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Review article

Tetranychids and occupational allergy

The taxonomic designation "tetranychids" encompasses a group of mites belonging to the Family Tetranychidae, within the Suborder Prostigmata (Fig. 1). These mites are phytophagous and commonly parasitise plants and trees, where they can be seen as a reddish stippling on the leaves together with long silken filaments (they build true spider webs) the aim of which is to establish a microclimate that is appropriate for their development. Because of this, these tetranychids are usually and widely known among Spanish farmers as *arañas rojas*, or "red spiders", while in English they are termed "red velvet mites"¹.

Their distribution is ubiquitous, particularly in warm, humid climates. In Spain they are predominant throughout the Mediterranean coastal regions, Andalusia, Extremadura and the Canary Islands. From the commercial point of view they represent a significant agricultural pest problem, and over the last few years there has been an increase in the occurrence of these tetranychid mites, which have become resistant to the usual pesticides. They can develop optimally on over 150 plant species, including fruit-bearing trees (citrus trees, rosaceae), other fruits (watermelon, cantaloupe, strawberry), cotton, grapes, vegetables (such as tomato, cucumber, courgette, pepper) and ornamental plants and flowers such as the carnation; particular mention should be made of greenhouse cultures².

ALLERGOLOGIC IMPORTANCE

The allergologically important tetranychids, or red velvet mites, belong to the genera *Tetranychus* and *Panonychus*. The species with the greatest number of occupational allergy cases reported are: *Panonychus ulmi*, a parasite of fruit trees of the *Rosaceae* family that has been reported as a cause of occupational allergy in workers harvesting these fruits³⁻⁵; *Panonychus citri*, which causes occupational disease in citrus fruit workers particularly in the eastern areas of Spain (the "Levante")⁶⁻⁸; *Tetranychus mcdanieli*, involved as an occupational allergen in grape harvesters⁹, and *Tetranychus urticae*, which causes occupational allergy problems in flower and leaf vegetable cultivators¹⁰⁻¹², particularly in greenhouse workers.

Other mites of the *Tetranychidae* family that have not yet been described as occupational allergens have however considerable economic importance. Table I summarises the types of cultures that are preferentially parasited by the various species.

The investigations examining the impact of these tetranychids on samples of symptomatic agricultural workers are summarised in Table II. When they are suspected to be involved as occupational allergens, red velvet mites have been observed to have considerable sensitising capacity¹³⁻¹⁵, and they have also been

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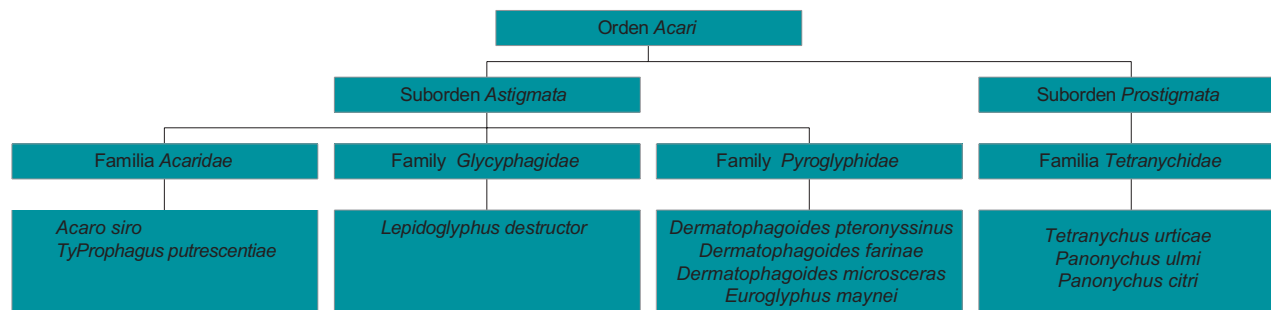


Fig. 1. Taxonomic classification of the mites.

Table I. Tetranychid species and cultivations they parasitise

Species	Type of cultivation
<i>Bryobia rubriocolus</i>	Apple and pear orchards
<i>Bryobia kissophylla</i>	Ivy
<i>Bryobia praetiosa</i>	Grass, herbaceous plants
<i>Metatetranychus ulmi</i>	Fruit-bearing trees, flowers
<i>Tetranychus turkestanii</i>	Cotton
<i>Panonychus ulmi</i>	Apple, pear and plum orchards
<i>Panonychus citri</i>	Citrus trees
<i>Tetranychus mcdanieli</i>	Grape
<i>Tetranychus urticae</i>	Vegetables, carnation

reported as the cause of occupational asthma in a high percentage of exposed agricultors¹⁴. However, Burches *et al.*¹⁶ have ascertained a lesser impact of this allergen (which was clinically significant in only 3.3% of the sample studied), perhaps because their study was carried out on agricultural workers with suspected allergic disease but with no clear occupational implication. The large number of monosensitised workers in the study of Astarita *et al.*¹³

is remarkable; this may perhaps be explained by the fact that this study was performed on a highly selected sample of agricultural workers in whom other occupational allergens had already been ruled out.

