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Therapeutic options for chronic hand dermatitis

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ABSTRACT: Hand dermatitis is a common skin condition that often has a chronic and/or relapsing clinical course. Several clinical forms of hand dermatitis have been described, including contact (i.e., allergic and irritant), hyperkeratotic (i.e., psoriasiform or tylotic), frictional, nummular, atopic, pompholyx (i.e., dyshidrosis), and chronic vesicular hand dermatitis. In the present review, therapeutic options for these types of hand dermatitis are discussed in detail, focusing on treatments for recalcitrant hand dermatitis.

KEYWORDS: dermatitis, eczema, hand, therapy

Prevalence

Hand dermatitis is a common problem. Its prevalence in the general population is approximately 2–8.9% (1–5). While earlier estimates of the prevalence of hand dermatitis in individuals with work-related skin diseases ranged from 80% (6) to 88% (7), more recent figures suggest that the proportion of occupational disorders caused by skin disease has decreased to 10–15% (8–10).

Clinical variants

Several clinical variants of hand dermatitis have been described, including contact (i.e., allergic and irritant), hyperkeratotic (i.e., psoriasiform or tylotic), frictional, nummular, atopic, pompholyx (i.e., dyshidrosis), and chronic vesicular hand dermatitis. Hybrids of these patterns exist and some experts do not agree on classifications. Diagnosis is made by obtaining a thorough history, physical exam (with special attention to evaluation of the feet), appropriate patch testing, and skin biopsy, if necessary.

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Contact dermatitis

Contact dermatitis is usually classified as either (1) irritant or (2) allergic contact dermatitis. Irritant contact dermatitis comprises approximately 80% of contact dermatoses, and results from direct skin exposure to irritants such as water, soap, and chemicals (14,15). Atopic individuals with impaired baseline epidermal function may be particularly susceptible to developing irritant hand dermatitis (11–13). Allergic contact dermatitis is a Type IV, delayed-type, cell-mediated, hypersensitivity reaction (14,15). Patch testing is the gold standard for diagnosis of responsible antigens. Several studies have found that 17% (16), 32% (17), 42% (18), and 47% (19) of individuals with hand dermatitis have allergic contact dermatitis. Discussion of specific allergens and occupational exposures related to hand dermatitis is beyond the scope of the present review, but interested readers may find the cited manuscripts helpful (20–31). Once the offending antigen is identified through patch testing, the mainstay of management of allergic contact dermatitis is allergen avoidance.

Clinical symptoms of contact dermatitis may include burning, stinging, itching, and tenderness at the site of exposure to the irritant or allergen. Acute signs of contact dermatitis may include the presence of edema, papules, vesicles, and/or bullae, often with superimposed weeping and crusting

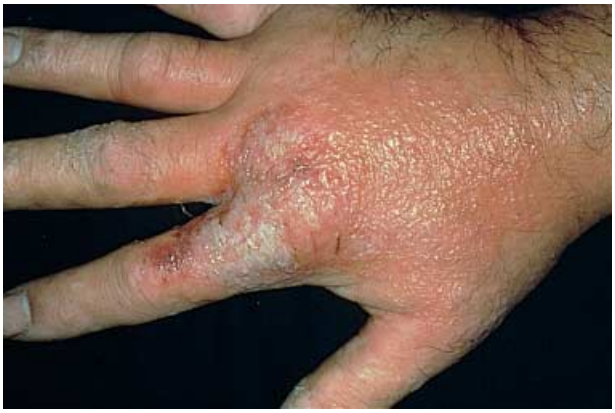

FIG. 1. Acute allergic contact dermatitis.

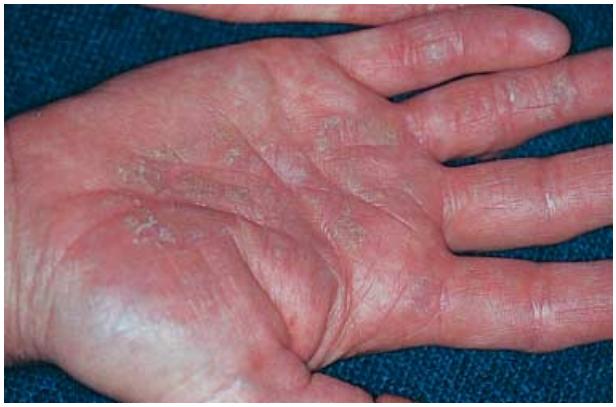

FIG. 3. Hyperkeratotic palmar hand dermatitis.

