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CLINICAL REPORT

Development and Validation of a Questionnaire for Diagnosing Atopic Dermatitis

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In this paper we describe the development and validation of a questionnaire for atopic dermatitis used in population surveys in Denmark. The Danish questionnaire was developed from the UK Working Party's questionnaire for atopic dermatitis and includes a severity score. The study included 61 children aged 3 to 14 years recruited from our Department of Dermatology, two kindergartens and a primary school. A validator was appointed to evaluate whether each child had current or previous atopic dermatitis. Compared to the validator's diagnosis, the sensitivity of the UK Working Party criteria was 90% (95% CI; 74–98) and the specificity was 97% (95% CI; 82–99). The criteria for atopic dermatitis have a satisfactory sensitivity and specificity for diagnosing current atopic dermatitis, but the natural course of the disease complicates the validation of investigational instruments. We suggest that future epidemiological studies aimed at establishing new knowledge on atopic dermatitis should include history, current symptoms and findings and a severity score. ***Key words: criteria diagnosis; sensitivity; specificity; severity score.***

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Although atopic dermatitis (AD) is the most common chronic inflammatory skin disease in childhood, population-based studies investigating possible risk factors and describing the course of AD have been sparse. One reason for this is the lack of an operational definition of AD that could be useful for population-based studies.

AD begins in childhood, with a peak incidence during the first 3 years of life (1). The disease varies from mild eczema of short duration to severe lifelong illness. AD can alternate between symptom-free intervals and relapses. The course of the disease is such that it is important not only to consider current symptoms and findings but also to focus on the history of symptoms and findings in order to identify persons with AD.

Two questionnaires have been validated for AD in epidemiological studies, Schultz et al. (2) and the UK Working Party (3), the latter study being the most well documented so far. The discriminators for the latter questionnaire were developed from the Hanifin & Rajka criteria (4).

These questionnaires have been used to estimate the prevalence of AD, including time trends. Prevalence measures are valid when studying risk factors assumed to maintain the disease, but when studying potential risk factors for initiating the disease process, incidence is the measure of choice. Few epidemiologic studies of risk factors for AD have been explicit as to the timing aspects of the hypotheses studied. The questionnaire presented in this paper was developed mainly to study the role of the factors in early life for initiating AD, and it differs from previous questionnaires in that it places more emphasis on information on past symptoms and findings.

A severity score is important in order to analyse the course of AD. Clinical scoring systems such as the Simple Scoring System of Costa et al. (5), the Scoring Atopic Dermatitis (SCORAD) index developed by the European Taskforce on Atopic Dermatitis (6) and SASSAD (7) have been devised in order to standardize a method of grading AD. These scoring systems are based on current symptoms and findings and are easy to use; they give a good picture of the severity of the disease. A new and simple method for assessing the severity of AD, the Nottingham Eczema Severity Score, was presented recently by Emerson et al. (8). This includes chronicity information in order to reflect the clinical course of AD.

The questionnaire presented in this paper (the Danish questionnaire) was developed to study the incidence of AD and to study associations between AD and hormonal contraception, measles vaccination and infection, and insulin-dependent diabetes mellitus. We present the experience from using the questionnaire, with results from a validation study, including estimates of sensitivity and specificity.

MATERIAL AND METHODS

Population survey

We conducted a population-based survey among a random sample of 9,744 children aged 3 to 15 years; the parents of 7,693 (79%) children replied to the questionnaire. In the population survey we attempted to conduct telephone interviews with the respondents in case of missing or inconsistent answers.

Development of the Danish questionnaire

The questions concerning AD in our questionnaire were developed from the UK Working Party questionnaire (3, 9–11). Some of the questions in the UK Working Party questionnaire were modified in order not to lose information (12). After a pilot study, the questionnaire was retranslated into English and sent to Dr. H. C. Williams, Queen's Medical Centre, Nottingham, UK, for critical comments and comparison with the original questionnaire. Table I shows in detail the differences between the UK Working Party questionnaire and the Danish questionnaire.

Criteria for atopic dermatitis

We applied the UK Working Party criteria in our study but used lifetime experience of AD instead of one-year prevalence. The UK Working Party criteria make a distinction between children less than 4 years of age and older children. Children less than 4 years old must

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Table I. *The UK Working Party's questionnaire on Atopic Dermatitis and the modified version used in Danish studies*

