

Irritant Contact Dermatitis: Mechanisms to Repair

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Abstract

Irritant contact dermatitis is an extremely common condition resulting from epidermal exposure to any number of skin irritants. Upon contact with skin irritants, the epidermis develops many identifiable problems including specific epidermal lipid deficiencies, elevated epidermal pH with concomitant suppression of epidermal lipid production, pH-dependent susceptibility to infection, inflammation, and aberrant calcium gradients. By addressing these problems simultaneously, and through irritant avoidance, the treatment of irritant contact dermatitis can be maximized.

Keywords: Allergen; Barrier dysfunction; Barrier repair, Ceramide; Contact; Dermatitis; Irritant; Petrolatum; Cholesterol ester; Niacinamide; Dimethicone; 18-B glycyrrhetic acid; Gluconolactone

Abbreviations:

ACD: Allergic Contact Dermatitis; CD: Contact Dermatitis; IL: Interleukin; ICD: Irritant Contact Dermatitis; TEWL: Transepidermal Water Loss; SLS: Sodium Lauryl Sulfate

Introduction

Contact dermatitis refers to any skin inflammation that occurs as a result of exposure to irritants or allergens. Irritant contact dermatitis (ICD) is a localized inflammatory reaction that occurs when a chemical or physical agent causes direct cytotoxic skin damage leading to skin barrier disruption, cellular changes, and release of proinflammatory mediators. This is a non immunologic mechanism that does not require sensitization, whereas allergic contact dermatitis (ACD) is a delayed-type hypersensitivity reaction, mediated by T cells [1].

The epidemiology of CD shows that 80% of all contact dermatitis is due to ICD with ACD accounting for the remaining 20% [2]. Irritant contact dermatitis is usually caused by frequent and repeated use of known irritating substances, such as soapy water, cleansers, and rubbing alcohol. Additional agents commonly reported to cause ICD include rubber, chemicals, wet work, resins and acrylics, nickel, petrolatum, cutting oils and coolants [3]. ICD can affect all people; however, individuals in the rubber, plastic, metal, petrochemical and automotive industries are most commonly affected due to high rates of irritant exposure [1]. Those with pre-existing skin disease (e.g. dry skin and atopic dermatitis), infants and the elderly, are also predisposed to developing ICD due, to a less resilient epidermal barrier. Research has demonstrated a different penetration profile in the stratum corneum (SC) of patients who have atopic dermatitis and who are exposed to irritants as compared to control subjects, thus illustrating the major role of skin barrier function in ICD [4].

Discerning ICD from ACD

Clinical distinction of irritant contact dermatitis from allergic contact dermatitis is difficult. Both conditions have similar clinical and histopathologic presentations, and often may coexist [5,6]. New evidence also indicates that the epidermal and dermal cell activity responsible for the cascade of inflammation in ICD and ACD is similar [7,8]. Because ICD is a frequently encountered clinical scenario that greatly impacts allergy evaluation, it is important to be able to discern between these two processes.

ICD is a complex biological syndrome with a distinct pathophysiology, diverse clinical appearance and natural history. ICD is influenced by the physical and chemical properties of the irritating substance, concentration, mode of exposure, host-related susceptibility factors, and concomitant environmental factors. These influences lead to a variety of clinical manifestations ranging from mild skin dryness and erythema, to more pronounced edema, coalescing vesicles, bullae, pustules, ulceration and even skin necrosis. Chronic ICD can lead to the appearance of relative tolerance to certain irritants and solvents when the acute signs of ICD evolve into a more chronic, lichenified form of ICD that is known as the hardening phenomenon (Figure 1).



Figure 1: The hardening phenomenon in a mechanic.

In ICD, lesions are usually sharply demarcated and confined to the contact area (Figure 2a), while in ACD, lesions are less circumscribed

and frequently disseminated (Figure 3a). Common symptoms in ICD include burning, stinging and soreness of the skin. Diagnosis of acute irritant dermatitis due to more potent agents is often obvious and is based upon distribution, location of the rash, and rapid onset of skin changes after exposure to the causative agent. A detailed history of the patient's chemical and physical environment and use of diagnostic patch testing will assist in differentiating between both types of dermatitis.



