

Skin prick test in the diagnosis of dog dander allergy

A comparison of different extracts with clinical history, provocation tests and RAST

T. VANTO, M. VIANDER and A. KOIVIKKO

Departments of Paediatrics and Medical Microbiology, University of Turku, Turku, Finland

(Received 8 May 1979; accepted for publication 14 June 1979)

Summary

Skin prick tests (SPT) were carried out on 164 asthmatic children using dog dander allergen preparations (A, B1, B2 and D) from three manufacturers. Bronchial and/or conjunctival provocation tests with allergen A were performed on all patients, as well as the Phadebas® RAST (allergen e5). There was a close agreement between the clinical history and the SPT with allergens A and D. The provocation tests and RAST gave results in good agreement with the SPT reactions to all allergens except B1. The overall agreement between the SPT reactions to the different allergens was good. However, significant differences were observed in the allergenic activity of the different preparations and between different batches from the same manufacturer (allergens B1 and B2).

Introduction

Dog dander and hair is recognized as a common inhalant allergen. However, opinions regarding the importance and prevalence of allergic disorders caused by it have varied a lot (Fontana, Wittig & Holt, 1963; Frankland, 1967; Rudolph *et al.*, 1975; Sarsfield *et al.*, 1976; Schultze-Werninghaus *et al.*, 1976 and Moore, Hyde & Manaligod, 1977). These variations may reflect the differences in the allergic populations studied: their age, degree of hypersensitivity and the severity of their symptoms etc. Perhaps other important reasons for these conflicting opinions have been the varying quality of the allergen extracts and the differing methods used in the diagnostic tests (Fagerberg & Wide, 1970; Varga & Ceska, 1972; Havnen *et al.*, 1974). Many of the present commercial dog allergen extracts lack proper immunochemical standardization and they are often weak or varying in their allergen contents. Animal dander extracts are also found to give many false-positive skin test reactions (Eriksson, 1977; Aas, 1970; Sarsfield *et al.*, 1976; Koers, Young & Berrens, 1977). Some of these reactions may be caused by non-specific irritants in crude extracts (Aas, 1975).

Correspondence: Dr Timo Vanto, Department of Paediatrics, University of Turku, SF-20520 Turku 52, Finland

The recent advances in the purification of dog dander and hair extracts (Blands, Löwenstein & Weeke, 1977; Lind, 1979) have provided allergists with a new well characterized purified extract. The efforts to standardize the methods used in allergy diagnosis have led to some recommendations for allergy test procedures (Aas & Belin, 1972; Aas, 1973; Aas *et al.*, 1978).

The purpose of the present study was to compare the skin prick test results of three different commercial dog dander allergen extracts with the clinical history, provocation tests and RAST in asthmatic children using standardized test techniques. We were interested in the possible advantages of the standardized extract compared to two other commercial extracts. It was also of interest to determine the biological activity of the allergens in HEP (histamine equivalent prick) units (Aas & Belin, 1972; Aas *et al.*, 1978).

Materials and methods

Patients

One hundred and sixty-four children from the Children's Asthma Register of the Paediatric Department of the University of Turku (Koivikko, 1977) were included in the study. The mean age of the children was 10.9 years (range 4 to 15 years). None of the patients had previously been hyposensitized with dog allergen extracts. Their clinical history was recorded by means of a detailed questionnaire, which was completed and corrected by the examining physician after an interview with the child and the parents. The children were divided into three groups according to the clinical history of allergy to dogs: (1) negative, (2) doubtful and (3) positive.

Allergens

The allergens for the skin prick tests were obtained from Allergologisk Laboratorium A/S, Denmark (allergen A). Bencard Ltd., England (allergen B) and Dome Laboratories, England (allergen D). All children were tested with allergen A (Soluprick® SQ containing purified freeze dried extract 1 mg/ml corresponding to approximately 1:20 w/v) and D (8590 PNU/ml) using a single batch of the allergen throughout the study. Sixty-five children were tested with allergen B (0.5%) using two different batches of this allergen: 37/65 subjects were tested by batch 1 (B1) and 28/65 by batch 2 (B2). Allergen A (aqueous SQ) was used in the provocation tests. The allergen used in RAST was prepared by Pharmacia AB, Sweden (e5).

