

Etiology and prognosis of hand eczema in a dermatology clinic in China: a follow-up study

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Background: Prognosis of hand eczema (HE) has not been reported in China.

Objectives: To investigate the etiology and outcome of HE in 655 consecutive patients patch tested with European standard series in Peking University Hospital in a 2-year period.

Methods: All patients were re-examined at 1 year after patch testing, and prognosis of dermatitis was evaluated by the rate of clearance of skin symptoms for at least 3 months without relapse before the evaluation.

Results: Of 599 patients examined, 82 (13.7%) were HE. Allergic, irritant, and unclassified HE accounted for 23.2%, 17.1%, and 51.3% of HE, respectively. The overall clearance rate of HE was much lower than that of eczema elsewhere (18.3% versus 29.6%, $P < 0.05$, chi-squared test). 35.7% of patients with allergic HE and 26.3% with irritant HE cleared their lesions, of those with unclassified HE only 11.9% ($P < 0.05$, chi-squared test). The lowest healing rate (5.7%) was found in unclassified HE patients with disease duration over 6 months.

Conclusions: The outcome of HE was worse than eczema elsewhere. Allergic HE had a better prognosis than unclassified HE. Longer disease duration was the main risk factor for poor prognosis of unclassified HE.

Key words: allergic; contact dermatitis; eczema; hand; outcome; patch test; prognosis. © Blackwell Munksgaard, 2007.

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Hand eczema (HE) is a very common skin disease. A recent review on epidemiology showed that its 1-year prevalence ranged from 7.3% to 11.8% in general population; the incidence of work-related HE in 3-years metal apprentices was 15.3%, and the 1-year prevalence of work-related HE in veterinarians in USA was 28% (1). A population-based twin study in Denmark including 6666 persons aged 20–44 years reported in 2000 showed a lifetime prevalence of self-reported HE of 21% in women and 12% in men (2). Non-specific symptoms of HE can be caused by environmental, occupational, and endogenous factors including unknown genetic factors (1, 3). In developed countries, irritant contact dermatitis, allergic contact dermatitis, and atopic dermatitis (AD) accounted for almost 80% of HE (1). AD is a significant risk factor for HE. The prevalence of HE in patients with a history of AD has been reported

to be 2 to 10-fold higher than that found in non-atopic patients (4).

The prognosis of HE was very poor. A 1-year follow-up of 564 occupational HE in Demark showed that 25% of all patients had persistently severe or aggravated disease, 41% improved, and 34% had unchanged minimal or mild to moderate disease (5). 15-year follow-up of HE in general population in Sweden showed that 66% of the responders still reported periods of HE, and 44% reported continues eczema during the previous year (6). The prognosis of HE in China has not been reported. China is a big developing country with a low prevalence of AD in mainland, where the point prevalence of AD was 0.7% in 6 to 20-year-old school children and 2.78% in 1 to 7 years children (7, 8). The visible flexural dermatitis in 9 to 11 years school children was 1.1% in Beijing and 0.8% in Guangzhou, which were

significantly lower than that in Hong Kong (9). The purpose of this study was to analyse the etiology and outcome of HE in Chinese eczema patients patch tested in a University Hospital Dermatology Clinic.

Patients and Methods

Diagnostic criteria

HE was diagnosed based on the presence of eczema-specific findings such as vesicles, papules, scaling, fissures, redness, swelling, exudation, and lichenification on the hands for at least 3 weeks (10, 11). Eczema was diagnosed and classified according to a standard textbook (12). Because other types of eczema with hand involvement would be finally diagnosed as other specific types of eczema and managed differently, they were excluded from this study. HE was further classified into following subtypes according to the literatures (1, 13): irritant HE, allergic HE, HE with a history of AD, nummular HE, pompholyx, and unclassified HE. Relevant irritant or allergic exposure was necessary to diagnosis of allergic and irritant HE. The UK diagnostic criteria were applied for the diagnosis of AD (14). Nummular HE and pompholyx were diagnosed accordingly based on the textbook (12). HE that could not fit any above subtypes was diagnosed as unclassified HE (1, 13).

Study population

655 consecutive eczema patients referred by other dermatologists to contact dermatitis clinic for patch testing between September 2003 and May 2005 were included. There were 187 men and 468 women with average age 40.5 ± 16.0 years. All patients were Chinese Han ethnics.

