Hand eczema: treatment

P. Elsner¹* | T. Agner²

¹Department of Dermatology, University Hospital Jena, Jena, Germany
²Department of Dermatology, Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark

*Correspondence: P. Elsner. E-mail: elsner@derma-jena.de

Abstract

Hand eczema is a highly prevalent, multietiological disease with a wide spectrum of severity and chronicity. The treatment of hand eczema, especially in severe and chronic cases, is a challenge to the dermatologist requiring not only diagnostic and therapeutic, but also excellent patient communication skills. This review discusses the spectrum of therapeutic options for hand eczema, the evidence for their efficacy and safety, and proposes a stepwise approach of intensity of treatment depending on disease severity and chronicity. In the near future, hand eczema patients may benefit from new therapeutic principles such as biologics for the treatment of atopic eczema and topical Janus Kinase inhibitors.

Conflict of interest

P.E. was study investigator and/or consultant for Leo, Novartis, Pfizer and Perre Fabre and received speaker’s honoraria from Galderma, Leo, Novartis, Pierre Fabre and Sanofi. TA was study investigator and/or consultant for Leo Pharma, Sanofi, Pfizer and Lilly and received speaker’s honoraria from Sanofi.

Funding source

None declared.

Introduction

Hand eczema is a socially significant disease because of its high prevalence, morbidity and the associated lost working time due to sick leave.¹ Clinically, it is a heterogeneous condition under the aspects of aetiology, clinical manifestations and acuteness. The aetiology is manifold from endogenous disease (atopy) to exogenous factors (irritant and/or allergic contact dermatitis) that frequently overlap.²,³ Clinical manifestations may be diverse, from vesicular and erosive to hyperkeratotic and desquamative. Its time course may be acute, recurring or chronic and long-lasting. With this wide diversity of aetiological and clinical factors, standard treatment approaches are frequently difficult, and individualized treatment plans developed in close communication between patient and dermatologist are required instead. Considering that the hands are human ‘tools’ in many professions, behavioural aspects have to be considered in the management of the disease more than it may be the case with other skin diseases.

Thus, the management of hand eczema has to extend beyond mere pharmacological or physical treatment, and requires an encompassing approach including removal or avoidance of causative factors, behavioural changes and social support.

This review takes into account these aspects with a view on the guidelines for the management of hand eczema that have been developed by various groups over the years (Table 1) and the recent Cochrane review on treatments for hand eczema.⁴ The latter clearly stated the current deficits of our knowledge on the treatment of hand eczema⁴: the quality of studies was frequently poor, and the duration of treatment was short, generally only up to 4 months, which is inconsistent with the need for a long-term management in chronic hand eczema defined as ‘an eczematous process that lasts for more than three months or relapses twice or more often per year’.⁵ Most of the guidelines (Table 1) take a similar approach to the hierarchy of treatments with some differences especially regarding the availability or reimbursement conditions of specific drugs.

In addition to established treatments, this review considers new substances that have not yet been licensed for the treatment of hand eczema but that may provide a benefit to patients.

Table 1  Guidelines for the management of hand eczema

| Organization                        | Date   | Ref. no. |
|-------------------------------------|--------|----------|
| German Society of Dermatology      | 2009   | 15       |
| Canadian Guidelines Expert Group   | 2010   | 85       |
| Danish Contact Dermatitis Group    | 2011   | 86       |
| European Society of Contact Dermatitis | 2015 | 6        |

JEADV 2020, 34 (Suppl. 1), 13–21

© 2019 The Authors. Journal of the European Academy of Dermatology and Venereology published by John Wiley & Sons Ltd on behalf of European Academy of Dermatology and Venereology.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.
Principles of hand eczema treatment

As stated in the ESCD guidelines,6 the diagnosis of hand dermatitis requires a thorough workup including a detailed patient history, signs and symptoms, evaluation of atopy, e.g. by the atopy score,7 patch testing and the exclusion of differential diagnoses. Frequent differential diagnoses such as mycoses or palmoplantar psoriasis have to be excluded. In older patients, the important differential diagnosis of acrokeratosis paraneoplastica (Bazex syndrome) should not be overlooked.8 Specific treatment should only be started if a consolidated diagnosis has been reached.

If no external causative factors are known, often morphological classification of hand eczema is used based mostly on its clinical appearance. However, different expressions of immunological patterns9 and genetical phenotypes might be considered in the future. To date, for different endotypes of atopic dermatitis,10 targeted endotype-specific treatment has been suggested.11,12 That is why in the future therapy might be pattern-oriented including the characteristics of the specific immunology and genetics of hand dermatitis.