FIG. 2. Irritant contact dermatitis with involvement of web spaces in an "apron" distribution.

(FIG. 1). Chronic irritant or allergic contact dermatitis often manifests as eczematous plaques with fissuring, hyperpigmentation, and/or lichenification (32). Localized involvement of the fingerwebs with extension onto the dorsal and ventral surfaces ("apron" pattern), dorsum of the hands or fingers (33), palms (18), and the ball of the thumb without vesicles may suggest irritant contact dermatitis (FIG. 2). Allergic contact dermatitis may favor the fingertips, nailfolds (18), and dorsal hands, but may also involve the palms; vesicles are often present. Often, irritant contact dermatitis precedes allergic contact dermatitis; a pattern that changes from webspaces to fingertips or from palms to dorsal surfaces should alert the practitioner to consider patch testing (or repatch testing). Both allergic and irritant contact dermatitis may be chronic, and aggravated by water, detergents, or household agents, sometimes called "wet work." Eczematous plaques may also develop from contact urticaria, a Type I, IgE-mediated reaction. Important causes of contact urticaria which may result in hand dermatitis include latex (especially in healthcare workers) (34), vegetables, fruit, and meat (35). Because both Type I and Type IV allergy, as well as irritant contact dermatitis, may coexist, it is important to consider evaluation for immediate allergy, in addition to patch testing.

Hyperkeratotic hand dermatitis of the palms

Hyperkeratotic hand dermatitis of the palms (FIG. 3) has also been called tylotic eczema (36). Hyperkeratotic plaques are characteristically symmetric, and localized to the proximal or middle part of the palms and/or soles. Painful fissures are not uncommon. In two different studies (1,37), hyperkeratotic hand dermatitis was found to represent approximately 2% of all hand dermatoses, and was most commonly found in males, aged 40–60 years. Patch testing is usually negative (19), and most patients with hyperkeratotic hand dermatitis tend to have a stable, chronic clinical course.

Frictional hand dermatitis

Mechanical factors such as trauma, friction, pressure, and vibration may induce skin changes, sometimes termed "wear-and-tear dermatitis." Frictional dermatitis (FIG. 4) has been reported from contact with carbonless copy paper, bus tickets (38), artificial fur (39), pantyhose (40), and carpet (41).

Nummular hand dermatitis

Nummular hand dermatitis (also called discoid hand dermatitis) consists of tiny papules, papulovesicles, or "coin-shaped" eczematous plaques

