

Hand Dermatitis in the Time of COVID-19: A Review of Occupational Irritant Contact Dermatitis

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Occupational contact dermatitis accounts for 95% of all cases of occupational skin disease with irritant contact dermatitis (ICD) constituting 80% to 90% of these cases. Health care workers, hairdressers, and food service workers are typically most affected by occupational ICD of the hands as these occupations require frequent hand hygiene and/or prolonged exposure to water, also known as “wet work.” In the context of the current COVID-19 pandemic, frequent hand hygiene has become a global recommendation for all individuals, and new workplace guidelines for hand sanitization and surface sterilization are affecting occupations not previously considered at risk of excessive wet work including grocery or retail workers, postal workers, sanitization workers, and others. In this review, we discuss the etiology and pathogenesis of occupational ICD with additional focus on treatment and interventions that can be made at an institutional and even national level for education and prevention of ICD resulting from frequent hand hygiene.

Occupational contact dermatitis (OCD) is overwhelmingly the most important cause of occupational skin disease, accounting for 95% of cases.^{1,2} The majority of these cases are caused by irritant contact dermatitis (ICD), further specified as occupational irritant contact dermatitis (OICD) with 80% to 90% of cases involving the hands.^{2,3} Occupational irritant contact dermatitis of the hands affects workers in many occupations, although it is observed most frequently in health care workers (HCWs). The true rate of cases is likely much higher as cases frequently go unreported, particularly in the health care sector.^{1,4} The rise in health care–associated infections observed in the last several decades prompted international campaigns for increasing hand hygiene in the health care setting, which has been accompanied by an increased incidence of hand OICD.⁵ As the act of hand hygiene cannot be reduced or eliminated in the setting of health care, these cases often become chronic and debilitating when left unrecognized and untreated.⁶ Hand dermatitis has been shown to significantly impact quality of life, both professional and personal, and leads to missed days of work and, in severe cases, change in career or early retirement with significant financial implications on a personal and societal level.^{7,8} In 1985, the national annual medical and indemnity cost of occupational skin disease was estimated to be between \$222 million and \$1 billion in

the United States, whereas more recently, it was estimated that in the European Union approximately \$5 billion is lost annually because of lost wages, lost productivity, and medical expenses for OCD.^{9,10}

The current climate of a global COVID-19 pandemic presents new challenges with regard to hand OICD. In the health care setting, recommended protocols have increased frequency of hand hygiene to include not only performing hand hygiene before and after patient care but also before and after application of personal protective equipment (PPE). Further, the Environmental Protection Agency released guidelines for surface disinfectants that target SARS-CoV-2 with many of the approved products containing known skin irritants or allergens.^{11,12} Traditionally, the greatest risk of OICD of the hands has been attributed to professions with frequent handwashing and/or wet work; however, in the setting of the COVID-19 pandemic, increased hand hygiene and exposure to harsh surface disinfectants have become a universal practice extending to all customer-facing occupations. Here, we will review the pathogenesis, triggers, and treatment of hand OICD, as well as system-wide approaches to early intervention and treatment, which have traditionally been thought of as health care specific, although now it may apply more broadly to many occupations.

OCCUPATIONAL CONTACT DERMATITIS

Occupational contact dermatitis is a general term that encompasses ICD, allergic contact dermatitis (ACD), and contact urticaria. Irritant contact dermatitis, ACD, and contact urticaria account for approximately one-third of all occupation-related medical complaints and 90% to 95% of occupation-related skin complaints.^{10,13,14} Each variant of contact dermatitis is the result of activation of a distinct immune response, thus resulting in their unique clinical presentations. Irritant dermatitis is the result of a physical injury to the

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stratum corneum, resulting in barrier dysfunction typically caused by repetitive friction, water, or chemical products. The compromised skin barrier and damage to keratinocytes lead to cytokine release and activation of the innate immune system. Approximately 80% of OCD is caused by ICD. Clinically, ICD is characterized clinically by erythema, scaling/hyperkeratosis, fissuring, burning, and pain.

