

Skin prick test reactions to brewer's yeast (*Saccharomyces cerevisiae*) in adult atopic dermatitis patients

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The sensitizing capacity of brewer's yeast (*Saccharomyces cerevisiae*) was studied with the skin prick test method in 449 subjects, including 226 atopic dermatitis (AD) patients, 50 patients with allergic rhinitis (AR) and/or asthma (A), and 173 nonatopic controls. A positive SPT reaction ($\geq ++$) was seen in 94% of patients with severe AD, in 76% with moderate AD, and in 25% with mild AD or no history of AD. Patients with AR and/or A and nonatopic controls displayed a positive reaction in only 8 and 2% of cases, respectively. There was also a parallel skin prick test reactivity with other yeasts including *Pityrosporum ovale* and *Candida albicans*, suggesting cross-reactivity. Parallel skin reactivity was observed also with molds and animal dander but not with pollen or house-dust mite. A significant correlation was also found between total serum IgE level and skin prick test (SPT) results with *S. cerevisiae*.

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Several patients with atopic dermatitis (AD) still suffer from the disease as adults, and in a certain patient group the dermatitis is chronic and widespread. In these cases it is not infrequent that high total serum IgE levels are detected. In recent studies positive skin prick test (SPT) results and IgE responses to two common commensal yeasts, *Pityrosporum orbiculare* (*P. orbiculare*) and *Candida albicans* (*C. albicans*), have been found in AD in especially severe forms (10). Savolainen & Broberg (11) have shown evident cross-reactivity between these two yeasts in an immunoblotting study.

Saccharomyces cerevisiae (*S. cerevisiae*), brewer's yeast, is a member of the same yeast family. It is present in our environment constantly, as it is part of our everyday nutrition. James & Warin (6) were aware of this yeast as a possible cause in chronic urticaria. Gröndahl-Hansen & Hjorth (4), in their pilot study of a yeast-free diet, suggested relief of AD symptoms in the majority of patients with positive SPT to *S. cerevisiae*. Possible allergenic cross-reactivity between *S. cerevisiae* and *C. albicans* was suggested by James & Warin (6) and later by Baldo & Baker (2).

In our investigation we wanted to study the frequency of positive SPT reactions to *S. cerevisiae* in patients with AD, allergic rhinitis (AR), or asthma (A). Simultaneous reactivity to other yeasts and

common allergens was also examined as well as changes in skin test response in a 5-year follow-up.

Material and methods

Patients

The study was carried out at the Department of Dermatology, University of Turku. A total of 226 patients with AD were selected for the study in 1984, comprising 101 males and 125 females (mean age 32.0, SD 5.4, with an age range from 16 to 45 years). In each case the diagnosis was established by a specialist in dermatology according to the criteria of Hanifin & Rajka (5). The eczema changes were further graded as follows: 1) group 0, only history of AD, no present dermatitis; 2) group I, mild AD, 10% or less of the body surface covered with eczema; 3) group II, moderate AD, 10–50% of the body surface covered with eczema; 4) group III, severe AD, more than 50% of the body surface covered with eczema. When the dermatologist graded these changes, localization and severity of eczema symptoms were also noted. Fifty patients with AR and/or A, mainly in combination (28 males, 22 females, mean age 30.6, SD 6.3, range from 17 to 41 years) and 173 non-atopics (C) (90 males, 83 females, mean age 30.9, SD 6.6, range from 18 to 46 years) served as controls (C).

Five years later, in 1989, another series of 114 AD patients, 37 of whom had attended the study earlier, were evaluated for eczema, skin prick tests, and serum sample (56 males and 58 females, mean age 31.3 years, SD 6.3, range from 22 to 49 years).

Patient investigations

The cytoplasmic *S. cerevisiae*, *C. albicans*, *Candida utilis*, *Cryptococcus albidus*, and *Rhodotorula rubra* antigens to be used for SPT were prepared as reported by Koivikko et al. (9). The protein content of these extracts was analyzed by SDS-PAGE. All extracts contained a variety of over 50 Coomassie stained protein bands. The protein composition of the *S. cerevisiae* extracts used in 1984 and 1989 was identical. The SPT extract was then obtained by reconstituting the lyophilized antigen with NSA-diluent (Pharmacia Ab, Uppsala, Sweden), as previously described (9). The final extract contained 1–2 mg/ml protein. In 1989 the commercial extracts of *P. ovale* (a different morphological form of *P. orbiculare*) and 12 aeroallergens (Allergologiske Laboratorium, Hørsholm, Denmark), including pollens, molds, house-dust mite, and animal epithelia were used for skin testing.

