

# Correspondence

## ***Pityrosporum ovale* allergens in conventional house dust mite extracts?**

To the Editor:

In their interesting article on the characterization of *Pityrosporum ovale* allergens, Jensen-Jarolim et al. (J ALLERGY CLIN IMMUNOL 1992;89:44-51) conclude that mild extraction of the yeast cells would release mainly cell-wall carbohydrates (probably mannans), and although it is not stated explicitly, their immunoblotting data suggest that these components would be of little allergenic relevance. We have recently confirmed the high prevalence of anti-*P. ovale* IgE antibodies in atopic dermatitis<sup>1</sup> and subsequently characterized the most important IgE-binding components. Instead of immunoblotting, however, we performed protease and periodate treatment, concanavalin A chromatography, and gel filtration. In contrast to the authors' conclusions, we have found that most of the IgE-binding activity of *P. ovale* resides in a heterogeneous pool of high molecular weight mannans.<sup>2</sup> We wonder whether the importance of high molecular weight mannans might be underestimated in immunoblotting, either because high molecular weight mannans do not enter the running gel during sodium dodecylsulfate-polyacrylamide gel electrophoresis, or because they would produce only diffuse staining in the high molecular weight region. Actually, the immunoblotting approach is based on the a priori assumption that "major allergens" should be proteins of distinct size.

Our study further revealed a marked cross-reactivity of IgE-binding mannans of *P. ovale* and of *Candida albicans*. A similar conclusion was recently reported by Savolainen and Broberg,<sup>3</sup> who have also observed a

high prevalence of IgE reacting with mannans of several yeast species in atopic dermatitis (J. Savolainen, personal communication, May 1992). Such mannan-specific IgE might account for the cross-reactivity of anti-*P. ovale* IgE with other yeasts, as reported by Jensen-Jarolim et al.

Like the authors, we also noticed an at-first-sight surprising cross-reactivity between *P. ovale* and house dust mite (DPT) extracts. Several commercial DPT extracts appeared to be effective fluid-phase inhibitors of anti-*P. ovale* and anti-*C. albicans* IgE antibodies (Table I). Such inhibition was also achieved with extracts of human dander but not with grass- or birch-pollen extracts (not shown). On the other hand, preincubation with yeast allergens did not have a significant effect on IgE reactions with a coating of DPT allergens (Table I), which suggests a partial identity of *P. ovale* and DPT extracts. We think that this might be simply due to the conventional culture procedures of mites for the production of DPT allergens. Because substrates in mite cultures usually contain human skin scales, members of the normal skin microflora such as *P. ovale* might be expected in the cultures; the presence of its IgE-binding components in the culture extract would imply that they are only partially degraded during the culture. The important consequence is that conventionally produced DPT extracts might contain significant amounts of IgE-binding allergens of microbial, and not of mite, origin.

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**TABLE I.** Inhibition by DPT extract of the anti-*P. ovale* and anti-*C. albicans* IgE reaction of a representative atopic dermatitis serum\*

| Fluid phase inhibitor | Reaction with ELISA wells coated with |                    |      |
|-----------------------|---------------------------------------|--------------------|------|
|                       | <i>P. ovale</i>                       | <i>C. albicans</i> | DPT  |
| None                  | 2.40                                  | 2.15               | 1.10 |
| DPT 1/100             | 0.40                                  | 0.25               | 0.14 |
| DPT 1/10              | 0.30                                  | 0.20               | 0.13 |
| <i>P. ovale</i> †     | ND                                    | ND                 | 1.07 |
| <i>C. albicans</i> †  | ND                                    | ND                 | 1.07 |

ND, Not done.

\*The ELISA for specific IgE (2) was performed after overnight incubation of 1/25 diluted serum (for the anti-DPT reaction 1/200) with or without added allergenic extracts. Similar results were obtained with four other sera and with several commercial DPT extracts.

†Diluted 1/10. In other experiments<sup>2</sup> preincubation with this concentration blocked for >80% the binding of IgE to both *P. ovale* and *C. albicans* extracts.

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### Intentional diagnostic insect sting challenges: A medical and ethical issue

#### To the Editors:

The recent JOURNAL article by van der Linden et al. (J ALLERGY CLIN IMMUNOL 1992;90:110-8) reports the relationship between the clinical severity of anaphylaxis-induced by intentional insect stings and assessment of mast cell activation by measurement of plasma levels of released mediators in a large number of insect-allergic patients. The results are most interesting; they show a correlation between the severity of anaphylaxis and the levels of plasma histamine and tryptase, adding an important contribution to the knowledge of the pathogenesis of anaphylaxis.

Two aspects of this study deserve comment. The first is the medical and ethical issue of intentional diagnostic sting challenges in patients who have had prior sting anaphylaxis and have not received venom immunotherapy. To potentially induce an anaphylactic reaction is fraught with peril, as pointed out many years ago by Smith et al.<sup>1</sup> who described profound life-threatening anaphylaxis after insect sting challenge despite intensive medical therapy in an intensive care unit. In their study, van der Linden et al. described 17 patients who had serious reactions after the sting challenges and required overnight observation in an intensive care unit. The authors defend the use of diagnostic sting challenges to select patients who need venom immunotherapy because other criteria have not been sufficiently specific.<sup>2, 3</sup>

There is clearly significant risk in reexposure to venom in patients who have had prior anaphylaxis. The likelihood of a severe reaction is related to the severity of the initial reaction; that is, patients who have had an initial severe reaction are likely to have a similar severe reaction when rechallenged. The incidence of such severe reactions appears to be greater in adults (65%) than in children (46%).<sup>4</sup> In their study, van der Linden et al. found an approximate 40% incidence of severe re-sting reactions primarily in adult patients who had initial severe reactions. In addition, an occasional severe re-sting reaction will occur in patients who have

had previous milder reactions.<sup>4</sup> The basic question then is whether the value of intentional challenges in selecting patients for immunotherapy is worth the risk of inducing a severe reaction. It is my opinion that patients at high risk, such as adults who have had prior severe anaphylactic sting reactions, should not be intentionally rechallenged and should be given immunotherapy on the basis of their history and skin test reactivity, recognizing that some of these patients may not need therapy.

Individuals with milder anaphylactic sting reactions might even be treated without immunotherapy and probably do not require intentional challenge. Thus I believe that in light of our current state of knowledge, the risks of serious potential reactions to intentional sting challenges in untreated patients cannot be justified.

As an accompanying issue, the failure to react to one sting challenge suggests the likelihood of continued lack of reactions to further stings; however, there are a minority of patients who do have subsequent allergic reactions.<sup>4</sup>

The second serious medical issue in the report by van der Linden et al., which needs to be addressed is the authors' use of an intravenously administered antihistamine as the initial treatment of acute anaphylaxis, reserving epinephrine until symptoms become very severe. Epinephrine is considered the drug of choice for anaphylaxis and should be administered as early as possible, preferably before symptoms become severe. Barnard<sup>5</sup> pointed out years ago that the administration of epinephrine may have been an important factor in differentiating the outcomes of fatal and serious non-fatal sting anaphylaxis. The appropriate treatment of anaphylaxis deserves emphasis.

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