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CLINICAL REPORT

Atopic Dermatitis in Adults: Does it Disappear with Age?

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There is limited knowledge of the prognosis in adult atopic dermatitis. We previously published a long-term follow-up questionnaire study of adults with atopic dermatitis. This study is a clinical examination of 79 adults (mean age 57 years) recruited 3 years after that study. Most patients (68%) still reported that they had atopic dermatitis and 53% had ongoing eczema at examination, mainly located on the head and neck. Severity was mainly mild to moderate, but 12% had severe atopic dermatitis. IgE antibodies to *Malassezia* (m70) were more common in patients with ongoing atopic dermatitis, while positive *Malassezia* culture was seen mainly in patients with no ongoing atopic dermatitis. *M. obtusa* and *M. globosa* were the most commonly cultured *Malassezia* species. In conclusion, considering increased prevalence of atopic dermatitis in children in recent decades and the fact that atopic dermatitis in most adults continues for many years, we should expect to see more adults with atopic dermatitis in the future. *Key words: atopic dermatitis; adults; severity; location; Malassezia.*

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Atopic dermatitis (AD) is a common inflammatory skin disease with a distinctive clinical appearance. The diagnostic criteria of Hanifin & Rajka (1) and the UK Working Party's Diagnostic Criteria (2) are used for diagnosis. Many studies indicate that AD with childhood onset is a chronic disease with a clearance rate of 50–70% after 10 years (3). There are only a few published follow-up studies in adults (4–7). In adults with AD the head and neck and hands are more frequently involved than other skin areas (8).

Malassezia yeasts (previously known as *Pityrosporum)* are members of the normal human cutaneous microflora, as well as being opportunistic pathogens (9). Seven species of *Malassezia* have been identified using a molecular biology system and a physiological typing system (10, 11). IgE antibodies to the opportunistic yeast *Malassezia* are often found in patients with AD (12). There are conflicting reports in the literature about the role of *Malassezia* in AD (11, 13).

The aims of this study were to investigate how many adults with AD had ongoing AD at examination among patients recruited from an earlier long-term follow-up questionnaire study (6) and to determine the location and severity of the AD at examination. Another aim was to investigate the concordance between the answers to the questionnaires given to the same patients in 1998 and in 2001. We also wanted to know if there was any difference in the occurrence of other atopic diseases (asthma, allergic rhinoconjunctivitis (AR)) and in the occurrence of the *Malassezia* yeasts between patients with ongoing AD and those with no ongoing AD. As seasonal variations in skin symptoms, and deterioration during winter are well known, the examinations took place in January and February.

MATERIALS AND METHODS

Subjects

Patients were recruited from a long-term follow-up questionnaire study in adult patients with AD performed in 1998 (6). A total of 100 (69 women and 31 men) out of the 420 individuals living in the Göteborg area were randomly selected for clinical examination and questions in 2001. The study was approved by the Ethics Committee of Göteborg University, Sweden.

Methods

The patients were contacted by letter in January 2001 and invited to participate in the study, which involved a clinical examination and a questionnaire. Patients were instructed not to shower or to use ointments or other local treatments on the day of examination. In January/February 2001 the patients were examined by one of the authors (MHSF) and they also answered a questionnaire at a visit to the Department of Dermatology, Sahlgrenska University Hospital. The UK Working Party's Diagnostic Criteria for AD were used for diagnosis (2, 14). Severity of AD was assessed using SCORAD (15, 16) and an assessment of skin type was made, according to Melski et al.(17). A blood sample was taken and analysed for total serum IgE antibodies, phadiatop and IgE antibodies to *M. sympodialis* extract (m70). The blood tests were analysed with ImmunoCAP™ (Pharmacia Diagnostics AB, Uppsala, Sweden). The reference range for total serum IgE was 2–120 kU/l and reference range for serum IgE antibodies to *M. sympodialis* (m70) < 0.35 kU/l. A value of 0.35 kU/l or higher for m70 was considered positive. Phadiatop® (serum IgE to any of 11 common aeroallergens) was specified as positive or negative. The patients were asked if they had or had had asthma or AR diagnosed by a physician.

Patients were given a questionnaire containing questions identical to those from the 1998 questionnaire (6).

