

ORIGINAL ARTICLE

Classification of hand eczema

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Abstract

Background Classification of hand eczema (HE) is mandatory in epidemiological and clinical studies, and also important in clinical work.

Objectives The aim was to test a recently proposed classification system of HE in clinical practice in a prospective multicentre study.

Methods Patients were recruited from nine different tertiary referral centres. All patients underwent examination by specialists in dermatology and were checked using relevant allergy testing. Patients were classified into one of the six diagnostic subgroups of HE: allergic contact dermatitis, irritant contact dermatitis, atopic HE, protein contact dermatitis/contact urticaria, hyperkeratotic endogenous eczema and vesicular endogenous eczema, respectively. An additional diagnosis was given if symptoms indicated that factors additional to the main diagnosis were of importance for the disease.

Results Four hundred and twenty-seven patients were included, 379 (89%) of the patients could be classified directly into one of the six diagnostic subgroups, with irritant and allergic contact dermatitis comprising 249 patients (58%). For 32 (7%) more than one of the six diagnostic subgroups had been formulated as a main diagnosis, and 16 (4%) could not be classified. 38% had one additional diagnosis and 26% had two or more additional diagnoses. Eczema on feet was found in 30% of the patients, statistically significantly more frequently associated with hyperkeratotic and vesicular endogenous eczema.

Conclusion We find that the classification system investigated in the present study was useful, being able to give an appropriate main diagnosis for 89% of HE patients, and for another 7% when using two main diagnoses. The fact that more than half of the patients had one or more additional diagnoses illustrates that HE is a multifactorial disease.

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Conflicts of Interest

None declared.

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None.

What is already known about this topic?

Several classification systems for hand eczema have been suggested, but none of these have been generally accepted.

What does this study add?

This study adds a clinical testing of a previously presented classification system, helping the clinicians to classify hand eczema.

Introduction

The term hand eczema (HE) refers to the manifestation of more than one disease. The specific location of eczema on the hands

[†]http://orgs.dermis.net/content/e05eecdrg/index_ger.html

reflects a common pathological pathway, leading to a clinical manifestation comprising erythema, vesiculation, infiltration, desquamation, hyperkeratosis and fissuration. However, the aetiology leading to this clinical picture may differ, and in the clinical picture only a few of the mentioned symptoms may be predominant, differing from case to case and ranging from acute to chronic states. The sub-diagnosis of HE should therefore optimally be based on aetiology (elicitation factors), as well as the present morphological picture, being aware, however, that this may change over time. A correct classification of HE is important with respect to the future care of the patient and to give the patient exact and correct information about skin protection and avoidance of specific irritants and allergens.¹ It is also important with respect to the prognosis, and for medico-legal purposes in case of work-related disease, and the diagnosis may also have implications for choice of medical treatment.² Classification of HE is mandatory in epidemiological research, and particularly in clinical trials and intervention studies evaluating new treatment strategies and preventive measures.

Classification of HE is further complicated by the fact that aetiology is not related to morphology or any specific clinical symptoms, and by the fact that morphology may change significantly over time.^{3–5} Allergic contact dermatitis (ACD) or irritant contact dermatitis (ICD) can be diagnosed by patch testing and exposure assessment. In protein contact dermatitis/contact urticaria (PCD/CU) immediate testing may also be helpful. With respect to atopic hand eczema (AHE) the medical history of previous or current atopic dermatitis is helpful.⁶ However, there is still a group of HE cases that cannot be explained from exposures to irritants and allergens or from previous or contemporary skin disease involving the skin barrier function. For these cases the aetiology is unknown or 'endogenous', and the classification here has to lean on the clinical symptoms of vesicles or hyperkeratosis,^{7,8} until, hopefully, we will achieve a better understanding of triggering factors in the near future. Several classification systems have been proposed over the last few years, including various aetiological subtypes of HE, and describing different clinical patterns,^{3–5} however, none of the classification systems found simple relationships between aetiological diagnoses and clinical patterns.

