Evidence-Based Management of Hand Eczema

Schuttelaar, Marie L.A.; Oosterhaven, Jart A.F.; Romeijn, Geertruida L.E.; Christoffers, Wietske A.; Voorberg, Angelique N.

Published in:
Kanerva's Occupational Dermatology

DOI:
10.1007/978-3-319-40221-5_89-2

Evidence-Based Management of Hand Eczema

Marie Louise A. Schuttelaar, Jart A. F. Oosterhaven, Wietske A. Christoffers, Geertruida L. E. Romeijn, and Angelique N. Voorberg

Contents

M. L. A. Schuttelaar (✉) · J. A. F. Oosterhaven · W. A. Christoffers · G. L. E. Romeijn · A. N. Voorberg
Department of Dermatology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands
e-mail: m.l.a.schuttelaar@umcg.nl; j.a.f.oosterhaven@umcg.nl; w.a.christoffers@umcg.nl; g.l.e.romeijn@umcg.nl; a.n.voorberg@umcg.nl

Abstract

Hand eczema is a common skin disease with a wide variation in morphology and a complex etiology based on endogenous and exogenous factors.

The diagnosis of hand eczema is based on patient history, exposure assessment,

S. M. John et al. (eds.), *Kanerva's Occupational Dermatology*, https://doi.org/10.1007/978-3-319-40221-5_89-2

physical examination, and the results of patch testing. Management of hand eczema starts with education of the patient on the etiology of the disease, and the needed changes in behavior regarding skin care and preventive measures, and avoidance of relevant exposure factors. In many cases, medical treatment is needed for successful management of the disease; use of medication can only be successful with proper education and avoidance of relevant exposure.

Keywords
Hand eczema · Management · Diagnosis · Topical therapy · Systemic therapy

1 Core Messages

- Hand eczema is a common skin disease with a wide variation in morphology and a complex etiology based on endogenous and exogenous factors.
- The diagnosis of hand eczema is based on patient history, exposure assessment, physical examination, and patch testing.
- Management of hand eczema starts with education of the patient on the etiology of the disease, and the needed changes in behavior regarding skin care and preventive measures, and avoidance of relevant exposure factors.
- In many cases, medical treatment is needed for successful management of the disease; use of medication can only be successful with proper education and avoidance of relevant exposure.

2 Introduction

Hand eczema, or hand dermatitis, is a common disease with a 1-year prevalence of approximately 10% in the general population (Thyssen et al. 2010). Clinically hand eczema is characterized by erythema, infiltration, hyperkeratosis, edema, and vesicles. In many cases, secondary signs such as scaling, hyperkeratotic areas, fissures, erosions, and bacterial infections, chiefly with *Staphylococcus aureus*, are seen. In addition to inflammation of the skin of the hands, often also the wrists and forearms are involved.

The disease tends to vary in clinical symptoms over years: as in many forms of eczema, the morphology of hand eczema in one case may substantially vary over time. In acute hand eczema erythema, edema and vesicles are characteristic. Over time infiltration, hyperkeratosis and fissures are more often seen. In most cases the acute inflammation passes into a skin disease with periods of acute eruptions. Some distinguished types of hand eczema are predominantly monomorphous: The typical form is known as hyperkeratotic palmar eczema (tylotic eczema). Typically the most important symptom in hand eczema, itch, is most often not present in tylotic eczema. As in other cases with hand eczema with fissures, pain is the predominant complaint of these patients.

3 Classification of Hand Eczema

To date, still no consensus has been reached on the classification of hand eczema. This is mostly because the disease is multifactorial, involving endogenous and exogenous factors.

One way of looking at this is from a clinical standpoint. Menné et al. proposed a classification based on hand eczema morphology as seen in daily practice, with types of hand eczema that may be distinguishable but can overlap and also change during the course of the disease:

- Chronic fissured hand eczema
- Recurrent vesicular hand eczema
- Hyperkeratotic palmar eczema
- Pulpitis
- Interdigital eczema
- Nummular hand eczema (Menné et al. 2011)

Because a clear link between morphology and etiology is still not found and because etiology is important for proper management of hand eczema, Menné et al. also put forward a separate etiological classification. This was updated a few

years later, and this resulted in a combined morphological/etiological classification:

- Irritant contact dermatitis (ICD)
- Allergic contact dermatitis (ACD)
- Atopic hand eczema (AHE)
- Protein contact dermatitis (PCD)/contact urticaria (CU)
- Vesicular endogenous hand eczema
- Hyperkeratotic endogenous hand eczema
- Unclassified (Diepgen et al. 2015; Agner et al. 2015)

An issue with this classification is that multiple items seem mutually exclusive by definition, while in clinical practice, they are still often taken together. This again reflects the multifactorial nature of hand eczema.

It seems that more knowledge is needed about what actually happens in the skin of hand eczema patients and whether a difference in function of (epi)dermal components could be linked to morphology. Until then, the classifications mentioned above should be used to characterize hand eczema.

4 Diagnosis

4.1 Patient History

The first step in the management of hand eczema is to make an accurate diagnosis. To do so a careful taken history is needed. The following aspects should be considered (see also Table 1):

Medical history
Localization of the lesions
Morphology of the lesions
Time course
Exposure assessment (Diepgen et al. 2007)

A history of atopic dermatitis is a risk factor for developing atopic dermatitis. Coenraads and Diepgen reported that an individual with a history of atopic dermatitis, without exposure to irritants, has twice as much chance on developing hand eczema. If this individual has a skin-risk occupation, the chance doubles again (Coenraads and Diepgen 1998). Previous episodes of hand eczema should also be asked for as well as previous episodes of allergic contact dermatitis.

The clinical pattern, i.e., the localization of the lesions and the morphology of the lesions, is also

Table 1 How to make the diagnosis

Medical history: Previous episodes of hand eczema History of atopic dermatitis Other skin diseases, e.g., psoriasis
Localization and morphology of the lesions according to Menné et al. 2011: Chronic fissured hand eczema Recurrent vesicular hand eczema Hyperkeratotic palmar eczema Pulpitis interdigital eczema Nummular hand eczema
Time course: Time of onset: changes in contact factors (occupational, domestic, hobby) Effect of days off and holiday Seasonal changes
Exposure assessment: Occupational, domestic, hobby – frequency and duration of contact with: Irritants Allergens Skin protection: glove use
Patch testing: with the European baseline series and with additional series (depending on exposure) In case of positive test: evaluate the relevance of the patch test reaction

of importance. Tylotic hand eczema, with a predominant hyperkeratotic aspect and with typical minimal signs of itching, for instance, has an unknown etiology but is most common in middle-aged men and is aggravated by mechanical trauma. Fingertip eczema (pulpitis), especially when localized on the first three digits of the nondominant hand, is often seen in chefs, due to repeated contact with irritants or allergens, e.g., garlic. Pulpitis on the same three digits of the dominant hand can occur in dentists and dental technicians due to contact with acrylic substances used in dental prostheses. Chapping on the dorsa of the hands and in particular in the finger webs is often a first sign of the development of irritant contact dermatitis.

The time of onset as well as the time course of the eczema sometimes can reveal the etiological factor, especially when it concerns eczema with a recent onset. For chronic hand eczema, the time of onset is less important, because it is usually ill-defined and not useful in establishing the final diagnosis. Other items to be asked for are seasonal variations, remission over weekend and holidays, and the time between re-exposure at the workplace and a flare-up. Seasonal variations may help to establish the type of eczema, e.g., atopic hand eczema improves in most patients during summer, whereas dyshidrotic eczema often is active during summer. Occupational hand eczema improves when a patient has a few days of work and can even disappear after a long period of vacation. After resumption of work, allergic contact dermatitis usually recurs relatively quickly, whereas irritant contact dermatitis recurs more slowly.

4.2 Exposure Assessment

A careful history about occupational and non-occupational exposure to irritants and allergens is necessary (Agner 2011; Veien 2011). The assessment of exposure to irritants and allergens must be tailored to the individual patient and should be quantified: frequency, duration, and combination of exposures. Exposure to physical irritants, cold air, and low relative humidity should be asked for. Information about the frequency of handwashing and the usage of soap and alcohol-based skin disinfectants is important. This should be supplemented by reviews of products, material safety data sheets, and, when relevant, contact with manufacturers, employers, and visits to the workplace.

