Acta Derm Venereol (Stockh) 1995; 75: 50–53

Prevalence and Some Clinical Aspects of Atopic Dermatitis in the Community of Sør-Varanger

LARS KÅRE DOTTERUD[1], BJØRN KVAMMEN[2], EILIV LUND[3] and EDVARD S. FALK[1]

Department of [1]Dermatology and [3]Institute of Community Medicine, University of Tromsø, and [2]The District General Practitioner, Sør-Varanger Community, Norway

A study of the prevalence of atopic dermatitis among 7–12-year-old children was carried out in a rural community in Northern Norway close to the Russian border. Of the 424 children investigated, 37% had a past and/or present history of atopic dermatitis (cumulative incidence), whereas 23% were classified as having atopic dermatitis by clinical examination (point prevalence). A history of atopic dermatitis during the past year was reported by 26% of the children. Flexural lichenified dermatitis was present in 88%, and 12% of the children had facial and extensor involvement with or without hand dermatitis.

Two thirds of the children showed mild and one third moderate symptoms; only 3 children had severe symptoms confirmed by clinical examination. The ratio of girls with atopic dermatitis to boys with atopic dermatitis was about 1.3:1. Onset of atopic dermatitis within the first 2 years of life occurred in 64% of cases, with no sex differences. Remission of atopic dermatitis occurred in 1 of 8 before the age of 5, with earlier cessation in boys. Mucous membrane atopy alone was reported by 13% of them and in combination with atopic dermatitis also in 13%.

Parental history of atopic diseases was reported by 37% of all children, more frequently in mothers than in fathers. In families with no parental history of atopic diseases, 41% of the children appeared to develop some kind of atopic disease; this increased to 63% with a single and to 75% with a double parental history. A strong, cumulative effect in both single and double parental history was seen for atopic dermatitis and mucous membrane atopy, with identical symptoms in parents and children. These observations suggest that atopy can be transmitted paternally as well as maternally.

The mean serum IgE levels were higher in children with atopic dermatitis and concomitant mucous membrane atopy (248 μ/ml) than in those with mucous membrane atopy only (132 μ/ml), atopic dermatitis only (76 μ/ml) and in children without atopic diseases (48 μ/ml). Moreover, we found that IgE levels increase with increasing severity of atopic dermatitis. ***Key words: clinical features; family history; immunoglobulin E; North Norwegian school children.***

(Accepted August 11, 1994.)

Acta Derm Venereol (Stockh) 1995; 75: 50–53.

L.-K. Dotterud, Department of Dermatology, University Hospital, N-9038 Tromsø, Norway.

Atopic dermatitis (AD) is a chronic, relapsing, pruritic dermatitis which, as well as allergic rhinoconjunctivitis (AR) and asthma, belongs to the atopies (1). AD is a common disease, particularly in childhood, but the prevalence and course show wide variations, depending on selection criteria, genetical and environmental factors (2–5). Population-based studies indicate that the frequency of AD has increased substantially during recent decades, and prevalence rates of up to 20% or more have been reported (3, 6–8). Hereditary factors have been shown to play an important role in the disposition of an individual to develop atopic diseases, and previous studies have suggested that the risk of developing atopy is higher for children of atopic mothers than for those of atopic fathers (5, 6, 8).

Disease onset occurs in many cases during the first year of life and in 80–90% of cases before the age of 7. However, at this age the signs and symptoms will have disappeared from many of those who had AD in early infancy. The clinical picture of AD is multi-faceted, and there is no definitive laboratory test or a primary or distinctive lesion with which to identify AD. Assessment methods for AD are not standardized, although several diagnostic point systems have been constructed (1, 9–12). The diagnosis has to be based on history as well as clinical signs and although typical cases of the disease are easy to recognize, the diagnosis in less typical cases may be difficult to state even for a trained dermatologist.

This report presents some epidemiological and clinical data resulting from a study of school children in Sør-Varanger, a rural community in Northern Norway close to the Russian border. Furthermore, we have investigated the diagnostic value of serum IgE in AD.

