

From the Allergology Division and the Pulmonary Division of the Department of Internal Medicine, University Hospital, Groningen, The Netherlands.

COMPARISON OF THE NASAL MUCOSA  
RESPONSE ON CHALLENGE OF HOUSE DUST  
AND MITES  
(*Dermatophagoides pteronyssinus*)  
ALLERGENS

By

Z. PELIKAN & K. de VRIES

Various authors have reported that mites of the "Dermatophagoides" genus may be responsible for the specific allergen in house dust (1, 2, 6, 8, 10, 11, 12, 13, 14, 15, 16, 19, 21, 22, 25, 26, 28, 29, 30, 31). The similarity of the allergenic component of house dust and *Dermatophagoides* (D.) *pteronyssinus* extracts seems probable from the results obtained by skin tests (1, 2, 3, 12, 14, 20, 21, 23, 24, 27, 28, 31, 32) and inhalation tests (2, 14, 31). Little is known about the response of the nasal mucosa to challenge with extracts of mites. Therefore a comparative study of the effects of the common house dust extract and of extracts of *D. pteronyssinus* on the nasal mucosa was performed.

MATERIALS AND METHODS

*Substances\*\*\**

*House dust* in a concentration of 5.0 mg of dry weight of dialyzed and lyophilized extract per 1 ml of Coca solution;

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\*\*\* All allergen extracts and dilution solutions were prepared by Pharmacy "Diephuis" (Groningen). The raw product of *D. pteronyssinus* was obtained

*Mites* (*D. pteronyssinus*) in concentrations of 100 and 250 Noon equivalent Units per 1 ml of phosphate solution.

*Coca solution* (5.0 g of NaCl; 2.0 g of  $\text{NaHCO}_3$ , 10  $\text{H}_2\text{O}$ ; 4.0 g of Phenol; Distilled water ad 1000 ml).

*Phosphate solution* (3.865 g of  $\text{NaH}_2\text{PO}_4$ , 1  $\text{H}_2\text{O}$ ; 4.98 g of  $\text{Na}_2\text{HPO}_4$ , 2  $\text{H}_2\text{O}$ ; 3.8 g of NaCl; 5.0 g of Phenol; Distilled water ad 1000 ml).

*The apparatus equipment* consisted of an one-channel recorder (Heath Built; Model 20 A; USA); an electric differential-pressure transducer (Godart NV; The Netherlands); a water manometer; a small rubber balloon of 5 mm diameter and 25 mm length (Lode NV; The Netherlands); polyethylene tubes as connecting system.

### *Principle of the Method*

After allergen challenge the nasal mucosa can react with swelling and hypersecretion. The swelling of the nasal mucosa influences the passage of air through the nose resulting in pressure differences between the nasopharyngeal cavity and the outside air. These pressure differences, so-called nasopharynx-nostril-pressure gradient (NPG), expressed in cm of  $\text{H}_2\text{O}$ , were recorded and considered as an index of the degree of nasal passage. The mean values of the NPG were calculated over a time interval of 90–120 seconds, during regular breathing (18).

### *Procedure*

After calibration of the recorder, the rubber balloon was introduced through one of the nasal cavities into the nasopharynx of the patient and the connecting tube was fixed to the alae nasi. The balloon was filled with 2 ml of air and then connected with the pressure transducer by a polyethylene tube. The patient breathed only through the other (non-intubated) nasal cavity, the mouth being closed, during the measurement and recording of the NPG. Five to fifteen minutes after the introduction of the balloon, while the patient breathed regularly, the actual investigation was performed in the following steps:

- the NPG was recorded during 3 minutes to obtain an "initial value".
- the appropriate control solution (Coca or Phosphate solution) was applied on the nasal mucosa under the lowest concha in the non-intubated nasal cavity, by means of a wad of cotton wool on a nasal probe, for 3 minutes. The NPG was then recorded three-times during 10 minutes. If the patient showed no changes of the mean NPG with respect to the initial value, the investigation was continued.
- the allergen was applied for 3 minutes in the same way as the control

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from the Dept. of Allergology of the State University of Leiden (Dr. R. Voorhorst).

solution and then the mean NPG was measured and recorded at 0, 5, 10, 20, 30, 45 and 60 minutes after the application.

