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Evaluation and Relevance of Atopic Basic and Minor Features in Patients with Atopic Dermatitis and in the General Population

T. L. DIEPGEN, M. FARTASCH and O. P. HORNSTEIN

Department of Dermatology, University of Erlangen, FRG

In a prospective computerized study on atopic dermatitis (AD) several basic and minor clinical features in patients with AD ($n=110$) and a sample of the normal population ($n=527$) was studied systematically and analysed statistically with regard to their diagnostic importance. On basis of chi-square values a diagnostic score system was constructed which might help to establish a firm diagnosis of AD in patients with ambiguous cutaneous inflammatory disease. Based on this score system patients with more than 10 points should be considered atopic, patients with 6 to 10 points are suspected to be atopics. An association between serum IgE and the amount of atopic points was found. Seven percent of the normal population sample proved to be obviously atopic, another 19% were suspected to be atopics. ***Key words: Atopic dermatitis; General population; Clinical features; Atopy score; Nickel allergy.***

T. L. Diepgen, Department of Dermatology, University of Erlangen, Hartmannstr. 14, D-8520 Erlangen, West Germany.

For the diagnosis of atopic dermatitis (AD) an array of basic and minor clinical features proposed by Hanifin and Rajka (1) are in common use. However, many of them can be found in normal individuals who never before had skin problems or eczema at the time of examination. In recent years atopic dermatitis seems to have become more frequent in the general population (2, 3, 4), yet there are only a few studies about the incidence rates of atopy in recent decades. The present study focuses on the evaluation and quantification of anamnestical and clinical features of atopy in clearly established cases of atopic dermatitis (AD) compared to a general German normal population (NP).

MATERIAL AND METHODS

Patients with atopic dermatitis (AD)

Patients with atopic dermatitis (AD: $n=110$; 64 females, 46 males; median age 21 years) were collected from the in- and out-patient divisions of our Department of Dermatology where a special atopy service has been instituted. Patients with all degrees of severity of the disease were seen. The diagnosis of AD was established according to Hanifin & Rajka (1). All patients revealed clinical or anamnestic data of recurrent flexural itching and lichenified eczema. The referral area was both urban and rural.

German normal population (NP)

A sample of the German normal population (NP; $n=554$) were taken from urban and rural areas. Persons with a history or the clinical picture of flexural eczema ($n=27$) were excluded. Thus the sample size of the controls was $n=527$ (178 females, 349 males) largely similar in age (median 23 years) and occupational distribution.

Clinical examinations and laboratory investigations

All anamnestical and atopic basic and minor clinical features described in the literature were examined in both groups. To achieve a good interobserver agreement (5) the clinical examination was performed by two dermatologists simultaneously. Serum IgE and Phadiatop (a RAST for screening inhalant allergy; "Pharmacia GmbH") were investigated in all test subjects.

Statistics

The chi-square test was used to analyse cross-classified data, nonparametric tests (Mann-Whitney rank-sum test and Kruskal-Wallis statistic) to analyse interval and ordinal scaled data (6). The level of significance chosen was $p<0.01$. A score system was constructed based on chi-square values. Relative risks were calculated according to Breslow & Day (7).

RESULTS

Atopic basic and minor features

Anamnestic data as well as clinical findings of atopic basic features in AD and NP are presented in Fig. 1 *a*, of minor features (arranged according to their frequencies in AD) in Fig. 1 *b*. Only those features are seen which had significantly higher incidences and were more frequent than 20% in AD. The frequencies, chi-square values and relative risks of atopic basic and minor features are listed in Table I. The term relative risk (RR) indicates how many times more frequent the disease is in the individuals positive for the atopic feature than in individuals negative for the atopic feature ($p<0.01$).

