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Irritant contact dermatitis: beyond a diagnosis of exclusion

Da Yeon Kim, Jin Ju Lee, Hae Young Choi*

Department of Dermatology, Ewha Womans University College of Medicine, Seoul, Korea

Irritant contact dermatitis (ICD) is the most common form of contact dermatitis and a leading cause of occupational skin disease, but remains underrecognized relative to allergic contact dermatitis (ACD). Direct chemical or physical injury to the epidermal barrier causes ICD, which can develop in anyone when exposure intensity or duration exceeds the skin's repair capacity. ICD is increasingly understood to involve more than barrier disruption: it is an innate immune-mediated inflammatory disorder involving keratinocyte-derived cytokines, neutrophil recruitment, C-C motif chemokine ligand 2–C-C motif chemokine receptor 2–interleukin-1β signaling, Toll-like receptor 3, and inflammasome activation. Host factors, particularly atopic dermatitis and filaggrin loss-of-function variants, further influence susceptibility. Clinical phenotypes range from acute irritant reactions to chronic cumulative dermatitis, and occupational wet work is a major preventable exposure. Distinguishing ICD from ACD is difficult because their clinical and histopathological features overlap, they may coexist, and ICD-related barrier damage may facilitate subsequent allergic sensitization. Diagnosis therefore requires assessment of exposure history, lesion distribution, symptom quality, and temporal course, with patch testing when ACD is suspected. Molecular biomarker panels and noninvasive imaging or barrier-assessment techniques may improve diagnostic precision, but remain investigational. Management should prioritize identifying and removing irritants, reducing exposure, implementing appropriate protective measures, and restoring the epidermal barrier. Recognizing ICD as a distinct clinical entity, rather than simply a diagnosis of exclusion, is essential for accurate diagnosis and effective management of contact dermatitis in clinical practice.

Keywords: Contact dermatitis; Irritant dermatitis; Occupational dermatitis

Introduction

Irritant contact dermatitis (ICD) is a nonspecific inflammatory skin reaction to direct chemical or physical damage to the epidermal barrier and is the most common form of contact dermatitis (CD). It accounts for approximately 80% of CD cases, representing a substantial clinical burden [1]. Its burden is particularly pronounced in occupational settings. Occupational CD accounts for most occupational skin diseases (OSD)—up to 95% in some reports—and irritant exposures or ICD constitute the predominant subtype, accounting for approximately 70%–80% of occupational CD or OSD in registry studies [2-4]. High-risk groups include healthcare workers, hairdressers and beauty workers, food handlers, construction workers, and people in other occupations involving wet work or chemical exposure [3].

Unlike allergic contact dermatitis (ACD), ICD requires no prior sensitization and can develop in virtually anyone after exposure to an irritant of sufficient concentration and duration. Despite this fundamental immunological distinction, ICD has long received less clinical and research attention than ACD. One reason is that the 2 conditions often cannot be distinguished reliably on clinical or histopathological grounds. They may coexist or develop sequentially in the same patient, and ICD often precedes and facilitates ACD. ICD should therefore be understood systematically as an independent clinical entity, rather than simply a diagnosis reached after excluding ACD.

This review begins with the definition and epidemiology of ICD, then examines its pathophysiological mechanisms and host risk factors. It also discusses clinical phenotypes, diagnosis, the relationship with ACD, occupational aspects and hand eczema, and current treatment and prevention approaches.

*Corresponding email: hychoi@ewha.ac.kr
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Ethics statement

Because this study is based on the literature, institutional review board approval and informed consent were not required.

Pathophysiology

Barrier disruption and cytokine cascade

Disruption of the epidermal permeability barrier is central to ICD. After an irritant passes through the stratum corneum into the viable epidermis, damaged corneocytes and activated keratinocytes release proinflammatory mediators that initiate an inflammatory cascade [2]. Conceptually, the process has 3 sequential steps: skin barrier disruption, epidermal cell activation, and cytokine release that stimulates innate immunity, leading to inflammation and tissue damage [2]. Implicated cytokines and chemokines include interleukin (IL)-1α, IL-1β, tumor necrosis factor-α (TNF-α), IL-6, C-X-C motif chemokine ligand 8/IL-8, C-C motif chemokine ligand 2 (CCL2), C-C motif chemokine ligand 20, C-C motif chemokine ligand 21, and interferon γ [2,5]. These events explain the current understanding of ICD as an innate immune response to direct barrier and cellular injury.