- when the NPG value after 60 minutes had not returned to the initial value, a 45-60 minutes' waiting interval followed, during which the NPG value always returned to the initial value.

- after the 45-60 minutes' waiting interval, the second allergen provocation followed in the same way as described above.

- if the patient had some nasal complaints after the investigation (obstruction, hypersecretion, sneezing), an aqueous solution of epinephrine (1:1000) was applied to his nasal mucosa for 1 minute.

The provocation tests were considered as positive, when the NPG values increased within 20 minutes after the end of the allergen challenge, by at least 1.5 cm of H<sub>2</sub>O, in respect to the initial value.

### *Patients*

Thirty-two patients, selected for this clinical experiment, were partly out-patients from the Pulmonary Division (University Hospital, Groningen) and partly hospitalized patients from the Department for Asthmatic Diseases of "Beatrixoord" (Haren-Groningen). All patients had positive skin tests to house dust and most of them also to mites. All these patients suffered from allergic rhinitis; often combined with chronic non-specific lung disease (CNSLD) (7, 9, 17). The patients were investigated in a period without manifest nasal complaints. Neither antihistaminics nor sympathicomimetics were given in a 24 hours' period before this clinical experiment.

The patients were investigated in 2 ways:

- I. In 24 patients the house dust extract was applied in a concentration of 5.0 mg/ml and the extract of mites in a concentration of 250 NU/ml. In 4 of these 24 patients no reaction of the nasal mucosa was observed after the house dust and mites challenge. Ten of the positively reacting patients were challenged with mites and then with house dust (subgroup 1) and 10 of them were challenged with house dust and then with mites (subgroup 2).

- II. In 8 patients the house dust extract was applied in a concentration of 5.0 mg/ml and the extract of mites in a concentration of 100 NU/ml. Four of these patients were challenged with mites and then with house dust (subgroup 3) and 4 of them were challenged with house dust and then with mites (subgroup 4).

The characteristics of the positively reacting patients of the 4 subgroups are presented in Table 1.

## RESULTS

The mean values of the nasopharynx-nostril pressure gradient (NPG), measured before the experiment ("initial value"),