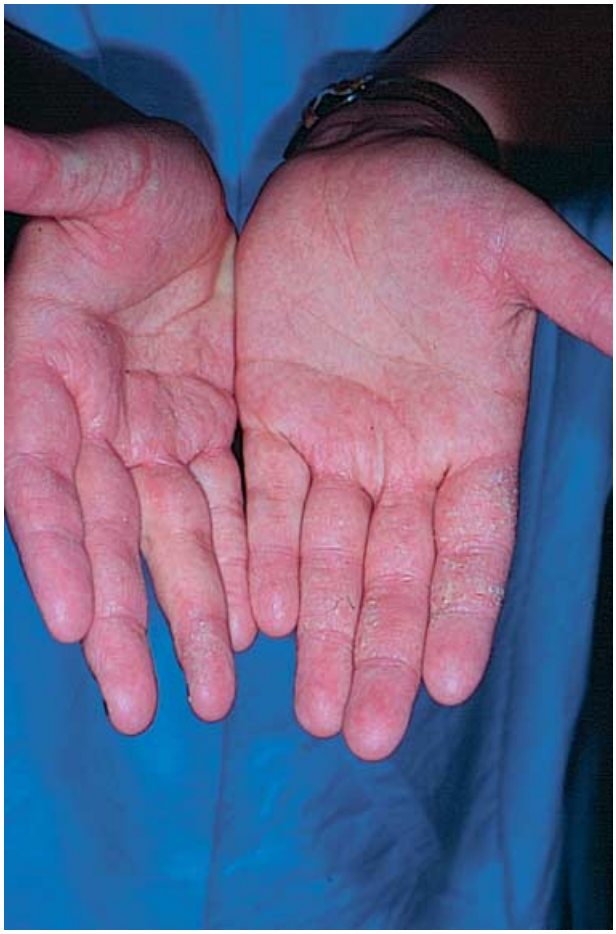

FIG. 4. Frictional hand dermatitis.

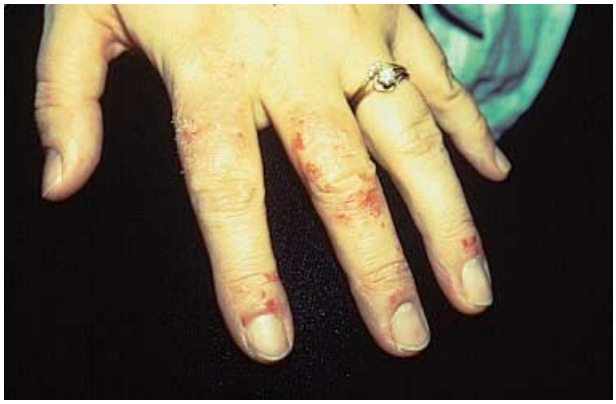

FIG. 5. Nummular hand dermatitis (photo courtesy of Frances J. Storrs, MD).

(FIG. 5). The dorsal hands and distal fingers are often involved. Contact urticaria (especially to natural rubber latex) may first present as nummular eczema. Nummular hand eczema has no known gender or age associations.

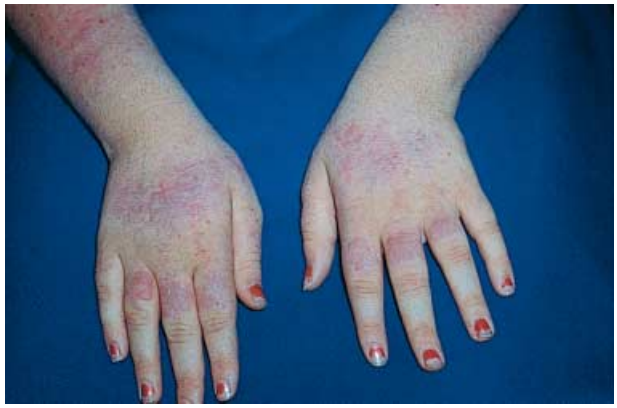

FIG. 6. Atopic hand dermatitis.

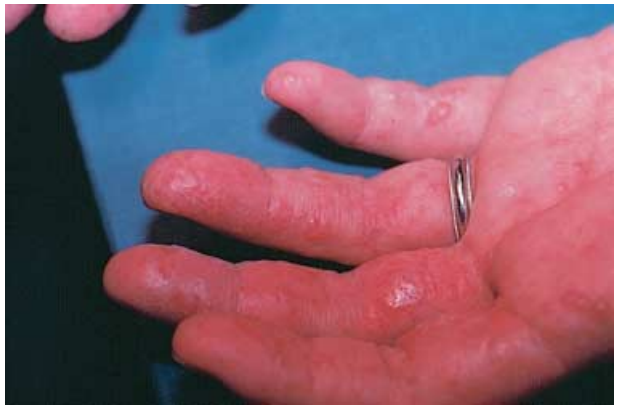

FIG. 7. Pompholyx (dyshidrosis).

Atopic hand dermatitis

It is well known that individuals with a history of childhood atopic dermatitis often develop hand dermatitis (FIG. 6) as adults (37,42). While atopic hand eczema has no uniform clinical presentation, several variants have been described. According to Moller (43), the most common form of atopic hand dermatitis involves the dorsal hands and fingers, with ill-defined, thin, light pink, xerotic, and lichenified plaques. Extension onto the volar wrist is characteristic (44,45).

