

Value of the case history in the diagnosis of allergic state and the detection of allergens

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Summary

Detailed histories taken in eighty-one patients suffering from perennial asthma and rhinitis were analysed independently by three trained allergists and their conclusions were compared to the results of three tests: (1) concentration of total serum IgE; (2) skin tests and (3) radioallergosorbent test (RAST). In eleven patients (14%), the three investigators disagreed when estimating the allergic nature of the symptoms. Ten out of forty-four patients (23%), unanimously predicted not to be allergic, had high levels of total serum IgE and skin tests and RAST clearly positive for one or more allergens. The allergists suspected 47% of the allergens detected by skin tests and 55% of those detected by RAST. The case history was the test which most often gave information at odds with that suggested by the other three tests. Our study indicates therefore that a case history not even suggestive of allergy should be complemented by additional tests.

Introduction

In patients suffering from bronchial asthma and chronic rhinitis, knowledge of the allergic nature of the symptoms and of the offending allergen(s) may help patient management through control of environment or, in some cases, specific immunotherapy. Traditionally, this has been achieved by the use of the case history and skin tests. Today the determination of the level of total serum IgE (Johansson, 1967) and of allergen-specific IgE (Wide, Bennich & Johansson, 1967) by the radioallergosorbent test (RAST) are routinely used in the allergic investigations. Several studies have compared the information obtained by case history with the results of skin tests or RAST (Aas & Johansson, 1971; Eriksson, 1977; Viljanen, Kreus & Viljanen, 1978; Østerballe, Malling & Weeke, 1979). We were interested in further characterizing the value of the case history; and have analysed the conclusions reached by three allergists who independently assessed the same case history. Also, an effort was made to determine which of four routinely used diagnostic methods (case history, total IgE,

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skin tests and RAST) was most often discrepant with that derived from the other three tests.

Materials and methods

Patients

Fifty adults with perennial bronchial asthma and thirty-one with perennial chronic rhinitis attending an allergy out-patient clinic were investigated. The patients with seasonal symptoms, occurring exclusively during the months of high pollen counts (April to June in our area) were excluded, since in these cases the diagnosis of allergy is generally not difficult. The asthmatic patients suffered from acute and reversible attacks of bronchial obstruction; those patient whose history fulfilled the criteria defined for chronic bronchitis were excluded. Patients with rhinitis complained of chronic nasal obstruction, rhinorrhea and sneezing. The patients' mean age was 38 ± 15 years ($\pm$ s.d., range 16–85 years), and the age of onset of the symptoms was 30 ± 15 years, (range 1–75 years). Seventy-two per cent of the patients with asthma had been hospitalized at least once for this disease. None of the patients were on steroids or antihistamines at the time of the investigation.

History

A careful and systematic history was taken by one trained allergist. In addition to questions concerning allergic diseases in their family, each patient was specifically asked about allergic illnesses other than asthma or rhinitis, age of onset of symptoms, their severity, the role of extrinsic factors as noticed by the patient; information was systematically obtained regarding contact with animals, and possible influence of dust or moulds, foods and non-specific stimuli such as exercise, cold and irritants. The data were written on a numbered sheet. The patients' histories were then analysed independently by three other trained allergists who did not know the patients and were unaware of the results of the other tests. They were asked to answer two questions: (1) On the basis of this history, do you think that this patient is allergic? and (b) if yes, to which allergen(s)?

Skin tests

In all patients (eighty-one) prick tests were performed with alum-precipitated extract of house dust, mites (*Dermatophagoïdes pteronyssinus* and *D. farinae*) and moulds (three mould mixtures): A13, *Alternaria tenuis*, *Aspergillus amsterlodami*, *As. niger*, *As. terreus*, *Cladosporium herbarum*, *Neurospora sitophila*, *Mucor mucedo*, *M. racemosus*, *M. spinosus*, *Rhizopus nigricans*, *Penicillium brevicompactum*, *P. expansum*, *P. notatum*; M₁₀: *Chaetomium globosum*, *Epicoccum purpurascens*, *Fusarium* sp., *Pullularia pullulans*; M₁₁: *Helminthosporium halodes*, *Phoma betae*, *Spicaria violacea*, *Sporobolomyces roseus* (Beecham, U.K.). They were read by the same investigator. In thirty-four patients, whose histories disclosed a possible contact with animal(s), extract of animal danders (cat, dog or horse) were further tested. Results were expressed on a scale of (–) to (4+) according to the recommendations from the Standardization Committee of the Northern Society of Allergology (Aas & Berlin, 1972). The definition of (–) is, the skin reaction produced by the administration of the control solution (NaCl 6%, phenol 0.5%) and (3+) by that of 1 mg/ml histamine. Hereafter only (2+)

or more reactions were considered positive, i.e. borderline results (1+) were considered negative.

The total serum IgE

This was determined in each patient by the paper radioimmunosorbent test (PRIST) (Pharmacia, Sweden) in serum obtained on the day of the investigation. According to the manufacturer a total IgE level was considered as increased, thus indicative of atopy, if above 100 PRIST units (> 200 ng/ml).

