

Clinical characteristics and consequences of hand eczema – an 8-year follow-up study of a population-based twin cohort

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Background: Few population-based clinical follow-up studies on hand eczema are reported.

Objectives: The aim of this study was to characterize clinical symptoms and to examine occupational and medical consequences as well as persistence of hand eczema in a population-based twin cohort.

Patients/Methods: A total of 274 individuals with and without hand eczema were examined, patch tested, and interviewed in 1997–1998 and 2005–2006. Data on 188 individuals with hand eczema in 2005–2006 were analysed.

Results: Erythema and scaling were the most frequent symptoms, and fingers and palms were most often affected. Mean hand eczema severity index score in individuals with clinical symptoms was 12.0. Sick leave was reported by 12.4%; job change by 8.5%. Being in the lowest socio-economic group and atopic dermatitis were risk factors for sick leave [odds ratio (OR) = 5.6; 95% confidence interval (95% CI) 1.5–22.9 and OR = 2.9; 95% CI 1.0–8.1]. The majority (63.4%) had seen a doctor at least once, and atopic dermatitis was a risk factor for more than 1 visit (OR = 3.0; 95% CI 1.4–6.4). Duration of >10 years was a risk factor for persistence of symptoms, which was reported by 67.7%.

Conclusions: The clinical picture and consequences of hand eczema vary; however, the majority experience chronic symptoms.

Key words: clinical study; consequences; follow-up; hand eczema. © Blackwell Munksgaard, 2008.

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Epidemiological studies on hand eczema have repeatedly confirmed that hand eczema is a frequent dermatological condition with a 1-year prevalence around 10% and a lifetime prevalence around 20% (1, 2). Symptoms may vary from mild to severe, affecting quality of life and potentially resulting in sick leave and/or job change (3, 4). Disease duration is variable; however, a tendency to chronicity is characteristic, and symptoms may persist for many years or recur after disease-free intervals (5).

Follow-up studies on hand eczema are regularly reported; however, only a few are population based (5–7). The majority of studies describe

selected groups, such as patients from dermatological departments and/or with occupational dermatitis (8–11). The disease pattern and prognosis in these selected groups may vary from what is seen in the general population. Moreover, many follow-up studies are solely questionnaire based and do not include clinical assessment of severity or symptoms.

The aim of this follow-up study was to characterize clinical symptoms and to examine occupational and medical consequences as well as persistence of hand eczema in a population-based twin cohort. The cohort consisted of twins; however, a twin design was not utilized in the study.

Materials and Methods

Study population

In 1997–1998, a total of 1076 twin individuals born between 1953 and 1976 participated in a clinical examination (denoted 'first examination'), interview, and patch testing (12, 13). The twin individuals were ascertained from a population-based twin cohort of 5610 same-sex twins participating in a questionnaire survey in 1996 on hand eczema (2). Results from a follow-up questionnaire study in 2005 have recently been published (14). To be invited to the first examination, both twins in a twin pair should have returned the questionnaire and at least 1 of them should have reported symptoms of hand eczema or hand eczema. In addition, both twin individuals in a twin pair had to live within 60 km from Copenhagen.

In total, 659 twin individuals had self-reported hand eczema themselves or had a co-twin with self-reported hand eczema in 1997–1998. The remaining twin individuals reported 1 or more symptoms of hand eczema. Invitation to participate in a new clinical examination (denoted 'second examination'), structured interview, and patch testing between May 2005 and June 2006 was restricted to twin individuals with self-reported hand eczema themselves or with a co-twin with self-reported hand eczema in 1997–1998. Addresses were obtained from the Danish Civil Registration System on 605 twin individuals. The remaining twin individuals had a protected address, had emigrated, or died. Participants were enrolled after informed consent, in compliance with the principles of the Helsinki Declaration.

Clinical examination and interview

The hand eczema severity index (HECSI) was used to score symptoms of hand eczema at the second examination (15). The score is based upon sites on involvement (i.e. fingertips, fingers, palm of hands, back of hands, and wrists) and signs (i.e. erythema, infiltration/papules, vesicles, fissures, scaling, and oedema) graded as no skin changes, mild disease, moderate disease, and severe disease. The minimum score is 0, and the maximum score is 360.

