Symposium - Contact Dermatitis

Hand eczema: An update

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ABSTRACT

Eczema, the commonest disorders afflicting the hands, is also the commonest occupational skin disease (OSD). In the dermatology outpatient departments, only the severe cases are diagnosed since patients rarely report with early hand dermatitis. Mild forms are picked up only during occupational screening. Hand eczema (HE) can evolve into a chronic condition with persistent disease even after avoiding contact with the incriminated allergen / irritant. The important risk factors for hand eczema are atopy (especially the presence of dermatitis), wet work, and contact allergy. The higher prevalence in women as compared to men in most studies is related to environmental factors and is mainly applicable to younger women in their twenties. Preventive measures play a very important role in therapy as they enable the affected individuals to retain their employment and livelihood. This article reviews established preventive and therapeutic options and newer drugs like alitretinoin in hand eczema with a mention on the etiology and morphology. Identifying the etiological factors is of paramount importance as avoiding or minimizing these factors play an important role in treatment.

Key words: Alitretinoin, barrier creams, emollients, hand eczema treatment, protective gloves

INTRODUCTION

Hand eczema (HE) is the most common form of occupational skin disease (OSD). OSDs comprises approximately 40% of occupational disease with variations in different countries related to the degree of industrialization.[1,2] The hands have been the affected site in 80% of the OSDs.[3] The increased prevalence in women as compared to men is seen in the younger age group.[4] Atopy (endogenous factor), wet work, irritants, friction, and contact allergy (chromate, nickel, fragrance, biocides, and rubber chemicals) are the major risk factors.[5,6] Ingested allergens may also provoke HE.[7]

HE is localized to the hands, which are important organs of expression, communication, and are necessary for carrying out daily household and work-related activity. Impairment in form or function can result in severe emotional and psychological distress associated with a poor quality of life comparable to diseases with extensive skin involvement. Skin protection measures and topical treatment are effective in the majority and form the mainstay of treatment regardless of any other additional treatment. Systemic therapy results in remission but cannot be continued indefinitely. No classification of hand eczema would be complete without addressing the etiological and morphological factors. There are several classifications of hand eczema, but are confusing including the recent one based on etiology and morphology proposed by Diepgen *et al*.[8] We propose a simple modified classification, which encompasses the varied clinical presentations based on previous classifications [Table 1].[9,10] The etiology is any one or a combination of the 4 listed in Table 1. Other skin diseases may mimic HE and may prove a diagnostic challenge initially [Figures 1 and 2]. Thus, in our classification, the differential diagnoses are also included since they closely mimic hand eczema and can be differentiated only by relevant investigations.

Access this article online	
Quick Response Code:	Website: www.ijdvl.com
	DOI: 10.4103/0378-6323.100547

How to cite this article: Lakshmi C, Srinivas CR. Hand eczema: An update. Indian J Dermatol Venereol Leprol 2012;78:569-82.
Received: September, 2011. **Accepted:** June, 2012. **Source of Support:** Nil. **Conflict of Interest:** None declared.

Table 1: Classification and differential diagnoses of hand eczema

Aetiology	Morphology
Atopic hand dermatitis	1. Pompholyx – vesicular hand eczema
Irritant dermatitis	2. Fissured hand eczema +/-scaling
Allergic contact dermatitis	3. Hyperkeratotic hand eczema
Protein contact dermatitis	4. Nummular hand eczema
Differential diagnoses	5. Fingertip eczema (pulpitis)
a. Disorders of Keratinisation: Psoriasis , PRP	6. Interdigital (web space) eczema
b. Lichen planus	
c. Bullous pemphigoid	
d. Scabies	
e. Tinea manuum	
f. Acrodermatitis enteropathica	
g. Keratodermas	
h. Malignancies – acute leukemia, lymphomas	
i. Pustular erythema multiforme	

Atopic hand dermatitis

A history of atopic dermatitis in childhood is a risk factor for the development of hand eczema in adulthood.[9] A history of mucosal atopy does not pose as much risk as atopic dermatitis.

Irritant dermatitis

Exposure to irritants like wet work, mineral oils, organic solvents, and friction [Figure 3] are known risk factors, especially in persons with underlying atopic dermatitis.[10]

Protein contact dermatitis

This presents as chronic or recurrent dermatitis, fingertips are commonly involved. Skin contact with the incriminated proteins (fruits, vegetables, spices, plants, animal proteins, grains, and enzymes) may result in flares characterized by urticarial or vesicular lesions within minutes of contact. Patients may complain of stinging, burning, or itching. Contact reactions to proteins are urticarial and last from 30 minutes to about 3 hours. With repeated exposure, eczema may develop. A preceding urticarial reaction is not always necessary for the development of protein contact dermatitis (PCD).[11,12] Food handlers, cooks, caterers, and housewives are at risk. It is a type I hypersensitivity reaction mediated by allergen-specific IgE in a sensitized person. The gold standard for diagnosis is skin prick testing with fresh material or commercial reagents.[11,12] Reactions appear within 20 minutes. The positive control is histamine, and negative control is saline [Figures 4 and 5].

Allergic contact dermatitis

Allergic contact dermatitis (ACD) diagnosed by patch testing is a known cause of hand eczema. It may be the sole causative factor or may be in combination with irritant dermatitis and/or atopic dermatitis.