MATERIAL AND METHODS

During the period of February 1992 to March 1993, school children, aged 7–12 years, in the community of Sør-Varanger were invited to participate in a clinical examination. Five hundred and fifty-one of all 575 children living in this community had previously (October 1991) completed a questionnaire about allergic disorders, and 424 (77%) of these attended a systematic clinical examination. The consultations were performed by a dermatologist (LK Dotterud), and all anamnestic data regarding allergic disorders were reviewed and further discussed with each child and the accompanying person. Information was obtained about past and/or present symptoms of AD, AR and asthma, age at onset of symptoms, prevailing factors, seasonal variation, pets at home, family history of allergic diseases, smoking habits in the family, adverse reactions to foods etc., but parts of this will be presented in a prospective paper.

Criteria for the diagnosis of AD were those given by Hanifin & Rajka (1), whereas the severity of the disease was graded as mild, moderate or severe, based on a score system given by Rajka & Langeland (12). Conditions connected to AD such as keratosis pilaris, ichthyosis vulgaris and juvenile plantar dermatosis were also recorded.

Mucous membrane atopy (MMA) was accepted if the child had a history of asthma and/or AR related to known or strongly suspected allergen(s) such as animal dander, pollens or foods.

In our study cumulative incidence is defined as the total proportion of children with past and/or present symptoms (lifelong at the time of investigation), and point prevalence is a measure of what prevails or exists at a designated point of time (the frequency of the disease at the time of investigation).

IgE was determined using the Pharmacia CAP-system, IgE FEIA (Pharmacia AB, Uppsala, Sweden). The upper limits for normal IgE values are 161 μ/ml at 7 years of age, 182 μ/ml at 10 years of age and

 ISSN 0001-5555

Table I. *Atopic dermatitis in 7–12-year-old school children, 223 boys and 201 girls*

		Point prevalence of AD %	Symptoms of AD in the past year %	Cumulative incidence of AD %
AD only	Boys	14	15	21
	Girls	16	18	27
AD with MMA	Boys	5	8	12
	Girls	11[a]	12	14
Total AD	Boys	20	23	33
	Girls	27	30	41

[a] AD with MMA significantly higher in girls than in boys ($p < 0.05$).

195 μ/ml at 14 years of age (Nyco, Oslo, Norway). For practical reasons an upper limit of 180 μ/ml for normal IgE was chosen.

The results were both computed and manually treated. The statistical analyses were performed using the statistical package SAS and Epi-Info. The Fisher exact test and the X^2-test were used to evaluate group differences.

The study was approved by the Ethical Committee of Tromsø University.

RESULTS

Of the 424 children investigated, 37% reported AD at the time of the investigation as well as having suffered from AD in early childhood (cumulative incidence). This was reported more frequently by girls (Table I). MMA was reported by 35% of the children with AD, and in addition 13% had MMA only. A history of AD during the past year was reported, more frequently in girls (30%) than in boys (23%). Clinical symptoms of AD at the time of investigation (point prevalence) were also found more frequently in girls than in boys (Table I). A cumulative incidence of 13% and 18% and a point prevalence of 7% and 5% were found for asthma and AR, respectively. Flexural lichenified dermatitis (wrists, elbows, ankles and knees) alone or in combination with other features diagnostic for AD was present in 88% of the children; the remaining 12% had facial and extensor involvement with or without hand dermatitis. The upper extremities were affected in 90% of cases, followed by the lower extremities (52%), face (41%), trunk/buttocks (24%), neck (21%), hands (15%) and scalp (13%). The severity of symptoms in children with AD is given in Table II.

The onset of AD occurred during the first 2 years of life in 58% of the children, for both sexes equally, whereas 80% of the boys with AD combined with MMA had such an early onset ($p < 0.05$). No association was found between onset and the severity score of AD. Cessation of AD had occurred in 13% of the 156 children before the age of 5 and in 17% of them before the age of 7. In 27 boys with both AD and concomitant MMA the cessation of AD before the age of 5 was more frequent (30%) than in boys with AD only (11%) ($p < 0.05$) and girls with AD + MMA (4%) ($p < 0.05$). An opposite but non-significant trend was seen in girls (RR = 1.34).

Dry skin (xeroderma) was a common finding, also in those children with a previous history of AD but without clinical signs of AD during the clinical examination. True ichthyosis vulgaris was observed in only one girl with AD, whereas 17% of the 212 atopic children were affected with keratosis pilaris, compared to 9% in the non-atopic group ($p < 0.01$). Keratosis pilaris was found more frequently in children with MMA (21%) than in children with AD (15%) (RR = 1.33). Juvenile plantar dermatosis occurred significantly more frequently in children with AD (15%) than in non-atopics (4%) ($p < 0.0002$). Of the 56 children with MMA, juvenile plantar dermatosis was observed in 2 boys (3.6%).