In a recently published study by the present research group, a HE classification system was presented, which consisted of seven subdiagnoses or combined subdiagnoses: ACD, ICD, AHE, ACD + ICD, AHE + ICD, vesicular endogenous HE and hyperkeratotic endogenous HE., as well as combined diagnoses of ACD + ICD and AHE + ICD.³ The aim of the present study was to test this classification system, with minor changes, in a clinical setting, using a prospective multicentre study design. Minor changes were that the combined subdiagnoses mentioned above were registered as a main and an additional diagnosis instead of combined diagnosis, and PCD/CU was added as a subdiagnosis.

Material and methods

Consecutive patients with HE were recruited from nine different centres all over Europe during the period October 2011–September 2012. Patients with widespread eczema on the body were not included. The centres were tertiary referral centres, and all patients underwent examination by one or two specialists in dermatology from each centre. Data on gender, age, duration of HE and previous skin diseases (with emphasis on atopic eczema and psoriasis) was registered. Previous or current atopic skin disease was defined according to the UK-criteria.⁹ Information as to whether the eczema was work-related, if the feet had been affected and whether patients underwent relevant allergy testing, was recorded.¹⁰ Advanced level patch testing was performed in all clinics: when considered appropriate by a trained dermatologist, patients were tested with allergens additional to the minimal European baseline series, and skin prick testing was also performed when relevant. Relevance for positive patch tests was assessed as recommended in the ESCD guidelines.¹¹ Based on the medical history, the clinical symptoms and the test results, the dermatologist responsible for the patient was asked to classify each patient into one of the following six diagnostic subgroups of HE: ACD, ICD, AHE, PCD/CU, hyperkeratotic endogenous HE and vesicular endogenous HE. The diagnostic criteria for each subgroup are given in detail in Table 1.¹¹ Further to this main diagnosis, an additional diagnosis (diagnostic subgroup) could be added by the dermatologist, if symptoms indicated that factors additional to the main diagnosis were of importance for the disease. Eczema which did not fit into any of the above mentioned subgroups was diagnosed as 'unclassified'.

Results

A total of 427 HE patients were included in the study from the nine participating centres. Mean number of patients recruited from each centre was 47 (range 36–55). Demographic data from the study population is given in Table 2. Mean age varied between centres from 34 to 47 years. Mean duration of HE in the study population was 6.1 years. In 47% the HE was assessed as work-related. Share of work-related cases for each subgroup is given in Fig. 1.

Of the 427 patients, 379 (89%) could be classified directly into one of the six diagnostic subgroups (ICD $n = 144$, ACD $n = 105$, AHE $n = 51$, PCD/CU $n = 12$, hyperkeratotic endogenous HE $n = 41$, vesicular endogenous HE $n = 26$) (Fig. 1). For 32 patients (7.4%) it had not been possible to provide just one main diagnosis, and multiple contributing factors were considered of equal importance, therefore more than one main diagnosis had been made. For these cases with multiple diagnoses the combination in most cases was ACD and ICD, see Table 3.

A total of 16 patients (3.7%) could not be classified. Of these patients six (38%) had previous or current psoriasis elsewhere

Table 1 Subgroups of hand eczema and definitions

Subgroup of HE	Defined as
ICD	A documented exposure of the hands to an irritant, which is quantitatively likely to cause contact dermatitis. No relevant contact allergy (no current exposure to allergens to which the patient has reacted positive in patch test). An example of a well-defined irritant exposure likely to cause contact dermatitis is wet work: wet hands or wearing of gloves for 2 h, or more than 20 hand washes daily. Relevance of the irritant exposure may be defined as either suspected or certified
Allergic contact dermatitis	Positive patch test reaction to the topical exposure to an allergen or a cross-reacting allergen, and a relevant – either documented or suspected – current exposure to this allergen on the hands. Relevance may be defined as either suspected or certified
Atopic HE	HE in a patient with a medical history of atopic eczema, previous or current, according to the UK criteria. No documented irritant exposure likely to cause ICD
PCD/CU	HE in patients exposed to proteins (food, latex and other biological material) with a positive prick test, or proven specific IgE, to suspected items. A considerable part of patients with <i>PCD/CU</i> will have atopic symptoms as well
Vesicular endogenous HE	Recurrent HE with vesicular eruptions. No relevant contact allergy, and no documented irritant exposure likely to cause dermatitis, and no personal history of atopic dermatitis
Hyperkeratotic endogenous HE	Chronic eczema with hyperkeratosis in the palms of the hands, or pulpitis, and no vesicles or pustules. No documented irritant exposure to the involved skin areas, likely to cause ICD
Unclassified	Eczema which does not fit into any of the above mentioned subgroups