The determination of specific IgE in serum

This was performed with a commercially available radioallergosorbent test (RAST) (Pharmacia). The technique modified in 1977 by the use of an antibody directed against the D_{e2} determinant of the IgE molecule was employed (Kurvits 1981, Pécoud *et al.*, 1982). All patients were tested for the presence of specific IgE against house dust (two antigens), mites (*D. pteronyssinus* and *D. farinae*) and moulds (*P. notatum*, *C. herbarum*, *As. fumigatus*, *M. racemosus* and *Al. tenuis*). In the thirty-four patients with possible animal contact, specific IgE against cat, dog or horse danders were also tested. The results were graded from 0 to (4+), 0 corresponding to an undetectable level of specific IgE and (4+) to a very high level. Hereafter only (2+) or more was considered positive, i.e. a borderline result (1+) was considered negative.

Statistical analysis of correlation was performed by χ^2 methods with Yates' correction test.

Results

Prediction of allergy

When answering the question 'On the basis of this history, do you think that this patient is allergic?', the three allergists agreed in seventy out of eighty-one patients (86%), i.e. forty-five out of fifty patients with asthma (90%) and twenty-five out of thirty-one with rhinitis (80.6%). Twenty-one asthmatic patients were unanimously judged to be allergic and twenty-four not allergic. In the rhinitis patients, these figures were respectively five and twenty. When the investigators disagreed, their judgements were randomly distributed: none of them showed a tendency to predict more allergic conditions than the others.

The prediction of allergy was then compared to the results of (1) total serum IgE, (2) skin tests, and (3) RAST. For these correlations, the eleven patients on which the three investigators disagreed were excluded in order to analyse only those whose diagnosis as allergic from the histories was agreed. The correlations between the prediction of allergy and the results of the other three tests performed in the seventy remaining patients are given in Table 1. Data obtained from patients with asthma and rhinitis were pooled since the same trends were observed in both conditions. It can be seen that no significant correlation was found between the prediction of allergy and the total IgE concentration, mainly because this concentration was high in twenty out of forty-four patients thought not to be allergic. The prediction based on history correlated well with the positivity of prick tests and of RAST for at least one allergen.

Among the forty-four patients considered not allergic by the three allergists, ten (23%) had a high level of IgE in addition to one skin test and RAST positive for at least one allergen. The allergen was house dust (or mite) in nine cases and dog dander in the

Table 1. Correlation between case history and total serum IgE, positivity of prick tests and specific IgE (RAST)

History prediction	Number of patients with					
	Total IgE (PRIST units)		Prick tests		Specific IgE (RAST)	
	> 100	< 100	One or more positive	all negative	For one or more allergens	none
Allergic (<i>n</i> = 26)	18	8	24	2	23	3
Not allergic (<i>n</i> = 44)	20	24	12	32	10	34
Concordance*	42 (60%)		56 (80%)		57 (81%)	
<i>P</i> value†	NS		< 0.001		< 0.0001	

* Concordance was achieved when a case history judged as allergic was associated with a serum IgE concentration > 100 PRIST units, with one or more positive prick tests or the presence of specific IgE directed against one or more allergens; or inversely.

† χ^2 , Yates' correction test; NS, not significant.

tenth. Conversely, among the twenty-six patients unanimously considered to be allergic, two had a low level of IgE, no positive prick test and no detectable amount of specific IgE.

Table 2 shows the degree of matching of the four tests. The results of the four tests suggested the same diagnosis in 57% of the patients (26% allergic and 31% not allergic). In only 7% of the patients, two tests were indicative of allergy and two were not. The test most often discrepant with the other three was the case history (twelve patients) followed by the total IgE level (eleven patients).

Prediction of the allergen

The three allergists were asked to predict the offending allergen(s) whenever they judged a case history as indicative of allergy. For the correlation studies, the individual

Table 2. Matching of history, total IgE, prick tests and RAST

	Tests indicative of allergy (<i>n</i>)*					Total
	4	3	2	1	0	
Patients (<i>n</i>)	18	13†	5	12	22	70
Percentage (%)	26	19	7	17	31	100

* Test indicative of allergy means: history judged as allergic, serum IgE level > 100 PRIST units, presence of prick test or RAST positive for at least one allergen.

† Discrepant test (non-allergic): case history (ten patients), total IgE (three patients).

‡ Discrepant test (allergic): total IgE (eight patients), case history (two patients) and skin test (two patients).

allergens were combined into three groups: house dust or mite, animal dander and moulds. Table 3 shows how many groups of allergens were detected by skin test or RAST in the eighty-one patients, as well as the proportion suspected by each allergist on the basis of the history alone. The three allergists predicted 47% of the allergens detected by skin test and 55% of those detected by RAST. There was no significant difference between allergens and these percentages were identical for asthma and rhinitis.