Serum IgE was elevated in 22% of the children with AD (with or without MMA). Table III shows the value for different

Table II. *Severity of AD in the 99 children presenting AD during the clinical examination*

		Mild %	Moderate %	Severe %
AD alone	32 Boys	63	31	6
	32 Girls	69	28	3
AD with MMA	12 Boys	50	50	0
	23 Girls	74	26	0
Total AD	44 Boys	59	36	5
	55 Girls	71	27	2

Table III. *Distribution of serum IgE values in the children with regard to different groups (AD only 97, AD with MMA 55, MMA 55 patients and 208 non-atopic subjects)*

S-IgE value	Non-atopy %	AD %	AD with MMA %	MMA %
0–180	95	86	65	86
181–499	4	12[a]	22[b]	11
500–2000	1	2	13[c]	4

Analysis of covariance:
a) = Children with AD have significantly higher serum IgE than non-atopic children ($p < 0.01$).
b) = Children with AD and concomitant MMA have significantly higher serum IgE than non-atopic children ($p < 0.00005$).
c) = Children with AD and concomitant MMA have significantly higher serum IgE than non-atopic children ($p < 0.0005$) and children with AD only ($p < 0.05$).

Table IV. *Atopic diseases in relation to a parental history of the same disease in 848 parents and 424 children*

AR = allergic rhinoconjunctivitis.

Child's history	Parental history		
+	None (%)	Single (%)	Double (%)
AD	33	49[b]	67[a]
Asthma	12	24[a]	33
AR	17	28[a]	
Total atopic diseases	41	63[c]	75[c]

[a] $p < 0.05$
[b] $p < 0.005$
[c] $p < 0.001$

Table V. *Atopic diseases in the children in relation to a maternal or paternal history of the same disease*

AR = allergic rhinoconjunctivitis.

Child's history	Mother's history		Father's history	
+	−(%)	+(%)	−(%)	+(%)
AD	33	57[b]	36	46
Asthma	12	30[a]	13	21
AR	17	29	18	21
Total atopic diseases	44	67	46	64

[a] $p < 0.01$
[b] $p < 0.001$

groups. Children with AD only had a mean IgE value of 76 μ/ml, compared to 248 μ/ml in children with both AD and concomitant MMA and 132 μ/ml in children with MMA only. Children without atopic diseases had a mean value of 48 μ/ml. When relating IgE to AD severity, we found that IgE levels increased with increasing AD severity (mild = 74 μ/ml, moderate = 188 μ/ml and severe = 427 μ/ml).

The atopic symptoms in the children and their parents are given in Table IV. Symptoms of atopy in one parent was reported by 30%, and in both parents by 7%.

If the mother had asthma, asthma could be expected in 30% of the children, compared to 21% if the father had asthma (Table V). AR in the mother increased the probability of the children developing this disease to 29%, as compared to 21% when the father had AR. If the mother had AD, AD could be expected in 57% of the children, compared to 46% if the father had AD.

DISCUSSION

The cumulative incidence of AD in this study was 37%, which is considerably higher than estimated in a recent questionnaire study of the same population (24%) (8). Information obtained from questionnaires can, of course, be criticized. However, parents of today are aware of allergic diseases and since each child was personally interviewed and examined, the information obtained was verified and complete. Seventy-seven per cent of the children in the questionnaire study participated in the clinical examination, and it is likely that more children with than without atopic diseases participated in the clinical examination. On the other hand it is well known that remission of AD increases with increasing age. Previous reports (6) of remission in one of 3 children before the age of 14 indicate that the cumulative incidence of AD found in our study may be reliable.

The point prevalence figure obtained from this study can also be regarded as reliable and as a minimum prevalence, since each child was carefully and clinically examined by a dermatologist. A point prevalence of 23%, however, is exactly as high as the cumulative incidence reported in the questionnaire study (24%), girls in both studies being more prone to get AD (27% and 28%, respectively) than boys (20% and 19%, respectively (8)). A good agreement between earlier information and recent symptoms was observed. All these figures are higher than comparable Scandinavian studies (6, 7, 13–15).