Allergic contact dermatitis is the result of a delayed type IV hypersensitivity reaction to an allergen or hapten, which elicits an adaptive immune response, specifically allergen-specific CD4 T lymphocytes. After the initial exposure or sensitization, cutaneous reexposure to the allergen will elicit a brisk T-lymphocyte response that results in the typical erythema, vesiculation, pruritus, and/or scaling observed in ACD.

Contact urticaria is a type I hypersensitivity reaction that can be accompanied by systemic symptoms such as rhinitis, conjunctivitis, wheezing, and in rare but severe cases anaphylactic shock.^{15,16}

Although each variant of contact dermatitis represents a distinct entity with its own pathophysiology, a single patient can be affected by multiple types of contact dermatitis. A Danish study demonstrated that ICD was responsible for 70% of cases of OCD, ACD constituted 15%, whereas an additional 10% was caused by a combined presence of ICD and ACD.⁴

OCCUPATION-SPECIFIC IRRITANTS

Although ICD is highly prevalent in the health care field, it is also a concern across many industries involving various irritant exposures.⁴ Wet work is well documented as the largest contributing irritant exposure to the development of OICD.^{4,17} Wet work has been loosely defined as (1) hands regularly in a wet environment for more than 2 h/d, (2) frequent hand washing (>20 times/d), (3) use of hand disinfectants 20 times in a working day, and (4) use of protective gloves for more than 2 h/d or change of gloves more than 20 times/d.¹⁸ Health care workers understandably account for a significant portion of the workforce involved in wet work; however, hairdressers, cleaning personnel, and food service workers also encounter significant wet work, as well as exposure to other irritants.^{4,17,19} In addition, skilled manual workers (such as craftsmen, construction workers, mechanics, technicians, and metalworkers) are also at risk of OICD, especially through exposure to both mechanical traumas and irritating substances.¹⁷ In the era of COVID-19, it is noteworthy that many professions not previously thought to endure significant exposure to wet work would now meet the aforementioned criteria for significant exposure because of hand hygiene practices, including those in customer-facing positions or other essential workers such as retail/grocery workers, sanitation workers, and postal workers. A recent review elegantly described the irritants contained in hand sanitizers and detergents used in the health care setting as related to the COVID-19 pandemic.¹²

Prolonged occlusion from rubber gloves is also considered an irritant exposure, even when unaccompanied by wet work.^{4,17} This is largely because of the humidity generated under occlusion, leading to prolonged skin exposure to moisture (primarily sweat), which

compromises skin barrier.²⁰ This is also relevant to note in the midst of the current pandemic given the increased use of medical-grade gloves by the general public. Cleaning agents, detergents, and disinfectant contribute an additional risk to developing OICD.^{17,21–24}

The occupations impacted by ICD extend beyond those listed here, ranging from agriculture workers immersed in soil and dust²⁴ to mail carriers and office workers exposed to paper irritants.⁴ The National Institute for Occupational Safety and Health labeled the prevention of OICD “imperative” because of its poor prognosis and the constant introduction of potential irritants into the workplace each year.²⁵ Given that all fields are likely to experience an exacerbation of OICD with the rise in necessary hand hygiene and cleaning precautions surrounding the COVID-19 pandemic,²⁵ it is now more important than ever to recognize the breadth of the problem across different occupations and specific irritants so as to properly spread prevention tactics and treatment knowledge to all employees.

PATHOGENESIS OF ICD

The skin serves an essential role in the innate immune system by acting as a barrier to irritants, allergens, and pathogens in the environment. The stratum corneum, composed of corneocytes and a lipid-rich extracellular matrix, functions both as a barrier to microbial entry and also in the prevention of transepidermal water loss (TEWL).²⁶ The extracellular lipids of the stratum corneum are derived from lamellar bodies, which release their polar lipid contents at the interface of the stratum granulosum and stratum corneum.²⁶ There, the lipids are processed into hydrophobic variants including ceramides, free fatty acids, and cholesterol in which the corneocytes are embedded generating a water-resistant barrier.²⁶