Skin prick tests (SPT)

To standardize the evaluation of the results, the method recommended by the Northern Society of Allergy (Aas, 1973) was followed. Each skin test reaction was compared with that of the diluent provided by the manufacturer. A weal size equal to the reaction of the histamine hydrochloride reference (1 mg/ml) was recorded as a +3 reaction. The skin tests were performed on the upper back of the patient. The skin reactions were recorded after 15–20 min. Criteria for positive and negative test results are presented in Table 2. Antihistamines, sympathomimetic drugs, sodium cromoglycate and corticosteroids were withdrawn 48 hr before the test.

Provocation tests

All patients were investigated by provocation tests. Most of the patients (88%) were

tested by the bronchial provocation test (BPT). Patients (1) with a low peak respiratory flow ($PEF \leq 60\%$ of the expected value, Murray & Cook, 1963), (2) with positive auscultatory findings (râles, wheezing) and (3) those lacking sufficient co-operation were excluded from BPT. Instead of BPT the conjunctival provocation test (CPT) was performed on these patients. CPT was carried out also on patients with a doubtful BPT result and on those with suggested dog dander allergy but a negative BPT result.

BPT. BPTs were usually started with allergen concentrations of $1 \mu\text{g/ml}$. The more sensitive the patients as judged from their history and skin test reactions, the lower the initial concentration. 1 ml of the extraction fluid was inhaled through a Pari nebulizator (Paul Ritzau Pari-Werk KG, Starnberg am See, G.F.R.), the concentration being progressively increased ten-fold until reactions occurred, or until 1 ml of the highest concentration (1 mg/ml) used had been nebulized. In the evaluation of the BPT three parameters were recorded immediately after the allergen inhalations as well as after 15–20 min: (1) peak expiratory flow (PEF) measured with a Wright Peak Flow meter, (2) auscultatory findings and (3) breathing discomfort or irritative cough. BPT was considered positive when a $\leq 20\%$ decrease in PEF was recorded along with positive auscultatory findings or the subjective symptoms of the patient.

CPT. CPT was performed instilling 0.05 ml of allergen extract fluid into the inferior conjunctival pouch with a disposable syringe. The other eye was used as a control by instilling the control solution. The concentration of the allergen extract was increased in ten-fold steps. CPT was considered positive, when distinct conjunctival injection, rhinorrhea or severe itching of the eye was recorded when compared to the eye used as a control.

RAST analyses

A blood sample for RAST analyses was obtained from each subject before the skin testing. Serum was stored at -20°C until the RAST determination was performed. RAST analyses were done with e5 dog dander and hair allergen (Pharmacia AB., Sweden) using commercially available Phadebas RAST materials. A conventional RAST reference was used (Lundkvist, 1975).

Determination of the biological activity of the allergens in HEP units

The biological activity of the allergen A was determined in twenty-seven subjects as described by Aas *et al.* (1978). These children had a positive clinical history of dog allergy, a previous positive routine skin test and a positive RAST (class 2–4) for dog dander, and they gave a reaction $\geq 4 \text{ mm}$ (D + d): 2 to the histamine reference solution.

Statistical methods

The difference in the skin reactivity between the allergens was tested by the Student's *t*-test for matched pairs. The χ^2 -test was employed to analyse the relationship between the prick test results by allergens A and D and the clinical history, RAST and the provocation tests. Because of the small number of patients tested by allergens B1 and B2, the Fisher exact probability test was employed combining relevant subgroups to form a four-fold table.

Results

The mean weal diameter [MWD = (D + d):2] of the SPT reactions by the different allergens was related to the MWD elicited by the histamine solution in each subject

Table 1. The relative mean weal diameters (RMWD) in the skin prick tests obtained by the three different allergens. Cases with negative skin reactions to all three allergens were excluded

Allergen	Concentration*	<i>n</i> _{total}	<i>n</i> _{excluded}	<i>n</i> _{RMWD}	mean RMWD
Allergen A	1 mg/ml	164	35	129	1.3
batch 1 (B1)	0.5%	37	9	28	0.3 ^{xxxA}
Allergen B					
batch 2 (B2)	0.5%	28	7	21	1.1 ^{xxxB}
Allergen D	8590 PNU/ml	163	35	128	0.5 ^{xxxA}

* = the concentration of the allergen extract given by the manufacturer

*n*_{total} = the total number of the patients tested by the allergen

*n*_{excluded} = the number of subjects excluded because of negative skin reactions to all three allergens.