Flexural lichenified dermatitis is regarded as the main clinical feature of AD in adolescents and was, in fact, diagnosed in 87 of the 99 children. Twelve children had a complex of other clinical signs which, according to the guidelines proposed by Hanifin & Rajka (1), classified them as having AD.

Our finding of a high incidence of AD during the first years of life is in accordance with others (6, 16, 17) and was found to occur even earlier when combined with MMA. Rajka reports onset of AD before the age of 1 in 55% of girls and 60% of boys, and before the age of 5 in 85% and 90%, respectively. The increasing difference between boys and girls, with the incidence ratio changing from 1:1 before the age of 2 to 1:1.3 over the course of childhood, was striking. This finding, in conjunction with the less common cessation of symptoms in girls, particularly in those with AD combined with MMA, would explain the apparently contrasting reports of higher prevalence of AD in girls than in boys of school age (6, 14) and equal incidence for both sexes in early life (18). The increasing incidence of dermatitis in girls in the age group 7–12 years, interpreted as AD in those with a history of but with no signs of AD during the clinical examination, might be explained by an addition of contact dermatitis, which is more common in girls than in boys (16, 19).

Ichthyosis vulgaris and AD are often said to regularly affect the same person. The true frequency of this association is unknown, because of the varied rigour with which the ichthyosis component has been diagnosed. Mild cases in the form of keratosis pilaris, however, occur frequently in patients with AD. In our study keratosis pilaris was found twice as frequently in AD children (15%) as in non-atopics (9%) ($p < 0.05$), but less frequently than proposed by Diepgen (28%) (10) and Rajka (50%) (4).

It is well known that atopics are prone to juvenile plantar dermatosis, but they do not usually have active AD, only a personal or a familial history of atopy. Various rates of AD among juvenile plantar dermatosis patients have been reported, but the rate is generally more than 50% (4). Our findings of juvenile plantar dermatosis were four times more frequent among children with AD (15%) than among non-atopics (4%) ($p < 0.0005$) and are comparable with the findings of others (4, 10).

The role of IgE in the etiology of AD is still unclear (2, 16); it may be a non-specific feature of the disease. Numerous previous investigations have shown that serum IgE is often elevated in AD (20–24) but that many patients have normal serum IgE values (9, 20, 22). Also, patients with MMA often have elevated serum IgE (24).

Previous studies have shown that IgE responsiveness to underlying MMA has a dominant inheritance with a linkage between the IgE responses and chromosome 11q13, but that transmission of atopy at the chromosome 11q locus is detectable only through the maternal line (5, 25). However, we found that the proportion of atopic children with two atopic parents was greater than the proportion affected when only one parent was atopic (Table IV). These observations suggest that atopy can be transmitted paternally as well as maternally and imply the presence of another gene (or genes) conferring atopy and not linking it to chromosome 11q13.

We found a clear correlation between serum IgE levels and

severity of skin lesions, which has also been found by others (21, 23). In this study the high incidence of increased serum concentrations of IgE in AD children with concomitant MMA compared to those with AD or MMA only, as has been found by others (21–23), may indicate an interaction or genetic linkage of IgE responses between AD and MMA, or simply that subjects with more than one organ manifestation have a more complex and severe type of atopic disease and thus increased IgE responsiveness.

The increased serum IgE found in some of the children with AD only indicates that IgE production may be stimulated by extrinsic allergens without, however, giving symptoms of MMA. Also, some children in the non-atopic group had increased serum IgE levels which might indicate latent atopy. Thus, as proposed by Wüthrich (26), there may be three main subtypes of AD: a mixed type with concomitant respiratory allergies, an extrinsic type of AD without MMA but with allergen-specific IgE, and an intrinsic type without immediate type sensitization.

In conclusion, the high frequency of atopic diseases and particularly AD found in a previous investigation (8) was confirmed in the present study. Although the frequency of atopic diseases has increased over recent decades, the high frequency found cannot simply be explained by this statement. Further studies to clarify this prevalence are in progress.