Endogenous cofactors such as hyperhidrosis need to be considered in the treatment planning.13 If exogenous factors are present, e.g. contact to allergens or irritants, these have to be avoided first which may require preventive measures or absence from work. Merely exogenous types of hand dermatitis may heal without any specific treatment under these conditions, but it has to be remembered that the recovery of the epidermal barrier takes many weeks. This is why, in cases of occupational hand dermatitis, rehabilitation programs provide that patients are routinely off work for a minimum of 6 weeks.14 Acute hand eczema should be treated promptly, effectively and thoroughly in order to prevent the condition from becoming chronic.15,16 Chronic hand eczema may require a stagewise treatment approach (Fig. 1) combining topical, physical (UV light) and systemic options depending on the severity of the disease. Since the spectrum of hand eczema severity varies widely, individual therapy should be based on an objective and subjective assessment of severity; clinical scores17,18 and specific quality of life questionnaires19 may be helpful. If hand dermatitis is associated with atopic dermatitis which is frequently the case, other therapies specific for atopic dermatitis including local and systemic agents should be considered, depending on severity of atopic dermatitis.

Topical therapy

Although a number of systemic compounds for the treatment of hand eczema have become available over the years, topical therapy should always be part of a treatment regimen, even with systemic therapies (Fig. 1). Topical therapies should consider the appropriate choice of vehicles, suitable pharmaceutical vehicle depending on the condition of the skin and the acuteness of the eczema.20 Generally, the principles ‘moist on moist’ and ‘greasy on dry’ propose to use hydrating vehicles on acute lesions of hand eczema and lipid-rich vehicles on chronic ones. This approach, however, is limited by the fact that patients may need to use their hands in everyday life not wishing to leave greasy marks on objects of their environment. Thus, the aspect of possible adherence to topical treatments has to be considered. In addition, the function of the pharmaceutical vehicle is to ensure a stable formulation and to facilitate the bioavailability of the active agent.20 Some pharmacologically active substances may only be available in cosmetically ‘unpleasant’ vehicles for this reason.

Basic topical therapy

A topical therapy with ‘base preparations’, i.e. emollients or moisturizers, is a key component in the treatment of any kinds of eczema. The treatment of xerosis cutis is a mainstay in the early forms of atopic and irritant hand dermatitis.21 Basic topical therapy helps to reduce inflammation and itching, has corticosteroid-sparing effects and promotes epidermal barrier recovery. In numerous experimental studies, basic topical therapy has been shown to promote the healing of eczema, without any specific pharmacological treatment.22,23 For acute and frequently oozing hand eczema, basic topical therapy should have drying, astringent and antibacterial effects; hand baths and soaks, moisturizing or moist dressings and hydrophilic creams or gels are indicated. In subacute hand eczema, basic topical therapy should have anti-inflammatory, antipruritic and moisturizing effects; this may be achieved by moisturizing water-in-oil and oil-in-water emulsions. Finally, in chronic hyperkeratotic hand eczema, keratolytic, anti-proliferative and moisturizing effects are needed with keratolytic ointments (containing salicylic acid up to 20% if necessary, urea 10–20%) and lipid-rich ointments, including water-in-oil and oil-in-water emulsions, to be used.24 The efficacy and safety of topical base preparations in the management
of hand eczema should be studied using the same stringent criteria as for specific pharmacological therapies; unfortunately, only few preparations are evaluated in studies and registered as medical devices.²⁻⁻² Basic topical therapy may be underestimated by patients and physicians as ‘bland’ and without active ingredients.¹ The result of such an attitude may be a reduced adherence, application that is inadequate or in insufficient quantity, ultimately compromising treatment.²⁶ This underscores the need of patient education interventions in the management of hand eczema.²⁷ Base therapy should be continued even after the visible signs of hand eczema have subsided, because the epidermal barrier damage will take longer to be restored.

Topical glucocorticosteroids
For over 50 years, topical corticosteroids have been the mainstay of the topical treatment of hand eczema. Considering their long history of use, it seems odd that the recent Cochrane review identified only nine studies that evaluated topical corticosteroids as the main intervention.¹⁻⁻¹ Globetasol propionate 0.05% foam and mometasone furoate cream probably improve control of eczema.²⁷ Base therapy should be continued even after the visible signs of hand eczema have subsided, because the epidermal barrier damage will take longer to be restored.

Topical immune modulators
Tacrolimus and pimecrolimus are calcineurin antagonists that inhibit the transcription of inflammatory cytokines released from T cells and mast cells via binding to FK-binding protein and blocking calcineurin phosphatase activity.³⁻⁻³ As the Cochrane review states, tacrolimus 0.1% over 2 weeks probably improves investigator-rated symptom control in hand eczema patients measured after 3 weeks compared with vehicle.⁴ Our group performed a prospective, open, multicentre study on 29 patients with occupational hand eczema treating with tacrolimus ointment 0.1% for 4 weeks followed by a 2-month optional treatment period.³⁴ Efficacy was evaluated by the use of a standardized hand eczema score and by clinical severity rating. The hand eczema score declined significantly after 2 weeks of treatment compared with baseline and further declined until the end of the study. Finally, 12 (44%) patients were clear of hand eczema. Worsening of the dermatitis occurred in two patients (7%). Overall tolerability was good.