Molecular pathways and innate immune activation

Recent studies have begun to clarify molecular pathways within this cytokine cascade. In surfactant-induced ICD, signaling through CCL2 and C-C motif chemokine receptor 2 (CCR2) in skin-resident cells drives IL-1β release and subsequent neutrophil recruitment to the injury site [5]. In a murine model of cumulative ICD induced by sodium lauryl sulfate (SLS; also called sodium dodecyl sulfate in some studies), CCL2 expression increased in SLS-treated skin. Both local CCL2 blockade and CCR2 deficiency reduced skin inflammation, epidermal thickening, and neutrophil accumulation [5]. Intradermal IL-1β restored neutrophil accumulation and ICD development in *CCR2*-deficient mice, further supporting a central role for the CCL2–CCR2–IL-1β axis in surfactant-induced ICD [5].

Molecular responses can begin soon after irritant exposure. Genome-wide expression analysis of human epidermis irritated in vivo by SLS or nonanoic acid (NON) identified distinct expression profiles within 30 minutes. NON transiently induced IL-6 and mitogen-activated protein kinase-related pathways, whereas SLS transiently downregulated pathways involved in cellular energy metabolism [6]. These results demonstrate early molecular responses in ICD pathogenesis and suggest that different irritants may produce distinct molecular signatures.

Innate immune receptor signaling also appears to contribute to ICD. Toll-like receptor 3 (TLR3) has been implicated in both ACD and ICD. In a croton oil-induced murine ICD model, *TLR3*-deficient mice had less inflammation, whereas *TLR3*-transgenic mice had more, suggesting that TLR3 amplifies antigen-independent cutaneous inflammation [7]. Inflammasome activation is another pathway of interest alongside Toll-like receptor signaling. Irritants can induce cell necrosis, cellular stress, and damage-associated molecular patterns, potentially activating the NLR family pyrin domain-containing 3 (NLRP3) inflammasome [8]. NLRP3 activation triggers caspase-1-dependent processing of pro-IL-1β and pro-IL-18, amplifying neutrophilic and innate inflammatory responses [8]. In a human patch-test model, topical inflammasome inhibition with disulfiram reduced SLS-induced irritation. This supports the relevance of inflammasomes to ICD and suggests that inflammasome-dependent IL-1 family cytokine signaling may be a therapeutic target [8].

Molecular distinction from allergic contact dermatitis

Molecular studies may help distinguish ICD from ACD: analyses of patch-test biopsies associate ICD with tissue remodeling and proliferative pathways, whereas ACD has a distinct immune activation signature [9,10]. A proposed small biomarker panel for distinguishing allergic from irritant reactions comprises *CD8A*, *CD4*, *GNLY*, *GZMB*, *CD69*, *IFNG*, *CXCL10*, *HLA-DRA*, *GPR183*, *PLEK*, *IL15*, and *IGFL3* [9,10]. Most allergy-associated biomarkers are not upregulated in ICD, consistent with the absence of allergen-specific T-cell activation [9]. In active dermatitis lesions, this approach showed substantial agreement with clinical diagnoses, supporting molecular profiling as a promising means of distinguishing ICD from ACD [10]. These tools remain investigational, however, and routine differentiation still requires patch testing with careful clinical correlation.

Host risk factors

The extent and outcome of barrier disruption differ substantially among individuals, reflecting variation in susceptibility to ICD [2,11]. Responsiveness also depends on the irritant, because different agents act through different mechanisms and elicit distinct molecular responses [2,6,11]. Greater susceptibility to one irritant therefore does not necessarily imply greater susceptibility to another [2,6,11]. Among personal risk factors, atopic dermatitis (AD) has the strongest supporting evidence: individuals with AD have a lower threshold for developing ICD and a poorer prognosis than nonatopic individuals [4,12]. This susceptibility is attributed to the intrinsic epidermal barrier defect in AD, which facilitates irritant penetration and amplifies inflammation. Consistent with this mechanism, a systematic review and meta-analysis of occupa-

tional CD risk factors found AD to be one of the most consistently supported personal risk factors, reinforcing the central role of barrier integrity in ICD pathophysiology [4].

Genetic factors have also been implicated: filaggrin loss-of-function mutations are associated with increased susceptibility to chronic ICD and chronic hand dermatitis, likely through impaired stratum corneum integrity and reduced barrier resilience [12]. Inflammatory responsiveness may also vary with *TNFA* polymorphisms. Greater susceptibility to hand ICD has been associated with *TNFA-308*, whereas *TNFA-238* appears relatively protective. These findings suggest that host cytokine response profiles may influence irritant reactivity [13].

Age, sex, and ethnicity may influence irritant responsiveness, although the evidence is inconsistent. Older adults may react less strongly despite impaired barrier repair, possibly because of reduced inflammation and cutaneous blood flow and smaller transepidermal water loss (TEWL) responses after irritant exposure in aged skin [2,11]. ICD and hand dermatitis are reported more often in women, but this is thought to reflect occupational and domestic exposure patterns, particularly greater wet-work exposure, rather than inherent biological susceptibility [11]. Some studies suggest stronger responses in Asian than in Caucasian skin; inconsistent findings, however, make ethnicity a possible modifier rather than a reliable predictor [14,15]. Overall, susceptibility to ICD depends on the combined effects of barrier integrity, inflammatory responsiveness, genetic background, anatomical site, demographic factors, and cumulative environmental exposure.