The causative allergens commonly detected include nickel, cobalt, fragrance-mix, balsam of Peru, and colophony.[13,14] Recently, allergy to formaldehyde[15] and methyl dibromo glutaronitrile[16] have been reported to be relevant in HE. In India, ACD to *Parthenium hysterophorus* may present as hand dermatitis [Figures 6 and 7].[17]

The various morphological forms include:[9,10]

1. **Pompholyx type** [Figure 8]
   This is characterized by tense, deep-seated crops of "sago-like" vesicles on palms, and/or palmar aspect and sides of the fingers with recurrences. The lesions are intensely pruritic. The plantar aspects of the feet may also be involved. Secondary infection with the development of pustules and lymphangitis may occur. Atopy is the most important factor [Table 2]. Irritants like soluble oils can cause pompholyx. Pustular lesions may occur in erythema multiforme and pustular psoriasis mimicking pompholyx. [Figures 9 and 10]
2. **Fissured hand eczema (Synonyms: dermatitis palmaris sicca, housewives' dermatitis)**
   This is dry eczema with scaling and fissuring and few hyperkeratotic areas. Exudation does not occur, and pruritus is minimal. Seen in longstanding HE persisting for months to years.
3. **Hyperkeratotic hand eczema**
   There are well-defined hyperkeratotic plaques on the palms and on the palmar aspects of the fingers. There is no scaling or vesicle formation. There is no increased incidence of atopy or psoriasis in this group of patients as compared to the general population. It can involve the plantar aspect of feet and is more common in middle-aged and older men. It may be refractory to treatment.
4. **Nummular eczema**
   These are well-circumscribed circular or oval lesions confined to the dorsum of hands or fingers and characterized by erythema, vesicles, oozing in the acute phase and are intensely pruritic. Hyperkeratosis may occur. This form of eczema frequently gets colonized by *S.aureus*. Atopy is commonly reported in these patients; similar lesions may occur in atopic eczema.
5. **Finger tip eczema; pulpitis [Figure 11]**
   This is hyperkeratotic eczema of the fingertips

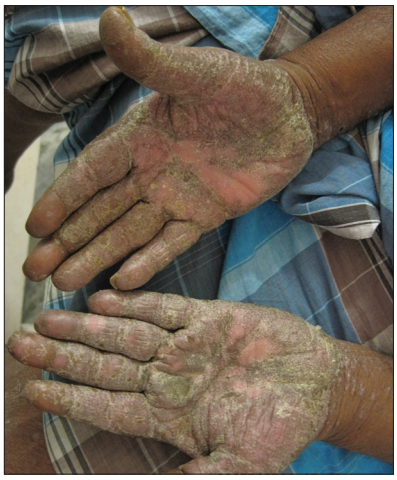

Figure 1: Hand dermatitis in a patient with immunofluorescence-proven bullous pemphigoid

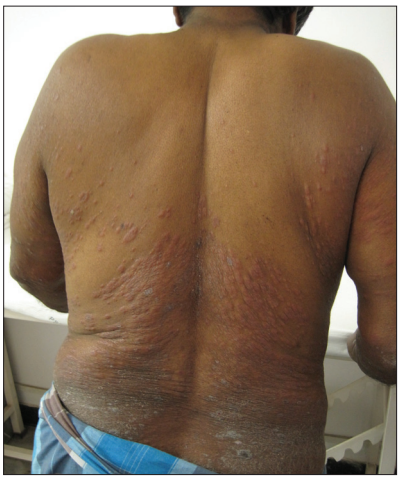

Figure 2: Urticarial plaques over the back in the same patient as in Figure 1

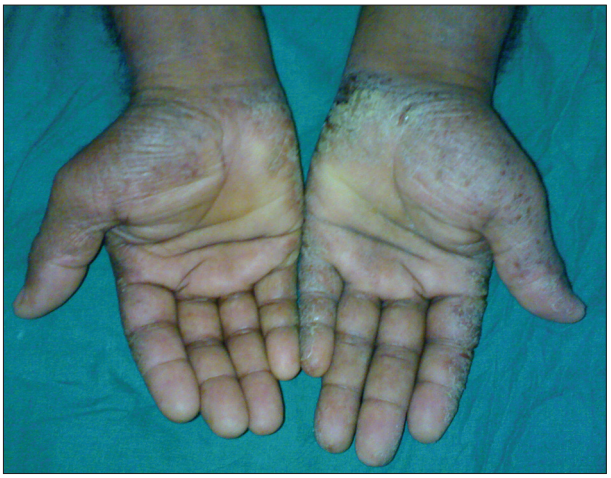

Figure 3: Frictional hand dermatitis in a power loom worker from Tirupur

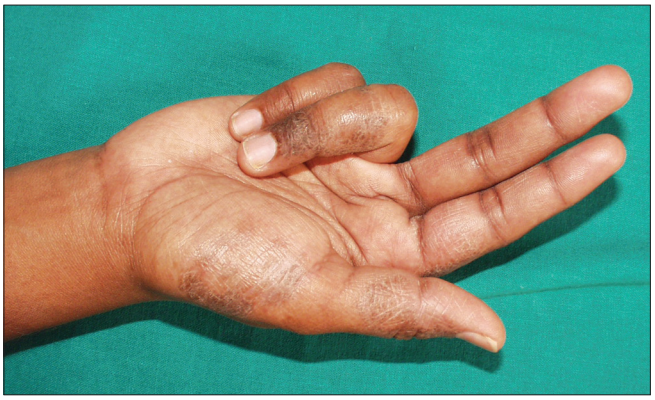

Figure 4: Hand dermatitis in a health care worker was investigated by prick testing (Figure 5)

