

# Diagnosis of nasal allergy to the house dust mite

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## SUMMARY

*Twenty-five patients with perennial rhinitis and a positive skin prick test (SPT) for Dermatophagoides pteronyssinus (Dp) and Dermatophagoides farinae (Df) were submitted to nasal provocation and the radioimmunosorbent test (RAST) for specific IgE-antibodies. We found a significant correlation in the reaction to both allergen extracts for all parameters examined. In addition, there was a significant correlation among the SPT, the RAST and the nasal provocation for Dp and between the SPT and the RAST for Df.*

*In patients with perennial rhinitis we recommend the combination of all three methods to differentiate unspecific rhinitis from an allergic rhinitis. Only the patients with proved allergic rhinitis could benefit from a specific hyposensitisation.*

## INTRODUCTION

After pollen, the house dust mite is the second most frequent allergen responsible for the induction of allergic rhinitis.

Major sensitizing allergen sources are faecal pellets and body surface proteins from house dust mites.

Dermatophagoides pteronyssinus and farinae are found in 50-90% of all samples of house dust in Europe and the U.S.A. (Smith et al., 1985).

The perennial presence of house dust mite allergens in the environment makes it difficult to ensure the diagnosis, which is based primarily on the history. Use of the prick test, the RAST and nasal provocation is important not only for reviewing the clinical relevance of the sensitization to the house dust mite but also for making a decision to initiate specific hyposensitisation therapy after preventive measures and symptomatic therapy have failed (Bousquet et al., 1985).

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## MATERIAL AND METHODS

Twenty-five patients with perennial rhinitis (15 males and 10 females, aged 12 to 54, mean 33) with a positive skin prick test (SPT) for both *Dermatophagoides pteronyssinus* (Dp) and *Dermatophagoides farinae* (Df) were included in our study. No patient suffered from allergic bronchial asthma or was on drug therapy at the time of the study.

### *Skin prick test*

The prick test was performed with an allergen extract 1:50 weight per volume (w/v), 50% glycerin and 0.4% phenol as a preservative, (Allergopharma, Reinbek) for Dp and Df.

The wheal diameter induced by the allergen extract was compared with that resulting from exposure to 1+99 w/v of histamine after 15 minutes. The same size was considered as (+), twice the size as (++) and three times as (+++); an allergen wheal at least three times the size of the histamine wheal and with pseudopodia was considered as (++++).

### *RAST*

Blood samples were drawn on the day of the prick test. Specific IgE antibodies against Dp and Df were determined by the Phadebas RAST (Pharmacia Diagnostic AB, Uppsala, Sweden). The results were expressed as RAST classes 0-4. A RAST  $\geq 2$  was considered positive.

### *Nasal provocation*

After anterior rhinoscopy, rhinomanometry was done with a Rhinotest 441 (Allergopharma, Reinbek). This procedure was repeated 10 min after the application of 0.04-0.05 ml of the diluent (0.9% NaCl, 0.4% phenol) in each nostril using a pump-nebulizer (Allergopharma, Reinbek). Patients with a nasal flow reduction of more than 10% after the application of the diluent were to be excluded from the study.

0.04-0.05 ml of the allergen solution (Dp, allergen extract for nasal provocation 1+99 w/v, 0.4% phenol, Allergopharma, Reinbek) were applied with pump-nebulizer in one nostril.

An anterior rhinoscopy and rhinomanometry were then performed 10 min later. The nasal provocation was evaluated according to the following scheme (Table 1). If the reaction to the Dp allergen extract was positive, the same provocation procedure was applied the next day with the Df allergen extract (1+99 w/v, 0.4% phenol, Allergopharma, Reinbek). If the reaction was negative, the provocation with the D.f. allergen extract was performed immediately afterwards in the other nostril.

Table 1. Evaluation of nasal provocation: negative (0-3 P), weak positive (4-7 P), positive (8-11 P) and strong positive (12-20 P)

rhinomanometry (RMM) volume/minute - difference in % from baseline values		clinical findings	secondary effects of nasal provocation
100 % and more	10 Point	<i>hypersecretion</i>	- conjunctivitis 1 P
99-90%	9 P	no secretion 0 P	- urticaria 6 P
89-80%	8 P	little secretion 1 P	- skin itching 2 P
79-70%	7 P	strong secretion 2 P	- throat itching 1 P
69-60%	6 P	<i>edema</i>	- ear itching 1 P
59-50%	5 P		- nose itching 1 P
49-40%	4 P	no edema 0 P	- coughing 1 P
39-30%	3 P	slight edema 1 P	- bronchoconstriction 3 P
29-20%	2 P	severe secretion 2 P	
19-10%	1 P	<i>irritation</i>	
9-0%	0 P		no irritation 0 P
			weak irritation 1 P
		strong irritation 2 P	

## RESULTS

*Skin prick test*

Dp allergen extract elicited the following reactions: (+) in 2/25 patients, (++) in 10/25, (++++) in 10/25 and (+++++) in 3/25.

