



# Review of Occupational Contact Dermatitis—Top Allergens, Best Avoidance Measures

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#### **Opinion statement**

Occupational contact dermatitis accounts for a significant proportion of occupational disease. Although dermatitis can occur anywhere on the body, hands are the most frequently affected location. Long-term or repetitive exposure to allergens and irritants can lead to chronic dermatitis resulting in significant reduction in quality of life. The first-line treatment for both irritant and allergic contact dermatitis is irritant and allergen avoidance. Modification of diet and lifestyle may be necessary to reduce exposures to certain substances. Well-established and user-friendly electronic databases are now available to help patients with avoidance of allergens and their cross-reactors by elimination or substitution. Barrier creams are another method of reducing contact with irritants, although their efficacy is not well proven. When avoidance measures fail, second-line treatments include topical and oral pharmacologic measures and interventional procedures including UV therapy. Emerging therapies for the treatment of allergic contact dermatitis aim to reduce inflammation via targeted alteration of cytokine pathways. Finally, in cases of occupational contact dermatitis refractive to treatment, a change of job task or even occupation may become necessary.

#### Introduction

Occupational contact skin disease includes irritant contact dermatitis (ICD), allergic contact dermatitis (ACD),

and contact urticaria. Occupational contact dermatitis accounts for 95 % of all occupational skin disease. ICD

accounts for about 70 % of all occupational dermatitis; the majority (68 %) of cases are caused by wet work  $[1 \bullet]$ .

Reliable epidemiologic data addressing occupational contact dermatitis has been challenging to obtain due to inconsistent diagnostic criteria and reporting requirements. That said, the incidence of occupational contact dermatitis is thought to range between 11 and 86 cases per hundred thousand workers per year [2]. One estimation believes that only 10–15 % of occupational contact dermatitis to be properly reported [3•]. In addition to the individual worker, occupational contact dermatitis impacts both the health system and the economy. The National Institute for Occupational Safety and Health (NIOSH) estimates that in the USA, occupational dermatitis costs the country at least 1 billion dollars per year [4].

Workers in certain occupations are known to be at higher risk for occupational contact dermatitis. These include the following: cooks, bakers, beauticians, painters, and mechanics [5], as well as health care workers [6] (Fig. 1), construction workers [7], shoe manufacturers [8], and poultry and manual laborers [9].

While several well-established allergens and irritants remain problematic in the occupational setting, novel occupational allergens and irritants have been identified in the literature and will be reviewed.



**Fig. 1.** Typical health care worker with allergic contact dermatitis of the hands.

Avoidance and prevention remain the fundamental and first-line approach to treatment of occupational contact dermatitis. Online electronic applications and programs have become available to help allergic patients identify allergen-free products. Patient education about avoidance and prevention remains a major barrier to successful implementation. Second-line treatment for occupational contact dermatitis includes personal protective barriers, steroids, steroid-sparing agents, and UV therapy. Systemic medications can be considered in some instances. Lifestyle and diet may also be modified to ameliorate systemic allergic symptoms.

# Common and novel allergens and irritants

Occupational contact dermatitis is generally caused by allergens and irritants specific to one's profession. Newly identified allergens and irritants are continually reported in the literature.

ICD is the result of exposure of a noxious stimulus to the skin and requires no prior sensitization. While inflammation may be localized to the insult, with activation of innate immune mechanisms, no immunologic memory develops. ACD differs from ICD in that a delayed-type hypersensitivity pathway mediates the inflammation. Initially, skin exposure to haptens causes an inflammatory response through antigen processing and activation of leukocytes resulting in sensitization. Subsequently, dermatitis develops when clonally produced memory T lymphocytes are reactivated by the immunogenic allergen, most commonly in the epidermis.

Differentiating clinically between occupational ICD and ACD may at times be difficult as the clinical presentations can be similar, especially in the chronic forms. Furthermore, these conditions can also coexist. One important clue is the timing from exposure to onset of symptoms. In ICD, the eruption usually occurs within hours of exposure, whereas in ACD, the response to re-exposure of an allergen, in a previously sensitized individual, usually occurs within 48–120 h.

# **Occupational irritants**

- Alkalis such as soaps, detergents, and cleansers cause ICD.
- Acids are directly toxic to skin and cause irritation.
- Frequent exposure to wet work, mechanical trauma, warm dry air, and prolonged use of occlusive gloves are well-known hand irritants [10, 11•].
- Wet work is perhaps the greatest cause of ICD and significantly contributes to occupational cases of hand dermatitis [1•].
- Gloves themselves can be very irritating and have been found to disrupt the epidermal barrier with prolonged use [12]. This, in turn, may make the epidermal barrier more susceptible to allergens or other irritants.
- Frictional hand dermatitis and hyperkeratotic hand dermatitis are types of irritant dermatitis resulting from repetitive handling of objects just as metal coins, fabric, and paper [13, 14]. Constant gripping of objects such as steering wheels can also cause this type of irritant dermatitis.
- Hydrocarbons such as oils and petroleum cause irritant dermatitis.
   Weathered oil, such as that from the Deep Water Horizon oil spill of 2010, resulted in contact dermatitis in rescue workers. Mouse models demonstrate that exposure to weathered oil results in epidermal thickening and neutrophil infiltration [15].
- Solvents such as isopropyl alcohol defat the skin, causing irritation [16].