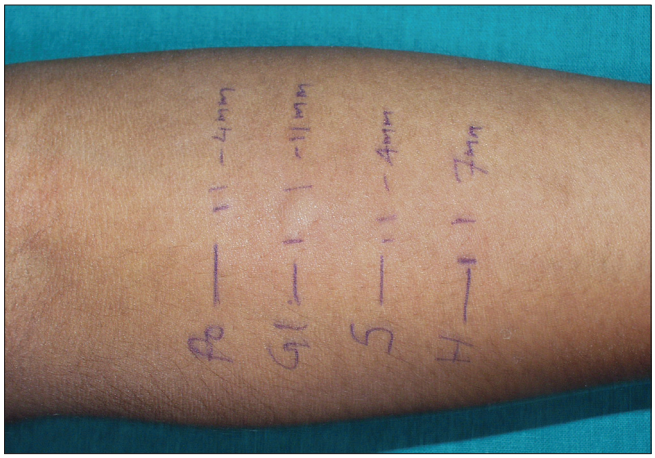

Figure 5: Positive prick test (Contact urticaria) to glove in a health worker

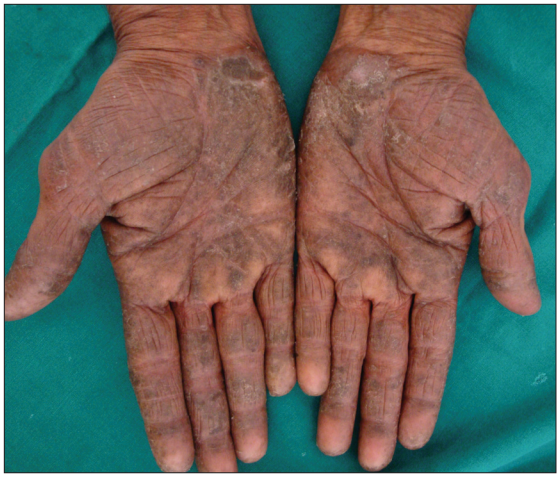

Figure 6: Hand dermatitis in a parthenium-sensitive patient

with painful fissures, which may extend to merge with eczema over the palm. Vesicles may occur. When all fingers, especially those of the dominant hand are involved, with aggravation in cold climate, this is possibly a cumulative irritant dermatitis where degreasing agents and trauma play a role. When localized to only the thumb, forefinger and third finger, especially

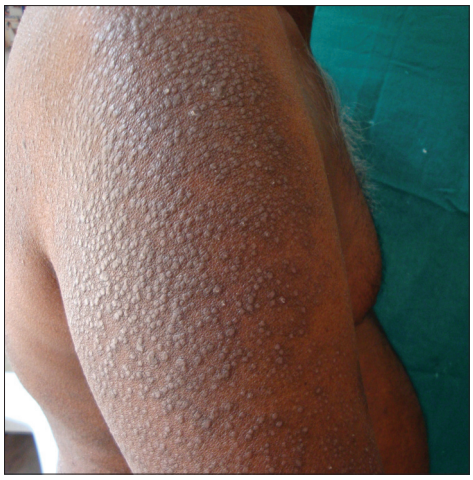

Figure 7: Papular lesions over the arm mimicking PRP in the same patient as in Figure 6

