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Recent investigations on the Relationship between Fungal Skin Diseases and Atopic Dermatitis

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Atopic dermatitis may be associated with chronic dermatophyte infections and Pityrosporum related disorders. Recent epidemiologic studies in school children and young recruits have confirmed that atopic individuals have an increased susceptibility to Trichophyton rubrum infections of the feet and an increased risk for persistant infections. In contrast, an investigation on skin reactivity in dermatophyte infected atopic patients indicated that a group of these patients is fully able to eliminate the fungi concomitant with the development of a delayed type skin reactivity. Facial erythema and scaling, often including neck and shoulders, is present in many young adults with atopic dermatitis. Preliminary data from a Danish-Swedish investigation have shown that atopic dermatitis patients with head-neck-shoulder dermatitis compared to a group without this disorder and normal individuals more often demonstrate positive prick test, RAST and specific histamin release using extract of Pityrosporum ovale. These findings indicate that the presence of Pityrosporum ovale in the skin may cause an allergic reaction leading to dermatitis.

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A multifactorial chain of different factors may cause exacerbations of atopic dermatitis (AD) including scratching, emotional stress, allergens, rapid temperature changes, exercise causing sweating, and microorganisms. Usually, the microorganisms related to are bacteria or virus, but recently it has been evident that also fungi i.e. Pityrosporum species may cause a deterioration of the disease (1). Lobitz et al. were the first to draw the attention to a correlation between AD and dermatophytosis (2, 3). Further studies showed that atopic patients were especially susceptible to chronic infections of the feet and hands caused by Trichophyton rubrum and at the first international symposium on AD in Oslo 1979 Jones suggested the term "the atopic-chronic dermatophytosis syndrome" (4). Thus, there may be two aspects of the relationship between fungi and atopic disease, an increased susceptibility to infection due to a compromized host defense and an exacerbation of the dermatitis caused by hypersensitization to the microorganisms.

ATOPIC DERMATITIS AND DERMATOPHYTOSIS

Previous epidemiologic studies showed that patients and families with chronic *T. rubrum* infections (CD) had a high incidence (40–70%) of atopic disease (5). A comprehensive study by Jones et al. showed that CD was three times more frequent in adults with AD than in non-atopic individuals (6). A recent study of tinea pedis in 15-year-old Danish school children showed a relative risk of 3 to contract tinea pedis in children with an atopic background (7). In a subsequent investigation of tinea pedis in Danish recruits examined before and after military service an increased susceptibility to tinea pedis in atopic individuals was not seen. However, an atopic predisposition was found in almost 50% of the soldiers with persistant infection at the final investigation (8).

Immunologic studies using intradermal application of trichophytin have previously shown that dermatophyte infected atopic patients react less often with a delayed type skin reaction than non-atopic patients. In a recent study on skin reactivity in atopic patients Kaaman (9) described two subgroups with different courses of dermatophyte infection. One group was characterized by the organisms *T. mentagrophytes, Epidermophyton floccosum* or *T. rubrum,* a short clinical course ending with cure and the presence of both delayed and immediate skin reactivity. Thirty percent of the patients in this group had atopic eczema without respiratory disease. The patients in the second group all had atopic respiratory disease, chronic *T. rubrum* infection and reacted with anergy or immediate type skin reactivity. The study indicates that AD patients infected with dermatophytes not necessarily develop CD, that this disease is related exclusively to *T. rubrum* and that atopic respiratory

Table I. *Frequency of positive prick test, RAST and Lucotest-HR using Pityrosporon ovale extract 5 mg/ml in 33 patients with atopic dermatitis complicated by erythematous scaling and itching dermatitis of head, neck and shoulders (HNS), 23 patients with atopic dermatitis without this disorder (AD), and 18 normal individuals without atopic dermatitis*

Group	No.	Calcofluor white* (% pos.)	Prick test** (% pos.)	Rast*** (% pos.)	Lucotest-HR**** (% pos.)
I HNS	33	77	79	24	70
II AD	23	18	44	4	48
III controls	18	0	6	6	0

