

Prognostic Factors in Atopic Dermatitis

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A long-term follow-up study (24 years minimum) was made of 955 individuals aged 24-44 years, who had atopic dermatitis (AD) in childhood. The material was divided into two groups: patients who in 1952-56 had been hospitalized on at least one occasion at the Department of Dermatology, Karolinska Hospital, Stockholm (Group 1), and patients who in 1955-56 had been out-patients in the same department (Group 2). At the time of investigation 62% and 40% of the patients in Groups 1 and 2 respectively had ongoing dermatitis, the majority with mild skin lesions. The frequency of healing of AD and severity of persistent or recurring dermatitis were influenced by several factors. In order of relative importance, disregarding sampling errors, persistent dry/itchy skin in adult life, widespread dermatitis in childhood, associated allergic rhinitis, family history of AD, associated bronchial asthma, early age at onset, and female sex were associated with low frequency of healing and increased severity of persistent or recurring dermatitis. *Key words: Atopic dermatitis; Follow-up; Prognosis.* (Received May 29, 1984.)

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Several investigations concerning the prognosis of atopic dermatitis (AD) have been performed during the last few decades (1-12). The percentage of persistent dermatitis has ranged as much as from 8% (10) to 83% (6). The studies have varied greatly in respect of number of patients, patient material, diagnostic criteria, observation period, method of investigation and response rate to the follow-up studies, which partly explains the big differences as regards the prognostic figures. Only a few investigators have concentrated on factors influencing the healing of AD and the severity of persistent dermatitis (3, 6, 7, 9, 10, 11). The aim of the present study has therefore been to define such prognostic factors by a long term follow-up of a large well-defined group of patients with AD in childhood.

PATIENT MATERIAL

955 patients were divided into two groups. *Group 1* comprised 549 persons, 290 men and 259 women, who during the years 1952-56 had been hospitalized at the Department of Dermatology, Karolinska Hospital, Stockholm, Sweden, with the diagnostic number for AD. Individuals not satisfying the criteria of AD set up by Hanifin & Rajka (13) were excluded from the follow-up after a scrutiny of the patients' records or after appropriate interviews. The age of the patients at the time of hospitalization was 0-14 years. The group comprised 90% (549/610) of the total number of the AD patients hospitalized during the five years under study. The 61 patients who were not included either could not be followed up because they had left the country or died, or were excluded because of doubtful diagnosis. Only 8 (1%) of the patients approached did not respond to repeated letters and telephone calls.

Group 2 comprised 406 (217 men and 189 women) out of a total of 460 individuals with AD who had visited the out-patient clinic during 1955-56 but had not been hospitalized. The criteria for inclusion in the study were otherwise the same as for Group 1. Only 11 (3%) of the patients who were approached did not respond to repeated letters and telephone calls.

The individuals in the two groups were 24-44 years of age. The follow-up time was a minimum of 24 years. A detailed report of the selection of the two groups has previously been published (14).

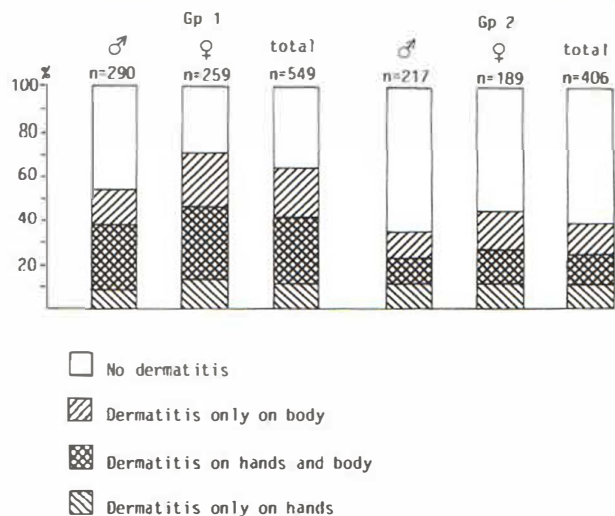


Fig. 1. Healing of atopic dermatitis and sites of persistent dermatitis.