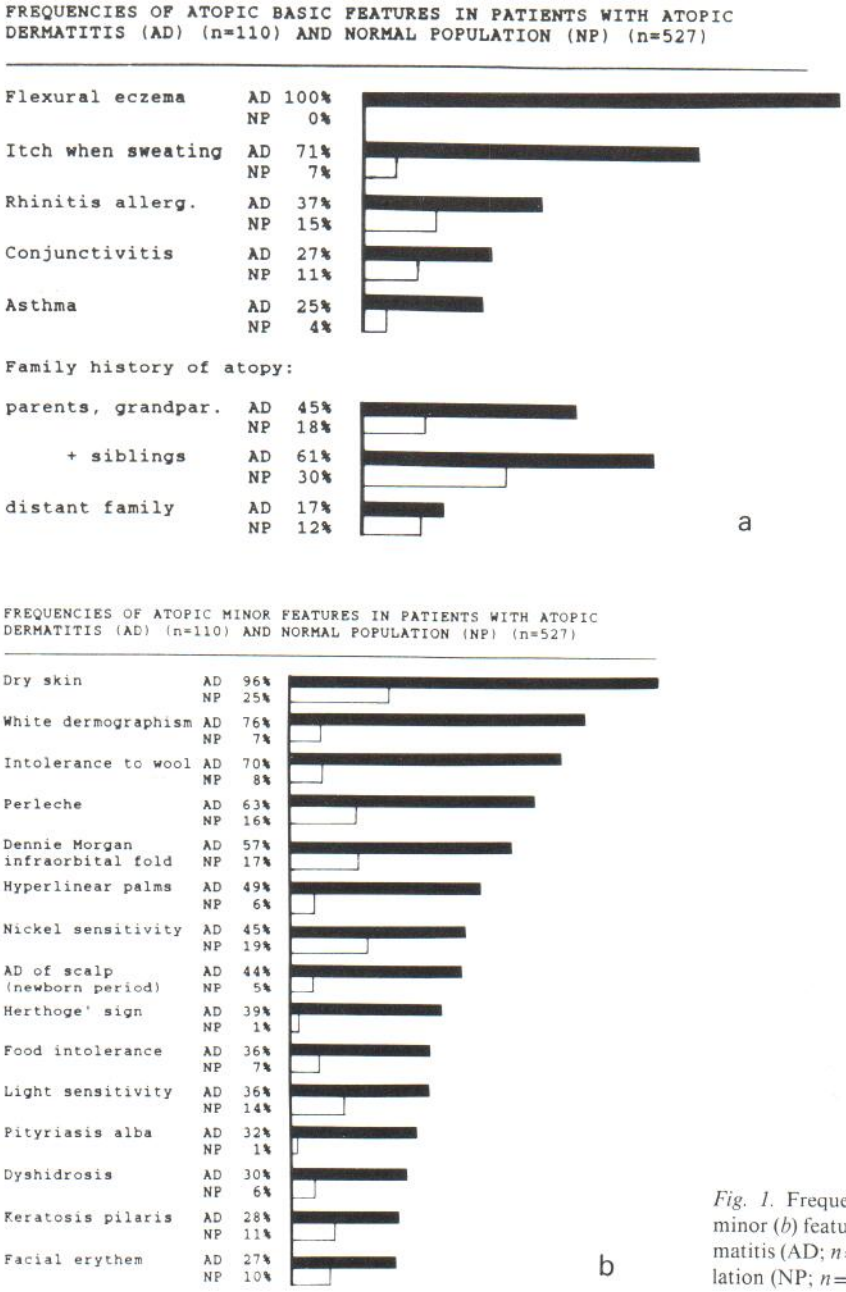

Fig. 1. Frequencies of atopic basic (*a*) and minor (*b*) features in patients with atopic dermatitis (AD; $n=110$) and in the normal population (NP; $n=527$).

The frequencies of a positive family history of atopy was dependent on the included relatives. An immediate positive history of atopy, i.e. of the parents or grandparents was found in 45% (AD) respectively 18% (NP), if the siblings were included as well the frequencies increased to 61% (AD) respectively 30% (NP). There were no statistically significant differences in the distant family history of atopy between AD (17%) and NP (12%) (Table I).

The frequencies, chi-square values and relative risk of some minor features were higher than the values found in basic features. Especially in dry skin, Hertoghe' sign and white dermographism the estimated relative risks were high (Table I). Comparing the fre-

Table I. *Frequencies, chi-square values (χ^2), relative risk[a] (RR) of atopic basic and minor features in atopic dermatitis (AD; n=110) and in the normal population (NP; n=527)*

Atopic features	AD (%)	NP (%)	χ^2	RR[a]
Basic features				
Itch when sweating	71	7	240	33.6
Rhinitis allerg.	37	15	27	3.2
Conjunctivitis allerg.	27	11	19	3.0
Asthma	25	4	57	8.1
Family history of atopy				
parents, grandparents	45	18	39	3.8
parents, grandparents, siblings	61	30	36	3.8
Distant family	17	12	NS	–
Minor features				
Dry skin	96	25	196	78.0
White dermographism	76	7	262	39.6
Intolerance to wool	70	8	222	25.7
Perleche	63	16	105	8.7
Dennie-Morgan's fold	57	17	78	6.6
Hyperlinear palms	49	6	140	15.1
Hist. of nickel sens.	45	19	32	3.4
AD of scalp	44	5	118	13.9
Hertoghe's sign	39	1	173	46.4
Light sensitivity	36	14	29	3.5
Pityriasis alba	32	1	137	35.0
Dyshidrosis	30	6	53	6.3
Keratosis pilaris	28	11	22	3.2
Facial erythem[a]	27	10	22	3.2

