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Management of Chronic Hand and Foot Eczema. An Australia/New Zealand Clinical Narrative.

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Management of Chronic Hand and Foot Eczema. An Australia/New Zealand Clinical Narrative.

Abstract

Chronic hand/foot eczemas are common, but treatment is often challenging, with widespread dissatisfaction over current available options. Detailed history is important, particularly with regard to potential exposure to irritants and allergens. Patch testing should be regarded as a standard investigation.

Individual treatment outcomes and targets, including systemic therapy, should be discussed early with patients; restoring function being the primary goal, with clearing the skin a secondary outcome. Each new treatment, where appropriate, should be considered additive or overlapping to any previous therapy.

Management extends beyond mere pharmacological or physical treatment, and requires an encompassing approach including removal or avoidance of causative factors, behavioural changes and social support. To date, there is little evidence to guide sequences or combinations of therapies.

Moderately symptomatic patients (e.g. DLQI ≥10) should be started on a potent/superpotent topical corticosteroid applied once or twice per day for 4 weeks, with tapering to twice weekly application. If response is inadequate, consider phototherapy, and then a 12-week trial of a retinoid (alitretinoin or

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acitretin). Second line systemic treatments include methotrexate, ciclosporin and azathioprine.

For patients presenting with severe symptomatic disease (DLQI ≥15), consider predniso(lo)ne 0.5-1.0 mg/kg/day (or ciclosporin 3 - 5mg/kg/day) for 4-6 weeks with tapering, and then treating as for moderate disease as above. In non-responders, botulinum toxin and/or iontophoresis, if associated with hyperhidrosis, may sometimes help. Some patients only respond to long-term systemic corticosteroids. The data on sequencing of newer agents, such as dupilumab or JAK inhibitors, is immature.

Introduction

The management of chronic hand and foot eczema can be challenging.[1-5] Distinguishing between dermatitis and psoriasis is often difficult, the thickened epidermis, in particular the stratum corneum, restricts percutaneous absorption making topical therapy less effective, and the effects on quality of life are often disproportionate to the area of cutaneous involvement.

Although chronic hand/foot eczemas are common, specific recommendations on their management are sparse.[2,3,6,7] The Australasian Medical Dermatology Group has developed the following narrative following an in-depth literature review (all languages, search terms included hand eczema/dermatitis, foot eczema/dermatitis, quality of life, reviews, and treatments, including an extensive list of individual drugs and treatment modalities). The narrative is structured around diagnosis, scoring systems, treatment modalities and a discussion on when to treat, what might be considered success, and sequencing of treatments. Specific management of allergic and irritant contact dermatitis of the hands and/or feet were excluded from the discussions, as was general hand/foot care.

Epidemiology and classification

The prevalence of chronic (i.e., persisting more than 6 months) hand eczema has been estimated at 1-5%, increasing to 10% if milder cases are included, with an

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incidence of 5.5 cases/1000 person-years.[5,8] The prevalence is higher in females, perhaps because of traditionally gender-based exposure, for example as hairdressers, nurses, domestic cleaning, food preparation and caregivers. An estimated 5-10% of hand dermatitis cases are chronic and treatment-resistant. There is very little information on the epidemiology of foot eczema, other than that 30% of patients with chronic hand eczema also have involvement of the feet.[9,10]

Several studies have assessed the prevalence of subtypes of hand eczema; a UK consensus statement reported that just over half of cases were allergic contact and/or irritant contact dermatitis, with the other common types being atopic hand eczema with or without irritant contact dermatitis, vesicular dermatitis, and hyperkeratotic dermatitis.[2] Seven categories of hand eczema have been proposed including allergic contact dermatitis, irritant contact dermatitis, endogenous atopic hand eczema alone or in combination, and vesicular and hyperkeratotic types.[4,11] No specific classification of foot eczema exists.

There is little that is distinctive about the aetiology of non-allergic chronic hand/foot eczema, with contributing factors including barrier dysfunction, genetic changes in filaggrin, a possible role of the skin microbiome, staphylococcal infection, and immune dysregulation.

