

In vitro diagnosis of farmers' IgE-mediated allergy by Phadiatop® and three new multiallergen RAST analyses

van Hage-Hamsten M, Johansson SGO. *In vitro* diagnosis of farmers' IgE-mediated allergy by Phadiatop® and three new multiallergen RAST analyses.

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Identification of persons with atopic allergy in a population is difficult if the pattern of sensitizing allergens is unique. Three new multiallergen tests, Professional Allergy Mixes (PAX) 1–3 (Pharmacia Diagnostics, Uppsala, Sweden), have recently been introduced to screen IgE-mediated allergy among farmers. PAX 1 contains animal danders and feathers, PAX 2 mites and insects, and PAX 3 pollens and molds. The value of these new tests for the determination of IgE-mediated allergy among farmers was compared with that of Phadiatop®, a test for general atopy. Of 440 farmers, 91 were positive to Phadiatop and 97 to any of PAX 1–3. None of the farmers were positive in all tests. Only 70/97 sera positive in RAST to PAX 1–3 had a positive Phadiatop, whereas of 91 sera positive in Phadiatop, 70 had specific IgE antibodies to PAX 1–3. The value of using either Phadiatop or PAX 1–3 is limited (sensitivity 74–79%), but, together, these four tests will detect almost all (95.9%) farmers with IgE-mediated sensitization and all (100%) with symptoms. We have also shown that the grain weevil *Sitophilus granarius* and the botfly *Gasterophilus intestinalis* are important sources of allergens in rural environments.

M. van Hage-Hamsten,
S. G. O. Johansson

Department of Clinical Immunology, Karolinska Hospital, Karolinska Institute, Stockholm, Sweden

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Marianne van Hage-Hamsten, MD
Department of Clinical Immunology
Karolinska Hospital
S-104 01 Stockholm
Sweden

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Farm workers are popularly supposed to lead a healthy, open-air life. Nevertheless, occupational hazards lurk in the rural environment, and several of these are important causes of lung disease. One major problem is IgE-mediated occupational allergy. Farmers and farm workers are exposed not only to common allergen sources, such as animal danders, pollens, molds, and mites, but also to insects such as the grain weevil *Sitophilus granarius* and the botfly *Gasterophilus intestinalis*. In the light of current knowledge, storage mites are the predominate source of allergens, causing both asthma and rhinoconjunctivitis (1, 4, 7, 10, 17). A simple screening technique for IgE-mediated allergy would not only facilitate diagnosis but also reduce the delay before appropriate medical treatment.

Until now a broad RAST panel has been needed for *in vitro* screening of atopic allergy in a rural population. The usefulness of Phadiatop® (Pharmacia Diagnostics, Uppsala, Sweden), an *in vitro* test for atopy in general, is limited, since it screens only for common inhalant allergens and not for occupational allergens. The same holds for the definition of atopy. However, since, for instance, storage mites, insects, and wheat and rye pollens are common in farming

environments, one should not overlook the possibility of sensitization to their frequently occurring allergens. Recently, three new multiallergen tests, Professional Allergy Mixes (PAX) 1–3 (Pharmacia Diagnostics, Uppsala, Sweden), were introduced to screen IgE-mediated allergy among farmers. PAX 1 contains animal danders and feathers, PAX 2 mites and insects, and PAX 3 pollens and molds. We wanted to compare the value of these new tests with that of Phadiatop for the determination of IgE-mediated allergy in a rural population. We also wanted to establish the importance of *S. granarius* and *G. intestinalis* as allergen sources in the rural setting.

Material and methods

Patients

Sera from 440 farmers who had earlier participated in an epidemiologic survey of respiratory diseases among farmers in Sweden were used in the study (7). These persons had been subjected to both clinical and laboratory investigations. A total of 123 farmers were sensitized to common inhalant allergens and/or storage mites, as confirmed by either skin

prick test or RAST. Of these, 114 had asthma and/or rhinoconjunctivitis and were considered to be allergic. Nine farmers were asymptomatic.

Determination of IgE antibodies

Specific IgE measurements by RAST, as described by Johansson et al. (11), were performed against PAX 1 (horse dander, cow dander, and chicken and goose feathers), PAX 2 (*Lepidoglyphus destructor*, *Acarus siro* (storage mites), *S. granarius*, and *G. intestinalis*), and PAX 3 (wheat pollen, rye pollen, *Aspergillus*, and *Alternaria*). *S. granarius* and *G. intestinalis* were analyzed as individual allergen sources. The reagents were obtained from Pharmacia Diagnostics, Uppsala, Sweden, and the tests were performed under standardized conditions, according to the manufacturer's recommendations. A positive RAST was defined as a value ≥ 0.35 kU/l. The results of the two insects were compared with the IgE response to allergens of *L. destructor* and *Dermatophagoides pteronyssinus* previously reported in the same farming population (8).