[a] The term relative risk (RR) indicates how many times more frequent the disease is in the individuals positive for the atopic feature than in individuals negative for the atopic feature ($p<0.01$).

quencies of the atopic features between females and males there were no significant differences except for the anamnestic sensitivity to nickel, which was highly correlated with females and ear-pierced. Specific features, like atopic winter feet (AD 16%; NP 0%), dirty neck (AD 10%; NP 0%) and nipple eczema (AD 9%; NP 0%) were not listed because their incidences were below 20%. Several minor features have been found worthless because they did not differ significantly: pronounced local insect reaction, herpes labialis, drug intolerance and urticaria.

IgE and Phadiatop were statistically associated with atopic dermatitis ($p<0.001$). There was elevated serum IgE (IgE > 100 U/ml) in 75% and a positive Phadiatop in 68% in AD. Especially in AD both parameters were statistically significant associated with rhinitis and conjunctivitis ($p<0.001$).

Table II. *Score system based on χ^2-values*

3 Points ($\chi^2>150$)
Itch when sweating
Intolerance to wool
Xerosis
White dermographism
Hertoghe's sign
2 Points ($100<\chi^2<150$)
AD of scalp (newborn)
Perleche, cheilitis
Hyperlinear palms
Pityriasis alba
1 Point ($\chi^2<100$)
Family history of atopy
Rhinitis
Conjunctivitis
Asthma
Dyshidrosis
Dennie Morgan fold
Nickel sensitivity
Food intolerance
Facial erythema
Light sensitivity
Keratosis pilaris

Score system

An atopic score system should be based on anamnestic and clinical features without laboratory investigations. Thus serum IgE and Phadiatop were not taken into consideration. The score system was based on statistical evaluation and should be restricted to the frequent important criteria. Specific features were excluded which were less frequent than 20% in AD (atopic winter feet, nipple eczema, dirty neck). The presence of an itching flexural dermatitis was not included since this was the selection basis. On the basis of chi-square values every atopic feature obtained a value between 1 and 3 points according to its statistical significance (Table II). By using the proposed score system both groups were separated fairly well with minimal overlapping (Fig. 2). The summarized atopic points were normally distributed in AD. There were different degrees of atopic severity based on the amount of atopic points. The median of serum IgE in the different groups classified by atopic points (Fig. 3) were significantly lower in NP than in AD

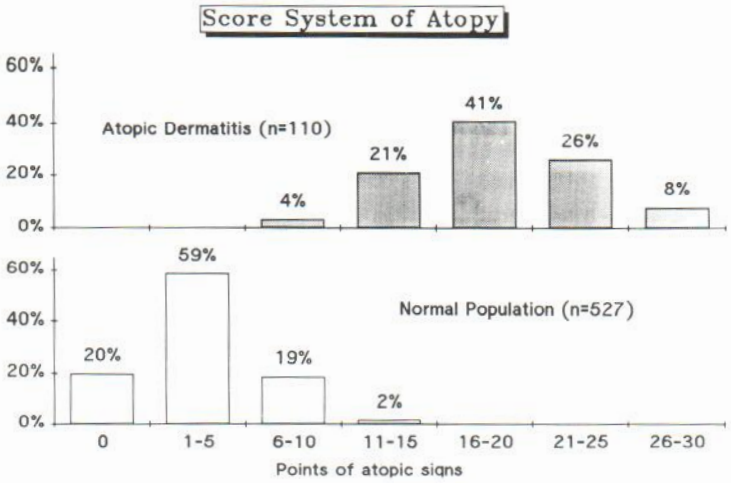

Fig. 2. Frequencies of classified atopic points in atopic dermatitis (AD; $n=110$) and in the normal population (NP; $n=527$). The score system is based on statistical evaluation of atopic basic and minor features according to chi-square values.

(Mann-Whitney rank sum test, $p<0.001$). In the different groups of AD classified by our score system the serum IgE increased significantly (Kruskal-Wallis test, $p<0.01$), but not in NP.

