

10. Atopic hand eczema and treatment strategies

KLAUS EJNER ANDERSEN

Chronic hand eczema is frequent among atopic dermatitis (AD) patients. Due to the multifactorial causes of hand eczema, careful clinical and allergological examination is important for classification of the individual case, and hence for advice, treatment and preventive measures to be recommended. The importance of patient information and preventive strategies cannot be overemphasized.

INTRODUCTION

There is no generally accepted classification system for hand eczema. The history of previous skin disease often includes either AD or psoriasis. Clinical examination shows a typical dermatitis pattern. The majority of cases can be grouped on morphological grounds: 80–90% are contact hand eczema type, 5–10% are dyshydrotic (pompholyx) and about 2% are keratotic hand eczema, which tend to come late in life and may follow the other two types of eczema.

CLASSIFICATION OF HAND ECZEMA

Hand eczema is a multifactorial disease and can be considered as endogenous and/or exogenous in origin. Endogenous hand eczema can present as AD, pompholyx or keratotic eczema. Exogenous eczema can be allergic contact dermatitis, irritant contact dermatitis, contact urticaria or microbial eczema. The classification of hand eczema in a particular patient may similarly vary over time depending upon when the patient presents at the clinic. For example, when the skin is dry it may resemble atopic eczema, whereas if the patient is working in wet conditions the presentation may resemble irritant contact eczema (1). Again, the relative importance of endogenous and exogenous factors may vary from time to time within the same patient.

In the case of atopic hand eczema, the absolute requirements for establishing the diagnosis are not defined. However, there should be a history of previous AD. There may also be evidence of mucosal atopy, a positive skin prick test to standard inhalant allergens and a family history of atopic diseases.

Endogenous hand eczema can present as:

- atopic dermatitis
- pompholyx
- keratotic eczema

Exogenous eczema can be:

- allergic contact dermatitis
- irritant contact dermatitis
- contact urticaria
- microbial eczema

TREATMENT OF HAND ECZEMA

The initial step in treating hand eczema effectively is to obtain a good history of the condition in order to rule out possible differential diagnoses. Patch tests should be conducted in patients having hand eczema for more than 3 months, and the type of hand eczema should be established as far as possible. It is essential to give patients information on the disease and to educate them as to its causes and management on a regular basis.

Diagnostic patch tests should always include the standard series of allergens and, if appropriate, selected additional allergens which might be present in the patient's working environment and topical agents, skin care products and gloves. An 'Allergen Bank' has been established in Denmark as a service for dermatologists in practice, who can order special contact allergens for testing individual patients (2). With patch tests it is important to take both early and late readings (days 3 and 5–7 post challenge). Careful interpretation of the results, particularly their relevance, is needed. Detailed discussion with the patient is needed to fully ascertain their exposure to allergens.

Patients who had relevant positive patch tests, enabling them to reduce exposure to the allergen, showed significant improvement in both perceived severity of their hand eczema and in the Dermatology Life Quality Index 2 months later (3). Patients with negative patch tests did not show significant improvement. Psychological factors are important in the condition, in that patients who are highly stressed seem to cope less well than patients who are less prone to stress (4).

MEDICAL TREATMENT OF HAND ECZEMA

A paramount feature of treating hand eczema is to provide information and education to the patient concerning the condition and its treatment. Amongst the medical agents used are:

- i) *Topical corticosteroids*: The topical corticosteroid treatment regimen of choice cannot be established from the literature (5). Neither the potency of corticosteroid preparation recommended nor the application schedule is established. Treatment tends to be based on teaching and past experience. Short-term glucocorticoid treatment compromises both skin permeability barrier homeostasis and stratum corneum integrity. For example, clobetasol applied twice daily topically for 3 days results in delayed barrier recovery and increased trans-epidermal water loss. In mice, there is decreased production and secretion of lamellar bodies, inhibition of lipid synthesis and decreased density of corneodesmosomes (6). Application of epidermal lipids reverses these findings. With these observations in mind the clinician should be aware of overusing topical steroids, particularly the more potent ones. However, a recent study could confirm that long-term control of hand eczema is possible in up to 80% of patients, if intermittent, prophylactic use of topical steroids is employed on a regular basis (7).
- ii) *Antimicrobial treatment*: The role of *Staphylococcus aureus* is well established and has been covered comprehensively by others. Secretion of staphylococcal superantigens causes potent T-cell activation and may induce steroid insensitivity (8). Whilst the relevance of these observations to hand eczema is not fully established, they do explain the effect of antibiotic treatment (with corticosteroids, e.g. Fucicort®) in severe hand eczema (9).
- iii) *Topical immunomodulators*: Preliminary studies indicate that topical immunomodulators may have a role in the treatment of hand eczema. In an open non-controlled study involving 13 patients with hand eczema receiving occlusive pimecrolimus cream 1% for 3 weeks, there was a good effect and minimal systemic absorption of the active component (10). In an observer-blinded crossover trial involving 16 patients with dyshidrotic hand eczema given 2 weeks of treatment with either tacrolimus 0.1% or mometasone fumarate, Schnopp et al. noted 50% improvement in palmar but not plantar eczema (11). These results suggest that rotational treatment might be appropriate.
- iv) *Potassium permanganate soaks*: Potassium permanganate soaks are often used in acute exacerbation of hand eczema as patients find them effective in relieving itching and oozing, in spite of the fact that evidence of effect is limited.
- v) *Oral immunosuppressive agents*: Efficacy of oral immunosuppressive drugs in hand eczema is not proven. Cyclosporine is no better than topical corticosteroids in clinical effect and in improving aspects of quality of life, and there are no

controlled trials with methotrexate and azathioprine (5). In our clinic we use azathioprine in severe cases of hand eczema, in multi-allergic cases and in AD. Our view (echoed by others present at the meeting) is that azathioprine is helpful as second-line therapy for those patients who can tolerate it.

- vi) *Oral retinoids*: Etretinate 30 mg daily is known to be effective in keratotic hand eczema (12) by reducing symptoms by 50% on average.
- vii) *Radiation therapy*: One placebo-controlled trial has shown that 3 Gy of Grenz rays applied on six occasions at intervals of 1 week improved chronic hand eczema 5 and 10 weeks after the start of treatment compared with the untreated control. However, due to concern about long-term effects, radiation therapy cannot be recommended (5, 13). PUVA and UVB are effective, but not proven to be more effective than conventional topical corticosteroids (5).

Some patients with irritant hand eczema apparently fail to respond, despite theoretically appropriate treatment and ceasing exposure to proven allergens and irritants. This could be due to poor compliance. There is, however, some evidence that autocrine regulation of TNF- α expression through the effect of keratinocytes may explain why some irritant hand eczema continues in spite of protection from the irritant stimulus (14).

SKIN CARE AND USE OF GLOVES

There is no established procedure for evaluating skin care products. Whilst multiple repeated short-time occlusive irritation tests have been developed and internationally validated, it is unclear whether these simulate real workplace conditions. Trials of skin care creams have serious limitations, including omission of a control group, small study populations or short study periods.

One 4-week field study among 111 cleaners and kitchen assistants showed in a crossover design that a moisturizer (Locobase®) effectively improved skin barrier function during everyday irritant exposure compared to no treatment (15).

PREVENTIVE THERAPY: EVIDENCE-BASED SKIN CARE PROGRAMMES

Evidence-based skin care programmes can help prevent work-related skin problems. In a study involving auxiliary nurses undergoing practical training, nurses receiving a skin care programme changed their behaviour and had less skin problems than did the control group (16), and in a large machine industry with 7000 employees in the production line the frequency of

occupationally related eczema decreased over a 10-year period simultaneously with increased use of emollients and moisturizers (17). The components of a typical skin care programme are shown in Table I (16, 18).