Conversely, Table 4 indicates the number of allergen groups which were predicted by the three investigators and the proportion later 'confirmed' by skin test and RAST. These figures were 20% higher in patients with asthma than in those with rhinitis.

Table 3. Allergen groups detected by skin tests and RAST in eighty-one patients. Proportion previously suspected by history taking

Allergen groups diagnosed by*	Allergen groups Total of positive tests (n)	Suspected by investigator (%)			Mean of three investigators (%)
		A	B	C	
Skin test	72	43	51	48	47
RAST	52	52	63	50	55

* Individual allergens were combined into three groups: house dust/mite, moulds and animal danders.

Table 4. Allergen groups predicted by taking history in eighty-one patients. Proportion later found positive by skin tests and RAST

	Investigator			Average
	A	B	C	
Allergen groups* (n predicted)	39	47	35	40
'Confirmed' by skin tests (%)	77	68	80	75
'Confirmed' by RAST (%)	67	60	69	65

* Individual allergens were combined into three groups: house dust/mite, moulds and animal danders.

Other correlations

A high concentration of IgE was in good agreement with the presence of at least one positive skin test (concordance 80%) or one positive RAST (75%). The mean concordance between skin test and RAST (all allergens considered together) was 84%: 19% skin test pos./RAST pos. and 65% skin test neg./RAST neg. Among the discordant results, the association of a negative skin test and a positive RAST was found in 3% of the cases.

Discussion

This study was performed on adults suffering from perennial asthma or rhinitis, i.e. a group of patients in which the diagnosis of allergy is more challenging than in those

suffering from seasonal symptoms. Many asthmatics were severely ill, as judged by the high proportion already hospitalized for this disease. The diagnostic tests available in a routine allergy consultation were used throughout. For this reason, bronchial provocation tests were not used, although they have been suggested to be the most reliable tests to detect the offending allergen (Aas, 1974).

First, there is some degree of divergence between three trained and experienced allergists who analyse the same anamnastical data. This should be remembered when comparing the different scores of agreement between the case history and other tests reported in the literature (Aas & Johansson, 1971; Eriksson, 1977; Viljanen *et al.*, 1978; Østerballe *et al.*, 1979). In our study, the three investigators depended on information provided to them by a fourth one; and it might be argued that a better consensus would have been reached if each investigator had interviewed the patient. However, some variation would be expected in the history given by the same patient on three different occasions.

Second, the case history may overlook an allergic component to the illness: 23% of the patients unanimously considered not to be allergic by three allergists were found to have an increased level of total IgE in addition to skin tests and RAST clearly positive for at least one allergen. There is no absolute way to determine an allergic basis for respiratory symptoms and it is generally agreed that none of the tests mentioned in this study, if used alone, can prove or exclude allergy. Many studies have shown that the best agreement with provocation tests, considered as the most accurate test, had been obtained by scores combining the results of several diagnostic methods (Ahlstedt *et al.*, 1974; Eriksson, 1977; Østerballe *et al.*, 1979). Therefore, in this subgroup of patients (23%) whose history did not suggest allergy but who had in fact high values of IgE, positive skin test and RAST, one can speculate that the case history gave a result 'falsely negative'. Further, the fact that the history underestimates a substantial number of allergic patients is reflected by the relatively small proportion of the allergens identified by the three allergists as compared to those found by skin tests or RAST. Since, in our study like in others (Apold *et al.*, 1974; Torsten, Berg & Johansson, 1974; Viljanen *et al.*, 1978), the vast majority of allergens diagnosed by RAST also gave positive skin tests, one estimates that the case history missed about 40% of allergens. This proportion is higher than the one found by Eriksson (1977) who reported that a convincing case history failed to predict 19% of the allergens found by bronchial provocation tests. As stated above, excluding the patients with allergy to pollen results in the loss of many allergens easy to diagnose. Our results, however, are in agreement with those of Viljanen *et al.* (1978) and Østerballe *et al.* (1979).

Third, from our data the history may also lead to an overestimate of patients judged as allergic, as a substantial number of predicted allergens were not 'confirmed' by another test. In the whole group of patients, 25% of the allergens suggested by case history were negative by skin test and 35% by RAST. Such an overestimation of allergens was also described in Eriksson's (1977) study, when comparing case history with bronchial provocation test.

In spite of these presumed 'false positive' and, to a lesser extent 'false negative' histories, the correlation between the prediction of allergy and the occurrence of positive skin tests and RAST was good. However, we did not find any relation between the prediction of allergy and an increased level of total serum IgE. The information given by this test was also often in disagreement with that suggested by the other three diagnostic means. In our patients, the predictive values of case history and of total IgE

were sufficient to correlate with the other tests (skin test and RAST) but not with each other.

Case history is the initial essential step in the diagnosis of asthma or chronic rhinitis, since it governs the choice of the allergens to be tested; it has, however, some limitations and our data indicate that a case history not even suggestive of allergy should be completed by additional tests and, conversely, all predicted allergens should be compared with the results of at least one, preferably two objective tests.

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