

Secular Change in the Occurrence of Atopic Dermatitis

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Atopic dermatitis is a common disease, and population-based studies indicate that the frequency of atopic dermatitis has increased substantially during recent decades. It has been generally accepted that disease onset occurs before 7 years of age in 80–90% of the cases, and consequently the epidemiology of atopic dermatitis has been studied mostly in children on admission of first grade school. Before 1960 about 2–3% of children suffered from atopic dermatitis. In the 1960s, some 4–8% was recorded in several studies, and for those born after 1970 most researchers found that 9–12% developed atopic dermatitis during childhood. The diagnostic criteria of Hanifin and Rajka are cumbersome for population studies not designed specifically for children. In order to compare epidemiologic data from varying times and locations, a framework for questionnaire studies in atopic dermatitis is proposed. Key words: Atopic dermatitis; Measures of disease frequency; Rising occurrence; Questionnaire proposal.

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The clinical picture of atopic dermatitis is multi-faceted. Even a trained dermatologist would find it hard to make an instant and definite diagnosis of atopic dermatitis (AD) in every case. There is no definitive laboratory test nor a primary or distinctive lesion with which to identify AD. In the eczematous patient the diagnosis has to be based on the history as well as on clinical signs. The most important features are the following: (a) a chronic, recurring course, (b) family/personal history of atopy, (c) pruritus, and (d) an often characteristic distribution of lesions (1). In some 80–90% of the cases, the onset of the disease occurs before 5–7 years of age (2). Consequently, it has been well-founded that the epidemiology of AD has been studied on admission of first-grade schoolchildren. However, at this age the signs and symptoms will have disappeared from many of those who had AD in early infancy. Thus, the first problem that confronts the researcher is to elaborate diagnostic guidelines for both those who still have and those who have had AD, in order to provide valid information on the occurrence of AD (3).

In an epidemiologic survey, the second problem is related to the confusing terminology of AD, especially in the first part of the century (4). Nowadays, the term atopic dermatitis should be the internationally accepted designation for this disease as already suggested by Wise & Sulzberger in 1933 (5). In passing, we prefer atopic dermatitis to atopic eczema, leaving the imprecise and misused term eczema to be reserved for lay speech.

The third problem is associated with the measures of disease frequency. The incidence of a disease is the number of cases of

the disease that arise during a specified period of time. However, it might not be possible in practice to measure incidence because the exact time of onset of a disease is uncertain, and the time required to confirm it is necessarily imprecise. The point prevalence is the frequency of a disease at a designated point of time. In contrast to incidence, which measures events, point prevalence is a measure of what prevails or exists. Period prevalence is a measure that expresses the total number of cases of a disease known to have existed at some point during a specified period. Thus, the period prevalence is the sum of point prevalence (the number of disease cases existing at the beginning of the period) and the incidence (the number of disease cases arising during the period).

With our current knowledge of the natural course of AD we are interested to know how many individuals have or have had at the age of 7 years, in order to provide reliable risk figures for the public. The ideal investigative design would be to follow a cohort of children from birth to 7 years of age. However, this approach is neither practical nor cost-effective. As AD is not associated with excess mortality, investigations at school admission can be regarded as a follow-up study of a theoretical cohort of livebirths (minus the small number of death infants). A proportion (in Denmark 15%) is exchanged by migration, and there is no reason to believe – at least in Denmark – that migration affects the occurrence of the disease. The relevant measure for this disease frequency is the cumulative incidence rate (0–7 years), which is the number of individuals developing the disease within this age interval, correlated to the number of individuals at risk at the start of the interval (6). Several of the studies cited below have not strictly defined the measures for disease frequency, and in this review the neutral designation ‘frequency’ or literary ‘incidence’ will be used to characterize those who have or have had AD at about 7 years of age. With the above-mentioned problems and limitations in mind, the following survey will specifically explore population-based studies dealing with the occurrence of AD.

