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A Diagnostic Tool for Atopic Dermatitis based on Clinical Criteria

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Forty-seven patients with atopic dermatitis was compared to non-eczematous controls with regard to the occurrence of different symptoms and signs. This comparison made it possible to analyze statistically atopic symptoms and signs with regard to their diagnostic importance. Hereby, a diagnostic point system was constructed which in 96% of probands gave the correct diagnosis. This diagnostic tool might be used when examining patients with obscure eczematous disease.

A clinical material of dermatologic patients contains a large amount of eczema cases the etiology of which may be obscure. It is probable that atopy is an essential cause of many eczematous diseases. In order to diagnose atopic dermatitis several clinical criteria have been proposed (1). The present study is an essay to quantify such symptoms and signs in established cases of atopic dermatitis comparing them to those in non-eczematous controls.

MATERIAL AND METHODS

Patients with atopic dermatitis (probands) were taken from the out-patient clinic, department of dermatology in Malmö. They were not selected by the authors but by departmental colleagues on the basis of a clinical picture of a recurrent flexural itching and lichenified eczema. The probands obtained a questionnaire and were referred to a further examination by one of us (Å. S.) There was no restriction with regard to age or sex. It is possible that the selection criteria implied a relatively severe dermatitis in the probands. The referral area is purely urban.

Control subjects matched to age and sex were randomly collected from out-patients at the Department of Dermatology, Central Hospital of Kristianstad 100 km from Malmö. The referral area is rural as well as urban. A matching age of ± 2 years was allowed. Patients with a present eczematous dermatitis or previous medical care for such disease were excluded from the control group. The controls obtained the same questionnaire as the probands and were examined by one of us (Å. S).

The two materials consisted of each 47 subjects; there were 32 females and 15 males. The age distribution is given in Fig. 1.

History and clinical examinations as well as laboratory investigations were performed in an identical manner in the two study groups with one exception: the counting of T and B lymphocytes was carried out in the probands only, the figures being compared with the reference values of the laboratory. All subjects were interviewed according to a standard formula.

The clinical findings were registered after thorough inspection (Table I). White dermographism was looked for with the patient in horizontal position. Normal skin of the foreleg was lightly stroked with a blunt instrument. Tetrahydrofurfuryl ester of nicotinic acid, the active constituent of Trafuril®, was dispersed in Essex cream® 0.25%, 1.0% and 4.0%, and applied to the other foreleg. The cream was wiped off after one minute's application, and the presence of erythema or paleness was registered 10 min later. Patch testing was performed with a conventional series of 18 allergens applied for 48 hours and read after a further 24 hours. The assay of serum IgE (PRIST)® and counting of T and B lymphocytes in peripheral blood was carried out in the Department of Medical Microbiology (head: A. Forsgren).

Statistics. The main statistical test used was the chi-square test. The level of significance chosen was $p<0.05$ with some specified exceptions.

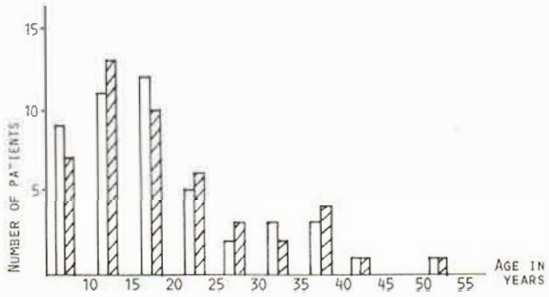

Fig. 1. Age distribution of proband (open columns) and control (hatched columns) materials.

In order to find the level of IgE (PRIST) which most significantly separates the two materials the following chi-square test was applied.

	IgE<X	IgE>X	Total
Control	a	b	e
Probands	c	d	f
Total	g	h	i

where a, b, c, d are the observed frequencies and e, f, g, h, i, j are totals.

The results of this test were:

X (IgE):	70	80	90	100	110
Chi-square:	22.1	24.4	22.6	20.9	19.2

with a maximal chi-square value 24.4 at IgE=80.