Patch testing

Patch testing was performed with a modified European standard series of allergens and improved quality Chamber (Chemotechnique Diagnostics, Malmö, Sweden; Table 1). Allergens were applied to the upper back, and the results were recorded at 2 and 3 days according to International Contact Dermatitis Group grading (15). If patients could supply the suspected substances, patch testing with the patients' own products was also performed. A relevant positive patch test result was considered, if the patient had exposed to the substance containing the positive allergen, and dermatitis was improved with the avoidance of that allergen. In patients with suspected allergic HE, but patch test was negative, a usage test was performed with the method similar to Maibach

Table 1. The standard patch test series of allergens and the test results [number (%)]

Allergen	Hand eczema (n = 82)	Eczema elsewhere (n = 517)
Benzocaine	0	12 (2.3)
Black rubber mix	1 (1.2)	9 (1.7)
2-bromo-2-nitropropane-1,3-diol (bronopol)	0	2 (0.4)
Carba mix	9 (11)	51 (9.9)
Colophonium	1 (1.2)	25 (4.8)
Epoxy resin	3 (3.6)	10 (2.0)
Ethylenediamine dihydrochloride	4 (4.9)	42 (8.1)
Formaldehyde	1 (1.2)	34 (6.6)
Fragrance mix	3 (3.6)	68 (13.1)*
Imidazolidinyl urea	0	8 (1.5)
Mercapto mix	1 (1.2)	5 (1.0)
N-(cyclohexylthio) phthalimide	2 (2.4)	26 (5.0)
Nickel sulfate	23 (28)	158 (30.6)
4-phenylenediamine base	4 (4.9)	42 (8.1)
Parabens	6 (7.3)	23 (4.4)
Potassium dichromate	7 (8.5)	42 (8.1)
Sesquiterpene lactone mix	2 (2.4)	7 (1.4)
Thiuram mix	2 (2.4)	5 (1.0)
Thimerosal (merthiolate)	12 (14.6)	68 (13.2)
Tixocortol-21-pivalate	1 (1.2)	7 (1.4)

* $P < 0.05$, chi-squared test.

reported, in which patient applied the suspected substance in the same way to a small area (1 cm $\times$ 1 cm) on the hand as when the dermatitis developed, twice daily for a week. If eczematous skin reaction occurred in the test period, the test was considered positive and stopped (16).

Investigation of suspected environmental agents by questionnaire

After patch testing, the suspected causal agent was investigated using a questionnaire (17). In the questionnaire, patient's personal data, present illness (patients' description, date of onset, effects of weekends, effects of vacation, and previous therapy), contactants existed in work, clothes, toiletries, household, and treatment, atopic diathesis as well as medications taking presently or within last 3 months were included.

Evaluation of prognosis

After patch testing, patients were treated based on acute, sub-acute, and chronic lesions accordingly with the well-accepted methods (1, 12). We also educated patients to (i) do their best to avoid any known allergic materials and any predisposing or exacerbating factors, (ii) washing hands as instructed in skin care (1), (iii) avoid any known intolerant food, and (iv) protect hands during work. 1 year after patch testing, all patients were asked a revisit, and prognosis of dermatitis was

evaluated by following categories: (i) healing: completely free of skin symptoms without recurrence for at least 3 months before the evaluation, (ii) relapse: skin lesions have been resolved but reappeared before evaluation, and (iii) improvement or no-improvement which was assessed globally by the same dermatologist.

Statistic analysis

The data were processed by chi-squared test and Rank Sum test with statistic software SPSS 11.0.

Results

Of 599 (91%) patients finished the study, 82 (13.7%) were HE. Allergic, irritant, and unclassified HE accounted for 17.1% (14/82), 23.2% (19/82), and 51.2% (42/82) of HE, respectively. 3 (3.7%) cases of nummular HE and 3 (3.7%) cases of pompholyx were also found. Only 1 patient (1.2%) was HE with a history of AD.

There was no significant difference between age (41.2 ± 15.8 versus 39.7 ± 16.4 , mean $\pm$ SD) and atopic diathesis (12.3% versus 9.9%, $P > 0.05$, chi-squared test) in patients with HE and eczema elsewhere. Male/female ratio was higher in HE group (0.78 versus 0.39, $P < 0.05$, chi-squared test). The healing rate of HE (18.3%) was much lower than that of eczema elsewhere (29.6%, $P < 0.05$, chi-squared test). No significant difference could be found between 2 groups in the relapse rate (24.4% versus 31.1%), improvement rate (31.6% versus 24.4%), and no-improvement rate (20.7% versus 13.9%).

63.4% (52/82) of HE patients reacted positively to at least 1 allergen in standard series, which was much lower than that of eczema elsewhere (75.2%, 389/517, $P < 0.05$, chi-squared test). A low frequency of positive patch test to fragrance mix in HE was noted (3.6% versus 13.1%, $P < 0.05$, chi-squared test; Table 1). The most common allergic material identified was metal (6/14, 42.9%) followed by rubber gloves (2/14, 14.3%), printing ink (2/14, 14.3%), and cosmetics (2/14, 14.3%), while the most common irritant was detergent (12/19, 63.2%), followed by water (2/19, 10.5%) and mechanical oil (2/19, 10.5%).

