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A Prospective Computerized Study of 500 Cases of Atopic Dermatitis in Childhood

I. *Initial Analysis of 250 Parameters*

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We report the initial results arising from analysis of a prospective computerized study of infantile atopic dermatitis in which, among other factors, the criteria of severity of the dermatitis was considered for the first time. Besides providing informations on the natural history of childhood AD, this study showed that onset of asthma was significantly earlier in children affected with severe AD. *Key words: Atopic dermatitis; Clinical features; Evolution; Prognosis.*

This paper reports some data resulting from a prospective computerized study of childhood atopic dermatitis (AD). The study was started in 1978, and therefore lacks one major factor at present: a long term follow up of the children to adulthood. However, the study as it stands provides some data that could help workers, either investigating the disease, or involved in the care of children suffering from it, to cope with questions from the parents and claims in the literature. We therefore took the opportunity offered by this symposium to publish this data. We believe it to be the first prospective study of AD in childhood; in addition, the severity of the disease, a variable which has never before been studied systematically, has been analysed.

MATERIAL AND METHODS

The study was conducted in both the in and out-patients department of a specialized paediatric dermatology unit located in a central children's hospital. Due to the system of referral, however, children with all degrees of severity of the disease were seen. (The criteria for estimating severity are mentioned later.) The data for each child were collected in standardized files which were tested firstly in a small number of patients before being modified to improve their accuracy. These files consisted of three parts:

Part one. At the first visit, parents were handed a questionnaire including questions concerning anamnestic data, which they were asked to complete and return at the next visit. The answers were reviewed with the parents by one of the authors during the second visit: in order to improve the accuracy, parents were regularly re-questioned about some important items during the subsequent follow-up. In a group of cases, a second questionnaire was given after a few months and was compared to the first one.

Part two. This comprised all the data which could be obtained during the first physical examination of the child.

Part three. This consisted of a series of sheets, of which one was to be completed during each subsequent visit; the patient's weight, height, severity score (see below) and any important new event not available when part I was completed were noted. The children were evaluated on a regular basis with approximately two visits per month for two months, then one per month for 6 months, followed by at least one every three months when the disease was under control.

About 250 parameters were analysed by using a specially tailored programme which was used in a microcomputer.

RESULTS AND DISCUSSION

Population studied

500 children with AD were studied. Three hundred of these were the first 300 patients to attend the clinic after the programme was ready for use (1). The other 200 were randomly selected out of about 800 known AD children. Separate analysis of the two groups gave similar results. The population studied consists of 57.9% boys and 42.1% girls. The mean age is at present 5.7 years (±3.2). 93.6% are caucasians with 45% of these having brown eyes and black hair, 4% are negro children, most of them from Antilles, and 1.8% are from south east Asia. 47% were blood group A, 44% O, and 9% B; these features are similar to the normal local population.

Onset of atopic dermatitis

Age at onset (Table I). The mean age at onset was 7.9 months. The peak was before 3 months of age (38.3%). In many children cutaneous lesions were reported by the parents to occur during the first days of life. Relevant questioning combined with a clinical picture of evolution to typical AD suggested that these very early lesions were probably early onset AD rather than seborrheic dermatitis. The small number of cases starting after 3 years is worth noting and is probably not due to a sampling bias since this clinic was involved in the care of children up to 16 years of age.

Localization of the initial lesions. When AD started before 1 year of age, the initial lesions were on the face (58%) and in the area of the hands and wrists (47%), whereas in those children whose AD started after 1 year of age, the hands (41%) were the most frequent site of initial involvement. During the first year of life, the napkin area was affected in 14% of the cases; in 63% of these children a "napkin dermatitis" was said to precede the atopic dermatitis. In 43% of children AD started in the flexural areas of the arms and legs; in these children the mean age at onset was higher (10.2 months) as compared to those (5.5 months) where the onset in flexural areas did not occur.

Initial "precipitating" factor(s). In 52% of the cases, the parents reported no obvious "precipitating" factor at the onset of AD. When such a factor was alluded to it was: changing of home (10%), diarrhoea (14%), dental problem (18%) and any change in the diet (27%). These episodes occur frequently in a child's life, and data relating to them should be regarded with caution as retrospective and potentially irrelevant. The season in which AD started was: winter 34.5%, spring 22.2%, summer 24.1% and autumn 19.2%. Of the children studied, 27.8% were born in winter, 23.2% in spring, 25.4% in summer and 23.6% in autumn.