The earliest report dates back to Service’s study (7) in 1939 in the City of Colorado Springs, USA. One thousand families (altogether 3,141 persons) were investigated through a house-to-house canvass. The study concentrated on the incidence of major allergies among those who had previously sought “medical relief for their symptoms”. Questionable cases were investigated by the author himself. The study showed that 91/3,141 (2.9%) had “eczema of allergic origin” not otherwise stated (Table 1).

At the opening lecture at the 4th Nordic Congress on Allergy in 1954, Eriksson-Lihr referred to a recent investigation on allergy in childhood among 4,832 schoolchildren in an area around Turku in southwest Finland (8). In addition to medical examination, further information was obtained from question-

Table I. Frequency of atopic dermatitis; year of birth before 1960.

	Frequency (%)
Service (7)	2.9
Eriksson-Lihr (8)	3.0
Eriksson-Lihr (8)	2.0
Walker & Warin (10)	3.1
Brereton et al. (11)	1.6
Freeman & Johnson (12)	1.4
Larsson & Lidén (13)	2.0

naires to the parents, school health records and local health centres. There were 145/4,832 (3.0%) with "infantile eczema" not otherwise defined. The author also referred to a similar study carried out among schoolchildren in Helsinki based on health records completed by school nurses and supplemented by clinical examinations made by school doctors. The material comprised 27,999 children aged 7-14 years, of whom 558/27,999 (2.0%) had eczema. Although it is not clear if those with a history of AD were taken into account, it is remarkable that the sex distribution female/male 335/248 (1.35%) is completely in accord with more recent Scandinavian population-based studies (9).

In a geographically delimited area around Bristol, England, the figures obtained by health visitors were scrutinized regarding the diagnosis of eczema on their health cards (10). When the diagnosis was in doubt, the child was clinically examined by one of the authors, and borderline cases were excluded. In addition, home visits were made in a subsample of 192 children, but only 1 case of previously unrecorded eczema was detected. The investigation took place in 1955 when the children were between 1 and 5 years of age. The overall incidence of infantile eczema was 32/1,024 (3.1%). However, there was no attempt to distinguish the exact type of eczema in these pre-school children.

From a different part of England, Brereton et al. (11) reported a survey designed to determine the incidence and prognosis of eczema and asthma in 1954-55 in Cambridgeshire schoolchildren. They were screened on starting school (usually at 5 years), at 8 and 11 years and at schoolleaving age. There were altogether 4,006 children, representing 37% of the pupils in the school district. In primary school (age range 5-11 years) about 69% of the parents attended the medical inspection at which a questionnaire form was completed. The methodological details are sparse and a complete cutaneous examination of all the children was presumably not performed. The authors found a total incidence of 46/4,006 (1.1%) who had eczema or a history of eczema, highest in the youngest age group, namely 19/1,223 (1.6%).

A mailed questionnaire study by Freeman & Johnson among 2,627 randomly selected adolescent students aged about 14 to 18 years of age formed the basis of a study of the incidence of allergic diseases in Denver, USA in 1963 (12). The strategy in this thoroughly reported investigation included pilot evaluation of the questionnaire, repeated mailing followed by telephone follow-up and an accompanying information sheet in which AD was defined as: "An allergic skin rash which appears in the creases of the elbows and knees, is

Table II. Number of pupils with atopic dermatitis in the County of Västerbotten, Sweden (13)

Year of birth	Time of examination	No. of pupils	Atopic dermatitis	
			n	(%)
1959-60	1975-76	557	11	(2.0)
1960-61	-	2571	72	(2.8)
1961-62	-	2672	80	(3.0)
1962-63	-	2249	74	(3.3)
1963-64	-	228	14	(6.1)

very itchy and lasts for months to years. Other skin areas can also be involved. Eczema usually starts in infancy". A response rate of 85.4% was obtained. A subsample of the non-responders were interviewed by phone or in person prior to the subsequent data processing. The authors emphasized the difficulty of obtaining reliable answers about dermatologic diseases by questionnaire, and only those cases which were established during the first 2 years of life were included. From one of the tables it can be deduced that 30/2,235 (1.4%) had AD defined as mentioned above.