A workplace visit is relevant when occupational contact dermatitis is suspected. It can be worthwhile to obtain information about the kind of substances the skin is exposed to and the duration of exposure. When a workplace visit is performed, it is important to bear in mind that the employee with hand eczema is probably the one with most knowledge of the work process and contact factors instead of, for instance, the personnel manager. Based on this assumption, a workplace visit should always be held in the presence of the involved employee. During a "walk through" of the workplace, specific information about chemicals and processes can be obtained. The work process has to be examined, and engineering controls such as exhaust hoods, ventilation, and the general environment of the workplace, including temperature and relative humidity, should be noted (Adams 1999). To obtain specific exposure information about allergens, several data sources are available:

Product labeling, product declarations, and material safety data sheets
Inquiries to manufacturers or suppliers
Chemical analysis
Product databases
Textbooks and other literature (Flyvholm 2001)

The process of documenting exposures to skin irritating circumstances includes:

Wet work: wet hands for more than 2 h per working day, frequent handwashing (>20 times daily), >2 h use of liquid-proof gloves per working day
Intensive contact with:
Detergents
Alkaline substances
Oil products, including cutting oils

Organic solvents
Mechanical traumas, such as friction (Menné et al. 2011)

A workplace visit can also reveal how hands are cleaned and if barrier creams, gloves, and emollients are used and in which way they are used. When protective gloves are used, it is important to evaluate if they are appropriate to the tasks (Adams 1999).

Based on the information obtained during a workplace visit, the relevance of occupational influences can be determined.

4.3 Physical Examination

Physical examination extent of hand eczema includes a description of the physical signs and if possible the clinical type of the hand eczema. During the course of treatment, possible variations in clinical aspects in relation to variations in exposure can be seen. This phenomenon of alterations in clinical aspects of the disease of hand eczema in relation to variations in day-to-day exposures has not yet been well described: No clear link between morphology and etiology is recognized yet (Johansen et al. 2011).

4.4 Patch Testing

Patch testing should be performed in every patient with chronic hand eczema. The test should be carried out according to the guideline of the European Society of Contact Dermatitis (Johansen et al. 2015). Additional information regarding patch testing can be found in chapters "▶ Patch Test Concentrations and Vehicles for Testing Contact Allergens" and "▶ Patch Testing with Patient's Own Materials Handled at Work" (Table 1).

5 Management of Hand Eczema

Based on several reviews performed by Bauer et al., Van Gils et al., and Van Coevorden et al., it can be concluded there still is a lack of evidence-based guidelines for the treatment and management of hand eczema (Bauer et al. 2018; van Coevorden et al. 2004; van Gils et al. 2011). Based on clinical practice, both etiological factors as well as morphological characteristics must be taken into account in the choice which treatment is best. The treatment of hand eczema has to be adjusted to the specific situation of the individual patient. It is important to treat acute hand eczema quickly and effectively, to prevent chronicity. At the same time, an effort should be made to determine the etiology of the eczema, and instruction on skin care and prevention should be given as described below.

5.1 Education

For the prevention of hand eczema, often a two-way approach is followed:

Relevant contact factors are to be eliminated if possible; for example, hand eczema is strongly related to wet/dirty activities and/or wearing occlusive gloves for long periods.
Skin barrier function should be maintained and supported by preventive measures (e.g., (cotton under) gloves or emollients) if avoidance of contact factors is not possible.

The review on effectiveness of prevention programs for hand dermatitis from Van Gils et al. (2011), however, reports on studies that have shown difficulties in the use of individual preventive measures, such as handwashing procedures, protective gloves (Meding and Swanbeck 1989), and recommended high-fat skin care products (Flyvholm et al. 2005; Mygind et al. 2006). To study workers' behavior in using preventive measures for hand dermatitis, the attitude, social influence, and self-efficacy (ASE) model is a useful theoretical framework (de Vries et al. 1988). The ASE model is based on the theory of planned behavior (Ajzen 1985). According to this model, the intention regarding the behavior of a person at risk for hand dermatitis is determined by three factors:

Attitude (awareness of risks and willingness to learn), which is important for the implementation of an intervention (Grol and Grimshaw 2003)

Social influence (e.g., the behavior of colleagues and/or the lack of role models [Erasmus et al. 2009]) and self-efficacy (confidence of a person in performing learned behavior)

Influence of barriers and resources and knowledge and skills for the prevention of hand dermatitis

The goal to maintain a normal healthy skin in a working population with increasing prevalence of atopy and increasing levels of exposure to skin irritating circumstances and allergens may be achieved only via primary education of the risks the skin is exposed to and how to prevent disease to evolve. In cases of developed skin disease, dermatological treatments, altered individual behavior, and skin exposure conditions (also in the working environment) as well as self-determination are needed. The correlation between health risks and individual behavior needs to be explained to the affected patient and the population at risk. In many professions consistent skin protection and skin care plays a significant role in the prevention of hand eczema. It cannot be taken for granted that preventive measures are applied in daily practice by the exposed worker in a correct and effective manner. That is why both the worker at risk and the patient with hand eczema actively need to be educated.

Prevention of occupational skin diseases and maintenance of a healthy skin can be achieved by the conditioning of individual behavior via specific educational programs in addition to dermatological care.

5.2 Secondary and Tertiary Prevention of Hand Eczema

Hand eczema can only be successfully managed, and recurrence of the disease can only be avoided when the etiology of the disease is attacked. Only a healthy skin can withstand the daily exposures to all kind of allergens and skin irritants. Moreover, after a period of skin inflammation, the skin is more vulnerable to the etiological factors for a long time. Ongoing exposure to etiological factors causing the hand eczema while the inflammation is treated with anti-inflammatory drugs is one of the major causes of the development of chronic hand eczema.

Several studies have shown a positive effect of educational interventions in the prevention of occupational hand eczema in different high-risk occupations (Van Gils 2011; Schwanitz et al. 2003; Wilke et al. 2012; Ibler et al. 2012). Whereas primary prevention aims to decrease the incidence of occupational hand eczema by limiting the exposure to relevant contact factors, secondary prevention measures aim to spot early skin changes in order to rapidly implement corrective measures. By motivating workers to use adequate skin protection and fostering a feeling of empowerment in terms of taking responsibility for one's own health, skin protection education is recommended as an important part of secondary prevention (Diepgen et al. 2015).

For those cases of severe and/or chronic occupational skin diseases in which outpatient prevention strategies have been ineffective, interdisciplinary (inpatient) prevention programs have been developed, including treatment, education, and rehabilitation measures to prevent work loss (tertiary individual prevention (TIP), Skudlik et al. 2009; Brans et al. 2016).

For more information about prevention strategies in occupational skin diseases, see chapter "► Prevention and Rehabilitation."

5.3 Avoidance Strategy

Avoidance can be used as a therapeutic as well as diagnostic tool. In many cases, contact to allergens and/or irritants is responsible for the development of hand eczema. Avoidance of these allergens and irritants is the first step in managing hand eczema. Based on clinical history exposure assessment and patch testing, the next step of avoiding possible relevant exposure will probably reveal the etiological factors that are of clinical relevance in a given case.

Management of (occupational relevant) hand eczema involves an (occupational) hygienist strategy which means try to avoid relevant exposure starting at the source of possible exposure factors. This means that prevention starts with first-line prevention strategies which are based on technical-organizational hazard control. Various procedures can be used for prevention and/or protection, for instance, use of potent allergens in closed systems, automation of processes, replacing the need of workers to expose their skin to irritants or allergens, and the replacement of dangerous substances to less dangerous, i.e., less irritant, less toxic, and less allergenic ones (Bauer et al. 2018; Lachapelle 2001). Furthermore, it is important to use irritants and allergens in an appropriate way, as advised by the manufacturer and to have better knowledge of the chemical nature of the different products used at work.

Management of (occupational relevant) hand eczema requires correct knowledge of working conditions as part of the exposure assessment. In many cases, unfortunately first-line preventive measures cannot practically be implemented at a sufficient level. In these cases, secondary (mostly individual) protective measures have to be used. These secondary (individual) preventive measures involve a three-step strategy:

1. The use of protective gloves and/or barrier creams
2. Correct cleansing
3. The use of moisturizers after work (Grief et al. 2000; Lachapelle 2001)

5.4 Gloves

In many occupations, the use of gloves is indispensable, and although the use of gloves is generally accepted as preventive measure against the development of irritant or allergic contact dermatitis, there is hardly any proof of their efficacy. Bauer et al. state in their comprehensive Cochrane review: "No RCT or CT on the efficacy of glove use in the prevention of OHID were identified. Actually, guidelines and recommendations on glove use are mainly based on rules and regulations as well as on expert opinion" (Bauer et al. 2018). However, this does not imply that the use of gloves is unnecessary, because the findings in several studies suggest a positive effect of the use of gloves as part of a prevention program in preventing the development of hand eczema (Jungbauer et al. 2004; Kutting and Drexler 2008). For more detailed information about the use of gloves, see chapter "▶ Protective Gloves," where Boman documents this area in detail.