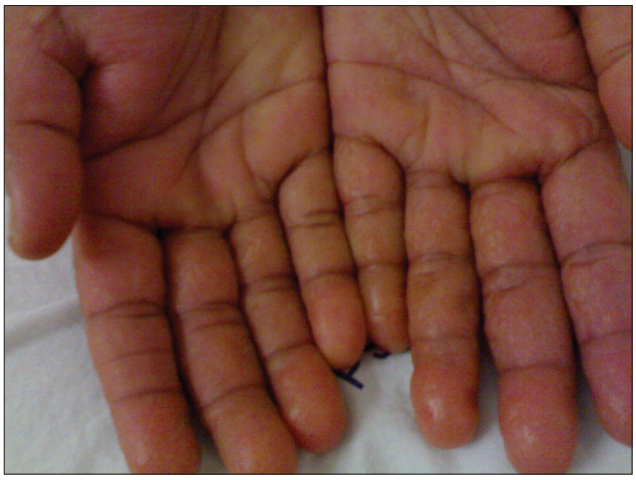

Figure 8: Deep seated vesicles on palms

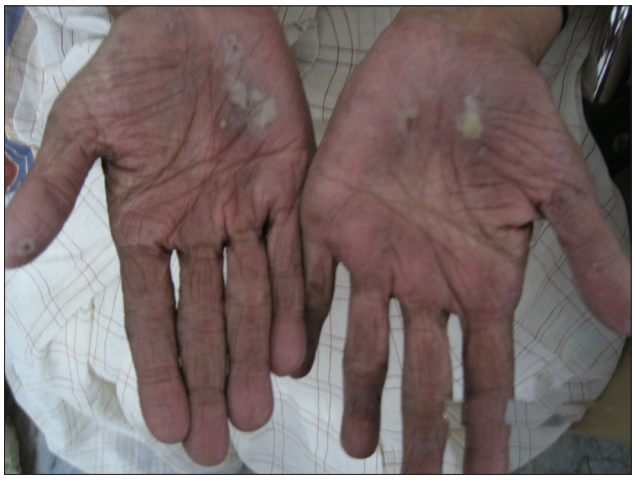

Figure 9: Pustular lesions in pustular psoriasis

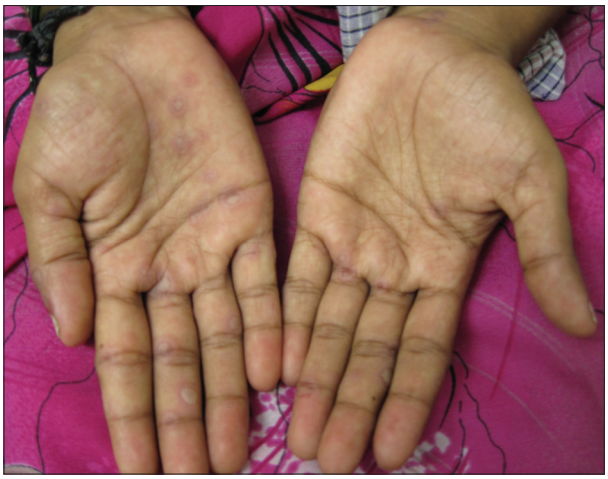

Figure 10: Pustular lesions in erythema multiforme

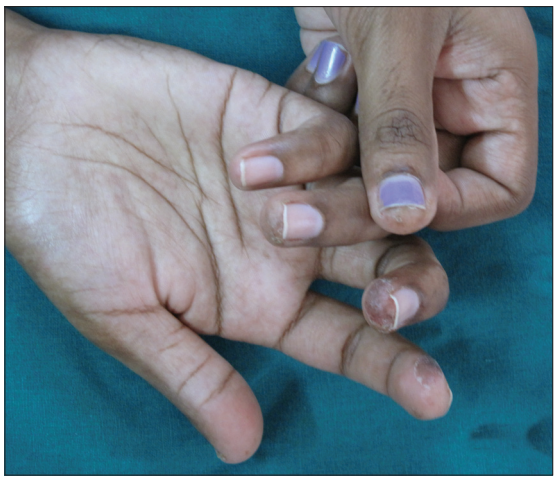

Figure 11: Finger tip eczema

Table 2: Causes of Pompholyx-type of reaction over palms

1. Atopy
2. Irritants – soluble oils
3. Contact allergens (on direct contact over palms)[18,19] Dichromates, nickel, cobalt benzoisothiazolones, isopropyl paraphenylenediamine, primin perfumes, fragrances, balsam of Peru
4. Ingested allergens:[18,20,21] nickel, chromium, cobalt, neomycin
5. Shoe allergens: rubber allergy may provoke a palmar eruption
6. Fungal infection elsewhere (feet) can result in vesicles over palms – dermatophytide[18]
7. Bacterial infection: pustular bacteride
8. Drugs: aspirin, oral contraceptives, cigarette smoking[22]
9. Others: Pustular psoriasis, vesiculo pustular lesions in EM (Figures 1, 2 & 9,10)

of the dominant hand, occupational dermatitis should be considered (irritant or allergic). The non-dominant hand is involved when vegetables and other items related to cooking are held in this hand (E.g., cutting onions, garlic)

6. Interdigital eczema

Erythema and scaling is seen in the interdigital spaces, rarely vesiculation may occur.

MANAGEMENT

The management of HE shall be discussed under 4 sub titles.

1. Assessment of severity
2. Diagnostic (history and investigations); identifying etiological factors
3. Preventive and protective measures
4. Treatment

1. Assessment of Severity

The severity of hand eczema can be assessed by various scoring methods.[23-27]

1. Osnabrück hand eczema severity index (OHSI) (Range 0-18).[24]
2. Hand eczema severity index (HECSI) (Range 0-360).[25]
3. Manu score (Range 0-6480).[26]
4. Hand eczema score for occupational screenings at the workspace (HEROS) (Range 0-2260).[23,27]

The description of these scoring systems is beyond the scope of this article, and readers are requested to access the references for detailed reading. Most of the skin scores have been developed for severe HE, except the HEROS, which quantifies an early hand eczema and would be useful in occupational screening.

These scoring systems for quantifying HE are useful in evaluating an outcome of treatment. Manu score has the highest range (0-6480). Itching, which is a subjective symptom, is included in this score. Ideally, subjective symptoms, which may be biased, should be excluded in scoring systems.

Localization of lesion may involve either or in combination the dorsa of hands, palmar aspects of hands, sides of fingers, finger web spaces, finger tips, and wrist.

2. Diagnostic (History and Investigations)

Exposure mapping of allergens and irritants[9]

Contact allergens

- Chemical constitution of product.
- Workplace visit

  Occupational exposure to paints, glues, cutting oils.

  Procure allergens for patch testing from manufacturer.
- Chemical spot tests: Nickel, chromate, and cobalt.[28-30]
- Testing for formaldehyde in products.
- Chemical analysis of product in specialized laboratories.

Irritants:

- Wet work
- Contact with detergents, alkaline substances, oil products, cutting oils, organic solvents
- Glove usage (hours spent with tight-fitting/ hours spent with wet hands/number of times hands are washed/number of glove changes)[31]
- Mechanical (frictional) trauma

Wet Work: Based on German standard, the following can give rise to irritant hand eczema[32]

Wet hands for more than 2 hours daily.
Frequent hand washing > 20 times / day
Wearing tight fitting gloves for more than 2 hours per day.

Investigations[17,33] Table 3 serves as a checklist for exposure assessment and investigations

1. Patch Testing

1. **For allergic contact dermatitis**
   - With Indian Standard series (ISS), which is the baseline series.[33]
   - With specific series based on results of baseline series.
   - Specific test series may be suggested based exposure related to occupation (hairdressing, health care workers) and hobbies/leisure/household activities
   - In addition, materials by the patient could be included while testing (skin care products, topical medicaments,gloves, etc.)
   - Strong irritants, corrosive or sensitizing products should not be tested. Patch testing is performed according to the International Contact Dermatitis Research Group (ICDRG) guidelines. Exposure is for 2 days, and readings are to be taken on D_2 and D_3 or D_4 and ideally on D_7 also.
2. **For irritant contact dermatitis**

   Detergents are a common cause for

Table 3: Diagnostic (history and investigations)

History of atopy (atopic dermatitis/asthma/rhinitis). Of these, dermatitis correlates most with hand eczema. Previous episodes of dermatitis, aggravating factors, remissions should be noted.
Exposure Assessment
Work place
• Allergens
• Irritants – wet work, mineral oils,
• Friction
• Foodstuffs
House hold and leisure
• Allergens
• Irritants
Relationship of HE to any of above exposures. Previous investigations / diagnosis of allergic sensitivity.
Treatment history
Course of HE
Investigations
Patch test
Prick testing with antigen or material
Serum IgE
RAST (radio allegro sorbent test for specific IgE)
RPA test (RNase Protection Assay)
Chemical spot tests for nickel, chromate , cobalt
Testing for formaldehyde in products

hand eczema in housewives, cleaners, and nurses. 24-hour patch testing with detergent and soap solutions (8% w/v), would help identify the cleanser/detergent producing the least irritation.[34,35]