Df allergen extract produced a (+) reaction in 3/25 patients, (++) in 11/25, (++++) in 9/25 and (+++++) in 2/25, (Figure 1a).

We found a highly significant correlation between the skin reaction of both house dust mite allergen extracts ( $r=0.71$ ,  $p < 0,0001$ ).

*RAST*

No specific IgE antibodies were detectable in two patients with a positive prick test to Dp. Four patients had specific IgE antibodies in a concentration of RAST class 1; seven patients reacted with RAST class 2, nine patients with class 3 and three patients with class 4. Four patients with a positive prick test to Df had no specific IgE antibodies; three patients reacted with RAST class 1, five patients with class 2, seven with class 3 and six patients with class 4 (Figure 1b).

The specific IgE antibody concentration against Dp and Df showed an excellent correlation ( $r=0.8$ ,  $p < 0,0001$ ).

Seventy-six percent of the patients with a positive prick test to Dp had clinically relevant levels of specific IgE antibodies to Dp (RAST class  $\geq 2$ ). 72% of patients with a positive prick test to Df had a RAST class  $\geq 2$  against Df (Figure 2b).

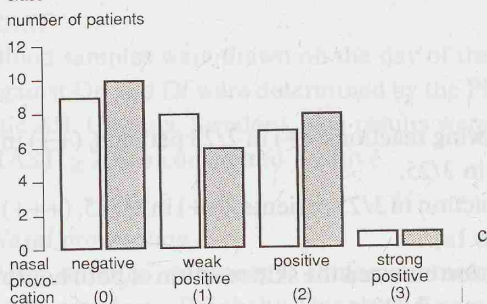
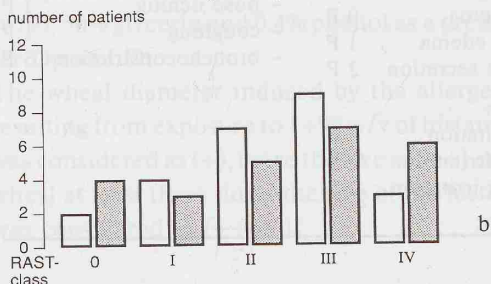
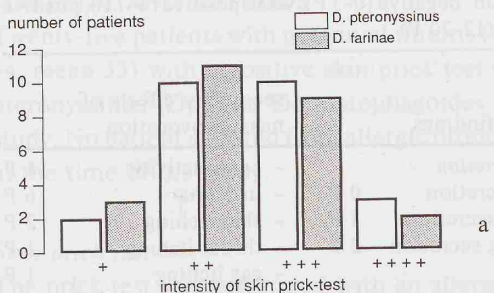


Figure 1. Grouping of patients according to the results of nasal provocation, skin prick-test and RAST-class.

Linear regression analysis showed a significant correlation between the prick test and the concentration of specific IgE antibodies (RAST class) for both house dust mites (Dp:  $r=0.51$ ,  $p < 0.01$ ; Df:  $r=0.41$ ,  $p < 0.05$ ).

#### Nasal provocation

Nasal provocation with Dp extract produced a negative reaction (0-3 P) in nine patients, a weak positive reaction (4-7 P) in eight, a positive reaction (8-11 P) in seven and a strong positive reaction (12-20 P) in 1 patient.

Nasal provocation with Df extract elicited a negative reaction in 10 patients, a weak positive reaction in six, a positive reaction in eight and a strong positive reaction in one patient (Figure 1c). As seen with other parameters examined, the correlation between the results of the nasal provocation to both house dust mite extracts was highly significant ( $r=0.76$ ,  $p < 0.0001$ ).

Prick-test (d <sub>1</sub> )	nasal provocation (d <sub>1</sub> )			
	0	1	2	3
+	1	/	1	/
++	5	2	2	1
+++	3	5	2	/
++++	/	1	2	/

Prick-test (d <sub>2</sub> )	nasal provocation (d <sub>2</sub> )			
	0	1	2	3
+	2	1	/	/
++	5	3	3	/
+++	3	2	3	1
++++	/	/	2	/

Figure 2a. Correlation between prick-test and nasal provocation for d<sub>1</sub> (*D. pteronyssinus*) and d<sub>2</sub> (*D. farinae*).

Prick-test (d <sub>1</sub> )	d <sub>1</sub> -RAST-class				
	0	I	II	III	IV
+	/	1	/	/	1
++	2	1	5	1	1
+++	/	2	2	6	/
++++	/	/	/	2	1

Prick-test (d <sub>2</sub> )	d <sub>2</sub> -RAST-class				
	0	I	II	III	IV
+	2	/	/	1	/
++	2	1	5	/	3
+++	/	2	/	5	2
++++	/	/	/	1	1

Figure 2b. Correlation between prick-test and RAST-class for d<sub>1</sub> (*D. pteronyssinus*) and d<sub>2</sub> (*D. farinae*).