The UK questionnaire	The Danish questionnaire	Authors' comments
1a. IN THE LAST YEAR Has your child had an ITCHY skin condition – by *itchy* we mean scratching or rubbing the skin? Yes ☐ No ☐ *If you answered "NO" please skip to question 4a.* 1b. Has your child had this ITCHY skin condition in the LAST WEEK? Yes ☐ No ☐	1. Has your child EVER had an itchy skin rash that lasted more than 24 hours? Yes ☐ No ☐ *If you answered "NO" please skip to question 5.* *If you answered "YES" please answer the questions in the shaded box below:*	In Danish there is no natural translation of "skin condition", and we chose two terms "skin rash" (*hududslæt*) and "skin disease" (*hudsygdom*). We wanted to record lifetime experience, not only recent experience of AD, in order to study associations with exposures and other diseases.
*2. How old was your child when this skin condition began? Under 2 ☐ 2 to 5 ☐ 6 to 10 ☐ Over 10 ☐	2. How old was your child when this skin disease began? _____ Years _____ Months	Age at onset is specified in a more precise, yet simple way, to study associations with exposures and other diseases.
3. Has this skin condition ever affected the skin creases in the past – *by skin creases we mean fronts of elbows, behind the knees, fronts of ankles, around the neck, or around the eyes?* Yes ☐ No ☐	3. Has the skin disease ever affected any of the following locations of your child's body? *Please answer YES or NO to all the below-mentioned possibilities.* In the scalp Yes ☐ No ☐ Around the eyes Yes ☐ No ☐ On the cheeks Yes ☐ No ☐ Around the mouth Yes ☐ No ☐ On the front or the back of the body Yes ☐ No ☐ In the bend of the arm or the hollow of the knee Yes ☐ No ☐ On the wrist or ankle Yes ☐ No ☐	We wanted detailed information on location, and we hereby avoided asking several questions in one. We included locations not specific to AD to make the question less leading.
	4. Has your child the itchy skin disease on one or more of the following locations of your child's body at the moment? *Please answer YES or NO to all possibilities.* In the scalp Yes ☐ No ☐ Around the eyes Yes ☐ No ☐ On the cheeks Yes ☐ No ☐ Around the mouth Yes ☐ No ☐ On the front or the back of the body Yes ☐ No ☐ In the bend of the arm or the hollow of the knee Yes ☐ No ☐ On the wrist or ankle Yes ☐ No ☐	Besides past locations, we also wanted to record current locations of AD manifestations.
*4a. Has your child ever suffered from asthma – *by asthma we mean bouts of wheezing with coughing?* Yes ☐ No ☐	5. Have you ever been informed by a doctor that your child has asthma? Yes ☐ No ☐	We chose to use a doctor's diagnosis instead of trying to define the condition to the parents. "Wheezing" can hardly be translated into Danish.
*4b. Has your child ever suffered from hay fever – *by hay fever we mean bouts of sneezing with a runny nose or itchy eyes in the summer?* Yes ☐ No ☐	6. Have you ever been informed by a doctor that your child has hay fever? Yes ☐ No ☐	We chose to use a doctor's diagnosis instead of trying to define the condition to the parents. The definition in the UK questionnaire is hardly specific to hay fever.
5. In the last year, has your child suffered from a dry skin in general? Yes ☐ No ☐	7. Has your child a tendency to a dry skin? Yes ☐ No ☐	Direct translation of the original wording seemed heavy. Our simplified version worked well in the studies.
*6. Does anyone in your child's immediate family (i.e. mother, father, brothers or sisters) suffer from eczema, hay fever or asthma? Yes ☐ No ☐	8. *Please indicate year of birth of your child, his/her siblings and parents, and put an X for the diseases which the child, his/her siblings and parents have had:* Siblings no./parents 1 2 3 4 5 6 Mother Father Year of birth *Atopic eczema* *Asthma* *Hay fever*	Our question seems complex at first sight, but we had good experience with the question in a previous study (1). Inheritance cannot be estimated from information about disease among siblings without knowing the number and rank of the siblings. Also we wanted to include information about inheritance for children with a late onset of AD. The self-reported information was validated with interviews and with information from the Danish National Population Register.

*In the UK Working Party questionnaire, question 2 is not used in children < 4 years and questions 4a and 4b are replaced by question 6.

at least have had an itchy skin rash and must fulfil 3 out of 4 possible criteria in order to qualify as AD cases. Children above 4 years of age must fulfil 3 out of 5 descriptive criteria.

Severity of atopic dermatitis

The Marselisborg Hospital severity score includes present extent of atopic dermatitis, periods of at least one week of disturbed sleep at night, onset during the first year of life, chronicity and relapses (Table II).

Validation study

We performed a study among 61 children aged 3 to 14 years from February 1999 to January 2000.

The children were recruited from the Department of Dermatology, Marselisborg Hospital, Aarhus, Denmark (children with definite AD and children with other skin disease) and from two kindergartens and a primary school in the municipality of Aarhus, Denmark.

Data collection

The appointed validator (KB) was instructed according to the manual of the UK Working Party's Diagnostic Criteria for AD (13), and the scores from Dr. K. Bang were sent to Dr. H. C. Williams, the Queen's Medical Centre, Nottingham, UK, for quality control. In this test the validator had a correct answer for 28 out of 30 possible answers, i.e. a mean pair agreement index of 0.93.