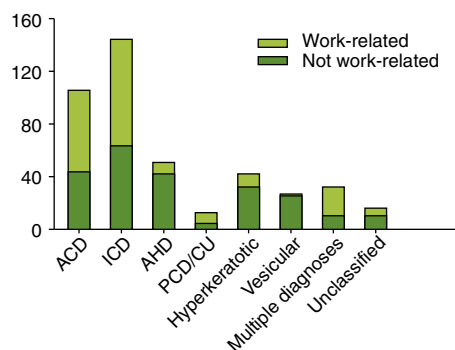
HE, hand eczema; PCD/CU, protein contact dermatitis/contact urticaria; ICD, irritant contact dermatitis.

on the body, while in 10 patients there was no indication why no classification could be made. The distribution of the different main diagnoses was found to differ significantly between the nine participating centres ($P < 0.001$).

With respect to diagnostic subgroups additional to the main diagnosis these can be seen in Table 4. One hundred and thirty-seven patients (36%) of the patients had no additional diagnosis, 145 (38%) had one additional diagnosis and 97 (26%) had two or more additional diagnoses.

Table 5 shows data on contact sensitization, as well as information about psoriasis and atopic dermatitis, in relation to main diagnostic subgroups. The number of patients with positive patch test reactions in other diagnostic subgroups than ACD varied between 31% and 37% (Table 5), showing that the positive patch test reactions in these cases were not considered to be of relevance to the current HE. Presence of psoriasis was highest in patients with hyperkeratotic endogenous HE, and with unclassified eczema, but no significant difference between the diagnostic groups was found with respect to this ($P > 0.05$). Atopic dermatitis was found to be more frequent in patients with PCD/CU than in the other diagnostic subgroups (AHE

being excluded), ($P < 0.001$). Eczema on feet in relation to the main diagnostic subgroups is given in Table 6. Eczema on the feet was most frequently found to be associated with hyperkeratotic and vesicular endogenous HE, as well as with the unclassified group, and was found to be less frequent in patients with ICD ($P < 0.002$).

**Figure 1** Share of work-related cases for each diagnostic subgroup.**Table 2** Demographic data for the study population

Total study population	427
Males/females	182 (43%)/245 (57%)
Mean age	40.6 years (SD: 14.9)
Mean duration time	6.1 years (SD: 8.8)
Work-related (assumed)	200 (47%)
Previous or current atopic eczema	107 (25%)
Psoriasis (elsewhere on the body)	22 (5%)
Eczema on feet (ever)/eczema on feet within last year	125 (29%)/99 (23%)

Table 3 The combined diagnosis for the 32 patients that were provided with more than one main diagnosis

Diagnoses	32
ACD + ICD*	19 (60%)
ACD + AHE	3 (9%)
ICD + AHE	3 (9%)
Other combinations	7 (21%)

ACD, allergic contact dermatitis; AHE, atopic hand eczema; ICD, irritant contact dermatitis.

*The diagnoses ACD and ICD were both used when the irritant exposure was estimated to be of independent significance, additional to the ACD.