The morphology of hand/foot eczema can include erythema, oedema, infiltration, scale, hyperkeratosis, fissures and erosions. Vesicular hand/foot eczema may have both acute and chronic features. Acute disease is characterised by recurrent vesicles with or without bullae on a non-erythematous base. Chronic disease has a more inflammatory base, often with a sharp border at the wrists.[12] Hyperhidrosis and attenuated sweating may be present.[13] Hyperkeratotic hand eczema has a distinct clinical presentation of sharply demarcated palmar hyperkeratosis with painful fissures. Some consider it to be distinct from hand eczema as it can resemble psoriasis histologically and often responds to psoriasis treatments.[14]

Severe chronic hand eczema interferes with daily activities, social functioning, and

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employment, with a third of patients reporting impairment while working and consequent productivity loss from both presenteeism and absenteeism.[15,16] The mean annual hand eczema patient cost has been estimated at between €1,712 to €9,792.[17] Common symptoms include dryness/flaking (81%), itchiness (75%), and cracking/tearing of the skin (71%), as well as sleep and mood disturbances.[16]

Assessment of chronic hand/foot eczema

Assessment of chronic hand/foot eczema requires a thorough history, particularly to exclude both irritant and allergic contact dermatitis. The history should include details on onset, evolution, duration, episodic or persistent nature, smoking as a risk factor, occupation, hobbies, family history, and symptoms which may include itching, soreness, cracking, fissuring, bleeding and hyper/hypo-hydrosis. Careful examination of the whole skin should be performed. Patch testing should be considered in all patients.

There is an extensive differential diagnosis, which includes papulosquamous disorders, infections, infestations, neoplasia, physical triggers (mechanical, chemical, thermal), metabolic disease and medications. Dermoscopy may assist the examination (e.g. looking for scabetic burrows); Wood lamp examination, microbiology swabs, skin/nail scrapings for mycology, and total serum IgE should be considered if the inflammation is unresponsive to general measures and first-line treatments. RAST or prick testing should be reserved for suspected cases of protein contact dermatitis.[4,6] Biopsy is generally unhelpful in distinguishing eczema from psoriasis, but may help with excluding lichen planus or other inflammatory skin conditions.

Once the diagnosis of chronic hand/foot eczema has been made, assessing severity is essential. The ideal clinical scoring system should take into account symptom type and severity, morphology, occupational factors, and quality of life measures including psychological burden, and be able to monitor the effects of treatment. Several groups have reviewed the available scoring systems.[18] Of these the Hand Eczema Severity Index (HECS), the Hand Eczema Extent Score (HEES), the Quality of

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Life in Hand Eczema Questionnaire (QOLHEQ), and the Patient-Oriented Eczema Measure (POEM) seem most useful.[19,20,21,22,23] There do not appear to be any specific validated scoring systems for chronic eczema of the feet. The commonly used Eczema Area and Severity Index (EASI), SCORring Atopic Dermatitis (SCORAD) and Dermatology Life Quality Index (DLQI) are less specific for chronic hand/foot eczema.

When to treat?

Treatment should be commenced: i) when the patient wants it, for example if there is a high impact on quality of life or function; ii) when the prescribing physician considers there are sufficient symptoms, visible disease, or high-impact disease; and iii) when treatment is available and affordable.

Treatment targets should be discussed, with restoring function being the main goal. Clearing the skin, whilst desirable, should be a secondary outcome. Each new treatment, where appropriate, should be considered additive or overlapping to the previous therapies. As palmoplantar disease can be slow to respond to treatment, each treatment requires a 'fair trial' before considering an alternative; distinguishing between a flare or fluctuation in disease and disease progression can be difficult. To date, there is little evidence to guide sequences or combinations of therapies.

General measures

Good hand/foot care is an essential first step in the management of chronic hand/foot eczema[5] and includes skin education programmes, lifestyle changes, and the use of barriers and soap substitutes, despite the evidence base for the latter being weak. Minimising relevant exogenous factors, e.g. exposure to allergens or irritants, is essential, which may require time away from work. Education needs to be repeated at each visit. Patient support and advocacy in the workplace, and interaction with the employer and /or insurers may be required from the treating dermatologist. (see Key points - General).

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Topical Treatment

The use of specific topical therapies is largely based on evidence of their efficacy elsewhere on the skin.