5.5 Barrier Creams

Barrier creams or protective creams are used in the workplace, to prevent the skin against the effect of hazardous agents. They are also known as invisible gloves. This term however is incorrect and leads to a false feeling of safety, because a barrier cream cannot give full protection against any workplace substance (Kresken and Klotz 2003; Loffler and Effendy 2002). Workers like the use of barrier creams, because they are easy to use and most of the times comfortable during use. Unfortunately, they most seldom are a satisfactory replacement for gloves (Lachapelle 2001). Although barrier creams cannot fully protect the skin, their use is seen as a common preventive measure in preventing the development of contact dermatitis in skin-risk occupations (Berndt et al. 2000; Kresken and Klotz 2003; Kutting and Drexler 2003). There are specific barrier creams for specific types of exposure available, e.g., detergents, metal working fluids, and solvents. The efficacy of these barrier creams has been investigated with several in vivo and in vitro test methods, but it is unclear if these test methods are suitable to simulate real workplace conditions (Kutting and Drexler 2003). Up to now there is a lack of evidence that barrier creams show a long-term protective effect in the primary prevention of contact dermatitis under real workplace conditions (Bauer et al. 2018; Kutting and Drexler 2003, 2008). According to 98% of experts participating in a worldwide survey, barrier creams are no more effective than moisturizers in the prevention of contact dermatitis (Hogan et al. 1990).

More important than the emphasis on special ingredients of a cream is the proper use of a cream: regular, frequent, and correct (Berndt et al. 2000) on a cleaned and properly dried skin (Kresken and Klotz 2003). For more detailed information about barrier creams, see chapter "▶ Protective Creams and Emollients," where Elnser documents this area in more detail.

5.6 Cleansing

Washing the skin with water and soap is, for most people, an everyday activity which in itself seems harmless. In several professions, however, skin cleansing with water and soap is a major cause of hand eczema. In several studies the irritant effect of water has been demonstrated. In an experiment in 30 normal young adult males, Willis demonstrated that continuous exposure to closed water cups for 72–144 h induced intense subacute dermatitis. Clinical observation of the test sides showed moderate to marked maceration, confluent erythema, and edema (Willis 1973). Kligman induced dermatitis in normal skin by applying water-soaked patches for up to 2 weeks. He noticed damage to epidermal cells after 2 days as well as swollen and detached corneocytes and signs of an inflammatory response after a week (Kligman 1996). Ramsing and Agner studied the effect of water on experimentally irritated skin in 21 healthy women. Subclinical skin irritation was elicited by immersing both hands into a 0.5% aqueous solution of sodium lauryl sulfate (SLS) for 10 min, once on day 1 and twice on day 2. Then the selected hand was exposed 15 min to water, twice a day over a period of 10 days. The other hand served as control. Based on their findings that there were no significant changes in transepidermal water loss (TEWL) but only a significant increase in skin blood flow, they concluded that water does not influence skin barrier function but is capable of aggravating subclinical inflammatory reactions in previously irritated skin (Ramsing and Agner 1997). The temperature of water also seems to be of importance. Berardesca et al. and Ohlenschlaeger et al. both demonstrated that water temperature influences the irritant capacity of a surfactant. Berardesca et al. demonstrated that a 5% SLS solution at a temperature of 40 °C caused significant more skin damage than SLS at 4 °C and 20 °C. Furthermore they showed that the only significant difference between untreated skin and SLS at 4 °C was a decrease in skin hydration induced by SLS at 4 °C. All other parameters (TEWL, reflectance, desquamation, and erythema) showed no significant differences. Based on these findings, they concluded that a low SLS solution temperature has a very mild effect on stratum corneum structures and that water temperature during washing has an important effect on the onset of irritant contact dermatitis (Berardesca et al. 1995). Ohlenschlaeger et al. performed a similar study. They divided 20 healthy volunteers into two groups. One group immersed one forearm in a 0.5% SLS solution at 40 °C and the other arm into a 0.5% SLS solution at 20 °C. The second group immersed their arms into sterile water of the same temperature as the SLS group. Immersion into the sterile water caused no significant changes in any parameter (clinical observations, TEWL, electrical capacitance, and erythema). Immersion into SLS at 40 °C caused a significant increase in TEWL in comparison to immersion in SLS at 20 °C. Based on their findings, they conclude that change in water temperature can be a simple way to prevent irritant contact dermatitis (Ohlenschlaeger et al. 1996).

Not only water and its temperature have a negative effect on skin barrier function. The use of soap also has a damaging effect. Cleansing the skin can lead to changes in basic properties of the skin such as change in pH of the skin surface and change of barrier function of the skin as measured by TEWL. Using a soap or detergent in general leads to an increase in pH (Dykes 1998) which in turn can lead to an increased growth of several bacteria (Korting and Braun-Falco 1996; Schmid-Wendtner and Korting 2006). A single washing is enough to increase TEWL and thus impair skin barrier function. Repetitive washing leads to further deterioration of TEWL, and even 12 h after finishing repetitive washing, there is still a marked change in skin function (Grunewald et al. 1995). Based on these findings, it seems logic to advise

the use of only water when washing hands, but in daily practice this is not attainable, especially not in workers with manual dirty work or in healthcare. The use of a "mild" soap seems second best, because manufactures claim these mild soaps to be suitable for the use on sensitive skin. Unfortunately the term mild does not imply that they are not irritating for the skin. Loden et al. demonstrated large differences in irritation potential between eight mild soaps, and some of them showed considerable damaging effects on skin. Furthermore they proved the presence of residues of surfactants on the skin after rinsing with water. These residues were large enough to produce barrier impairment (Loden et al. 2003).

In some occupations skin becomes dirty due to exposure to grease, oil, metal particles, carbon black, or lubricants. In these occupations, skin cleansing with an ordinary liquid detergent generally is not enough for proper removal of dirt. Therefore, so-called heavy duty cleansers are used. Generally they contain a higher percentage of detergents, combined with a scrubbing agent and/or a solvent (Tupker and Coenraads 1996). Both scrubbing agents (Klotz et al. 2003; Mahler et al. 2010; Wigger-Alberti et al. 1999) and solvents cause increased TEWL values and thus impairment to the skin barrier function. Klotz et al. demonstrated that products without solvents but with a mild natural oil/surfactant combination can clean skin comparable to cleansers with solvents. They also demonstrated that the use of scrubbing agents is often unnecessary (Klotz et al. 2003). If the use of a cleanser with scrubbing agent cannot be avoided, one should seek for a scrubbing agent with the least irritating potential. Based on their research on effects of various grit-containing cleansers on skin barrier function, Wigger-Alberti et al. demonstrated that a polyethylene-grit-containing cleanser is less irritating compared to apricot kernel grit-containing cleansers (Wigger-Alberti et al. 1999). Mahler et al. performed a similar study with walnut shell powder and castor wax beads and showed the castor wax beads to be less irritant for the skin with comparable cleaning properties (Mahler et al. 2010). If a heavy duty cleanser is used, wiping off the mixture of dirt and cleanser with paper before rinsing with water can be more effective in removing dirt than rinsing the dirt and cleanser with water without prior paper wiping (Tupker and Coenraads 1996).

In healthcare not dirt but nosocomial pathogens must be removed from the skin, because transmission of these pathogens, which can lead to infections, mostly occurs by the hands of healthcare workers (Kampf et al. 2009; Rocha et al. 2009). Two types of hand hygiene procedures are available: handwashing with water and soap or hand disinfection with an alcohol-based rub. Handwashing with water and soap should be an exception, because water and soap have a more irritant effect on the skin than the use of a disinfectant (Pedersen et al. 2005; Slotosch et al. 2007), and frequent handwashing may result in skin damage (Grunewald et al. 1995). In healthcare workers, this skin damage can lead to a higher bacteria count on the hands compared to healthy hands (Rocha et al. 2009), and when damaged hands are being washed, this is not effective in reducing their contamination (de Almeida et al. 2007). This does not mean that hands should not be washed at all, but handwashing should be limited to only a few circumstances: before and after work, when visible soiling has to be removed, after visiting the bathroom, and occasionally to reduce microbial colonization of the skin, for example, in the case of contamination by spores of *Clostridium* difficile. In all other situations, hand disinfection is preferred (Kampf et al. 2009). Although many healthcare workers complain about burning sensations after the use of an alcohol-based hand rub, this is not caused by an irritating effect of the hand rub but rather caused by a pre-irritated skin due to frequent handwashing and the use of occlusive gloves. If this burning sensation results in more handwashing instead of using a hand rub, more skin damage will occur (Kampf et al. 2009; Kampf and Loffler 2003, 2007). Based on the information in this paragraph, some advice concerning hand cleansing can be derived, as summarized in Table 2.