Cultures of the *Malassezia* yeasts were taken from normal-looking skin from the upper back of all patients, and from

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patients with ongoing AD from lesional skin, using contact plates containing a modification of the Leeming & Notman's medium (18, 19). The cultures were incubated in plastic bags at 37°C for 6 days and the various *Malassezia* species were then identified using a combination of a metabolic and growth typing system (11).

Statistical analysis

When analysing the data, patients were divided into two categories: those who had ongoing AD, i.e. visible eczema at examination, and those who did not. Objective SCORAD was used for grading AD into mild (<15), moderate (15–40) and severe (>40) AD (16). SCORAD was divided into 0–14 and ≥15 for the statistical analysis. Differences between groups in categorical data were tested by means of Fisher's exact test and χ^2 test, and for numerical data Student's *t*-test was used. Significance level was set to 5% ($p< 0.05$).

RESULTS

Clinical examination

Eighty-eight of the 100 patients invited agreed to participate. However, for various practical reasons, only 79 were able to participate (Table I). The age range at the time of examination was 47–82 years (mean 57 years). The majority (86%) of the 79 patients considered that their AD had improved over the years, and only 4% considered that it had deteriorated. Fifty-six percent of the patients had ongoing treatment with topical steroids and 84% had ongoing treatments with emollients. Fifty-four patients (68%) reported that they had had AD at some time during the last 12 months (i.e. persistent AD).

Forty-two patients (53%) had ongoing AD at examination, of which 60% reported duration of 6 months or more. The most common localization of the eczema was head and neck (52%) and hands (50%). However, most of the patients had eczema in several locations (43% on the arms, 40% on the legs, 36% on the trunk and 7% on the feet). Ninety-five percent fulfilled the UK Working Party's Diagnostic Criteria. The reason the remaining 5% (2 patients) did not fulfil the criteria was that they no longer had itching, which is the main criterion. However, they were still included in the group with ongoing AD. SCORAD was 12–78 (median 26) (Table I) and objective SCORAD 11–71 (median 23). The AD was mild in 24%, moderate in 64% and severe in 12% measured by objective SCORAD (16). There was no difference in AD severity (SCORAD 0–14, ≥15) between patients with and without AD in the head and neck area (p=1.00).

Thirty-seven patients (47%) had no eczema at examination, i.e. no ongoing AD. Eighty-four percent of these had not had AD for many years (5–41 years, mean 26 years). Sixty-eight percent fulfilled the UK Working Party's Diagnostic Criteria. The reason the majority of the remaining patients did not fulfil the criteria was that they no longer experienced itching. They considered their AD to be healed because they had not had eczema for a long time, and they were included in the group with no ongoing AD.

Comparisons of the answers from the 1998 and 2001 questionnaires

The answers from the patients in the 2001 questionnaire were compared with their answers to identical questions in the 1998 questionnaire (Table II). The concordance of identical answers was 86–99%. Concerning skin type, the clinical examination in 2001 corresponded well with the patients' reported skin type in the 1998 questionnaire.

Among those with AD located in the head and neck area at examination in 2001, 84% had reported the same eczema location in the 1998 questionnaire. For AD on the hands, the corresponding figure was 78%.

Total serum IgE, phadiatop, allergic rhinoconjunctivitis and asthma

Total serum IgE levels and phadiatop results for the patients with ongoing vs. no ongoing AD at examina-

Table I. Characterization of the patients with and without ongoing atopic dermatitis (AD)

		Gender F/M	Age (years) Median (range)	SCORAD[a] Median (range)	Head/neck AD[b]	AR[c]	Asthma[c]	AR and/or asthma[c]	Total serum IgE[d] (kU/l) Median (range)	Total serum IgE[d] >120kU/l	Phadiatop® positive[e]	m70+[f] > 0.35 kU/l
	n (%)				*n* (%)	*n* (%)	*n* (%)	*n* (%)		*n* (%)	*n* (%)	*n* (%)
Ongoing AD	42 (53)	28/14	55 (47–74)	26 (12–78)	22 (52)	31 (73)	21 (50)	33 (79)	158 (2–55100)	25 (60)	29 (69)	18 (43)
No ongoing AD	37 (47)	26/11	58 (47–82)	NA	NA	22 (59)	11 (30)	27 (73)	82 (2–841)	15 (41)	20 (54)	5 (15)

[a]Assessed using SCORAD (15).
[b]With or without other AD locations.
[c]With present or earlier occurrence.
[d]ImmunoCAP™ (Pharmacia Diagnostics), reference range 2–120 kU/l.
[e]Phadiatop® (Pharmacia Diagnostics); Serum IgE antibodies to any of 11 common aeroallergens;
[f]Serum IgE antibodies to *M. sympodialis* extract (m70); ImmunoCAP™ (Pharmacia Diagnostics).
NA, not applicable; AR, allergic rhinoconjunctivitis.