Table III presents the epidemiological studies related to red velvet mites¹⁷⁻¹⁹, and shows that up to one quarter of the workers exposed become sensitised to these tetranychids. The prevalence of occupational allergic disease among such workers has been estimated to be slightly lower, ca. 19%¹⁹.

POPULATION AT RISK

Considering the extensive distribution of the red velvet mites in both greenhouse and open-air cultures, tetranychids should be included in the standard allergen panel to be tested on any agricultural worker with suspected occupational disease. Whether the extract to be used should be prepared from mites of the genus *Panonychus* or of the genus *Tetranychus* should be decided considering the particular cultivation involved.

Table II. Studies performed with tetranychids on samples of symptomatic workers

Authors	Red velvet mite	Type of cultivation	No. of cases	Positive prick tests (%)	Monosensitised (%)	Positive specific IgE (%)
Astarita <i>et al.</i> ¹³	TU	Open air	30	78	73	78
		Greenhouse	16			
Burches <i>et al.</i> ¹⁶	TU	PC	150	36	0	36
		Horticulture and citrus				
Delgado <i>et al.</i> ¹⁴	TU	Greenhouse	24	75	54	66
Kim <i>et al.</i> ¹⁵	PC	Citrus	16	100	62.5	81.3

TU = *Tetranychus urticae*; PC = *Panonychus citri*.

Table III. Epidemiologic studies of red velvet mites

Authors and year	Red velvet mite species	No. of cases	Type of cultivation	Positive prick test (%)	Occupationally encountered mite (%)
Kim et al. ¹⁷ (1999)	PC	725	Apple orchards	23,2	6,6
	TU			16,6	4,4
Kim et al. ¹⁸ (1999)	PC	181	Citrus	25	6
Navarro et al. ¹⁹ (1999)	TU	241	Carnation (greenhouse)	25	7,6

TU = *Tetranychus urticae*; PC = *Panonychus citri*.

As is the case with other high molecular weight occupational allergens, atopy is a significant predisposing factor for sensitisation in the occupational environment^{18,20}, so that atopic individuals working in agriculture should be advised to undertake early and vigorous eradication measures for the elimination of the red velvet mite pest.

Considering the ubiquity of these mites, the susceptible and at risk population encompasses not only the agricultural workers themselves, but also manipulators of agricultural products and flowers²¹. Besides the occupational involvement, and considering the widespread diffusion of red velvet mites in gardening, sensitisation may also occur in other environments, such as households or gardens where ornamental plants exist.

CHARACTERISATION

Using SDS-PAGE immunoblotting procedures, and in the case of *Tetranychus urticae*, a relevant protein band has been described in the 19 kDa range, and the binding

intensity of this band correlates with the RAST values for each of the sera used²². Further minor protein bands have been described in the 46, 37, 25 and 15-16 kDa ranges^{12,23}.

Studies with this same mite using SDS immunoblotting and RAST inhibition have demonstrated high antigenic similarity in extracts of *Tetranychus urticae* from three different types of cultivation environments (courgettes, cucumbers and carnations), and also similar allergenic capacity when assessing the skin response in the workers tested²³. This implies that this tetranychid is sensitising by itself, regardless of the actual cultivation it has parasitised.

CROSS-REACTIVITY

A joint assessment of the different studies which tested red velvet mite extracts on a control population (Table IV) showed that among 124 non-atopic subjects the test results had always been negative; this further emphasises the specificity of the test.

Table IV. Control subjects (atopics and non-atopics) and positive prick tests with red velvet mites

Authors	NON-ATOPICS		ATOPICS			
	N	Positive prick	MITES		OTHER	
			N	Positive prick	N	Positive prick
Kroidi et al. ⁵	20	0	–	–	–	–
Burches et al. ¹⁶	15	0	50	50	–	–
Delgado et al. ¹²	4	0	8	9	4	0
Delgado et al. ¹⁴	–	–	7	0	8	0
Astarita et al. ¹³	10	0	?	?	10?	0
Navarro et al. ¹⁹	75	0	68	11	84	8
Total	124	0	133	61	106	8

N = Number of patients.