Table 2 Hand cleansing advices

Use lukewarm water
Do not use soap if it is not necessary
If soap with a scrubbing agent has to be used, make sure to use a scrubbing agent that is the least irritating for skin
If a heavy duty cleanser is used, wipe off the mixture of dirt and cleanser with a paper towel and then rinse off the remnants thoroughly with running water
Rinse hands thoroughly when soap is used
For healthcare workers: the use of an alcohol-based hand rub is the preferred hand hygiene procedure

5.7 Emollients

Emollients, also referred to as moisturizers, are the most prescribed products in dermatology, and their use aims at maintaining skin integrity and well-being of the individual by providing a healthy appearance (Loden 2005). Emollients are commonly used by patients with hand eczema and are considered to be its maintenance treatment. Although they are used for prevention and treatment of hand eczema, there is only little evidence for their effectiveness. In a systematic review on interventions for prevention of occupational irritant hand dermatitis (OIHD), Bauer et al. found four randomized controlled trials about the use of moisturizers that met the inclusion criteria. Included patients in these studies were metal workers who are exposed to cutting fluids. All trials found reduced risk of developing OIHD when applying moisturizers. Two of these studies reported a higher skin barrier function, measured as transepidermal water loss, due to the usage of moisturizers. This outcome was however not significant. Only one study found a significant higher rate of skin hydration in the treatment period compared to baseline (Bauer et al. 2018). In a randomized controlled trial about the use of emollients by Kucharekova et al., an emollient with ceramides was compared to a regular petrolatum-based emollient. The study showed a significant improvement in clinical signs of hand eczema in both groups. The difference between the groups, however, was not significant (Kucharekova et al. 2003). In a different randomized controlled trial about the use of emollients by McCormick et al., an oil-based lotion was compared to a barrier cream based on Vaseline in a group of healthcare providers. This study showed a significant improvement in clinical signs and patient reported outcome for both groups, with significant better results in the oil-based lotion group, even though the frequency of handwashing was remarkably higher in this group (McCormick et al. 2000). One study by Lodéo et al. looked into emollients versus no treatment at all. The emollient that was used in this study contained 5% ureum. The group that wasn't allowed to use any treatment had an exacerbation of their hand dermatitis in a median time of 2 days, while the median time until exacerbation was 20 days for the emollient using group. For severity, no significant difference was found between both groups (Lodén et al. 2010).

Looking at four different guidelines for the use of emollients in the treatment for hand dermatitis, all recommend the use of emollients to protect and restore the damaged skin barrier (Johnston et al. 2017; Diepgen et al. 2015; Menné et al. 2011; Lynde et al. 2010). The guideline by Menné et al. bases their recommendation on two studies in which it was proven that the skin barrier on both hands and arms had improved in 5 to 12 days after using emollients.

For more detailed information about emollients, see chapter "▶ Emollients: Effects, Evidence, and Side Effects", where Agner documents this area in detail.

6 Treatment of Hand Eczema

Various treatment modalities exist, such as topical and systemic corticosteroids, phototherapy, topical calcineurin inhibitors, oral retinoids, and systemic immunosuppressive; however, the number of randomized controlled trials regarding the treatment of hand eczema is limited.

6.1 Topical and Systemic Corticosteroids

In the treatment of hand eczema, the use of topical corticosteroids is generally accepted. Topical steroids have an anti-inflammatory, immunosuppressive and antiproliferative mechanism of action. They are considered to be the first-line therapy (Diepgen et al. 2007; English et al. 2009; McFadden 2001) and are the most prescribed treatment for hand eczema (Soost et al. 2012).

As a rule, potent topical steroids are used for approximately 1 month, followed by either a treatment-free period or a maintenance treatment of two or three times a week (Drake et al. 1996). Treatment with topical steroids has to be combined with treatment with emollients at all times. The choice of the steroid potency and vehicle is influenced by eczema severity, morphology and location, age of the patient, and the duration of treatment (Agner 2000; Drake et al. 1996). It is important to keep in mind that topical corticosteroids can have disadvantages as well: skin atrophy, tachyphylaxis, adrenal suppression, and allergic reactions (English et al. 2009; Robertson 2009). Furthermore, there is a small group that is refractory to treatment with topical steroids. Patients are classified refractory to treatment with topical steroids if they are referred to a dermatologist and were prescribed phototherapy or systemic immunosuppressive/immune-modulating treatment, such as oral corticosteroids, alitretinoin, or acitretin. In the study by Diepgen et al., the prevalence of being refractory to topical steroids was estimated to be 0.2–0.4% (Diepgen et al. 2007). Furthermore, in a study by Crane et al., a strong age pattern corresponding with the working age was found. Through the working years, prevalence increased and showed a small decline in old age (Crane et al. 2017).

Multiple studies have compared different topical corticosteroids with each other, but only two studies evaluated the benefits of corticosteroids on hand eczema in comparison to a placebo vehicle. Veien et al. compared mometasone furoate cream three times a week and a group of mometasone furoate cream twice a week with a group using placebo for a period of 9 weeks or until patients were clear of hand eczema. Emollients were allowed in all groups. Both mometasone groups showed a significant difference in no occurring relapses of hand eczema compared to the placebo group. Minimal adverse advents occurred, suggesting that long-term intermittent treatment of hand eczema with topical corticosteroids such as mometasone is effective and safe (Veien et al. 1999). In a trial by Kircik et al., clobetasol propionate 0.05% foam was compared to a vehicle foam. Both were applied twice daily for 15 days. There was a significant improvement of the severity of hand eczema based on a subjective global assessment score in both groups, with a significant higher percentage of improvement in the clobetasol using group. This significant difference only applied to improving 1 degree in severity scores, since the difference between both groups disappeared when compared for improvement of at least 2 degrees in severity scores (Kircik et al. 2013).

Although systemic treatment with corticosteroids might be beneficial for short-term treatment, there are no randomized controlled trials found to support this assumption. In textbooks and articles on treatment of hand eczema, it is advised to avoid long-term use because of the severe adverse side effects of long-term therapy (Agner 2000; McFadden 2001; Soost and Worm 2009).

More detailed information about the use of topical and systemic corticosteroids is given by Worm in chapter "► Topical and Systemic Corticosteroids".

6.2 Phototherapy

Phototherapy can be used in various forms to treat hand eczema, e.g., UVA-1, oral PUVA, topical PUVA, topical bath PUVA, and UVB. UV phototherapy is, together with topical corticosteroids, the major standard treatment for hand eczema, but there is only little evidence of a comparative advantage within these categories. An upcoming review found in total ten randomized controlled studies in which the use of phototherapy (UVA, UVB, and PUVA) was investigated. The studies

all differed in design, duration of treatment, and number of treatments per week and included different subtypes of hand eczema. Moreover, the studies, especially the older studies, had various methodological flaws. The question whether PUVA is more effective than UVB could not be answered. Only two randomized controlled trials addressed this question (Brass et al. 2015; Sezer and Etikan 2007). The study of Brass et al. compared the efficacy of narrowband UVB with localized PUVA in 60 patients for 12 weeks. Sezer et al. compared local UVA on the one hand with local narrowband UVB on the other hand thrice a week in 12 participants over a 9-week period. Both studies did not find a comparative advantage of one treatment modality over the other. The question whether phototherapy should be preferred over topical corticosteroids was addressed in only one study (Said et al. 2011). Said et al. studied topical betamethasone valerate 0.1% cream twice daily versus UVA-1 phototherapy thrice weekly in 47 patients with vesicular hand eczema for 6 weeks. The study claimed localized UVA-1 phototherapy was as effective as topical corticosteroids, and even superior in the reduction of itch, though the study was based on a small number of participants and the data was not reproducible.

Although seen as one of the standard treatments for hand eczema, UV phototherapy is due to the numerous hospital visits that are required for this treatment, inconvenient for patients.

For more detailed information about phototherapy, see chapter "▶ Phototherapy," where Breuer documents this area in more detail.

6.3 Topical Calcineurin Inhibitors

The topical calcineurin inhibitors, tacrolimus (Protopic®) and pimecrolimus (Elidel®), are relatively new therapeutic options in the treatment of hand eczema. They provide an alternative to topical corticosteroids, especially since their mode of action is more selective than corticosteroids and do not cause skin atrophy.

Tacrolimus (FK506), produced by the fungus *Streptomyces tsukubaensis*, is a macrolide lactone which binds to calcineurin (Nghiem et al. 2002). The penetration of tacrolimus depends on the concentration, vehicle, and integrity of the epidermal barrier. Most reported side effect of short-term treatment is a transient burning or heat sensation. This starts a few minutes after application and can last for 30–90 minutes (Bornhovd et al. 2001).