HNS versus AD: $*p=0.006$; $**p=0.008$; $***p=0.05$; $****p=0.09$ not sign.

disease is a more important susceptibility factor than atopic eczema. The significance of the trichophytin reactivity in AD was studied by Rajka and Barlinn (10). The results suggested that immediate type reactions not necessarily mean sensitization to dermatophytes but may be a sign of cross reactivity to other moulds. Furthermore, that patients with CD without AD reacted even more frequently than the infected AD patients with an immediate type reaction indicating that other factors than AD play a role in the development of this type immune reaction in CD. Thus, recent studies have confirmed previous results concerning an increased susceptibility to persistent dermatophyte infection in atopic patients. However, it was also shown that the type of atopy i.e. respiratory plays a role and that a complete normal response to infection ending with cure may take place. Finally, it is noteworthy that CD in atopic patients usually is a restricted mild to moderate inflammatory condition indicating a relatively well functioning immune system compared to the widespread severe dermatophyte infections seen in the heavily immunocompromized patients with the acquired immune deficiency syndrome (AIDS).

ATOPIC DERMATITIS AND PITYROSPORUM SPECIES

Pityrosporum orbiculare/ovale (PO) are saprophytic lipophilic yeasts belonging to the normal microbial flora of the human skin. They mainly colonize the head, neck and upper part of the trunc. Various factors may cause the species to become pathogenic from simply the application of fatty lotions (11) to general immunosuppression during systemic corticosteroid treatment of AIDS. The disorders considered related to PO are Pityriasis versicolor, Pityrosporon folliculitis, confluent and reticular papillomatosis, seborrhoic dermatitis and psoriasis of the face and scalp (12).

In 1983, Clemmensen and Hjorth (1) reported on the benefit of ketoconazole in the treatment of atopic patients with a pronounced dermatitis of the head, neck and shoulders (HNS). They found many patients with AD to react positively to prick test with PO extract.

To further clarify the role of PO in AD and, in addition in seborrhoic dermatitis and psoriasis, an investigation including the history of the disease, a clinical description, identification of the fungus and immunologic studies was carried out as a co-operation between three dermatological departments. In this presentation in only the main preliminary results are given, as a more detailed report is under preparation (13). The first part of the study included group I, 33 AD patients with HNS, group II, 23 patients with AD without HNS, and group III, 18 control patients without atopy. In the clinical evaluation was used a simple score system, including grades of inflammation and area involved, location, diagrams and photo. Clinical involvement of head, neck and shoulders with scores higher than the remaining locations indicated HNS.

Identification of the fungus was done microscopically using calcofluor-white which makes the chitin-cellulose in the fungal membranes display an apple-green fluorescence in blue, ultraviolet or violet light. The material was skin scrapings taken by curette from the submandibular region.

The immunologic investigations included i) prick test with PO 5 mg/ml (ALK Laboratories, Denmark), ii) specific IgE antibodies against PO measured by RAST (ALK Laboratories, Denmark), iii) specific histamine release from basophilic leucocytes measured by Lucotest-HR (H. Lundbeck Diagnostics,

Denmark) (14), iv) total serum IgE (RIST), v) total leucocyte and different count, vi) T-lymphocyte ratio determination, vii) epicutaneous test with X-ray radiated PO and, viii) specific IgG antibodies against PO.

The most important preliminary data are given in the table. A positive microscopy means that a large amount of yeast spores were present per field of vision compared to normal skin, in which Pityrosporum is also present but in far less numbers. A more reliable quantitative method for the evaluation of the fungus is under investigation. Prick test and Lucotest-HR, an in vivo and an in vitro test for histamine liberation were both positive to a higher degree in the HNS group than in the pure AD group. The RAST test in which only allergy classes 3 and 4 were considered positive was excellent distinguishing the HNS from the pure AD group, but unfortunately gave many false negative results compared to the other methods.

Many of these patients were for a while treated with topical or systemic antimycotics with success, even relapses were observed after weeks to months. However, our investigations have shown that colonization of the HNS region in patients with AD may take place and cause a sensitization to the fungus leading to a flare of the eczema as an erythematosus scaling and itching dermatitis.

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