In comparison with tacrolimus, pimecrolimus seems to have a lower anti-inflammatory potency.³⁵ While Belzito et al.³⁶ reported some benefit by topical treatment with pimecrolimus in a multicenter, randomized, vehicle-controlled, 3-week study in 294 patients with chronic hand eczema, the efficacy of pimecrolimus in a later study on 652 hand eczema patients randomized to pimecrolimus 1% or vehicle cream twice daily for 6 weeks, followed by a 6-week open-label pimecrolimus treatment, was not significant.³⁷ Also in a sequential maintenance therapy study of atopic hand eczema, pimecrolimus 1% cream twice daily was not superior to vehicle.³⁸

Despite the limited evidence, the current ESCD guidelines suggest to consider topical calcineurin inhibitors for hand eczema patients with a need of long-term treatment.⁶ The most valuable advantage of the compounds is their safety over long-term usage, without the induction of atrophy or interference with barrier repair. It should be remembered, however, that tacrolimus and pimecrolimus are only licensed for the treatment of atopic dermatitis. If they are to be used in other types of hand dermatitis not involving atopy, their use will be off-label requiring specific informed consent.³⁹ According to the ‘black box’ warning for topical calcineurin inhibitors, they should not be applied parallel to topical UV therapy,⁴⁰ and UV protection, such as sunscreens and appropriate clothing, is advisable in patients undergoing treatment, although there is no robust evidence to support the association of skin cancer and lymphoma with the use of topical calcineurin inhibitors.¹

Topical calcipotriol
Calcipotriol is a vitamin D 3 derivative approved for the topical treatment of psoriasis. Anecdotal evidence exists on its use in hyperkeratotic hand eczema that may mimic palmar psoriasis;¹¹⁻⁻¹²; its use for this condition would be also off-label. A recent prospective study in 13 patients with in-patient control compared the efficacy of calcipotriol ointment with desoximetasone ointment, a superpotent glucocorticosteroid, twice daily for 8 weeks.⁴³ The hand eczema severity index (HECSI) scores revealed up to a 75% reduction in both treatments (P < 0.001) without significant differences between the groups (P > 0.05).⁴³ Thus, calcipotriol may have a potential as a steroid-sparing agent in the management of hand eczema. Clearly, further studies are necessary including more patients and differentiating better between hand eczema and psoriasis.

Coal tar, pine tar and sulfonated shale oil preparations
While topical tar preparations have been used widely in the treatment of recalcitrant hand dermatitis in the past, no clinical
studies exist proving their efficacy and safety in this condition according to modern evidence-based criteria. Due to the possible risk that tar is a possible carcinogen and the proven urinary excretion of 1-hydroxypyrene in patients with atopic dermatitis treated with topical coal tar, the use of coal tar for the treatment of hand dermatitis has been widely discontinued in recent years. However, sulfonated shale oil preparations seem to have a better safety profile and have been proven to be efficacious in mild-to-moderate atopic eczema in children; thus, they might be tried for topical therapy of hand dermatitis, although no studies on their efficacy and safety in hand dermatitis are available.

UV-Phototherapy

As a special feature of dermatology, various procedures of light therapy may be used for the treatment of dermatoses. Depending on the indication, the entire light spectrum from the ultraviolet to the visible to the infrared range may be used. Light therapy has the particular advantage for the patients that, in contrast to systemic therapeutics, no systemic side effects are to be expected in many cases despite high efficacy.

According to the Cochrane review, local combination ultraviolet light therapy (PUVA) may lead to improvement in investigator-rated symptom control when compared to local narrowband UVB after 12 weeks of treatment. Due to the side effects of systemic psoralen application, especially nausea and the need for full body UV protection and specific sunglasses, some clinics have abandoned systemic PUVA and use bath or cream PUVA treatment in hand eczema instead. Both regimens seem to be comparably effective with the advantage of PUVA-cream therapy to reduce organizational efforts and expenses.

The current ESCD guidelines suggest phototherapy of the hands in adult patients with chronic hand eczema refractory to first-line treatment with topical corticosteroids. It should be considered, however, that long-term use of phototherapy may not only be time-consuming and stressful for patients, but also increase the risk of skin malignancy. The home use of UV units by patients as suggested by some authors should therefore be critically reviewed considering possible liability risks.