TABLE 1  
*Characteristics of the Positively Reacting Patients.*

| Subgroup | Patient | Sex | Age | Nasal complaints |                |          |                          | Blood eosinophilic cells per mm <sup>3</sup> | Skin tests (i.c.) |       |
|----------|---------|-----|-----|------------------|----------------|----------|--------------------------|----------------------------------------------|-------------------|-------|
|          |         |     |     | obstruction      | hypersecretion | sneezing | Lividity of nasal mucosa |                                              | House dust        | Mites |
| 1        | 1       | ♂   | 42  | ++               | +++            | ++       | —                        | 825                                          | +                 | ±     |
|          | 2       | ♂   | 17  | +                | +              | —        | +                        | 660                                          | ++±               | ++    |
|          | 3       | ♂   | 30  | ++               | ++             | +        | —                        | 308                                          | ++±               | ++    |
|          | 4       | ♀   | 38  | +                | —              | +        | —                        | 704                                          | +±                | +     |
|          | 5       | ♂   | 20  | +++              | ++             | ++       | +                        | 594                                          | +                 | ++    |
|          | 6       | ♂   | 23  | +++              | +++            | +        | —                        | 825                                          | ++±               | ++    |
|          | 7       | ♂   | 20  | +                | +              | —        | —                        | 363                                          | +++               | ++    |
|          | 8       | ♂   | 15  | +                | ++             | +++      | —                        | 308                                          | ++                | +++   |
|          | 9       | ♂   | 47  | ++               | ++             | +++      | +                        | 308                                          | +±                | —     |
|          | 10      | ♀   | 23  | ++               | ++             | ++       | —                        | 253                                          | +±                | —     |
| 2        | 11      | ♂   | 35  | +++              | —              | ++       | —                        | 583                                          | ++                | —     |
|          | 12      | ♂   | 19  | +++              | ++             | ++       | —                        | 583                                          | ±                 | ±     |
|          | 13      | ♂   | 30  | ++               | +              | —        | +                        | 297                                          | +++               | ++±   |
|          | 14      | ♂   | 51  | +                | +              | +        | —                        | 715                                          | +                 | +     |
|          | 15      | ♂   | 24  | +++              | +              | —        | —                        | 473                                          | ++±               | ++±   |
|          | 16      | ♂   | 21  | ++               | ++             | +        | +                        | 583                                          | ++                | +     |
|          | 17      | ♀   | 41  | ++               | +++            | ++       | —                        | 319                                          | +++               | +     |
|          | 18      | ♂   | 39  | +++              | —              | +        | —                        | 231                                          | +                 | ×     |
|          | 19      | ♀   | 15  | —                | ++             | +        | —                        | 385                                          | +±                | +±    |
|          | 20      | ♂   | 46  | —                | +              | —        | —                        | 385                                          | ++                | ++    |
| 3        | 21      | ♂   | 24  | ++               | —              | +++      | +                        | 242                                          | ++±               | ±     |
|          | 22      | ♀   | 41  | —                | —              | ++       | —                        | 110                                          | ++±               | ++    |
|          | 23      | ♂   | 24  | +++              | +++            | ++       | —                        | 220                                          | +±                | +     |
|          | 24      | ♂   | 21  | +                | +              | +        | —                        | 880                                          | +++               | ×     |
| 4        | 25      | ♂   | 19  | +++              | +++            | +++      | —                        | 264                                          | ±                 | ±     |
|          | 26      | ♂   | 30  | ++               | +              | +        | —                        | 473                                          | ++                | +     |
|          | 27      | ♂   | 20  | ++               | +              | ++       | —                        | 165                                          | ++                | +     |
|          | 28      | ♂   | 33  | ++               | +              | ++       | —                        | 264                                          | +++               | +++   |

♂ = male, ♀ = female, × = unknown.

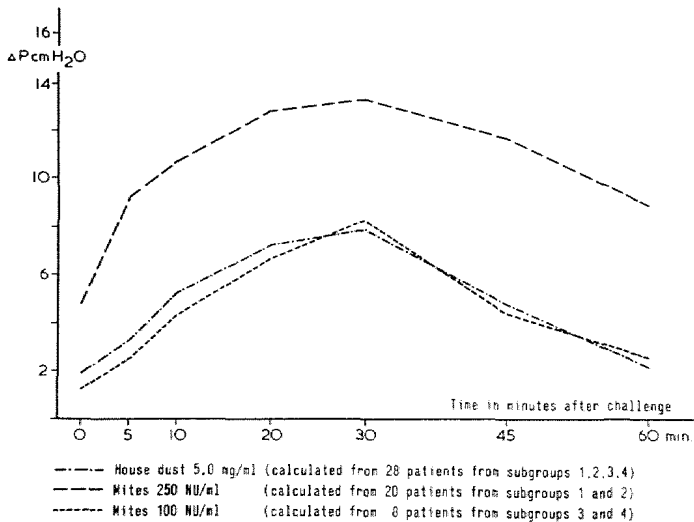
The evaluation of the intracutaneous tests:

— = normal skin appearance.

± = wheal not greater than original injected papule.

after the application of control solutions, and after the application of the allergens in all subgroups of patients, are given in Table 2 and their statistical evaluation in Table 3 (2 samples t-test). The mean increase of the NPG after challenge with the allergens, in respect to the NPG after challenge with the appropriate control solutions, are summarized in Fig. 1.

The control solutions had no effects on the nasal mucosa of any patient. Every patient who had a positive response to house dust also exhibited a positive response to mites. The



Time response  $\Delta P$  relationship after challenge with different allergens, in respect to the control solutions.

Table 1. (Cont.)

- + = wheal increase up to 7.5 mm in diameter.
- + ± = wheal increase up to 10.0 mm in diameter.
- ++ = wheal increase up to 12.5 mm in diameter.
- + + ± = wheal increase up to 15.0 mm in diameter.
- + + + = wheal increase greater than 15 mm, with surrounding erythema, and sometimes with "pseudopodia".