Table 4 Combination of main diagnosis and one additional diagnosis. Number of cases with only one diagnosis is given in the shaded boxes. Those with more than one additional diagnosis are listed in the column at the right ('more combinations'). *N* = 379 (patients with multiple main diagnoses and unclassified patients not included)

Main diagnosis	Total	Additional diagnosis					
		ICD	ACD	AHE	PCD/CU	Hyperkeratotic	More combinations
ICD	144	71	21	21	0	5	23
ACD	105	34	31	7	0	3	26
AHE	51	16	1	10	0	0	22
PCD/CU	12	1	2	1	0	0	8
Hyperkeratotic	41	10	5	0	0	16	10
Vesicular	26	3	2	2	0	2	9

ICD, irritant contact dermatitis; ACD, allergic contact dermatitis; AHE, atopic hand eczema (HE); PCD/CU, protein contact dermatitis/contact urticarial; Hyperkeratotic, hyperkeratotic endogenous HE; Vesicular, vesicular endogenous HE.

Table 5 Number of patients with positive patch tests, and data for psoriasis and previous atopic dermatitis given for the main diagnostic subgroups

Main diagnosis	Patients with positive patch test (%)	Medical history of atopic disease (%)	Psoriasis (%)	Total
ICD	45 (31)	23 (16)	6 (4)	144
ACD	103 (98)*	17 (16)	3 (3)	105
AHE	17 (33)	41 (80)	3 (6)	51
PCD/CU	5 (42)	7 (58)	0	12
Vesicular	9 (35)	3 (12)	1 (4)	26
Hyperkeratotic	15 (37)	4 (10)	5 (12)	41
Multiple diagnoses	24 (75)	10 (31)	1 (3)	32
Unclassified	7 (44)	2 (17)	2 (13)	16
Total	223 (52)	107 (25)	22 (5)	427

ICD, irritant contact dermatitis; ACD, allergic contact dermatitis; AHE, atopic hand eczema (HE); PCD/CU, protein contact dermatitis/contact urticarial; Vesicular, vesicular endogenous HE; Hyperkeratotic, hyperkeratotic endogenous HE; Multiple diagnoses, patients with more than one main diagnosis; Unclassified, patients which could not be classified.

*Two patients were assessed as ACD due to typical medical history of contact dermatitis following exposure for allergen, but did not show up for planned patch testing.

Table 6 Eczema on the feet (foot eczema) in relation to main diagnostic subgroups, evaluated in 419 of the 427 patients

	Eczema on feet (%)	Total
ICD	26 (18)	141
ACD	33 (31)	101
AHE	17 (35)	50
PDC/CU	3 (25)	12
Vesicular	13 (50)	26
Hyperkeratotic	20 (49)	41
Unclassified	8 (50)	16
Multiple diagnoses	5 (16)	32
Total	125 (30)	419

ICD, irritant contact dermatitis; ACD, allergic contact dermatitis; AHE, atopic hand eczema (HE); PCD/CU, protein contact dermatitis/contact urticarial; Vesicular, vesicular endogenous HE; Hyperkeratotic, hyperkeratotic endogenous HE; Multiple diagnoses, patients with more than one main diagnosis; Unclassified, patients which could not be classified.

Discussion

Distribution of gender, age and previous atopic dermatitis in the study population was similar to previous studies on

HE.^{1,3–5} Work-relation was reported in almost half of all cases, which is higher than in most HE populations, mean duration time was 6 years, and the distribution irritant/allergic dermatitis was 1.3:1, which shows a higher proportion of ACD than reported in some other studies.^{12,13} The patients were recruited from tertiary referral centres, which explains the relatively high number of work-related cases and patients diagnosed as ACD.

A total of 89% of the patients could be diagnosed in the classification system using just one main diagnosis. Only 4% of the patients were assessed as unclassifiable. Of the patients assessed as unclassifiable, one-third had previous or current psoriasis elsewhere on the body, indicating that these patients might not be HE patients, but rather psoriasis patients. These data confirm the capacity of the presented classification system to classify the different subgroups of HE. Since the classification is – among other factors – based on patch testing and interpretation of relevance of patch test results, the conclusion is limited to diagnoses given by dermatologists, and cannot be extrapolated to other groups of physicians.