Pompholyx

Pompholyx (called dyshidrosis by some) is characterized by recurrent crops of vesicles and bullae on the lateral aspects of the fingers, as well as the palms and soles on a background of non-erythematous skin (FIG. 7). Papulovesicles characteristically are symmetric and heal after desquamation. Patients may complain of pruritus

or pain. Pompholyx is a term that has often been used interchangeably with dyshidrotic eczema. However, some authorities, consider pompholyx to be a distinct clinical entity. While pompholyx is characterized by an explosive onset of large bullae, usually on the palms, dyshidrosis tends to be more chronic with small papulovesicles usually located on the sides of the fingers. Each lasts two to three weeks and resolves, leaving normal skin, only to recur again at varying intervals. These two conditions are idiopathic and closely related, if not identical. Symptoms recur frequently, and may be associated with exogenous factors [e.g., nickel (46,47) or hot weather] or endogenous factors [e.g., atopy or stress (48,49)]. A large European population study on hand eczema in twins involving almost 400 patients found that tinea pedis, but neither nickel allergy nor atopy, was statistically associated with vesicular eruptions on the hands (50).

Two reported series of patients with vesicular hand dermatitis found that patients who ingested low-nickel diets showed improvement of their dermatitis (51,52). Hyposensitization with a combination of ultraviolet (UV) B light therapy and subcutaneous nickel sulfate administration was found to induce clinical improvement in a study of 21 patients with allergic contact dermatitis to nickel, suggesting that this may be of benefit in individuals with hand dermatitis and nickel allergy (53). Interestingly, nickel chelators such as disulfiram have been reported to improve dermatitis caused by nickel allergy (54,55). However, some patients may experience a flare of their dermatitis during initial disulfiram treatment (56,57), possibly as a result of the release of nickel from nickel-albumin or nickel-histidine complexes in the serum (58).

Chronic vesicular hand dermatitis

When hand dermatitis is chronic, pruritic, vesicular, and mostly palmar, it is called chronic vesicular hand eczema (FIG. 8). This entity is differentiated from pompholyx by a more chronic course and the presence of vesicles with an erythematous base. The eruption often stops at the wrist, and either spares the dorsal hands or involves the fingertips only. The soles of the feet may also be involved. This probable "hybrid" hand eczema may be extremely difficult to treat. Patch testing to rule out allergic contact dermatitis is important; in one series, 55% of patients with this pattern of hand dermatitis were found to have positive patch test results (19).

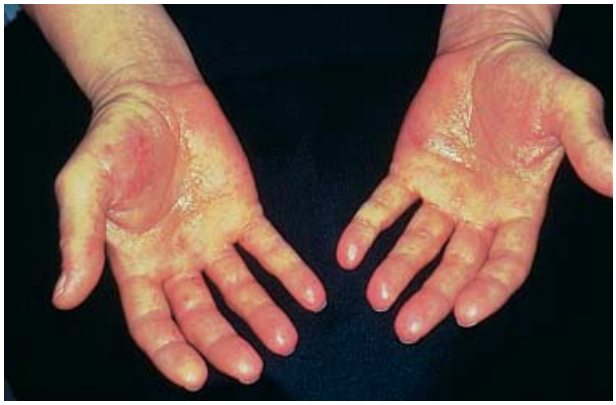

FIG. 8. Chronic vesicular hand dermatitis (photo courtesy of Frances J. Storrs, MD).

Therapies for chronic hand dermatitis

Prevention and lifestyle management

Regardless of the type of hand dermatitis, life-modifying factors, as listed in Table 1, are essential but often difficult for patients to implement (59). Education of atopic individuals to avoid irritants and "wet work" at home and at work is especially important (60). Exposure to irritants can be minimized by eliminating their use, substituting products, creating a physical barrier with cotton gloves under vinyl gloves, or by changing jobs (61–64). Aggressive use of emollients is critical to help restore normal skin-barrier function. Simple, inexpensive, petrolatum-based emollients were found to be equally as effective as an emollient containing skin-related lipids in a two-month study of 30 patients with mild to moderate hand dermatitis (65). A summary of the recommended therapeutic agents for different types of hand dermatitis is listed in Table 2 and discussed in detail below.