Both tacrolimus and pimecrolimus were initially only approved for the treatment of atopic dermatitis, but in the last decade, some publications showed an effect in the treatment of hand eczema. In a randomized observer-blind study with a within-patient left and right design, Schnopp et al. compared tacrolimus with mometasone furoate in 16 patients with dyshidrotic palmoplantar eczema. After 4 weeks, an improvement was shown for both treatments when used for treatment of palmar eczema. Mometasone furoate was superior to tacrolimus in the treatment of palmar eczema. They concluded that treatment with tacrolimus is suitable for use in rotational therapy with mometasone furoate in patients with long-standing disease (Schnopp et al. 2002). Katsarou et al. used a similar scheme of mometasone furoate and tacrolimus. Both groups showed a significant difference in all studied parameters, but there was no difference between the two groups (Katsarou et al. 2012). Krejci-Manwaring et al. performed a randomized double-blind controlled trial in 32 patients with moderate to severe hand eczema. The patients received a 3-week taper of prednisone. Simultaneous to the prednisone taper, a treatment with either twice daily application of topical tacrolimus or vehicle was started to study the effectiveness of tacrolimus in keeping hand eczema in remission after prednisone use. In the tacrolimus group, the mean time to recurrence was 48 days versus 39 days in the vehicle group. Although no statistical differences were found, the reduction in disease symptoms from baseline to week 14 favored tacrolimus over vehicle (Krejci-Manwaring et al. 2008).

Pimecrolimus has only been compared to placebo in studies, while tacrolimus has been compared to both topical corticosteroids as placebo treatments. A large multicenter study by Belsito et al. compared pimecrolimus cream with vehicle cream in patients with chronic hand

eczema. After 3 weeks, at the end of the study, there was a trend toward greater clearance in patients who were treated with pimecrolimus than in those treated with vehicle cream. The difference between the groups was significant only when there was stratification according to palmar involvement (Belsito et al. 2004). In a randomized controlled study by Bauer et al., the time to relapse was compared between pimecrolimus 1% cream and placebo, both applied twice daily. This study did not show any difference between the treatment and placebo group (Bauer et al. 2012). Hordinsky et al. compared pimecrolimus 1% and a vehicle cream, both applied daily and with overnight occlusion. The percentage of success of treatment was equal in both groups, measured by an improvement of patients' investigator global assessment (IGA) score. However, a significant higher proportion of patients experienced relief of pruritus in the pimecrolimus group (Hordinsky et al. 2010).

Further studies need to be done to compare the effects of topical immune modulators such as tacrolimus and pimecrolimus to judge their beneficial effects in relation to other topical treatments. Concluding from the previous mentioned studies, calcineurin inhibitors do not have a more beneficial effect on the severity of hand eczema than topical corticosteroids such as mometasone.

6.4 Retinoids

Retinoids are vitamin A derivatives. Oral retinoids are used since the early 1980s, mainly in patients with hyperkeratotic dermatitis of the palms. The use of oral retinoids is associated with several side effects such as teratogenicity, dry skin, cheilitis, metabolic effects, and hepatic effects. The use of acitretin was studied by Thestrup-Pedersen et al. in a single-blind placebo-controlled study. No additional treatment was given other than emollients. In the patient group treated with acitretin, an overall reduction of 51% in clinical symptoms was seen, compared with 9% reduction in the placebo group. It was concluded that treatment with 30 mg acitretin is efficacious and safe in patients with hyperkeratotic dermatitis of the palms (Thestrup-Pedersen et al. 2001). A downside of acitretin is its prolonged teratogenic effect after withdrawal of the drug.

Alitretinoin (9-*cis*-retinoic acid) is another retinoid for systemic use. The European guideline on hand eczema recommends this systemic drug as first choice treatment of severe chronic hand eczema, refractory to potent topical corticosteroids (Diepgen et al. 2015). Alitretinoin is teratogenic, like acitretin, but this effect wears off quickly within the first month following withdrawal. Its effectiveness was studied by Ruzicka et al. in two large multicenter studies. In the first study, three different dosages (10, 20, and 40 mg/day) of alitretinoin were compared with placebo capsules. The use of alitretinoin led to a significant improvement (Ruzicka et al. 2004) on a physician global assessment scale comprising five categories (clear, almost clear, mild, moderate, severe). In the second study, alitretinoin 10 or 30 mg/day was compared with placebo: a status of clear or almost clear was achieved in 47.7% of patients using 30 mg alitretinoin. In the 10 mg group, this was 27.5% and in the placebo group 16.6%. The difference was statistically significant for both doses compared with placebo (Ruzicka et al. 2008). Fowler et al. found a response rate of 39.6% for alitretinoin 30 mg/day versus 14.8% in placebo. The dropout percentage was high in this study (Fowler et al. 2014). In the trials the hyperkeratotic subtype of hand eczema better to alitretinoin than the vesicular subtype. Four large observational trials generally found similar results for effect. Most reported side effects are headache, dry skin/mucosa, elevated triglycerides/cholesterol, and a lowered TSH (Dirschka et al. 2011; Diepgen et al. 2012; Politiek 2016a, b; Thaçi et al. 2016).

Bissonnette et al. studied the retreatment with alitretinoin in patients who had responded to the treatment in the second study of Ruzicka et al. and relapsed within a 24-week observation period. Response rates (clear or almost clear hands) were 80% in patients retreated with alitretinoin 30 mg/day and 48% in patients retreated with alitretinoin 10 mg/day, compared to, respectively, 8% and 10% in the placebo group. It was concluded that intermittent treatment with alitretinoin is suitable for long-term management of chronic

hand eczema (Bissonnette et al. 2010). Lynde et al. performed a similar study but in patients that did only partially reacted to alitretinoin treatment before. They found lower success rates: 39% for alitretinoin 30 mg/day and 50% for alitretinoin 10 mg/day in inpatients that were treated with these respective doses before (Lynde et al. 2012).

6.5 Systemic Immunosuppressants/ Immunomodulatory Drugs

Systemic immunosuppressants such as cyclosporine, azathioprine, mycophenolate mofetil, and methotrexate are used off-label in severe cases of hand eczema. Although the use of these systemic immunosuppressants is mentioned in several textbooks and articles, there is only little evidence of their effectiveness in the treatment of hand eczema, and head-to-head studies lack. In case treatment with alitretinoin fails, these drugs can be considered as third-line therapy (Diepgen et al. 2015).

Pickenacker et al. described the only case study on the use of mycophenolate mofetil in a patient with dyshidrotic eczema (Pickenacker et al. 1998).

For azathioprine, one randomized controlled trial was performed (Agarwal and Besarwal 2013). In this study azathioprine 50 mg/day was combined with topical application of clobetasol propionate crème 0.05% and compared with application of this crème alone. After 24 weeks, 91% reached complete remission on an unnamed measurement instrument in the azathioprine group versus 39% in the topical corticosteroid group. No side effects were reported. Oosterhaven et al. retrospectively described 30 patients treated with azathioprine in dosages between 50 and 250 mg/day, looking at drug survival. Fifteen patients stopped therapy within 3 months because of side effects. Reported side effects were elevated liver enzymes, lowered hemoglobin, gastrointestinal discomfort, flu-like symptoms, arthralgia, headache, and tiredness (Oosterhaven et al. 2017). Scerri did a retrospective study on the use of azathioprine as monotherapy for non-bullous inflammatory disease. He studied a total of 24 patients of which only 6 had pompholyx (Scerri 1999).

The use of methotrexate in hand eczema treatment is advocated on the bases of only three observational studies. Egan et al. describe an uncontrolled series of five patients with severe palmoplantar pompholyx, who were treated with low-dose methotrexate of 15–22.5 mg/week. Treatment with methotrexate was effective and acted steroid sparing (Egan et al. 1999). O'Shea et al. treated 12 adults with chronic hand eczema with methotrexate in a mean dosage of 12.8 mg/week. After 6 months, none of the patients reached full remission. After 12 months, 40% reached full remission, but at that time only five patients remained in the study (O'Shea and Lugo-Somolinos 2015). Another retrospective study included 42 patients treated with methotrexate 5–10 mg/week with a maximum of 20 mg/week. After 8–12 weeks of treatment, 37% showed a good effect on a retrospective physician global assessment scale. After 1 year, 34% of patients had stopped treatment because of side effects (Politiek et al. 2016a, b). Reported side effects in the studies were elevated cholesterol, triglycerides, and liver enzymes, as well as xerosis cutis, gastrointestinal discomfort, flu-like symptoms, headache, urinary tract infection, hematoma, and tiredness.