Severity. The severity of the AD was analysed according to a standardized method

Table I. *Age at onset of atopic dermatitis in this population*

Age at onset[a]	%[b]
Before 3 months	38.3
Before 6 months	26.6
Before 12 months	16.6
Before 24 months	9.6
Before 36 months	5.6
3 to 6 years	1.3
After 6 years	1.6

[a] Mean age at onset 7.9 months.
[b] Out of 500 cases.

previously described (2) taking into account both (i) the intensity of each type of skin lesion as measured by the existence of 10 possible parameters (erythema, oedema, vesicles, excoriations, crusts, scaling lichenification, xerosis, pruritus and loss of sleep) each evaluated on a scale from 1 to 7 and (ii) the surface involved, scored from 0 to 30. The maximum score possible for (i) and (ii) combined was 100. The error on the reproducibility of this scoring system amongst the staff involved in this study was about 5%. The severity at inclusion in the programme as measured by the lesional score at the first visit (subsequently termed initial lesional score or ILS) was highly correlated to the mean of subsequent lesional scores obtained during follow up for 20 months (see below).

Children with "mild" AD had an ILS below 20, a "moderate AD" corresponded to an ILS between 20 and 40 and "severe AD" to an ILS 40 greater than and up to 100. 22% of the children had "mild AD", 44.5% "moderate AD", and 33.5% "severe AD". These figures emphasize the fact that this population does not only include severe cases with an hospital bias, but due to the mode of referral, probably gives a representative picture of the severity of AD within this age range.

No correlations were seen between severity and either the sex of the child or the age at onset. Severity was, however, correlated to incidence of asthma in the population studied and the duration of the infantile AD (see below).

ILS was highly correlated to subsequent scores during the follow-up of these children given a standardized treatment including topical steroids (3). The mean of severity scores observed at regular visits (see methods) was 9.5±2.1 in "mild AD" (ILS 13.7±4.4), 14.5±1.8 in "moderate AD" (ILS 27.7±4) and 20±4.2 in "severe AD" (ILS 52.8±9.1). This illustrates the degree of stable clinical improvement to which each group was amenable, as well as verifying the ILS chosen in this study as a measure of severity.

Anamnestic data

Family history. The data concerning the family history of atopic diseases were very similar to that found in the literature. In 16% of the cases no familial history of atopy was recorded.

Pregnancy and birth. 75% of the mothers had no known illness, nor took any drug during pregnancy. 12% were treated with progesterone. Infections during pregnancy included those of the upper respiratory tract, bronchi and urinary tract which were treated with several types of antibiotics. 60% of the children were born at full term, 33% were born after the 36th week of gestation and 7% between 32 and 36 weeks; these figures are similar to the normal population. No prevalence of AD was noted when the month of birth was considered. Delivery was uneventful in 76% of the children, 15% had forceps and 9% Cesarean section. Apgar score (at 1 min) was not significantly different from the normal population.

Breast feeding. The incidence of breast feeding (BF) before inclusion in the study was 54.8%; of these 25% were exclusively breast fed (duration 2.0±1.5 months) and 29.8% had mixed BF (duration 2.1±1.7 months with less than one week of exclusive BF). The incidence of both types of BF was similar in the three severity groups. AD started during exclusive BF in 28% of cases and during mixed BF in 23% of cases. The mean age at onset was 7.4 months in children having had exclusive BF and 5.5 m in those with mixed BF; this does not reach significance. There is a linear correlation between age at onset and duration of mixed BF ($R=0.2059$, $p<0.05$) but not for exclusive BF.

Course and environmental factors

Environmental factors. 82% of the children were living in a big city, 15% in the country and 1.6% by the sea. Analysis of flare-up rates in relationship to environmental factors

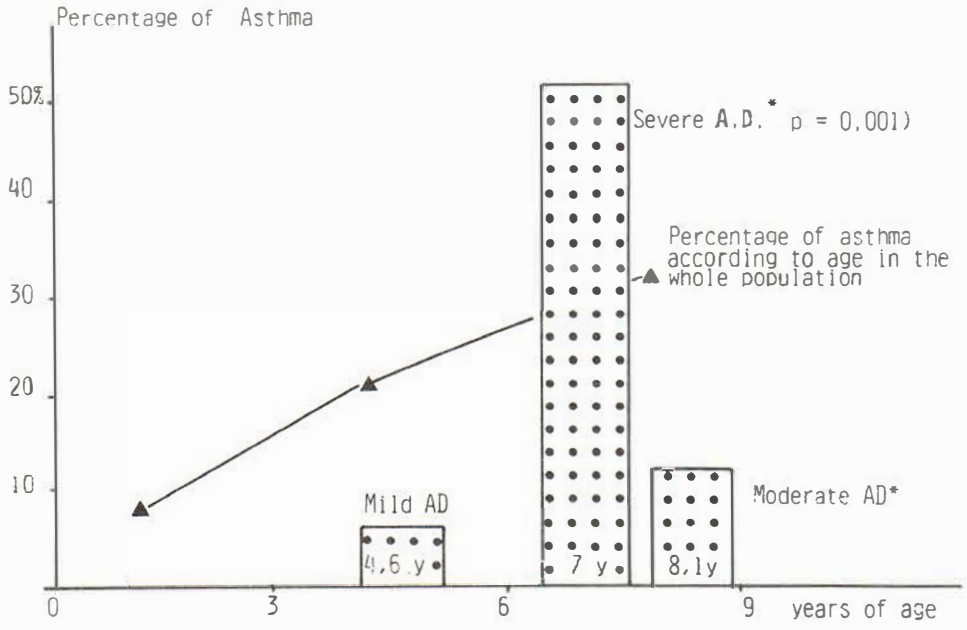

Fig. 1. Incidence of asthma according to age and to severity (see text).