Patients with hand eczema should avoid using alkaline soaps as these are known to disturb stratum corneum integrity by activation of serine proteases and degradation of corneodesmosomes. They also delay skin barrier recovery by decreasing beta-gluco-cerebrosidase activity (19). Liquid soaps also present a problem as patients tend to use too much, so conventional soap bars are better.

CONCLUSION

Effective management of hand eczema requires a good doctor–patient relationship. Time must be spent on discussing the causes, prevention and treatment with every patient. Educating the patient as to the causes of hand eczema and its avoidance is particularly important. Treatment of occupational hand eczema should be evidence-based, if the evidence exists, and involve effective drug treatment regimens and skin care programmes, the three components of which are skin protection before work, cleansing and the use of emollients after work.

DISCUSSION

Thestrup-Pedersen; Some years ago a company in Denmark introduced a health care programme for workers, because they had hand eczema problems. Free emollients and advice were given by company doctors. The incidence of hand eczema fell from around 7% to 2–3% over a 5-year period.

Diepgen; I think we all have similar personal experience, but controlled clinical trials are lacking. A literature search showed the lack of controlled trials.

Andersen; I agree, but a suitable trial design is difficult, as is adequate patient compliance over the long term.

Diepgen; The response criterion is also difficult to decide upon. Data show a poor correlation between severity

and response scores graded by clinicians and patients. Quality of life assessment is equally poor, when compared to clinicians' outcomes.

Agner; We need a suitable scoring system for hand eczema. We have in a pilot study found quite a good correlation between a self-graded score for hand eczema and that of the clinician.

McFadden; What is your attitude to the use of liquid soaps and how do you deal with the period after a response, but before the skin barrier is re-established? When do you use second-line therapies?

Andersen; Liquid soaps should not be used – too much is commonly taken; use a soap bar instead. Tell patients to be careful during the vulnerable period, which can last 6 months. It is difficult if the patient has young children, where there is a lot of washing required. We have an interest in Compositae dermatitis, and in suitable patients we use azathioprine during the plant growing season. For people with recurrent severe hand eczema we use azathioprine as third-line therapy.

Agner; In experimental studies you see a hardening of the skin in 6 weeks after exposure to detergents, but how this relates to the clinical situation is not known.

Thestrup-Pedersen; You talked about the chronicity of hand eczema. Is it possible to stop this progression?

Andersen; I believe so. If you get the patient early you may be able to control this, but I have no evidence.

Agner and Thestrup-Pedersen; We have the same opinion.

Traulsen; Do you have any views on the skin barrier after corticosteroid use?

Andersen; We know steroids can cause skin atrophy and patients say that they are not good for them. This may be a matter of dose, I advise intermittent use of steroids.

Agner; We do not know for certain if intermittent use is any better, but no doubt this could be studied.

Table I. Evidence-based skin care programme

Wash hands in lukewarm water	Do not wear rings on fingers
Use protective gloves during 'wet' work	Do not use disinfectants, unless specifically required
Use gloves for as short a period as possible	Use a lipid-rich moisturizer, repeatedly
Gloves must be clean and intact	Apply the moisturizer all over the hands
Use cotton gloves underneath	Be careful about exposure to allergens at home

Taken from Held et al. (16, 18).

REFERENCES

1. Bruze M. Principles of occupational hand eczema. In: Menne T, Maibach HI, eds. Hand eczema. Boca Raton: CRC Press, 2000: 181–194.
2. Andersen KE, Rastogi SC, Carlsen L. The Allergen Bank: a source of extra contact allergens for the dermatologist in practice. *Acta Derm Venereol* 1996; 76: 136–140.
3. Thomson KF, Wilkinson SM, Sommer S, Pollock B. Eczema: quality of life by body site and the effect of patch testing. *Br J Dermatol* 2002; 146: 627–630.