When the control subjects were atopic, in a total sample of 133 individuals with house dust mite allergy positive prick tests with red velvet mites were seen in 45.8%, while the positivity rate was only 7.5% among 106 atopic subjects with no mite allergy. This suggests that the probability of a positive skin prick test with a tetranychid extract in a patient with mite allergy is sixfold that of any other atopic subject.

An analysis of the in vitro studies assessing cross-reactivity shows that Kroidl et al.⁵ found 67% partial cross-reactivity between *Dermatophagoides pteronyssinus* and *Panonychus ulmi* (and 20% cross-reactivity in the reverse RAST inhibition test), using the serum from a single patient.

Other authors have not detected cross-reactivity between *Tetranychus urticae* and *Dermatophagoides pteronyssinus* extracts^{10,13}, particularly when the sera used were mainly from patients monosensitised to *Tetranychus urticae*²⁰.

Burches et al.¹⁶, using sera from patients who were allergic both to *Dermatophagoides pteronyssinus* and to *Tetranychus urticae*, found 80% cross-reactivity both for this particular red velvet mite and for *Panonychus citri*, although the reverse RAST inhibition was positive in only 55% and 68% of the cases, respectively, for each of the red velvet mites and *Dermatophagoides pteronyssinus*.

Ashida et al.⁸ observed no cross-reactivity between *Panonychus citri* and *Dermatophagoides pteronyssinus* and *D. farinae* extracts with the exception of the serum from one patient, which showed 94%, 81% and 87% inhibition, respectively.

All these apparent discrepancies might have their explanation in the results of Kim et al.¹⁸, who observed two distinct cross-reactivity patterns: (a) with a serum pool from patients with positive prick tests to *Dermatophagoides pteronyssinus* and *Panonychus citri*, the inhibition between the two extracts was greater than 52% and dose-dependent, while (b) with a serum pool from patients monosensitised to *Panonychus citri* there was no inhibition with the *Dermatophagoides pteronyssinus* extract.

It might thus be suggested that subjects monosensitised to any of the red velvet mites recognise a specific protein with no cross-reactivity to the house dust mites. In the case of *Tetranychus urticae*, this specific protein might be the 19 kDa one observed as the most relevant one in the immunodetection study²². The remainder of the subjects might recognise any other protein belonging to the minor bands (46, 37, 25 or 15-16 kDa) detected in other extracts

of this allergen^{12,23}. In the case of the 25-kDa protein, this might explain a partial cross-reactivity between red velvet mites and house dust mites in some patients.

In the case of *Panonychus ulmi*, the cross-reactivity to *Dermatophagoides pteronyssinus* might be due to one protein observed in both extracts at the 4.1 and 4.5 pH range⁵.

DIAGNOSTIC METHODS IN TETRANYCHID SENSITISATION

The red velvet mites are known occupational allergens in the agricultural environment, able to induce respiratory and skin symptoms through type I and type IV immunologic hypersensitivity mechanisms^{5,24}. As in any other study of presumed occupational allergy, the necessary steps are the assessment of the occupational symptomatology, the demonstration of sensitisation and the demonstration of a causal relationship to the allergen.

Anamnesis

It must be assessed whether the patient recognises the presence of the red velvet mite pest in the actual cultivations in which he or she works. As these mites are macroscopic in size, they are easily identified by the workers, as demonstrated in up to 93% of the cases when the patients are directly questioned in this regard¹⁹. When the exposed worker reports worsening of his or her symptoms in relation to the exposure to red velvet mites, there is usually a significant association to the diagnosis of tetranychid sensitisation¹⁹, so that this aspect should be kept in mind when establishing the diagnostic suspicion.

The severity of the symptoms may be variable along the year; in greenhouse cultures it is in Spring when the red velvet mites achieve their greatest reproduction level; in the case of fruit-bearing trees, the seasonal symptomatology is most evident at the time of the harvest^{3,4}.

Occupational rhinitis, conjunctivitis, asthma and urticaria through an IgE-mediated mechanism have been reported in relation to red velvet mites, and the symptoms may be of immediate or delayed onset. Rhinitis is usually the earliest-occurring clinical picture²⁵, and also the most frequent one¹³.