Systemic therapy

In systemic treatment of hand dermatitis, considering that it is not a life-threatening, but the quality of life significantly impairing disease, the benefit-risk ratio of available therapies should be critically considered, especially regarding comorbidities, pregnancy, immunosuppression and cancer risk.

Systemic corticosteroids

Systemic corticosteroids may be required in severe acute hand eczema and exacerbations of chronic disease, with usually short-term 0.5–1 mg/kg/day prednisolone equivalents with tapering depending on the improvement of signs and symptoms. Their long-term or frequent use is not indicated in hand eczema due to their well-known side effects such as osteoporosis, osteonecrosis, glaucoma, cataracts, hypothalamic-pituitary-adrenal axis suppression, hyperglycaemia, hypertension and immunosuppression. Nevertheless, according to German registry data, a significant percentage of patients with chronic hand eczema seem to be treated with systemic corticosteroids in contrast to current guidelines.

Alitretinoin

Alitretinoin is an endogenous vitamin A derivative which binds with high affinity in a saturable manner to all 6 known retinoid receptors (RAR-α, RAR-β, RAR-γ, RXR-α, RXR-β and RXR-γ). It is the only approved systemic treatment licensed specifically for hand eczema. The approval was received in 2008 following a randomized, double-blind, placebo-controlled, prospective, multicentre phase 3-trial (BACH) in Europe and Canada. A total of 1032 patients with severe refractory CHE were randomized in a 1 : 2 : 2 ratio to placebo, or 10 mg or 30 mg of oral alitretinoin once daily for up to 24 weeks. Safety was assessed for all patients during a follow-up period of 4 weeks, and responders were observed for relapse for 24 weeks after the end of therapy. The primary efficacy parameter was physician global assessment of overall CHE severity, with response defined as clear or almost clear hands. Responses, defined as clear or almost clear, were achieved in up to 48% of patients treated with alitretinoin, compared with 17% for placebo (P < 0.001), with up to 75% median reduction in disease signs and symptoms. Treatment was well-tolerated, with dose-dependent adverse effects comprising headache, mucocutaneous events, hyperlipidaemia, and decreased free thyroxine and thyroid-stimulating hormone. The median time to relapse, defined as recurrence of 75% of initial signs and symptoms, was 5.5–6.2 months in the absence of anti-eczema medication. Similar efficacy was reported in a later study (HANDEL) from the United States. Data from real-world clinical use are consistent with those from clinical trials. According to the Cochrane review, alitretinoin 30 mg achieved investigator-rated control in 432 compared with 157 participants per 1000 with placebo. Similar results were shown for participant-rated control (high-certainty evidence). Consistently with the marketing approval, the ESCD guidelines recommend the use of alitretinoin for treating severe, chronic hand eczema that does not respond, or responds inadequately, to topical corticosteroids. As all retinoids, however, alitretinoin is teratogenic which limits its use in women of child-bearing age. Strict pregnancy prevention 1 month before, during and for 1 month after cessation of treatment is necessary. The most frequently reported side effect is headaches that are mostly transitory and well controllable by NSAIDs; in addition, triglycerides, cholesterol, liver enzymes and TSH should be monitored. The combination of retinoid therapy with PUVA therapy in hand dermatitis is possible as...
frequently practised in psoriasis, but it has not been systematically studied.68

**Acitretin**

In contrast to alitretinoin, acitretin is not approved for the treatment of hand eczema, but efficacy in the management of patients with hyperkeratotic hand eczema has been reported. Thøstrup-Pedersen compared oral acitretin vs. placebo in 29 patients with chronic hand eczema and found a significantly greater reduction of symptoms among patients receiving acitretin ($P < 0.01$) compared with the placebo group.59 In an open study on nine patients with severe hand eczema treated with up to 30 mg acitretin daily if well-tolerated, three patients achieved a PGA of clear or almost clear.60 No recommendation for acitretin in the management of hand eczema is given by the current ESCD guidelines, and even stricter safety issues regarding pregnancy prevention (up to 3 years after discontinuing treatment) and monitoring of side effects apply.

**Cyclosporine**

Cyclosporine is a lipophilic cyclic polypeptide that effectively inhibits the transcription of interleukin 2 and several other cytokines. This leads to an inhibition of the activation of T cells, which play a key role in the pathogenesis of psoriasis, but also atopic dermatitis.61 Cyclosporine is approved for systemic treatment of these diseases, but not hand dermatitis. Its use in the management of hand dermatitis is thus limited to cases of atopic hand dermatitis; otherwise, the use would be off-label. In a double-blind study with 41 patients, cyclosporine 3 mg/kg/day for 6 weeks was as effective as topical betamethasone dipropionate, leading to a 57% reduction in hand eczema severity score.62 According to the ESCD guidelines, cyclosporine may be considered for hand eczema patients with long-term need for treatment if first- and second-line therapy has been insufficient or contraindicated.6 Therapy with cyclosporine should be conducted for up to 6 months at the minimum effective dose, followed by 3 months’ tapering. In some patients, longer therapy may be required, whereas with good responders, earlier discontinuation is advisable considering the risk of hypertension and nephrotoxicity with this drug. If no clinical response is observed within 8 weeks, cyclosporine should be withdrawn.1 An increased risk for skin cancer may result under long-term use; thus, UV protection is recommended.