In the structured interview, participants answered questions on self-reported hand eczema, atopic dermatitis, socio-economic status, age at onset, time of last hand eczema eruption, current exposure to wet work, current glove use, and current frequency of hand washing. Also, questions on ever having been on sick leave, having changed job because of hand eczema, or to have notified the Danish National Board of Industrial Injuries and number of medical consultations were asked.

Patch testing

All participants were patch tested with the ready-to-use TRUE Test[®] system (Mekos Laboratories AS, Hilleroed, Denmark) panels 1 and 2 in 1997–1998 and 2005–2006. Reading of the patches was carried out on day 3 according to the International Contact Dermatitis Research Group's guidelines (16).

Definitions

Hand eczema – a diagnosis of hand eczema was based on a positive answer to a question on self-reported hand eczema (Have you ever had hand eczema?), given either in the questionnaire survey in 1996 or at the second examination. *Age at onset* – participants were asked about age at onset of hand eczema at the first examination. Participants with onset in the follow-up period were asked at the second examination. Participants were subdivided into 2 groups with age at onset ≤ 15 years and > 15 years. This division was arbitrarily chosen as a way to distinguish between individuals with onset in childhood and onset in adulthood. *Socio-economic status* was based on Socio (Statistics Denmark's Socio-economic classification), 1st edition, 1997. This classification system is based upon educational skills. Participants were divided into 3 groups: (i) highest/medium level (minimum 15 years of educational training), (ii) basic level (11–14 years of educational training), and (iii) lowest level (up to 10 years of educational training and/or unemployed or pensioner). *Atopic dermatitis* was defined according to the UK Working Party's diagnostic criteria (17). *Persistent hand eczema* was defined as hand eczema within the year prior to the second examination. Participants having their last hand eczema eruption > 1 year prior to the first examination were excluded from the analysis on persistence of hand eczema. *Wet work* was defined as skin exposed to liquids > 2 hr/day or use of occlusive gloves > 2 hr/day or very frequent hand washing (> 20 times/day) (18). *Duration* at the first examination was calculated by subtracting year at onset from year at first examination, thus ignoring periods with complete healing in between. Participants were subdivided into 2 groups having had hand eczema ≤ 10 years and > 10 years, respectively.

Statistical analyses

Data management, descriptive statistical analyses, and the chi-squared test used in the drop-out analysis were performed in SPSS version 11.0. Logistic regression analyses were performed with STATA statistical software. All P values are 2 sided,

and a 5% significance level was used. As the twins in a twin pair are not statistically independent, the confidence intervals were corrected for intra-twin correlation using the option 'cluster' in STATA.

In a multiple logistic regression analysis, the potential influence of sex, zygosity, age at onset, socio-economic status, atopic dermatitis, and positive patch test in 1997–1998 on the risk of sick leave and medical consultations was explored. Likewise, the influence of sex, zygosity, age at onset, socio-economic status, atopic dermatitis, positive patch test in 1997–1998, current wet work, and duration of hand eczema at the first examination on the risk of persistent hand eczema was evaluated in a multiple logistic regression analysis.

Results

A total of 274 twin individuals volunteered to participate in the clinical examination and interview, resulting in a participation rate of 41.5% (274/659).

Hand eczema and descriptive data

174 individuals had self-reported hand eczema at the first examination in 1997–1998. 14 new cases were detected at the second examination; thus, the total number of individuals with self-reported hand eczema in 2005–2006 was 188. The following data relate to these 188 individuals. The group comprised 128 women and 60 men with a mean age of 42 years (SD 6.4). The group comprised 34 twin pairs and 120 single twin individuals (101 monozygotic twin individuals, 75 dizygotic twin individuals, and 12 with unknown zygosity). The mean follow-up period was 8.6 years (range 7.4–9.4 years). Regarding socio-economic status, 72/188 (38%) were in the highest/medium level, 87/188 (46%) were in the basic level, and 29 (15%) were in the lowest level. A total of 58/188 (30.9%) had wet work according to the definition.