There was no significant difference between the average age (mean $\pm$ SD) of allergic (40.7 ± 14.5), irritant (45.7 ± 16.6), and unclassified HE (40.0 ± 15.4), so did the male/female ratio (0.56, 0.73, 0.91, respectively, $P > 0.05$, chi-squared test). 2/14 of allergic HE, 2/19 of irritant HE, and 4/42 of unclassified HE were atopic ($P > 0.05$, chi-squared test). 92.9% of allergic HE patch tested positive, which was much higher than those

of irritant HE and unclassified HE (47.4% and 61.9%, respectively, $P < 0.05$, chi-squared test). 53.8% of these positive results were relevant in allergic HE, while none of those was found relevant in irritant HE and unclassified HE. All allergic HE improved at 1 year after patch testing. 5/14 (35.7%) of allergic HE, 5/19 (26.3%) of irritant HE healed, of those with unclassified HE only 5/42 (11.9%, $P < 0.05$, chi-squared test). More allergic HE (42.9%) relapsed, compared with that in irritant HE (26.3%) and unclassified HE (16.7%, $P < 0.05$, chi-squared test). The lowest healing rate (5.7%, 2/35) was found in unclassified HE patients with disease duration over 6 months.

Discussion

Although the proportion of allergic and irritant HE in our study was consistent with the literature, of which 19% of HE was allergic, and 35% was irritant (1), AD in our hands was much less, with only 1 case (1.2%) was found. Atopic diathesis in HE was no different to that of eczema elsewhere suggesting that atopy was not a risk factor for HE currently in China. The reason of this difference is unclear. It may be partly because of the fact that most cases of AD with skin lesions on other locations had been excluded from our study, however, the low prevalence of AD in mainland China may also contribute greatly to it (7–9).

Another interesting find in this study was the high percentage of unclassified HE (51.2%). The mechanism of unclassified eczema is still unknown. Some postulated that it might be a kind of undiagnosed AD because they found that 12/34 of these patients had an elevated IgE level (18). Although we did not perform intracutaneous test or prick test in this study, high-positive rate of intracutaneous test to aeroallergens had been observed previously (19). Nevertheless, these patients could not be diagnosed as AD so far because they could not meet any known diagnostic criteria of AD. The high-positive rate (61.9%) of patch testing to standard series of allergens in this study also suggested that some unclassified HE might be undiagnosed allergic contact dermatitis, however, none of these positive results was found relevant. Because we only tested 20 allergens from European standard series, some allergic HE might be missed. Patch testing patients with more allergens may help to identify this.

Contact allergy had been reported to be a risk factor for HE (1, 3). In this study, the positivity rate to standard allergens in HE was much lower than that of eczema elsewhere (63.4% versus 75.2%). This result was consistent with our previous studies of 2002 and 2004 (20, 21) suggesting that contact allergy is less common in our HE and

other factors, such as skin irritation or unknown endogenous factors may play more of a role in HE. Again, because we only tested limited number of allergens, some contact allergy might be missed. Patch testing patients with more allergens may help to elucidate it.

Nickel allergy had been found related to HE, however, after exposure regulation and public education, although the prevalence of HE was raising significantly, the association between nickel allergy and HE was lost (22). In our study, the positivity rate to nickel in HE was not different to that in eczema elsewhere (Table 1) suggesting that nickel allergy is not a risk factor for HE. Interestingly, the positivity rate to nickel in current study was consistent with that of 29.1% in women with HE in the study of Bryld et al. (3), but increased significantly from our 2002 report of 9.5% and 2004 of 10.7% (20, 21) implying that with the economic development in China, more nickel allergy may be found. The relationship between nickel allergy and HE must be studied further.

A low frequency of fragrance allergy was found in HE in this study; however, it was not found in our previous studies (20, 21). More women and cosmetic dermatitis patients in eczema elsewhere group (data not shown) may cause this difference.

Consistent with occupational HE, of which most cases were persistent (1, 3), the 1-year healing rate of HE in this study (18.3%) was also low. It was in accordance with the prognosis of contact dermatitis reported, of which complete clearance of dermatitis were ranged from 18% to 72% of patients, while 60% between 18% and 40% (23). The mechanism of this poor prognosis is unclear. Older age and female sex had been reported related to poor prognosis (5, 24). In this study, because the number of each subgroup of HE was too small, the influence of age and sex was not analysed.

The healing rate of unclassified HE was much lower in the patients with longer disease duration before testing suggesting that long duration of HE is an important factor for the poor prognosis. Our study further demonstrated that all HE lasting more than 1 month should be patch tested (1).

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