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# Hand eczema:

## A common and challenging disease

*Treatments range from emollients to immunosuppressive agents*

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**H**and eczema affects about 10% of the general adult population. The main causes are exposure to irritants (e.g., water, soap) or allergens (e.g., nickel) and endogenous factors such as atopic dermatitis. Since clinical manifestations are usually multifactorial, identifying and eliminating all causative factors is challenging.

Most cases are mild and can be well-managed by the mainstay therapies, including avoidance of irritants and allergens, plus the use of skin protection, moisturization and topical corticosteroids. But in many patients, hand eczema progresses into a chronic condition and eventually becomes refractory to this mainstay regimen. Persistent and disfiguring changes in hand appearance can develop in severe cases and cause substantial occupational, functional and psychosocial disability. Since hand eczema has a tendency to become chronic, early and effective intervention is critical.

### Emollients and skin protection

Application of emollients (moisturizers) is recommended for all patients with hand eczema. Emollients prevent drying of the skin and protect the hands from irritants and allergens. For best results, emollients should be applied immediately after showering or hand-washing to lock in the moisture, followed by frequent application throughout the day. Ointments are preferred over creams (which are preferred over lotions) because creams may contain preservatives and emulsifiers that can irritate the skin. However, creams are often more cosmetically elegant than ointments and more readily available to patients. Recently, physiologic emol-

lients containing key skin lipids, such as ceramides, have become widely available and appear to be quite helpful.

The use of gloves is a standard skin protective measure recommended to reduce the incidence of contact dermatitis. However, paradoxically, prolonged occlusion from wearing gloves may itself aggravate hand eczema; cotton liners are recommended to reduce the incidence of this problem. Barrier creams are another form of skin protection and are often recommended for the prevention of occupational hand dermatitis, although there is insufficient evidence that such creams have a long-term protective effect. Patient education on proper skin care, skin protection, and avoidance of irritants and network is especially important to prevent the progression and relapse of hand eczema.

### Topical corticosteroids

Topical corticosteroids are first-line treatment for hand eczema. They help reduce the inflammation that disrupts the skin barrier and leaves the skin vulnerable to irritants. The active ingredient and vehicle of the corticosteroid formulation determine its potency, and the selection of a particular corticosteroid depends on the severity, morphology and area of skin involved. In more severe cases and in areas with thicker stratum corneum—such as the palms and soles, for example—more potent preparations are required.

The recommended regimen is daily use for up to one month followed by a maintenance therapy of two to three times per week. Thorough moisturization of the hands prior to application and subsequent occlusion with plastic wraps or thin cotton gloves can enhance the efficacy of corticosteroids. Skin

atrophy is a potential adverse side-effect with prolonged use, although this is rarely observed on the palms or soles. When possible, tapering to discontinuation (or transition to a topical calcineurin inhibitor) is recommended with topical steroids. If hand eczema persists or worsens despite adequate treatment, patch testing should be considered to rule out allergy to corticosteroid or other contact allergens.

A randomized trial of topical mometasone furoate for chronic hand eczema showed that of the 120 patients treated daily with topical mometasone furoate, almost half had clearing at three weeks and another quarter at six weeks.<sup>1</sup> Those whose hand eczema had cleared were then enrolled in a trial of maintenance therapy for up to 36 weeks. Participants were randomized to one of three groups: three times a week, two times a week and emollients alone. Recurrence rates were significantly lower in the groups receiving mometasone furoate treatment (17% and 32%, respectively) than the group using emollients only (74%). This confirms the benefit of maintenance therapy in preventing recurrences.

For moderate and more severe hand eczemas, more potent corticosteroids such as clobetasol propionate or halobetasol propionate can be prescribed, although high-quality studies are lacking for these stronger agents.

### Topical calcineurin inhibitors

The biological effects of tacrolimus and pimecrolimus are mediated by the suppression of T-cells and mast cells, which are critical for the inflammatory process. They are widely used to treat atopic dermatitis, but evidence of their efficacy in hand eczema is limited.

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Twice daily application of pimecrolimus 1% produced a slightly greater clearance than vehicle cream alone in two large randomized clinical trials of three and six weeks' duration. However, the difference was not statistically significant.<sup>2,3</sup> Another small randomized trial compared the efficacy of tacrolimus 0.1% twice daily with twice daily mometasone furoate 0.1% in chronic dyshidrotic palmar eczema. Both treatments resulted in similar improvement rates of over 50%.<sup>4</sup> Consequently, an option is to rotate the use of these agents with topical corticosteroids in the management of chronic hand eczema, or to use these agents to transition off corticosteroids.

**Phototherapy**

Phototherapy is widely used as second-line treatment when topical therapy has failed. During therapy, a patient's hands are exposed to ultraviolet light (UVA, UVB). UVB has been used to treat hand eczema for more than 80 years. Narrow-band UVB (311 nm) is now more commonly used and it can deliver more energy into the lower epidermis than the conventional broadband UVB, which is advantageous for treating palmar regions with thicker stratum corneum. UVA is typically coupled with psoralen, a photosensitizing compound found in plants, in a therapy known as psoralen plus UVA (PUVA).