From the immunosuppressants mentioned above, only cyclosporine was studied in a randomized, double-blind study in which the use of cyclosporine was compared with the use of topical betamethasone-17,21-dipropionate. Forty-one patients with chronic hand eczema were assigned to either 3 mg/kg/day oral cyclosporine or 0.05% betamethasone-17,21-dipropionate cream. Both cyclosporine and betamethasone-17,21-dipropionate cream improved the eczema. No statistical differences were found between the two treatments regarding effectiveness and adverse events. It was concluded that cyclosporine at 3 mg/kg/day is as effective as topical betamethasone-17,21-dipropionate cream in the treatment of chronic hand eczema (Granlund et al. 1996). In a retrospective study, 102 patients were reported who were treated with two different doses of

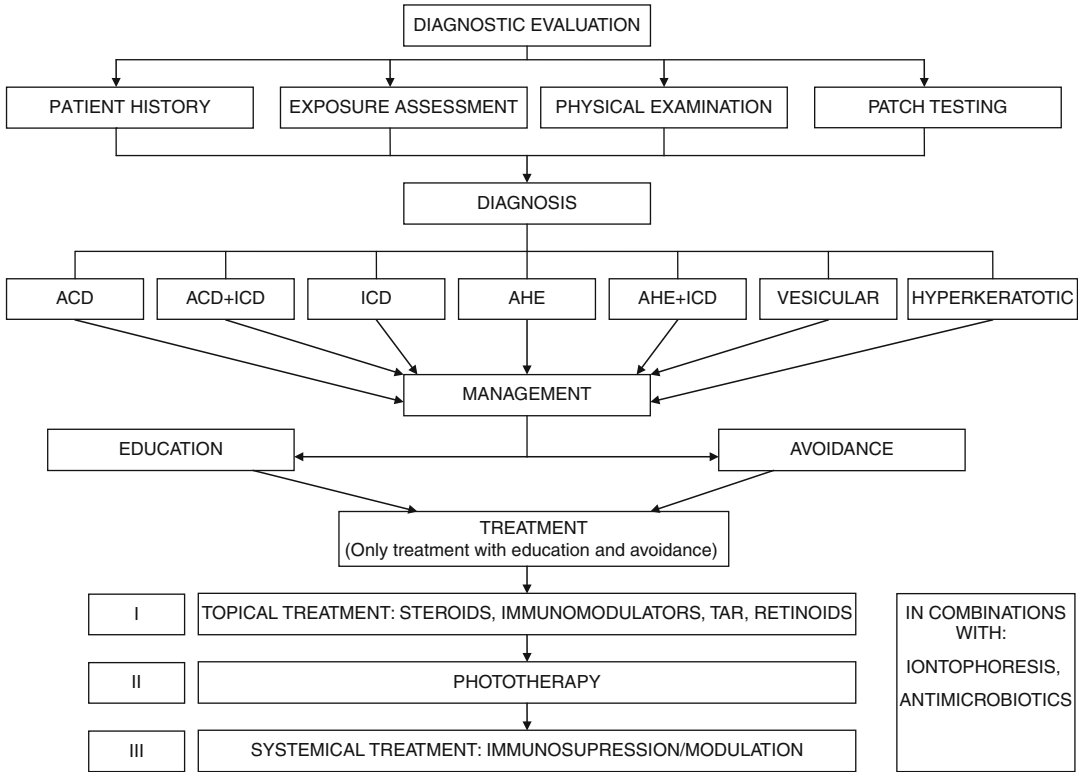

Fig. 1 Hand eczema: from diagnosis to management. ACD, allergic contact dermatitis; ICD, Irritant conctact dermatitis; AHE, Atopic hand eczema

cyclosporine: a step-up regime with a dose of ≤3.5 mg/kg/day gradually increased to a maximum of 5.0 mg/kg/day and a step-down regime with a starting dose of >3.5–5.0 mg/kg/day which was gradually tapered. Primary outcome was drug survival. After 1 year, 45% of patients were still using cyclosporine. Most important reason for drug discontinuation was side effects, mainly hypertension, gastrointestinal discomfort, headache, fatigue, and serum creatinine increase of >30% compared to baseline (Christoffers et al. 2016).

6.6 Tar

Tar is one of the oldest dermatological preparations and is used in the treatment of several disorders, e.g., psoriasis, atopic dermatitis, and seborrheic dermatitis. In clinical setting it is also used in the treatment of hand eczema, but this is done without any evidence of its effectiveness: no literature could be found on this subject.

Hand eczema is treated mainly with immunosuppressive and immunomodulating medication such as topical steroids and UV. As mentioned, in chapters "► Phototherapy" and "► Topical and Systemic Corticosteroids," the use of immunosuppressive medication and its place in dermatitis management is described in more detail. In addition to topical or systemic treatment, other types of therapy can be chosen: iontophoresis and antimicrobiotics (including antimycotics). For the indications and their place in treatment of eczema/dermatitis in general, see chapters "► Therapy: Iontophoresis" and "► Occupational MRSA Infection: Risk Factor, Disposition, Prevention, and Therapy."

Figure 1 summarizes the process from diagnosis to management of hand eczema. The

importance of an adequate etiological diagnosis in addition to the morphologic description of the disease cannot be emphasized enough. Management of the diseased is based on the diagnosis and consists of three pillars:

1. Education of the patient: Each patient with hand eczema needs to know the important etiological factors.
2. Avoidance: The needed changes in behavior regarding skin care and preventive measures and avoidance of relevant exposure factors.
3. Therapy: In many cases a third pillar of medical treatment is needed for successful management of the disease. Many years of experience, however, revealed that medical treatment of hand eczema can only be successful with proper education and avoidance of relevant exposure factors.

References

Adams RM (1999) Prevention, treatment, rehabilitation, and plant inspection. In: Adams RM (ed) Occupational skin disease, 3rd edn. W.B. Saunders, Philadelphia

Agarwal US, Besarwal RK (2013) Topical clobetasol propionate 0.05% cream alone and in combination with azathioprine in patients with chronic hand eczema: an observer blinded randomized comparative trial. Indian J Dermatol Venereol Leprol 79:101–103

Agner T (2000) Guidelines for the management of hand eczema. In: Menné T, Maibach HI (eds) Hand eczema, 2nd edn. CRC Press, Boca Raton

Agner T (2011) Hand eczema. In: Johansen JD, Frosch P, Lepoittevin JP (eds) Contact dermatitis, 5th edn. Springer, Heidelberg

Agner T, Aalto-Korte K, Andersen KE, Foti C, Gimenez-Arnau A, Goncalo M, Goossens A, Le Coz C, Diepgen TL, E.E. and C.D.R. Group (2015) Classification of hand eczema. J Eur Acad Dermatol Venereol 29:2417–2422

Ajzen I (1985) From intentions to action: a theory of planned behaviour. In: Kuhl J, Beckmann J (eds) From cognition to behaviour. Springer, Heidelberg

Bauer A, Lange N, Matterne U, Meurer M, Braeutigam M, Diepgen TL (2012) Efficacy of pimecrolimus 1% cream in the long term management of atopic hand dermatitis. A double-blind RCT. J Dtsch Dermatol Ges 10:426–432

Bauer A, Rönsch H, Elsner P et al (2018) Interventions for preventing occupational hand dermatitis. Cochrane Database Syst Rev 4:CD004414

Belsito DV, Fowler JF Jr, Marks JG Jr et al (2004) Pimecrolimus cream 1%: a potential new treatment for chronic hand dermatitis. Cutis 73(1):31–38

Berardesca E, Vignoli GP, Distante F et al (1995) Effects of water temperature on surfactant-induced skin irritation. Contact Dermatitis 32(2):83–87

Berndt U, Wigger-Alberti W, Gabard B et al (2000) Efficacy of a barrier cream and its vehicle as protective measures against occupational irritant contact dermatitis. Contact Dermatitis 42(2):77–80

Bissonnette R, Worm M, Gerlach B et al (2010) Successful retreatment with alitretinoin in patients with relapsed chronic hand eczema. Br J Dermatol 162(2):420–426

Bornhovd E, Burgdorf WH, Wollenberg A (2001) Macrolactam immunomodulators for topical treatment of inflammatory skin diseases. J Am Acad Dermatol 45(5):736–743

Brans R, Kolomanski K, Mentzel F et al (2016) Multicentre cohort study 'rehabilitation of occupational skin diseases – optimization and quality assurance of inpatient management (ROQ)': results from a 3-year follow-up. Contact Dermatitis 75(4):205–212

Brass D, Farr P, Reynolds N, Stocken D, Macdonald C, Wahie S et al (2015) An observer-blinded randomized controlled pilot study comparing localised psoralen-ultraviolet A with localized narrowband ultraviolet B for the treatment of hand eczema. Br J Dermatol 173:13