*n*_{RMWD} = the number of subjects used for the calculation of mean RMWD

$$\text{RMWD} = \frac{\text{MWD allergen}}{\text{MWD histamine}}$$

xxxA = $P < 0.001$, compared to allergen A (*t*-test for matched pairs)

xxxB = $P < 0.001$, compared to allergens B1 and D (*t*-test for matched pairs for comparison with allergen D; *t*-test for comparison with allergen B1).

Table 2. Comparison of the prick tests results between the different allergens

		Allergen B								
		Allergen D			Batch 1 (B1)			Batch 2 (B2)		
		-	-	+	-	-	+	-	-	+
Allergen A		0	1, 2	≥3	0	1, 2	≥3	0	1, 2	≥3
-	0	38	0	0	8	0	0	7	0	1
-	1, 2	34	9	1	9	0	0	2	2	1
+	≥3	15	44	22	16	2	2	1	4	10
<i>n</i>		163			37			28		
χ^2		82.8			—			—		
<i>P</i>		<0.001			ns			<0.05		
d.f.		2			—			—		

+ = regarded as a positive prick test result.

- = regarded as a negative prick test result.

The sum of the cases in the squared areas were used for the statistical tests.

(MWD allergen/MWD histamine). These relative MWDs (RMWD) were calculated in all the cases in which a skin test with at least one of the allergens was positive. The results are shown in Table 1. Allergen D and B1 elicited significantly smaller reactions than allergen A and B2 ($P < 0.001$). The SPT reactions elicited by allergen B2 were equal in size with those by allergen A. Allergen B1 was found to be very weak and it mostly gave a negative reaction in the SPT.

Because of this variation in the strength of the allergen extracts, the SPTs with allergen A and B2 (RMWD > 1) were considered positive only with prick test result $\geq +3$, while the SPTs with allergen D and B1 were considered positive with a result $\geq +1$ (Table 2).

In spite of the differences in the strength of the skin test reactions the over-all agreement between these allergens was good with the exception of allergen B1, as shown in Table 2. However, in 17% of the cases with a negative SPT result by allergen D, a positive ($\geq +3$) reaction by allergen A was found. Allergen B1 gave a positive SPT reaction in only 20% of cases with a positive reaction by allergen A. One case with a positive ($\geq +3$) reaction to allergen A and a totally negative (0) reaction to allergen B2 was observed, also a case with reverse results was noticed.

General agreement between the clinical history and the SPT results was good ($P < 0.001$) with allergens A and D as shown in Table 3. The agreement was best with allergen A. Allergen D gave a negative SPT result in 34% of the cases with a positive clinical history, allergen A in 24%, respectively.

The agreement of the SPT results with RAST classes 0 and 3-4 was excellent with allergens A, B2 and D (Fig. 1). The correlation seemed to be best with allergen A. The cases with a RAST class 1 or 2 generally gave a negative or slightly positive reaction in the SPT. The SPT results with allergen B1 had a poor agreement with RAST.

A positive provocation test result was recorded in seventy-two of the 164 subjects

Table 3. Comparison of the prick test results with clinical history

	Skin prick tests							
	Allergen B							
	Allergen A		Batch 1		Batch 2		Allergen D	
	-	+	-	+	-	+	-	+
Negative	44	9	11	1	0	0	42	11
Doubtful	22	18	8	1	7	3	22	18
Positive	17	54	14	2	9	9	24	47
<i>N</i>	164		37		28		163	
χ^2	42.8		—		—		24.5	
d.f.	2		—		—		2	
<i>P</i>	< 0.001		ns		ns		< 0.001	

Criteria for the positive and negative prick test results are presented in Table 2.