Clinical phenotypes and diagnosis

Clinical subtypes

ICD has diverse clinical phenotypes, reflecting interactions among the irritant, exposure concentration and mode, exposure duration and frequency, anatomical site, and individual endogenous factors [2,11,16]. It can follow either a single intense exposure or repeated low-level exposures that cumulatively exceed the skin's capacity to repair its barrier.

Table 1 summarizes the major ICD subtypes [17]. Chronic cumulative ICD is the most common and clinically important phenotype. It develops when repeated subthreshold exposures to weak irritants occur before the epidermal barrier has recovered fully from the previous exposure [16]. Typical features are xerosis, erythema, scaling, hyperkeratosis, and fissuring, usually without marked vesiculation [2,16]. Chronic cumulative ICD often overlaps clinically with ACD, contact urticaria, or AD, particularly in occupational hand dermatitis [16].

Anatomical site-specific manifestations

ICD can have characteristic presentations at specific anatomical sites because of regional differences in stratum corneum thickness, hydration, occlusion, friction, barrier recovery, and exposure patterns. Thin or frequently exposed skin, including the eyelids, face, genital area, and dorsal hands, is generally more susceptible to irritants. The palms and soles are relatively resistant because their stratum corneum is thicker [2]. Table 2 summarizes these site-specific manifestations [2,17].

Diagnosis

ICD is diagnosed primarily by integrating exposure history, lesion morphology, anatomical distribution, symptom quality, temporal course, and exclusion of relevant allergic sensitization [2,11,16]. Its traditional description as a diagnosis of exclusion should not imply a passive or residual diagnosis. Clinicians should actively suspect ICD when dermatitis begins where a plausible irritant contacts the skin, remains largely confined to that area, and correlates with exposure intensity, frequency, and duration [2,16].

Diagnosis requires a detailed history and physical examination focused on lesion distribution and morphology. Clinicians should assess occupational exposures, hobbies, domestic activities, environmental conditions, personal protective equipment (PPE), wet work, hand hygiene, glove use, cosmetics, topical and oral medications, and personal or family history of chronic skin disease [2,16]. Assessment should also cover the dose, frequency, and duration of exposure, the extent of exposed skin, and the cumulative exposure pattern [16]. A characteristic pattern in hand ICD is the apron pattern, in which interdigital dermatitis extends onto both palmar and dorsal surfaces [1]. Symptom timing is particularly informative: as noted above, ICD generally develops sooner after exposure than ACD [16]. Acute ICD usually peaks rapidly and then resolves in a decrescendo pattern, whereas ACD follows a delayed crescendo pattern over 24–96 hours after allergen exposure [1,16].

On examination, sharply defined lesions restricted to the directly exposed area favor ICD when burning, stinging, prickling, pain, or soreness predominate; predominant pruritus favors ACD [1,2,16]. ICD may also show accommodation, or the hardening phenomenon: skin reactivity gradually decreases and dermatitis resolves despite continued or repeated exposure to the same irritant. Experiments with repeated SLS exposure have shown that TEWL may peak after approximately 2 weeks and then improve during the third week despite ongoing exposure. This adaptive response may favor ICD over ACD [18].

Patch testing remains essential when ACD is suspected; when dermatitis is chronic, recurrent, occupational, or refractory to

