

Management of Atopic Hand Dermatitis



Anne-Sofie Halling-Overgaard, MS^a, Claus Zachariae, MD, DmSci^a,
Jacob P. Thyssen, MD, PhD, DmSci^{a,b,*}

KEYWORDS

• Atopic dermatitis • Hand eczema • Irritant contact dermatitis • Allergic contact dermatitis

KEY POINTS

- Atopic dermatitis in childhood is associated with occupational hand eczema in adulthood.
- Patients with filaggrin gene mutations have an increased risk of developing hand eczema but only in the context of atopic dermatitis.
- It is important to identify and prevent exposure to culprit irritants and allergens that may cause or worsen hand eczema.
- First-line therapy in patients with atopic dermatitis and hand eczema includes emollients and topical corticosteroids.

INTRODUCTION

Atopic dermatitis (AD), a common chronic inflammatory skin disease characterized by pruritus and eczematous lesions, affects 10% to 20% of the population.¹ The condition often begins during early childhood; although some patients obtain full remission, AD persists or relapses in many patients during adolescence and adulthood.¹

Hand eczema (HE) occurs often in children and adults with AD.^{2–4} In this clinical review article, the authors provide an overview of the most important clinical aspects of HE in AD, with a special emphasis on management.

CLASSIFICATION AND CLINICAL SUBTYPES OF HAND ECZEMA

HE is divided into various subtypes based on either cause or morphology (**Table 1**), and several proposals exist in the literature.^{5–7} It can be difficult to clinically appreciate such complex

classification because there is often no apparent link between the etiologic and morphologic picture and because the morphology of lesions, and even the cause, often change over time in affected patients.^{5,7,8} Interested readers may access a clinically meaningful guideline with photographs showing the different subtypes.⁵

Acute HE is characterized by erythema, edema, and vesicles, whereas chronic HE predominately displays hyperkeratosis, scaly skin, and fissures.^{2,5} The location of HE depends to a certain degree on the different etiologic subtypes. Hence, HE, primarily located to the dorsal aspects of the fingers and hands, is a common anatomic predilection site of AD in children and adults² but importantly also a frequent comorbidity due to irritant contact dermatitis (ICD) and/or allergic contact dermatitis (ACD) to for example, rubber chemicals.^{9–11}

The most frequent HE etiologic subtypes include ICD, ACD, protein contact dermatitis (PCD), and HE as a natural part of AD, so-called atopic HE (AHE).^{6–8} According to a cross-sectional multicenter study

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^a Department of Dermatology and Allergy, Herlev and Gentofte Hospital, University of Copenhagen, Kildegårdsvej 28, Hellerup DK-2900, Denmark; ^b National Allergy Research Centre, Herlev and Gentofte Hospital, University of Copenhagen, Kildegårdsvej 28, Hellerup DK-2900, Denmark

* Corresponding author. Department of Dermatology and Allergy, Herlev and Gentofte Hospital, University of Copenhagen, Kildegårdsvej 28, Hellerup DK-2900, Denmark.

E-mail address: Jacob.p.thyssen@regionh.dk

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Table 1
Subtypes of hand eczema

Morphologic Subtypes	Etiologic Subtypes
• Chronic fissured HE • Recurrent vesicular HE • Hyperkeratotic palmar eczema • Pulpitis • Interdigital eczema • Nummular hand eczema	• Allergic contact dermatitis • Irritant contact dermatitis • Protein contact dermatitis • Atopic HE

Data from Menne 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(1):3–12.

including 319 European patients with HE, the most frequent subtypes were ICD (21.5%), combined ACD and ICD (15.2%), ACD (15.2%), vesicular HE (9.3%), combined AHE and ICD (7.8%), AHE (5.8%), and hyperkeratotic eczema (5.3%).⁶

ACD is diagnosed by a positive patch test reaction and a concomitant history of exposure to the contact allergens. Acute inflammation due to ACD is often characterized by the presence of vesicles and erythema, particularly if allergen exposure is significant; but chronic ACD can be noncharacteristic with hyperkeratosis and fissures. The location of ACD normally begins at the site of skin contact (Fig. 1) but may spread to involve major parts of the hands, and even body, if exposure persists.⁸ Traditional clinical examples of ACD include glove-related ACD on the wrists and dorsal aspects of the hands, nickel-related ACD on finger tips (pulpitis), and chromium-related ACD from cement on the palms.