**Azathioprine**

Azathioprine is an immunosuppressant introduced in the 1960s that is approved in combination with other immunosuppressants for the prevention of graft rejection and the treatment of several autoimmune diseases. In dermatology, it is used off-label for a variety of diseases, especially autoimmune bullous diseases, because of its steroid-saving effect, although the evidence varies widely.63 Azathioprine is a prodrug metabolized to 6-mercaptopurine Mercaptopurine is further metabolized via three metabolic pathways, including 6-thioguanine nucleotides (6-TGN), which are responsible for most of the immunosuppressive activity of thiopurines, but also cause their bone marrow toxicity.64 Further side effects may include gastrointestinal disturbances and infections.65

Oosterhaven et al.66 published a retrospective review of 30 adult patients with severe chronic hand eczema who were treated with azathioprine. Seven patients showed a satisfactory response at the 3-month assessment, but 17 of 30 patients discontinued treatment, 15 of those because of adverse effects. Five of the remaining 13 patients discontinued treatment at some point following the 3-month assessment, because of insufficient responsiveness or non-responsiveness.66 In conclusion, the efficacy of azathioprine in the management of hand dermatitis seems to be rather limited, and careful monitoring of the drug is required. As for cyclosporine, an increased risk for skin cancer under long-term use and UV protection should be considered.

**Methotrexate**

Methotrexate has been widely used in dermatology for the treatment of psoriasis and psoriatic arthritis where its efficacy is well established.67 The evidence for its use in hand eczema is limited. It has been reported in case series of patients with unresponsive hand dermatitis68 and other types of recalcitrant eczema.69 In a retrospective chart review study, 17 patients were treated systemically with acitretin and/or methotrexate.68 Of these 17 patients, four patients received courses of both acitretin and methotrexate independently after failing the alternative treatment course. At 6 months, acitretin achieved clearance/almost clearance in 44% of patients, compared to 0% of those treated with methotrexate. At 12 months, 100% of patients treated with acitretin achieved clearance/almost clearance compared to 40% of patients treated with methotrexate.68 A similar retrospective study reported that after 8–12 weeks of treatment, 36.8% of patients treated with methotrexate for hand eczema showed a good effect of treatment.70 Regarding the subtypes, a good effect was achieved in hyperkeratotic hand eczema in 47.6% compared with 25.0% in the non-hyperkeratotic subgroup. The general safety precautions with methotrexate therapy should be observed, such as monitoring the serum liver enzymes and complete blood count, as well as the cumulative dosage; a weekly dose of 30 mg should not be exceeded.71 The ESCD guidelines mention the lack of evidence for the efficacy of methotrexate for the treatment of hand eczema, but since this treatment has been used over the years, it may be considered if first- and second-line therapy has been insufficient or contraindicated.6

**Emerging therapeutic options for hand eczema**

**Biologics**

Atopic dermatitis is an inflammatory, pruritic, chronic or chronically relapsing skin disease characterized by persistent itch,
erythema and lichenification. Treatment options have been mainly limited to topical and systemic immunosuppressive treatments and to UV light therapy, but with the advent of biologics, therapies targeting the atopic inflammation more specifically have become available. These substances may also have an impact on the management of hand eczema. Dupilumab became the first biologic to receive approval, while the anti-IL-13 monoclonal antibodies lebrikizumab and tralokinumab, which target different IL-13 epitopes with potentially different effects, are currently in advanced-stage trials.71

**Dupilumab**

Dupilumab is a fully human monoclonal antibody directed against the interleukin (IL)-4 receptor α (IL-4Rα) subunit inhibiting the signalling of the type 2 cytokines IL-4 and IL-13 approved for use in the treatment of adult patients with moderate-to-severe atopic dermatitis since 2017.72

Oosterhaven et al.73 reported about a patient with a longstanding combination of very severe chronic atopic hand eczema and moderate-to-severe atopic dermatitis who had been treated with several systemic drugs. Dupilumab treatment was initiated with a loading dose of 600 mg subcutaneously, followed by 300 mg once every 2 weeks. Over 12 weeks, her hand eczema improved from ‘very severe’ and a hand eczema severity index (HECSI) score of 244 (of 360) to ‘almost clear’ with a HECSI score of 11.73

