

Respiratory allergies (bronchial asthma and rhinitis) due to sensitization of type I allergy to red spider mite (*Panonychus ulmi* KOCH)

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Summary

The inhabitants of a fruit growing area often report spontaneously of sensitization to the red spider mite (RSM) (*Panonychus ulmi* KOCH). These are for the most part sensitizations with low clinical symptoms (rhinitis, conjunctivitis and erythema). Severe clinical developments with bronchial asthma have been observed. We investigated six patients working in a fruit growing area sensitized by RSM. The sensitizations corresponded to a Type I allergy. Skin tests and provocation tests (nasal as well as bronchial) with RSM showed immediate reactions and RAST positive results were obtained using RSM allergen disks. RAST measurements of sera from nine house-dust mite *Dermatophagoides pteronyssinus* allergic patients using RSM allergen disks showed RAST-class > 1 for eight patients. RAST inhibition and immunoprint suggest a possible cross-reaction between RSM and *D. pteronyssinus*.

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Introduction

Patients from a nearby fruit-growing area came for allergy consultation and reported that they had noticed 'other allergies'. Each complained of symptoms of conjunctivitis, rhinitis, erythema and shortness of breath. They were clearly able to attribute these complaints to contact with red spider mite (RSM). Despite the degree of familiarity of this allergy in the affected laymen, the effect of sensitization to RSM is rarely mentioned in literature [1]. The information revealed by the affected patients caused us to continue with *in vivo* and *in vitro* allergy tests using an allergen extract prepared from RSM.

As some of these patients also showed allergic reactions to house dust mite *Dermatophagoides pteronyssinus* (*D. pteronyssinus*), sera from these patients were also measured by RAST using RSM and *D. pteronyssinus* allergen disks.

Classification of RSM and its occurrence in fruit-growing areas

RSM (*Panonychus ulmi* KOCH) belongs to the order of mites, to the family of spider mites (*Tetranychidae*) and represents its own species (see Table 1).

RSM passes the winter in the branches and barks of trees. In the spring (with the onset of the pink stage of the apple blossoms) it moves to the lower side of the leaves. It remains there for 6–8 generation cycles, well into September. All generation stages are found on the leaves and branches: eggs, nymphs and the adult animal. RSM is primarily found on apple and plum trees. It is considered a plant pest and so is subjected to intensive plant pesticide measures.

Patients and methods

All patients ($n=6$) were able to attribute their complaints either to working in orchards or on fruit trees. They all assumed that contact with RSM had triggered their problem. Two sample case histories follow.

A 46-year-old fruit-grower's wife complained, in October 1985, of recurrent colds accompanied by eye and nose irritation, erythema and considerable asthmatic

Table 1. Classification of RSM. Relationship of RSM to the house dust mite *D. pteronyssinus*

Category (sub-class)	Acari (mites)	
Sub-category	Prostigmata	Astigmata
Family	Tetranychidae (spider mites)	Acaridae (storage mites)
Species	'Red Spider "Mite"' (<i>Panonychus ulmi</i> KOCH)	'House dust mites' (Pyroglyphidae)
Type	Fruit tree spider (vulg.: 'Red Spider')	<i>Dermatophagoides pteronyssinus</i> <i>Dermatophagoides farinae</i> <i>Dermatophagoides microceras</i> <i>Euroglyphus maynei</i>

Table 2. Data of the six patients with considerable allergy symptoms due to contact with RSM

Patients	Age (years)	Problems	Prick-test RSM	Prick-test <i>D. pteronyssinus</i>	RAST RSM/ <i>D. pteronyssinus</i>	Provocation test nasal/bronchial	Atopy
1 R.K. (f)	28	Rhinitis, conjunctivitis in autumn	+++	0	0/0	Nasal + to RSM bronchial n.d.	No
2 F.K. (m)	19	Asthma +++ itching due to RSM	++++	+++	2/4	Bronchial + to RSM and <i>D. pteronyssinus</i> nasal n.d.	Yes
3 F.M. (m)	58	Asthma for 10 years	+++	+++	0/4	Bronchial + to RSM and <i>D. pteronyssinus</i> nasal n.d.	No
4 S.S. (f)	24	Cough +++ Asthma + Conjunctivitis during harvest of fruits	+++	++	2/0	Nasal + to RSM bronchial n.d.	No
5 H.A. (f)	47	Asthma for 15 years Rhinitis during harvest of fruits	++++	++	3/2	Nasal and bronchial + to RSM	No
6 D.G. (m)	57	Asthma for 24 years during harvest of fruits	+++	0 +++	0/0 0	Bronchial + to RSM nasal n.d.	No

0, negative. ++, < histamine control (0.1%). +++, histamine control. +++, > histamine control. n.d., not done.

problems. These symptoms had appeared for the last 15 years and always began in September when the apples were picked. The complaints increased considerably throughout late October and then stopped spontaneously. The asthmatic symptoms were progressive so she had to be given corticosteroids. Her history offered no further allergy data (patient 5, Table 2).