Table II. Answers to the questions in the questionnaire 1998 compared with the answers to the same questions in 2001

Factors studied in the 1998 and 2001 questionnaire[a]	Concordance between answers[b] (%)
Change of occupation due to eczema	74/77 (96)
Age at onset of symptoms of AD	71/78 (91)
Experienced progression of eczema	64/74 (86)
Eczema the last 12 months	67/78 (86)
History of asthma	77/78 (99)
History of AR	69/77 (90)
Siblings with AD	64/71 (90)
Siblings with asthma	65/71 (92)
Siblings with AR	62/70 (89)
Hospitalized due to eczema	69/77 (90)
Skin type[c]	71/77 (92)
UV treatments of the AD in a dermatological clinic	71/78 (91)
Private use of UV light	67/77 (87)

[a]In the 79 patients. Most of the questions were answered Yes or No.
[b]Number of patients who answered in the same way on both occasions.
[c]Measured by one of the author (MHSF) at examination in 2001 and compared with the patients' answers in the 1998 questionnaire.
AD, atopic dermatitis; AR, allergic rhinoconjunctivitis; UV, ultraviolet.

tion are shown in Table I. There was no statistically significant difference between the two groups in relation to total serum IgE ($p = 0.13$), phadiatop ($p = 0.47$), occurrence of AR ($p = 0.23$) or asthma ($p = 0.11$) (Table I). In all but one of the patients who reported asthma history, the asthma had been diagnosed by a doctor. Those who reported AR and/or asthma had positive phadiatop to a greater extent than those without airway symptoms: 44 out of 58 patients as compared with 5 out of 18 patients ($p<0.001$).

Malassezia and atopic dermatitis

Cultures for *Malassezia* were positive in 64% of the patients with ongoing AD and in 70% of the patients with no ongoing AD. Among those with ongoing AD, 40% had positive *Malassezia* cultures from lesional skin and 50% positive cultures from non-lesional skin. The distribution of the various *Malassezia* species is shown in Table III. No *M. furfur, M. restricta* or *M. pachydermatis* were found.

Of all the patients, 29% had IgE antibodies to *M. sympodialis extract* (m70): m70 was positive to a higher extent among those with ongoing AD than those with no ongoing AD ($p = 0.01$) (Table I). Fifty-five percent of the patients with head and neck location – with or without involvement of other locations – had m70 antibodies while 20% of those without head and neck location were positive ($p<0.01$). In patients with increased total serum IgE (>120) the frequency of m70 was higher than in those with low total serum IgE (≤120) ($p<0.0001$). However, there was no correlation between m70 and the mean total serum IgE values ($p=0.085$).

DISCUSSION

Our results demonstrate that when AD has persisted to adulthood, it will usually then continue for many years. Considering the increasing prevalence of AD in childhood in recent decades (20), and the overall persistence rates of AD after puberty of 40–60% among patients seen in outpatient clinics and university hospitals (21), we can expect an increase in adults with AD in the future. Our findings from this study and our earlier questionnaire study (6) show that in the majority of patients who have AD as young adults, the AD has persisted in 59–68% after 25–41 years of follow-up. AD is already a worldwide problem and a heavy financial burden (22), and the costs are only going to increase. One important cost factor is treatment. We showed in our earlier questionnaire study (6) and in this study, that majority of the adults with AD use emollients and topical steroids.

Similar to the findings in the earlier questionnaire study (6), in this study in approximately half the patients, the AD was located in the head and neck region or on the hands. However, in most cases the patients' eczema had several locations. The head and neck distribution has been shown to be a prognostic factor for the persistence of AD (6).