- Emollients: A number of small studies have examined the use of emollients in chronic hand dermatitis.[24,25] A 3 week trial of a 'medical device repairing emollient cream' reported decreased pain and pruritus at days 8 and 22 compared to baseline, in 40 patients with mild to moderate chronic hand dermatitis.[26] An open-label study of an emulsion containing sucralfate, with copper and zinc sulfates, resulted in patient- and investigator-rated improvements after 7 days in 32 subjects with contact or climatic hand dermatitis.[27]
- Keratolytics: salicylic acid, up to 20%, and urea 10–20%, have often been added to emollients, but the clinical trial evidence is generally of low quality.[28] A barrier strengthening moisturiser containing 5% urea prolonged the disease free interval of treated hand dermatitis, from 2 days to 20 days, compared to no treatment, in study of 53 patients.[29]
- Topical corticosteroids: After a suitable trial of emollients, barriers, and soap substitutes, potent topical steroids are regarded as the first line pharmacological treatment of moderate/severe hand and foot eczema, despite limited data from randomised, controlled trials to confirm their efficacy.[30,31,32] Although there are insufficient data on which to base a choice between short-duration potent/super-potent agents, compared with continuous application of less strong corticosteroids, it has been recommended that potent topical corticosteroids be used once daily for 1 month, followed by twice weekly (e.g. at weekends) maintenance therapy.[33,34]

  In an open-label study topical mometasone furoate applied freely for up to 9 weeks by patients with hand eczema resulted in clearing at 3 weeks in almost half the patients, and another quarter had cleared at week 6.[35] Those who had clearing of eczema participated in a trial of maintenance therapy for up to 36 weeks, in which recurrence-free rates were significantly higher in the groups applying glucocorticoid three times weekly (83%) or twice weekly (68%) compared to emollients alone (26%).

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As a general rule once daily application is sufficient; ointment formulations are more effective than creams. There is insufficient evidence of any additive benefit from a combined topical antibacterial/corticosteroid agent.

- Topical calcineurin inhibitors: In 294 patients with chronic hand dermatitis, three weeks of pimecrolimus 1% cream was associated with a greater improvement in Investigator Global Assessment (IGA) compared to vehicle control.[36] However, another study in 40 patients found that initial benefit after 3 weeks was not sustained during maintenance therapy.[37]

  Studies of tacrolimus are limited by lack of a placebo control, small sample sizes and short duration. A study of 29 adults,[38] with occupationally-induced hand dermatitis showed complete clearance in 44% and ≥ 50% improvement in two-thirds of patients (based on the Jena Hand Eczema Score) who used tacrolimus 0.1% ointment twice daily for 4 weeks. An earlier study of 25 adults with moderate to severe hand and/or foot eczema treated with tacrolimus 0.1% ointment three times daily for up to 8 weeks reported a significant improvement in a composite severity score.[39]

  Alternating a topical corticosteroid with a topical calcineurin inhibitor may reduce adverse events, although the long-term efficacy and safety are unknown.

<u>Other topical agents</u>

- Bexarotene: In 55 patients with chronic severe hand dermatitis bexarotene gel monotherapy was associated with a 50% clinical improvement in 79% of patients and 90% improvement in 39% using both a physician assessment score and a modified Hand Eczema Area Severity Score (HEASI).[40]
- Calcipotriol: In 13 patients with chronic hand eczema, 0.005% calcipotriol ointment was as effective as 0.25% desoximetasone ointment twice daily for 8 weeks.[41] Nine patients experienced ≥ 75% reduction in Hand Eczema Severity Index (HECSI) with calcipotriol. Calcipotriol/betamethasone ointment was used successfully in 3 Chinese patients with chronic hand eczema.[42]
- Coal tar: Tar preparations have long been used for inflammatory skin conditions, but have largely fallen out of favour. Sulfonated shale oils

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(ichthammol) and pine tars are still being used, but with limited clinical trial evidence.[43]