The sum of the cases in the squared areas were used for the statistical tests

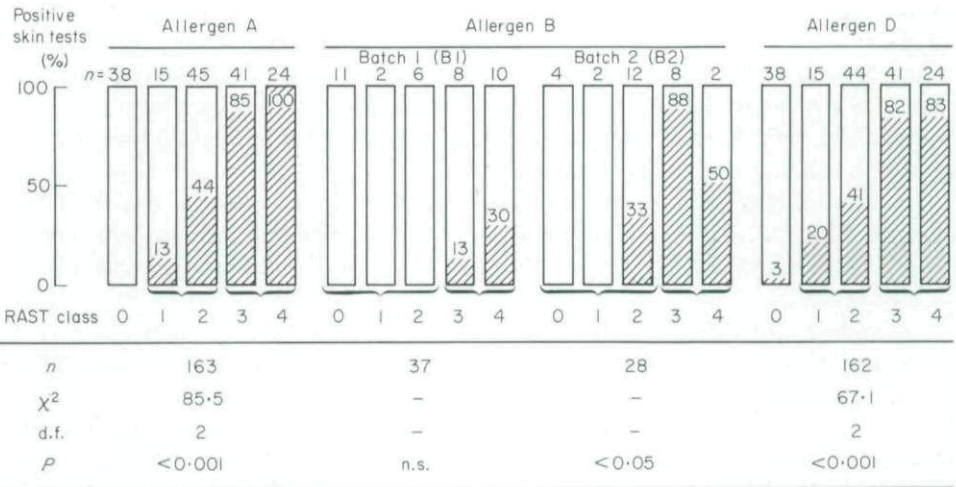


Fig. 1. The distribution of positive and negative skin test results by RAST class. □, negative skin test; ▨, positive skin test. Criteria for the positive and negative prick test results are presented in Table 2.

(44%). Of these, 20/72 (28%) had a positive provocation test only in the conjunctival provocation test. The agreement between the provocation test and the SPT results was good with allergens A, B2 and D: 84, 86 and 79%, respectively (Tables 4 and 5). Allergen D seemed to give slightly more false negative SPT results than allergens A or B2. The skin test results with allergen B1 had a poor agreement with the provocation test. The best agreement with the SPTs and provocation tests was observed in the most sensitive patients.

Table 4. Comparison of the prick test results with provocation tests

		Skin prick tests							
		Allergen B							
		Allergen A		Batch 1		Batch 2		Allergen D	
Provocation test		- *	+ *	-	+	-	+	-	+
Negative		73	6	16	0	12	0	70	8
Doubtful		2	11	1	0	1	0	4	9
Positive		8	64	16	4	3	12	13	59
n		164		37		28		163	
χ^2		77.3		—		—		62.1	
d.f.		1		—		—		1	
P		<0.001		ns		<0.001		<0.001	

*=Criteria for the positive and negative prick test results for all allergens are presented in Table 2.

The sum of the cases in the squared areas were used for the statistical tests.

Table 5. Correlation between provocation tests and skin prick tests

Provocation test†	Results in agreement with skin prick test*							
	Allergen A		Allergen B1		Allergen B2		Allergen D	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Negative	73/79	92	16/16	100	12/12	100	70/78	90
Positive in any concentration of allergen	64/72	89	4/20	20	12/15	80	59/72	82
Positive with concentration 10 ⁻³ w/v	26/31	84	1/9	11	9/12	75	27/32	82
Positive with concentration 10 ⁻⁴ w/v	32/35	91	3/9	33	3/3	100	29/34	85
Positive with concentration ≤10 ⁻⁵ w/v	6/6	100	0/2	0	—	—	3/6	50

* = Criteria for the positive and negative prick tests results are presented in Table 2.

† = Allergen A was used in the provocation tests.

Patients with doubtful provocation test results are omitted.

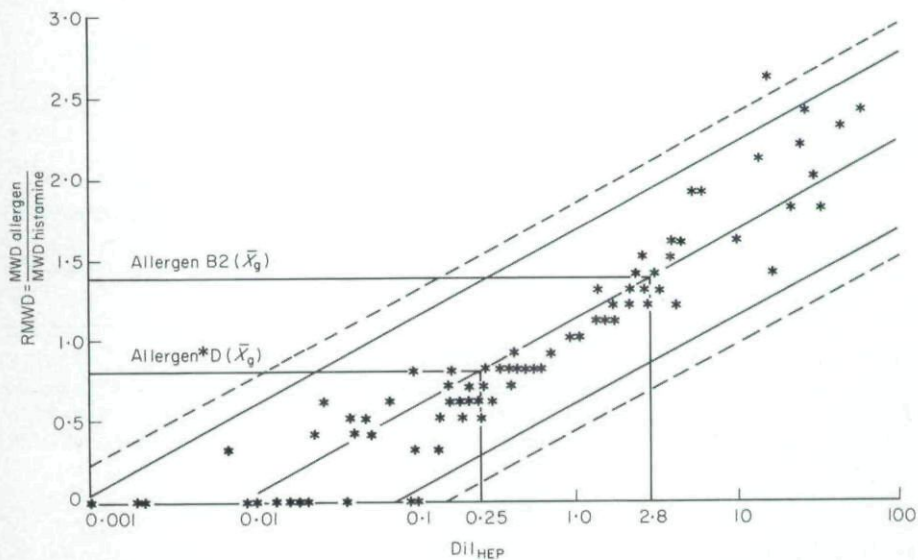


Fig. 2. Linear regression function between the individual RMWD and Dil_{HEP}-values for different concentrations of allergen A (1.0, 0.1 and 0.01 mg/ml). HEP-values corresponding to the RMWDs for allergen B2 (0.5%) and allergen D (8590 PNU/ml) are estimated. The mean RMWD for allergen B1 was 0. Results of individual patients are shown in Table 6. Patient No 25 is excluded from the figure. --- 99% confidence limit; —, 95% confidence limit.