METHODS

The basic material for the study consisted of the answers to a detailed questionnaire together with previous medical records. 183 individuals from Group 1 and 162 from Group 2, selected at random, were clinically examined by the author (14). The other individuals in the two groups were interviewed by telephone and their answers were recorded. None of the patients answered the questionnaire by mail.

In the following, family atopy is defined as a family history of atopic dermatitis (AD), bronchial asthma (BA) or allergic rhinitis (AR) in parents or siblings. Dry/itchy skin refers to history of dry/itchy skin in adult life.

All the information was computerized and analysed. Differences in frequencies between different parts of the material were tested with the chi-square test. Differences between mean values were tested with Student's *t*-test. The null hypothesis that no difference or no correlation existed was rejected at the significance levels 5% ($p < 0.05$), 1% ($p < 0.01$) and 0.1% ($p < 0.001$).

The validity of the comments on the figures and tables in the present study is mainly in agreement with those in a report on a stepwise logistic regression analysis of the importance of the factors for healing and severity of AD (14).

RESULTS

Prognosis of AD

At the time of the interview and investigation 38% of the individuals in Group 1 and 60% in Group 2 were free of symptoms ($p < 0.001$). Thus 62% and 40% respectively had eczematous lesions on hands and/or other parts of the body (Fig. 1). The hands were the most common sites of the dermatitis. In the 12 months preceding the investigation 28% in Group 1 and 49% in Group 2 had been completely healed ($p < 0.001$).

The number of sites was used as a measure of the severity of the dermatitis. Each of the following sites was assessed as one site: one or both hand(s), head and/or neck, antecubital fossa(e), popliteal fossa(e), other arm site(s), other leg or foot site(s), trunk. Only 17% in Group 1 and 5% in Group 2 had eczematous lesions at more than three sites.

No significant differences as to frequency of healing of AD or distribution and severity of persistent or recurring dermatitis were found between the clinically examined groups and the total Groups 1 and 2 (14).

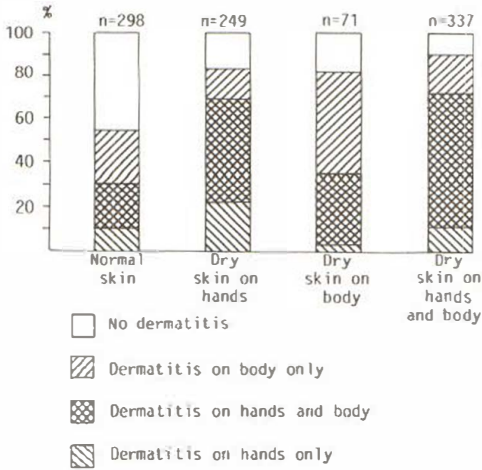


Fig. 2. Persistent dermatitis in relation to dry/itchy skin in adult life. Figures obtained from pooled Group 1 and 2 patients.

Prognostic factors in AD

Apart from age the following factors were associated with poor healing of AD and with increased severity of persistent or recurring eczema.

Dry/itchy skin. Dry and/or itchy skin was associated with persistent or recurring AD to a significantly ($p < 0.001$) higher degree than normal skin (Fig. 2). Individuals with dry/itchy skin also had more widespread persistent dermatitis at the time of the investigation ($p < 0.001$).

Severe dermatitis in childhood. The severity of eczema in childhood was assessed by number of sites in the same way as for adults. As shown in figures for both Groups 1 and 2, the more widespread the dermatitis in childhood, the lower the frequency of healing and the more widespread the persistent dermatitis at the time of investigation (Figs. 3 and 4).