Table III. *Distribution of the various Malassezia species on lesional and non-lesional skin in patients with ongoing atopic dermatitis (AD) (n=42) and in skin of patients with no ongoing AD (n=37)*

	Ongoing AD, lesional skin[a] *n* (%)	Ongoing AD, non-lesional skin[a] *n* (%)	No ongoing AD Normal-looking skin *n* (%)	Non-lesional skin vs. normal-looking skin *p*-value[b]
M. sympodialis	–	3	–	0.24
M. obtusa	7	10	15	0.15
M. globosa	9	8	11	0.30
M. slooffiae	1	–	–	
No. of individuals with positive *Malassezia* culture	17 (40)[c]	21 (50)[c]	26 (70)[d]	0.11

[a]Patients may have one *Malassezia* species in lesional skin and another species in non-lesional skin.
[b]Fisher's exact test. Level of significance $p < 0.05$.
[c]Percent of 42 patients.
[d]Percent of 37 patients.

The majority (86%) of patients considered their AD to have improved over the years. This has also been shown in previous studies (5, 6). The severity of the AD measured by objective SCORAD was mainly mild to moderate. In other clinical follow-up studies of patients with AD, mainly mild to moderate AD has also been found (5, 7). The figure of 12% for severe AD at examination in this study was in accordance with the severity reported by the patients in the earlier questionnaire study (6).

When we applied the UK Working Party's Diagnostic Criteria for AD, some of the patients did not fulfil the criteria because they no longer satisfied the main criterion; itching. One possible reason could be their ongoing treatment with topical corticosteroids. Another possibility is that they had become accustomed to the itching and learned to live with it. However, little is known about the validity of the diagnostic criteria for AD in adults (23).

The patients who were invited to participate in the study were randomly selected from a previous questionnaire study in 1998 (6). There was good concordance when we compared the patients' answers to their answers to identical questions in the 1998 questionnaire, which indicates the reliability of the answers. There was also good concordance between the answers and the clinical findings at examination.

The earlier questionnaire study found it to be more common to have asthma and/or AR if the respondent had persistent AD, compared with patients who stated that they had had no visible eczema the last 12 months (6). We did not find any statistically significant difference in this study between patients with ongoing and no ongoing AD at examination as concerned occurrence of asthma and/or AR. This is probably attributable to a dilution effect, since there are also patients with persistent AD among the patients with no ongoing AD at examination, i.e. with no visible eczema at that time.

In our study the majority of the patients had elevated total serum IgE, which is in agreement with the literature (24). Nordvall et al. (25) reported higher IgE levels of antibodies to *P. ovale (Malassezia)* in patients with current AD than in patients who had recovered from lesions. Head and neck dermatitis was also associated with high levels of IgE to the yeast. In our study the number of patients with IgE antibodies to *M. sympodialis* extract (m70) was higher among patients with ongoing AD and also higher among patients with AD located on the head and neck. Although this is in agreement with earlier investigations (26), it is still unclear whether or not it is of clinical importance.

Fewer positive *Malassezia* cultures were found in lesional skin than in non-lesional skin, as has also been seen in earlier studies (13). One explanation for this may be the antifungal activity of mediators and/or inflammatory cells present in the lesions. It is also interesting that fewer patients with ongoing AD were culture positive than those with no ongoing AD. It has been shown in earlier studies that patients with AD had fewer positive *Malassezia* cultures than healthy controls (13). One reason could be the reduced amounts of lipids in the skin of patients with AD, compared with healthy controls (27): it is well known that skin lipids are essential for *Malassezia* to thrive. In the *Malassezia* cultures we mainly found *M. globosa* and *M. obtusa*, but more seldom *M. sympodialis*. The species found were the same as in an earlier study (13), but with fewer *M. sympodialis* positive cultures.

The probable reason for antibodies to *M. sympodialis* (m70) being found in spite of the fact that *M. sympodialis* was not found in the cultures is that *Malassezia* species contain both species-specific and common allergenic components that react with IgE antibodies (13). In a previous study we found serum IgE antibodies to *M. obtusa*, *M. globosa* and *M. restricta* in 100% of patients with IgE antibodies to *M. sympodialis* (m70+) (13). Sometimes, although one *Malassezia* species was cultured from the skin, no IgE antibodies to this species were found, while IgE antibodies to other *Malassezia* species were still often present.

In conclusion, the present study has shown that the majority of adults who had AD earlier in life still had AD, and that the majority had ongoing disease. More than half of the patients had AD including the head and neck region, and the severity of the disease was mainly mild to moderate, but 12% had severe AD. The number of patients with IgE antibodies to *Malassezia* was higher among those with ongoing AD and also among AD located on the head and neck. However, further studies are necessary to prove the exact role of *Malassezia* in AD.

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