

In vitro diagnosis of atopic allergy in children

A comparison between total IgE, conventional RAST and a new multi RAST (Phadiatop®)

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A new multi RAST (Phadiatop®) was compared with conventional RAST and total IgE determination (PRIST) for the diagnosis of IgE-mediated allergy in children. Serum specimens were tested from 100 children with a suspected IgE-mediated allergy, restricted to the eyes and/or the respiratory tract, to inhalant allergens. Compared with a RAST panel of 12 allergens representing seven groups, the new multi RAST showed a sensitivity of 95% and a specificity of 100% with a predictive value for positive test of 100% and for negative test of 91%. Corresponding figures for total IgE elevated > 2 SD above mean determined with PRIST were 47%, 88%, 84% and 56% respectively. We conclude that multi RAST might be a good adjunct to the clinical diagnosis of IgE-mediated allergy to inhalant allergens.

Key words: total IgE determination; inhalant allergens; multi RAST (Phadiatop®); PRIST; RAST.

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After the discovery that reaginic antibodies belong to a particular immunoglobulin class, IgE (3, 4), sensitive radioimmunoassays were developed to quantitatively measure total IgE (RIST, PRIST) and to demonstrate specific IgE antibodies (RAST) in serum (1, 7, 8). These *in vitro* methods have proved to be good adjuncts to the clinical diagnosis of atopic allergy. Even though a significantly increased level of serum total IgE has a relatively high specificity for atopic allergy there is a general clinical experience that the sensitivity of this *in vitro* test is low. The determination of serum total IgE has therefore a limited value in screening for atopic allergy.

Recently, a new multi RAST (Phadiatop®), Pharmacia Diagnostics, Uppsala, Sweden) was introduced and reported to have both a high sensitivity and specificity for *in vitro* diagnosis of atopic allergy in adults against common inhalant allergens (9). As this would seem preferable to total IgE determinations, we wanted to investigate the value of this test in

children by comparing it with the demonstration of specific IgE antibodies with conventional RAST and the determination of total IgE. Our results indicate that this new multi RAST has a significantly higher sensitivity and specificity than total IgE determinations. It might therefore be a potential *in vitro* screening test to identify children with atopic allergy to common inhalant allergens.

MATERIAL AND METHODS

Serum specimens

Blood samples were obtained from 100 children, 3-15 years old, who attended the Department of Pediatrics at our hospital or one of the out-patients clinics in our county. They were subjected to clinical and laboratory investigations because of a suspected IgE-mediated inhalant allergy with symptoms restricted to the eyes and/or respiratory tract.

The serum specimens were stored frozen at -20°C and were retested with RAST, PRIST and multi RAST as described below.

PRIST, RAST and multi RAST

The serum specimens were tested with conventional RAST for specific IgE antibodies against seven groups of allergens representing 12 different allergens. These were birch and alder pollens (Group I), timothy pollen (Group II), mugwort pollen (Group III), dust (Group IV), mites: *Dermatophagoides* (Group V), cat, dog & horse (Group VI), the moulds *Aspergillus fumigatus*, *Cladosporium herbarium* and *Alternaria alternata* (Group VII). In addition, sera were tested with PRIST for total IgE concentration, and with the new multi RAST, which according to the manufacturer is adapted for a group of common inhalant allergens. All reagents were obtained from Pharmacia Diagnostics, Uppsala, Sweden, and the tests were performed under standardized conditions

according to the manufacturer's recommendations. A serum specimen was considered positive for RAST when a class 1 reaction was obtained for at least one allergen. Elevated total IgE concentrations were age group-related according to Kjellman et al. (5) and expressed as > 1 SD or > 2 SD above mean. The results obtained with the multi RAST were expressed as positive or negative according to the manufacturer's recommendations. A positive RAST was considered as a true positive test for the presence of specific serum IgE antibodies.

Statistical evaluations

The results of the determinations of total serum IgE and multi RAST were compared with those of RAST. Sensitivity, specificity and predictive values of positive and negative tests were calculated (2). The so-called sign-test was used to calculate for differences (6).