In a retrospective chart review, the outcome of 38 dupilumab-treated patients with hand dermatitis was evaluated.74 From the publication, it is unclear if these were only patients with atopic dermatitis, or if also other aetiologies were included. The authors reported that after treatment with dupilumab, the Investigator’s Global Assessment (IGA) of patients with hand dermatitis decreased by 1.54 points from 3.26 to 1.72, with 40.0% of treated patients achieving IGA of 0 and 1.74

In an observational prospective study, 47 adult patients with hand eczema and atopic dermatitis were treated with dupilumab at a 600 mg loading dose, followed by 300 mg every 2 weeks.75 Primary outcome was a minimum improvement of 75% on the hand eczema severity index after 16 weeks (HECSI-75). HECSI-75 was achieved by 28 (60%).75

Thus, dupilumab seems to have a potential to control hand eczema in a significant proportion of patients with concomitant atopic dermatitis, but further studies are needed to assess its use in patients with other aetiologies of hand eczema.

**JAK Inhibitors**

The Janus kinase (JAK)—signal transducer and activator of transcription (STAT) pathways modulate multiple important immune pathways, including Th2 {IL-4, IL-5, IL-6, IL-10, IL-13, IL-31, CCL [chemokine (C-C motif) ligand] 18}, Th22 (IL-22, S100A8), Th1 {IL-2, IFN-γ and TNF (tumour necrosis factor)-β} and Th17 (IL-17A, IL-17F, IL-21, IL-22, IL-23R).76 They are currently assessed for use in a number of dermatological conditions such as psoriasis, atopic dermatitis, alopecia areata, vitiligo, dermatomyositis and graft-versus-host disease.77 Since they are small molecules, they may penetrate the epidermal barrier thus being of potential not only for systemic, but also for topical use in hand eczema.

**Delgocitinib**

Delgocitinib is a novel, pan-JAK inhibitor specific for JAK1, JAK2, JAK3 and TYK2 kinases.78 It blocks several cytokine-mediated signalling cascades, thereby inhibiting inflammation and might, therefore, be a suitable therapeutic agent for topical use in hand eczema. In a recent proof-of-concept study79 comparing topical delgocitinib vs. placebo (vehicle), 91 patients were randomized. Significantly more patients receiving delgocitinib (45.7%) compared with vehicle (14.9%) {odds ratio 4.89 [95% confidence interval (CI) 1.49–16.09]; P = 0.009} achieved treatment success (PGA 0–1).79 The mean HECSI score at Week 8 was significantly lower with delgocitinib (13.0) compared with vehicle (25.8) [adjusted mean difference −12.88 (95% CI −21.47 to −4.30); P = 0.003].79 The incidence of adverse events was similar with delgocitinib and vehicle; none led to discontinuation of delgocitinib.79 A phase 3 study with the compound may be expected.

**Real-life management of patients with chronic and severe hand eczema**

How scientific evidence on the efficacy and safety of treatment regimen is put into practice in patient care, depends on many additional factors such as physician training and preferences, nationalk differences and traditions, availability of health services and drugs, and cost restraints and insurance limitations. Register studies that allow the analysis of treatments under real-life conditions may identify shortcomings and help to optimize health services. Currently, data on only one register on patients with chronic hand eczema are available (CARPE80 and a Swiss ”sister-registry”81). Patients are prospectively assessed by dermatological examination and patient questionnaire, and socio-economic data and data on diagnostics, skin status, severity and treatment of chronic hand eczema and atopy criteria are repeatedly evaluated. An early analysis of CARPE data stated that a significant proportion of patients may not receive adequate treatment according to guidelines.82 However, a recent 5-year follow-up of this cohort of 1281 patients reported that chronic hand eczema improved substantially over time, whether considered clinically or from the patients’ own perception.83 As possible reasons apart from the natural course of the disease and optimization of treatments, the authors mentioned that regular visits may improve hand eczema through psychological effects of monitoring and feedback and that regular visits mean that there is room to optimize both treatment and the prevention of disease progression.83 This stresses the importance of time-
intensive individualized dermatological care for patients with chronic hand eczema. 

**Adherence to treatment in hand eczema patients**

Since hand eczema may be a chronic disease with a severe impact on quality of life, intensive physician–patient communication, but also active patient self-management play an important role to achieve adherence to treatment regimen like in other chronic skin diseases. Provision of creams, electronic monitoring and feedback on cream consumption may be used to improve adherence to topical therapy.83 Integrated care by a multidisciplinary teams, combining clinical and occupational care to optimize treatment, and the patient’s quality of life and social functioning will improve outcomes.84 Specific teaching interventions have been developed for the management of patients with hand eczema that should be incorporated into therapeutic concepts.27

**Conclusion**

While the spectrum of therapeutic options for hand eczema has expanded in recent years, the condition remains a challenge for dermatologists and patients alike. The therapeutic algorithms encompassing topical, physical and systemic treatments proposed in the guidelines should be followed actively in order to prevent chronicity and relapses that may severely impair patients’ wellbeing. New therapeutic principles such as biologics and topical Janus Kinase inhibitors may be available for the management of hand eczema patients in the near future.