In late summer of 1988, a 57-year-old fruit-grower reported considerable asthmatic complaints since the mid 1960s. He was also clearly able to relate his asthma to his

work in the orchard and especially to contact with RSM. Asthma progressed and he had to be treated with corticosteroids (patient 6, Table 2).

In vivo tests

Skin tests were performed with a specially prepared RSM-extract (1000 PNU/ml and 5000 PNU/ml; [Allergopharma, Joachim Ganzer KG, Reinbek, Germany]). Skin titration with extracts of 1000 and 5000 PNU/ml, nasal and bronchial challenge tests were also performed. Nasal

Table 3. RAST results for house dust mite (*D. pteronyssinus*) allergic patients measured with *D. pteronyssinus* and RSM allergen disks. The non-allergic serum pool (NC) served as negative control.

Allergen disks Sera	RSM RAST-class	<i>D. pteronyssinus</i> RAST-class
1	3	2
2	3	2
3	2	3
4	2	3
5	2	2
6	1	1
7	1	4
8	0	2
9	2	3
NC	0	0

challenge tests were done recording symptoms score and rhinomanometric results. Bronchial challenge tests were done according to the recommendations of the DGAIF (Deutsche Gesellschaft für Allergie- und Immunitätsforschung [German Society of Allergy and Immunology]). The extracts were prepared from RSMs kindly provided by BASF, Ludwigshafen, FRG.

In vitro investigations

RAST. The specific IgE level in the patients' sera to RSM and to *D. pteronyssinus* was determined by RAST using RSM- and *D. pteronyssinus*-allergen disks (Allergopharma Joachim Ganzer KG). As reference the RAST reference sera and ^{125}I -anti-IgE from Pharmacia (Freiburg, Germany) were used. Furthermore sera of nine *D. pteronyssinus* allergic patients who showed a positive skin prick test with *D. pteronyssinus* extract (Allergopharma) were measured by RAST using *D. pteronyssinus* and RSM allergen disks. A non-allergic serum pool ($n = 154$) served as negative control.

RAST inhibition. To examine the degree of crossreactivity between RSM and *D. pteronyssinus* the allergen extracts were calibrated to the same protein content $750 \mu\text{g}$ protein/ml and were measured by RAST inhibition [2,3] using *D. pteronyssinus* and RSM allergen disks, the serum of patient no. 5 (see Table 2: serum diluted 1:5) and ^{125}I -anti-human-IgE (Pharmacia) as tracer for IgE.

IEF. IEF was done according to the Pharmacia-LKB prescription. Protein ($25 \mu\text{g}$) of the RSM and *D. pteronyssinus*

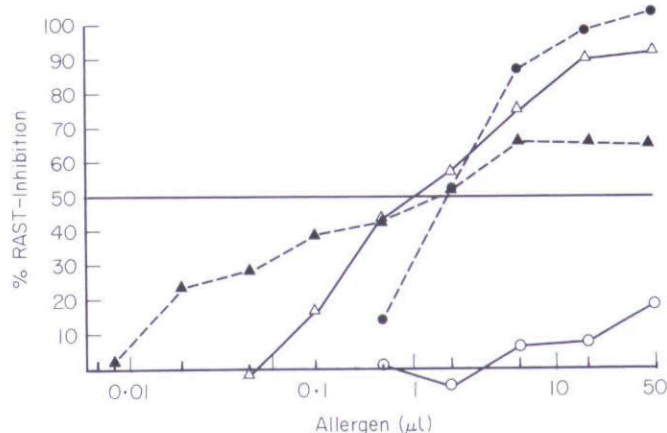


Fig. 1. RAST-inhibition of the *D. pteronyssinus* and RSM extracts. ●, *D. pteronyssinus* extract, *D. pteronyssinus* disks. ▲, RSM extracts, *D. pteronyssinus* disks. △, RSM extract, RSM disks. ○, *D. pteronyssinus* extracts, RSM disks.

sinus extract were applied on the gel. The proteins were made visible by Coomassie brilliant blue (E. Merck, Darmstadt, Germany) staining.