Topical agents

Topical corticosteroids are usually first-line agents for inflammatory hand dermatitis. The discussion of various formulations of topical corticosteroids is beyond the scope of the present discussion. In general, ointments are more effective and contain fewer preservatives and additives than creams. Generic preparations such as 0.1% triamcinolone ointment are widely available and cost-effective. Long-term use of topical corticosteroids is limited by local and, potentially, systemic side effects, such as skin atrophy, striae, and telangiectasia (66).

Table 1. Sample patient handout on lifestyle management of hand dermatitis[a]

Hand washing and moisturizing:
- Use lukewarm or cool water, and mild cleansers without perfume, coloring, or antibacterial agents, and with minimal preservatives. In general, bar soaps tend to have fewer preservatives than liquid soaps (Cetaphil or Aquanil liquid cleansers or generic equivalents are exceptions to this statement).
- Pat hands dry, especially between fingers.
- Immediately following partial drying of hands (e.g., within three minutes), apply a generous amount of a heavy cream or ointment (not lotion); petroleum jelly, a one-ingredient lubricant, works well.
- It is helpful to have containers of creams or ointments next to every sink in your home (next to the bed, next to the TV, in the car, and at multiple places at work).
- Moisturizing should be repeated as often as possible throughout the day, ideally 15 times per day.
- Avoid using washcloths, rubbing, scrubbing, or overuse of soap or water.

Occlusive therapy at night for intensive therapy:
- Apply a generous amount of your doctor's recommended emollient or prescribed medicine on your hands.
- Then put on cotton gloves and wear overnight.

When performing "wet work":
- Wear cotton gloves under vinyl or other non-latex gloves.
- Try not to use hot water and decrease exposure to water to less than 15 minutes at a time, if possible.
- Use running water rather than immersing hands, if possible.
- Remove rings before wet or dry work.

Wear protective gloves in cold weather and for dusty work. For frictional exposures, wear tight-fitting leather gloves (e.g., baseball, riding, or golfing gloves).

Avoid direct contact with the following, if possible:
- shampoo;
- peeling fruits and vegetables, especially citrus fruits;
- polishes of all kinds;
- solvents (e.g., white spirit, thinners, and turpentine);
- hair lotions, creams, and dyes;
- detergents and strong cleansing agents;
- fragranced chemicals;
- "unknown" chemicals.

Heavy-duty vinyl gloves are better than rubber, nitrile, or other synthetic gloves because vinyl is less likely to cause allergic reactions.

[a]Modified from Buxton (123) and Drake et al. (124), and reprinted with permission from FIG. 9 in "Hand dermatitis: a review of clinical features, therapeutic options, and long-term outcomes" by B. C. Decker, E. Warshaw, G. Lee and F. J. Storrs (Amer J Contact Derm 2003: **14**: 126).

Table 2. Recommended therapies for hand dermatitis variants[a]

	Hand dermatitis variant						
Therapeutic agent	Irritant contact	Allergic contact	Hyper-keratotic	Nummular	Pompholyx (dyshidrosis)	Frictional	Chronic vesicular
Corticosteroids:							
topical	✓	✓		✓	✓	✓	✓
oral		✓			✓[b]		✓
Cyclosporine		✓			✓		✓
Methotrexate		✓	✓		✓		✓
Mycophenolate mofetil		✓		✓	✓		✓
Tacrolimus or pimecrolimus (topical)	✓	✓		✓	✓		✓
Phototherapy (UVB, PUVA and Grenz)	✓	✓	✓	✓	✓	✓	✓
Retinoids (topical and/or oral)			✓			✓	✓
Calcipotriene (topical)			✓			✓	✓

[a]Reprinted with permission from Table 3 in "Hand dermatitis: a review of clinical features, therapeutic options, and long-term outcomes" by B. C. Decker, E. Warshaw, G. Lee and F. J. Storrs (Amer J Contact Derm 2003: **14**: 128).
[b]Acute flares.