REFERENCES

1. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. Acta Derm Venereol (Stockh) 1980; Suppl. 92: 44–47.
2. Hanifin JM. Atopic dermatitis. J Allergy Clin Immunol 1984; 73: 211–222.
3. Taylor B, Wadsworth J, Wadsworth M, Peckham C. Changes in the reported prevalence of childhood eczema since the 1939–45 war. Lancet 1984; ii: 1255–1257.
4. Rajka G. Essential aspects of atopic dermatitis. Berlin: Springer-Verlag, 1989.
5. Cookson WOCM, Young RP, Sandford AJ, Moffatt MF, Shirakawa T, Sharp PA, et al. Maternal inheritance of atopic IgE responsiveness on chromosome 11 q. Lancet 1992; 340: 381–384.
6. Åberg N. Allergic diseases in childhood and adolescence in relation to background factors. Thesis. Gothenburg University, Sweden, 1988.
7. Foucard T. Allergy and allergy-like symptoms in 1050 medical students. Allergy 1991; 46: 20–26.
8. Dotterud LK, Kvammen B, Bolle R, Falk ES. A survey of atopic diseases among school children in Sør-Varanger Community. Possible effects of subarctic climate and industrial pollution from Russia. Acta Derm Venereol (Stockh) 1994; 74: 124–128.
9. Svensson Å. Diagnosis of atopic skin disease based on clinical criteria. Thesis. Lund University, Sweden, 1989.
10. Diepgen TL, Fartasch M, Hornstein OP. Evaluation and relevance of atopic basic and minor features in patients with atopic dermatitis and in the general population. Acta Derm Venereol (Stockh) 1989; Suppl. 144: 50–54.
11. Stalder JF, Atherton DJ, Bieber T, Bonifazi E, Broberg A, Calza A, et al. Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis. Dermatology 1993; 186: 23–31.
12. Rajka G, Langeland T. Grading of the severity of atopic dermatitis. Acta Derm Venereol (Stockh) 1989; Suppl. 144: 13–14.
13. Hattevig G, Kjellman B, Bjørksten B, Johansson SGO. The prevalence of allergy and IgE-antibodies to inhalant allergens in Swedish school children. Acta Paediatr Scand 1987; 76: 349–355.
14. Haahtela T. Allergy in young people. An epidemiological study of immediate skin test reactivity and allergic disorders among adolescents and conscripts in southeast Finland. Thesis. Helsinki University, Finland, 1980.
15. Varjonen E, Kalimo K, Lammintausta K, Terho P. Prevalence of atopic disorders among adolescents in Turku, Finland. Allergy 1992; 47: 243–248.
16. Rystedt I. Hand eczema and long term prognosis in atopic dermatitis. Acta Derm Venereol (Stockh) 1985; Suppl. 117: 1–59.
17. Musgrove K, Morgan JK. Infantile eczema. A long-term follow-up study. Br J Dermatol 1976; 95: 365–372.
18. Fergusson DM, Horwood LJ, Shannon FT. Parental asthma, parental eczema and asthma and eczema in early childhood. J Chronic Dis 1983; 36: 517–524.
19. Dotterud LK, Falk ES. Metal allergy in North Norwegian schoolchildren and its relationship with ear piercing and atopy. Contact Dermatitis 1994; 31: 000.
20. Juhlin L, Johansson SGO, Bennich H, Högman C, Thyresson N. Immunoglobulin E in dermatoses. Arch Dermatol 1969; 100: 12–16.
21. Ogawa M, Berger PA, McIntyre OR, Clendenning WE, Ishizaka K. IgE in atopic dermatitis. Arch Dermatol 1971; 103: 575–580.
22. Øhman S, Johansson SGO. Immunoglobulins in atopic dermatitis. Acta Derm Venereol (Stockh) 1974; 54: 193–202.
23. Wüthrich B. Serum IgE in atopic dermatitis. Clinical Allergy 1978; 8: 241–248.
24. Zetterstrøm O, Johansson SGO. IgE concentrations measured by PRIST® in serum of healthy adults and in patients with respiratory allergy. Allergy 1981; 36: 537–547.
25. Sandford AJ, Shirakawa T, Moffatt MF, Daniels SE, Ra C, Faux JA, et al. Localisation of atopy and β subunit of high-affinity IgE receptor (FcεRI) on chromosome 11 q. Lancet 1993; 341: 332–334.
26. Wüthrich B. Atopic dermatitis flare provoked by inhalant allergens. Dermatologica 1989; 178: 51–53.