The stratum corneum must retain approximately 10% to 13% water content to maintain its biomechanical and barrier properties.^{27,28} This is primarily accomplished by the humectant natural moisturizing factor. Humectants maintain the moisture level in the stratum corneum by recruiting water from the dermis into the epidermis and also absorbing ambient water from humid environments.²⁹ Natural moisturizing factor is composed of the byproducts of filaggrin degradation, lactate, urea, and sodium and chloride ions and constitutes 20% of the total weight of the stratum corneum.^{27,30} Natural moisturizing factor is involved in maintaining the low pH of the stratum corneum, which is essential for barrier function.³¹ It is thus not surprising that mutation or deficiency in profilaggrin or filaggrin has been associated with ICD.^{32,33}

Irritant contact dermatitis is the result of damage to the epidermal barrier that generates inflammation and activation of the innate immune system. Dehydration of the stratum corneum and loss of integrity of the hydrophobic lipid barrier have been identified as inciting events of both ACD and ICD.^{34–36}

The mechanism by which irritants induce skin barrier disruption is dependent on the intrinsic nature of the irritant. Exposure to water results in an immediate increase in the pH of the skin surface.^{37,38} To maintain its barrier function, the stratum corneum maintains

an acidic pH, which is required for optimal functioning of enzymes that function in lipid and ceramide metabolism.³⁹

Detergents and surfactants are common irritants in hand hygiene practices and OICD. Sodium lauryl sulfate (SLS), a surfactant found in many detergents, is toxic to keratinocytes.⁴⁰ Sodium lauryl sulfate and other anionic surfactants can denature proteins including keratin, profilaggrin, involucrin, and loricrin.⁴¹ Acetone, an organic solvent and common irritant, disrupts the lipid composition of the stratum corneum, leading to lipid loss and thus a compromised barrier while also promoting proliferation of basal layer keratinocytes.^{42,43} Exposure to either acetone or surfactants results in an increase in density of Langerhans cells in the area of damage, thus inducing and promulgating the innate immune response.⁴⁴

Both the physical compromise of the skin barrier and the irritant inciting the damage contribute to the inflammatory response that produces the clinical symptoms of ICD. The type and quantity of cytokines released in response to an irritant are dependent on the nature of the irritant and the dose of exposure.² Disruption of the skin barrier itself leads to the release of cytokines interleukin 1 α , interleukin 1 β , and tumor necrosis factor α primarily by keratinocytes, Langerhans cells, and macrophages.^{2,43} These proinflammatory cytokines promote recruitment of Langerhans cells, neutrophils, and lymphocytes.⁴³ This cytokine and proinflammatory milieu promotes the recruitment of other inflammatory cells such as neutrophils, macrophages, lymphocytes, and mast cells to the epidermis.² Specific irritants may be recognized by Toll-like receptors and Nod-like receptors, which subsequently activate nuclear factor κ B and inflammasome pathways, respectively.²

Environment also contributes to pathogenesis of ICD. One study demonstrated a greater incidence of hand ICD in HCWs who work in colder/drier climates when compared with age-matched controls in warmer climates.⁴⁵ Several studies in HCWs have shown worsening xerosis of the hands, particularly dorsum and knuckles, as well as increased erythema and symptoms of burning or itching in winter months compared with summer months.^{46,47} Low-humidity environments have been associated with up to 6- to 7-fold increase in TEWL with cold temperatures exacerbating this finding.^{48,49}

Stressful environments may also impact the barrier function of the skin. Increased levels of circulating glucocorticoids, either from psychological stress or exogenous administration, have been associated with impaired cohesion of the stratum corneum and altered permeability of the barrier.^{26,50,51} This is particularly relevant in the setting of the global pandemic in which psychological stress seems to be universally elevated with implications that this stress alone could exacerbate ICD.

TOPICAL TREATMENTS

The definitive treatment of ICD of any cause is the identification and avoidance of the causative agent. If complete avoidance cannot be attained, PPE can be used to protect from exposure to the irritant and subsequent disease worsening. However, frequently, patients are unable to completely remove an irritant from their daily work

requirements. Various topical therapies have been demonstrated to help alleviate symptoms and reduce inflammation.