Nonsteroidal topical immunomodulating agents such as tacrolimus (FK 506) and pimecrolimus (SDZ ASM 981) inhibit release of inflammatory cytokines from T-lymphocytes and mast cells (67), and have been studied in treating chronic eczematous skin diseases such as atopic dermatitis (68–71). In these studies, the most commonly reported adverse side effect of topical use of these agents was transient skin burning or a sensation of warmth (68,69), occurring in approximately 50% of patients treated with topical tacrolimus and 10% with pimecrolimus. The vast majority of patients treated with either tacrolimus or pimecrolimus had no significant systemic absorption although the lipophilicity of pimecrolimus, and negligible systemic immunosuppression may make it a safer agent for widespread or long-term use. Neither tacrolimus nor pimecrolimus induce skin atrophy, telangiectasia, or tachyphylaxis, unlike glucocorticoids (72,73). These characteristics make topical tacrolimus and pimecrolimus particularly advantageous for use in sensitive skin areas such as the face and neck, as well as for treatment of chronic skin diseases such as hand dermatitis.

Both topical tacrolimus and pimecrolimus have been evaluated for treatment of hand dermatitis. Belsito and colleagues evaluated the efficacy of pimecrolimus 1% cream under occlusion for three weeks in 294 individuals with mild to moderate chronic hand dermatitis (i.e., dyshidrosis, atopic, irritant, and chronic allergic dermatitis) in a randomized, double-blind, vehicle-controlled study. There was an overall statistical trend toward greater improvement in the pimecrolimus group ($P = 0.068$), with greater efficacy noted in participants without involvement of the palms (74). An open-label study by Thaci et al. utilized twice-daily, occlusive therapy (including ≥ six hours of occlusive therapy overnight) with pimecrolimus 1% cream in 12 patients with moderate to severe chronic hand dermatitis (both irritant and allergic contact dermatitis) for 22 days. Investigator global assessments showed a 49% improvement from baseline and pharmacokinetic evaluations demonstrated low pimecrolimus blood levels (75). Thelmo and colleagues evaluated 25 patients with hand and foot dermatitis in an open-label study. Participants applied tacrolimus ointment 0.1% to affected areas three times daily for eight weeks. Statistically significant improvements from baseline were reported for erythema, scaling, induration, fissuring, and pruritus, but not for vesiculation (76).

Other topical agents not reported in the literature, but anecdotally prescribed to treat hand dermatitis, include tazarotene and calcipotriene, both of which act to regulate epidermal cell maturation (77). Both may be particularly helpful for hyperkeratotic hand dermatitis.

Ionizing radiation

Two different types of ionizing radiation, i.e., conventional superficial X-rays and Grenz rays, have been used to treat skin disorders. Fairris et al. compared a combination of superficial X-ray (100 rad at 50 kV every three weeks for three sessions) and topical therapy with topical therapy alone in a double-blind, right–left hand comparison study in 24 patients with chronic hand eczema. Hands receiving the combination treatment showed significant improvement as compared to hands receiving topical treatment alone (78). King and Chalmers performed a similar double-blind, right–left hand comparison trial of superficial X-ray (100 rad at 45 kV weekly for three weeks) in 15 patients with chronic hand dermatitis (seven with pompholyx eczema and eight with hyperkeratotoic eczema). Statistically significant improvement was seen at one month after therapy, but this difference was no longer apparent by 6 months (79).

Grenz rays (ultra-soft X-rays or Bucky rays) are almost entirely absorbed in the superficial portion of the epidermis and dermis (80). Treatment for hand dermatitis usually requires 200–400 rad (2–4 Grays or Gy) every one to three weeks for up to a total of six treatments, followed by a six-month hiatus (80–82). Low voltages are typically used (5–20 kV) (83). Although anecdotally considered effective, a double-blind, right–left hand comparison study by Cartwright and Rowell found that treatment of chronic hand eczema with Grenz rays (a total dose of 900 rads given in three equal doses at 21-day intervals) was no more effective than placebo in the treatment of chronic hand eczema in 30 patients evaluated at multiple occasions up to 18 weeks after initiation of therapy (84). Fairris and colleagues conducted a double-blind study of 25 patients with chronic bilateral hand dermatitis and found that conventional X-rays (300 rad) were superior to Grenz rays (900 rad) (85).