When the exposure to red velvet mites such as *Tetranychus urticae* occurs within a greenhouse, a greater incidence of bronchial asthma²² has been observed as com-

pared to similar studies performed on open-air cultivation workers¹³; this might indicate a greater allergenic aggressiveness of this tetranychid in the greenhouse environment as compared to open spaces.

The average exposure time required for the development of symptoms ranges in most cases between two and four years¹³ but might be shorter, down to 1.6 years, for greenhouse workers²², or longer in the case of open-air exposure, up to 12.9 years for the development of asthma and 11.5 years for rhinitis¹⁵.

Skin symptoms in the form of contact urticaria are a frequent companion to respiratory symptomatology; the development of whealing is occasionally reported to be related to contact with the leaves parasitised by the pest¹⁰, or even to stings or bites from these mites in individuals in direct contact with them⁷. There have also been reports of contact dermatitis through a type IV hypersensitivity mechanism²⁴.

Prick test

Red velvet mite extracts are not commercially available, and such extracts must be prepared *ex profeso* for performing this test and the other *in vitro* and *in vivo* studies. Two procedures have been described for the preparation of the extract. One of them¹⁴ uses as the antigen source leaves or stalks from the strongly parasitised culture so as to include possible allergens secreted by the mite, and particularly those contained in its web. If this procedure is selected, a control prick test must be performed with an extract prepared from the same cultivation, but parasite-free. In the other procedure, the extract is prepared from the whole bodies of the red velvet mites^{13,23}. In both cases, the concentration of the extract is usually 1-2 mg/ml, or 1000-5000 PNU/ml⁵.

Conjunctival challenge test

This is performed with the same aqueous extract used for the prick test, at 1:10,000 dilution and with a single dose in the case of *Tetranychus urticae*¹⁶.

Nasal challenge test

Adequate responses are achieved beginning with a 1000 PNU/ml extract in the case of *Panonychus ulmi*, although concentrations up to 5000 PNU/ml may be used⁵.

Specific bronchial challenge test

In asthmatic subjects, this test usually elicits an immediate positive result and, in up to one half of the cases,

a dual-type response^{14,22}. Although the diagnostic yield is good, it is not greater than that of the prick test or the specific IgE detection, so that its use does not appear to be necessary except in the context of research protocols²⁶. Based on the existence of well-documented cases^{4,6,12} and on the studies of patient series¹⁴, at present the association of positive clinical features, prick test results and a nonspecific bronchial hyperreactivity test are considered to suffice for a diagnosis of allergic occupational asthma caused by these tetranychids^{15,18}.

For the specific bronchial challenge test, dilutions from a 1 mg/ml (or 1000 PNU/ml) mother extract are usually applied^{5,14}.

Red velvet mite exposure test

The recommended exposure time is two hours, in a pesticide-free work environment with red velvet mites and with the patient performing his usual work or chores. The expiratory peak flow rate is assessed at 30-minute intervals during the exposure, and at 6-hourly intervals thereafter¹³.

Specific IgE

The quantitation of the specific IgE is a useful complement for the diagnosis of red velvet mite allergy²⁶, although it is less sensitive than the prick test^{4,19}.

Some authors^{13,18} have observed a statistically significant association between the diameter of the wheal in the prick test and the specific IgE levels.

Patch test

An open patch test should be performed when contact urticaria is suspected, or a traditional epicutaneous test when the clinical manifestation is an eczema. In the case of *Tetranychus urticae*, the test material used is a⁵⁻⁶ mg/ml aqueous extract¹³.

THERAPY PERSPECTIVES

As for any other occupational allergic disease, the first step in the management should be that of avoidance of the aetiologic agent. This, however, is a not-at-all-easy task for the agricultural worker, who recognises the red velvet mites as one of the most difficult agricultural pests to eradicate. Thus, when the diagnosis of occupational allergy caused by tetranychids is established, the specific advice given shall be to quit the occupational exposure.

The social and economic implications render this advice most often impossible to follow, and thus the induced symptoms should be prevented and palliated with the help of the therapeutic armamentarium appropriate for the particular clinical manifestations of each patient.

Therapeutic control remains difficult as long as the patient continues to be exposed to his occupational environment. As for other high-molecular-weight occupational allergens, immunotherapy might have a very important role in this context. Up to the present date, however, and with the exception of one report of a patient treated with a *Panonychus ulmi* extract⁴, only a single summary has been published stating that, after one year of immunotherapy with *Tetranychus urticae*, a decrease in symptomatology and in the specific serum IgE levels of the treated patients was observed. The number of patients so treated and the methodology used are however unknown, as that work was not published in full¹¹.

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