ICD is diagnosed by a history of significant exposure to an irritant as well as a temporal relationship between irritant exposure and onset of HE. ICD can be located on both the palmar

and dorsal aspects of the hands, the distal dorsal aspects of the fingers, as well as in the interdigital space (Figs. 2–4). From a clinical experience, wet workers often experience their first onset of ICD on the knuckles and interdigital space and then experience a gradual spread to the hands; but, as opposed to ACD, generalization is less pronounced. Although the risk of ICD is clearly increased in adult patients with AD, particularly those who are engaged in risk occupations,^{9–11} ICD may also develop in young children who play with their hands in wet sandboxes or frequently suck on their hands to seek comfort. Notably, ICD is mostly limited to the sites of skin exposure.⁸

PCD is diagnosed by a positive skin-prick test and a history of exposure to protein-containing material, such as food that results in instant urticarial eruptions, pruritus, or erythema. Following repeated exposure to the allergenic proteins, there is a gradual development of eczema.⁸ PCD is particularly common among patients who handle food professionally. The presence of PCD is often overlooked, if patch testing is not supplemented by skin-prick testing with the suspected allergens. A retrospective study found a high prevalence of AD (48.6%) in patients with PCD and in patients with other food-related hand dermatoses, indicating that patients with AD are more susceptible to cutaneous food allergen exposure.¹²

Traditional AHE is located on the wrists and dorsal aspects of the hands (Figs. 5 and 6),⁵ where patients are exposed to cold temperatures, dry air, solar irradiation, and air pollution, all factors that may negatively affect the skin barrier and cause dermatitis.^{13–15} Notably, the different subtypes often co-occur, because AHE may be complicated by ICD, ACD, and even PCD.⁵ In these multifactorial cases, there is often vesicular dermatitis in the palms or interdigital space as well.

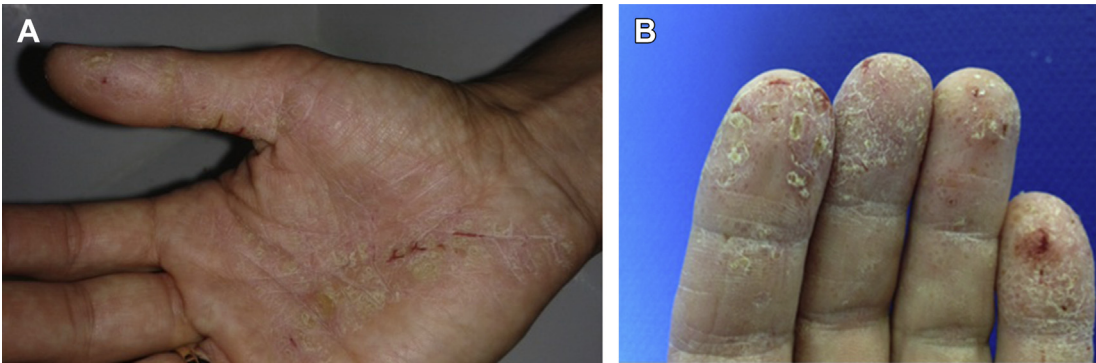


Fig. 1. (A) Chronic allergic contact dermatitis of the palms with hyperkeratosis and fissures caused by nickel allergy. (B) Acute and chronic allergic contact dermatitis on the fingers due to methyisothiazolinone exposure with erythema and vesicles as well as scales, hyperkeratosis, and fissures.