Figure 2: (A) Signs of irritant contact hand dermatitis include dry, cracked and oozing plaques on the dorsal hands. (B) Irritant contact dermatitis after twice daily treatment for 14 days using skin barrier optimized 1% hydrocortisone cream and a lipid barrier optimizing ointment.



Figure 3: (A) Allergic contact dermatitis due to iodine two days after an epidural in a nursing mother. (B) After 11 days BID treatment with skin barrier optimizing hypoallergenic lipid barrier ointment compounded with 0.05% clobetasol.

In the case of ACD, the distribution, location and chronology of exposure to potential allergens are all important considerations when differentiating ICD from ACD. When the dermatitis is distributed in a symmetrical or recognizable pattern, or, if it is in a typical/likely location that may implicate sensitizing contact with an allergen, then ACD can often be easily differentiated from ICD. However, in subacute or chronic contact dermatitis where no obvious distribution or demarcation of the dermatitis is present, it is clinically challenging to determine if the etiology is one of ICD versus ACD [9]. Equally confounding, is that some haptens can cause both ICD and ACD depending on the concentration [10].

In this paper, we will specifically focus on the pathophysiology of and mechanisms to repair the skin barrier in ICD.

Pathophysiology of Irritant Contact Dermatitis

The pathogenesis of ICD is multifactorial. Physical and chemical irritants that contact the skin damage epidermal cells and remove epidermal lipids from the epidermis. An increase in skin permeability

and transepidermal water loss (TEWL) ensues. This is considered the initiating event in ICD, and results in the release of cytokines, chemokines and adhesion molecules, which are potent chemoattractants for leukocytes and may induce T-cell activation independent of exogenous antigen [11,12]. Different mechanisms have been associated with ICD and these are largely dependent on the nature of the irritant. Experimental and animal models have demonstrated that solvents such as acetone extract lipids from the stratum corneum [13], and anionic surfactants like sodium lauryl sulphate (SLS), cocobetaine and sodium dodecan sulphate (SDS) damage keratin, involucrin, profilaggrin, and other protein structures responsible for preventing oversaturation of the stratum corneum and disorganization of the lipid bilayers [14-16].

Cytokine Cascade

In ICD, a cytokine cascade is initiated by contact and penetration of irritants into the epidermal skin barrier which leads to activation of the keratinocytes. The innate immune system is turned on leading to the release of proinflammatory cytokines, such as interleukin (IL) 1 alpha, IL-1 beta, IL-6, and tumor necrosis factor (TNF) alpha [17-19]. T cells are activated by TNF alpha, IL-1 beta and IL-6. The cytokine and chemokine cascade is perpetuated, leading to the characteristic upregulation of intercellular adhesion molecule-1 (ICAM-1) [20] found in ICD. CCL20 and CXCL8 release are also triggered, leading to attraction of mononuclear and polymorphonuclear cells to the site of injury [21,22]. Fibroblasts also stimulate active mediators such as CXCL8, CXCL1, and CCL2. This leads to migration of Langerhans cells out of the epidermis [23,24] and the simultaneous upregulation of adhesion molecules that result in recruitment of more immune cells into the skin [25].

Chronic ICD

With repeated exposure to solvents and surfactants, the skin develops the hardening phenomenon, a characteristic of chronic ICD (Figure 1). This condition is thought to be due excessive and chronic extraction of skin lipids as a result of the insidious exposure to surfactants and solvents. Transepidermal water loss promotes cell proliferation and hyperkeratosis, which is exhibited as the chronic eczematoid irritant reaction of the hardening phenomenon [26,27].