Emollients

Emollients offer an effective and accessible option for treating ICD and function by attracting water to and softening the stratum corneum and reducing TEWL.^{28,52–54} Several studies have demonstrated the efficacy of emollients to decrease irritation and restore barrier function^{55–59}; of note, most studies have been done on experimentally induced irritated skin.⁶⁰ Six commonly used lipid-rich moisturizers were demonstrated to be effective in reducing erythema, scaling, and TEWL in skin irritated by SLS.⁵⁷ The use of moisturizers with higher lipid content, such as petrolatum, was shown to improve barrier function more rapidly than less lipid-rich moisturizers.⁵⁷ Petrolatum, an occlusive, slows and reduces TEWL.^{57,61} Other occlusives include lanolin, mineral oil, vegetable oils, beeswax, ceramides, and silicones. Their high lipid content is crucial in barrier recovery.^{57,62} In a double-blind, randomized study of 5 different moisturizers on skin barrier function, Williams et al⁵⁹ determined that regular application of moisturizers to normal skin offers a protective effect against repeated exposure to irritants, and thus regular use among HCWs may prevent development of ICD. The proper use of emollients and compliance with daily care are important behaviors for treatment success in ICD and represent a huge obstacle to treatment. A recent study demonstrated that hand eczema patients who received text message reminders used moisturizer more frequently and had decreased severity of disease and overall improved treatment success.⁶³

Humectants

Humectants are hydrophilic substances that attract water from the deeper epidermis, dermis, and atmosphere to the stratum corneum.^{28,62} Natural moisturizing factor functions as the predominant endogenous humectant, whereas topical urea is the classic humectant used in therapeutically in clinic. Other compounds that function as humectants include amino acids, glycerin, sorbitol, lactic acid, and other sugars, which are often combined with an occlusive emollient in commercial products.⁶⁴ In a single-blind study, Lodén⁶² reported that a urea-containing moisturizer speeds skin healing and decreases sensitivity to SLS. Barrier function, skin hydration, and clinical symptoms were all significantly improved compared with an untreated control site.⁶²

Barrier Creams

Barrier creams aim to protect the skin from contact with exogenous irritants. They are designed to prevent or delay penetration and absorption of irritants to reduce the risk of developing and worsening ICD.^{28,64,65} Ideally, barrier creams should also improve stratum corneum hydration to maintain skin integrity and epidermis barrier function.²⁸ Although there is not one definition for barrier cream composition, the Food and Drug Administration came out with a finite list of approved active ingredients and their concentrations for

skin barrier protection.^{28,66} Despite their approval, the efficacy of barrier creams in preventing and treating ICD is not entirely clear. Two reviews have looked at rates of occupational irritant hand dermatitis among those who used barrier creams compared with control^{64,67}; however, randomized controlled trials with better assessment methods are needed.⁶⁴

Application dose and technique also should be considered when counseling patients and evaluating efficacy of therapeutic intervention.^{68,69} Schliemann et al⁶⁸ postulate that the actual amount of creams applied in the occupational setting is likely lower than recommended for protective effect. The dose-effect relationship observed in their single-blind randomized controlled study emphasizes the importance of workplace application education, because when inadequately applied, products that may have been proven to have protective potential will lose efficacy.⁶⁸ Although barrier creams are commonly used and recommended, quality evidence of its effectiveness is still lacking, and better-standardized studies are needed.^{64,65,67,68}

Topical Corticosteroids

Topical corticosteroids are routinely used in the treatment of ICD, although controversy regarding their efficacy remains.⁷⁰ Clemmensen et al⁷¹ found a dose-dependent treatment response for the corticosteroids and demonstrated clobetasol propionate to be more effective than triamcinolone acetonide on SLS-irritated skin. In a double-blind, vehicle-controlled study, betamethasone valerate significantly reduced TEWL on experimentally induced irritant skin reactions.⁷² However, other studies have called its efficacy into question⁷³ and raised concern about the adverse effects of prolonged therapy and detrimental effects on the skin barrier.^{51,65,74} Although topical corticosteroids reduce inflammation and can provide symptomatic relief, long-term use may impair restoration of lipids in the stratum corneum, thus leading to new treatment challenges.^{65,75}