- Crisaborole: Crisaborole, a phosphodiesterase type 4 (PDE4) inhibitor, has been used in the treatment of atopic dermatitis with anecdotal benefit reported in atopic hand dermatitis.[44]
- Delgocitinib: Topical delgocitinib, a pan-Janus kinase (JAK) inhibitor, was compared to vehicle ointment in 91 patients with chronic hand eczema, treated for 8 weeks.[45] More patients receiving delgocitinib (46%) than vehicle (15%) achieved treatment success, defined as the proportion achieving clear/almost clear skin with ≥2-point improvement in Physician Global Assessment (PGA).
- Fumaric acid: In a double-blind randomised controlled trial in 58 patients with hand eczema, topical fumaric acid 5% cream was less effective than triamcinolone 0.05% cream when used twice daily for one month.[46]
- Retapamulin: A randomised study of 60 adults with hand-foot eczema showed that the addition of retapamulin 1% ointment, a pleuromutilin antibiotic which targets gram-positive bacteria, to clobetasol propionate 0.05% foam, was more effective than clobetasol propionate plus vehicle placebo ointment at 14 days, but with no difference at 28 days.[47]
- Bacterial therapy: A double-blind randomised placebo-controlled trial in 75 patients concluded that a cream containing 5% lysate of the non-pathogenic bacterium *Vitroscilla filiformis* significantly reduced the severity and pruritus of atopic dermatitis as well as transepidermal water loss and cutaneous colonization by *S. aureus*.[48] Commensal strains of coagulase-negative *S. epidermidis* and *S. hominis* from healthy donors have also been applied to atopic dermatitis skin and found to decrease colonisation by *S. aureus*.[49]

Physical therapies

- Phototherapy: Several small trials have shown that ultraviolet B (UVB) may improve chronic hand eczema over a period of 10 weeks, but topical psoralen plus ultraviolet A (PUVA) was superior.[2] In a 12 week trial of PUVA versus narrow-band UVB (nb-UVB) treatment of palmar hand eczema in 60 patients,

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43% of the PUVA group achieved PGA 'clear' or 'almost clear' compared to only 23% in the nb-UVB group.[50] However, wide confidence intervals suggested PUVA did not achieve clear superiority. Adverse events, mainly erythema, were reported by 9 patients receiving nb-UVB versus none in the PUVA group.

- Excimer laser: A chart review of 30 patients with refractory chronic hand and foot eczema concluded that Excimer laser demonstrated excellent and sustained efficacy.[51] The response was assessed using PGA and a modified total lesion/symptom score (mTLSS). The authors stated that compared to other UV therapies, Excimer laser offers lower cumulative doses of UV radiation by targeting specific areas and should be considered alone or in combination with other established or newer therapies.
- Grenz rays: Small case series show some benefits from Grenz rays in the treatment of chronic hand eczema,[52,53] but a NICE guideline notes the evidence is very limited.[54] There is some concern about the risk of skin malignancy in the long term, but Grenz remains an option for recalcitrant hyperkeratotic hand eczema.
- Botulinum toxin: In a trial in 10 patients with vesicular hand dermatitis, botulinum toxin A (mean dose - 162 units) was injected in one hand, using the untreated hand as a control.[55] Self-assessment 5 to 6 weeks later showed that 7 of 10 patients experienced good or very good effect; reported benefits included reduced itch and less severe clinical signs. In a study of 8 patients with dyshidrotic hand eczema, the more severely-affected hand was treated with 100 units of botulinum toxin A, whilst using topical corticosteroids on both hands.[56] Six patients completed the study. At week 8 the mean Dyshidrotic Eczema Area and Severity Index (DEASI) reduced from 28 to 17 with topical therapy alone and from 36 to 3 with adjuvant botulinum toxin.
- Iontophoresis: In 20 patients with chronic dyshidrotic hand eczema, tap water iontophoresis (15-minute daily treatments over 3 weeks) was performed on one hand, using the untreated hand as a control.[13] The hand treated with iontophoresis cleared slightly faster (20 vs. 22.3 days; p=not significant); however the relapse-free interval was significantly prolonged at 24.8 weeks

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vs.8.35 weeks for the non-treated hand ($p<0.0001$). This was confirmed in a larger study of 54 patients with hand/foot eczema.[57] The authors hypothesise that galvanization with tapwater iontophoresis interrupts the neurogenic inflammation and prolongs the relapse-free interval in hyperhidrotic palmoplantar eczema. Studies also suggest a role for leaky tight junctions in eczema with eccrine sweat leaking into the dermis potentially flaring itch and eczema.

