

# Hand Dermatitis: Utilizing Subtype Classification to Direct Intervention

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## Opinion statement

Hand dermatitis is a common inflammatory skin condition with typical clinical signs including redness, hyperkeratosis, scaling, edema, vesicles, and fissuring. It often becomes chronic and disabling, leading to significant morbidity, disability, and economic loss. The pathogenesis of hand dermatitis is multifactorial, and the treatment is challenging. The most common exogenous cause of hand dermatitis is contact with irritants such as soap and water, leading to an irritant contact dermatitis. Atopic dermatitis is a significantly associated endogenous cause of hand dermatitis. Exposure to a contact allergen is also an important cause of hand dermatitis, and it is recommended that all patients with persistent or treatment refractory hand dermatitis undergo patch testing, especially prior to the initiation of systemic immunosuppressive therapy. Preventative measures including the identification and elimination of irritants or allergens are essential in all cases of hand dermatitis. In addition, a stepwise approach of escalating therapy is advised. Initially, we recommend frequent application of emollients, along with the use of a potent topical corticosteroid daily for up to 6 weeks. A concomitant short, 1–2-week course of oral steroids may also be needed in severe cases to achieve rapid resolution. Once well controlled, maintenance therapy with either twice weekly topical corticosteroid application or topical calcineurin inhibitor application may be indicated for cases of chronic dermatitis. If topical corticosteroids are ineffective and the patient has access to phototherapy, we would next recommend a course of localized PUVA or UVB therapy. In severe, refractory cases of hand dermatitis unresponsive to topical steroids and phototherapy, systemic therapy such as an oral retinoid or immunosuppressive medication may be considered.

## Introduction

Hand dermatitis (HD) is a common inflammatory skin condition with an estimated lifetime prevalence of 15–20 % and a 1-year prevalence of about 10 % [1]. The most important risk factors for persistent and chronic hand dermatitis include female sex, atopic dermatitis, and disease onset before the age of 20 [2–6]. Due to its chronic relapsing course, HD has a high public health impact, often resulting in long-term sick leave or unemployment [4, 7]. Furthermore, the vast majority of patients experience negative psychosocial consequences and a lower quality of life [1, 8, 9]. The incidence of occupationally related cases of HD is estimated to be >0.7 persons per 1000 per year [10]. Based on a survey of 621 Danish patients with occupational HD, 19.9 % were on prolonged sick leave while 23 % had lost their jobs over the course of 1 year [7]. A higher prevalence has been seen in occupational groups engaged in wet work or frequently exposed to irritants and allergens such as hairdressers, cooks, health care workers, florists, housewives, machine operators, and cleaners [11]. In a cross-sectional survey of 24 outpatient centers in Germany, the estimated financial cost of HD was >\$2000 per year [12].

Classification of HD is often based on etiology and morphology (Table 1); however, it should be noted that HD is often of a multifactorial etiology. Furthermore, causative factors are not necessarily related to the clinical morphology, which may vary over time. A recommended approach toward the diagnostic evaluation of HD is provided in Table 2. Common exogenous causes of HD are irritant contact dermatitis (ICD), caused by cumulative

exposure to irritants, and allergic contact dermatitis (ACD), a delayed-type hypersensitivity reaction to contact allergens. A significant endogenous risk factor for HD is atopic dermatitis, as approximately one third of HD patients have a history of being diagnosed with atopic dermatitis [13]. Not only is atopic dermatitis associated with an earlier onset of HD, it also portends a poor prognosis with increased severity and duration of disease [13].

Morphologically, HD may have a varied presentation. Vesicular dermatitis, or pompholyx, presents as a vesicular eruption on the palms, sides of fingers, and soles that recurs every few weeks to months [2, 14]. It is strongly related to an atopic diathesis and/or ACD, especially nickel sensitization [15]. ACD may generalize beyond the hands, and the dorsal hands may be preferentially involved [16]. Hyperkeratotic HD is characterized by erythematous, infiltrated, oozing plaques that evolve into dry hyperkeratotic plaques with fissuring on the palms and fingers [2, 14]. Hyperkeratotic HD is classically endogenous and treatment refractory. ICD may also present with hyperkeratosis [16, 17]. Pulpitis is a variant of hyperkeratotic dermatitis with fissuring that is localized to the fingertips [14]. It is associated with atopy and worsens in the winter. Predominance of the first three fingers may suggest occupational ICD or ACD, especially when localized to the dominant hand. Interdigital dermatitis involves the finger web spaces with erythema and scaling and is often irritant in nature [2, 14]. Finally, nummular dermatitis may be localized to the dorsal hands but more commonly is a part of a generalized eruption [2, 14].