The Skin Barrier

Human skin is composed of three main regions-epidermis, dermis, and hypodermis, creating an impervious barrier that protect underlying tissue from dehydration, infection, and physical, chemical and mechanical stress. The outermost layer of the epidermis, the stratum corneum, serves as the first line of defense against absorption and irritation due to chemical exposure [28]. Within the stratum corneum, stacked cornified keratinocytes are separated by highly ordered extracellular lipid bilayers [29]. The lipid bilayer prevents excessive loss of water from the skin and acts as a barrier against the permeation of many topically applied substances. The lipid bilayer also contributes to the acid mantle of the epidermis and contributes another intrinsic line of defense within the epidermis; a naturally acidic pH. An epidermal calcium gradient influences desquamation, cellular turnover and differentiation of the epidermis, as well as the cutaneous immune system [30].

After exposure to irritants, the stratum corneum is damaged and the skin barrier is impaired. Excessive water loss and increased

penetration of irritants and allergens ensue. Alteration in the epidermal calcium gradient [31], slow/deficient lipid production [32], and an increase in pH [33], all play a role in the development of irritant contact dermatitis.

Mechanisms to Repair

To prevent and treat irritant contact dermatitis, it is important to understand the many ways in which the skin can develop ICD (Table 1) and to address the many areas of epidermal vulnerability through skin barrier optimization. Skin barrier optimization occurs via optimization of epidermal skin barrier lipid content, restoration of the pH of the acid mantle, prevention of irritant and allergen penetration into the skin, controlling inflammation, and by helping to maintain natural calcium gradients across the epidermis. Additionally, all common allergens and pro-inflammatory excipients should be avoided. In cases where inflammation is so intense that barrier repair alone is insufficient to restore the skin barrier, additional benefits can be seen by compounding glucocorticoids into skin barrier optimized moisturizers. The skin barrier can be optimized while severe inflammation is also addressed (Figures 3b).

| Occupation | Common irritants encountered |
|----------------------------------|---------------------------------|
| Agriculture | Oils |
| | Solvents |
| | Cleansers and detergents |
| | Plants |
| | Animal hair, saliva, secretions |
| | Wet work |
| Automobile industry | Oils (cutting oils) |
| | Solvents |
| | Cleansers and detergents |
| Cement and construction industry | Cement |
| | Wood preservatives |
| | Oils |
| | Acids and alkalis |
| | Fiberglass |
| Cleaners and housework | Wet work |
| | Cleansers and detergents |
| | Abrasives |
| Electrical/electronics | Solvents |
| | Soldering flux |
| | Cleansers and detergents |
| | Acids and alkalis |
| Food Industry | Wet Work |
| | Cleansers and detergents |

| | |
|-------------------------|--|
| | Vegetables, fish, meat, fruit, spices, flour |
| Hairdressing/beautician | Wet work |
| | Shampoos |
| | Permanent wave solutions |
| | Oxidizing agents, bleaching agents |
| Healthcare and dental | Cleansers and detergents |
| | Wet work |
| | Alcohol |
| | Disinfectants |
| | Medications |
| | Solvents |
| Painting | Oils and cutting fluids |
| | Acids and alkalis |
| | Solvents |
| Metal industry | Cleansers and detergents |
| | Paints |
| | Glues and adhesives |
| | Clay, plaster |
| Plastic industry | Plastics |
| | Solvents |
| | Fiberglass |
| Rubber industry | Acids |
| | Solvents |
| | Cleansers and detergents |
| Woodwork | Frictional/mechanical factor |
| | Plastics |
| | Solvents |
| | Wood preservatives |
| | Detergents |
| | Sawdusts |

Table 1: High-risk occupations and common irritants encountered. Adapted with kind permission from: Chew AL, Maibach HI (2003) Occupational issues of irritant contact dermatitis. Int Arch Occup Environ Health 76: 339.

Prevent Chemical-Induced Transepidermal Water Loss

Transepidermal water loss (TEWL) is a reflection of the barrier function of the stratum corneum. When injured, the stratum corneum's ability to maintain hydration is reduced, leading to increased TEWL and decreased water content in the skin. This impaired skin barrier facilitates the entry of irritants and is one of the

fundamental defects in irritant contact dermatitis pathophysiology [34].

