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**Pityrosporum ovale** (Malassezia furfur) and Atopic Dermatitis
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ABSTRACT

Allergy to a saprophytic yeast of the human skin, *Pityrosporum ovale* (*P. ovale*), an oval form of Malassezia furfur, has been suspected to play a role in atopic dermatitis (AD), especially in patients with head, neck and shoulder dermatitis. The aim of this study was to investigate the importance of *P. ovale* as a source of allergens in adult patients with AD.
To establish standardized extracts for diagnostic work we characterized the allergen extract of *P. ovale*. In immunoblotting we found a total of 39 IgE-binding protein bands. Two of the protein bands were regarded as major allergens: 9 kDa (73% of patients reacting) and 96 kDa (65% of patients reacting) bands. The RAST index levels measured against *P. ovale* mannan, a polysaccharide, and analysed by nitrocellulose RAST, were elevated in 77% of the patients with AD. According to these results, the *P. ovale* allergen extracts used to establish the IgE response in patients with AD should contain at least the major allergens, including mannan.

The stability of allergens in *P. ovale* extracts during storage is also important from the clinical point of view and it was analysed with immunoblotting and densitometry. It appeared that the proteins of *P. ovale* were poorly preserved at +20°C even when stored in 50% glycerol. The extract stored at +4°C was better preserved, but completely only for one month. In general the 9 kDa band was the most stable protein allergen. The reliability of negative skin prick test results should be questioned with currently used commercial *P. ovale* extracts.

Hypersensitivity to yeasts appears to cluster. Therefore cross-reactivity between yeasts (*P. ovale*, *Candida albicans*, *Saccharomyces cerevisiae*, *Rhodotorula rubra* and *Cryptococcus albidos*) was examined with RAST and ELISA inhibition assays. The cross-reactivity between yeast mannans was observed, but the cross-reactivity was also seen between *P. ovale* mannan and *C. albicans*, *S. cerevisiae* and *C. albidos* crude extracts, but to a lower degree. This cross-reactivity of yeasts may be misleading in clinical practice, if a patient have simultaneous positive yeast RASTs.

Both Th1 and Th2 type cytokines appear to be involved in the pathogenesis of AD. Therefore the *P. ovale* and *C. albicans* specific lymphoproliferative and cytokine (IL-2, 4, 5 and IFN-γ-ELISA) responses were evaluated in patients with AD. *C. albicans* induced IFN-γ production and IL-5 production. IL-4/IFN-γ ratio induced by *P. ovale* was higher than that induced by *C. albicans*. *P. ovale* was associated with IgE production. *C. albicans* was also associated to IgE production, but also strongly to IgG production. Our findings suggest that *P. ovale* induces predominantly a Th2-like immune response and *C. albicans* a Th1-like response.

To establish the role of yeasts in the pathogenesis of AD, the effect of yeast eradication by antifungal medication was studied. In a double-blind placebo controlled study with systemic ketoconazole, a significant improvement was seen on clinical SCORAD scale with patients in the ketoconazole group only. Also the number of positive *P. ovale* cultures from skin decreased only during ketoconazole treatment. As a whole, the results of this study suggest that *P. ovale* is an important source of allergens and can trigger cutaneous inflammation in patients with head, neck and shoulder-type dermatitis. Systemic antifungal medication is useful for patients with elevated IgE antibodies to *P. ovale* and positive yeast culture results.

Key words: allergy, atopic dermatitis, *Malassezia furfur*, *Pityrosporum ovale*, yeast, ketoconazole.

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