Table 1. Clinical subtypes of irritant contact dermatitis

Subtype	Description	Typical irritants or triggers
Acute ICD	Rapid inflammation after a single intense exposure, clinically indistinguishable from ACD. Lesions are generally sharply demarcated and limited to the contact area; severity determines whether erythema, edema, vesiculation, bullae, erosions, or necrosis occurs.	Strong acids or alkalis, solvents, oxidizing agents, chemical spills, concentrated disinfectants
Delayed acute ICD/ subacute ICD	Develops several hours to 1–2 days after exposure. The delayed onset can mimic ACD, although the clinical presentation resembles acute ICD.	Anthralin, benzalkonium chloride, acrylates, benzoyl peroxide, nonanoic acid, certain topical medications
Chronic cumulative ICD	The most common form, arising from repeated subthreshold exposure to weak irritants before the barrier has fully recovered. Features include dryness, erythema, scaling, lichenification, hyperkeratosis, and fissuring, generally with less vesiculation than ACD.	Water, wet work, soaps, detergents, cleansers, shampoos, low-concentration disinfectants, repeated glove occlusion
Subjective/sensory irritation	Reproducible stinging, burning, prickling, pain, tightness, or itching within seconds to minutes, without visible lesions. May occur independently of susceptibility to other irritants.	Propylene glycol, hydroxy acids, lactic acid, tretinoin, ethanol-containing products, cosmetics
Non-erythematous/ suberythematous irritation	Early or subclinical barrier damage without visible erythema, detectable only by bioengineering methods such as TEWL, capacitance, or other barrier measurements.	Low-grade repeated exposure to surfactants, detergents, water, occlusion
Frictional ICD	Caused mainly by repeated mechanical friction or rubbing, often on the hands. May coexist with chemical irritation.	Repetitive manual work, paper handling, tools, textiles, gloves, rubbing from masks or devices
Traumatic ICD	Chronic ICD that uncommonly develops at a site of prior mechanical injury, abrasion, or laceration.	Repeated trauma, abrasions, wound care products, occupational microtrauma
Hyperkeratotic ICD	Well-demarcated hyperkeratotic plaques with minimal erythema and little vesiculation, occurring most often on the hands or feet. Biopsy may reveal chronic spongiotic dermatitis.	Chronic mechanical irritation, repeated wet work, detergents, occupational hand exposure
Asteatotic ICD	Dry, fissured, cracked eczema, usually in older adults or people with xerotic skin.	Low humidity, frequent washing, soaps, winter climate, decreased skin lipids
Acneiform/follicular ICD	Follicular papules or sterile pustules caused by irritant or occlusive exposure.	Metals, tars, asphalt, oils, greases, cutting fluids, cosmetics, occlusive topical products
Airborne ICD	Caused by airborne irritants and predominantly affects exposed areas. Particle deposition and runoff can also produce involvement of "shadowed" areas or skin folds.	Fiberglass, dusts, cement particles, sprays, volatile chemicals, aerosols

Adapted and revised from Ale and Maibach [17].
ICD, irritant contact dermatitis; ACD, allergic contact dermatitis; TEWL, transepidermal water loss.

treatment; or when patients are exposed to common allergens such as rubber accelerators, preservatives, fragrances, metals, hair dyes, topical medications, disinfectants, or cosmetics [1,4,16]. A negative result supports ICD only if the clinical history and exposure pattern are compatible. Such results require caution: in a North American Contact Dermatitis Group analysis, dermatitis was ultimately attributed to a relevant irritant in only 23% of patients with negative patch tests [19]. A negative test alone therefore does not establish ICD.

Noninvasive tools can assess barrier impairment, although most remain investigational. TEWL is widely used to measure barrier disruption, but variability due to external factors such as temperature and humidity limits its clinical utility [11,20]. It is therefore more useful in research or controlled occupational settings than in routine practice. Natural moisturizing factor (NMF) has been proposed as a more sensitive molecular marker of stratum corneum integrity. The dermal texture index, derived from corneocyte surface topography, has been investigated alongside NMF as a potential biomarker of irritant-induced barrier alterations [21,22]. Reflectance confocal microscopy (RCM) allows repeated, real-time observation of affected skin and can show stratum corneum disruption, parakeratosis, spongiosis, corneocyte separation, and inflammatory infiltrates [11,23]. These techniques nevertheless cannot yet replace careful clinical evaluation and patch testing.

Skin biopsy has limited diagnostic value because ICD, ACD, and other eczematous dermatoses can share patterns of spongiotic dermatitis [1,2,4]. Histopathological differentiation may help in early lesions, ideally within 24–48 hours of exposure [2]. Early ICD may show more pronounced epidermal necrosis, keratinocyte ballooning in the upper and middle epidermis, neutrophilic infiltration, and upper epidermal injury. ACD may instead show more pronounced lower-epidermal spongiosis, spongiotic vesicles, and persistent intraepidermal Langerhans cell infiltration [1]. Bains et al. [2] also noted that eosinophils favor ACD, neutrophils may support ICD, increased mast cells are more characteristic of AD, and granular layer changes can offer additional clues; none is