RESULTS

The results obtained with conventional RAST, PRIST and the multi RAST are summarized in Tables 1 and 2. Compared with the RAST results the specificity of PRIST is 74% and 88% for total IgE elevated > 1 SD and > 2 SD, respectively, above the mean values. The sensitivity, however, is only 47% for an elevated total IgE of > 2 SD and 86% for total

Table 1

Serum specimens from 100 children tested with RAST for specific IgE antibodies and PRIST for total IgE. The results of "positive" and "negative" IgE refer to values above mean $+1$ SD or $+2$ SD (in parenthesis)

Total IgE	RAST		Total
	positive	negative	
Positive	49 (27)	11 (5)	60 (32)
Negative	8 (30)	32 (38)	40 (68)
Total	57 (57)	43 (43)	100 (100)

Table 2

Comparison of results obtained with RAST and the multi RAST. The results of "positive" RAST refers to a RAST result with at least RAST class 1, in parentheses at least RAST class 2

Multi RAST	RAST		Total
	positive	negative	
Positive	54 (52)	0 (2)	54
Negative	3 (2)	43 (44)	46
Total	57 (54)	43 (46)	100 (100)

Table 3

Children with positive RAST (at least class 1) restricted to only one group of allergens compared with multi RAST results

Allergen group	No. of children	Positive multi RAST result
Trees (I)	4	3
Grass (II)	4	4
Herbs (III)	1	0
Dust (IV)	0	0
Mites (V)	2	1
Animals (VI)	1	1
Moulds (VII)	0	0
Total	12	9

IgE > 1 SD. This will also give relatively low predictive values for positive tests: 84% for total IgE > 2SD, and 81.6% for total IgE > 1 SD above means, and for negative tests 56% and 80%, respectively.

Corresponding comparisons for the multi RAST give a sensitivity of 95% and specificity of 100%. Correspondingly, the predictive value for a positive test will be 100% and for a negative test 91%. If at least a class 2 result is required for a positive RAST, the figures will be 96.3% and 95.6%, respectively, for sensitivity and specificity, and corresponding figures for predictive values for positive and negative tests.

In all, there were three children with a positive RAST but negative multi RAST. Analysis of the results showed that they had a RAST class of 1 or 2 for only one allergen, restricted to one of the allergen Groups I, III, or V (see Methods), respectively. Table 3 shows that another nine children had a positive RAST restricted to only one of the allergen groups, and all were positive with multi RAST.

DISCUSSION

RAST results are in good agreement with clinical allergic manifestations, we used a broad RAST panel of 12 allergens, representing seven groups, as reference test. The multi RAST used in this study of children showed both a high sensitivity and a high specificity compared with RAST for common inhalant allergens. Our results also showed that determination of total IgE has a significantly lower efficiency than multi RAST, which is in agreement with those recently reported for adults by Zetterström et al. (9).

Twelve of the 57 children with a positive RAST had specific IgE antibodies restricted to only one particular group of allergens. The three children with negative multi RAST but positive RAST were among these. No child had positive RAST restricted to allergens in the mould or dust group only. One child was RAST positive to mugwort pollen only, an allergen within the herb group, but negative

in multi RAST. This means that in the present study we have not been able to evaluate the efficiency of multi RAST for dust, mould and herbs.

The cost for RAST may be high if many allergens are to be analysed. From a cost benefit point of view the multi RAST is therefore an attractive alternative. However, multi RAST results are given only as "positive" or "negative", and the test does not specify a specific allergen. RAST for specific allergens should be used when this is needed.

A careful case history is of utmost importance for the diagnosis of atopic disease. Clinical signs and symptoms on exposure to specific allergens may give clearcut information but on some occasions the diagnosis needs confirming. The present study shows that multi RAST is better correlated to RAST results than the total IgE level for children older than 3 years. Thus multi RAST might be used as screening for IgE antibodies against inhalant allergens instead of total IgE determinations.

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