Table 6. Determination of the biological activity of allergen extracts in HEP-units

Patient No.	Dil _{HEP} allergen A	Relative mean diameter (RMWD)							Provocation test (Allergen A)	
		Allergen A (mg/ml)			Allergen B (0.5%)		Allergen D	RAST (e5) class	BPT	CPT
		1.0	0.1	0.01	Batch 1 (B1)	Batch 2 (B2)	8590 PNU/ml			
1	4.0 × dil.	1.6	0.7	0.5	—	—	0.5	4	+	n.d.
2	22 × dil.	1.8	1.2	0.7	—	—	0.9	3	n.d.	+
3	2.4 × dil.	1.4	0.6	0.4	—	—	0.8	2	+	n.d.
4	0.1 × dil.	0.3	0	0	—	—	0	2	0	0
5	45 × dil.	2.3	1.6	0.8	—	—	1.3	4	+	n.d.
6	14 × dil.	2.1	1.3	0.3	—	—	1.8	3	n.d.	+
7	10 × dil.	1.6	1.0	0	—	—	0.6	3	n.d.	+
8	34 × dil.	1.8	1.3	0.8	0	—	0.8	4	+	n.d.
9	31 × dil.	2.0	1.4	0.6	0	—	0.8	3	+	n.d.
10	3.8 × dil.	1.5	0.8	0	0	—	0.8	4	n.d.	+
11	0.2 × dil.	0.5	0	0	0	—	0	2	n.d.	0
12	1.0 × dil.	1.0	0.8	0	0	—	0.6	3	+	n.d.
13	0.5 × dil.	0.8	0.5	0.9	0	—	0.5	2	0	n.d.
14	27 × dil.	2.4	1.3	0.7	0	—	0	4	+	n.d.
15	17 × dil.	1.4	1.1	0.8	0	—	0.7	4	+	+
16	16 × dil.	2.6	1.1	0.7	0	—	0	4	+	n.d.
17	0.2 × dil.	0.6	0	0	0	—	1.0	2	0	0
18	5.5 × dil.	1.9	0.8	0.4	—	1.4	0.4	3	+	n.d.
19	2.2 × dil.	1.3	0.6	0	—	2.6	0.9	2	0	+
20	1.4 × dil.	1.1	0.5	0	—	0.8	0.5	2	n.d.	+
21	0.7 × dil.	0.9	0.6	0.3	—	1.5	0.5	2	n.d.	+
22	2.8 × dil.	1.2	0.8	0.6	—	1.1	0.7	3	n.d.	+
23	60 × dil.	2.4	1.9	0.8	—	2.3	1.9	3	±	+
24	1.7 × dil.	1.2	0.6	0	—	1.0	0.5	3	+	n.d.
25**	0 × dil.	0	0	0	—	1.1	0	3	n.d.	+
26	26 × dil.	2.2	1.5	0.5	—	1.7	0.8	2	+	n.d.
27	4.2 × dil.	1.2	0.9	0.4	—	1.2	0.4	2	+	n.d.
$\bar{X}$	12.3 × dil.	1.5	1.0	0.4	0	1.5	0.7	n.d. = not done		
s.d.	15.9	0.6	0.5	0.3	0	0.6	0.5	0 = negative		
n	27	27	27	27	10	10	27	+ = positive		
$\bar{X}_g$	4.1 × dil.				0	1.4	0.8			

$P < 0.001$, compared to allergens A (10^{-3} w/v) and B2 (0.5%) (t-test for matched pairs).

Dil_{HEP} = dilution of the allergen A extract (1 mg/ml) eliciting a SPT reaction equal to that of histamine control solution (1 mg/ml) in an individual patient.

** In repeated SPT with allergen A using concentrations 1.0, 0.1 and 0.01 mg/ml the RMWD results were 1.0, 1.0 and 0.5, respectively, and the BPT was positive.