RAST class (d <sub>1</sub> )	nasal provocation (d <sub>1</sub> )			
	0	1	2	3
0	2	/	/	/
I	1	3	/	/
II	4	2	/	1
III + IV	2	3	7	/

RAST class (d <sub>2</sub> )	nasal provocation (d <sub>2</sub> )			
	0	1	2	3
0	3	/	1	/
I	/	3	/	/
II	4	1	1	/
III + IV	3	2	6	1

Figure 2c. Correlation between RAST and nasal provocation for d<sub>1</sub> (*D. pteronyssinus*) and d<sub>2</sub> (*D. farinae*).

64% of patients with a positive prick test to Dp showed a positive nasal provocation to Dp, whereas 60% of patients whose prick test was positive to Df had a positive nasal provocation to Df (Figure 2a).

52% of the patients with RAST  $\geq 2$  had a positive nasal provocation for Dp and 44% for Df (Figure 2c).

The linear regression analysis revealed a correlation between the nasal provocation with Dp and the RAST ( $r=0.43$ ,  $p < 0.05$ ) as well as between the nasal provocation and the SPT ( $r=0.43$ ,  $p < 0.05$ ). For Df, the correlation between the nasal provocation and the RAST was significant ( $r=0.55$ ,  $p < 0.005$ ), but no correlation was detectable between the nasal provocation and the SPT.

#### DISCUSSION

Our results showed a significant correlation between the SPT reaction and the specific IgE antibodies to both house dust mites. These findings confirm the results of Kersten (1978) and Kerrebijn et al. (1976). After allergen contact, atopic patients are able to produce specific IgE antibodies. Via circulation, these antibodies reach the basophils and mast cells in skin and mucosa and bind to their Fc-receptors. These basophils and mast cells are able to react with allergen and release mediators through IgE bridging.

There is an equilibrium between the level of the specific IgE in blood and the basophil/mast-cell-bound antibodies (Conroy et al., 1977). This balance explains the good correlation between the RAST, the SPT and the nasal provocation. This correlation is influenced by many factors, including the different reactivity of mast cells in skin and mucosa, different antigen preparations, priming effects with other allergens and unspecific mucosal hyperreactivity.

The immunological similarity of Dp and Df (cross-reactivity) (Lind, 1986) explains the highly significant correlation between Dp and Df in the SPT, the RAST, and the nasal provocation. This cross-reactivity is not 100%, and our results show that Dp extract yields a better correlation between the SPT and the nasal provocation than Df extract. The clinical relevance of the sensitization to house dust mites can only be evaluated by performing an allergen provocation of the target organ. Because of the afore mentioned cross-reactivity we recommend using the Dp extract first. A Df provocation is only necessary in cases of questionable or negative reactions. If the history raises suspicion of house dust mite sensitization and nasal provocation yields negative results or cannot be performed (e.g. active allergic or unspecific rhinitis, local steroid or  $\alpha$ -mimetic therapy), a conjunctival provocation test might be necessary. We recommend a specific hyposensitization in cases where a clinically relevant sensitization to house dust mites has been confirmed (positive SPT, RAST, and provocation tests), an unspecific component is not dominant, and local therapy is ineffective.

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SUMMARY

Endothelin (ET) is a newly discovered peptide that was first cultured from bovine endothelial cells. Amino acid analysis discovered ET-1 as the only one that was reported to be an endothelin potent vasoconstrictor in vivo. In this study we have determined the structure of ET-1 and its biological activity.

ET produces a potent vasoconstrictor effect in the blood vessels both of the canine and the human basal arteries. The dose effect of ET-1 in canine circulation was 10<sup>-10</sup> M concentration and 10<sup>-11</sup> M threshold.

This response was found to be endothelial cell dependent. In vitro ET-1 also contracts a preparation of rat aortic smooth muscle. A subthreshold concentration of ET-1 when is continuously applied to endothelial cells induced endothelial cell contraction. An endothelial derived substance such as ET-1 might have a role in the regulation of vascular tone. ET-1 may play an important role in the regulation of vascular tone of the normal blood vessels and in the pathogenesis of hypertension.

INTRODUCTION

Vascular tone depends on several substances contraction of vascular smooth muscle not demonstrating dependence on stimuli from outside (1). This was first described by Mellander and Johnson (1967). Although the mechanism for the development of inherent tone has not yet been clarified, it can be considered as the integrated result of shape twitches initiated by action potentials of smooth muscle cells. Continuous release of noradrenaline (NA) from the sympathetic nerve plexus with the liberation of its release by acetylcholine (ACh), which is received from

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