In order to find correlations among the 40 variables tables were set up for all possible combinations as:

Variable Y	Variable X			
	Level 1	...	Level n	Total
Level 1				
...				
Level m				
Total				

and a chi-square test was applied on the tables.

The expected frequencies of each cell were found as:

row total × column total/grand total.

In order to find the border value of points, confidence limits were used as mean $\pm t \times$SD. It was found that the confidence limits of 90% separated the two groups very well:

Probands:	14.5–36.5
Controls:	0 –14.4

RESULTS

Anamnestic data as well as clinical and laboratory findings are presented in Table II for probands and controls. It can be seen from the table that the presence of an itching flexural dermatitis is not included since this was the selection basis. Among the most frequent findings in the probands it was a good agreement between a history of dry skin and the

Table I. *Signs registered at examination*

Xerosis
Ichtyosis
Keratosis pilaris
Facial pallor/facial erythema
White dermographism
Lichenified eczematous dermatitis on the knuckles
Nummular eczematous patches
Pompholyx
Orbital darkening
Dennie-Morgan infraorbital fold
Nipple eczema

Table II. *Findings from history and examination in the proband and control materials*

	Probands (%)	Controls (%)
Dry skin periodically or continuously	98	53
Irritation from textiles	72	36
Seasonal variation	72	4
Personal history of allergic rhinitis	53	9
Family history of atopic dermatitis	49	17
Itch in uninvolved skin when sweating	47	2
Deterioration by psychological tension	47	0
Family history of allergic rhinitis	45	9
Food intolerance	43	15
Personal history of asthma	30	6
Family history of asthma	26	13
Hand eczema in childhood	23	0
Drug intolerance	12	12
Pronounced local or systemic insect reaction	9	17
White dermographism	100	100
Xerosis	98	34
Facial pallor/erythema	64	32
Dennie-Morgan fold	60	38
Orbital darkening	47	32
Keratosis pilaris	43	15
Lichenified eczematous knuckle dermatitis	23	2
Nummular eczematous patches	17	0
Nipple eczema	15	0
Pompholyx	13	0
Ichtyosis	13	0
Positive patch test	22[a]	11
Petechial reaction to cobalt	7[a]	10
Poritic reaction to nickel	7[a]	2
Poritic reaction to chromium	7[a]	4
Poritic reaction to cobalt	4[a]	10
Serum IgE >80 kU/l	39[a]	15
White reaction on 4% tetrahydrofurfuryl nicotinate	9	0
White reaction on 1% tetrahydrofurfuryl nicotinate	9	0
White reaction on 0.25% tetrahydrofurfuryl nicotinate	9	0

[a] $N=46$.

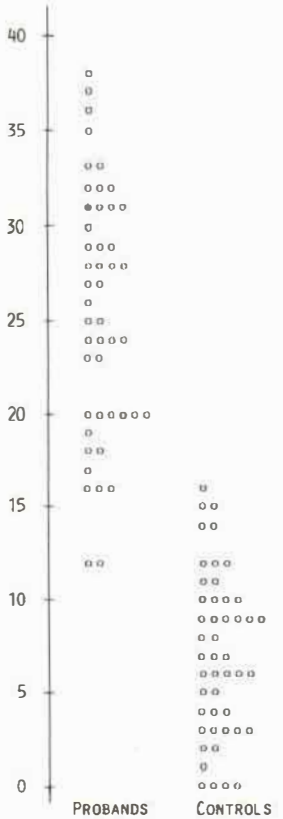

Fig. 2. The point sum of significance values for each patient in the proband and control materials.

Table III. *Significant and highly significant correlations between certain signs and symptoms in the probands*

$p<0.001$
Asthma and high age
Asthma and psychological tension
Dennie-Morgan fold and low age
$p<0.01$
Allergic rhinitis and absence of orbital darkening
Asthma and absence of orbital darkening
Asthma and absence of Dennie-Morgan fold
Asthma and elevated serum IgE
Facial pallor/erythema and low age
Hand eczema in childhood and absence of dry skin
Hand eczema in childhood and late onset of eczema
Hand eczema in childhood and drug intolerance
Hand eczema in childhood and lichenified eczematous knuckle dermatitis
Orbital darkening and low age
Pompholyx and ichtyosis
Psychological tension and high age

presence of xerosis. The agreement was not so good in the control group. White dermographism was provoked in all cases of atopic dermatitis but this was also the case in the controls. Determination of lymphocyte subgroups gave the following results: T cells 62.2%, SD ± 3.7 (normal 58–70%), B cells 4.1%, SD ± 1.4 (normal 3–8%).