In the validation study the mothers of the children were asked to fill in the Danish questionnaire. Next, the validator interviewed the mother about earlier and present skin conditions of the child, including symptoms, locations and course. Information about family history of atopy was obtained during the interview and the validator performed a clinical investigation of the skin and used the SCORAD index to estimate the severity of AD. After the interview and clinical examination the validator determined whether the child had present AD, previous AD, another skin condition or no skin condition. Previous AD was defined according to the Hanifin & Rajka diagnostic criteria for AD (4), if there was no report of disease relapse during the last 2 years prior to the study.

Statistics

Data entry was performed with SPSS Data Entry (14). The analysis was performed with SPSS for Windows, version 9.0 (15). The study was approved by the Ethics Committee of the County of Aarhus and by the Danish Data Protection Agency.

RESULTS

Telephone interviews among respondents in the population survey

Among 7,693 returned questionnaires in the population survey, 109 (1.4%) were incompletely or inconsistently filled in concerning AD-related questions. The main problems were missing information on age at symptoms onset and inconsistencies between responses to different questions. Most of the problems were resolved afterwards by telephone interview (data not shown).

The validation study of our questionnaire

Out of a total of 66 families who initially agreed to participate in the study, 61 families completed the full programme and were thus available for detailed analysis. The children included 32 boys and 29 girls between 3 and 14 years of age. Out of 28 children from the Department of Dermatology, Marselisborg Hospital, 23 children had AD. Of the 33 children from the school or kindergarten, 8 children had AD.

According to the validator's judgement, 31 out of 61 children had AD; of these 23 had present AD and 8 had previous AD, defined as no relapses in the 2 years leading up to the examination. According to the UK criteria applied to the questionnaire information, 29 children had AD. Table III shows the distribution of symptoms and findings in AD and non-AD children.

The joint distribution of children according to the two diagnostic criteria shows a high degree of agreement between the two criteria. Using the validator's diagnosis as a reference, the sensitivity of the UK criteria was 90% (28/31) (95% CI 74%–98%) and the specificity 97% (29/30) (95% CI 82%–99%). Omitting family history among children younger that 4 years did not change the results.

The mean SCORAD score among children with AD was 28.1 (range 0 to 97.9). The mean score of the Marselisborg Hospital severity score was 4.9 (range 0 to 7). The SCORAD and the MH severity scores among children with AD ($n = 31$) are shown in Fig. 1. In the group with current AD, the SCORAD shows only a slight association to the Marselisborg Hospital severity score, whereas no association was observed among children with previous AD.

Table II. *The Marselisborg Hospital severity score. The scoring index used in two epidemiological studies*[1,2] *performed in Denmark*

The Marselisborg Hospital severity score	
Extent	Visible eczema on at least 3 different locations at the time the questionnaire was completed: 1 point
Subjective symptoms	Disturbed sleep at night in periods of at least one week: 2 to 5 periods: 1 point > 5 periods: 2 points
Onset of atopic dermatitis	Onset ≤12 months: 1 point
Chronicity and flare-up of atopic dermatitis	Eczema during 3 successive months for at least 3 successive years: 1 point
Chronicity of atopic dermatitis	Eczema ≥ 25% of lifetime since onset: 1 point Eczema ≥ 50% of lifetime since onset: 2 points

[1]Olesen AB, Juul S, Birkebæk N. Thestrup-Pedersen K. Association between atopic dermatitis and insulin-dependent diabetes mellitus: a case-control study. Lancet 2001; 357: 1749–1752. Ref. 19.

[2]Olesen AB, Juul S, Thestrup-Pedersen K. Atopic dermatitis following vaccination for measles, mumps and rubella or measles infection (in manuscript).

Table III. *Frequency of positive answers to the Danish questionnaire regarding atopic dermatitis (AD). Comparison of the diagnosis by validator and UK Working Party criteria*

	Diagnosis by validator[a]		Diagnosis by UK criteria	
Questionnaire information	AD ($n = 31$)	Non-AD ($n = 30$)	AD ($n = 29$)	Non-AD ($n = 32$)
Itchy skin rash	31 (100%)	2 (6.7%)	29 (100%)	4 (12.5%)
Onset 2 years	26 (83.9%)	1 (3.3%)	25 (86.2%)	2 (6.3%)
History of flexural involvement	31 (100%)	2 (6.7%)	29 (100%)	4 (12.5%)
Visible flexural involvement	21 (72.4%)	0 (0%)	21 (72.4%)	0 (0%)
History of asthma and/or hay-fever	9 (29.0%)	2 (6.7%)	9 (31.0%)	2 (6.3%)
Dry skin	27 (87.1%)	3 (10.0%)	27 (93.1%)	3 (9.4%)
Positive family history of atopy among one or more first-grade relatives[b]	16 (51.6%)	13 (43.3%)	14 (48.3%)	15 (46.9%)

[a]The validator diagnosis was made by KB after an interview and clinical examination.
[b]The UK Working Party uses this criterion for children less than 4 years of age.