Family history of AD. A family history of AD (parents/siblings) was reported by 51% and 43% respectively of the two groups. Individuals with a family history of AD exhibited a significantly lower frequency of healing and a significantly higher degree of severity of persistent dermatitis at the time of the investigation than those without atopy in the

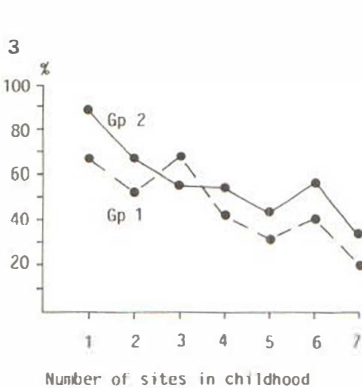


Fig. 3. Healing of atopic dermatitis in relation to severity (number of sites) in childhood.

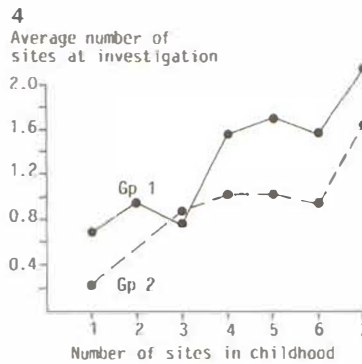


Fig. 4. Severity (average number of sites) of persistent dermatitis in relation to number of sites of AD in childhood.

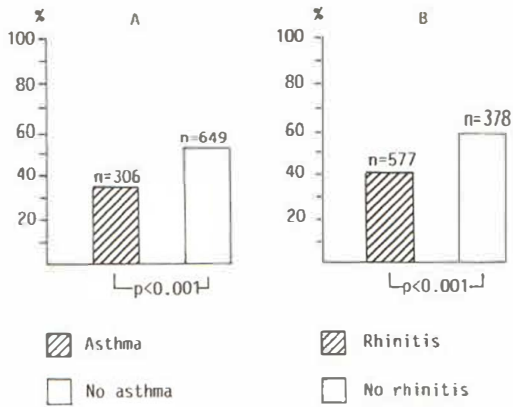


Fig. 5. Healing of atopic dermatitis in patients with and without associated asthma (A) and rhinitis (B). Bars indicate % of healed individuals in pooled Groups 1 and 2.

immediate family as shown in Table I ($p < 0.001$ for both calculations). This table also shows that a family history of BA/AR alone had no prognostic significance either for healing or for severity of persistent or recurring eczema.

Associated bronchial asthma (BA) and allergic rhinitis (AR). In the two groups taken together, 32% had or had had BA and 60% AR during some period of their lives. Individuals with BA or AR had a significantly lower frequency of healing than individuals without history of respiratory diseases ($p < 0.001$ for both calculations) (Fig. 5). The same level of significance was found as regards BA and AR in relation to the severity of persistent or recurring dermatitis (Fig. 6). Ongoing BA and/or AR were more important unfavourable factors than past respiratory allergy.

Early age at onset. In 73% of Group 1 and 58% of Group 2, AD had started before one year of age, and in 98% of Group 1 and 90% of Group 2 before five years of age. In Group 1 it was found that individuals with early age at onset (< 1 year) were free of symptoms to a significantly lower extent ($p < 0.01$) and had more severe (widespread) dermatitis ($p < 0.01$) than individuals with comparatively late age at onset of AD (> 3 years) (Fig. 7). In Group 2 no such significant correlation was found.

Female sex. At the time of the investigation, 44% of the men and 30% of the women in Group 1 ($p < 0.001$) and 65% of the men and 56% of the women in Group 2 (NS) were free of symptoms. The women also had more widespread eczema ($p < 0.001$ in Group 1 and $p < 0.05$ in Group 2).

Table I. Healing of atopic dermatitis and severity of persistent dermatitis (average number of sites) in relation to family atopy

Figures obtained from pooled Group 1 and 2 patients

Family atopy	Number of patients	Healing in percentage	Average number of sites
AD	238	35***	1.42**
AD+BA/AR	214	33***	1.59***
BA/AR	157	51	1.08
None	346	49	1.07

Asterisks indicate statistical significance of the difference between patients with and those without family atopy: ** $p < 0.01$; *** $p < 0.001$.

