

Atopic dermatitis: an increasing problem

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It is well known that atopic dermatitis is an extremely common disease in the industrialized world, and in recent decades an alarming increased frequency has been observed in several investigations. However, some of the main problems in studies on the changing pattern in the epidemiology of atopic dermatitis are related to the definition of the disease, which is notoriously hard to define in writing – and the few reliable data on its frequency in the past. In this paper we report and discuss examples on solid and long-term population-based studies and a recently suggested framework for questionnaire investigations on atopic dermatitis.

Questionnaire studies on the frequency of atopic dermatitis

One of the first studies on this issue was published by Taylor et al. in *Lancet* in 1984 (1). This was a wide-scale epidemiological study in which health visitors surveyed randomly selected 5- to 7-year-old children by a structured questionnaire. The question was: "Is there a history of eczema in the first year? Or after the first year? The results suggest a convincing increase since the Second World War (Table 1). These three national British birth cohorts was set up to evaluate the quality of the maternity services in Great Britain, and the structured questionnaire contained a battery of questions on the medical, social and environmental background of the child, and the questions were slightly different at the three surveys which each included 10,000–15,000 children born during a certain week in the years in question. However, it might be that these vague questions on eczema overestimate the actual number of atopic dermatitis cases.

Another study from Great Britain concentrates on respiratory symptoms and atopy in Aberdeen schoolchildren (2). Two surveys were carried out 25 years apart with slightly different sampling technique. The precise questions on atopic dermatitis are not reported. However, the results fits very well into those previous reported from England (Table 2).

In 1986, we published a genetic-epidemiologic investigation on atopic dermatitis in a population-based twin sample. The study was specifically directed towards examining the occurrence of atopic dermatitis and the relative importance of genetic factors in the etiology of the disease. The investigation has been described elsewhere in detail (3). In short, we encircled a representative twin series with atopic dermatitis by a mailed questionnaire study among twins living in the Danish island of Fyn and performed a subsequent clinical examination of all who answered affirmatively to the inquiry. The conventional clinical twin study was widened to include a control series of the non-atopic study population in an attempt to obtain an unbiased estimate of the genetic as well as the epidemiologic aspects of atopic dermatitis. The study indicates a significant increase in the frequency of the disease since the early 1960s. In order to evaluate and expand the original findings we have conducted a new twin study in younger age groups in the same area (4). This investigation likewise indicates a still rising disease frequency and that the cumulative incidence rate (0–7 years) of atopic dermatitis in 1987 was about 12% for children born from 1975 to 1979 in Denmark (Table 3).

Reliability of questionnaire studies

The reliability of questionnaire studies has been studied to some extent. In an investigation from the south-west coast of Norway, about 5000 persons were asked about atopic symptoms in a mailed questionnaire study (5). The response rate was 90%. A subsample of about 600 subjects were invited to a clinical examination. They found that the predictable value of a positive answer to the question: "Have you ever had eczema?" was 50%, while the predictable value of a negative answer was 98%. In our own 1986 study we asked: "Have you or have you had infantile eczema?", and the questionnaire was accompanied by an informative letter giving

Table 1. Frequency of atopic dermatitis

The frequency of atopic dermatitis in a large-scale epidemiological study in Great Britain - health visitors asked parents of randomly selected 5- to 7-year-old children - "Is there a history of eczema in the first year? Or after the first year?"

Year of birth	Frequency (%)
1946	5.1
1958	7.3
1970	12.2

Taylor, Lancet ii, 1255, 1984

atopic dermatitis a wide and elastic description to give the fewest possible false-negative answers. The predictable value of positive answers rose to 80% and that of a negative answer to 100% (3). However, for many reasons it is not always practicable or economically feasible to conduct clinical investigations on representative subsamples of participants in questionnaire studies. For epidemiologic purposes we need a definition of atopic dermatitis that is specific, sensitive and suitable for large-scale studies. Furthermore, the guidelines have to be immune to changes in the diagnostic fashion or a supposed greater readiness to use the label atopic dermatitis that might occur in interview studies.