Any substance capable of denaturing keratin, removing natural moisturizing factor or interrupting the lipid bilayer component of the epidermis can result in increased transepidermal water loss. Irritants most frequently associated with increased TEWL include solvents, detergents, and excessive use of water and soap. Irritating potency of different surfactants and detergents has been previously studied using TEWL, with sodium lauryl sulfate (SLS), sodium dodecan sulphonate (SDS) and cocobetaine (COCO) noted to most markedly influence the loss of water through the skin [35-37].

Prevent Contact with Irritants

In addition to TEWL prevention, irritants should be inhibited from coming in contact with the skin. Several substances have been found to effectively inhibit transepidermal water loss in addition to preventing irritants from coming in contact with the skin. Petrolatum, paraffin wax and dimethicone are commonly and effectively used as skin protectants as well as TEWL inhibitors for ICD. Recently, a lipid fraction, isostearyl isostearate, has been identified as one of the most effective lipid-based TEWL inhibitors in the world [38-40].

To be considered an ideal skin barrier protectant, the relative hydrophobicity, water solubility and melting point should be considered. As the hydrophobicity of a substance increases, its water solubility decreases making it less likely to be washed off and more resistant to water-soluble irritants. An increased melting point also confers higher resistance to washing off in hot or cold water.

Petrolatum, the gold standard TEWL inhibitor, is a complex semi-solid combination of paraffin wax, microcrystalline wax and white mineral oil [41]. Wigger-Alberti and Elsner evaluated the protective effects of petrolatum against four standard irritants: 10% SLS, 1% sodium hydroxide (NaOH), 30% lactic acid (LA), and undiluted toluene (TOL) in the repetitive irritation test (RIT) in humans for 12 days. Irritation was assessed by visual scoring, TEWL, and colorimetry. Petrolatum was effective against SLS, NaOH, and LA irritation, and moderately protective against TOL [42]. The melting point of petrolatum is between 36-60°C [43].

Paraffin is a mixture of saturated aliphatic hydrocarbons and is considered to be the most hydrophobic water-repelling agent. Paraffin wax is even more impermeable to water than petrolatum and, when combined with petrolatum, is an extremely efficient TEWL inhibitor [44]. Paraffin is also a natural moisturizer, assists with exfoliation, and helps to heal dry, cracked skin. If injected into the skin, paraffin has been reported to induce granuloma formation. This has not been the case when applied directly to the skin as it would be in the context of irritant dermatitis. The melting point of paraffin wax ranges from 47-65°C depending on which grade of wax is used [45].

Dimethicone is a man-made polymer of the naturally occurring element silica or silicon. It is used as an emollient to soften and moisturize the skin, decrease itching and flaking, facilitate epidermal exfoliation and provide a protective barrier from irritants [46]. Lotion containing dimethicone has been shown to be efficacious against insult from sodium lauryl sulfate (SLS)-induced ICD [47]. Dimethicone-containing ointment has also proven to be effective in protecting the skin against contact irritants from sunscreens, intra-abdominal drainage, and from the discharge of cutaneous ulcers [48,49]. Unfortunately, an increasing number of reports of sensitization and

inflammatory reactions to silicon polymers limit their use. When silicon was incubated with human monocytes, elevated levels of inflammatory cytokines including IL-1 beta, IL-6 and TNF-alpha were noted [50]. Furthermore, a local lymph node assay in mice showed weak to moderate skin sensitization potential in four out of five silicon materials tested for skin sensitization [51,52]. The melting point of dimethicone is generally below 50°C depending on which polymer is used.