Drop-out analysis

Drop-out analysis of twin individuals participating in the second examination (274) versus those where 1 or both twin individuals had self-reported hand eczema in 1997–1998 (659) showed no statistically significant differences regarding sex, zygosity, hand eczema status, co-twins hand eczema status, patch test status, or atopic dermatitis status (data not shown). Age was the only statistically significant factor influencing willingness to participate. The group was subdivided into 3 groups of equal size. Only 35% from the young-

est age group (born 1969–1976) participated, and in the middle age group (born 1961–1968), 41% participated, whereas 50% from the oldest age group (born 1953–1960) volunteered to the study ($P = 0.009$).

Clinical signs and severity

In total, 77/188 (41.0%) had 1 or more clinical signs of hand eczema at the second examination. Erythema and scaling were the most frequently encountered clinical signs, and fingers (excluding fingertips) and palms were most often affected (Figs 1 and 2). A total of 98/188 (56.9%) had signs of hand eczema at either 1 of the examinations. The mean HECSI score was 4.9 (SD 13.3, range 0–120). If only individuals with clinical signs were counted, the mean HECSI score was 12.0 (SD 18.7). The mean HECSI score in males and females was 4.0 (SD 7.2) and 5.4 (SD 15.4), respectively. The mean HECSI score in individuals with atopic dermatitis was 9.9 (SD 25.8), as opposed to a mean HECSI score of 3.6 (SD 6.6) in individuals without atopic dermatitis.

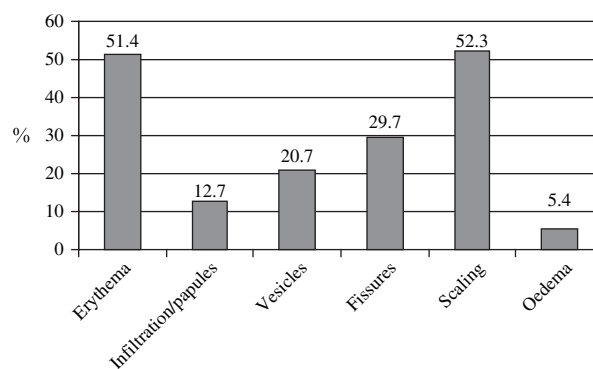


Fig. 1. Clinical signs of hand eczema observed at clinical examination ($n = 77$).

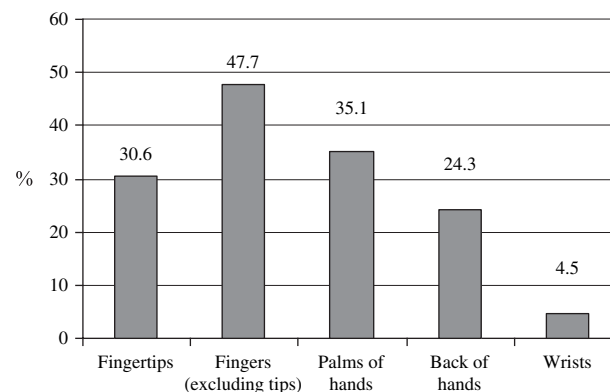


Fig. 2. Extension of clinical signs observed at the clinical examination ($n = 77$).

Atopic dermatitis

A subgroup of 39/188 (20.7%) had current or previous atopic dermatitis.

Patch test results

The frequency of a positive patch test in 1997–1998 and 2005–2006 was 53/188 (28.2%) and 59/185 (31.9%), respectively. 3 participants were not patch tested in 2005–2006 because of breast feeding and immunosuppressive therapy. A total of 40 (21.6%) had a positive patch test to nickel sulfate. Further details on the results of the patch testing are presented elsewhere (19).