Phadiatop

The Phadiatop test (Pharmacia Diagnostics, Uppsala, Sweden) was performed according to the manufacturer's instructions, and the results were expressed as positive or negative.

Results

Of the 123 farmers, 91 were positive to Phadiatop and 97 to any of PAX 1–3. Sixteen were positive in RAST to PAX 1, 62 to PAX 2, and 35 to PAX 3. None of the farmers were positive to all tests (Fig. 1). PAX 2 gave the highest geometric mean kU levels of the three PAX tests (Table 1). However, the maximum kU level was found against PAX 3.

A total of 118 farmers were positive to Phadiatop

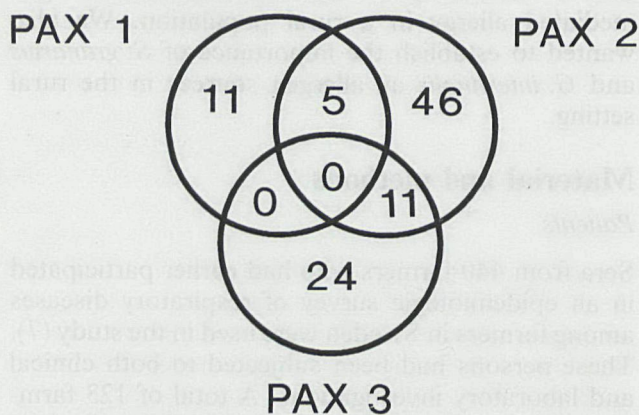


Fig. 1. Distribution of PAX 1–3 among farmers positive in the three tests.

Table 1. Number, mean strengths, and range of positive RAST against PAX 1–3

Test	No.	kU/l (geom. mean)	Range kU/l
PAX 1	16	0.9	0.4–2.3
PAX 2	62	1.7	0.4–70
PAX 3	35	1.3	0.4–110

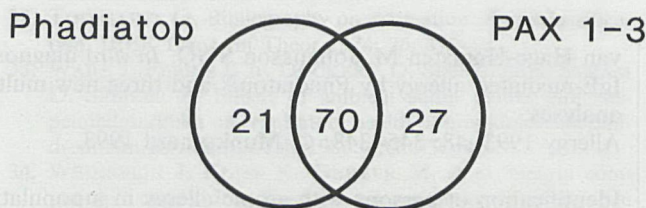


Fig. 2. Distribution of Phadiatop and PAX 1–3 analyses among 118 of 123 farmers with IgE-mediated sensitization.

and/or PAX 1–3, and 70 were positive to all four tests. Only 70/97 sera which were positive in RAST to PAX 1–3 had a positive Phadiatop, and of the 91 sera which were positive in Phadiatop, 70 had specific IgE antibodies to PAX 1–3. PAX 2 and Phadiatop picked up 110/123 subjects, and the combination of these tests was superior to PAX 1 (100/123) and PAX 3 (92/123) in the combination with Phadiatop in screening for IgE-mediated sensitization. In addition, 118/123 farmers with IgE-mediated sensitization and all subjects with allergic symptoms (114/114) were detected by the four tests. However, 5/123 farmers lacked IgE antibodies to all four tests in spite of being skin-prick-test positive to either pollens or animal danders. The distribution of the analyses among the 118 subjects is shown in Fig. 2.

Twenty-nine of the 440 farmers were positive in RAST to *G. intestinalis* (geometric mean 0.9 range 0.4–3.2 kU/l), and six to *S. granarius* (range 0.7–2.3 kU/l). Twenty-one and four, respectively, were also positive in Phadiatop. The calculated overall prevalences of a positive RAST to *G. intestinalis* and *S. granarius* in the whole farming population ($n = 2578$) of Gotland were 5.2% and 1.1%, respectively (Table 2). However, *L. destructor* gave a higher prevalence of a positive RAST than did *G. intestinalis* or *S. granarius* (8).

Table 2. Prevalence of positive RAST against mites and insects among 2578 farmers

Allergen source	%
<i>Gasterophilus intestinalis</i>	5.2
<i>Sitophilus granarius</i>	1.1
<i>Lepidoglyphus destructor</i>	6.8*
<i>Dermatophagoides pteronyssinus</i>	5.2*

* van Hage-Hamsten et al. Clin Allergy 1987; 17: 417–23.