The entire proband material was analyzed with regard to statistically significant correlations between different anamnestic data as well as clinical and laboratory findings. Several positive correlations were demonstrated and are given in Table III.

In order to establish the most reliable symptoms and signs in the diagnosis of atopic dermatitis their frequency in the two groups was compared. The results are presented in Table IV; this is a ranking list based on the chi-square value.

The proband material was divided into two groups; the group aged 15 years and younger was compared to that over 15. There was a very good agreement between the findings in older and younger probands except for some slight displacements in the ranking list.

On the basis of this ranking list every individual parameter obtained a value of statistical significance (1 for $p<0.05$, 2 for $p<0.01$, 3 for $p<0.001$). The sum of all significance values for the probands and controls is given in Fig. 2. The different sums were compiled and the means given below the figure. As can be seen from the figure the sums of significance values of the two groups are fairly well separated with little overlapping.

DISCUSSION

The purpose of the present study was to evaluate the importance of individual symptoms and signs for the diagnosis of atopic dermatitis. Therefore, it can be questioned if our

Table IV. *Chi-square values and significance grouping of atopic symptoms and signs*

	Chi-square value	
		$p<0.001$
Seasonal variation	46.1	
Xerosis	42.9	
Deterioration by psychological tension	28.4	
Periodically or continuously dry skin	25.7	
Itch in uninvolved skin when sweating	22.9	
Serum IgE >80 kU/l	22.8	
Personal history of allergic rhinitis	21.3	
Family history of allergic rhinitis	15.4	
Irritation from textiles	12.3	
Hand eczema in childhood	12.2	
Family history of atopic dermatitis	10.9	
		$p<0.01$
Facial pallor/erythema	9.64	
Lichenified eczematous knuckle dermatitis	9.50	
Personal history of asthma	9.17	
Keratosis pilaris	8.95	
Food intolerance	8.90	
Nummular eczematous patches	8.70	
Nipple eczema	7.60	
		$p<0.05$
Pompholyx	6.50	
Ichtyosis	6.50	
Dennie-Morgan fold	4.55	
White reaction on tetrahydrofurfuryl nicotinate	4.2	

material is representative for the disease. We feel this is the case for several reasons. Thus, the sex distribution with females twice as frequent as males agrees with earlier reports (2–4). The occurrence of asthma and/or allergic rhinitis has been given as 50% (5–7) and in our material the equivalent figure amounted to about 60%. Our slightly higher figure may be explained by the inclusion of anamnestic data of respiratory atopic disease, past as well as present.

Age at onset was 51% below the age of one year, 13% between 1–5 years, and 36% over the age of 5 years. In agreement with earlier studies (2, 7, 8) the group with early age of onset predominates. However, in our material a rather high proportion had a late onset. This has been shown to imply a poor prognosis (9) which therefore might indicate a certain selection of more severe cases in our material.

It should be pointed out that our selection basis was a chronic flexural dermatitis whereby patients lacking this sign were excluded. Of course it would have been of interest to include patients with all atopic skin manifestations but without the presence of a flexural dermatitis the diagnosis of atopic dermatitis was impossible to establish with available methods.

About 90% of the patients with childhood atopic dermatitis are supposed to heal by the age of 20 years (9, 10). The mean age in our material (23 years) therefore is rather high. This is probably explained by our selection basis being a recurrent flexural dermatitis which is more characteristic of the adult than the childhood phase. For this reason, the findings in patients below and over 15 years of age were compared but important differences were not found.