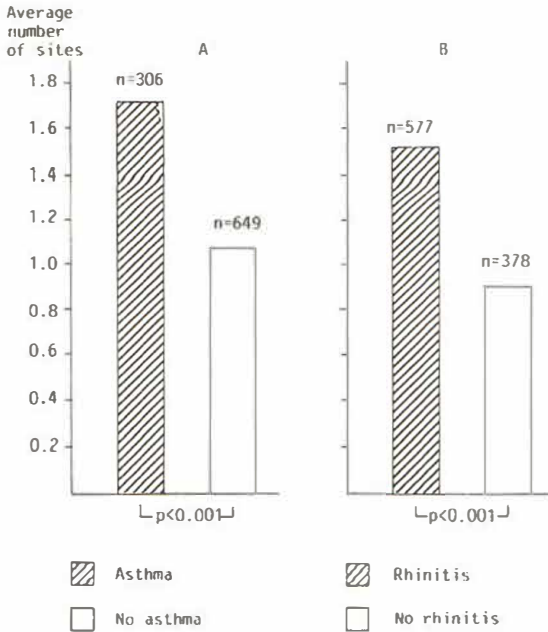


Fig. 6. Severity (average number of sites) of persistent dermatitis in patients with associated asthma (A) and rhinitis (B). Bars indicate average number of sites in pooled Group 1 and 2 patients.

Predictive capacity of the various factors

The tabular analyses showed that in order of relative importance (disregarding sampling errors) dry/itchy skin in adult life, widespread dermatitis in childhood, associated allergic rhinitis, family history of AD, associated bronchial asthma, early age at onset, and female sex had significantly lowered the frequency of healing and increased the severity of persistent or recurring dermatitis. Even though dry/itchy skin in adult life turned out to be a predominantly unfavourable factor, this factor cannot for natural reasons serve as a predictor in childhood. As regards the other factors mentioned, the correlation between widespread (severe) dermatitis in childhood and low frequency of healing was very strong,

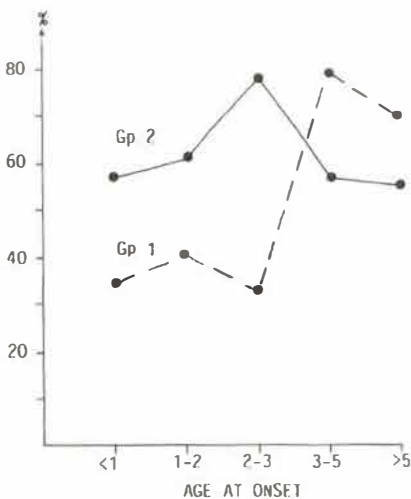


Fig. 7. Healing of atopic dermatitis in relation to age at onset. Graphs indicate % of healed individuals in various age ranges at onset.

while the factors female sex and early age at onset were of limited importance compared to the other factors.

A detailed presentation of the results of the statistical analyses including a stepwise logistic regression analysis, which in substance confirmed the results of the present study, has been given in a previous report (14).

DISCUSSION

The present study was based on a large well-defined group of individuals with AD in childhood (14) (excluding all with doubtful diagnosis), with a long follow-up period (minimum 24 years) and with a high rate of response to follow-up. With one exception (10) none of the studies have fulfilled all these requirements. In the following discussion of individual findings, comparative aspects will be further emphasized.

Aspects of the prognosis of AD

Considerably higher figures for persistent dermatitis than in the present study have been reported by Burrows (6), who found 83% with persistent eczema among those who had had severe dermatitis in childhood; and by Roth & Kierland (7) with 71% among those with a history of severe and 60% among those with a history of mild dermatitis. These studies, however, were performed on small numbers of patients who gave a low response rate at follow-up. Lower figures have been presented in several other studies, but in these the number of patients and the response rates were usually low. An exception is the study by Vickers (10), who followed up about 2000 children with AD and reported an average rate of persistent dermatitis of only about 10%. As Vickers's patient material comprised solely out-patients and hitherto the investigation has only been briefly reported, it is difficult to make any direct comparisons between his results and those of the present study.

The discrepancy between the results of the present study and previous investigations as regards healing of AD may have several explanations.