2. Prick Testing

- With standardized allergens[17,33]
- Prick test with fresh food stuffs.
- Procedure – done by standard method with histamine as positive control and saline as negative control. The maximum wheal diameter is measured in mm. Whenever possible, record the late phase reaction (LPR) in mm at 24 hours at the prick tested site.[17]

3. Serum IgE estimation
4. RAST (Radio Allergo Sorbent Test).
5. RPA test (R Nase Protection Assay)[36]
   This measures small quantities of RNA obtained from tape stripping of human skin and is very sensitive. The RPA test discriminates between irritant and allergic patch test reactions. Interleukin-4 (IL-4) was found to be increased in allergic but not in irritant reactions.
6. Chemical spot tests: For nickel, chromate, and cobalt
7. Test for formaldehyde in product

3. Preventive and Protective measures

Preventive measures

High risk groups such as those with history of atopic dermatitis, hairdressers, health-care workers, food-handlers, and those working with solvents and cutting oils should be identified and educated.[37] In work-related disease, occupational screening and education reduce the incidence of HE. During occupational screening evaluation, issues related to hazardous chemicals, their attributable risk, and reduction of exposure should be addressed. Pre-employment patch testing of healthy subjects identified culprit allergens in 7% of subjects.[38]

Long hours of wet work, low humidity, and hard water increase the risk for dermatitis.[39]

Hand outs on skin care in HE are advised for all patients. (Refer Appendix I)

Protective measures

At the workplace, skin protection is achieved by[14,40]

1. Pre-exposure barrier/protective creams to be used on intact skin before and during work. (o/w emulsions, w/o emulsions, tanning agents (cause hardening and increase resistance to irritants. They are also useful under occlusive gloves to reduce skin maceration), aluminium chlorohydrate, zinc oxide which has a shielding effect, talcum, perfluoropolyethers, chelating agents, quarternium-18, bentonite, uv absorbers.)
2. Cleansing during and after work with mild skin cleansers[41]
3. Post-exposure skin care after work with emollients, moisturizers, humectants (glycerol, sorbitol, urea), lipids (complex mixtures of ceramide, fatty acid, cholesterol).[42] It has to be kept in mind that some ingredients like urea in moisturizers may increase skin permeability and enhance penetration of hazardous substances.[43]

Emollients and moisturizers are post-exposure skin products that are advisable on diseased skin; they are the mainstay in the prevention and treatment of HE.

Barrier creams or protective creams are to be used on intact skin and should be used prior to the exposure to the irritant. Rarely, barrier creams may trap allergens,

and result in worsening of the dermatitis. Allergy to some component of the barrier cream may also rarely occur.

Greasy creams are helpful in restoring barrier function of skin. Preparations, which are fragrance-free and preservative-free, are preferred. Petrolatum is effective against water-soluble and water-insoluble irritants, it is recommended as a standard substance against which barrier creams are compared.[44] White petrolatum (pet.) is a refined, purified, and hydrogenated derivative from mineral oil, consisting of a complex combination of long-chained aliphatic hydrocarbons.[45] Experimental studies using *in vivo* techniques have proved that white petrolatum effectively protects the skin from water-soluble skin irritants in moderate concentrations and accelerates barrier recovery.[44,46]

Alcohol-based disinfectants with or without glycerin are less irritant than soap and water and are preferred.[47]

Protective Gloves

Gloves provide an effective protection against most irritants.[41,48,49] No single glove protects against the various causes of dermatitis, and wrong selection of gloves may not only lead to increased chance of injury or aggravation of dermatitis but also reduce efficiency during work. Some glove materials are permeable to certain chemicals and thus do not protect against those exposures. Occlusion, latex sensitivity, and contact allergy to other additives in rubber limits their use.

The standards of protective effect conferred by gloves include the EN standard (European Standard, European committee for Standardization) and the ASTM (American Society of Testing and Materials).

In Europe, gloves for protection (PG- protective gloves) are referred to as Personal Protective Equipment (PPE) and are covered under the PPE Directive 89/686/EEC "Gloves intended for protection." The PPE Directive is a part of European Legislation, which defines essential requirement for the product.[50] Medical gloves (MG) are separately covered under the Council Directive 93/42/EEC for medical devices.[51] In the USA, the American society of testing and materials - (ASTM), F-23 on protective clothing includes standards for gloves.[52] Under the EEC-directive, protective gloves are divided into 3 categories.[51]

1. Category I: Gloves of simple design – minimal risk
2. Category II: Gloves for intermediate risk
3. Category III: Gloves for irreversible / life-threatening risks

Methods for testing the level of protection conferred by protective gloves are given in EN 374 of the EEC Directive.[50] The properties tested include penetration, permeation, biocompatibility, and degradation.

Penetration or leakage is the passage of chemicals through macroscopic holes or pores. Faults in the manufacturing process or in storage are possibly responsible. Storage conditions are most important for medical gloves from natural rubber latex. The EN 374- 2 and ASTM F903 have laid down the regulations for testing of penetrability.[49,51] The British Standard (BS 3574:1989) also has guidelines for storage.