The results of the determination of the biological activity of allergen A in HEP-units are shown in Table 6. The relative mean weal diameters (RMWD) for allergen A (1.0, 0.1 and 0.01 mg/ml), allergen B (0.5%) and allergen D (8590 PNU/ml) are shown in the same table. The correlation between RMWDs and HEP-values is presented in Fig. 2.

Discussion

The present study revealed marked differences in the biological activity of the three commercial dog dander allergen extracts. A distinct difference was also found between the two batches of one of the allergens, one of the batches being extremely weak and the other comparatively good in its allergenic activity. Previously, similar differences in the allergen contents of various allergen extracts, even up to a thousand-fold, have been demonstrated using the RAST titration method, by several authors (Foucard *et al.*, 1972; Pepys *et al.*, 1975; Gleich *et al.*, 1976). This variability has also been demonstrated in regard to commercial dog dander allergen extracts by Varga & Ceska (1972). Though the RAST-based allergen assay mostly gives concordant results with *in vivo* methods (Pepys *et al.*, 1975), it cannot, however, always be regarded as a reliable method, and *in vivo* methods may be needed for testing the allergenicity of extracts (Stenius-Aarniala *et al.*, 1978), as was done in the present investigation.

Also qualitative differences between various dog dander extracts, possibly due to breed-specific allergens, have been shown by Hooker (1944) and by Fagerberg & Wide (1979). Blands *et al.* (1977) were not able to demonstrate with certainty any breed-specific allergens, even though they demonstrated qualitative and quantitative variations in the antigen content of the extracts from different dog breeds. They explained this variation as a concentration phenomenon, there being more dandruff relative to hair in the short-haired breeds. Whether or not the differences between the allergen extracts in the present study are based on qualitative or quantitative variations, cannot be evaluated.

In this study a highly significant relationship ($P < 0.001$) between the clinical history and the prick test results was obtained with two of the allergens, while the association was not significant with both batches of the third allergen. Previously, Eriksson (1977) has reported a highly significant correlation between the clinical history and the skin tests with a dog dander allergen. However, Moore *et al.* (1977) could not show any association between the cutaneous test results and the clinical history. These conflicting results could be explained by the differences in the allergen extracts used, as shown by the present study. It is also possible that the analysis of the clinical history has been slightly different in these studies.

A significant correlation between the skin test results and RAST with dog dander allergens has previously been reported by Eriksson (1977) and Moore *et al.* (1977). The opposite, however, has been shown by Sarsfield *et al.* (1976), who reported that out of thirty-six children with a positive skin test only ten (28%) had a positive RAST for dog dander. These conflicting results may be caused by differences in the allergens used in RAST (Havnen *et al.*, 1974) or by difficulties in the coupling of the allergens to the paper discs used in RAST (Brighton, Lampard & Fordham, 1975). Also non-specific irritants in the extracts may cause a false-positive skin test with a negative specific IgE result.

The provocation test is often regarded as the definitive criterion in allergy diagnosis (Aas, 1970; Ahlstedt *et al.*, 1974; Eriksson, 1977). In this study, a highly significant relationship between the provocation tests and the skin tests with the most allergens used was observed. Significant correlation has also been reported by Eriksson (1977). Naturally, the correlation found in various studies depends on the test techniques and the interpretation of their results as well as on the allergens used both in the skin test and in the provocation tests. This was also shown in our study; a weak batch of one of the allergens gave prick test results which were not in significant relationship with the

provocation tests. The results of the provocation tests depend also on the selection of the target organ for the test, and this selection is usually done on the basis of the clinical history. Nasal and conjunctival provocation tests in asthmatic subjects have been reported to be more sensitive than the bronchial provocation test (Stenius-Aarniala, Malmberg & Holopainen, 1978). The selection of the target organ may sometimes be difficult because of a doubtful or negative clinical history, and often multiple provocation tests are needed to exclude a specific allergy. Also in the present study 28% of the positive cases were not detected by the bronchial provocation test, but only by the conjunctival test.

The calculation of the biological activity of the allergens in HEP-units was found to be clinically relevant in selecting the best allergens for allergy diagnosis. It detected weak and unreliable allergens in a simple way. A difficulty with the HEP-determinations is the selection of the patients for the prick tests. In the present study we used criteria recommended by Aas *et al.* (1978). However, all of the criteria recommended are susceptible to errors and misinterpretations. The required positive clinical history may be false-positive. The previous positive routine skin test may have been performed with a poor allergen extract, which may have elicited a false-positive reaction. The required positive RAST (class 2-4) may be misleading, because most patients with a RAST class 2 for dog dander have a negative provocation test. Differences have also been found between various dog dander allergen extracts used in RAST (Vanto *et al.*, 1979). If a positive provocation test were required for the patients selected for the HEP-determinations of a specific allergen, it would probably increase the reliability of the determination. This would, however, make it more difficult to find an adequate number of patients for the HEP-determinations.