Table 2. Site-specific manifestations of irritant contact dermatitis

Anatomical site	Clinical features	Common irritants or predisposing factors
Hands	The most common site of occupational ICD, with dryness, erythema, scaling, fissuring, hyperkeratosis, and soreness. The dorsal hands and interdigital spaces are often more susceptible than the palms.	Wet work, handwashing, detergents, soaps, disinfectants, gloves, solvents, friction, occupational exposure
Interdigital spaces	Highly susceptible because of the thin epidermis and frequent occlusion. Interdigital dermatitis can be an early sentinel sign in hairdressers.	Shampoo, hair dyes, bleaching agents, wet work, occlusion, detergent residue
Eyelids/periorbital skin	Even limited exposure can cause prominent erythema, burning, stinging, scaling, or edema because eyelid skin is thin and highly permeable. Hand-to-eyelid transfer is common.	Eye cosmetics, mascara solvents, cleansers, airborne particles, nail products transferred by hand
Face	May resemble ACD, rosacea, seborrheic dermatitis, or photodistributed dermatitis. Burning and stinging may be prominent.	Cosmetics, sunscreens, retinoids, hydroxy acids, masks, cleansers, shaving products, airborne agents
Lips/perioral area	Irritant contact cheilitis occurs more often than allergic cheilitis, with sharply bordered perioral erythema, scaling, cracking, burning, or soreness.	Saliva, lip licking, toothpaste, mouthwash, spicy foods, lip cosmetics, musical instruments
Scalp	May cause burning, stinging, pruritus, erythema, scaling, erosions, or oozing after hair-care product exposure. Because the scalp is hair-bearing and seborrheic dermatitis is common, ICD may go unrecognized or be mistaken for seborrheic dermatitis, psoriasis, or ACD.	Shampoos, hair dyes, bleaching agents, permanent-wave solutions, relaxers, alcohol-containing tonics, exfoliating scalp products, prolonged product contact
Vulva/genital skin	Hydration, occlusion, friction, and high permeability facilitate vulvar ICD, which may cause burning, soreness, erythema, fissuring, or erosions.	Urinary incontinence, excessive hygiene, wipes, occlusive underwear, bidet
Perianal area	May cause burning, soreness, erythema, maceration, or fissuring. Infection or inflammatory dermatoses can coexist with chronic irritation.	Fecal soiling, diarrhea, wipes, cleansers, topical hemorrhoid preparations, occlusion
Feet	May affect the dorsal feet, interdigital areas, or soles. Hyperkeratotic ICD can develop at weight-bearing or friction-prone sites.	Occlusive footwear, sweating, friction, detergents, topical medications, occupational exposure

Adapted and expanded from Bains et al. [2], incorporating additional information from Ale and Maibach [17].
ICD, irritant contact dermatitis; ACD, allergic contact dermatitis.

independently diagnostic. Histopathological distinction between chronic ICD and ACD is generally unreliable.

The broad differential diagnosis of ICD should be guided by anatomical site and morphology. Conditions that can mimic ICD include ACD, AD, psoriasis, dyshidrotic eczema, tinea manuum or tinea pedis, nummular eczema, and cutaneous infection [2]. Because ICD and ACD often coexist, evaluation should identify all relevant irritant and allergic contributors rather than simply assign one label. Treatment can then combine irritant reduction, barrier repair, and targeted allergen avoidance.

Relation to allergic contact dermatitis

Mechanistic interplay: irritant contact dermatitis as a precursor to allergic contact dermatitis

ICD and ACD are linked mechanistically as well as diagnostically. Nedorost [24] proposed that the allergen strength needed for sensitization depends on the underlying skin condition. In healthy skin, only strong allergens capable of acting as irritants themselves, such as para-phenylenediamine, can induce ACD [24]. By contrast, chronic inflammation or barrier impairment permits sensitization even to weak or moderately potent allergens [24,25]. This difference has been attributed to predominantly T helper 1-skewed responses in healthy skin versus T helper 2-skewed responses in chronically inflamed skin [24].

Clinical evidence supports this relationship: barrier impairment due to AD or wet work is associated with greater susceptibility to contact sensitization by less potent allergens. Kohli and Nedorost [25] found that childhood-onset flexural dermatitis predisposed patients to contact allergy to weak sensitizers, whereas current wet work predisposed them to allergy to moderate sensitizers. Neither factor was associated with sensitization to strong sensitizers [25]. Thus, ICD may do more than mimic ACD: it may create an inflammatory environment with a disrupted barrier that facilitates subsequent allergic sensitization.

Clinical example: rubber glove allergy

Rubber glove allergy illustrates the interaction between ICD and ACD. Workers with pre-existing ICD from frequent wet work, hand hygiene, or cleaning agents may wear protective gloves more often, increasing their exposure to rubber additives. With an already impaired barrier, they may subsequently become sensitized to rubber accelerators such as thiurams, carbamates, thiazoles, thioureas, and guanidines and develop ACD [26]. This sequence is particularly relevant in occupations such as healthcare, where glove use, wet work, and repeated hand hygiene often coexist [26].

Thiurams and carbamates have long been important rubber ac-

celerator allergens. Carba mix and diphenylguanidine have also become increasingly relevant, particularly with synthetic rubber gloves [26]. Affected patients should avoid the offending gloves and choose alternatives, such as accelerator-free nitrile or polyvinyl chloride/vinyl gloves, according to workplace protection requirements [26]. ICD and ACD are therefore not mutually exclusive. In chronic, recurrent, or occupational dermatitis, particularly of the hands, clinicians should assess both irritant exposure and allergic sensitization [16,19,27].