Systemic therapies

Consideration of systemic therapy should be discussed early with the patient. The traditional immunomodulators azathioprine, ciclosporin, methotrexate and mycophenolate are widely considered second/third-line systemic agents in hand and foot eczema, after topical therapies, phototherapy and retinoids. Their use is based primarily on evidence of their efficacy in atopic dermatitis at other sites.[58] (see Key points – Specific treatments).

- Systemic corticosteroids: Despite almost no clinical trial data, oral corticosteroids remain very popular in the treatment of chronic hand/foot eczema, in particular for the vesicular subtype.[8,16] A 2012 review advised that oral corticosteroids should only be used for one week.[3] However, in Australia and New Zealand, systemic corticosteroids, 0.5–1 mg/kg/day predniso(lo)ne equivalents is used for up to 4 weeks with dose tapering, similar to the treatment of moderate/severe atopic eczema.[57]
- Acitretin: A number of small trials and case series have demonstrated a benefit of acitretin. Nine patients with severe hand dermatitis received 10-30mg/day; at 24 weeks a third were clear or almost clear, and 44% were almost clear or had mild symptoms.[59] A Korean open label study of 28 patients with 2 years of chronic hand dermatitis refractory to high-potency topical corticosteroid were treated with 10 mg acitretin twice daily for 8 weeks. The Hand Eczema Severity Index (HECSI) fell by 58%, from 21.9 at baseline to 9.2, with the hyperkeratotic subtype showing the most improvement.[60]

  An 8 week single-blind, placebo-controlled study randomised 29 patients with hyperkeratotic hand eczema to 30 mg/day acitretin or placebo. After 4 weeks

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there was a 51% reduction in a semi-quantitative score with acitretin (hyperkeratosis, fissuring, scaling, itch, redness and vesicle count) compared to 9% with placebo.[61] In a single-blind study of chronic hyperkeratotic palmoplantar dermatitis, 42 patients received either acitretin 25-50 mg/day for 1 month or topical betamethasone/salicylic acid ointment. Using a 10-point severity scale, acitretin was significantly better than the conventional topical treatment after 30 days (two-sided P<0.0001) and the improvement persisted for >5 months after discontinuing acitretin.[62]

A retrospective review of 17 patients with chronic hand dermatitis treated with either methotrexate or acitretin found that, at 6 months, acitretin achieved clearance/almost clearance in 44% of patients, compared to none 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. Adverse effects were minimal and as expected.[63]

The largest real-world study to date retrospectively reviewed 109 Dutch patients with severe chronic hand eczema treated with acitretin. Patients with hyperkeratotic hand eczema did best: 50.7% had a good effect. The drug survival rates of acitretin at 12, 24, 36, and 52 weeks were 74.3%, 45.5%, 33.8% and 23.2%, respectively.[64] Dose related adverse effects, in particular the teratogenic risks, limits its potential use.

- Alitretinoin: A large randomised placebo controlled trial of 1,032 patients with chronic hand eczema (all types) assessed two dosages of alitretinoin (30 or 10 mg/day) against placebo, for up to 24 weeks. The percentages of patients rating their hand eczema as ‘clear’ or ‘almost clear’ at the end of therapy were 40%, 24%, and 15%, respectively.[65] Patients with hyperkeratotic eczema had the highest response rates, but those with vesicular eczema also appeared to benefit. The beneficial effects were confirmed in a retreatment trial among a subgroup of patients who had relapse.[66] In a real world setting, a quarter (27.4%) of 95 patients’ hand eczema cleared with alitretinoin, with 68.3% of patients with a hyperkeratotic subtype clearing. The drug survival rates of alitretinoin after 12, 24, 36, and 52 weeks were 69.3%, 45.1%, 19.6% and 7.0%, respectively.[64] Multiple other studies report a consistent 40-50% response

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rate.[67-71] The response to alitretinoin appears better when combined with potent topical steroids.[72]

A Cochrane review of hand eczema treatments assessed 60 RCTs: 18 topical steroids/calcineurin inhibitors trials, 10 phototherapy, 3 systemic immunosuppressives, and 5 oral retinoids studies. In total, they included 5,469 participants with mild to severe chronic hand eczema.[5] The review concluded that alitretinoin 10 mg improves investigator-rated symptom control compared to placebo (risk ratio (RR) 1.58; 95% CI 1.20 to 2.07), with numbers needed to treat for an additional beneficial outcome (NNTB) being 11 (95% CI 6.3 to 26.5). Alitretinoin 30 mg also improves this outcome compared with placebo, RR 2.75 (95% CI 2.20 to 3.43) with a much better NNTB of 4 (95% CI 3 to 5). Adverse events including headache did not differ between alitretinoin 10 mg and placebo, but the risk of headache increased with alitretinoin 30 mg.[73]