In northern Sweden, schoolchildren between the ages of 12 and 16 years took part in a clinical investigation of skin diseases (13). The clinical examination was performed by a dermatologist (Larsson) who filled in a form for each pupil. He managed to examine 8,277 (86.3%) of all school-children registered for the school year 1975-76 in the County of Västerbotten. All pupils diagnosed as having AD "had dry eczema and/or lichenification in flexures or in other predilection sites". The investigation is undoubtedly one of the few studies which gives the point prevalence for the skin disease in question. The overall point prevalence of AD was 3.0%, but an increasing trend was suggested by tabulating individual year groups (Table 2).

In 1967, Albeiter (14) published a questionnaire study on the incidence of allergy in 5-15-year-old schoolchildren in Munster, a suburb of Chicago, USA. A 1-page questionnaire along with a letter of explanation to the parents was distributed to 2,001 pupils, from whom 1,842 (92%) replies were deemed satisfactory. The author only calculated as positive those children whose diagnosis of an allergic disorder was confirmed by a physician. Without giving exact figures, it was reported that 4.4% had eczema, highest in the 7-8 year age group, which had 6.4% (Table 3). Females exceeded males in a ratio of 1.3:1. It was stressed that the validity of the investigation may be high, as most of these upper-middle income parents were college graduates, familiar with answering inquiries reliably, and as the children were frequently seen by

Table III. Frequency of atopic dermatitis; year of birth 1960-70

	Frequency (%)
Arbeiter (14)	6.4
Turner et al. (15)	8.8
Kjellman (16)	8.3
Larsson & Lidén (13)	6.1
Engbæk (17)	3.8

Table IV. Numbers of 6-year-old pupils with atopic dermatitis in two Danish municipalities (17)

Year of birth	Time of examination	No. of pupils	Atopic dermatitis	
			n	(%)
1968-69	1975-76	183	7	(3.8)
1972-73	1979-80	382	37	(9.7)
1973-74	1980-81	430	37	(8.6)

physicians because of the better education and economic status of their parents.

In 1970 Turner et al. (15) studied the incidence of atopic disease and its relationship to serum IgE levels in school-children aged 6-17 years who were resident in Brusselton, a rural town in Western Australia. Questionnaires were sent home from school with the children, and collected by their local doctor. The following questions were asked: "Did the child have eczema under the age of 2 years? Has the child had eczema over the age of 2 years?" The overall incidence of eczema was stated to be 141/1,598 (8.8%), and infantile eczema (onset before 2 years of age), 89/1,598 (5.6%). The study concentrated on serum IgE, and no further relevant details were reported.

In 1975 in Linköping, in Sweden, all schoolchildren were questioned by trained school nurses about atopic disease, in connection with the ordinary medical inspection at school admission, 7 years of age. This investigation by Kjellman (16) resulted in a response rate of 1,325/1,473 (90%). The study demonstrated, among many other things, that the overall incidence of atopy was 15.1%; 110/1,325 (8.3%) of these children had AD defined as "in the case of evident symptoms and/or signs of atopic dermatitis".

In two Danish rural municipalities with 4,400 schoolchildren, annual examinations from 1968 to 1974 by a school medical officer (Engbæk) formed the background of a survey of the morbidity in school age (17). Fewer than 1% of the children within the municipalities was unable to attend school owing to severe physical or mental handicap. The number of diagnosed cases of AD in the kindergarten class (children approximately 6 years of age) is given in Table 4.