TABLE 2  
*The Mean Values of NPG (in cm H<sub>2</sub>O) at Different Times in the Subgroups.*

| Sub-group | Initial value | Coca solution | House dust                      |     |     |      |      | Phosphate solution | Mites                           |     |     |      |      |      |      |      |      |
|-----------|---------------|---------------|---------------------------------|-----|-----|------|------|--------------------|---------------------------------|-----|-----|------|------|------|------|------|------|
|           |               |               | Time in minutes after challenge |     |     |      |      |                    | Time in minutes after challenge |     |     |      |      |      |      |      |      |
|           |               |               | 0'                              | 5'  | 10' | 20'  | 30'  | 45'                | 60'                             | 0'  | 5'  | 10'  | 20'  | 30'  | 45'  | 60'  |      |
| 1         | 2.1           | 2.3           | 5.4                             | 6.8 | 8.1 | 9.3  | 9.2  | 7.2                | 4.9                             | 1.8 | 5.0 | 8.0  | 8.8  | 11.2 | 11.8 | 10.9 | 10.2 |
| 2         | 2.1           | 2.0           | 4.2                             | 5.9 | 8.3 | 10.2 | 11.1 | 8.4                | 5.0                             | 2.3 | 8.7 | 14.8 | 16.8 | 18.7 | 18.9 | 16.4 | 11.2 |
| 3         | 1.9           | 1.9           | 3.0                             | 4.2 | 6.6 | 9.0  | 9.7  | 6.5                | 4.0                             | 1.8 | 2.8 | 4.0  | 6.1  | 8.8  | 9.5  | 7.0  | 4.6  |
| 4         | 2.1           | 2.0           | 3.3                             | 4.1 | 5.9 | 8.6  | 10.4 | 5.5                | 2.8                             | 2.0 | 3.4 | 4.5  | 6.1  | 8.8  | 10.4 | 5.4  | 3.3  |

Subgroup 1 (10 patients) : 1st challenge with Mites 250 NU/ml; 2nd challenge with House dust 5.0 mg/ml.  
 Subgroup 2 (10 patients) : 1st challenge with House dust 5.0 mg/ml; 2nd challenge with Mites 250 NU/ml.  
 Subgroup 3 ( 4 patients) : 1st challenge with Mites 100 NU/ml; 2nd challenge with House dust 5.0 mg/ml.  
 Subgroup 4 ( 4 patients) : 1st challenge with House dust 5.0 mg/ml; 2nd challenge with Mites 100 NU/ml.

TABLE 3

*Survey of Significance of Differences Among the NPG Values Measured After the Challenge of Individual Allergens.*

|          | Initial values | Control solutions | Differences of the NPG between  |    |     |     |     |     |     |
|----------|----------------|-------------------|---------------------------------|----|-----|-----|-----|-----|-----|
|          |                |                   | Allergens                       |    |     |     |     |     |     |
|          |                |                   | Time in minutes after challenge |    |     |     |     |     |     |
|          |                |                   | 0'                              | 5' | 10' | 20' | 30' | 45' | 60' |
| I - II   | —              | —                 | —                               | +  | +   | +   | +   | +   | +   |
| I - III  | —              | —                 | —                               | +  | +   | +   | +   | +   | +   |
| I - IV   | —              | —                 | +                               | +  | +   | +   | +   | +   | +   |
| II - III | —              | —                 | —                               | ±  | —   | —   | —   | —   | —   |
| II - IV  | —              | —                 | ±                               | ±  | —   | —   | —   | —   | —   |
| III - IV | —              | —                 | —                               | —  | —   | —   | —   | —   | —   |

- I. Mites 250 NU/ml (The NPG values of 20 patients from subgroups 1 and 2).  
 II. House dust 5.0 mg/ml (The NPG values of 20 patients from subgroups 1 and 2).  
 III. Mites 100 NU/ml (The NPG values of 8 patients from subgroups 3 and 4).  
 IV. House dust 5.0 mg/ml (The NPG values of 8 patients from subgroups 3 and 4).

— =  $p > 0.05$ .