Occupational aspects and hand eczema

Wet work and occupational exposures

ICD is the most common form of OSD, and the hands are affected most often because of repeated workplace irritant exposure [4,11]. A recent systematic review and meta-analysis found moderate-quality evidence identifying wet work as an important risk factor for occupational ICD [4]. The standard definition of wet work requires at least one of the following during a working day: wet hands for more than 2 hours, more than 20 handwashing episodes, or occlusive glove use for more than 2 hours [28]. These exposures increase stratum corneum hydration and skin permeability, extract lipids and NMF, and impede barrier recovery, lowering the threshold for irritant-induced inflammation [2,29].

Wet work rarely occurs alone. Workplace water exposure often accompanies exposure to soaps, detergents, disinfectants, or other irritants. Occlusion, friction, pressure, and repeated minor trauma further damage the epidermal barrier, while heat, sweating, cold, low humidity, and poor ventilation may intensify irritation [2,11,29]. This cumulative pattern explains why occupational ICD often develops gradually as chronic cumulative hand eczema rather than after a single acute irritant exposure.

High-risk occupations

Table 3 summarizes occupations at particularly high risk of ICD, including hairdressers, food service workers, healthcare workers, metalworkers, and cleaners [29,30]. Their shared exposures include repeated wet work, frequent hand hygiene, detergents or disinfectants, alkaline or solvent-based materials, glove occlusion, and repetitive mechanical trauma.

Hairdressers are a well-recognized high-risk group. Interdigital dermatitis often develops early in their apprenticeship and is considered a sentinel event preceding more severe hand dermatitis [11]. This early involvement of the web spaces reflects repeated exposure to shampoo, water, hair dyes, bleaching agents, and glove occlusion. Prompt recognition matters because timely education and exposure modification may prevent progression to chronic occupational hand eczema.

Protective strategies: gloves and barrier measures

Prevention and management depend on reducing irritant exposure while maintaining occupational protection. Measures include substituting irritants, limiting wet work, drying hands thoroughly, using moisturizers, and wearing appropriate protective equipment [2,11].

Gloves are essential for protection against irritants, but prolonged occlusion can itself impair the barrier and increase susceptibility to irritation [31]. Experiments help clarify this damage. Wearing occlusive gloves for 6 hours daily over 3 days did not significantly impair barrier function in normal skin, but significantly worsened it in skin previously irritated with SLS [32]. After 6 hours of daily glove wear for 2 weeks, even normal skin showed significant barrier impairment, indicated by increased TEWL [32]. These findings suggest that occlusion may be particularly harmful to an already compromised barrier and that glove-wear

Table 3. High-risk occupations and common irritant exposures in occupational irritant contact dermatitis

Occupation	Major irritants and exposure patterns
Healthcare workers	Frequent handwashing, alcohol-based hand rubs, soaps, disinfectants, chlorhexidine, detergents, prolonged glove occlusion, sweating under gloves
Hairdressers	Wet work, shampoos, detergents, hair dyes, bleaching agents, permanent-wave solutions, thioglycolates, persulfates, glove occlusion
Food service workers/cooks	Wet work, soaps, detergents, food juices, spices, acids, alkalis, repeated handwashing, glove occlusion
Butchers/fishmongers	Wet work, animal proteins, blood, brine, detergents, disinfectants, cold exposure, glove occlusion, friction from tools
Cleaners/housekeeping workers	Detergents, surfactants, disinfectants, bleach, ammonia, solvents, frequent wet work, glove occlusion
Metalworkers/machinists	Cutting oils, metalworking fluids, coolants, solvents, degreasers, metal particles, friction, occlusive gloves
Construction workers/cement workers	Wet cement, alkaline materials, chromate-containing cement, dust, solvents, friction, trauma, cold or heat exposure
Beauticians/nail technicians	Solvents, acetone, acrylates, nail products, detergents, disinfectants, cosmetics, repeated handwashing
Dental workers	Frequent hand hygiene, disinfectants, acrylics, impression materials, glove occlusion, wet work
Agricultural workers/florists	Plant sap, soil, fertilizers, pesticides, wet work, mechanical trauma, cold exposure

Adapted and revised from Ale and Maibach [30].

duration has clinical importance.

Cotton glove liners may lessen the adverse effects of prolonged occlusion by absorbing sweat, reducing friction, and improving comfort. They reduced barrier impairment from prolonged glove wear in the long-term occlusion model [32]. Cotton liners should therefore be considered for workers who need prolonged occlusive glove use, especially those with pre-existing ICD, AD, or chronic hand eczema (CHE).

Barrier creams and moisturizers are adjuncts to, rather than substitutes for, gloves and exposure reduction. Moisturizers help restore stratum corneum hydration and barrier function. Barrier creams may provide partial protection against selected irritants, but are often inadequate for intense or prolonged exposure [11].