Prick tests were carried out and interpreted according to Nordic recommendations (1). Skin prick tests were performed in duplicate. The results were evaluated after 15 min. Histamine-HCl (1 mg/ml) was used as a positive control and NSA-diluent as a negative control. Serum samples were taken for total serum IgE determinations (Pharmacia IgE-RIA, Uppsala, Sweden) from 73 AD patients.

Statistics

Spearman rank order correlation and Kolmogorov-Smirnov goodness of fit test for two groups were used for statistical analyses.

Results

Among the 449 subjects tested in 1984, 92 (20%) were SPT positive ($\geq ++$) for *S. cerevisiae*. Of these, 85 were AD patients, 4 had AR or A, and 3 were nonatopic controls. Of these 92 SPT-positive patients, 77% showed at least a histamine equivalent ($+++$) test reaction, and 23% a $++$ skin test reaction. SPT was negative in 353 cases, i.e. in 138 AD, 46 AR/A, and 169 nonatopic controls.

There was a significant correlation with the severity of eczema and the frequency of positive skin test results to *S. cerevisiae*, as illustrated in Fig. 1. The patients with severe or moderate dermatitis displayed positive SPT reactions significantly more fre-

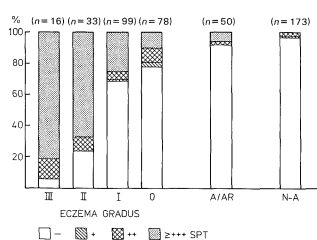


Fig. 1. Skin prick test results for *S. cerevisiae*. Patients are grouped according to symptoms. Atopic dermatitis (AD) graded as III: severe and widely distributed eczema, II: moderate eczema, I: mild eczema. Patients with allergic rhinitis and/or asthma, mainly in combination (A + AR). Healthy controls (C). The vertical axis shows % of skin test positive in each group. Number of patients tested is indicated in parentheses above each bar.

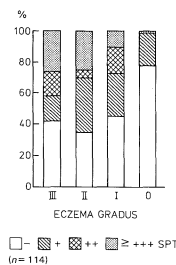


Fig. 2. Skin prick test results for *S. cerevisiae* in patients grouped according to head, neck, and shoulder symptoms. Atopic dermatitis is graded as in Fig. 1. The vertical axis shows % of skin test positive in each group. Number of patients tested is indicated in parentheses above each bar.

quently than AR/A patients or nonatopic controls ($P < 0.001$).

When *S. cerevisiae* SPT results and eczema grades were compared 5 years later, there was also an obvious association between positive SPT results with *S. cerevisiae* and the localization of eczema in the head, neck, and shoulder regions ($P < 0.01$) (Fig. 2).

When the SPT results with five other yeasts were compared to *S. cerevisiae*, it appeared that all five reacted in parallel with *S. cerevisiae* ($P < 0.001$) (Fig. 3, A and B). In comparison with common aeroallergens, a significant association was shown