± =  $0.05 > p > 0.025$ .

+ =  $p \leq 0.01$ .

reactions of the nasal mucosa after the application of house dust and after the application of mites in both concentrations, follow a similar time pattern.

The degree of response after the challenge with the mites in a concentration of 100 NU/ml is identical with the degree of response after the challenge with the house dust in a concentration of 5.0 mg/ml. The degree of response after the challenge with the mites in a concentration of 250 NU/ml is quantitatively higher than the degree of response both after the house dust in a concentration of 5.0 mg/ml, and after the mites in a concentration of 100 NU/ml (Table 3). When both the allergens are applied in the following concentrations, house dust 5.0 mg/ml and mites 100 NU/ml, the sequence of their application does not play any role in the degree of response of the nasal mucosa. The effect of one of them is not influenced by a previous application of the other.

The provocation effect of house dust (5.0 mg/ml) as well as of mites (100 NU/ml and 250 NU/ml) reaches a maximum within 30 minutes and the time of recovery to the initial NPG value depends on the degree of the response. Generally it can be stated that the provocation effects of the house dust (5.0 mg/ml) as well as of mites in both the concentrations tested do not disappear completely within 60 minutes after the end of the allergen challenge, in most of patients.

A refraction stage has not been observed after the allergen application. All patients with a positive response of their nasal mucosa to the house dust (5.0 mg/ml) as well as to the mites (100 NU/ml; 250 NU/ml) challenge, also showed one or more of nasal complaints (obstruction, hypersecretion, sneezing), after the allergen challenge. The course of the nasal complaints runs parallel to the course of the NPG changes.

No reactions of the nasal mucosa were observed in these series of patients 2-8 hours after the allergen challenge.

#### DISCUSSION

The purpose of this investigation was to compare quantitatively the response of the nasal mucosa after the house dust challenge with the response after the mites challenge. The possibility that the apparatus equipment and the method used may influence the reaction of the nasal mucosa was examined in a number of control investigations in another similar group of patients. No significant NPG changes occurred during a 60 minutes' period following introduction of the balloon if no challenge was performed (first control test) or if Coca (or Phosphate) solution was used for the challenge (second control test).

The results of our experiment show that all patients who had a positive response of the nasal mucosa to the house dust had also a positive response to the mites. A positive response to only one of the allergens tested was not observed. The

provocation effects of the mites in a concentration of 100 NU/ml are similar to those of the house dust in a concentration of 5.0 mg/ml. The provocation effects of the mites in a concentration of 250 NU/ml are quantitatively higher than those of the house dust in a concentration of 5.0 mg/ml; there is a clear dose-response effect. The results are in accordance with the findings of the skin tests that the concentration of 5.0 mg of house dust per 1 ml is equivalent to a concentration of 100 NU of mites per 1 ml.

The relationship between house dust and mites that we found in our study on the nasal mucosa, is in accordance with observations of other authors who reported a highly significant correlation between house dust and mites, either in skin tests (1, 2, 3, 12, 14, 20, 21, 23, 24, 27, 28, 31, 32) or in inhalation tests (2, 14, 31). The results of this investigation may suggest that mites are an important constituent of house dust. A definitive solution of the problem of similarity or identity of the mites allergen and of the house dust allergen cannot be reached by clinical experiment only, but immunochemical analysis of both the allergens is necessary (4, 5, 8, 13).

#### SUMMARY

The response of the nasal mucosa to the house dust (5.0 mg/ml) and to the mites *Dermatophagoides pteronyssinus* (100 NU/ml and 250 NU/ml) challenge was demonstrated in 28 patients suffering from allergic rhinitis, often combined with chronic non-specific lung disease (CNSLD). All patients had positive skin tests to house dust and most of them also to mites. All patients who showed a positive reaction of the nasal mucosa to house dust also showed a positive reaction to mites. The provocation effects of the mites in a concentration of 100 NU/ml are equivalent to those of the house dust in a concentration of 5.0 mg/ml. The provocation effects of the mites in a concentration of 250 NU/ml are quantitatively higher than those of the mites in a concentration of 100 NU/ml. There is a distinct dose-response effect.

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