Symptoms and signs in diminishing frequency among our probands are given in Table II. The findings are well known among dermatologists and the following ones in particular agree with earlier studies. Thus, a history of permanently dry skin was obtained in 64% and periodically in 34% of our probands. Irritation from textiles was obtained in about 2/3 of our patients. Intolerance to wool in particular has been pointed out by Sulzberger & Goodman (5) and by Rajka (11). Almost half of the atopic patients, 43%, reported some type of food intolerance (oral irritation 23%, generalized or localized itch 21%, flare-up of eczema 9%, gastrointestinal disturbance 4%, urticaria 4%). The figures are surprisingly high for this material with a relatively advanced mean age. The high frequency of oral irritation in particular is seldom commented upon in the literature. On the other hand, reactions to drugs and insect bites were few, in agreement with the experience of other authors (11–13).

The normal value for total amount of IgE antibodies varies between different materials. We have chosen to consider a PRIST® value above 80 kU/l as pathologic, since this level discriminates best between values found in the proband and control groups (see Material and Methods). Thereby 39% of our probands had increased IgE level.

A history of a particular seasonal variation was given in 72% of our probands which is somewhat lower than in other materials: 83% (2), 90% (14), 90% (15). A recent Swedish material (16) showed a seasonal variation in about 70%.

A history of atopic diseases in the family is often obtained, also in our material (Table II). Atopic dermatitis and rhinitis were much more common than asthma. Thus, at least one of the three atopic diseases was found in the family in 68%. Exactly the same figure was obtained by Hellerström & Lidman (8) and by Rajka (7) while Nexmand (2), Baer (17) and Roth & Kierland (10) reported 43%, 62% and 66%, respectively. It should be pointed out that in some materials "family history" embraced more than parents, brothers and sisters.

Almost all patients reported their skin to be markedly dry, periodically or continuously. This coincided with objective signs of xerosis. Furthermore, an ichtyosis with diamond-

formed scales sparing the big folds was observed in 13% which frequency is somewhat higher than that given by Nexmand (2) and Rajka (11).

After computerizing the isolated symptoms and signs among atopic subjects several interesting correlations emerged (Table III). Some of the correlations were statistically highly significant. One of these was the connection between a late onset and a dry skin, another the connection between the Dennie-Morgan folds and a low proband age. This might speak for a disappearance of the eyelid folds with increasing age (18, 19). Furthermore, there was a negative correlation between the occurrence of eyelid folds and orbital darkening on the one hand, and the presence of asthma on the other. It may be concluded that these eye signs seem to be more related to the skin disease than to the asthma.

A lichenified eczema on the knuckles was often correlated to a previous hand exzema in childhood. Hand eczema occurs frequently among atopic patients, both the dorsal type and pompholyx (20). It seems to appear in adult age, irrespective of occupational influence (21).

The diagnostic criteria for atopic dermatitis proposed by Rajka (11) and Hanifin & Rajka (1) are based on traditional clinical experience. These criteria have recently been tested in two materials, one infantile (22), the other of a more advanced age (23). There was an incomplete agreement between the proposed criteria and the clinical reality in both studies. The present study is the first in which the occurrence of different signs and symptoms in atopic dermatitis have been compared to those in a control material. Thereby a list of important criteria has appeared that in several aspects differs from that previously proposed. Several typical findings have thus been found worthless because of their high frequency in control material (e.g. white dermographism, orbital darkening). True, the white dermographism is frequent and strong in atopic dermatitis but lacking a quantitative method for eliciting and reading the reaction, its occurrence cannot be differentiated from that in normal individuals.

Other findings have emerged as important factors because of reverse conditions (e.g. presence of knuckle eczema, history of hand eczema in childhood).

In Table IV the different signs and symptoms are listed with their chi-square values. The sum of significance values obtained in individual patients may be used as a diagnostic instrument in doubtful eczema cases. When the instrument was applied to our two materials the discrimination was very good with minimal overlapping (Fig. 2). Based on this experience we suggest that a patient with >15 points should be considered atopic.

Using this method two probands, or 4%, were underdiagnosed. They both reach a level of 12 points in spite of a clear-cut atopic dermatitis. This might be explained by the design of the method, founding much of the diagnosis on anamnestic data.