Occupational consequences

A subgroup of 23/185 individuals (12.4%) had been on sick leave because of hand eczema. When summing all sick leave periods, 4 individuals (2.2%) reported sick leave for <1 week, 8 (4.3%) for 1–2 weeks, 5 (2.7%) for 3–5 weeks, and another 6 (3.2%) for >6 weeks. 3 did not answer the question. Being in the group with the lowest socio-economic status, compared with the group with the highest socio-economic status, and atopic dermatitis were the only statistically significant factors influencing the risk of ever having been on sick leave [odds ratio (OR) = 5.6; 95% CI 1.4–22.3 and OR = 2.9; 95% CI 1.0–8.1] (Table 1). A smaller group of 16 individuals (8.5%) had changed their job because of hand eczema. All, but 1, had changed job once. Notification to the Danish

National Board of Industrial Injuries Registry was reported by 19 individuals (10.1%).

Medical consultations

The majority had seen a doctor because of hand eczema (118/186, 63.4%). 2 individuals did not remember. An approximately equal number (25.3% and 22.6%) had seen a doctor only once or 2–5 times, respectively, whereas a smaller group (15.6%) had seen a doctor >5 times. Atopic dermatitis was associated with an increased risk of reporting more than 1 medical consultation compared with no or just 1 medical consultation (OR = 3.0; 95% CI 1.4–6.4) (Table 1).

Persistence of hand eczema

Of those with self-reported hand eczema within 1 year prior to the first examination ($n = 142$), a total of 96 (67.6%) still had hand eczema within the last year prior to the second examination. Individuals with duration of hand eczema >10 years at the first examination had an increased risk of persistent hand eczema (OR = 2.5; 95% CI 1.0–6.0). Also, in the analysis, being a dizygotic twin was associated with an increased risk of persistence when compared with monozygotic twins (OR = 2.6; 95% CI 1.2–5.4) (Table 2).

Discussion

The present follow-up study confirmed that hand eczema is a chronic disease, with 67.6% still

Table 1. Results of the multiple regression analysis on sick leave and more than 1 medical consultation because of hand eczema

		Sick leave ever ^a ($n = 185$)			More than 1 medical consultation ^b ($n = 186$)		
		n (total)	OR (95% CI)	P value	n (total)	OR (95% CI)	P value
Sex	Male (ref)	4 (59)	1	0.278	21 (60)	1	0.552
	Female	19 (126)	2.1 (0.6–7.7)		50 (126)	1.2 (0.6–2.6)	
Zygosity	Monozygotic (ref)	9 (74)	1	0.837 ^c	33 (75)	1	0.327 ^c
	Dizygotic	13 (99)	0.8 (0.3–2.1)		33 (99)	1.5 (0.8–2.9)	
	Unknown zygosity	1 (12)	1.5 (0.2–11.9)		5 (12)	2.1 (0.6–7.3)	
Age at onset	≤15 years (ref)	5 (49)	1	0.543	21 (49)	1	0.398
	>15 years	18 (136)	1.4 (0.5–4.4)		50 (137)	0.7 (0.4–1.5)	
Socio-economic status	Highest (ref)	4 (72)	1	0.050^c	23 (72)	1	0.163 ^c
	Basic	12 (86)	3.0 (0.8–10.6)		33 (86)	1.4 (0.7–2.8)	
	Lowest	7 (27)	5.6 (1.4–22.3)		15 (28)	2.5 (1.0–6.4)	
Atopic dermatitis	No (ref)	14 (147)	1	0.049	48 (147)	1	0.006
	Yes	9 (38)	2.9 (1.0–8.1)		23 (39)	3.0 (1.4–6.4)	
Positive patch test ^d	No (ref)	16 (133)	1	0.516	52 (133)	1	0.408
	Yes	7 (52)	0.7 (0.2–2.1)		19 (53)	0.7 (0.3–1.5)	

95% CI, 95% confidence interval; OR, odds ratio; ref, reference.

^aSick leave ever because of hand eczema.

^bMore than 1 medical consultation ever because of hand eczema.

^cTest if equal odds in all 3 groups.

^dIn 1997–1998.