The HEP-determination measures only the total allergenic activity of allergen preparations; an allergen extract with a high activity in HEP-units may still lack some major or minor allergens, which can be important in individual cases. This may lead to errors in the diagnosis and treatment of these patients. This disadvantage can be eliminated only by a reliable immunochemical characterization of the allergens and by a reliable immunochemical standardization of the allergen extracts (Marsh, 1975).

In the present study marked differences were observed in the biological activity between three dog dander allergen extracts by an *in vivo* method. The SPTs with the immunochemically standardized allergen (A) were shown to be in an excellent agreement ($P < 0.001$) with the clinical history, RAST and the provocation tests, and this extract was also found to have good biological activity determined in HEP-units. One batch of allergen B (B2) was found to have good allergenic activity, and no significant differences between it and allergen A were detected. On the other hand, the other batch of the same allergen preparation (B1) was found to be weak and unreliable. Even though the allergenic activity of the third allergen preparation (allergen D) was shown to be relatively low, it still gave prick test results with a good agreement to clinical history, RAST and provocation tests. However, false negative skin test results were more abundant with allergen D than with allergen A. This study emphasizes the urgent need for relevant standardization of the allergens used in allergy diagnosis and specific immunotherapy.

Acknowledgments

We are grateful to Allergologisk Laboratorium A/S for supplying some of the allergens, and to Pharmacia Diagnostics AB for supply of the RAST reagents. We wish

to thank Ms Mailis Ulmanen, Ms Tuulikki Hellsten and Ms Raija Raulimo for their excellent technical assistance. This work was supported by the Finnish Allergy Research Foundation and the Finnish Paediatric Research Foundation.