Skin Lipid Depletion and Supplementation

While many skin barrier repair products have focused on "physiologic lipid replacement" in a 3:1:1 ratio of ceramides, cholesterol, and fatty acids, the major lipid species of the stratum corneum are actually present in the following relative concentrations; ceramides (47%), fatty acids (11%), cholesterol (24%), and cholesterol esters (18%). Physiologic lipid replacement that follows the 3:1:1 rule does not specifically focus on lipid species that are particularly deficient in SDS-induced contact dermatitis, aged skin, dry skin and eczema-prone skin [53,54]. The structure, concentration and ratio of epidermal lipids allow the epidermis to act as a barrier to irritants, allergens and microbes and limits water loss and regulates temperature. Many skin conditions such as ICD, xerosis, aged skin and atopic dermatitis are attributed in some regard to deficiencies or aberrations in ratios of specific lipid classes [55,56]. Because this is the case, it may be most beneficial to rely on the medical literature and identify the specific lipid species that are deficient in irritant contact dermatitis and supplement those lipids to the irritated skin rather than supplying physiologic levels of lipids.

Epidermal Lipids

Ceramides are a lamellar granule-derived sphingolipid. Lamellar granules produce and excrete stacked lipid structures that bathe the corneocytes and provide a barrier that limits TEWL and prevents the leaching of natural moisturizing factor from the stratum corneum. With the progression of age, intercellular lipid production and concentration decreases sharply. Phytosphingosine and phytosphingosine-containing ceramides become deficient and the skin becomes increasingly susceptible to dryness, irritation and the development of ICD [57,58]. Interestingly, ceramide 3 (a phytosphingosine-based ceramide) has also been shown to be markedly deficient in atopic skin and is correlated to increased TEWL.

Many common skin irritants such as (SLS) and (SDS) have been shown to reduce ceramide production. This is partially due to their ability to solubilize stratum corneum lipids. Examination of ceramide content following SLS application showed an inverse relationship between baseline ceramide weight and clinical irritation including erythema, scaling, dryness and roughness [59]. This suggests a proclivity towards surfactant-induced irritant contact dermatitis. Other irritants known to damage lipid bilayers and decrease ceramide content include alkalis such as soaps, soda, ammonia, potassium and sodium hydroxides, as well as solvents including benzene, toluene and acetone.

A beneficial skin barrier repair product for the treatment and prevention of irritant contact dermatitis would specifically supplement the skin with phytosphingosine and phytosphingosine-containing ceramides and would induce ceramide production. Ceramide production can be induced with niacinamide. Niacinamide up-regulates expression of serine palmitoyltransferase, the rate-limiting

enzyme in sphingolipid synthesis [60]. Niacinamide has also been shown to increase epidermal thickness and filaggrin formation [61].

Cholesterol, cholesterol esters and their relative ratios also play an important role in skin barrier function. An excess concentration of cholesterol with a relative deficiency of cholesterol esters has been identified in SDS-induced dry skin, xerotic skin and atopic skin [57,62,63]. When skin was irritated with SDS to induce ICD and was then treated with either a 1% cholesterol base or 1% cholesterol ester base, the skin that was treated with cholesterol showed no improvements in conductance values while the cholesterol ester base-treated skin did show improvements in conductance values [63]. This illustrates the benefits of supplementing the skin with lipid species that are particularly deficient in ICD, such as cholesterol esters, rather than simply following traditional physiologic lipid supplementation where cholesterol would be supplemented rather than cholesterol esters.

Inflammation

Anti-inflammatory molecules have been shown to be effective in many forms of skin barrier disruption [64], with glucocorticoids being the most-commonly prescribed. Prescription medical device creams have also been introduced and subsequently found to be comparable in efficacy to an over the counter product [65]. Here we will review the many benefits of two well-studied non-steroid anti-inflammatory molecules: niacinamide and 18 β -Glycyrrhetic Acid.