A prospective study of the cumulative incidence rate of AD and infant diet was carried out by Ferguson and co-workers (18,19) in a birth cohort of 1,265 infants born in 1975 in maternity units in Christchurch, New Zealand. The infants were clinically assessed at birth, at 4 months, and at 1, 2 and 3 years, at which age 1,143 (90%) remained in the study. Be-

Table V. Frequency of atopic dermatitis; year of birth after 1970

	Frequency (%)
Fergusson et al. (19)	20.4
Engbæk (17)	9.1
Taylor et al. (20)	12.2
Schultz Larsen et al. (3)	10.2
Storm et al. (21)	8.9
Schultz Larsen (24)	11.5

Table VI. Frequency of atopic dermatitis in widescale epidemiological study in Great Britain - health visitors asked randomly selected 5-7-year-old children about eczema (20)

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

sides the drop-out there was a small amount of missing data. The cumulative incidence rates for the first, second and third year were, respectively: 7.4%, 16.6% and 20.4% (Table 3 in reference 19). The diagnosis of AD was based on diaries kept by the mothers (61% at 2 years of age), maternal recall, or from the child's doctor. However, only about 80% of the infants were prescribed a steroid cream, and the skin changes were not evaluated by a dermatologist. The above-mentioned figures probably overestimate the occurrence of AD (Table 5).

In 1984, Taylor et al. (20) published data on the reported frequency of childhood eczema from three national birth cohort set up to assess the quality of maternity services in Great Britain. When the children were about 5-7 years of age the mothers were interviewed at home by a health visitor using a structured questionnaire with a list of disorders including eczema not otherwise defined. The results suggest a convincing increase in AD since the Second World War (Table 6), although at a higher level than found in a twin population in Denmark (3). However, we believe that such vague questions on eczema tend to overestimate the number of AD cases, and the figures merely reflect the incidence of miscellaneous eczemas in childhood.

A Danish paper with an English summary (Storm et al.) describes an investigation of atopy in a representative sample of a cohort of 1,210 children born 1974-75 in the city of Viborg (21). At the age of 7 years, 1,073 (89%) of the children were traced, and their parents answered a mailed questionnaire on predisposition, atopy and atopic-like symptoms. Based on the answers, all children with definite or probable atopic diseases were examined physically and allergologically and atopic dermatitis was defined as "itching eczema with a characteristic distribution". They found a cumulative incidence rate of 96/1,073 (8.9%). Although lacking application of internationally accepted diagnostic guidelines (1) and a control group from the presumably non-diseased study population, the frequency

Table VII. Cumulative incidence rate of atopic dermatitis for twin individuals born 1960-64, 1965-69 and 1970-74 (3).

Year of birth	Twins n	Cumulative incidence (0-7 year) of atopic dermatitis		
		n	%	95% confidence interval
1960-64	348	11	3.2	1.3-4.9
1965-69	416	19	4.6	2.8-6.6
1970-74	362	37	10.2	6.8-13.6