## Treatment

HD is often multifactorial in nature; thus, the treatment of HD is challenging and typically requires multiple treatment approaches, including identification

**Table 1. Classification of hand dermatitis**

| Causative factors           | Morphological variants |
|-----------------------------|------------------------|
| Irritant contact dermatitis | Hyperkeratotic         |
| Allergic contact dermatitis | Vesicular              |
| Protein contact dermatitis  | Interdigital           |
| Atopic dermatitis           | Pulpitis               |
| Idiopathic                  | Nummular               |

**Table 2. Diagnosis of hand dermatitis**

## Careful history including:

- Occupational and recreational exposures to irritants and allergens
- Quantitation of wet work, including frequency of hand washing
- Time course of dermatitis in relation to exposures
- Personal/ Family history of atopic dermatitis

## Physical exam of hands:

- Distribution and morphology of dermatitis
- Involvement of wrists, finger webs, nails
- Correlate physical exam with irritant or allergen exposure

## Full skin exam with focus on:

- Feet
- Atopic findings

and avoidance of contributing triggers. Acute hand dermatitis should be treated quickly and aggressively to avoid the progression to chronic dermatitis, and information on proper preventative measures should be given to each patient.

## Prevention

### Irritant avoidance

ICD constitutes one of the most common causes of HD, resulting from wet work, long-term glove use, and exposure to irritants such as detergents, organic solvents, or metal fluids [18–20]. Wet work is considered any activity where there is skin exposure to water or occlusive gloves for >2 h per day or washing of the hands >20 times per day [21].

Irritant avoidance is one of the most important elements in the successful treatment of HD. Primary prevention involves decreasing incidence in the at-risk, healthy population by limiting exposures. Secondary prevention aims to decrease the prevalence of already existing HD through timely diagnosis and treatment. For prompt resolution, clinically relevant irritants need to be identified and eliminated both at home and in the work place. Preventive programs targeting occupations with increased wet work have been hugely successful [22–25]. These programs have emphasized educating at-risk populations on specific protective measures: [24, 26–28]

- Use of work-appropriate gloves when performing wet work or working with irritants
- Use of gloves for as short of a time as possible
- If wearing gloves for >10 min, wear cotton gloves underneath
- Keeping gloves intact, clean, and dry inside
- Washing hands with lukewarm water only when visibly soiled and drying completely before donning gloves

- Using alcohol disinfectant instead of water whenever hands are not visibly soiled
- Avoid wearing rings at work
- Application of moisturizers after work and before bedtime

## Allergen avoidance

ACD should be considered in any patient with chronic treatment refractory dermatitis [17]. This is especially true if vesicles or dorsal hand involvement are present or if the patient is in the working population [29]. Common allergens in HD include preservatives, rubber chemicals, fragrances, topical antibiotics, metals, and plant allergens [29]. Contact allergens can be identified by patch testing to a standard series along with personal care products, with addition of supplemental series as appropriate based on exposure history.

Protein contact dermatitis is a less common cause of HD characterized by urticaria or vesicles that occur within minutes of contact with specific foods, enzymes, grains, animal protein, and latex. It is thought to be due to a combination of immediate and delayed-type hypersensitivity reactions [30, 31]. In the case of suspected protein hand dermatitis, prick testing or IgE testing is warranted [32•]. There is currently insufficient evidence to recommend for or against atopy patch testing.

## Topical treatments

### Emollients

Emollients are essential in the prevention and treatment of HD, providing hydration and contributing to improved skin barrier function [23, 33, 34]. Ointments are preferred over creams, as creams are more likely to contain preservatives and irritating emulsifiers. Emollients have been shown to be effective in treating contact dermatitis and decreasing pruritus and flares [23, 34]. Adherence is key and can be increased by allowing the patient to choose a preferred emollient that he/she will more likely use. Lipid rich moisturizers have been found to be most effective [35]. Plain petroleum jelly may be considered as effective as more specialized emollients containing skin lipids, although further studies are required given the emerging evidence suggesting enhanced improvements utilizing lipid-based barrier repair therapies [36, 37]. Furthermore, in a small fraction of patients, there can be intolerance to the polycyclic aromatic hydrocarbons contained in plain petrolatum [38]. In the case of hyperkeratotic HD, keratolytic emollients may be beneficial, and fissures can be sealed with glue to improve pain and healing.