The distribution of the diagnosis used was found to differ significantly between the participating centres. However, an equal distribution was not to be expected, due to differences in age and disease patterns among the referral populations of the different centres.

For a minor part of the patients (7%) it was necessary to use two main diagnoses to classify the HE, and in these cases by far the most common combination was ACD and ICD. This combination is well-known from previous clinical studies,^{1,3} and reflects the difficulty of judging whether an irritant eczema has resulted in contact sensitization and a following ACD, or whether an allergic eczema has been complicated by an additional ICD. The combinations ACD and AHE, as well as ICD and AHE, were both present in 9% of the patients. This is consistent with some newer findings indicating that ACD may be a frequent complication in atopic individuals,¹⁴ and certainly underlines the importance of patch testing, also in cases where atopic dermatitis is considered to be the obvious aetiology of the eczema.

It is interesting that in the majority of the patients one or more additional diagnoses were given. This reflects the fact that, in most cases, HE is a multifactorial disease, and this becomes even more prominent in severe and long-lasting cases, as in the present study.

Positive patch test reactions were found in one-third of patients with diagnosis different from ACD as the main diagnosis, indicating that in these cases the finding of a positive patch test was not considered to be of current relevance. Although mandatory before establishing a correct diagnosis, a positive patch test needs further interpretation, and may not be relevant to the present dermatitis. Moreover, a negative patch test result, if the correct allergen was not tested, cannot completely eliminate ACD. Our conclusion on the presented classification systems is therefore based on diagnoses made by dermatologists, with experience of interpretation of patch test results.

With respect to psoriasis it is well-known that the distinction between hyperkeratotic endogenous HE and psoriasis can sometimes be difficult,⁷ and sometimes only the development of the eczema or psoriasis over time will solve this dilemma. However, no statistical difference between the groups was found with respect to previous or current symptoms of psoriasis elsewhere on the body, and in the present study the hyperkeratotic endogenous HE did not predominantly represent cases of psoriasis.

The increased frequency of atopic dermatitis in patients with PCD/CU as the main diagnosis is not surprising, since atopic patients are more prone to develop type 1 allergies and PCD/CU.¹⁵

With respect to concomitant eczema on the feet there is little data on this subject in the literature. It is well-known that HE is related to eczema on the feet, and in the present population we found additional foot eczema in a total of 30% of the patients. However, in patients with endogenous eczema as the main diag-

nosis (vesicular and hyperkeratotic endogenous HE), the frequency was as high as 50%, while in patients with ICD the frequency of foot eczema was significantly lower. Previous studies have shown a relationship between foot-localized dermatosis, such as tinea pedis, and vesicular eczema on the hands,¹⁶ and it cannot be ruled out that this could be a possible explanation for at least some cases. In a previous study foot eczema was accepted as an indication of idiopathic (endogenous) eczema in patients without ACD,⁵ and our data confirms this finding.

Previous publications on classification of HE includes suggestions for clinical as well as aetiological classifications,^{3–5} and emphasize the importance of identifying exposures, as well as previous medical history of the patients.⁸ It is generally agreed that no simple relationships between clinical patterns and aetiological diagnoses can be found. The classification system tested in this study includes both morphological patterns as well as aetiological causes for HE.

The strength of the present paper is the high number of patients included, as well as the multicentre approach, all centres confirming the usefulness of the classification. A weakness is that although the diagnoses were based on detailed criteria,¹¹ there is currently no gold standard for HE diagnosis, which may be influenced by clinical judgement from the dermatologist. However, to test the classification further, a methodological set-up, where the same patients were tested in different centres and the given diagnoses were compared, would be ideal.

In conclusion, we found that the classification system used in the present study was capable of giving one appropriate main diagnosis to at least 89% of HE patients and additional 7% could be characterized by use of two main diagnoses. The diagnoses used in the present classification system are based on the clinical history and patch testing, to reveal or exclude ACD. The fact that the majority of the patients had at least one additional diagnosis confirms that HE is a multifactorial disease.

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