$\chi^2 = 16.71, p < 0.001.$

ATOPIC DERMATITIS

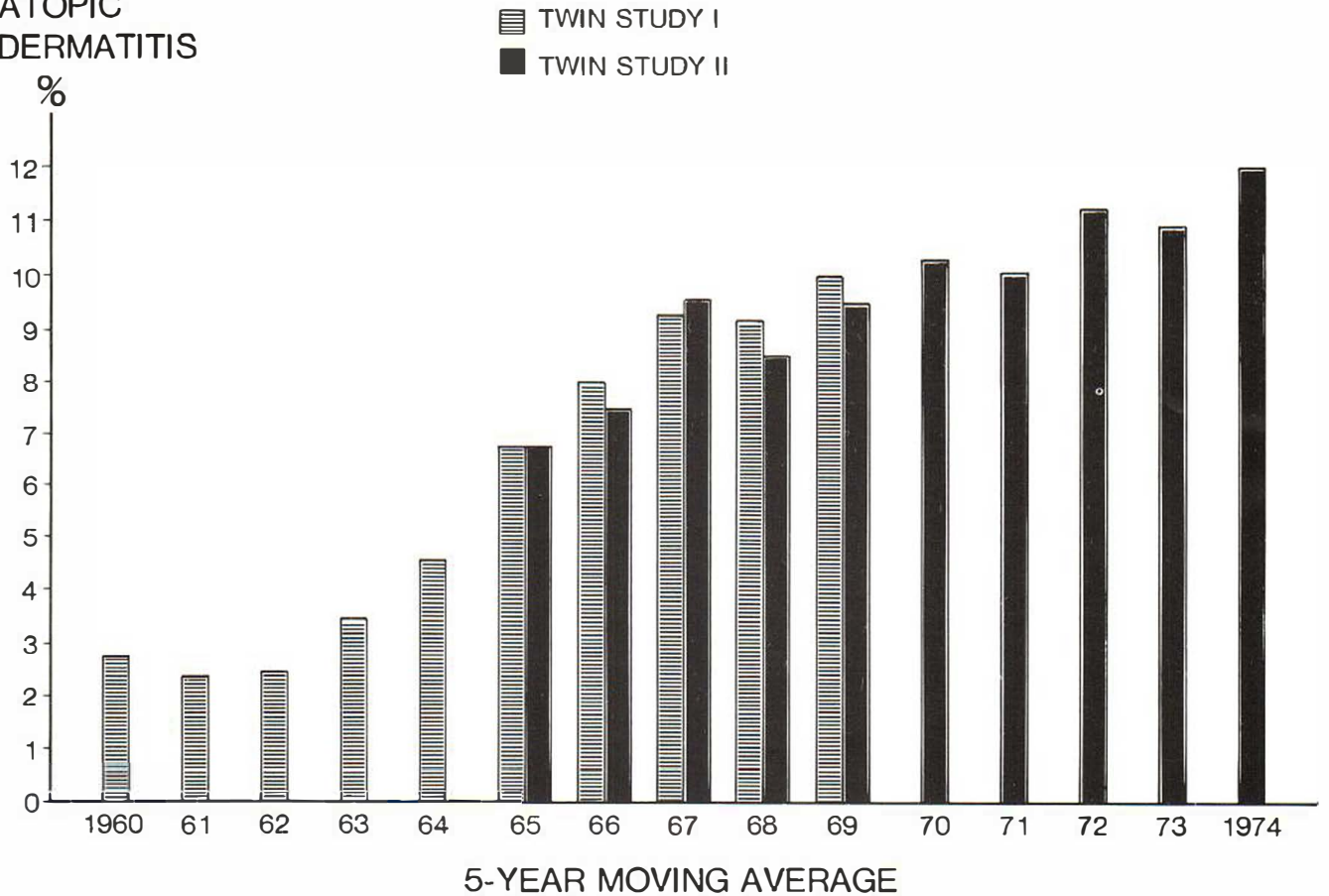


Fig. 1. The cumulative incidence rates (0–7 years) for atopic dermatitis according to year of birth between 1960 and 1979 (depicted as 5-year moving average).

of AD in this prospective study agreed well with those found in other Danish studies from the same period (3,17).

Since some criticism can be directed against several of the studies referred to above, we initiated a Danish population-based twin study with the purpose of studying the relative importance of genetic factors and the occurrence of AD. The methodological details have been presented elsewhere (3, 9, 22, 23). The main epidemiological data of the investigation are given in Table 7. The study clearly indicates a rising frequency of AD within recent decades. In order to evaluate and expand this finding, we have conducted a new twin study (II), which shows that there is a continuing statistically significant increase in AD among individuals born during the 1960s and 1970s (Fig. 1), and that the cumulative incidence is – at least in Denmark – about 12% in the present generation, who will develop AD during childhood (24).