18 β -Glycyrrhetic Acid

18 β -Glycyrrhetic acid is a potentially viable agent for the treatment of contact dermatitis due to its corticosteroid-like anti-inflammatory and anti-allergic activity. In vitro, Glycyrrhetic acid attenuates the generation of excessive NO, PGE₂, and ROS and suppresses expression of pro-inflammatory genes by inhibiting NF- κ B and PI3K activity [66]. Additionally, it is known to inhibit Δ 4 β -reductase, an enzyme that competitively inactivates steroid hormones, and 11 β -hydroxysteroid dehydrogenase, an enzyme that deactivates cortisol [67,68]. This possibly potentiates the body's anti-inflammatory capacity by increasing naturally occurring cortisol levels. When used in formulation by itself or with a glucocorticoid, glycyrrhetic acid may extend the effectiveness of glucocorticoids, allowing for use of less-potent glucocorticoids and/or a shorter course of treatment (Figure 2b). This could limit overall glucocorticoid exposure and side effects. Incidence of contact dermatitis in mice was minimized when given a metabolic precursor of 18 β -glycyrrhetic acid intraperitoneally versus prednisolone. When administered orally, it was ineffective [69], possibly highlighting the necessity to deliver the active molecule directly to the area of contact dermatitis.

Niacinamide

Niacinamide is a physiologically active form of vitamin B3 that has been shown to have anti-cancer effects [70] and to be beneficial in treating a variety of inflammatory skin diseases including acne vulgaris, rosacea, and bullous pemphigoid [71-73]. The broad clinical effects of niacinamide are felt to be from a variety of potential mechanisms of action including anti-inflammatory effects via inhibition of leukocyte chemotaxis, lysosomal enzyme release, lymphocytic transformation, mast cell degranulation, bacteriostatic effects against *Propionibacterium acnes*, inhibition of vasoactive amines, preservation of intracellular coenzyme homeostasis, and decreased sebum production [74,75]. Niacinamide also increases the

thickness of the epidermis [76] while inducing de novo ceramide production through up-regulated expression of serine palmitoyltransferase, the rate-limiting enzyme in sphingolipid synthesis. This increase in ceramide production directly correlates with a reduction in TEWL in subjects with xerotic skin [77]. By creating a more formidable skin barrier with the use of topical niacinamide, patients may be less prone to ICD following irritant exposure.

Skin pH Fluctuation and Modulation

Skin pH and the organic factors influencing it are important in the pathogenesis, prevention and treatment of irritant contact dermatitis. Healthy skin typically has an acidic stratum corneum with the pH ranging between 4.6 and 5.6. Optimizing skin pH helps maintain activity levels of lipid-producing enzymes β -glucocerebrosidase and acid sphingomyelinases [78,79]. These enzymes are vital for ceramide and lipid production, as well as maintaining a healthy microbiome [79]. When ceramides, lipid content, and the natural skin flora are disturbed, a cycle of increased alkalinity, infection, dry skin and a disrupted epidermal barrier ensues. This can be further exacerbated following repeated exposure to alkaline substances such as soap, bleach, solvents and even tap water.

In contrast, hyperacidification of the stratum corneum in hairless mice using lactobionic acid (LBA) and gluconolactone (GL) has been shown to enhance permeability barrier homeostasis, stratum corneum desquamation and skin appearance while preventing skin irritation [80]. These polyhydroxy acids (PHA) are ideal for optimizing epidermal pH and decreasing TEWL.

Restoring the Disrupted Calcium Gradient to Optimize Cell Turnover

Keratinocytes are generated in the stratum basale and differentiate as they move towards the skin surface. These epithelial cells are instrumental in maintaining barrier homeostasis. They provide structural support for the stratum corneum by undergoing terminal differentiation to produce corneocytes and intercorneocyte lipids. Corneocytes contain rigid proteins and play a hydrating role in the stratum corneum, while intercellular lipids create a hydrophobic interface between the corneocytes and the highly hydrophobic lipid lamellae to enhance the ionic skin barrier [81].

Terminal differentiation of the epidermis is regulated by the concentration of extracellular calcium ions. Keratinocytes cultured in low calcium concentrations produce an undifferentiated, basal cell-like phenotype, whereas keratinocytes cultured in higher calcium concentrations undergo terminal differentiation. In vivo and in vitro studies using human and murine epidermis have reinforced these findings, demonstrating lower calcium levels in the basal, proliferating spinous layers, with a progressive increase in calcium as one proceeds to the outer, differentiated stratum granulosum [82-84].