# Common occupational allergens

- In North America, the most common occupational allergens are carbamates, thiurams, epoxy resins, nickel, and formaldehyde (Table 1) [17].
- A recent (2012) study from Canada not only endorsed these allergens, but also reported additional occupational allergens: glyceryl thioglycolate, para-phenylenediamine, glutaraldehyde, cobalt chloride, and potassium dichromate [18].
- Top workplace allergens in Denmark include rubber allergens and epoxy [1•].

#### Novel occupational allergens

#### **Coconut derivatives**

- Coconut fatty acid diethanolamide (cocamide DEA) is a derivative of coconut oil, which is commonly found in cleaning agents, cosmetic products, waxes, metalworking fluid, and even skin barrier creams. In Finland, an industrial hand cleanser was found to be the main source of cocamide DEA sensitization in two thirds of occupational contact dermatitis to the allergen [19].
- Cocamide MEA, or tall oil fatty acid monoethanolamide, caused occupational ACD and was found in metal working fluid in Finland [19].

Table 1. Common occupational allergens

| Top allergens Carba mix (carbamates) | Use or function Rubber accelerator Pesticide Herbicide Fungicide | Sources Elastic, boots, gloves, masks, waistbands, rubberized computer accessories, pesticides, herbicides, fungicides.                           | Commonly exposed occupations  Health care workers, dental workers, pesticide applicators, farmers, trade workers, rubber manufacturers, any occupation with rubber or elastic uniform |
|--------------------------------------|--|---|---|
| Thiuram mix                          | Rubber accelerator Pesticide Germicide Fungicide Preservative    | Similar to carba mix  | Similar to carba mix  |
| Epoxy resin                          | Resin to produce plastics<br>and glues                           | Plastic molds and dye casts,<br>sealants, glues, adhesives,<br>protective finishes, epoxy<br>composite, paints,<br>dental products                | Automobile and boat industry,<br>construction and mechanical<br>workers, shoemakers,<br>woodworking, electronics<br>industry  |
| Formaldehyde                         | Preservative<br>Disinfectant                                     | Soaps, cleansers, paper,<br>pressboard, fabric, urea-<br>formaldehyde foam insulations,<br>textile finishing treatments,<br>metalworking fluids   | Beauticians, textile workers,<br>heath care workers, construction<br>workers, metalworkers, trade<br>workers  |
| Nickel                               | Metal imparting strength and luster                              | Tools, jewelry, machine parts,<br>metalworking fluids, batteries,<br>musical instruments, office<br>supplies, foundries,<br>incinerators, hangers | Trade workers, machinists, retail clerks, beauticians, metalworkers, cleaners, food workers, jewelers, musicians  |

- Capryldiethanolamine, another coconut fatty acid derivative causing ACD, is present in metalworking fluids and was not listed on the fluid's Material Safety Data Sheet (MSDS) in Finland [20].
- Sodium cocoamphopropionate is a surfactant that was found to cause occupational dermatitis in fast-food workers in Sweden [21].

# Preservatives—the isothiazolinones

- Methylisothiazolinone (MI) is said to be "causing a current epidemic of contact dermatitis in Europe," with MI patch test positivity increasing from 4.8 to 6.5 % in 2 years [22•].
- Occupations at high risk for methylchloroisothiazolinone/ methylisothiazolinone (MCI/MI) occupational ACD include painters, welders, blacksmiths, machine operators, and cosmetologists [5].
- Some occupational sources of the isothiazolinones are reported: paints, varnishes, cleaners, and polishing liquids. Concentration of MCI/MI may be high in some occupational sources, as industrial regulation allows higher concentration than for personal use [23].

- Water cooling tower technicians are susceptible to occupational ACD from MCI/MI [24].
- An ultrasonographer reacted to MI in ultrasound gel in Denmark [25].

#### Medications

- Airborne benzodiazepine particles can cause occupational contact dermatitis in health care workers who crush drug tablets [26]. In particular, tetrazepam has triggered hand and facial dermatitis [27, 28].
   Of note, there may be significant cross-sensitization to other benzodiazepines, which in turn demonstrates the importance of through patch testing and consideration of cross-reactors.
- The first reported case of systemic allergic dermatitis to sevofluorane occurred in 2014. The pattern of eruption was flexural, and diagnosis was confirmed with repeated open application test (ROAT) [29].
- Race horses are susceptible to stomach ulcers, and omeprazole paste is
  often administered as a preventive medication. Both a horse trainer [30]
  and a "head lad" caring for horses [31] developed ACD to omeprazole via
  cutaneous contact with this paste. Another horse trainer suffered airborne
  ACD from the breath of an omeprazole-treated horse [32].