Statistically significant results are highlighted in bold.

Table 2. Results of the multiple regression analysis on persistent hand eczema

		Persistent hand eczema ^a (n = 142)		
		n (total)	OR (95% CI)	P value
Sex	Male (ref)	32 (41)	1	0.098
	Female	64 (101)	0.4 (0.2–1.2)	
Zygosity	Monozygotic (ref)	34 (60)	1	0.041^b
	Dizygotic	57 (76)	2.6 (1.2–5.4)	
	Unknown zygosity	6 (6)	3.4 (0.3–42.4)	
Age at onset	≤15 years (ref)	23 (34)	1	0.316
	>15 years	73 (108)	1.7 (0.6–4.7)	
Socio-economic status	Highest (ref)	35 (52)	1	0.226 ^b
	Basic	44 (69)	1.1 (0.5–2.6)	
	Lowest	17 (21)	2.7 (0.8–8.8)	
Atopic dermatitis	No (ref)	72 (106)	1	0.981
	Yes	24 (36)	1.0 (0.4–2.5)	
Positive patch test ^c	No (ref)	72 (102)	1	0.284
	Yes	24 (40)	0.6 (0.2–1.5)	
Wet work	No (ref)	65 (94)	1	0.830
	Yes	31 (48)	1.1 (0.5–2.6)	
Duration	≤10 years (ref)	39 (65)	1	0.044
	>10 years	57 (77)	2.0 (1.0–6.0)	

95% CI, 95% confidence interval; OR, odds ratio; ref, reference.

^aHand eczema within the last year prior to the second examination. Analysis restricted to individuals with hand eczema within 1 year prior to the first examination.

^bTest if equal odds in all 3 groups.

^cIn 1997–1998.

Statistically significant results are highlighted in bold.

reporting persistence of hand eczema within the previous year after 8 years of follow-up.

Erythema and scaling were the most frequently recorded signs, and palms and fingers were the most frequently affected areas. This is in line with a previous report (20). Severity scoring, judged by signs and sites of involvement, was generally mild. Recently, a number of different hand eczema severity scores based on clinical evaluation of signs and localisation or based on photographs have been developed, but none has yet been employed in clinical epidemiological studies or gained general acceptance (15, 21, 22).

Atopic dermatitis was defined according to the UK Working Party's diagnostic criteria, and 20.7% met the criteria. Meding and Swanbeck, in a population-based cohort study on hand eczema, found a similar estimate – 22% had atopic hand eczema (23). Also, the frequency of contact sensitization of 30.3% found in this study is comparable to a previous population-based study, reporting a positive patch test in 32% of individuals with hand eczema (24).

Possible consequences of hand eczema are sick leave and/or change of job. In the present study, 12% had been on sick leave at some time because of hand eczema. The proportion ever having been on sick leave varies among different studies, reflecting among other things a variable length of follow-up and difference in study populations. Also, variation in social insurance systems between coun-

tries and the state of the market influences the sick leave rate, which may thus also vary over time in the same country. Occupational hand eczema often causes sick leave (4). Meding et al., in a 12-year follow-up study on occupational hand eczema, found that 48% had been on sick leave for at least 1 week, whereas in a population-based 15-year follow-up study, only 6% had been on sick leave in the follow-up period (5, 9). In this study, 8.5% stated that they had changed their job because of hand eczema. The corresponding numbers in the two above-mentioned studies from Meding et al., were 44% and 3%. 1 in 10 reported that the hand eczema had been notified to the Danish National Board of Industrial Injuries Registry. To our knowledge, no data on the proportion of notified cases in a population-based cohort have previously been published. The proportion of notified cases will likely vary greatly between countries because of the differences in insurance systems and registries.

Although the majority of individuals with hand eczema had seen a physician, one-third did not seek medical advice and 25.3% had only 1 contact. This finding is in agreement with data previously reported (25). Thoughts on how these individuals manage their disease, the reasons for not seeing a doctor, and what characterize their hand eczema can only be speculative. Atopic dermatitis was associated with an increased risk of more than 1 medical consultation, also in agreement with previous findings (25).