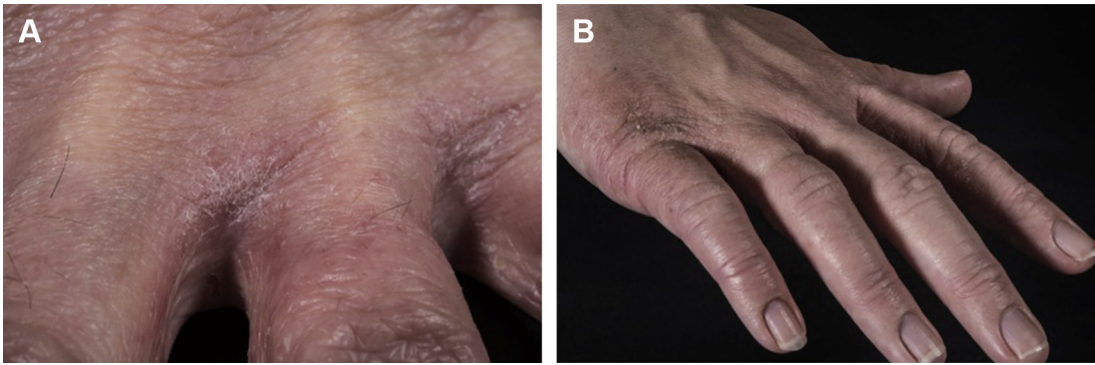


Fig. 2. (A) Irritant contact dermatitis in the interdigital space with erythema and scales. (B) Irritant contact dermatitis with spread to the knuckles following initial interdigital space eczema.

THE SKIN BARRIER IN PATIENTS WITH ATOPIC DERMATITIS

Patients with AD display skin-barrier impairment due to epidermal filaggrin deficiency caused by exogenous and/or inherited factors. These factors include a low relative humidity, excessive UV exposure, water, detergents, topical corticosteroids, and filaggrin gene (*FLG*) mutations. Epidermal filaggrin deficiency affects several important pathways, which puts further stress on the barrier.¹⁶

The dysfunctional skin barrier makes patients with AD significantly more susceptible to irritant exposure and increases their risk of developing ICD.^{9–11} For example, application of an irritant sodium lauryl sulphate (SLS) (0.5% of SLS in an aqueous solution) result in a significantly higher skin reaction and transepidermal water loss in patients with AD irrespective of their *FLG* mutations status compared with controls.¹⁷



Fig. 3. Severe, irritant contact dermatitis on the dorsal side, caused by water exposure.

EPIDEMIOLOGY OF HAND ECZEMA IN PATIENTS WITH ATOPIC DERMATITIS

In 1985 Rystedt¹⁸ found an association between the occurrence of AD in childhood and presence of HE in adulthood. Since then, several studies have confirmed the potent association between these clinical entities, with the highest prevalence of HE in adolescents and young adults.^{2–4} Rystedt¹⁹ showed that HE is most common in patients with AD aged 25 to 29 years, likely because of a combination of risk factors including domestic and occupational wet work.^{2,20}

The association between AD and HE is strongest in patients with severe AD, in patients with AHE since childhood, and in patients with persistent AD on other parts of the body.^{3,4,18} Furthermore, AD is associated with more severe HE^{21,22}; the resolution of HE is less likely in patients with AD compared with patients without AD.¹⁹ In general, studies that examined the association between AD and HE have not addressed the difference between AHE and HE due to ICD and/or ACD.^{3,4,18} Although it has been a topic of



Fig. 4. Irritant contact dermatitis on the palms with typical vesicles.



Fig. 5. Severe AHE on the dorsal aspects in (A) a patient with ichthyosis vulgaris and (B) a child with AD.

intensive discussions, it remains unclear whether AD also increases the risk of ACD; but it is likely nickel allergy and AD are associated.^{23,24} It is well known that *FLG* mutations represent a major predisposing factor for AD²⁵; mutation carriers have characteristic palmar hyperlinearity, xerotic skin, as well as incidental skin fissures. Epidemiologic studies have examined whether *FLG* mutations increase the risk of HE, and it seems that mutations primarily increase the risk of HE in the context of AD.^{26–29} Affected patients have characteristic early onset of HE and tend to have more persistent and severe disease.^{10,26,28,29}

Most studies investigating the risk of occupational HE (OHE) in patients with AD have not addressed the difference between OHE due to ICD and ACD, respectively. However, Rystedt¹⁹

found that 77% of OHE cases were due to ICD, whereas only 6% were due to ACD. Studies have found that patients with AD have an increased risk of developing OHE when in health care, hairdressing, and metalwork.^{4,9–11,21,22,30,31} Furthermore, patients with AD tend to have more severe OHE, which results in a higher number of sick-leave episodes, job loss, and use of topical corticosteroids.^{10,22} Interestingly, a recent questionnaire study found the prevalence of AD to be significantly lower among hairdresser apprentices compared with general population controls.³² This finding indicates that patients with AD now may tend to avoid risk occupations, likely as a result of information given by physicians.