### Topical corticosteroids

Topical corticosteroids are very effective at decreasing inflammation and are the mainstay in the acute treatment of HD. In acute and severe episodes, a potent topical steroid should be employed to rapidly and effectively decrease inflammation [39, 40]. Side effects of potent topical steroids include atrophy [41], decreased repair of the stratum corneum [42, 43], and possibly tachyphylaxis, although this remains to be substantiated. Thus, it is recommended to use potent topical steroids for a short period of time at a once daily application,

which has been shown to be as effective or even superior to twice a day application [44]. The American Academy of Dermatology recommends once daily use of topical steroids for 1 month followed by maintenance therapy two to three times per week [45••]. Chronic HD can be treated with an intermittent dosing regimen to decrease the risk of adverse effects including atrophy. In ICD, limited data suggests that topical steroids are somewhat effective [46, 47]. If the disease does not respond to or worsens despite treatment, it is important to consider development of ACD to topical corticosteroids [48]. In these cases, patch testing to topical corticosteroids, their vehicle agents and the patients' current therapeutics should be considered. It is important to note that a 7-day read is essential, as up to 30 % of positives may not appear with a standard day 5 reading [49••].

### Topical calcineurin inhibitors

Topical calcineurin inhibitors (TCI), tacrolimus and pimecrolimus, are approved for the treatment of atopic dermatitis and are usually used in conjunction with topical steroids at an alternating dose to decrease adverse effects of steroids. Side effects of TCI include temporary burning, sensitivity to ultraviolet light, and worsening of skin infection. In a small trial involving patients with chronic HD, tacrolimus was as effective as mometasone furoate [50]. In two randomized clinical trials, pimecrolimus was not significantly more efficacious than vehicle cream likely due to its lower potency [51, 52]. Concerns about potential risk of lymphoma and photo-carcinogenesis based on effects of systemic therapy with calcineurin inhibitors have been raised, but an expert review and observational data have not substantiated these concerns [51–55].

### Topical retinoid

In a phase I–II open-label randomized clinical trial, 55 patients with chronic severe hand dermatitis were treated with bexarotene 1 % gel with or without hydrocortisone 1 % ointment or mometasone furoate 0.1 % ointment. After 22 weeks of treatment, 79 % patients treated with bexarotene gel monotherapy had a response rate of  $\geq 50$  % clinical improvement while 39 % patients had a  $\geq 90$  % clearance rate. These outcomes were not significantly improved by combination with topical steroids [56]. Adverse events included irritation, transient stinging and burning, and flaring of existing hand dermatitis, especially in patients with atopic dermatitis. Five patients withdrew from the trial due to inadequate response and four due to adverse events. As a potent topical retinoid, bexarotene gel is contraindicated in pregnancy and is considered pregnancy category X.

### Phototherapy

When HD is refractory to first-line treatments with topical steroids, phototherapy can be used as a second-line treatment, including psoralens ultraviolet A (PUVA) and ultraviolet B (UVB) therapy. Psoralens are available in both oral as well as topical formulations, with no significant difference in efficacy between these two formulations [57, 58]. In a randomized control trial of 35 patients, both PUVA and UVB were effective in treating HD, though PUVA was more effective [59]. In another smaller, prospective comparison study of 12 patients

with HD, UVB was just as effective as PUVA [60]. Adverse effects of UV-treatment include erythema, swelling, and burning, along with nausea from oral methoxsalen. There is also an increased risk of non-melanoma skin cancer with long-term use of phototherapy, especially in the case of PUVA. A practical drawback to phototherapy is lack of inconvenience, as multiple clinical visits are required. Oftentimes, phototherapy is used in conjunction with topical steroids to treat chronic HD.

## Systemic therapies

### Oral retinoids

Oral retinoids can be used in chronic HD, especially when hyperkeratosis is present. Though not approved in the USA, alitretinoin is approved in Europe and Canada for the treatment of severe chronic HD. In a large, randomized clinical trial of 1032 patients with chronic HD, 48 % of patients were clear or almost clear within 12–24 weeks of alitretinoin when compared to 17 % of patients treated with placebo [61, 62]. Acitretin is another oral retinoid that is often used to treat recalcitrant HD. It should be noted that this is an off-label use of this medication. In a smaller, open-label, placebo-controlled study of 29 patients with hyperkeratotic dermatitis of the palms, there was a 51 % improvement in patients treated with acitretin 30 mg daily when compared to a 9 % improvement in the placebo group [63]. Common side effects of retinoids include dry skin, dry lips, and hyperlipidemia. Retinoids are teratogenic; therefore, pregnancy prevention and monthly pregnancy tests are mandatory in all women of child bearing potential. In the case of alitretinoin, pregnancy prevention 1 month before, during, and 1 month after completion of the medication is required in women of childbearing potential. For acitretin, in the USA, pregnancy prevention measures are indicated during treatment and for at least 3 years after discontinuation of the drug.