**References**

1 Antonov D, Schliemann S, Elsner P. Hand dermatitis: a review of clinical features, prevention and treatment. Am J Clin Dermatol 2015; 16: 257–270.
2 Diepgen TL, Andersen KE, Brandao FM et al. Hand eczema classification: a cross-sectional, multicentre study of the aetiology and morphology of hand eczema. Br J Dermatol 2009; 160: 353–358.
3 Agner T, Elsner P. Hand eczema: epidemiology, prognosis and prevention. J Eur Acad Dermatol Venereol. (in print) 2020; 34(Suppl 1): 13–21.
4 Christoffers WA, Coenraads P-J, Svensson Å et al. Interventions for hand eczema. Cochrane Database Syst Rev 2019; 4: CD004055.
5 Diepgen TL, Andersen KE, Chosidow O et al. Guidelines for diagnosis, prevention and treatment of hand eczema. J Dtsch Dermatol Ges 2015; 13: e1–e22.
6 Diepgen TL, Andersen KE, Chosidow O et al. Guidelines for diagnosis, prevention and treatment of hand eczema – short version. J Dtsch Dermatol Ges 2015; 13: 77–85.
7 Diepgen TL, Fartasch M. Recent epidemiological and genetic studies in atopic dermatitis. Acta Derm Venereol Suppl 1992; 176: 13–18.
8 Räßler F, Goetzs S, Elsner P. Acrokeratosis paraneoplastica (Bazex syndrome) – a systematic review on risk factors, diagnosis, prognosis and management. J Eur Acad Dermatol Venereol 2017; 31: 1119–1136.
9 Eyerich K, Eyerich S. Immune response patterns in non-communicable inflammatory skin diseases. J Eur Acad Dermatol Venereol 2018; 32: 692–703.
10 Czarnowicki T, He H, Krueger JG, Guttman-Yassky E. Atopic dermatitis endotypes and implications for targeted therapeutics. J Allergy Clin Immunol 2019; 143: 1–11.
11 Guttman-Yassky E, Krueger JG. Atopic dermatitis and psoriasis: two different immune diseases or one spectrum? Curr Opin Immunol 2017; 48: 68–73.
12 Li R, Hadi S, Guttman-Yassky E. Current and emerging biologic and small molecule therapies for atopic dermatitis. Expert Opin Biol Ther 2019; 19: 367–380.
13 Oda S, Vocks E, Rakoski J, Ring I. Successful treatment of dyshidrotic hand eczema using tap water iontophoresis with pulsed direct current. Acta Derm Venereol 1996; 76: 472–474.
14 Skudlik C, Weisshaar E, Scheidt R et al. Multicenter study 'Medical-Occupational Rehabilitation Procedure Skin–optimizing and quality assurance of inpatient-management (ROQ)’. J Dtsch Dermatol Ges 2009; 7: 122–126.
15 Diepgen TL, Elsner P, Schliemann S et al. Guideline on the management of hand eczema ICD-10 Code: L20, L23, L24, L25, L30. J Dtsch Dermatol Ges 2009; 7(Suppl 3): S1–S16.
16 Coenraads P-J. Hand eczema. N Engl J Med 2012; 367: 1829–1837.
17 Held E, Skoet R, Johansen JD, Agner T. The hand eczema severity index (HECSI): a scoring system for clinical assessment of hand eczema. A study of inter- and intraobserver reliability. Br J Dermatol 2005; 152: 302–307.
18 Coenraads P-J, Van Der Walle H, Thestrup-Pedersen K et al. Construction and validation of a photographic guide for assessing severity of chronic hand dermatitis. Br J Dermatol 2005; 152: 296–301.
19 Ofenloch RF, Weisshaar E, Dumke A-K et al. The Quality of Life in Hand Eczema Questionnaire (QOLHEQ): validation of the German version of a new disease-specific measure of quality of life for patients with hand eczema. Br J Dermatol 2014; 171: 304–312.
20 Wohlrab J, Staubach P, Augustin M et al. S2k guidelines for the use of topical preparations on the skin. J Dtsch Dermatol Ges 2018; 16: 376–392.
21 Augustin M, Wilsmann-Theis D, Körber A et al. Positionspapier: Diagnostik und Therapie der xerosis cutis. J Dtsch Dermatol Ges 2018; 16(Suppl 4): 3–35.
22 Ramsing DW, Agner T. Preventive and therapeutic effects of a moisturizer. An experimental study of human skin. Acta Derm Venereol 1997; 77: 335–337.