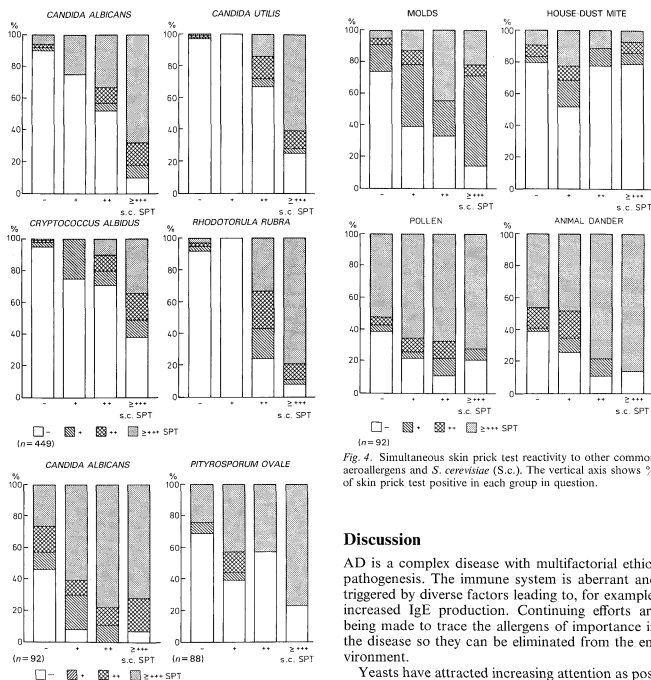


Fig. 4. Simultaneous skin prick test reactivity to other common aeroallergens and *S. cerevisiae* (S.c.). The vertical axis shows % of skin prick test positive in each group in question.

Discussion

AD is a complex disease with multifactorial ethio-pathogenesis. The immune system is aberrant and triggered by diverse factors leading to, for example, increased IgE production. Continuing efforts are being made to trace the allergens of importance in the disease so they can be eliminated from the environment.

Yeasts have attracted increasing attention as possible pathogenic agents in diverse dermatological diseases as well as in AD. We wanted to focus on *S. cerevisiae*, as it is a constantly present sensitizing agent and can be eliminated from the environment by keeping it out of food.

According to our results, AD patients with chronic widespread dermatitis showed significantly more positive SPT reactions to *S. cerevisiae* than AR/A patients or nonatopic controls, suggesting that exposure to brewer's yeast has led to sensitization. There was also a significant association with total serum IgE level and positive SPT results, reflecting the activated specific and also nonspecific IgE production in these patients.

between SPT reactions to *S. cerevisiae* and molds ($P < 0.001$) and to animal dander ($P < 0.01$), whereas no association to reactions with house-dust mite or pollen could be found (Fig. 4). A clear correlation between total serum IgE and positive SPT results with *S. cerevisiae* was seen ($r = 0.53$, $P < 0.001$) (Fig. 5).

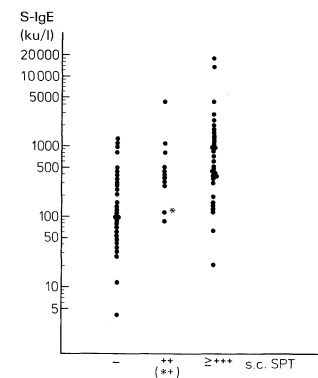


Fig. 5. Total serum IgE concentration and SPT reactivity to *S. cerevisiae*. On the vertical axis total serum IgE values are expressed on a logarithmic scale. The horizontal axis shows skin test reactivity to *S. cerevisiae*.

Recently, allergenic cross-reactivity between *P. ovale* and *C. albicans* has been demonstrated (11) and has been suggested between *S. cerevisiae* and *C. albicans* (2, 6). Our study supports these findings. Allergic cross-reactivity is possible since overlapping in SPT results was highly significant, not only among *S. cerevisiae*, *P. ovale*, and *C. albicans* but also among *S. cerevisiae*, *P. ovale*, and *C. albicans*. This suggests that molds could be structurally related to yeasts. With animal dander the association is more unlikely. The patients reacted also to pollens and house-dust mite, but in these cases the SPT results with *S. cerevisiae* were not parallel.

P. ovale is a common commensal in human skin. In AD patients it has been cultured in 18 to 77% of the cases in different studies (8, 13). *C. albicans* is frequently found in the gastrointestinal tract and has been cultured in 48% of atopic patients (12). On the other hand, treatment trials have been carried out with systemic antifungal preparations, with promising results in certain patients, but with poor results in others with severe disease (3, 7, 14). It could be speculated that, as in some patients chronic exposure to *S. cerevisiae* could affect the result, all these yeasts should be considered at the same treatment occasion.

It is evident that *S. cerevisiae* is an allergen leading to sensitization. However, the allergenic properties, the stability of allergens in food, and the significance of *S. cerevisiae* in the pathogenesis of AD must be further investigated before a definite decision about treatment schedules can be made.

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