References

- AAS, K. (1970) Bronchial provocation tests in asthma. *Archives of Disease in Childhood*, **45**, 221.
- AAS, K. (1973) Standardization of diagnostic work in allergy. *Clinical Allergy*, **3**, 481.
- AAS, K. (1975) *The Bronchial Provocation Test*, p. 13. Charles C. Thomas, Springfield.
- AAS, K. & BELIN, L. (1972) Standardization of diagnostic work in allergy. *Acta Allergologica*, **27**, 439.
- AAS, K., BACKMAN, A., BELIN, L. & WEEKE, B. (1978) Standardization of allergen extracts with appropriate methods. *Allergy*, **33**, 130.
- AHLSTEDT, S., ERIKSSON, N., LINDGREN, S. & ROTH, A. (1974) Specific IgE determination by RAST compared with skin and provocation tests in allergy diagnosis with birch pollen, timothy pollen and dog epithelium allergens. *Clinical Allergy*, **4**, 131.
- BLANDS, J., LOWENSTEIN, H. & WEEKE, B. (1977) Characterization of extract of dog hair and dandruff from six different dog breeds by quantitative immunoelectrophoresis. Identification of allergens by crossed radioimmunoelectrophoresis (CRIE). *Acta Allergologica*, **32**, 147.
- BRIGHTON, W.D., LAMPARD, J. & FORDHAM, R. (1975) Activated paper as an immunosorbent. *Developments in Biological Standardization*, vol. **29**, 1.
- ERIKSSON, N.E. (1977) *Diagnostic methods in reaginic allergy. A clinical evaluation in patients with bronchial asthma and allergic rhinitis*. M.D. thesis, University of Göteborg, Göteborg, Sweden.
- FAGERBERG, E. & WIDE, L. (1970) Diagnosis of hypersensitivity to dog epithelium in patients with asthma bronchiale. *International Archives of Allergy and Applied Immunology*, **39**, 301.
- FONTANA, V.J., WITTIG, H. & HOLT, L.E. (1963) Observations on the specificity of the skin test. The incidence of positive skin tests in allergic and non-allergic children. *Journal of Allergy*, **3**, 348.
- FOUCARD, T., JOHANSSON, S.G.O., BENNICHT, H. & BERG, T. (1972) *In vitro* estimation of allergens by a radioimmune antiglobulin technique using human IgE antibodies. *International Archives of Allergy and Applied Immunology*, **43**, 360.
- FRANKLAND, A.W. (1967) Allergy to animals. *Acta Allergologica*, **22**, 175.
- GLEICH, G.J., LEIFERMAN, K.M., JONES, R.T., HOOTON, M.L. & BAER, H. (1976) Analysis of the potency of extracts of June grass pollen by their inhibitory capacities in the radio-allergosorbent test. *Journal of Allergy and Clinical Immunology*, **58**, 31.
- HAVNEN, J., APOLD, J., HVATUM, M., OSEID, S. & AAS, K. (1974) The radioallergosorbent test in the *in vitro* diagnosis of multiple reaginic allergy. *Clinical Allergy*, **3**, 411.
- HOOKE, S.B. (1944) Qualitative differences among canine danders. *Annals of Allergy*, **2**, 281.
- KOERS, W.J., YOUNG, E. & BERRENS, L. (1977) Animal dander allergy. *Clinical Allergy*, **7**, 245.
- KOIVIKKO, A. (1977) Children's asthma register. Description of a data system and a patient material. *Acta Allergologica*, **32**, 350.
- LIND, P. (1979) Commercial extracts of horse, cat and dog dander—characterization of specific allergen content and standardization of extract potency' *Abstracts of the Annual Meeting of the European Academy of Allergy and Clinical Immunology*, May 24–26, p. 108, Helsinki.
- LUNDKVIST, U. (1975) Research and development of the RAST technology. *Proceedings of the First North American Conference on RAST*, Febr 21–22, p. 85. *Symposia Specialists*, Miami.
- MARSH, D.G. (1975) Allergens and genetics of allergy. *The Antigens*, vol. III (ed. M. Sela), p. 271. Academic Press, New York.
- MOORE, S.B., HYDE, J.S. & MANALIGOD, L.M. (1977) A comparative study of allergens of canine origin. *Annales of Allergy*, **39**, 240.
- MURRAY, A.B. & COOK, C.D. (1963) Measurement of peak expiratory flow rates in 220 normal children from 4.5 to 18.5 years of age. *The Journal of Pediatrics*, **62**, 186.
- PEPYS, J., TANGEN, O., PERKINS, F.T., TATE, H. & BRIGHTON, W.D. (1975) Examination of cocksfoot pollen (*Dactylis glomerata*) extracts by skin prick test in man, RAST-based allergen assay and protein content. *Developments in Biological Standardization*, **29**, 284.
- RUDOLPH, R., MEIER-DUIS, H., KUNKEL, G., STAUD, R.-D. & STOCK, U. (1975) Ueber die Bedeutung von Tierhaarallergien bei Erkrankungen der oberen Luftwege. *Deutsche Medizinische Wochenschrift*, **100**, 2557.

- SARSFIELD, J.K., BOYLE, A.G., ROWELL, E.M. & MORIARTY, S. (1976) Pet sensitivities in asthmatic children. *Archives of Disease in Childhood*, **51**, 186.
- SCHULTZE-WERNINGHAUS, G., GONSIOR, E., THIEL, C., KROIDL, R. & MEIER-SYDOW, J. (1976) Häufigkeit und korrelative Beziehung von diagnostischen Kriterien der Tierschuppenallergie. *Acta Allergologica*, **31**, 44.
- STENIUS-AARNIALA, B.S.M., MALMBERG, C.H.O. & HOLOPAINEN, E.E.A. (1978) Relationship between results of bronchial, nasal and conjunctival provocation tests in patients with asthma. *Clinical Allergy*, **8**, 403.
- STENIUS-AARNIALA, B.S.M., MALMBERG, C.H.O., HOLOPAINEN, E.E.A. & BJÖRKSTEN, F. (1978) *In vivo* tests with pollen extracts previously investigated by means of direct RAST titration allergen assay. *Clinical Allergy*, **8**, 411.
- VANTO, T., VIANDER, M., KOIVIKKO, A. & SCHWARTZ, B. (1979) Diagnosis of dog dander allergy: A comparison between two allergen preparations using two variants of RAST. *Abstracts of the Annual Meeting of the European Academy of Allergology and Clinical Immunology*, May 24-26, p. 81, Helsinki.
- VARGA, J.M. & CESKA, M. (1972) Characterization of allergen extracts by polyacrylamide gel isoelectrofocusing and radio-immunosorbent allergen assay. II. Dog and cat allergens. *International Archives of Allergy and Clinical Immunology*, **42**, 438.

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.

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.