MANAGEMENT OF HAND ECZEMA IN PATIENTS WITH ATOPIC DERMATITIS

The therapy for HE is similar in patients with and without AD. Moreover, AD on the hands is treated the same way as AD on other parts of the body. Useful guidelines on AD therapy have been published, and the authors refer interested readers to these.^{33–36}

Regarding the particular management of AHE, it is obviously important to first determine if there is another cause than AD (**Box 1**). A careful patient interview should, therefore, be performed whereby irritant, allergen, and protein exposure at work and home is evaluated. Irritant exposure should be quantified, for example, by the number of hand washes per work day, frequency of hand disinfectant use, frequency of glove changes per work day, and finally accumulated time of wet work, including total glove use. Also, pH and the presence of irritant chemicals in products should be examined. Protein exposure is often related to food exposure; here it is important to ask about instant pruritus, edema, and erythema following



Fig. 6. AD on the wrist.

Box 1**Recommended management of hand eczema in patients with atopic dermatitis**

- Categorize HE subtypes: morphologically and etiologically.
- Evaluate occupational and domestic irritant and allergen and protein exposure.
- Quantify possible irritant exposure, for example, the number of hand washes per work day, frequency of hand disinfectant use, frequency of glove changes per work day, and presence of low or high pH as well as irritant chemicals in products.
- Identify contact allergen exposure from ingredient labels and material safety data sheets, and consider examination of products for their exact chemical content with advanced chemical analysis.
- Diagnose possible PCD by examining whether patients have experienced instant pruritus, edema, and erythema (urticarial) following skin contact with food.
- Assess whether resolution of dermatitis occurs over holidays and weekends.
- Consider patch testing and skin-prick testing.
- Educate patients in the management of HE and AD.

skin contact. Also, remember to ask about resolution of dermatitis over holidays and weekends and about episodes of sick leaves and change in job routines. Allergen exposure should be assessed by reading ingredient labels of cosmetic products (sometimes easier to have patients bring in their products), performing spot tests for allergen release (eg, for nickel, cobalt, chromium, and formaldehyde), and collection of material safety data sheets. Some clinics may also examine products for their exact chemical content with advanced chemical analysis, such as high-performance liquid chromatography.

The next step is often patch testing. Recommendations on patch testing patients with AD were recently published.³⁷ Notably, patch testing in patients with AD might be associated with misdiagnosing, because irritant reactions can be misinterpreted as allergic reactions.³⁷ If a clinically relevant contact allergy is identified, patients are recommended to avoid future allergen exposure. Similar for irritants, patients should protect their hands and avoid triggers.⁸ Among patients with suspected PCD, skin-prick testing is recommended.³⁸

Apart from the etiologic categorization of HE, the clinician should describe the development and morphology of HE, as it sometimes provides information related to cause. Always begin by asking where dermatitis began anatomically and how it spread to other parts. Moreover, ask for the presence of vesicles, as this could indicate ACD, whereas interdigital and dorsal location could indicate ICD; but again, there should be an exposure. It is also very important that patients are educated in the management of HE and AD. Randomized controlled trials have found educational programs to be very effective.^{39,40}

MEDICAL THERAPY FOR PATIENTS WITH ATOPIC DERMATITIS WITH HAND ECZEMA

The main purposes of medical therapy are to relieve symptoms, suppress inflammation, and improve the skin barrier (**Box 2**). Therapeutic guidelines vary between countries; however, the variation seems to be small.^{5,8} The combination of emollients and topical corticosteroids (TCS) represents the first-line treatment.^{5,8,33,37,41} Lipid-rich hypoallergenic emollients improve the skin barrier and are always indicated in patients with AD.^{5,8} Moderately potent TCS should be applied daily, often in periods of weeks to months,⁵ and should then be replaced by application twice per week for a maintenance regimen.⁴² However, TCS can cause atrophy, hereby limiting its chronic use. Albeit it is uncommon, patients with AD also have an increased risk of contact allergy to TCS, sometimes warranting patch testing.^{43,44} It is the authors' experience that AHE, even in children, often requires mometasone furoate therapy, or a similar strength, to obtain adequate control. Topical calcineurin inhibitors (TCIs) are an alternative to TCS^{5,8} because they do not cause atrophy, but they are rarely efficient in case of palmar dermatitis.⁴¹ Coal tar represents an effective therapy that has antiproliferative, anti-inflammatory, and antipruritic effects.⁴⁵ A study found that coal tar partly works through restoration of *FLG* expression in patients with AD.⁴⁶ Coal tar can be mixed with emollients in 5% or 10% solutions and works well for nightly therapy with cotton gloves.