DISCUSSION

The diagnostic criteria for atopic dermatitis proposed by Hanifin & Rajka (1) are based on traditional clinical experience. There was an incomplete agreement between the proposed criteria and the results of some other studies (8, 9, 10). In the present prospective standardized study the occurrence of different atopic features have been compared to those in the general population because the proposed score system is based on relative risks which depend on the frequencies of atopic symptoms and signs in the general population. Some typical basic features were found to be of minor importance because of their high frequency in control material. For example a history of atopic disease in the family is often obtained. Dependent on the number of included family members the frequencies ranged between 45 and 61% in AD and between 18% and 30% in NP (Table I). Frequencies between 43 and 73% were obtained by other studies (8, 10, 11, 12, 13). Most of the former studies did not investigate the frequencies of a positive family history in the normal population simultaneously. Kjellman (13) studied the incidence of atopic disease in a sample of children aged 7 years and its relation to the family history. In our study the relative risk of a history of atopic disease in the immediate family was only 3.8 because of the high incidence in the normal population. A distant family history of atopy was found to be of no diagnostic relevance. Other minor features have emerged as important factors because of their high relative risks (Table II). The frequency of intolerance to wool in AD (Table I; 70%) is in good accordance with Svensson et al. (8) who in 72% found irritations from textiles in AD and in 36% in non-eczematous out-patients. In our general population of young adults only 8% reported an intolerance to wool.

According to Hanifin & Rajka (1) an intolerance to metals is not a diagnostic feature of atopic dermatitis. Romaguera et al. (14) found an atopic history in 49% of 627 patients who complained of intolerance to

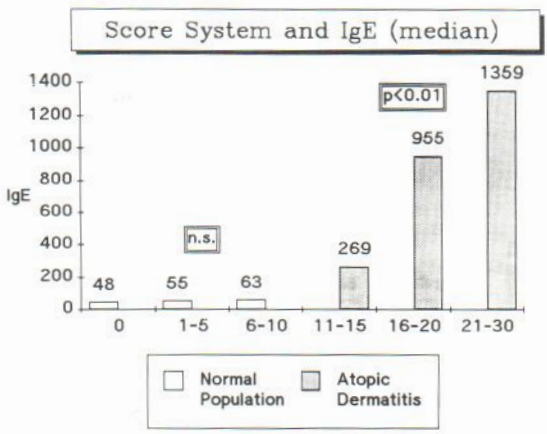

Fig. 3. Median of serum IgE in different groups of the normal population (NP; $n=527$) and atopic dermatitis (AD; $n=110$) classified according to atopic score system which is based on statistical evaluation of atopic basic and minor features according to chi-square values. (Differences of serum IgE between the three groups of AD resp. NP are calculated by Kruskal-Wallis test.)

metals and had a positive patch test to nickel sulfate. In our former prospective study (15) where we investigated the occurrence of delayed-type hypersensitivity in a sample ($n=143$) of patients with AD and comparing them to control subjects similar in age and occupational distribution, atopics were found to have a significantly higher incidence of reactions to nickel. Thus sensitivity to nickel may be regarded as a further minor feature. Because of the frequency in the normal population the relative risk was only 3.4. Sensitivity to nickel can therefore not be regarded as a hard criterion for the diagnosis of AD.

The purpose of the score system was to summarize atopic features in a way that best discriminates atopic risk on the basis of frequent clinical signs without laboratory investigations. Serum IgE, Phadiatop and some specific signs of atopy which were less frequent than 20% were therefore not taken into consideration. In AD the serum IgE were associated with the different groups of AD classified by the proposed score system (Fig. 3). The individual atopic symptom and signs were elevated with regard to their diagnostic importance. The study emphasis the presence of subgroups of atopic dermatitis (Fig. 2). This score system based on traditional atopic features may also be a tool to estimate the atopic risk in non affected individuals. Based on the score system a patient with more than 10 points may be considered atopic, a patient with 6 to 10 points is suspected to be an atopic. Because of a history or clinical manifestation of flexural eczema 5% of the normal population were excluded. Using the proposed score system (Fig. 2) in our sample of the general population another 2% may be considered atopic, another 19% were suspected to be atopics (calculated atopic points: 6 to 10 points). In conclusion the prevalence of atopy in the investigated Caucasian normal population is estimated to be more than 7% and an additional 19% are suspected to be atopics.

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