4. Niemeier V, Nippesen M, Kupfer J, Schill W-B, Gieler U. Psychological factors associated with hand dermatoses: which subgroup needs additional psychological care? *Br J Dermatol* 2002; 146: 1031–1037.
5. Coenraads P-J, van Coevorden AM, Diepgen T. Hand eczema. In: Williams H, Bigby M, Diepgen T, Herxheimer A, Naldi L, Rzany B, eds. *Evidence-based dermatology*. London: BMJ Publishing, 2003: 132–143.
6. Kao JS, Fluhr JW, Man MQ, Fowler AJ, Hachem JP, Crumrine D, et al. Short-term glucocorticoid treatment compromises both permeability barrier homeostasis and stratum corneum integrity: inhibition of epidermal lipid synthesis accounts for functional abnormalities. *J Invest Dermatol* 2003; 120: 456–464.
7. Veien NK, Larsen PØ, Thestrup-Pedersen K, Schou G. Long-term, intermittent treatment of chronic hand eczema with mometasone furoate. *Br J Dermatol* 1999; 140: 882–886.
8. Hauk PJ, Hamid QA, Chrousos GP, Leung DYM. Induction of corticosteroid insensitivity in human PBMCs by microbial superantigens. *J Allergy Clin Immunol* 2000; 105: 782–787.
9. Hill VA, Wong E, Corbett MF, Menday AP. Comparative efficacy of betamethasone/clioquinol (Betnovate-C) cream and betamethasone/fusidic acid (Fucibet) cream in the treatment of infected hand eczema. *J Dermatol Treat* 1998; 9: 15–19.
10. Thaçi D, Steinmeyer K, Ebelin M, Scott G, Kaufmann R. Occlusive treatment of chronic hand dermatitis with pimecrolimus cream 1% results in low systemic exposure, is well tolerated, safe, and effective; an open study. *Dermatology* 2003; 207: 37–42.
11. Schnopp C, Remling R, Mohrenschlager M, Weigl L, Ring J, Abeck D. Topical tacrolimus (FK506) and mometasone furoate in treatment of dyshidrotic palmar eczema: a randomized, observer-blinded trial. *J Am Acad Dermatol* 2002; 46: 73–77.
12. Thestrup-Pedersen K, Andersen KE, Menne T, Veien NK. Treatment of hyperkeratotic dermatitis of the palms (eczema keratoticum) with oral acitretin. A single-blind placebo-controlled study. *Acta Derm Venereol* 2001; 81: 353–355.
13. Lindelof B, Wrangsjö K, Liden S. A double-blind study of Grenz ray therapy in chronic eczema of the hands. *Br J Dermatol* 1987; 117: 77–80.
14. Lisby S, Hauser C. Transcriptional regulation of tumor necrosis factor- α in keratinocytes mediated by interleukin-1 β and tumor necrosis factor- α . *Exp Dermatol* 2002; 11: 592–598.
15. Halkier-Sørensen L, Thestrup-Pedersen K. The efficacy of a moisturizer (Locobase) among cleaners and kitchen assistants during everyday exposure to water and detergents. *Contact Dermatitis* 1993; 29: 1–6.
16. Held E, Wolff C, Gyntelberg F, Agner T. Prevention of work-related skin problems in student auxiliary nurses: an intervention study. *Contact Dermatitis* 2001; 44: 297–303.
17. Halkier-Sørensen L. Occupational skin diseases. *Contact Dermatitis* 1996; Suppl 1: 106.
18. Held E, Mygind K, Wolff C, Gyntelberg F, Agner T. Prevention of work related skin problems: an intervention study in wet work employees. *Occup Environ Med* 2002; 59: 556–561.
19. Hachem J-P, Crumrine D, Fluhr J, Brown BE, Feingold KR, Elias PM. pH directly regulates epidermal permeability barrier homeostasis, and stratum corneum integrity/cohesion. *J Invest Dermatol* 2003; 121: 345–353.