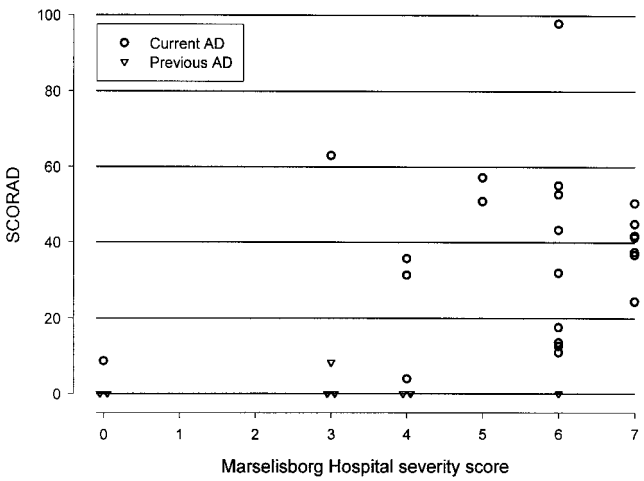

Fig. 1. Comparison of SCORAD (range 0 to 100 points) and the Marselisborg Hospital severity score (range 0 to 7 points) among 31 cases with current or previous atopic dermatitis.

DISCUSSION

Our study showed a sensitivity of 90% and a specificity of 97% when comparing the Danish questionnaire with the validator's diagnosis of AD. This result is as good as any previous validation of the criteria, even in non-translated versions, and much better than results obtained by most translated versions. We are aware that our sample size is small, which is also reflected in the confidence intervals. However, we are satisfied with the high specificity, which is of major importance for the purpose of studying risk factors.

The UK Working Party's own validation study showed a sensitivity of 80% and a specificity of 97% among 695 children aged 3 to 11 years (16). The validation of these criteria was performed among schoolchildren, with the main focus on current symptoms (within the previous 2 weeks) and current findings defined as visible flexural eczema. Several studies have validated the UK Working Party criteria. All studies have shown a specificity of 90% or higher, whereas the sensitivity has varied from 10% in a study from Iran (17) to 88% in a study from Germany (18).

Our questionnaire was developed from the UK Working Party questionnaire to estimate the incidence of AD and to study associations between AD and factors in early life. We intended that it would yield information that would enable the use of the UK Working Party criteria for AD, but we wanted more information on the onset and course of AD than is obtained from the UK Working Party questionnaire.

AD is a disease that can vary in degree of severity, and the dichotomy between diseased and non-diseased cases is a matter of definition. Furthermore, the manifestations of AD vary over time, and in an affected child the disease may sometimes be dormant, sometimes active. These characteristics complicate the defining of criteria for the disease and validation of investigational instruments. The natural course of AD emphasizes the importance of measuring both current and previous symptoms and findings.

No external standard exists for examining the validity of the information obtained on the onset and course of the disease. However, the internal consistency of the information obtained from 7,693 questionnaires in our population survey concerning disease onset and course was satisfactory, and only in a very few questionnaires was the information on timing of events inconsistent.

In a study of the association between AD and insulin-dependent diabetes mellitus (19), we decided not to include information on family history in the AD criteria because there may be common genetic or environmental factors that affect the risk of both diseases, and including genetic information (family history) in the definition of AD may confound the interpretation of results. Apart from this consideration, another problem is the interpreting of information about atopic disease among siblings: the probability of a positive family history is much higher for a child with several older siblings than for an only child. This may be of minor importance in the clinical setting, but it could confound the results of epidemiological studies.

We also intended to obtain information on disease severity, but unlike SCORAD, which describes the current state only, we wanted to apply a severity index including information on chronicity. For longitudinal studies, a simple and easy scoring system including information on the clinical course of the disease is a must. The severity score should not include treatment and use of doctors, since many patients with AD are not seen by a doctor and some of the associations that we wish to examine may be connected to health behaviour which

could lead to confounding. In this context the recently presented Nottingham Eczema Severity Score seems a promising investigational instrument for future epidemiological research.

In conclusion, the criteria for AD used in the Danish studies have a satisfactory high sensitivity and specificity for diagnosing current AD, while the validity concerning lifetime experience of AD cannot be determined. The characteristics of AD complicate the validation of investigational instruments and of the criteria of the disease. Inclusion of aetiological information in the definition of AD may be useful in the clinical setting, but it may confound the interpretation of results in epidemiological studies.

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