Workplace assessment

Workplace assessment can help when occupational ICD is suspected, especially in chronic, recurrent, or severe cases. A detailed occupational history should identify potential workplace irritants and allergens, establish how exposure relates temporally to onset or exacerbation, and determine whether symptoms improve away from work [33]. Evaluation should directly assess the worker's tasks, wet-work duration, handwashing, PPE, and opportunities to reduce or substitute exposures [4,34,35]. Product labels and material safety data sheets (MSDS) should also be reviewed to identify possible irritants and recommended precautions [33]. MSDS require cautious interpretation because they may omit clinically relevant irritants [35].

Persistent post-occupational dermatitis

Persistent post-occupational dermatitis (PPOD) persists or recurs long after occupational exposure has ended [36]. It challenges the assumption that removing exposure necessarily leads to complete resolution. Barrier dysfunction and inflammatory susceptibility can persist for years, particularly after severe, prolonged, or recurrent occupational hand dermatitis [36]. Patients should be told that improvement may be slow even after exposure reduction or a job change and that long-term protection and maintenance therapy may remain necessary. PPOD reinforces the occupational-health need for early recognition, prompt exposure control, and prevention before dermatitis becomes chronic. Clinicians should consider it when counseling patients whose dermatitis began at work and who continue to have persistent or recurrent eczema resembling endogenous dermatitis [36].

Prevention and treatment

Barrier recovery kinetics

Epidermal barrier recovery after ICD takes considerably longer than is generally recognized. In human experimental models using SLS, complete recovery from acute ICD took approximately 4 weeks [37]. In a chronic model, 1% SLS was applied for 30 minutes daily for 5 days, with this schedule repeated over 3 consecutive weeks. Previously irritated sites remained hyperreactive even 10 weeks later, indicating that biophysical markers may take a long time to normalize [38].

Recovery also depends on the surfactant. In detergent patch tests, SLS caused persistent, concentration-dependent TEWL increases even 10 days after exposure, whereas sodium laureth sulfate allowed faster recovery and alkyl polyglucoside caused little detectable irritation [39]. Undetectable irritation does not mean an absence of irritant potential: even mild surfactants may cause irritation with repeated or prolonged exposure [39]. Because recovery is prolonged, renewed irritant exposure before full barrier restoration is a key mechanism in progression from acute or subclinical irritation to chronic cumulative ICD.

Irritant avoidance and skin protection

Prevention underpins ICD management. The 4R principle organizes practical care into 4 actions: recognize the causative irritant, remove it from the patient's environment, reduce inflammation, and restore the skin barrier [40]. Recognition requires detailed assessment of occupational, domestic, and recreational exposures, including the irritant, exposure frequency and duration, work practices, and PPE use [2,11,40]. Patch testing should be performed if concomitant ACD is suspected [1,16,40]. Removal means eliminating the irritant from the workplace and home wherever feasible [40]. If complete avoidance is impractical, particularly in occupational ICD, clinical benefit may still come from reducing exposure frequency, duration, or intensity and substituting less irritating products [11,40].

Reducing inflammation requires treatment tailored to the acuity, severity, morphology, and anatomical site of active dermatitis [40]. Anti-inflammatory therapy may be needed when irritant avoidance is insufficient, particularly in persistent ICD or with coexisting endogenous dermatosis such as AD; it nevertheless remains secondary to adequate exposure control [2,16,40]. Restoration requires continued skin protection and appropriate basic topical therapy to help the damaged epidermal barrier recover [40]. Because clinical improvement may precede full functional recovery, protective measures and regular use of a suitable moisturizer should continue after visible dermatitis resolves [37-40].

Barrier-restorative products should be selected individually: effects vary by formulation and irritant, and some products may paradoxically increase susceptibility [40].

Moisturizers and barrier restoration

Both prevention and treatment rely on moisturizers. Emollients such as lanolin, fatty acids, cholesterol, and ceramides fill gaps between corneocytes to smooth the skin. Occlusives, including petrolatum, mineral oil, and silicones, reduce water loss by forming a hydrophobic film. Humectants such as glycerin and urea draw water into the stratum corneum. Many formulations combine these functions. Lipid-rich, fragrance-free moisturizers with low irritant potential are recommended for occupational ICD and CHE [2,11]. Greasy preparations rich in lipids or free fatty acids may be particularly helpful for barrier restoration.

Anti-inflammatory agents

Topical corticosteroids (TCS) have a more limited and less consistent role in ICD than in ACD or AD. Reviews covering acute and chronic ICD found a consistent lack of significant TCS efficacy in experimental models [41]. One proposed explanation is that their antiproliferative effects and suppression of epidermal lipid synthesis may impede barrier recovery despite their anti-inflammatory action. Short-term glucocorticoid treatment has been shown to compromise permeability barrier homeostasis and stratum corneum integrity by inhibiting epidermal lipid synthesis [42]. TCS should therefore not be considered primary barrier-restorative treatment for ICD.