23 De Paepe K, Hachem JP, Vanpepe E et al. Beneficial effects of a skin tolerance-tested moisturizing cream on the barrier function in experimentally elicited irritant and allergic contact dermatitis. Contact Dermatitasis 2001; 44: 337–343.
24 Surber C, Schmid-Grendelmeier P. General principles of topical therapy of the skin. In: Brockow K, Mortz C, eds. Global Atlas of Skin Allergy, EAACI, 2019. https://www.eaaci.org/images/Atlas/Global_Atlas_IV_v1.pdf p. 220–223.
25 Thouvenin M-D, Bacquey A, Nocera T, Rossin AB. Tolerability and efficacy of a medical device repairing emollient cream in adults with chronic hand dermatitis. J Cosmet Dermatol 2018; 17: 1158–1164.
26 Lodén M. The clinical benefit of moisturizers. J Eur Acad Dermatol Venereol 2005; 19: 672–688; quiz 686–7.
27 Seyfarth F, Schliemann S, Antonov D, Elsner P. Teaching interventions in contact dermatitis. Dermatitis 2011; 22: 8–15.
28 Luger T, Loske KD, Elsner P et al. Topical skin therapy with glucocorticoids–therapeutic index. J Dtsch Dermatol Ges 2004; 2: 629–634.
29 Levin C, Zhai H, Bashir S et al. Efficacy of corticosteroids in acute experimental irritant contact dermatitis? Skin Res Technol 2001; 7: 214–218.
30 van der Valk PG, Mailbach HI. Do topical corticosteroids modulate skin irritation in human beings? Assessment by transepidermal water loss and visual scoring. J Am Acad Dermatol 1989; 21: 519–522.
31 Ramsing DW, Agner T. Efficacy of topical corticosteroids on irritant skin reactions. Contact Dermatitis 1995; 32: 293–297.
32 Kao JS, Fluhr JW, Man M-Q 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.
33 Lee GR, Maarrow M, Hendricks AK et al. Current and emerging therapies for hand eczema. Dermatol Ther 2019; 32: e12840.
76 He H, Guttman-Yassky E. JAK inhibitors for atopic dermatitis: an update. Am J Clin Dermatol 2019; 20: 181–192.
77 Cinats A, Heck E, Robertson L. Janus kinase inhibitors: a review of their emerging applications in dermatology. Skin Therapy Lett 2018; 23: 5–9.
78 Tanimoto A, Ogawa Y, Oki C et al. Pharmacological properties of JTE-052: a novel potent JAK inhibitor that suppresses various inflammatory responses in vitro and in vivo. Inflamm Res 2015; 64: 41–51.
79 Worm M, Bauer A, Elsner P et al. Efficacy and safety of topical delgocitinib in patients with chronic hand eczema: data from a randomised, double-blind, vehicle-controlled Phase 2a study. Br J Dermatol 2019 Aug 29. doi: 10.1111/bjd.18469. [Epub ahead of print]
80 Apfelbacher CJ, Akst W, Molin S et al. CARPE: a registry project of the German Dermatological Society (DDG) for the characterization and care of chronic hand eczema. J Dtsch Dermatol Ges 2011; 9: 682–688.
81 Cazzaniga S, Ballmer-Weber BK, Grani N et al. Chronic hand eczema: a prospective analysis of the Swiss CARPE registry focusing on factors associated with clinical and quality of life improvement. Contact Dermatitis 2018; 79: 136–148.
82 Apfelbacher C, Molin S, Weisshaar E et al. Characteristics and provision of care in patients with chronic hand eczema: updated data from the CARPE registry. Acta Derm Venereol 2014; 94: 163–167.
83 Soltanipoor M, Rustemeyer T, Sluiter JK et al. Evaluating the effect of electronic monitoring and feedback on hand cream use in healthcare workers: Healthy Hands Project. Contact Dermatitis 2019; 80: 26–34.
84 van Gils RF, Boot CRL, Knol DL et al. The effectiveness of integrated care for patients with hand eczema: results of a randomized, controlled trial. Contact Dermatitis 2012; 66: 197–204.
85 Lynde C, Guenther L, Diepgen TL et al. Canadian hand dermatitis management guidelines. J Cutan Med Surg 2010; 14: 267–284.
86 Menné T, Johansen JD, Sommerlund M et al. Hand eczema guidelines based on the Danish guidelines for the diagnosis and treatment of hand eczema. Contact Dermatitis 2011; 65: 3–12.