NICE recommends alitretinoin be started when severe disease is present, as defined by the PGA and a DLQI score of ≥15, and stopped as soon as an adequate response has been achieved, or if the eczema remains severe at 12 weeks, or if an adequate response (hands clear or almost clear) has not been achieved by 24 weeks.[74] Alitretinoin has the usual dose-related retinoid adverse effects; women of childbearing potential need adequate contraception during treatment, and for four weeks after stopping.

- Anti-staphylococcal treatments: Whilst more than half of patients with chronic hand eczema are colonized by *Staphylococcus aureus*,[75,76] including methicillin-resistant *S. aureus* (MRSA),[77] there is little evidence from clinical trials that systemic antibiotics, or decolonisation, are beneficial, particularly as *S. aureus* counts reduce significantly following monotherapy with topical corticosteroids.[78]

  In an open label trial in 30 adult patients with mild to severe chronic hand eczema receiving daily supplementation with *Lactobacillus acidophilus*, *Lactobacillus casei* and *Lactobacillus rhamnosus* for 12 weeks, 5 patients achieved a PGA score of 0 or 1.[79]
- Azathioprine: Azathioprine is used off-label in atopic dermatitis and is generally considered as a third-line option. About one-third of patients with atopic

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dermatitis have a good response, typically after about 6 months.[58] In an observer-blinded, randomised controlled trial in 91 patients with chronic hand eczema, clobetasol propionate 0.05% cream in combination with azathioprine 50 mg daily led to significantly higher mean percent improvement in the Hand Eczema Scoring Index (HESCI) at 24 weeks than clobetasol alone (92% vs. 65%, p=0.001).[80] In a drug survival study in 30 patients with chronic hand eczema, half discontinued azathioprine in the first 3 months because of adverse effects, but 7 of the 15 patients who continued azathioprine for 3 months, remained on therapy at 1 year.[81] Concomitant oral corticosteroids were given to 13 patients. The addition of allopurinol to azathioprine may improve clinical response, but the dose of azathioprine should be decreased by 25-50%.[82]

A head-to-head study of azathioprine and alitretinoin in 116 patients with chronic non-hyperkeratotic hand eczema was due to be completed during 2019.

- Ciclosporin: A head-to-head study compared ciclosporin and topical betamethasone dipropionate 0.05% for 6 weeks in 41 patients with chronic hand eczema.[83] The disease activity score decreased to 57% of baseline in the ciclosporin group and to 58% in the betamethasone group, suggesting equal effectiveness.

  A retrospective review of 102 patients with chronic hand eczema identified an average treatment duration of 10.3 months at doses to 5 mg/kg/day; two-thirds of patients achieved a PGA of 1 at three months, with the best response in the vesicular subtype, but with a significant rate of side effects and frequent relapses.[84] A more recent open-label study in 16 patients with chronic hand eczema used ciclosporin at a dose of 200 mg/day maintained until >50% clearance then tapered to 25-100 mg/day for 10-12 weeks.[85] Topical corticosteroids and emollients were permitted. At week 4, 25% achieved a PGA of 0 and 39% improved from 'moderate' to 'mild' disease. At week 10, 14 patients had PGA 0 or 1.

  In a 24 week, open-label trial of 118 patients with chronic hand eczema comparing alitretinoin and ciclosporin, 68.2% and 40.9% respectively, were categorized as responders.[86]

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- Methotrexate: Despite no reliable data on the use of methotrexate in hand and foot eczema, it is often used as the first additional immunomodulator after topical therapy, phototherapy, retinoids, and systemic corticosteroids.[8] A retrospective review of 42 Dutch patients with chronic hand eczema treated for a median of 139 days found 37% had a good effect on the Physician Global Assessment (PGA) after 8-12 weeks.[87]
- Mycophenolate mofetil: There are no specific trials of mycophenolate mofetil in the treatment of chronic hand/foot eczema, but this agent has been shown to be of benefit in some patients with atopic dermatitis.[58,88] Its effectiveness is limited by gastrointestinal side effects, drug interactions and potential teratogenicity.
- Ranitidine: A randomised placebo-controlled trial of ranitidine for the treatment of hand eczema in patients with atopic dermatitis demonstrated benefits of the active treatment using a modified HEASI.[89]