Eczema in patients with AD is frequently colonized by *Staphylococcus aureus*⁴⁷; patients may, therefore, benefit from antimicrobial medicaments and antiseptic potassium permanganate baths.⁴⁸

Box 2**Recommended medical therapy for hand eczema in patients with atopic dermatitis**

- The main purposes of medical therapy are to relieve symptoms, suppress inflammation, and improve the skin barrier.
- Lipid-rich hypoallergenic emollients are always indicated in patients with AD.
- TCS is first-line therapy and should be applied daily, often in periods of weeks to months, and then replaced by maintenance therapy 2 times per week.
- TCIs can be used as an alternative to TCS but are normally less effective on palms.
- Coal tar is an alternative to TCS and TCI and can be mixed with emollients in 5% or 10% solutions and work as nightly treatment with cotton gloves.
- Patients with AD colonized with *Staphylococcus aureus* can sometimes benefit from antimicrobial therapy and antiseptic potassium permanganate baths.
- UV therapy is used as second-line therapy when topical therapy is insufficient, but it requires that patients can come for irradiation 2 to 3 times per week for 8 to 12 weeks or more.
- As last options, patients can receive systemic therapy, including acitretin, alitretinoin, azathioprine, enteric-coated mycophenolate sodium, cyclosporine, and methotrexate; but few of these are labeled for HE and AD, and efficacy is variable.

Abbreviations: TCIs, topical calcineurin inhibitors; TCS, topical corticosteroid.

A study showed that the antimicrobial therapy and a daily potassium permanganate bath significantly improved AD in patients with *Staphylococcus aureus* colonization.⁴⁸ The authors sometimes advise patients to use potassium permanganate baths for their hands 1 to 2 times per week with good results.

If topical therapy is insufficient, UV therapy (UV-B or psoralen-UV-A) can be used as second-line therapy.^{5,36,41} UV therapy has many positive effects, including suppression of the immune system, improvement of the skin barrier, reduction of *Staphylococcus aureus* counts, as well as pruritus.⁴⁹ However, patients should be willing, or able, to come for irradiation 3 times per week for 12 weeks or more.

As a last option, patients can receive systemic therapy. Apart from prednisolone, which should only be used on very rare occasions, there are different medicaments available to treat AHE or other types of HE, including acitretin, alitretinoin, azathioprine (AZA), enteric-coated mycophenolate sodium (EC-MCP), cyclosporine, and methotrexate.^{5,8,36,41} Alitretinoin and acitretin should in general be reserved for hyperkeratotic HE, and remember that they may worsen the already impaired skin barrier in AD. Although cyclosporine in many countries is labeled for AD, continuous treatment of extended periods greater than 1 year should be avoided. A randomized controlled trial compared cyclosporine with EC-MCP and found both medicaments to be effective in patients with severe AD; however, EC-MCP resulted in longer relapse-free periods and a more favorable

side effect profile.⁵⁰ Another randomized controlled trial found AZA and methotrexate to be equally effective in the treatment of severe AD, as about 40% in each group improved.⁵¹ Recently, studies have examined drug survival of systemic therapy in patients with AD.^{52,53} One study found that the median overall drug survival was 201 days for AZA, whereas it was 322 days for EC-MCP. Discontinuation of AZA was mainly due to side effects, whereas discontinuation of EC-MCP was mainly due to ineffectiveness.⁵³ Another study found that methotrexate's overall drug survival was 223 days and discontinuation of methotrexate was mainly due to side effects (25%) and ineffectiveness (15%).⁵²

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