Topical calcineurin inhibitors (TCIs), including tacrolimus and pimecrolimus, have also been investigated; these agents inhibit calcineurin-dependent T-cell activation and reduce inflammatory cytokine production [43]. Repeated TCI application in experimental studies compromised stratum corneum integrity, epidermal permeability, and antimicrobial barrier function to an extent comparable to TCS [44]. Applying tacrolimus after SLS irritation has been shown to increase inflammation [16]. Pimecrolimus, however, has a more cell-selective pharmacological profile, downregulates proinflammatory mediators such as TNF-α and IL-8, and has shown anti-inflammatory activity in the SLS irritation test [43,45]. It may therefore be considered when sensitive sites require anti-inflammatory treatment.

Systemic and advanced therapies

Systemic or advanced therapies have limited use in uncomplicated ICD, which is sustained primarily by direct barrier injury rather than a systemic immune-mediated process [2,16]. Systemic anti-inflammatory treatment is rarely needed for pure ICD, and robust controlled clinical evidence does not support its use. It may be considered when ICD is part of severe refractory CHE, but this should not be interpreted as ICD-specific treatment.

Alitretinoin has the strongest support among systemic agents for severe refractory CHE. Korean clinical studies and real-world data indicate that it can be effective and generally well tolerated in moderate-to-severe CHE [46-48]. CHE is heterogeneous, however, and can include irritant, allergic, atopic, hyperkeratotic, and endogenous components [49]. Cyclosporine, methotrexate, and azathioprine have also been used off-label for severe CHE, but ICD-specific evidence is limited [49]. These agents should therefore be reserved for selected cases in which ICD forms part of a severe CHE phenotype, after ongoing irritant exposure and clinically relevant allergic sensitization have been carefully excluded.

Oral antihistamines do not directly address ICD pathophysiology, which is driven mainly by barrier disruption and innate inflammatory activation rather than histamine-mediated inflammation [2,16]. They should therefore not be considered disease-modifying treatment for ICD. Sedating agents may serve only as symptomatic adjuncts for sleep disturbance or prominent itch. Evidence for dupilumab is emerging in chronic recalcitrant hyperkeratotic ICD and CHE [11,50]. Further studies are needed to determine its efficacy in ICD; it is not yet an established treatment for pure ICD.

Phototherapy may be an adjunct for cumulative ICD through enhancement of skin barrier function by repeated low-level ultraviolet exposure [11]. In one study of eczematous hand dermatitis that included patients with ICD, both psoralen–ultraviolet A and narrowband ultraviolet B phototherapy were associated with clinical improvement [16]. More than half of the patients relapsed after treatment stopped, however, suggesting an adjunctive role and a possible need for maintenance therapy [16]. Overall, systemic and advanced therapies remain exceptional, adjunctive, or investigational options for ICD; treatment should continue to prioritize exposure reduction, skin protection, and barrier restoration.

Conclusion

ICD is the most common type of CD and the most frequent presentation of OSD. It is a distinct inflammatory disorder driven by barrier dysfunction and mediated by innate immunity, with its own pathophysiology, clinical spectrum, occupational relevance, and treatment principles. It should therefore be recognized as more than a diagnosis reached after ACD has been excluded.

Advances in ICD research have extended understanding beyond simple barrier damage. CCL2–CCR2 signaling, TLR3 activation, and inflammasome-related IL-1 family cytokine signaling

are being clarified within the broader context of epidermal barrier disruption and innate immune activation [5,7,8]. AD and other host determinants of barrier susceptibility further influence individual risk [2,4]. Clinical presentations range from subjective sensory irritation and suberythematous barrier damage to acute, chronic cumulative, occupational, airborne, and site-specific forms [2,16]. Wet work remains the most important occupational exposure, and accurate risk assessment and protective strategies such as cotton glove liners can help prevent disease [4]. The 4R principle summarizes management: recognize, remove, reduce, and restore [40].

Future research should convert mechanistic and diagnostic advances into clinical tools. RCM and molecular biomarker panels need validation in real-world populations with overlapping ICD, ACD, AD, and CHE. Studies should also clarify the role of dupilumab and other targeted therapies in recalcitrant ICD. These developments may improve the precision of diagnosis, prevention, and management for this common, underrecognized condition.

ORCID

Da Yeon Kim: https://orcid.org/0009-0001-5040-8042
Jin Ju Lee: https://orcid.org/0000-0002-6188-6306
Hae Young Choi: https://orcid.org/0000-0003-3460-2539

Authors' contribution

Conceptualization: HYC. Data curation: DYK, HYC. Investigation: DYK, JJL, HYC. Methodology: DYK, JJL, HYC. Validation: DYK, JJL, HYC. Resources: DYK, JJL, HYC. Project administration: HYC. Supervision: HYC. Writing–original draft: DYK. Writing–review & editing: DYK, JJL, HYC. Final approval of the manuscript: all authors.

Conflict of interest

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