Novel therapies

- Apremilast: A single case report has described a good response to apremilast in chronic hand eczema.[90]
- Biologics: There is very little information on the use of biologics specifically for hand/foot eczema. A case report describes some efficacy of etanercept in recalcitrant hand pompholyx.[91]

  A number of case reports have described the use of dupilumab in chronic hand eczema. A retrospective case series of patients with dermatitis treated with dupilumab identified six with dermatitis involving only the hands and 32 with hand and body involvement.[92] Diagnoses included dyshidrotic eczema, atopic dermatitis and contact dermatitis. After treatment the Investigator Global Assessment (IGA) of patients with hand dermatitis decreased from 3.3 to 1.7, with 40% achieving an IGA score of 0 or 1. Almost all patients with hand dermatitis reported improvement in pruritus, dermatitis-related pain and resolution of fissures.

  In an observational prospective study of 47 adult patients with atopic

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dermatitis, who also had hand dermatitis, commenced on dupilumab, HECSI-75 was reached in 28 patients (60%) by week 16.[93,94] There are currently no reports of studies of biologics specifically in foot dermatitis

- JAK inhibitors: A number of recent reviews have discussed the potential role of JAK inhibitors in atopic dermatitis but they do not describe their use specifically in hand and foot dermatitis. Anecdotally, as with dupilumab, patients in phase 3 clinical trials of upatacitinib for atopic eczema are showing excellent early responses in their hand/foot dermatitis.

Sequencing of treatments

The management of hand/foot eczema extends beyond mere pharmacological or physical treatment, and requires an encompassing approach including removal or avoidance of causative factors, behavioural changes and social.[7] Although several consensus guidelines and treatment algorithms have been proposed,[2,3,6,16] there are no studies to help recommend sequencing of treatments. The group recommends detailed hand/foot care education, specifically targeting avoidance of irritants and potential allergens, at each visit. Patients should be informed of the importance of application of liberal amounts of emollients and barrier creams.

Moderately symptomatic patients (e.g. DLQI ≥10) should be started on a potent/super-potent topical corticosteroids applied once or twice per day for 4 weeks, with tapering to twice weekly (or at weekends) if adequate response is achieved. If no significant improvement, consideration should be given to adding phototherapy (if available). If inadequate response to phototherapy within 4-6 weeks, or phototherapy is not available, a trial of alitretinoin 30 mg/day should be considered. If alitretinoin is not available, acitretin 10-30 mg/day may be considered as an alternative. When pregnancy is a concern, ciclosporin may be considered in at risk female patients. If there is limited response to retinoids after 12 weeks, the addition of a conventional systemic immunomodulator may be appropriate; there was some disparity within the group, with the addition of methotrexate slightly preferred over ciclosporin and then azathioprine. These should be used in accordance with experience gained from atopic dermatitis.[58]

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For patients presenting with severe symptomatic disease (DLQI ≥15), consider predniso(lo)ne 0.5-1.0 mg/kg/day for 4-6 weeks (or ciclosporin 3 - 5 mg/kg/day), and then treating as for moderate disease described above. In non-responders, if significant hyperhidrosis is present, consider botulin toxin or iontophoresis. Some patients only respond to systemic corticosteroids, which may need to be continued long term. The data on sequencing of newer agents, such as dupilumab or JAK inhibitors, is still immature.

In case of no response, reconsider the diagnosis with repeat patch testing including for topical corticosteroids and assessing microbiology/mycology. Consider an empirical course of anti-staphylococcal therapy (e.g. flucloxacillin).

How to measure success

Success should be measured by improvement in patient symptoms. Although DLQI is not ideal for measuring response, it is the most widely used patient reported outcome measure. The minimum clinically important difference is a reduction of DLQI by 4, but ideally the DLQI target should be an absolute score of below 5. A patient specific outcome should also be negotiated, e.g. able to shampoo hair without discomfort, be able to play a round of golf, be able to access fingerprint scanning on their cell phone, etc.

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