Non-ionizing radiation (UVA and UVB)

Psoralen and UVA irradiation (PUVA) has been used to treat patients with all forms of hand dermatitis (86–88). Psoralen and its derivatives (e.g., 8-methoxypsoralen or 8-MOP, 5-MOP, and trioxsalen) are available as topical agents (i.e., creams, gels, lotions, or solutions) and oral preparations

(i.e., 8-MOP and psoralen-ultra). Topical PUVA has been evaluated for chronic vesicular hand eczema (89), chronic hand eczema (90), and other recalcitrant hand dermatoses (91–94). Sheehan-Dare and colleagues (95) compared topical PUVA and conventional superficial radiotherapy in a randomized, double-blind, controlled study of 21 patients with chronic hand eczema. One hand of each patient was treated with PUVA and the other was treated with superficial X-ray. Hands treated with superficial radiotherapy demonstrated rapid initial clearing, although both groups showed clinical improvement at 12 weeks follow-up, and there was no statistically significant difference between the two treatment modalities. The recommended starting UVA dose for topical 1% psoralen is 0.25–0.5 J/cm (2) with incremental increases of 0.25 J/cm (2) per treatment, administered three times weekly (96,97).

Oral psoralen and UVA irradiation (PUVA) has been evaluated for chronic eczematous hand dermatitis (94,98) and dyshidrotic eczema (99). Rosen and colleagues (98) compared PUVA with UVB in a randomized, controlled study of 35 patients with chronic hand dermatitis (i.e., allergic and irritant contact dermatitis, and hyperkeratotic and idiopathic dermatitis). Patients were randomized to either PUVA or UVB on one hand; the contralateral hand served as a control. The length of treatment ranged from three to nine weeks with standard psoralen doses (0.6 mg/kg body weight) and a maximum UVA dose of 15 J/cm (2). All 14 patients who completed the study in the PUVA group were completely cleared of disease in contrast to none in the UVB group. Different results were found in a different, similarly designed study by Simons and colleagues in which 13 patients with chronic hand dermatitis were treated with topical PUVA to one hand and UVB to the other; no differences in clinical improvement at six weeks between the two treatment modalities were found (100).

Ultraviolet A light without psoralen may also be beneficial. Schmidt and colleagues used UVA1 (40 J/cm^2 per day given five times per week for three weeks) to treat 12 patients with chronic vesicular dyshidrotic hand eczema in an open-label trial. Post-treatment scores were significantly improved (101).

Systemic glucocorticoids

Prednisone may be useful for recurrent pompholyx and dyshidrotic hand dermatitis, if treatment is started early, at the onset of itching prodrome. Short bursts of 60 mg as a single dose in the morning for three to four days, repeated every two to four months, as needed, may be especially helpful (Frances J. Storrs, MD, personal communication). While systemic glucocorticoids often produce dramatic improvement of skin inflammation, long-term side effects such as osteoporosis, glaucoma, cataracts, hypothalamic–pituitary–adrenal axis suppression, hyperglycemia, hypertension, and immunosuppression limit their use (102). These side effects may also occur from intramuscular glucocorticoid administration, making it a poor choice for the treatment of chronic hand dermatitis (103).

