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Publication date
2001

Published in
International archives of allergy and immunology

[Link to publication](#)

Citation for published version (APA):

Aalberse, R. C., & Vermeulen, E. (2001). Immune reactivity to mite allergens in nonatopic subjects: Immune deviation or immune ignorance. *International archives of allergy and immunology*, 24((1-3)), 208-209.

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Immune Reactivity to Mite Allergens in Nonatopic Subjects: Immune Deviation or Immune Ignorance

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Key Words

Allergy · Immune deviation · Mite allergen · Crossreactivity · IgG

Abstract

Most subjects without IgE to *Dermatophagoides pteronyssinus* do not have IgG to Der p 1 or Der p 2 (as measured by RIA). However, by immunoblot or ELISA, IgG reactivity (mostly IgG1) to mite components is easily detectable. This discrepancy is caused largely by immune reactivity to mite components with a high molecular weight under native conditions (possibly mite gut flora cross-reactive with human gut flora) and partially by the presence of IgG with low affinity for fluid-phase antigen. We conclude that the pattern of IgG antibody in subjects without IgE to mites does not support the notion of immune deviation, but rather indicates a lack of a mite-induced high-affinity immune response.

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Introduction

Controversy exists regarding the immune status of nonatopic subjects towards mite (and pollen) allergens. One view holds that virtually all infants are immunologically sensitized, but that nonatopic children (in contrast to atopic children) fail to switch their immune reactivity towards a low-grade Th1-type pattern (i.e. immune deviation in nonatopic subjects) [1–3]. An alternative view is that mite allergens usually do not activate the immune system in nonatopic subjects (i.e. immune ignorance in nonatopic subjects). This is mainly based on the striking difference in IgG reactivity between IgE-positive and IgE-negative subjects observed for purified grass pollen allergen [4] and purified mite allergen [5, 6].

Materials and Methods

We investigated the human IgG (IgG1 and IgG4) response to mite extract and to purified mite allergens in atopic and nonatopic subjects, using RIA, radioimmunoprecipitation/SDS-PAGE, ELISA and immunoblot. For RIA, we used affinity-purified Der p 1 and Der p 2. For radioimmunoprecipitation/SDS-PAGE, we used a radiolabeled partially purified (i.e. size exclusion chromatography, 10–60 kD cut) mite extract from which Der p 1 and Der p 2 had been removed by absorption with Sepharose-coupled monoclonal antibodies. Serum was incubated with the iodinated antigen preparation and Sepharose-coupled protein A. Radioactivity bound to Sepharose was analyzed by SDS-PAGE and autoradiography.

Results

The IgG1 mite ELISA did not discriminate between atopic and nonatopic subjects. However, by RIA (using purified radiolabeled Der p 1 or Der p 2), we found a marked difference between these two groups: IgG reactivity in nonatopic subjects was usually undetectable, whereas the majority of subjects with IgE to *Dermatophagoides pteronyssinus* had detectable IgG to Der p 1 and/or Der p 2.

We next analyzed the characteristics of the mite components that were IgG-reactive in nonatopic subjects. Size exclusion chromatography indicated that these mite components were substantially larger than the 70- to 100-kD cutoff found for well-established aeroallergens. This presumably indicates that this IgG reactivity was not induced via inhalation of mite-derived material. It possibly reflects either IgG to components present in the culture medium or IgG to human gut flora cross-reactive with mite gut flora.

The results obtained by analysis by SDS-PAGE of IgG reactivity to an iodinated, size-fractionated (10–70 kD), Der p 1- and Der p 2-depleted mite extract were consistent with the results with the purified major allergens, i.e. marked reactivity in atopic subjects and a lack of reactivity in nonatopic subject. IgG reactivity detectable in the ELISA, but not in the RIA, presumably represents low-affinity (i.e. cross-reactive?) antibody.

Discussion

We conclude that it is most likely that nonatopic subjects usually lack a high-affinity antibody response to mite-derived allergens. The observed immune reactivity towards mite-derived antigens [7] is of low affinity and might well represent natural immune reactivity, i.e. immune reactivity present without stimulation by antigen. Alternatively, (part of) this immune reactivity may be due to exposure to cross-reactive antigens.

Two important questions need to be answered: (1) Is this immune reactivity dependent on antigen exposure? and (2) Does this low-grade immune reactivity have consequences for subsequent exposure to antigen? The answer to the first question can in principle be obtained by statistical comparisons between IgE-negative subjects from human populations with high and low mite exposure. The main problem for this type of analysis is that these populations should be matched for other relevant factors affecting immune responsiveness. The answer to the second question will become clear from analyses of serum samples from the ongoing prospective studies of birth cohorts. The availability of purified allergens that can be used in assays selectively detecting high-affinity responses is an important step towards answering this question.

Acknowledgment

These investigations were supported by the Netherlands Asthma Foundation (grants 96.41 and 98.24).

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