Immunoprint. The allergen patterns of RSM and *D. pteronyssinus* on the basis of their isoelectric points were performed by immunoprint [4]. From each extract $25 \mu\text{g}$ protein [5] were applied on the agarose gel. The proteins were transferred by capillary blotting onto a nitrocellulose membrane (NC) (Schleicher and Schüll, Dassel, Germany), the NC was blocked and then incubated with the serum of patient no. 5 (1:5 diluted). After washing, the NC-membrane was incubated with radiolabelled anti-human-IgE (3 KBq/ml) and the autoradiographs were developed after 7 and 14 days at -20°C on Kodak x-Omat AR film. Marker proteins were purchased from Pharmacia.

Results

In vivo tests

The results are shown in Table 2.

Skin-prick tests. Control tests in 20 non-allergic subjects from the fruit-growing area were all negative with the RSM-extract. Skin-prick tests in patients with allergic complaints caused a +++ to ++++ positive reaction with the RSM-extract.

Challenge tests. Nasal provocation using 1000 PNU/ml of the RSM extract was clearly positive (+) in patients 1, 4 and 5. Bronchial provocation tests using the same

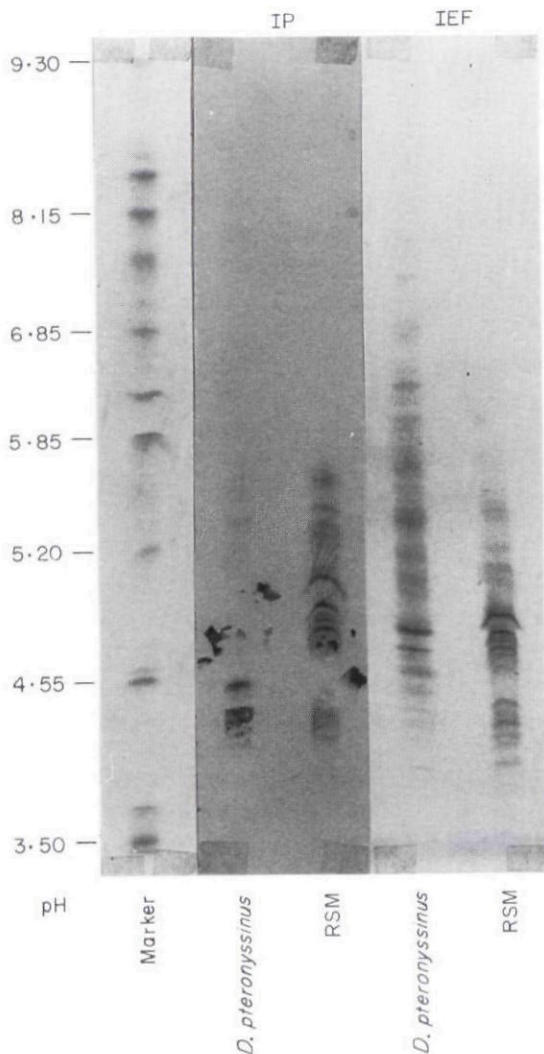


Fig. 2. IEF (on the right) and immunoprint (on the left) of the RSM and *D. pteronyssinus* extracts.

concentration were carried out on four patients (patients 2, 3, 5 and 6; Table 2), revealing definite immediate-type reactions, but no late reactions.

In vitro tests

RAST Positive RAST was found in three of the six patients using RSM allergen disks (RAST-class 2 and 3, respectively). Two of the six patients had RAST-class 4 and one RAST-class 2 when using *D. pteronyssinus* allergen disks (Table 2). Out of nine house dust mite *D. pteronyssinus* allergic patients, eight showed RAST-classes between 1 and 3 when using RSM allergen disks (Table 3). With both allergen disks, the non-allergic control pool serum showed RAST-class 0, i.e. the positive

RAST-classes could not be attributed to unspecific binding. The total IgE levels of tested sera were between 120 and 320 ku/l.