A 12-week randomized, controlled trial compared the efficacy of PUVA with UVB alone in treating chronic hand eczema in 35 patients.<sup>5</sup> In both groups, one hand was treated and the other hand served as an untreated control. The results showed that the treated hands in both groups had statistically significant improvements over the untreated hands, and while UVB was effective, PUVA was even more effective. However, for various reasons including access and photosensitivity, PUVA is not as widely available and much less commonly used. More recent clinical trials have further demonstrated the efficacy of phototherapy, although the overall sample sizes were small.

Side-effects include rashes, pain and edema. There is an increased risk of skin cancer associated with PUVA, particularly squamous cell carcinoma. Tablets of methoxsalen, a derivative of psoralen, may also cause nausea. Therefore, many clinics prefer topical formulations of psoralen (a cream, a gel, or bath preparation), which two randomized trials have shown to have no significant difference in efficacy compared with the oral forms.<sup>6,7</sup>

**Oral immunosuppressives**

Oral immunosuppressive therapy is less commonly used to treat chronic hand eczema that is unresponsive to all other treatments. These drugs include cyclo-

**Application of emollients (moisturizers) is recommended for all patients with hand eczema.**



sporine, azathioprine, mycophenolate mofetil and methotrexate, although there is limited evidence of their efficacy in hand eczema from randomized trials. Oral corticosteroids are used in some cases for a short course to achieve rapid control. The recommended dosage is 1 mg of prednisone per kilogram of body weight per day, tapered over two to three weeks.

A randomized, double-blind study involving 41 patients compared the effectiveness of oral cyclosporine at 3 mg per kilogram per day to topical 0.05% betamethasone dipropionate cream.<sup>8</sup> Total disease activity, which scores the severity of hand eczema, noticeably decreased in both treatment groups (57% and 58%, respectively) but there was no statistically significant difference between them. The relapse rates for both groups were also similar (50% after two weeks of followup. This study suggested oral cyclosporine as a useful alternative in patients unresponsive to conventional therapies.

Importantly, however, with the use of cyclosporine (as with any immunosuppressive agents), close monitoring is required as the treatment can be associated with potentially serious adverse events, including hypertension, decreased kidney function and sequelae of immune suppression. The burden of hand eczema must be weighed against these risks.

**Oral alitretinoin**

Alitretinoin is a newly approved treatment in Canada and several European countries indicated for severe chronic hand eczema refractory to potent topical corticosteroids. As with other retinoids, the biological effects of alitretinoin are mediated by retinoic acid receptors, although the precise mechanisms behind the therapeutic benefits in chronic hand eczema are not yet known. Alitretinoin is preferred over oral immunosuppressive agents because of its better safety profile. The most common side-effect is headache, and less commonly dry skin, hyperlipidemia, and decreased free thyroxine and thyroid-stimulating hormone. Since retinoids are teratogenic, all women of reproductive age are required to be on contraceptives for a month

before treatment, during treatment and for at least one month after the end of treatment (similar to isotretinoin).

An international, multicentre phase III trial conducted in Europe and Canada evaluated the therapeutic benefits of alitretinoin in severe chronic hand eczema.<sup>9</sup> A total of 1,032 patients with severe disease refractory to standard therapy were randomized to 30 mg or 10 mg of alitretinoin once daily or placebo. The percentages of patients rating their hand eczema as "clear" or "almost clear" at the end of therapy (which is the definition of a response) were 40% and 24%, respectively, for 30 mg and 10 mg of alitretinoin, both of which were higher than the placebo rate of 15%. Further, 62% and 50% of the patients achieved a partial response on 30 mg and 10 mg of alitretinoin respectively, compared with 36% in the placebo group.

A followup study was conducted in 2010 retreatting 117 of the responders who had had a relapse from the previous trial: 80% retreated with alitretinoin responded compared with 8% for placebo, confirming the therapeutic bene-

fits of alitretinoin.<sup>10</sup> Of note, patients with hyperkeratotic eczema had the highest response rates to alitretinoin, but those with dyshidrotic eczema also appeared to benefit. Another U.S. phase III trial (596 patients) reported in early 2012 confirmed consistent therapeutic benefits of alitretinoin for severe chronic hand eczema.<sup>11</sup>

**Conclusion**

Hand eczema is an important skin disease that has a high incidence and a high disease burden. In some patients, hand eczema can become chronic and difficult to manage, which can be frustrating for both physicians and patients. Appropriate lifestyle changes and preventive measures, such as minimizing exposure to irritants, are key to breaking the recurrence cycle. Consequently, patient education alongside proper treatment is critical to ensuring therapeutic success. The recently approved oral alitretinoin is a new addition to the armamentarium of treatments that may help physicians better manage patients with severe chronic hand eczema. More large-scale and well-designed trials are needed to evaluate and compare the various available treatments. **MP**

**For further reading**

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