Cyclosporine

Cyclosporine is a potent immunomodulating agent that suppresses T-lymphocytes and has been used to treat many inflammatory skin disorders (104–106). In a double-blind fashion, Grandlund and colleagues randomized 41 patients with hand dermatitis to either oral cyclosporine (3 mg/kg/day) or a potent topical corticosteroid for six weeks, and found that disease activity decreased in 50% of participants in the cyclosporine group, as compared to 32% in the steroid group. However, both groups showed a 50% relapse rate at a two-week follow-up (104). In another series of 75 patients treated with six weeks of oral cyclosporine (3 mg/kg/day), the long-term success rate (based on patient assessment at one year) for chronic hand dermatitis was 74% (105). A case report of using oral cyclosporine at a higher dose (5 mg/kg/day) reported success after two weeks of treatment, but relapse occurred immediately after discontinuation of cyclosporine (106).

Mycophenolate mofetil

Mycophenolate mofetil is a relatively new immunomodulating agent that inhibits the synthesis of guanosine nucleotides. Typical doses used in treatment of inflammatory skin diseases such as psoriasis, bullous pemphigoid, and dyshidrotic eczema range from 2 to 3 g/day (107–110). Side effects may include nausea, loose stools, diarrhea, abdominal cramping, leukopenia, anemia, and herpes zoster (111). A case report described a patient with a four-year history of recurrent dyshidrotic eczema resistant to corticosteroids, iontophoresis, and phototherapy who responded to 1.5 g of mycophenolate mofetil administered twice daily. Complete clearing was achieved in four weeks and the dose was tapered gradually over 12 months without recurrence (110). Another case report,

however, described mycophenolate-mofetil-induced, biopsy-proven dyshidrotic eczema, which cleared on discontinuation of mycophenolate mofetil and flared on reinstitution (112).

Methotrexate

Methotrexate inhibits dihydrofolate reductase, an enzyme important in cell proliferation, making it a useful therapy for a wide range of skin diseases including psoriasis and cutaneous T-cell lymphoma (113,114). In a report by Egan and colleagues, methotrexate was found to partially or completely clear chronic dyshidrotic eczema in five patients at doses ranging from 12.5 to 22.5 mg/week (115). Side-effects of methotrexate include nausea, vomiting, diarrhea, hepatitis, liver cirrhosis, pancytopenia, and pulmonary fibrosis (116).

Retinoids

An experimental oral retinoid that is currently approved for use in Europe, 9-*cis*-retinoic acid (9-*cis*-RA or alitretinoin), has been reported to work especially well for patients with chronic hyperkeratotic hand eczema. Common side effects include cheilitis, headache, and flushing. One study evaluated 38 patients resistant to other therapies, including corticosteroids, X-ray, PUVA, tretinoin, isotretinoin (13-*cis*-RA), and acitretin who were mostly treated with a "high" dose of 40 mg daily for an average of 2.3 months. In this preliminary study, 89% of the patients reported "good" to "very good" responses to 9-*cis*-RA. This response is more favorable than previous reports using oral etretinate (0%, $n = 11$), acitretin (6%, $n = 17$), or isotretinoin (0%, $n = 7$) (117).

Other therapies

Both iontophoresis and intradermal botulinium toxin are effective therapies for hyperhidrosis (118), and have been reported to be effective for treatment of hand dermatitis. Iontophoresis is the transfer of ions through the skin induced by direct current. In one open-label study of 20 patients, iontophoresis was reported to be effective for treatment of dyshidrotic hand eczema (119). Swartling and colleagues conducted an open label study of 10 patients with recurrent vesicular hand dermatitis in which the hand of each patient received intradermal botulinium toxin injections and the other hand served as a control. Seven out of the ten patients reported good or very good control at six weeks; responders were more likely to have concomitant hyperhidrosis of the palms (120). A similar study compared topical corticosteroids plus intradermal botulinium toxin with topical corticosteroids alone in six patients with dyshidrotic eczema and found improvement in the combination group (121). Since dyshidrosis and pompholyx have no relationship to sweat gland obstruction or hyperhidrosis, the improvement of patients in these small, uncontrolled studies may be spurious or secondary to decreased irritation from sweat, as has been documented to occur in atopics (122).

Discussion

Hand dermatitis is a common dermatological condition. History, distribution of dermatitis, general physical exam, and/or patch testing may help elucidate causative and/or contributing factors. Therapies that may be effective include PUVA, topical and oral immunomodulators, antimetabolites, and retinoids.

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