Christoffers WA, Politiek K, Coenraads PJ et al (2016) Drug survival of cyclosporine in the treatment of hand eczema: a multicentre, daily use study. J Eur Acad Dermatol Venereol 30:63–66

Coenraads PJ, Diepgen TL (1998) Risk for hand eczema in employees with past or present atopic dermatitis. Int Arch Occup Environ Health 71(1):7–13

Crane M, Webb D, Watson E, Cunliffe T, English J (2017) Hand eczema and steroid-refractory chronic hand eczema in general practice: prevalence and initial treatment. Br J Dermatol 176:955–964

de Almeida E, Borges LF, Silva BL, Gontijo Filho PP (2007) Hand washing: changes in the skin flora. Am J Infect Control 35(6):417–420

de Vries H, Dijkstra M, Kuhlman P (1988) Self-efficacy: the third factor besides attitude and subjective norm as a predictor of behavioural intentions. Health Educ Res 3:273–282

Diepgen TL, Agner T, Aberer W et al (2007) Management of chronic hand eczema. Contact Dermatitis 57(4): 203–210

Diepgen TL, Pfarr E, Zimmermann T (2012) Efficacy and tolerability of alitretinoin for chronic hand eczema under daily practice conditions: results of the TOCCATA open study comprising 680 patients. Acta Derm Venereol 92:251–255

Diepgen TL, Andersen KE, Chosidow O, Coenraads PJ, Elsner P, English J et al (2015) Guidelines for diagnosis, prevention and treatment of hand eczema. J Dtsch Dermatol Ges 13:e1–e22

Dirschka T, Reich K, Bissonnette R, Maares J, Brown T, Diepgen TL (2011) An open-label study assessing the

safety and efficacy of alitretinoin in patients with severe chronic hand eczema unresponsive to topical corticosteroids. Clin Exp Dermatol 36:149–154

Drake LA, Dinehart SM, Farmer ER et al (1996) Guidelines of care for the use of topical glucocorticosteroids. American Academy of Dermatology. J Am Acad Dermatol 35(4):615–619

Dykes P (1998) Surfactants and the skin. Int J Cosmet Sci 20(1):53–61

Egan CA, Rallis TM, Meadows KP et al (1999) Low-dose oral methotrexate treatment for recalcitrant palmoplantar pompholyx. J Am Acad Dermatol 40(4):612–614

English J, Aldridge R, Gawkrodger DJ et al (2009) Consensus statement on the management of chronic hand eczema. Clin Exp Dermatol 34(7):761–769

Erasmus V, Brouwer W, van Beeck EF et al (2009) A qualitative exploration of reasons for poor hand hygiene among hospital workers: lack of positive role models and of convincing evidence that hand hygiene prevents cross-infection. Infect Control Hosp Epidemiol 30(5):415–419

Flyvholm MA (2001) Exposure assessment. In: Rycroft RJG et al (eds) Textbook of contact dermatitis, 3rd edn. Springer, Berlin

Flyvholm MA, Mygind K, Sell L et al (2005) A randomised controlled intervention study on prevention of work related skin problems among gut cleaners in swine slaughterhouses. Occup Environ Med 62(9): 642–649

Fowler JF, Graff O, Hamedani AG (2014) A phase 3, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of alitretinoin (BAL4079) in the treatment of severe chronic hand eczema refractory to potent topical corticosteroid therapy. J Drugs Dermatol 13:1198–1204

Granlund H, Erkko P, Eriksson E et al (1996) Comparison of cyclosporine and topical betamethasone-17,21-dipropionate in the treatment of severe chronic hand eczema. Acta Derm Venereol 76(5):371–376

Grief C, Wigger-Alberti W, Elsner P (2000) Emoillients and barrier creams in the prevention of hand eczema. In: Menné T, Maibach HI (eds) Hand eczema, 2nd edn. CRC Press, Boca Raton

Grol R, Grimshaw J (2003) From best evidence to best practice: effective implementation of change in patients' care. Lancet 362(9391):1225–1230

Grunewald AM, Gloor M, Gehring W et al (1995) Damage to the skin by repetitive washing. Contact Dermatitis 32(4):225–232

Hogan DJ, Dannaker CJ, Lal S et al (1990) An international survey on the prognosis of occupational contact dermatitis of the hands. Derm Beruf Umwelt 38(5): 143–147

Hordinsky M, Fleischer A, Rivers JK, Poulin Y, Belsito D, Hultsch T (2010) Efficacy and safety of pimecrolimus cream 1% in mild-to-moderate chronic hand dermatitis: a randomized, double-blind trial. Dermatology 221(1): 71–77

Ibler KS, Jemec GB, Diepgen TL et al (2012) Skin care education and individual counselling versus treatment as usual in healthcare workers with hand eczema: randomized clinical trial. BMJ 12(345):e7822

Johansen JD, Hald M, Andersen BL et al (2011) Classification of hand eczema: clinical and aetiological types. Based on the guideline of the Danish Contact Dermatitis Group. Contact Dermatitis 65(1):13–21

Johansen JD et al (2015) European Society of Contact Dermatitis guideline for diagnostic patch testing – recommendations on best practice. Contact Dermatitis 73(4):195–221

Johnston GA, Exton LS, Mohd Mustapa MF, Slack JA, Coulson IH, English JS et al (2017) British Association of Dermatologists' guidelines for the management of contact dermatitis 2017. Br J Dermatol 2:317–329

Jungbauer FH, van der Harst JJ, Groothoff JW et al (2004) Skin protection in nursing work: promoting the use of gloves and hand alcohol. Contact Dermatitis 51(3):135–140

Kampf G, Loffler H (2003) Dermatological aspects of a successful introduction and continuation of alcohol-based hand rubs for hygienic hand disinfection. J Hosp Infect 55(1):1–7

Kampf G, Loffler H (2007) Prevention of irritant contact dermatitis among health care workers by using evidence-based hand hygiene practices: a review. Ind Health 45(5):645–652

Kampf G, Loffler H, Gastmeier P (2009) Hand hygiene for the prevention of nosocomial infections. Dtsch Arztebl Int 106(40):649–655

Katsarou A, Makris M, Papagiannaki K, Lagogianni E, Tagka A, Kalogeromitros D (2012) Tacrolimus 0.1% vs mometasone furoate topical treatment in allergic contact hand eczema: a prospective randomized clinical study. Eur J Dermatol 22(2):192–196

Kircik LH, Eastman WJ, Gwazdauskas J (2013) A randomized, double-blind phase 4 study of the efficacy and safety of ethanol-free clobetasol propionate foam, 0.05%, vs vehicle foam in the treatment of chronic hand dermatitis. J Drugs Dermatol 12(3):328–334

Kligman AM (1996) Hydration injury to human skin. In: van der Valk PG, Maibach HI (eds) The irritant contact dermatitis syndrome. CRC Press, Boca Raton

Klotz A, Veeger M, Rocher W (2003) Skin cleansers for occupational use: testing the skin compatibility of different formulations. Int Arch Occup Environ Health 76(5):367–373

Korting HC, Braun-Falco O (1996) The effect of detergents on skin pH and its consequences. Clin Dermatol 14(1):23–27

Krejci-Manwaring J, McCarty MA, Camacho F et al (2008) Topical tacrolimus 0.1% improves symptoms of hand dermatitis in patients treated with a prednisone taper. J Drugs Dermatol 7(7):643–646

Kresken J, Klotz A (2003) Occupational skin-protection products – a review. Int Arch Occup Environ Health 76(5):355–358

Kucharekova M, Van De Kerhof PC, Van Der Valk PG (2003) A randomized comparison of an emollient containing skin-related lipids with a petrolatum-based emollient as adjunct in the treatment of chronic hand dermatitis. Contact Dermatitis 48(6):293–299

Kutting B, Drexler H (2003) Effectiveness of skin protection creams as a preventive measure in occupational dermatitis: a critical update according to criteria of evidence-based medicine. Int Arch Occup Environ Health 76(4):253–259

Kutting B, Drexler H (2008) The three-step programme of skin protection a useful instrument of primary prevention or more effective in secondary prevention? Dtsch Med Wochenschr 133(5):201–205

Lachapelle JM (2001) Principles of prevention and protection in contact dermatitis (with special reference to occupational dermatology). In: Rycroft RJG et al (eds) Textbook of contact dermatitis, 3rd edn. Springer, Berlin

Loden M (2005) The clinical benefit of moisturizers. J Eur Acad Dermatol Venereol 19(6):672–688

Loden M, Buraczewska I, Edlund F (2003) The irritation potential and reservoir effect of mild soaps. Contact Dermatitis 49(2):91–96