Discussion

Farming is an occupation involving hundreds of millions of people in the world. On a farm, one is exposed not only to common inhalant allergens in large amounts, but also to special allergens such as cattle dander, grain flour, and insects. Sensitization to pollens, molds, and other common allergen sources seems to be rare among rural workers (8, 10). However, several studies have shown that a large proportion is allergic to storage mites (1, 4, 7, 10, 17). In our survey of respiratory diseases in a Swedish farming population, storage mites were responsible for more than one-third of IgE-mediated reactions (7). Allergy to storage mites has also been demonstrated in other occupations such as grain handling (2, 15) and baking (13, 16).

Farmers who suffer from allergy are often prepared to endure it, since they neither can afford time off work nor are able to seek alternative employment. However, it is crucial to detect these persons since their condition over the years may lead to deterioration of respiratory function and nonspecific bronchial hyperreactivity. Chan-Yeung and colleagues have shown that approximately half the patients with western red cedar asthma continue to have nonspecific bronchial hyperreactivity for as long as 5 years after removal of the offending agent (3).

The most common diseases associated with atopy are asthma, rhinoconjunctivitis, and eczema. The first step in screening for atopic allergy is to establish whether the subject is atopic. The Phadiatop test is, like the definition of atopy, based on the detection of an IgE-mediated sensitization to common inhalant allergens (14). Not only is it a valuable test to screen for an atopic constitution (18), but in clinical trials it has also given excellent correlations to the final diagnosis of atopic allergy (5). However, Pepys has defined atopy as "that form of immunological reactivity of the subject in which IgE antibody is readily produced in response to ordinary exposure to common allergens of the subject's environment" (14). Since storage mites, insects, and wheat and rye pollens are part of the rural environment, they should, according to Pepys' definition, be checked when screening for atopic allergy. This makes it difficult for the physician to decide which RAST test to choose. Therefore, mixed allergen tests are of great value. Recently, three new multiallergen mixes, PAX 1-3, typical of rural environments, were introduced.

When comparing Phadiatop and the three PAX analyses for screening of atopic allergy among farmers, we found that PAX 1-3 and Phadiatop detected about the same number of farmers with IgE-mediated sensitization, 97 and 91, respectively. However, Phadiatop used alone failed to detect more than one-

fifth of allergic farmers. Thus, some farmers have only IgE antibodies against allergens specific to farming surroundings, since they were not detected by Phadiatop. Only 59.3% (70/118) of farmers were positive to both Phadiatop, and PAX 1-3, indicating that they were sensitized to a broad panel of allergens. When Phadiatop and PAX 1-3 were used together, they apparently detected all allergic persons and nearly all farmers with IgE-mediated sensitization.

A majority of farmers positive in RAST to PAX 1-3, 62 of 97, had specific IgE antibodies restricted to PAX 2. These analyses, which comprise mites and insects, also gave the highest geometric mean value of specific IgE of the three PAX tests. It was not surprising that PAX 2 gave the highest number of positive RAST tests, since we have earlier shown that storage mites are the predominant source of allergens, in both sensitization and numbers (9). The combination of PAX 2 and Phadiatop was also superior to PAX 1 and PAX 3 in screening for IgE-mediated sensitization.

To detect all sensitized persons in a rural setting, one needs to find out which are the main allergens for this particular environment. Insects and mites are one source of inhalant allergens. Frankland & Lunn reported three decades ago that *S. granarius* caused asthma in two laboratory workers who were exposed to the dust of grain infested by this weevil (6). One cause of millworkers' asthma has been shown to be *S. granarius* (12), a common pest in stored grain, particularly wheat. It causes IgE-mediated reactions, but less than does the insect *G. intestinalis*. We found that *G. intestinalis* is a rather common allergen source, yielding the third highest prevalence figure of a positive RAST among 2578 farmers. This botfly is parasitic to the horse; thus, a large number of farmers may be exposed to it.

The cost of screening for allergy among farmers with RAST would be very high if all allergens included in PAX 1-3 are to be analyzed individually. From a cost-benefit point of view, the three new multiallergen analyses are an attractive alternative. The present study showed that carefully selected and well-characterized allergen mixes will not only simplify the diagnostic procedure but also increase the accuracy, since a negative RAST test would exclude, not only a specific sensitization, but also the atopic constitution of the patient.

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