Calcineurin Inhibitors

The use of topical calcineurin inhibitors in treatment of ICD remains off-label because data are limited and somewhat controversial.^{71,76–78} Although some studies have shown topical calcineurin inhibitors to be effective in treatment, others have found them to be ineffective and potentially irritating. Topical calcineurin inhibitors are notorious for inducing a burning sensation when applied to clinically inflamed skin. Engel et al⁷⁸ found that erythema induced by a 24-hour SLS patch test was significantly reduced by pimecrolimus compared with vehicle and untreated sites, whereas no effect on TEWL was found. Tacrolimus has been demonstrated to have a positive effect on ceramide-to-cholesterol ratio compared with treatment with emollient, as well as a diminished response to application of an irritant (SLS).⁷⁷ Conversely, in 2 other studies, the use of tacrolimus enhanced the irritancy in SLS-irritated skin.^{71,79} The conflicting results may reflect differences in compounds, concentrations, level, or irritant, as well as exposure.⁷¹

OPPORTUNITIES FOR INSTITUTIONAL IMPROVEMENTS

Irritant contact dermatitis is a widespread and often debilitating problem among HCWs. A recent literature review found that chronic hand eczema has a similar or higher burden on health-related quality of life compared with other chronic conditions including hepatitis, vision disorders, and some types of cancer.⁸⁰ A study in the United Kingdom demonstrated an increased incidence of ICD in HCWs in response to national-level interventions to increase hygiene-related activities over a 16-year period.⁵ This suggests that the increased attention to hand hygiene among frontline HCWs during the COVID-19 pandemic may result in increased incidence of ICD. This has already been supported by early studies showing frequent hand hygiene among all HCWs to be associated with a higher incidence of hand dermatitis, independent of direct care for COVID-19 patients.^{81,82} Risk factors for development of ICD are known and inherent in the field, which allows for great opportunity for institution-wide improvement aimed at prevention.

Prevention strategies can be broken down into primary, secondary, and tertiary, differentiated by the timing of their intervention in disease stage.⁸³ Primary prevention refers to interventions that occur before any skin changes or symptoms occur.⁸³ This is known to be the most effective method of disease prevention^{83,84} and involves action both at the institutional and individual levels.⁸³ Specifically, primary prevention at the institutional level involves providing workers with quality, less-irritating disinfectants such as alcohol-based hand rubs (ABHRs) containing emollients that will improve HCW skin health.⁸³ Primary prevention also encompasses efforts to educate individuals on proper use of PPE and ABHRs to optimize hand hygiene practice and limit irritant exposure. Alcohol-based hand rubs have been shown to be less irritating than soap and water,¹² but they are also a more effective decontaminant.^{5,85,86} The Centers for Disease Control and Prevention guidelines for HCW hand hygiene during the COVID-19 pandemic include the use of ABHRs with greater than 60% ethanol or 70% isopropanol and emollients within the formulation.²⁵ This recommendation should be minimally irritating^{83,87}; however, ABHRs require correct use to be effective, which is where education becomes crucial. Improper use of ABHRs includes application to preirritated skin and handwashing before and/or after application. If applied to preirritated skin, ABHRs may cause a burning sensation as the alcohol stimulates nerve receptors in the disrupted epidermis.⁸³ Handwashing before and after disinfection are both unnecessary and can compound damage. If hands are washed before, protective superficial skin sebum will be removed, and if washed after, both the skin sebum and emollients of the sanitizer will be removed.⁸³ Education regarding optimal hand hygiene practices that minimize irritation can be reinforced by placing posters including simple graphics as visual reminders above sinks in the workplace such as at nurses' stations on hospital floors.