Permeation is the migration of chemicals through the glove at a molecular level from the outer surface to the inner surface contacting the hand. This includes the processes of sorption, diffusion, and desorption. 3 parameters are measured:

1. Breakthrough time (BT, min) is defined as the time between the initial application of a test chemical to the time when a specific permeation rate (PR) is achieved (This is a PR of 1 μg/min/cm^2 - EN standard, or 0.1 μg/min/cm^2- ASTM standard.) This standard determines permeation under a laboratory environment and not under real working environment where stretching and rise in temperature transmitted from the occluded skin occurs. This will affect the BT.
2. Permeation rate (PR) is the mass of chemicals migrating through the material per unit time per unit area (μg/min/cm^2).
   Steady-state permeation (SP) when the permeation rate becomes constant
3. Protection index (PI) is the protective effect conferred by combination of protective glove / test chemical and is based on the BT measured after constant contact with the chemical.
   i. BT (min) > 10 PI = 1
   ii. BT > 30 PI = 2
   iii. BT > 60 PI = 3
   iv. BT > 120 PI = 4
   v. BT > 240 PI = 5
   vi. BT > 480 PI = 6
4. *Degradation* relates to the glove material and chemical substance interactions. At present,

there is no standard, and manufacturers use different test methods to determine degradation occurring with different chemicals in contact with their glove product.

Other test methods include

Biocompatibility (As health care workers are reporting adverse reactions to latex proteins in gloves and other rubber chemicals). No complete guidelines available on this as yet for *in vivo* testing in man or in experimental animals.

Based on the results of the testing for penetration and permeation parameters, different pictograms are marked on each glove.[49] [Table 4]

Glove materials

The various materials used to manufacture gloves have been elaborated by Mellstrom and Boman.[46] Table 5 lists the various materials suitable for use as protective gloves or medical gloves modified from their classification.[48] Protection is conferred by the type of material, manufacturing processes, additives, etc. The protective effect increases with the thickness of the glove as the BT increases with the thickness of glove materials.

Newer protective gloves[41] include the:

1. Semi-permeable gloves: Selective semi-permeable membranes from manufacturers like GoreTex® (W. L. Gore and Associates Inc., www.goretex.com) or Sympatex® (Sympatex TechnologiesInc., www.sympatex.com) allow the transport of water-vapour from inside the medium to outside, but prevent penetration of water from outside. These gloves avoid the damaging effects of occlusion on the barrier properties of healthy skin.[53] However, they do not provide adequate protection against chemicals, and therefore, may be used under a protective glove in situations which entails an exposure to wet work but not chemicals.
2. "Hypoallergenic gloves" are gloves which are free of vulcanization accelerators.

Table 4: EN374 - Pictograms[47]

The 'Micro-organism' pictogram is to be used when the glove conforms to at least a performance level 2 for the Penetration test.

The 'Chemical resistant' glove pictogram must be accompanied by a 3-digit code. This code refers to the code letters of 3 chemicals (from a list of 12 standard defined chemicals), for which a breakthrough time of at least 30 minutes has been obtained.

The 'Low Chemical resistant' or 'Waterproof ' glove pictogram is to be used for those gloves that do not achieve a breakthrough time of at least 30 minutes against at least three chemicals from the defined list, but which comply with the Penetration test.

Table 5: Various glove materials for protection and medical use

Protective Gloves (PG)	Material	Medical Gloves (MG)
+	Natural Rubber latex (NR)	+
	Synthetic rubber materials	
+	Butyl Rubber (BR)	-
+	Chloroprene / Neoprene (CR)	+
+	Flour Rubber / Viton (V)	-
+	Polyisoprene rubber / Isolex P/R	+
+	Nitrile rubber / N-Dex, Nitrilite (NI)	+
-	Styrene butadiene/Elastyrene (SBR)	+
-	Styrene ethylene butadiene/Tactylon	+
-	Styrene isoprene	+
	Plastic polymeric materials	
+	Ethylene methacrylate (EMA)	+
+	Polyethylene (PE)	+
+	Polyvinyl alcohol (PVA)	-
+	Polyvinyl chloride (PVC)	+
+	Polyurethane	-
+	E+Ethylen vinyl alcohol EVOH+ PE/Laminate, 4-H glove	+
+	Leather	-
+	Textiles (silk, cotton, nylon)	-
	Special cut resistant fibres	
+	Kevlar	-
+	Lycra	-
+	Spectra fibre	-

Newer Protective Gloves (Hypoallergenic gloves, Semi-permeable gloves, Rip-up gloves)

3. Rip-up gloves are used for protection against cutting fluids (containing allergens like colophony, monoethanolamine) in the metal industry where gloves are not permitted to be worn on account of the risk from rotating machinery. These easy-tearing gloves may help overcome these problems. However, studies have not been conducted on the protection conferred by them.

Adverse effects of gloves include[41]

1. The right gloves for the substance(s) to be handled should be selected. Without the manufacturer's recommendations, the false sense of protection conferred by the gloves would pose a chemical hazard.
2. Internal contamination with chemicals occur if macroscopic holes or increased permeability is present. Incorrect use, incorrect wearing, removal, and disposal of gloves would still predispose to contamination in the absence of structural defects of the glove.
3. Occlusion may result in irritant contact dermatitis.
4. Contact urticaria to latex in gloves (Type I allergy). Legal and preventive measures have brought down the incidence of this condition.[54]
5. Allergic contact dermatitis. The list of allergens include:
    1. Thiurams (commonest)[55]
    2. Dithiocarbamates, mercaptobenzothiazol, and derivatives[56]
    3. 1,3 – diphenylguanidine causes false positive reactions though it is never used
    4. In Polyvinyl chloride (PVC) gloves, the culprit allergens are bisphenol A, formaldehyde, or benzisothiazolinon.[57]
    5. Natural rubber latex (rarely Type IV hypersensitivity)[58]