and to travelling for holidays revealed extreme variations from child to child. Similar variable influences were noted for seasonal factors: no influence was observed in 37.6% of the cases, whereas in the others the classical aggravation seen in winter was the most frequent seasonal effect. Foods were considered by parents as aggravating factors in 38% of the cases, wool in 34%, pets in 14.5%, grass in 7.5% and sand in 8%. These figures are only indicative and confirm previous observations in the literature.

Course and associations. Only 4.6% of the children have a delayed growth of −2 SD; half of these are asthmatic and had been treated with systemic steroids, while those remaining have severe AD alone (score >40). Acute urticaria (as distinct from the vasomotor flare of AD) was noted in 11% and was considered as being induced by food in 46.5% and by drugs in 19.5%. Contact urticaria was suspected in 35.7%. Allergic rhinitis was present in 6.8% when the mean age of the population was 4 years and increased to 21.84 when the mean age was 5.7 years.

Asthma: Fig. 1 shows the incidence of asthma in this population according to age. After 6 years of age, the incidence of asthma reaches 34.5%; no preponderance for one sex was noted. Most interestingly (Fig. 1), children with severe AD had asthma significantly more often than those, although older, with moderate AD. We do not know if this is due to either an increase in the risk or earlier onset of asthma in severe AD; however, since the mean percentage in the population studied over 6 years of age is 34.5%, a figure similar to that observed in adults with persistant AD (4), we suspect that there is indeed an increased risk.

Duration of infantile AD

It is difficult to gain accurate information concerning the duration of infantile AD with the present length of follow-up, since even in those children whose AD cleared it cannot be confidently stated that AD will not recur at a later date or during adolescence. However,

we feel it useful to show our present observations which can be considered as valid for what could be termed the "infantile phase" of AD. For practical reasons (moving of the authors to another institution) only 200 children could be reviewed. The parents considered that AD was cleared for a period of 18 months (except for dry skin) in 52 children (26%), with no inflammatory itching or lichenified lesions. In this population of 52 children, the mean age is 4.5±2.2 years, the mean age at onset was 4.7±4.8 months and the mean age at clearing 3±2.3 years. The mean duration of AD was 27.7±17.8 months and the mean ILS 27±13. The duration of this infantile phase of AD, now cleared, was taken as a parameter to be correlated with several items included in the files such as sex, age of onset, initial lesional score, flexural onset, respiratory manifestations and familial history of atopy.

Sex: The AD cleared at 24.5±11 months of age after a duration of 20.6±10.4 months in girls whereas in boys it cleared at 40±29 months of age after a duration of 29±19 months. The mean age at onset was 8.4 months in boys and 9.5 months in girls. Although this suggests a longer duration in boys the figures do not reach statistical significance.

Age at onset: Although the coefficient of linear regression is close to statistical significance (R=0.2736 ddl 47) a definite correlation between age at onset and duration could not be demonstrated.

Initial lesional score (ILS): The duration was 20±11 months in children with ILS below 20 (mild AD) and 34±18 in those with ILS superior to 40 (severe AD); the difference is statistically significant ($p<0.05$). Children with moderate AD had an intermediate duration of AD (26±20 months).

Flexural onset: The duration was 36±21 months when AD started in flexural areas whereas it was 23±14 months when it did not ($p<0.01$). This is in accordance with previous observations by Vickers (5).

Respiratory manifestations: The duration of AD was 23±17 months in pure AD whereas it was 37±15 months in AD associated with respiratory manifestations (asthma and asthmatiform bronchitis) ($p<0.02$).

Family history of atopy: AD was of shorter duration (24±14 months) when neither the father nor the mother had asthma or AD as compared to when both parents exhibited atopic disease (35±21 months) ($p<0.05$). A similar situation is observed when all the family is considered, but the figures do not reach statistical significance.

As stated earlier, these observations can only be considered as prognostic for *the infantile phase of AD* since the population is now only 4.1±2.25 years of age. A recurrence may well be observed in these children later in life. It is possible, however, that most of these children will never show recurrence for two reasons: (i) a great proportion of childhood AD is known to clear early in life and never recur, (ii) several of the parameters found to have a prognostic significance in this study (except initial severity which has never been considered previously) are similar to those reported in other studies dealing with older subjects (5, 6, 7).

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