On the other hand, in the control material one patient will be diagnosed as atopic, and a few come close to the point level for atopic dermatitis. Although these patients never before had sought medical attendance for skin problems or had eczema at examination they showed so many atopic criteria that, in retrospect, they may be presumed to be atopic subjects. With the prerequisites given it is almost impossible to avoid such atopic subjects in a control material. In clinical practice, a lower point sum might therefore be used for the diagnosis of atopic dermatitis than that preferred by us. On the basis of the statistical calculation (see above) a level of >14 points could have been chosen.

REFERENCES

1. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. Acta Derm Venereol (Stockh) 1980; suppl 92: 44–47.
2. Nexmand PH. Clinical studies of Besnier's Prurigo. Copenhagen: Rosenkilde and Bagger Publishers, 1948.

3. Schnyder UV. Neurodermitis asthma-rhinitis. Basel, New York: Karger, 1960.
4. Cronin E, Bandmann H-J, Calnan CD, Fregert S, Hjorth N, Magnusson B, Maibach HI, Malten K, Meneghini CL, Pirilä V, Wilkinson DS. Contact dermatitis in the atopic. Acta Derm Venereol (Stockh) 1980; 50: 183–187.
5. Sulzberger MB, Goodman J. The relative importance of specific skin hypersensitivity in adult atopic dermatitis. JAMA 1936; 106: 1000–1003.
6. Schnyder UW. Konstitutionelle Neurodermitis-atopic dermatitis-Prurigo Besnier. In: Schuppli R., ed. Aktuelle Probleme der Dermatologie 1959; 1: 216–233.
7. Rajka G. Prurigo Besnier (atopic dermatitis) with special reference to the role of allergic factors. Acta Derm Venereol 1960; 40: 285–306.
8. Hellerström S, Lidman H. Studies of Besnier's prurigo (atopic dermatitis). Acta Derm Venereol (Stockh) 1956; 1: 11–22.
9. Vickers CFH. The natural history of atopic eczema. Acta Derm Venereol (Stockh) 1980; suppl 92: 113–115.
10. Roth HL, Kierland RR. The natural history of atopic dermatitis. Arch Dermatol 1964; 89: 209–214.
11. Rajka G. Atopic dermatitis, London, Philadelphia, Toronto: Saunders, 1975.
12. Rytel MW, Klion FM, Arlander TR, Miller LF. Detection of penicillin hypersensitivity with penicilloylpolylysine. JAMA 1963: 894–898.
13. Juhlin L, Wide L. IgE antibodies and penicillin allergy. In: Dash CH, Jones HEH, eds. Mechanisms in drug allergy, Edinburgh, London: Churchill Livingstone, 1972: 139.
14. Schnyder UW. The importance of intracutaneous test in various types of constitutional neurodermatitis. Int Arch Allergy 1957; 11: 64–72.
15. Rajka G. Prurigo Besnier (atopic dermatitis) with special reference to the role of allergic factors. Acta Derm Venereol 1961; 41: 363–395.
16. Bleeker JJ. Atopisk dermatit. Stockholm: Liber Tryck, 1980.
17. Baer RL. The development of the concept of atopic dermatitis. In: Baer RL, ed. Atopic dermatitis. New York University Press, 1955: 1.
18. Holzegel K. Unterlidfalte beim endogenen Ekzem. Hautarzt 1977; 28: 45.
19. Meenan FOC. The significance of Morgan's fold in children with atopic dermatitis. Acta Derm Venereol (Stockh) 1980; suppl 92: 42–43.
20. Bandmann HJ, Agathos M. Die atopische Handdermatitis. Dermatosen in Beruf und Umwelt 1980; 28: 110–113.
21. Rystedt I. Long-term follow-up in atopic dermatitis. Paper read at the conference "Contact dermatitis in the 80's", Copenhagen, 1980.
22. Yates VM, Kerr REI, MacKie RM. Early diagnosis of infantile seborrhoeic dermatitis and atopic dermatitis—clinical features. Br J Dermatol 1983; 108: 633–638.
23. Svensson Å, Månsson T. Unpublished results, 1984.

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