Firstly, the present investigation included both in-patients with severe AD and out-patients with moderate AD in childhood. Since, according to the present results, severe AD in childhood is connected with poor healing, a higher frequency of persistent dermatitis should be expected in this study than in those that included out-patients only.

Secondly, strict criteria were adopted in the selection of patients in this study. Only those with a clear diagnosis of AD were included. Patients with, for example, the diagnostic number for seborrhoeic type of infantile eczema, who are known to have a very favourable prognosis (1), were, in contrast to many other studies, excluded.

Thirdly, the criteria used for diagnosis of AD in the patients followed up have not been uniform in the various studies. In the present study, all patients with a type of eczema which could be connected with AD in childhood, including irritant hand eczema on an atopic basis, were recorded as not healed.

Fourthly, the high risk of recurrence among patients with AD in childhood may have been underestimated in other studies, in particular in those with short follow-up periods. In the present study, nearly 25% of the patients had remained free of symptoms for long periods of childhood but as adults had a recurrence of AD, often localized to the hands.

Prognostic factors in AD

The severity of dermatitis can be assessed in different ways: by counting the number of sites, by evaluating the size of eczematous lesions, by the activity of dermatitis, etc. Since it is difficult to measure the activity of dermatitis over a long period of time in a

standardized way, the number of sites was chosen as the only measure of severity of dermatitis in the present study.

Similarly to previous observations (3), *dry/itchy skin* in adult life was associated with an unfavourable prognosis of AD in the present study. Since, however, dry/itchy skin might be a consequence of dermatitis, the cause and effect relationship is unclear.

The finding that patients with *severe AD in childhood* had persistent and widespread dermatitis as adults to a significantly higher degree than those with moderate dermatitis in childhood is in accordance with the results of several other studies (3, 7, 9, 11), but contradicts Vickers's conclusion (10) that no relation exists between severity of AD in childhood and persistent dermatitis in adult life.

The unfavourable effect of *associated BA as well as AR* on the prognosis of AD has been reported previously (9, 11). In Vickers's study (10) BA, but not AR, was found to influence the prognosis of AD. However, it has not previously been reported that ongoing BA/AR is of particular importance, nor has the observed correlation between severity of persistent dermatitis and active BA/AR been described before.

The results concerning the frequency of *family history of atopy* are in accordance with the previous report of Musgrove & Morgan (9). No uniform line has been followed in the various investigations (3, 6, 7, 11) as to which family members should be included in a family history. In some studies, reference has been made simply to a family history of atopy, without further specification. Direct comparisons of the results are therefore difficult to make. The correlation between family history of AD and severity of persistent dermatitis found in the present study has not been reported before.

Detailed medical records were available for the patients in Group 1. This strengthens the reliability of the results that show a correlation between frequency of healing, as well as the degree of severity of persistent or recurring dermatitis, and *early age at onset*. The results contradict earlier findings (10) that late age at onset is associated with poor healing. The reason for this discrepancy is not clear. However, Group 2 patients, who had a history of milder AD in childhood than Group 1 patients, and possibly were similar to Vickers's patients (10), did not have a prognosis that was dependent on age at onset. Therefore it is possible that there are subgroups of AD, one a severe type with unfavourable prognosis if it has an early onset, and another milder form, with a prognosis that is independent of age at onset.

Sex as a factor of possible importance for healing of AD has been dealt with by Burrows (6) who, in a very small group of patients, found no evidence of the prognosis being different with regard to sex. Since in the present study the difference in healing frequency between the sexes was significant only in Group 1, the importance of this factor must be regarded as limited.

In conclusion, the present study showed that, in order of importance, dry/itchy skin, widespread dermatitis in childhood, associated AR, family history of AD, associated BA, early age at onset, and female sex were prognostically unfavourable factors for the healing of AD. The same factors were also associated, in the same order, with increased severity of persistent or recurring dermatitis. Even though the present study was based on a selected material of patients with severe to moderate AD in childhood, it seems reasonable to attempt a generalization as to all patients with AD in childhood: that the fewer and the less important the unfavourable factors involved, the better the prognosis.

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