### Systemic corticosteroids

Short courses of oral glucocorticoids can be used to rapidly control acute severe HD or acute flare-ups of chronic HD. Frequent or long-term use of systemic corticosteroids is discouraged because of well-known side effects of osteoporosis, osteonecrosis, hyperglycemia, hypertension, immunosuppression, glaucoma, cataracts, and suppression of the hypothalamic-pituitary-adrenal axis.

### Other oral immunosuppressive agents

Oral immunosuppressants are used as a third-line treatment for recalcitrant chronic HD. Large randomized controlled trials are lacking; instead, the use of oral immunosuppressive agents is largely based on studies showing efficacy of their use in treating atopic dermatitis. Limited data, however, are available regarding the treatment of hand dermatitis.

#### *Cyclosporine*

Cyclosporine is the most frequently used oral immunosuppressive medication in treating recalcitrant HD. In a randomized, double-blinded study

of 41 patients with chronic HD, patients treated with cyclosporine 3 mg/kg/day had a 50 % improvement in disease when compared to those treated with betamethasone dipropionate cream, who had a 32 % decrease in disease activity [64]. These results, however, were not statistically significant. Cyclosporine requires careful monitoring as potential side effects include nephrotoxicity, hypertension, hyperkalemia, hyperlipidemia, hypertrichosis, and increased risk of infection and malignancy secondary to immunosuppression [65]. Blood pressure and lab studies including a comprehensive metabolic panel, magnesium level, complete blood count, fasting lipids, urinalysis with microscopic examination, and/or uric acid levels should be checked at baseline and routinely [65].

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#### *Azathioprine*

In a retrospective study looking at patients with severe refractory non-bullous inflammatory dermatoses, azathioprine was seen to improve atopic dermatitis and pompholyx [66, 67]. Azathioprine can result in profound bone marrow toxicity, especially in patients who lack adequate levels of thiopurine methyltransferase (TPMT) enzyme [65]. Thus, it is advised to measure blood levels of TPMT before starting azathioprine. Other adverse effects of azathioprine include hypersensitivity reaction, nausea, vomiting, diarrhea, hepatotoxicity, fatigue, respiratory distress, hepatotoxicity, and an increased risk of infection and malignancy [65]. A comprehensive metabolic panel, complete blood count, urinalysis, pregnancy test, TPMT testing (as mentioned above), and/or quantiferon testing should be done at baseline and complete blood count should be checked routinely thereafter while on azathioprine [65].

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#### *Methotrexate*

In a case series of five patients with severe, recalcitrant pompholyx, the addition of methotrexate (MTX) 15–20 mg weekly to the treatment regimen led to improvement of their disease and a decreased oral corticosteroid requirement [68, 69]. Side effects of methotrexate include hepatotoxicity, liver cirrhosis, pancytopenia, pulmonary fibrosis, and teratogenicity [65]. These side effects can be minimized through careful monitoring of complete blood count and comprehensive metabolic panel. At baseline, hepatitis B and C serologies should be checked as well. A liver biopsy will need to be considered for patients on long-term and high cumulative doses of MTX [65].

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#### *Mycophenolate mofetil*

The use of mycophenolate mofetil (MMF) at doses of 2–3 g per day is mostly supported anecdotally with a few case reports in the literature [70, 71]. MMF is an immunosuppressive medication that was originally used to prevent graft rejection. It blocks de novo purine synthesis by inhibiting inosine monophosphate, and its action is primarily in lymphocytes. At doses of 2 or 3 g per day, MMF is well tolerated. Major side effects include gastrointestinal symptoms such as nausea, loose stools, and cramping, along with an increased risk of infection [65]. In transplantation studies,

leukopenia and anemia have been observed. At baseline, a complete blood count, comprehensive metabolic panel, pregnancy test, hepatitis B and C serologies, and/or quantiferon test should be checked. Routine lab studies including liver function tests, kidney function, basic metabolic function, and complete blood counts are monitored while patients are on MMF [65].

## Conclusions

Hand dermatitis is a multifactorial disease that is challenging to treat. The identification and elimination of potential irritants and allergens is essential in the successful treatment of HD, and a stepwise approach of escalating treatment is recommended. Frequent application of emollients and daily application of topical corticosteroids for up to 6 weeks is initially recommended. A concomitant short course of oral corticosteroids may also be needed to achieve complete and rapid resolution. Second-line treatment includes PUVA or UVB therapy. In severe, refractory cases of HD, systemic treatment with an oral retinoid, cyclosporine, or other oral immunosuppressive medications may be warranted.

## Compliance with ethical standards

### Conflict of interest

Gina P. Kwon declares that she has no conflict of interest.

Caroline A. Tan declares that she has no conflict of interest.

Jennifer K. Chen declares that she has no conflict of interest.

### Human and animal rights and informed consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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