In total, 67.6% reported persistent hand eczema, defined as hand eczema within the last year of the second examination. A 12-year follow-up study on farmers found that 40% still had symptoms within the last year; the 12-year follow-up study on occupational skin disease found that 70% reported symptoms within the last year; and the 15-year population-based study estimated that 44% experienced symptoms within the last year (5, 9, 11). The seemingly high frequency of persistent hand eczema in this study may partly be explained by the shorter follow-up period. Duration above 10 years at start of follow-up was a risk factor for persistent hand eczema. In a study on occupational chromate dermatitis, duration of symptoms for >12 months before diagnosis of chromate sensitivity was associated with persistence of dermatitis (10). The significantly increased OR for dizygotic twins concerning persistent hand eczema was unexpected. The limited sample size is a probable cause.

The diagnosis of hand eczema relied on a questionnaire-based self-report of hand eczema using a question very similar to 1 that has previously been validated and shown to have a high specificity, but less sensitivity (26). Misclassification, especially mild cases misclassified as not having hand eczema and thus not being invited to participate, is possible. The opposite scenario, i.e. cases without hand eczema misclassified as having hand eczema, is less likely; however, it may occur if individuals with other skin diseases on the hands (i.e. tinea, psoriasis, and pustulosis palmoplantaris) are classified as having hand eczema (26). In approximately half of the individuals, the diagnosis could be confirmed by objective symptoms at either 1 of the clinical examinations, and in the remaining individuals, verification of the diagnosis was attempted by asking thoroughly to history, symptoms, and treatment. However, the self-reporting of a disease may be influenced by an increased awareness of the disease, which can be anticipated in a twin pair with an affected member. In that case, sensitivity and specificity may change. A decrease in specificity is of greatest concern and cannot be excluded. A clinical diagnosis would have been preferable in all cases, but was impossible, as many of the cases in the sample only had historic symptoms.

Selection bias is a concern in this study because of the limited participation rate. Drop-out analysis showed no differences between participants and non-participants with regard to sex, zygosity, hand eczema status, co-twins hand eczema status, atopic dermatitis status, or patch test status. However, a selection bias with a tendency for more severe cases and cases with recent

symptoms to attend cannot be excluded. Thus, the proportion with persistent symptoms and occupational and medical effects may be increased in this sample, and the analysis on factors associated with persistence may be hampered by loss to follow-up of already recovered cases. Supporting this, Meding et al., in a drop-out analysis of individuals participating in a dermatological examination, found that more individuals had continuous symptoms among those attending in the study than among those not attending (1). Also, recall bias may influence the results as information on occupational and medical effects, age at onset, year of last eruption, and atopic dermatitis was based on questions answered by the participants. The effect of a potential recall bias is more unpredictable, and both underestimation and overestimation of the estimates are possible.

Specific statistical twin analyses were not performed in this study. Extrapolation of the results from a twin study to the general population requires that the twin population is representative of the background population. The study population was drawn from twin cohorts in the Danish Twin Registry that is based on the Danish Civil Registration System and covers 74.4% of all twins born 1953–1967 (inclusive) and 97.4% of those born 1968–1982 (inclusive) (27, 28). The prevalence of hand eczema and atopic dermatitis in twins has been shown to be comparable to prevalences in non-twin populations (2, 14). Whether twin individuals have an increased frequency of sick leave or medical consultations because of hand eczema or persistent hand eczema compared with a non-twin population is unknown. However, the results obtained in this study are comparable to previous reports.

In conclusion, this population-based study confirms the diversity in clinical characteristics and consequences of hand eczema. A total of 12.4% had ever been on sick leave, while 8.5% had changed their job. The majority had seen a doctor at least once (62.7%). Low socio-economic status and atopic dermatitis were risk factors for sick leave, and atopic dermatitis in addition a risk factor for more than 1 doctor visit. Persistent hand eczema was reported by 67.7%, and long duration (>10 years) was a risk factor for persistent hand eczema.

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