This historical survey of population-based studies has provided an opportunity to highlight some general problems in epidemiologic studies on AD. Uncertainty in the diagnosis of the disease as well as in the measurements for the disease frequency is evident in some of the publications. Nor have previous reports thoroughly considered the implications of incomplete ascertainment or evaluated the generalizability, i.e. to what extent the investigations can be generalized to groups other than the study sample. In addition, none of the

above-mentioned studies have been exclusively designed to examine the epidemiology of AD. In spite of these obstacles, this review fully supports the statement: atopic dermatitis is a very common disease and it is becoming more and more common. Before 1960 about 2–3% of children had AD. For those born in the 1960s, 4–8% was recorded in several studies, and for the rising generation born after 1970 in Denmark – and presumably in other areas of the industrialized world too – we can confidently estimate that 9–12% will suffer from AD during childhood (Tables 1, 3, 5).

The increasing occurrence of the disease is an alarming phenomenon that has attracted public attention. Concerted action in future research efforts into the study of the nature of AD has been encouraged. As a practical and cost-effective model in the epidemiological surveillance of AD we suggest a 1-page questionnaire to be used in representative samples of primarily 7-year-old school children (Appendix 1). This suggestion is based on personal experience and on studies on the validity of the Hanifin & Rajka criteria (1) by Svensson (25,26) and Diepgen et al. (27). These studies evaluate anamnestic and clinical features in established cases of AD vis-à-vis control groups. Although reporting disparate results in several of the findings, the two investigations commonly agree that criteria such as itching when sweating, dry skin and personal history of respiratory atopy discriminate fairly well between

cases and controls (25,27). In addition, it has been our basic consideration that a minimum number of reliable characteristics should be present in order to diagnose AD by questionnaire. These essential features are: flexural itchy rashes, onset during infancy or early childhood, chronicity, and personal/family atopy. Furthermore, we have tried to elaborate the questions in easily understood language. An assessment scale is giving in Appendix 1. We consider

- > 60 points: denoting definite atopic dermatitis
- 25-55 points: possible atopic dermatitis
- < 20 points: no atopic dermatitis.

The questionnaire should be evaluated in one or several forthcoming studies by a clinical examination of a representative subgroup of those deemed as having definite, possible, and no AD. The points for each answer should of course not be printed on the form, which should be accompanied by an informative letter emphasizing the approval by the medical ethics committee, confidentiality, the rising frequency of AD and preventive measures. In our opinion the information sheet should not contain further description of AD, as differences in 'common language' definitions would make comparisons between different studies unnecessarily difficult. It is quite possible that this concept could also be utilized in front of a patient with a questionable history of AD. Finally, it is our hope that this accessible and reproducible questionnaire instrument would be an efficient and powerful method with which to obtain new and valid information on the occurrence of atopic dermatitis.

APPENDIX 1

Questionnaire

Did your child ever have itchy rashes (infantile eczema)? (Circle all those that apply for each question):

- Points
- 20 1) in the elbow or knee folds
 - 10 2) at the wrists or ankles
 - 10 3) over the face or neck
 - 10 4) on the hands, arms or legs
 - 5 5) on the trunk

Did your child have any of the following?

- 5 6) unusually dry skin
- 5 7) irritation of the skin from textiles (wool)
- 5 8) itching of the skin when sweating
- 5 9) seasonal variation in severity
- 5 10) worsening by psychological tension or stress

At what age was the first appearance of the skin problem?

- 20 11) less than 2 years of age
- 10 12) 2-5 years of age
- 5 13) 5-10 years of age
- 0 14) more than 10 years of age

For how long did your child have itchy rashes (infantile eczema)?

- 0 15) less than 1/2 year
- 5 16) 1/2-2 years
- 10 17) 2-5 years
- 20 18) more than 5 years

Has your child had asthma or hay fever?

- 10 19) yes
- 0 20) don't know
- 0 21) no

Did your child have other relatives (e.g. siblings, parents, children) who have or have had infantile eczema, asthma or hay fever?

- 10 22) yes
- 0 23) don't know
- 0 24) no

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