Treatment

In the acute stage, it is important to soothe the irritated skin with wet compresses or soaks (saline, aluminium acetate, potassium permanganate solution may be used), and not use occlusive ointments. In the sub-acute stage, creams may *be introduced and in the chronic stage, ointments (Soothe the acute with compresses and anoint the chronic with occlusive ointments*). Topical treatment with emollients and topical corticosteroids in addition to skin protection measures form the mainstay of therapy.[6,59-63]

Elimination diets**:** Ingested allergens may cause variety of skin and mucocutaneous lesions including perioral dermatitis, gingivostomatitis, pruritis ani related to sites of contact. In addition, systemic contact dermatitis and a flare-up of dermatitis in previously sensitized sites may also occur. Ingestion of nickel in diet may provoke these reactions, and a nickel elimination diet may lead to clinical improvement or clearance of hand eczema.[59] A low cobalt diet is also proposed in some patients.[57]

The **rule of the 4 R's**can be applied in the management of hand eczema.[60]

1. **Recognition of** the culprit irritant/allergen
2. **Removal** of the irritant/allergen
3. **Reduction of** skin inflammation
4. **Restoration of** the skin barrier

The various treatment modalities are listed in Table 6.

Emollients and Barrier creams

Following an episode of dermatitis, it takes weeks to months for the skin barrier to be restored.[60] Emollients and moisturizers help to restore the barrier. Sometimes, the demarcation between moisturizers used to restore the barrier and barrier creams, which are used to prevent dermatitis (irritant/contact), is not clear. They may prove harmful to the skin barrier. White petrolatum would be an effective emollient and barrier cream, so would be the topical emollient of choice.

Barrier repair

The concomitant treatment of dermatitis influences the barrier repair.[60] Topical and systemic

Table 6: Therapeutic armamentarium in hand eczema

Topical	Systemic
1. Emollients and barrier creams	1. Corticosteroids
2. Keratolytics (salicylic acid 20%), urea 5-10%	2. Ciclosporine
3. Topical corticosteroid ointments	3. Azathioprine
4. Topical calcineurin inhibitors (tacrolimus, pimecrolimus)	4. Retinoids (acitretin, alitretinoin)
5. Wet wraps	5. Methotrexate
6. Photo(chemo)therapy: with broad and narrow band UVB, (PUVA), UV A1	
7. Topical retinoid – bexarotene	
8. Tar based products (coal tar, ichthyol)	
9. Radiotherapy: X rays/Grenz rays	
10. Botulinum toxin	
11. Iontophoresis	

corticosteroids, retinoids control the inflammation well but have a negative effect on barrier recovery. Topical calcineurin inhibitors allow normal recovery while UV- phototherapy exerts its beneficial effect by skin hardening or accommodation (strengthening the barrier), thus making it less sensitive to irritants and control of ACD even with continued exposure.

Keratolytics used include salicylic acid up to 20%, and urea 5-10%. Urea softens the horny layer, and increases its water-binding and penetration-enhancing capabilities. Occlusion may cause skin irritation and burning. The potential to enhance penetration of noxious chemicals should also be kept in mind.

Topical Steroids

They, along with emollients are the mainstay of therapy.[61]

Potent topical steroids are used daily for about 4 weeks and then tapered to alternate day regimen.[63] Long term intermittent monotherapy with moderately-potent steroid-like mometasone furoate has been found to be effective.[63-65] Potent steroids are more effective and reduce the risk of recurrences as compared to moderately-potent steroids.[66] The adverse effects of long term topical corticosteroid usage are well-known (skin atrophy, tachyphylaxis, and adrenal suppression). Alternating a moderately-potent topical steroid with a topical calcineurin inhibitor reduces these side effects and clinically found to be effective. Topical tacrolimus is reported to be as effective as mometasone furoate in dyshidrotic palmar eczema, while the efficacy of pimecrolimus is comparable to a mild potent steroid.[67] Hypersensitivity to corticosteroids or other ingredients should be suspected if there is worsening. Patch testing with corticosteroid series would help in confirmation. Wet wrap dressings have been found to be effective in atopic eczema.[68]

Phototherapy improves the skin barrier. Topical psoralen UVA (PUVA) has been found to be superior to phototherapy with UVB[69] although pigmentation may be of concern in Indian patients. PUVA should be considered first for hyperkeratotic eczema as it is relatively safe. Broad and narrow band UVB, PUVA, and UVA1 have been reported to be beneficial.

UVA1 is considered to be less carcinogenic than PUVA and UVB.[70] Moderate to high doses give long remissions. [40 J/cm^2 5 times per week for 3 weeks (~ 600 J/cm^2) per treatment cycle.[70]

Topical bexarotene gel, a retinoid used for the treatment of lymphoma, has been reported to be effective although irritation, stinging, burning, and a flare of dermatitis has been reported.[71]

Coal tar-based products are effective in sub-acute and chronic eczema and have an anti-inflammatory, anti-pruritic, and anti-proliferative effect.

Radiotherapy (Grenz rays / superficial X-rays)

Grenz rays are safer than X-rays since penetration is only skin deep. Superficial X-rays was found to be more effective than Grenz rays, possibly due to deeper penetration.[72]

Other rarely tried therapies

When hand dermatitis is combined with hyperhidrosis, aluminium chloride hexahydrate and tap water iontophoresis may be effective; botulinum type A toxin may also be effective.[73]

Systemic Therapy

There are several drugs which are commonly used in treatment. Excepting alitretinoin, most of these drugs are not licensed for the treatment of hand eczema. Alitretinoin is approved in adults for the treatment of HE unresponsive to topical steroids, based on evidence from a larger randomized trial.[74]

Systemic corticosteroids

Oral corticosteroids are used in the short term management of acute hand eczema or during an exacerbation of chronic HE (0.5 - 1 mg/kg/day) with rapid tapering; long term use is not advocated due to their side-effects.