There are also opportunities for primary prevention with regard to proper use of PPE. The use of certain irritating surface disinfectants is necessary against SARS-CoV-2, and all workers performing

surface disinfection should be reminded to avoid direct contact with skin.⁸⁸ The use of occlusive gloves can exacerbate ICD, and education regarding the proper use of occlusive gloves in the workplace is essential in preventing OICD.^{18,89,90} Tight-fitting gloves should be used only as long as necessary, for the shortest time possible, and should be accompanied underneath by cotton gloves, which are changed as soon as they become damp.^{18,90} Interestingly, it has been demonstrated that skin occlusion with glove material on its own does not negatively impact skin barrier function provided occlusion is not extensive (6 hours daily for >10 days) or combined with exposure to irritants.⁸⁹ Skin barrier impairment is increased if occlusion follows trauma or pretreatment with irritant.⁸⁹ Workplace education regarding the selection of the proper glove for the job and exposure, restricted time in the glove, and replacing gloves when they become damaged is important if the glove is to serve a protective purpose while minimizing skin irritancy.⁹¹

Secondary prevention refers to screening, identification of symptoms, and early intervention when ICD initially develops.⁸³ Failure to recognize symptoms of ICD leads to delays in care, which can result in severe disease that is more difficult to treat.^{92–95} Employee health surveillance is one way to mitigate this risk. Institutions should follow an occupational health protocol that clearly defines a plan for treatment and referral for all employees with symptoms of skin irritation.⁹⁵ Early detection can be encouraged through education and establishing a culture of compliance with regulations. For example, instead of HCWs getting discouraged from using ABHRs if they experience a burning sensation, this should be identified as a warning sign of potential ICD and prompt additional monitoring.⁸⁷ The use of emollients should also be implemented as they support skin barrier regeneration and help mitigate symptoms.^{83,93} Institutions can support this by making high-quality moisturizers available at convenient locations such as sinks and nurse stations.⁹⁵

Tertiary prevention refers to treating established disease to slow or stop disease progression with the goal of reducing disability in those already diagnosed with the condition.⁹⁵ One study demonstrated that people who exhibited knowledge of their diagnosis and its causes are less symptomatic and are more likely to show improvement than those who are not informed.⁹⁶ Knowledge ideally leads to compliance, which will help mitigate disease progression.

Given the current SARS-CoV-2 pandemic, there is great opportunity for dermatologists to assist in education regarding OICD both at the institutional and individual level. By collaborating with institutional administrators, dermatologists can assist in primary prevention by ensuring the products provided to employees are both effective for hand hygiene and also for minimizing irritancy. We can advocate for availability of emollients at workstations. Regarding secondary and tertiary prevention, dermatologists can assist in educating both employees and primary care colleagues regarding symptom recognition and basic treatment strategies for OICD.

CONCLUSIONS

Occupational irritant contact dermatitis is the most commonly reported occupational skin disease with significant impact on patient

quality of life and substantial economic burden because of losses in productivity, compensation, and cost of medical treatment. In this review, we have attempted to summarize the etiology and pathogenesis of OICD and discuss interventions, both behavioral and medicinal, at the individual and institutional levels. Education is fundamental in the prevention of OICD and should occur not only at initial job training but also at regular and pertinent intervals for those employed in at risk groups.^{83,95} This typically applies to HCWs, hairdressers, cleaning personnel, and food service workers because these professions encounter a substantial occupational risk. With the current global COVID-19 pandemic, individuals working in occupations not previously associated with excessive wet work are now being encouraged to perform frequent hand hygiene and sterilization procedures to ameliorate risk of viral transmission. For instance, a grocery worker who may at baseline perform hand hygiene only after a cash transaction or after going to the restroom is now more likely to sanitize after each customer-facing encounter. In a recent study, more than 75% of surveyed adults felt the need to wear gloves and sanitize hands frequently, with 85% reporting compliance with frequent handwashing.⁹⁷ One defining criterion for wet work is the “performance of hand hygiene more than 20 times in a day,” and it is easy to assume that many individuals in the United States currently meet this criterion regardless of his/her occupation. With flu season rapidly approaching and no SARS-CoV-2 vaccine available at this time, it is clear there is currently no end in sight to recommended practices of social distancing and hand hygiene precautions. Further, the dry, cold environment of the approaching winter season is likely to exacerbate the development and symptoms of ICD. Therefore, we are likely to experience an increased number of cases of ICD nationally, affecting many workers who would benefit from broad-reaching national or institutional educational interventions so as to be able to recognize symptoms and seek treatment before disease advances to the point of disability, missed work, and lost compensation.

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