The epidermal calcium gradient has a significant role in skin barrier homeostasis via its influence on keratinocyte terminal differentiation. Following acetone-induced barrier disruption, Menon et al. showed that the intracellular calcium gradient disappears and reappears with lamellar body secretion and barrier recovery over a 24 hour period. When immersed in iso-osmolar sucrose plus calcium, however, the epidermal calcium gradient was replenished and both lamellar body secretion and the process of barrier recovery were significantly

decreased. These results show that barrier disruption leads to loss of the epidermal calcium gradient, which may be the signal that initiates lamellar body secretion leading to barrier repair [83]. Patients with psoriasis, dry atopic skin and contact dermatitis are particularly vulnerable to irritants such as sodium lauryl sulphate and polyethylene glycols (PEGs) due to chronically impaired barrier function [84,85]. Research using scanning nuclear microprobes has demonstrated that these patients have an epidermal calcium gradient higher than normal skin [86]. Additionally, strong irritant compounds such as 2-4-hexadienal, piperazine, DMIPA, heptylamine and SLS have all been shown to induce keratinocyte release of intracellular calcium leading to a systematic activation of pro-inflammatory cytokines IL1 α , IL6 and IL8, or mediators such as ATP and prostaglandins [87]. These chemical irritants are therefore linked to acute irritant contact dermatitis activated by calcium-dependent pathways.

Calcium inhibits normal desquamation. Chelation with EDTA has been shown to foster the final steps of desquamation in hyperkeratotic skin [88,89]. Normal skin likely has a natural chelating agent, which Rawlings et al. postulate is due to the naturally-occurring fatty acids [54]. If true, it would be logical that skin disorders deficient in fatty acids would also have increased levels of calcium as was noted by Forslind et al. [85]. For products that are intended to treat irritant contact dermatitis wherein the fatty acids are often stripped from the skin, the inclusion of weak calcium chelating agents may help to normalize cell cycling and desquamation.

Prevention of ICD

Educating patients about how to avoid irritants in the home and work place is very important. Reducing contact with irritants such as soap, solvents, oils, alkalis, acids or abrasive materials decreases the incidence of ICD. However, when avoidance of the irritant is not possible, protective skin products are the next alternative [90].

When selecting skin protection products it is important to consider the specific substances and exposure conditions they are designed to protect against. Barrier creams and ointments protect against low-grade irritants, benefiting wet-workers who regularly utilize water, soaps, and detergents. They also shield the skin from chemicals, oils and other potential irritants [91]. Moisturizing barrier products may prevent ICD and accelerate the rate of healing in damaged skin by increasing skin hydration and modifying endogenous epidermal lipids [92,93]. Individuals who are regularly exposed to irritants should be encouraged to regularly apply moisturizers not only prevent but to treat mild ICD.

Conclusion

Water, organic solvents, detergents, alkalis and acids are the most common irritants in ICD. Human exposure to these irritants leads to stratum corneum damage causing skin barrier impairment. Because avoidance of these irritants is not always practical, prophylactic measures aimed at reducing the signs and symptoms of inflammation and restoring the epidermal barrier are necessary. The ideal topical product should address the many areas of vulnerability and pathology that can lead to ICD and should be effective regardless of environment, age group, or occupation. Utilization of existing and recent data on the interaction of various chemicals with the stratum corneum leads to the development of novel products based on evidence-based medicine. Our understanding of the pathophysiology of irritant contact dermatitis is continually clarified, allowing for the

development of more innovative and more advanced treatment options.

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Conflict of Interest

Cheryl Lee Eberting, MD, owns CherylLeeMD[®], Sensitive Skin Care and is the inventor of TrueLipids[®] skin barrier repair technology. Other authors have no conflicts of interest to disclose.

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