Oral retinoids

Retinoids are vitamin A derivatives which are either endogenous (physiological) or synthetic.

Acitretin, a synthetic retinoid, 40 mg oral daily showed 50% improvement at 4 weeks in a study (n = 14) of patients with hyperkeratotic hand eczema. There was no further improvement at week 8.[75] Combined therapy with other drugs may prove more beneficial.

Alitretinoin (9-cis-retinoic acid)

Isotretinoin is a naturally-occurring retinoid found in the body in small quantities. Alitretinoin is an isomer of isotretinoin (13-cis-retinoic acid) and is an endogenous physical retinoid. Although structurally similar to isotretinoin, sebum secretion is not suppressed significantly, which could explain the lower incidence of mucocutaneous side-effects like dryness, cheilitis, etc. and also the lack of efficacy in acne.[76]

There are 2 families of nuclear receptors associated with retinoids – retinoid acid receptors (RARs) and retinoid X receptors (RXRs). Alitretinoin binds to both RARs and RXRs.

Alitretinoin is currently the only evidence-based therapy for patients with severe chronic hand eczema, unresponsive to potent topical corticosteroids. There are 3 large phase II clinical trials assessing its safety. The first is a large, randomized, multi-centric, placebo controlled, double blind study in 111 dermatology clinics in Europe and Canada. The BACH study (Benefit of Alitretinoin in Chronic Hand Eczema) is currently the largest-controlled trial in hand eczema.[74] The commonest side-effect was headache; other less common side-effects were muco-cutaneous side-effects and dryness, decreased TSH levels and hyper-triglyceridemia.[74] Alitretinoin is a teratogen-like other retinoids, but has a shorter half life (mean t1/2 2-10 hours) than acitretin (mean t1/2 39-96 hours). Contraception is recommended 1 month post-treatment with alitretinoin as compared to 3 years for acitretin. In the BACH study, patients who relapsed within 24 weeks after completion or those who didn't respond were retreated with alitretinoin 30 mg for 24 weeks, of which, 50% achieved 'clear' or 'almost clear' hands.[77] These patients were included in the second trial, which was a double-blind, placebo-controlled, randomized study.[75] The third trial was an open-label, single-fixed dose study in 249 patients.[78]

Cyclosporine

Cyclosporine at 3 mg/kg/day for 6 weeks was reported to be as effective as topical betamethasone dipropionate.[79] It has been studied extensively in the treatment of atopic dermatitis.[80] Very slow tapering over a period of 6 months is recommended. A lack of response beyond 8 weeks should suggest discontinuation of therapy. Blood pressure, serum potassium, and creatinine should be monitored.

Azathioprine

It is an effective steroid-sparing agent and can also be used alone in hand eczema (2 mg/kg/day). Hand eczema seen with parthenium dermatitis responds well to azathioprine.[17] Atopic hand eczema also shows good response.[81] Due to genetic polymorphisms, 11% of the population have intermediate TPMT activity and are predisposed to toxic effects. 1 in 300 people has low or no activity and is susceptible to life-threatening pancytopenia; other frequencies are also reported.[82] Dosage should be advised after checking the TPMT levels.

Methotrexate

Low dose methotrexate (5-20 mg weekly) has been reported to be effective in chronic hand eczema.[83] In an atopic patient with parthenium dermatitis presenting as hand dermatitis, methotrexate has been found to be effective.[17]

Mycophenolate mofetil

Beneficial effects have been reported in a single patient with hand eczema.[84]

The treatment of chronic hand eczema still remains an arduous task since the majority do not derive adequate benefit from the multitude of therapies. Newer superpotent steroids like halometasone monohydrate once-daily for a limited period during the initial phase of chronic-fissured HE should be studied. Cyclosporine and azathioprine are beneficial in HE with an atopic background. Alitretinoin is a new drug licensed for use in severe chronic HE, with good results in a clinical trial, having the side-effects of retinoids, at a lesser degree.

When chronic hand eczema is characterized by combined allergic and irritant contact dermatitis, filaggrin gene mutations may play a role.[85] Identifying the cause and avoiding it could result in complete clearance in a case of ACD; however, in irritant and atopic dermatitis, avoiding the irritant factor is not always feasible.

Lifestyle change is recommended for all patients, avoiding all possible irritants and allergens.

Skin care and personal protection measures should be individualised for each person and his/her environment.

Appendix I

Patient Information Brochure: HAND ECZEMA

1. Avoid handling food items (raw vegetables, especially onion and garlic, raw meat, and fish) with bare hands. Also, try to avoid eating with bare hands.
2. Direct contact with solvents, polishes (metal, shoe, furniture, car, etc.), adhesives, and epoxy resins has to be avoided. Use protective gloves.
3. Vinyl gloves can be used for these jobs. Do not use latex gloves since solvents pass through latex rubber gloves. Vinyl gloves are less likely to cause allergic reactions.
4. For some chemicals like hair perming chemicals, a plastic polymer glove – 4H glove is recommended. Thin cotton gloves underneath the gloves may be used to absorb perspiration.
5. Woolen gloves may cause irritation in many people, especially atopics.
6. Use lukewarm water and mild cleansers without perfume, colors, anti-bacterial agents for washing hands. Take off rings before washing. Pat hands dry, especially the fingerwebs and wrist.
7. Use corticosteroid ointments and emollient creams as advised. Do not use any other hand creams. Repeat application of emollients (Vaseline) as many times as possible.
8. Thin polyethylene gloves at night after applying corticosteroid ointment will provide occlusion and enhance the effect of ointment.
9. Protect hands from cold weather. Use leather gloves; thin cotton gloves may be first worn.
10. Cut off the tips of the gloves or fingers if necessary, based on the requirement of occlusion. Normal skin need not be occluded.

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