms". We would like to supplement the statement in the following way: a positive RAST score of 3–4 to an inhaled allergen is a strong indicator of clinical allergy, while low RAST scores of 1–2 are frequently found in healthy young people and have little clinical relevance. To what degree these asymptomatic subjects with positive skin prick tests and/or RAST scores of 1–2 will develop clinical allergy in the course of years can only be determined by means of a long-term follow-up.

There were also subjects with asthma, allergic rhinitis or atopic dermatitis without demonstrable IgE-antibodies or positive skin tests. This group with "intrinsic" type of symptoms is known to increase with age. In conclusion, respiratory allergy and to a lesser degree atopic dermatitis were found to be connected with both positive skin tests and RAST reactivity. However, tests which screen for immediate, IgE-mediated reactions cannot identify correctly all cases.

ACKNOWLEDGEMENTS

We are grateful to Mrs. Anita Nummelin for laboratory assistance and to Docent Fred Björkstén for constructive criticism. Pharmacia Diagnostics AB kindly supplied us with the reagents necessary for the RAST analyses. This work was supported by Allergiatutkimussäätiö.

REFERENCES

1. Aas, K.: Clinical and experimental aspects of standardization and purification of allergens. *Int. Arch. Allergy Appl. Immunol.* 49, 44–54, 1974.
2. Aas, K. & Lundkvist, U.: The radioallergosorbent test with a purified allergen from cod-fish. *Clin. Allergy* 3, 255–263, 1973.
3. Berg, T. & Johansson, S. G. O.: IgE concentration in children with atopic disease: a clinical study. *Int. Arch. Allergy* 36, 219–232, 1969.
4. Berg, T. & Johansson, S. G. O.: In vitro diagnosis of atopic allergy. IV. Seasonal variations of IgE antibodies in children allergic to pollens: a study of non-treated children and of children treated with inhalation of disodium cromoglycate. *Int. Arch. Allergy* 41, 452–462, 1971.
5. British Thoracic and Tuberculosis Association: Immunological features of asthma (Part III). *Clin. Allergy* 5, 403–416, 1975.
6. Brown, W. G., Halonen, M. J., Kaltenborn, W. T. & Barbee, A.: The relationship of respiratory allergy, skin test reactivity, and serum IgE in a community population sample. *J. Allergy Clin. Immunol.* 63, 328–335, 1979.
7. Foucard, T. & Johansson, S. G. O.: Indications and interpretations of RIST and RAST. *Paediatrician* 5, 228–236, 1976.
8. Godfrey, R. C. & Griffiths, M.: The prevalence of immediate positive skin tests to *Dermatophagoides pteronyssinus* and grass pollen in school children. *Clin. Allergy* 6, 79–82, 1976.
9. Haahtela, T., Björkstén, F., Heiskala, M. & Suoniemi, I.: Skin prick test reactivity to common allergens in Finnish adolescents. *Allergy* 35, 425–431, 1980.
10. Haahtela, T., Heiskala, M. & Suoniemi, I.: Allergic disorders and immediate skin test reactivity in Finnish adolescents. *Allergy* 35, 433–441, 1980.
11. Johansson, S. G. O.: In vitro diagnosis of reagin-mediated allergic diseases. *Allergy* 33, 292–298, 1978.
12. Miyamoto, T., Johansson, S. G. O., Ito, K. & Horiuchi, Y.: Atopic allergy in Japanese subjects: studies primarily with radio-allergosorbent test (RAST). *J. Allergy Clin. Immunol.* 53, 9–18, 1974.
13. Pepys, J., Roth, A. & Carroll, K. B.: RAST, skin and nasal tests and the history in grass pollen allergy. *Clin. Allergy* 5, 431–442, 1975.
14. Pepys, J. & Davies, R. J.: Allergy. In Clark, T. J. H. & Godfrey, S. (eds.): *Asthma*, p. 126, Chapman and Hall, London, 1977.
15. Stenius, B. & Wide, L.: Reaginic antibody (IgE), skin, and provocation tests to *Dermatophagoides culinae* and house dust in respiratory allergy. *Lancet* ii, 455–458, 1969.
16. Wide, L.: Clinical significance of measurement of reaginic (IgE) antibody by RAST. *Clin. Allergy* 3, (Suppl.), 583–595, 1973.

Address:

Dr. Tari Haahtela
Tiuru Hospital
SF-55330 Tiuruniemi
Finland

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.