Evaluation of a questionnaire model for the epidemiology of atopic dermatitis

At an international symposium on atopic dermatitis in 1991, we suggested an appropriate questionnaire model to the epidemiological surveillance of atopic dermatitis (6). We decided to evaluate this model and at the same time study the occurrence of atopic dermatitis in Denmark, Germany and Sweden in schoolchildren born in the 1980s (7). The proposed questionnaire technique is based on the idea that if a person answers affirmatively to certain key questions, it is very likely that the person has or has had atopic dermatitis. The elaboration of the questions relies on investigations on the validity of the Hanifin-Rajka criteria (8) by Diepgen (9) and Svensson (10), who had evaluated clinical and anamnestic features in established cases of atopic dermatitis against control groups. It has been our basic consideration that a minimum list of reliable characteristics should be fulfilled in order to diagnose atopic dermatitis by a questionnaire. These features include: flexural itchy rashes, onset during infancy or early childhood, chronicity, and personal or family atopy. The study, including the exact questions, is published in detail elsewhere (7). In short, we informed the schoolmasters of all the schools in Fredericia, Erlangen and Kristianstad about the project, and the questionnaire was handed out by the class teachers to all the school beginners in a certain week in October 1992. A short informative letter ex-

Table 2. Frequency of atopic dermatitis

Respiratory symptoms and atopy in Aberdeen schoolchildren. Two surveys 25 years apart but with different sampling technique, and the precise questions on atopic dermatitis are not reported

Year of birth	Age	Frequency (%)
1951-56	8-13	5.3
1976-81	8-13	12.0

Ninan, BMJ, 304,873,1992

Table 3. Frequency of atopic dermatitis

Population-based twin study of 7-year-old twins living in Fyn County, Denmark - validated questionnaire studies - "Have you or have you had infantile eczema?" - accompanying informative letter

Year of birth	Frequency (%)
1960-1964	3.2
1965-1969	4.6
1970-1974	10.2
1975-1979	11.5

Schultz Larsen, JAAD, 15, 487, 1986

Schultz Larsen, JAAD, 28, 719, 1993

plained the purpose of the investigation to the parents, and the child was asked to bring the questionnaire back to the schoolteacher before the end of the week. The reply rate reached 90%. A total of 2,655 questionnaires with about 1% missing data were available for assessment. A positive answer to each question was assigned a certain number of points, and if the total score surpassed a certain points, the diagnosis of atopic dermatitis could be considered likely (11). In order to evaluate the questionnaire, it was handed out to the parents of 105 out-patients of the same age and who fulfilled the Hanifin-Rajka criteria, and to 100 out-patients without known atopic dermatitis, both groups from the Department of Dermatology in Kristianstad in Sweden. Furthermore, a population-based control group of the supposedly non-atopic dermatitis patients was created from the whole material minus the 7.5% who had onset before 2 years of age, a duration of more than 3 years and flexural involvement. In accordance with previous investigations (9, 10) it was demonstrated that, for example, dry skin, seasonal variation and emotional worsening discriminate fairly well between patients and controls. In total, a responder could have 140 points, and previously we were fairly convinced that those who had 60 points or more could definitely be deemed to have or have had atopic dermatitis (6). The analyses revealed that this statement was almost correct. With a slight change in the value of each question we could show that the sensitivity and specificity were about 90%, if those who had 50 points or more

were considered to have atopic dermatitis (11). In that way the frequency of atopic dermatitis for those 7-year-old children born in 1985 in northern Europe could be calculated to be 16% with some regional differences. This still increasing frequency of atopic dermatitis in schoolchildren has recently been confirmed in others and independently performed investigations from Århus in Denmark (18%) and Birmingham in England (20%) for children born in the 1980s (12, 13).

Risk factors of atopic dermatitis

Unfortunately, nothing definitely is known of the explanation of the rising occurrence of atopic dermatitis. Heredity, race and social class has been shown to be risk factors (14, 15). One of the new theories has focused on the increasing maternal age at the birth of the first child and a suspected dysmaturation of the immune system in older mothers (16). It might be that the slow progress in our understanding of the probably heterogeneous disease that we call atopic dermatitis is related to a lack of the necessary conceptual instrument to combine risk factors. It is greatly to be hoped that the proposed questionnaire model will add a greater deal of standardization to the study of atopic dermatitis in the future. Of course, it is much more informative to compare the results of the same survey technique applied in different areas, at different times or at different levels of exposure.

Conclusion

Several studies have suggested that the prevalence of atopic dermatitis has increased over the last decades. However, definition and measures of atopic dermatitis in the population have been hampered by difficulties in separating real changes in the occurrence of the disease from secular change in the diagnosis. After the Second World War, the frequency of atopic dermatitis in childhood seems to have been steadily increasing from about 3% in 1960 to at least 15% in 1990. Recently, we conducted a cross-sectional questionnaire study in nearly 3000 7-year-old schoolchildren in the autumn of 1992 in Denmark, Germany and Sweden. The frequency of atopic dermatitis was calculated to be 16%, with regional differences. This simple questionnaire model works well and is sufficient sensitive and specific to measure the occurrence of the disease and could be used to study suspected risk factors in the etiology of atopic dermatitis in schoolchildren.

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