Lodén M, Wirén K, Smerud K et al (2010) Treatment with a barrier-strengthening moisturizer prevents relapse of hand-eczema. An open, randomized, prospective, parallel group study. Acta Derm Venereol 6:602–606

Loffler H, Effendy I (2002) Prevention of irritant contact dermatitis. Eur J Dermatol 12(1):4–9

Lynde C, Guenther L, Diepgen TL, Sasseville D, Poulin Y, Gulliver W et al (2010) Canadian hand dermatitis management guidelines. J Cutan Med Surg 6:267–284

Lynde C, Cambazard F, Ruzicka T, Sebastian M, Brown TC, Maares J (2012) Extended treatment with oral alitretinoin for patients with chronic hand eczema not fully responding to initial treatment. Clin Exp Dermatol 37:712–717

Mahler V, Erfurt-Berge C, Schiemann S et al (2010) Dirt-binding particles consisting of hydrogenated castor oil beads constitute a nonirritating alternative for abrasive cleaning of recalcitrant oily skin contamination in a three-step programme of occupational skin protection. Br J Dermatol 162(4):812–818

McCormick RD, Buchman TL, Maki DG (2000) Double-blind, randomized trial of scheduled use of a novel barrier cream and an oil-containing lotion for protecting the hands of health care workers. Am J Infect Control 4:302–310

McFadden J (2001) Hand Eczema. In: Rycroft RJG et al (eds) Textbook of contact dermatitis, 3rd edn. Springer, Berlin

Meding B, Swanbeck G (1989) Epidemiology of different types of hand eczema in an industrial city. Acta Derm Venereol 69(3):227–233

Menné T, Johansen JD, Sommerlund M et al (2011) Hand eczema guidelines based on the Danish guidelines for the diagnosis and treatment of hand eczema. Contact Dermatitis 65(1):3–12

Mygind K, Sell L, Flyvholm MA et al (2006) High-fat petrolatum-based moisturizers and prevention of work-related skin problems in wet-work occupations. Contact Dermatitis 54(1):35–41

Nghiem P, Pearson G, Langley RG (2002) Tacrolimus and pimecrolimus: from clever prokaryotes to inhibiting calcineurin and treating atopic dermatitis. J Am Acad Dermatol 46(2):228–241

O'Shea PM, Lugo-Somolinos A (2015) Methotrexate versus Acitretin in the treatment of chronic hand dermatitis. J Drugs Dermatol 14(12):1389–1391

Ohlenschlaeger J, Friberg J, Ramsing D et al (1996) Temperature dependency of skin susceptibility to water and detergents. Acta Derm Venereol 76(4):274–276

Oosterhaven JAF, Politiek K, Schuttelaar M-LA (2017) Azathioprine treatment and drug survival in patients with chronic hand eczema – results from daily practice. Contact Dermatitis 76:304–307

Pedersen LK, Held E, Johansen JD et al (2005) Short-term effects of alcohol-based disinfectant and detergent on skin irritation. Contact Dermatitis 52(2):82–87

Pickenacker A, Luger TA, Schwarz T (1998) Dyshidrotic eczema treated with mycophenolate mofetil. Arch Dermatol 134(3):378–379

Politiek K, Christoffers WA, Coenraads P-J, Schuttelaar M-LA (2016a) Alitretinoin and acitretin in severe chronic hand eczema; results from a retrospective daily practice study. Dermatol Ther 29:364–371

Politiek K, van der Schaft J, Christoffers WA et al (2016b) Drug survival of methotrexate treatment in hand eczema patients: results from a retrospective daily practice study. J Eur Acad Dermatol Venereol 30: 1405–1407

Ramsing DW, Agner T (1997) Effect of water on experimentally irritated human skin. Br J Dermatol 136(3): 364–367

Robertson L (2009) New and existing therapeutic options for hand eczema. Skin Therapy Lett 14(3):1–5

Rocha LA, Ferreira de Almeida E, Borges L, Gontijo Filho PP (2009) Changes in hands microbiota associated with skin damage because of hand hygiene procedures on the health care workers. Am J Infect Control 37(2): 155–159

Ruzicka T, Larsen FG, Galewicz D et al (2004) Oral alitretinoin (9-cis-retinoic acid) therapy for chronic hand dermatitis in patients refractory to standard therapy: results of a randomized, double-blind, placebo-controlled, multicenter trial. Arch Dermatol 140(12): 1453–1459

Ruzicka T, Lynde CW, Jemec GB et al (2008) Efficacy and safety of oral alitretinoin (9-cis retinoic acid) in patients with severe chronic hand eczema refractory to topical corticosteroids: results of a randomized, double-blind, placebo-controlled, multicentre trial. Br J Dermatol 158(4):808–817

Said NH, Lim KS, Chong WS, Theng CTS (2011) A comparative study of UVA-1 phototherapy versus betamethasone valerate 0.1% cream for chronic

vesicular hand eczema. Ann Acad Med Singap 40(11 Suppl 1):S28
Scerri L (1999) Azathioprine in dermatological practice. An overview with special emphasis on its use in non-bullous inflammatory dermatoses. Adv Exp Med Biol 455:343–348
Schmid-Wendtner MH, Korting HC (2006) The pH of the skin surface and its impact on the barrier function. Skin Pharmacol Physiol 19(6):296–302
Schnopp C, Remling R, Mohrenschlager M et al (2002) Topical tacrolimus (FK506) and mometasone furoate in treatment of dyshidrotic palmar eczema: a randomized, observer-blinded trial. J Am Acad Dermatol 46(1): 73–77
Schwanitz HJ, Riehl U, Schlesinger T et al (2003) Skin care management: educational aspects. Int Arch Occup Environ Health 76(5):374–381
Sezer E, Etikan I (2007) Local narrowband UVB phototherapy vs. local PUVA in the treatment of chronic hand eczema. Photodermatol Photoimmunol Photomed 23(1):10–14
Skudlik C, Weisshaar E, Scheidt R et al (2009) Multicenter study "medical-occupational rehabilitation procedure skin – optimizing and quality assurance of inpatient-management (ROQ)". J Dtsch Dermatol Ges 7: 122–127
Slotosch CM, Kampf G, Loffler H (2007) Effects of disinfectants and detergents on skin irritation. Contact Dermatitis 57(4):235–241
Soost S, Worm M (2009) Therapy of occupational skin diseases. Hautarzt 60(9):718–721
Soost S, Abdollahnia M, Kostev K, Worm M (2012) Topical therapy of hand eczema – analysis of the prescription profile from dermatologists in private practice. J Dtsch Dermatol Ges 10:180–184
Thaçi D, Augustin M, Westermayer B, Kamps A, Hennig M (2016) Effectiveness of alitretinoin in severe chronic hand eczema: PASSION, a real-world observational study. J Dermatolog Treat 27:577–583
Thestrup-Pedersen K, Andersen KE, Menné T et al (2001) Treatment of hyperkeratotic dermatitis of the palms (eczema keratoticum) with oral acitretin. A single-blind placebo-controlled study. Acta Derm Venereol 81(5):353–355
Thyssen JP, Johansen JD, Linneberg A, Menné T (2010) The epidemiology of hand eczema in the general population – prevalence and main findings. Contact Dermatitis 62(2):75–87
Tupker RA, Coenraads PJ (1996) Cleansing. In: van der Valk PG, Maibach HI (eds) The irritant contact dermatitis syndrome. CRC Press, Boca Raton
Van Coevorden AM, Coenraads PJ, Svensson A, Bavinck JN, Diepgen TL, Naldi L, Elsner P, Williams HC, European Dermato-Epidemiology Network (Eden) (2004) Overview of studies of treatments for hand eczema-the EDEN hand eczema survey. Br J Dermatol 151(2):446–451
van Gils RF, Boot CR, van Gils PF et al (2011) Effectiveness of prevention programmes for hand dermatitis: a systematic review of the literature. Contact Dermatitis 64(2):63–72
Veien NK (2011) Clinical features. In: Johansen JD, Frosch P, Lepoittevin JP (eds) Contact dermatitis, 5th edn. Springer, Heidelberg
Veien NK, Ølholm Larsen P, Thestrup-Pedersen K, Schou G (1999) Long-term, intermittent treatment of chronic hand eczema with mometasone furoate. Br J Dermatol 140:882–886
Wigger-Alberti W, Fischer T, Greif C et al (1999) Effects of various grit-containing cleansers on skin barrier function. Contact Dermatitis 41(3):136–140
Wilke A, Gediga K, Schlesinger T et al (2012) Sustainability of interdisciplinary secondary prevention in patients with occupational hand eczema: a 5 year follow-up survey. Contact Dermatitis 66(2):79–86
Willis I (1973) The effects of prolonged water exposure on human skin. J Invest Dermatol 60(3):166–171