RAST inhibition When measuring RSM- and *D. pteronyssinus* allergen-extracts by RAST inhibition with *D. pteronyssinus*-allergen disks, the *D. pteronyssinus*-extract (homologous system) produced an inhibition of 100% compared with 67% for the RSM-extract in the heterologous system. On testing the extract with RSM-allergen disks, the RSM-extract achieved a total of 93% (homologous system) and the *D. pteronyssinus*-extract a total of 20% inhibition (heterologous system) (Fig. 1).

IEF By IEF the *D. pteronyssinus* and RSM extracts showed most of the proteins in the acidic region (Fig. 2).

Immunoprint The *D. pteronyssinus*- and the RSM-extract both showed allergen bands in a pH-range between 4.1 and 4.5 and 5.2 and 5.4 (Fig. 1). With regard to the intensity of radiostaining, of the individual allergen bands, the most pronounced common allergen bands were discovered in a pH-range between 4.1 and 4.45. In both extracts the radiostaining for equivalent allergen bands was of similar intensity. Using a non-allergic control serum pool no allergen bands could be detected (not shown).

Discussion

The clinical-allergological relevance to sensitization with RSM (*Panonychus ulmi* KOCH) is well known to the inhabitants of the fruit-growing region we studied.

Allergological data were gained from six patients with severe respiratory complaints. They revealed a considerable degree of sensitization towards RSM. Skin tests, provocation tests (bronchial and nasal) and RAST showed positive reactions to this allergen. RAST inhibition and immunoprint provided the evidence for possible crossreactions to the house dust mite *D. pteronyssinus*. From the results of RAST inhibition, it can be supposed that different concentrations of common allergens may exist in the tested extracts. Also by RAST measurements of *D. pteronyssinus* allergic patients with RSM allergen disks, common allergens in both species can be suspected.

There was a better correlation in the RAST-class between RSM and *D. pteronyssinus* in the group of the nine mite allergic patients than in the group of the actual patients. From the mite group it was only known by prick testing that they were *D. pteronyssinus* allergic patients. RSM was not tested in prick test in this group. Besides *in vitro* investigation, *in vivo* investigation like skin-prick test, and bronchial provocation tests should be performed

to establish that there is crossreactivity of clinical relevance between RSM and *D. pteronyssinus*. Recently *in vivo* and *in vitro* investigations were performed with sera of five RSM allergic patients from Austria who showed an actual sensitization to RSM and *D. pteronyssinus* (own laboratory data).

Although by *in vitro* investigations like RAST inhibition and immunoblot crossreactivity between RSM and *D. pteronyssinus* can be suspected, nevertheless an independent sensitization to RSM cannot be totally excluded. An exclusive sensitization, however, seems not very reasonable because of the relatively rare chance to come into contact with RSM.

Table 2 shows that some patients had a positive prick test to RSM but a negative RAST. The sera of these patients were taken 6 months after allergen exposure and it can be supposed that by avoiding the allergen the specific RSM IgE level decreased. Sera taken at the same time as prick testing showed a good correlation to the RSM-RAST.

Despite the fact that RSM is well-known to medical laymen in fruit-growing regions, a lack of information exists in allergy literature [1]. In 1986 Schlegel & Schulz [6] reported the history of a fruit-grower in a liability insurance matter. In this case, sensitization to RSM with bronchial asthma was recognized as a professional illness. In the field of general medicine as well, colleagues have been consulted on this subject when relevant questions arose [1].

Thus the actuality of this allergen in certain regional and professional fields (primarily fruit-growing regions) has been recognized and confirmed. Recently Astarita *et al.* [7] reported allergic reactions associated with bronchial asthma to the spider mite *Tetranychus urticae* in farmworkers. Thirty-five investigated farmworkers showed relevance of this spider mite as an allergen source in the environment.

Contact with the allergen to RSM is not unavoidable. Complaints have 'only' been observed as the results of immediate exposure, such as when picking apples, working on the trees in the orchards, etc. Therefore, therapy lies in the avoidance of allergens and is (theoretically) feasible. For many patients, however, the simple avoidance of the allergen (which amounts to not working in the

orchards) is not really practicable or if so, causes considerable economic and family problems. In our series of patients, two (no. 5 and 6) were classified as having occupationally caused ailments.

As our investigations showed, RSM can be an important allergen in occupational allergy especially for persons working in a fruit-growing area. For a more precise statement of crossreactivity between the house dust mite *D. pteronyssinus* and RSM, further *in vitro* and clinical investigations must be done.

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