### **Fragrance**

- d-Limonene is used as a fragrance in cosmetic and personal cleaning products; it is a well-known cause of contact allergen in consumers.
   Occupational contact allergy to d-limonene has been described in workers who use occupational detergents and cleansers contained dlimonene [33].
- Other components of citrus essence are also known to cause occupation dermatitis. As early as 1989, a bartender that was diagnosed with sensitivity to citrus peel was found to react to geraniol and citral [34]. More recently, nine beauticians in a high-end spa presented with hand and arm ACD to citral [35].

# **Treatment**

# Diet and lifestyle

Cutaneous allergen avoidance is the mainstay of treatment for ACD, but in select patients not improved with this approach, a low-allergen diet can be considered. Only a few allergens have possible oral contribution to overall exposure.

#### Nickel

 Nickel allergy affects about 10 % of the population [36]. While most patients and providers are aware of cutaneous contact dermatitis to nickel, oral intake of nickel found in many foods has been linked to systemic contact dermatitis [37, 38].

- Systemic symptoms can range from gastrointestinal distress to cutaneous eruptions in sensitized individuals. The absolute amount of nickel consumed has been found to directly correlate with symptom severity, but more recent studies have shown that foodstuffs release nickel in the gastrointestinal (GI) system at different rates resulting in modified total nickel exposure [39].
- A scoring system has been created to aid patient adherence to a lownickel diet [40••]

# Balsam of Peru (Myroxylon pereirae)

- Balsam of Peru (BOP) is a well-recognized allergen causing contact dermatitis.
- In some sensitized patients, both cutaneous and systemic exposure to BOP must be limited.
- Citrus, tomatoes, spices, and chocolates are common foods containing BOP [41].

### **Formaldehyde**

- Formaldehyde exposure is widespread; this allergen has been named the 2015 American Contact Dermatitis Society (ACDS) Contact Allergen of the Year [42].
- Formaldehyde-releasing preservatives are found in around 20 % of cosmetic products and also in other household and personal items including soaps, fabric softeners, and adhesives [42]. While the cutaneous avoidance of formaldehyde and formaldehyde-releasers is the mainstay of treatment in ACD, in some sensitive individuals, oral avoidance may also be necessary.
- Consumption of aspartame results in release of methanol and formaldehyde [43]. We believe that avoidance of aspartame is a rare consideration in very sensitive individuals who do not completely improve with cutaneous avoidance.

### Additional systemic allergens

- Low-allergen diets are also described for cobalt [44], chromate [45], and propylene glycol [46], among others.

#### **Irritants**

- Frequent wet work is a known risk factor for hand dermatitis, and modification of lifestyle may be necessary.
- Exposure to air pollutants including tobacco smoke and volatile organic compounds may be risk factors for development of atopic dermatitis [47].

 Patients may consider lifestyle changes to reduce both airborne and cutaneous irritant exposure both at work and at home.

# Pharmacologic treatment

Pharmacologic treatment for occupational contact dermatitis may be necessary while attempting to limit exposure to the offending agent.

### **Topical treatment**

#### **Barrier creams**

- Barrier creams may be used in industrial settings in an attempt to prevent ICD. Theoretically, this treatment method could provide irritant protection while allowing full mobility of the hands. Practically, numerous problems have been encountered which prevent barrier creams from achieving their full protective potential.
- First, the amount of barrier cream applied per unit of skin surface area is correlated to its efficacy in preventing contact dermatitis [48]. Actual amount used in the practical setting is much less than the amounts reported. Thus, studies on barrier creams should be carefully reviewed for methodology. The average amount of cream applied by nurses in one study was under 1 mg/cm², and studies on barrier cream use dosages ranging from 4 to 25 mg/cm² [49••].
- Furthermore, after application, the barrier cream needs to remain on the skin to be effective. In many professions, frequent hand washing or manual manipulation can decrease the amount of protective cream on the hand over the course of a day. When a barrier cream was tested for protection against sodium lauryl sulfate under occlusive conditions, barrier cream afforded some protection against skin irritation but did not completely prevent it [50]. One could surmise that repeated application may be required.
- Barrier creams function as another protective layer to supplement the stratum corneum's role as the permeability barrier.
   Furthermore, barrier creams act as emollients to moisturize and maintain the epidermal integrity. Common ingredients to achieve these dual goals include petrolatum, dimethicone, and paraffin [51]. Petrolatum is cost-effective, hydrophobic, and occlusive. Dimethicone, also known as simethicone, and paraffin are other hydrophobic barriers.
- Some restorative barrier creams contain additional active ingredients to reduce inflammation or to augment the stratum corneum's intracellular lipids. Ceramide is one such lipid and can protect against transepidermal water loss to counter the drying properties of irritants such as detergents. When a group of hairdressers used a pseudo-ceramide barrier cream, they

experienced decreased dryness, scaling, cracking, redness, and itching [52]. Linoleic acids, present in sunflower and coconut oils, as well as hyaluronic acids are also thought to promote intracellular lipid production [53]. Colloidal oatmeal is a commonly used anti-inflammatory which contains various natural compounds including a polyphenol which decreases levels of prostaglandin, cytokine, and nuclear factor-kappaB [54].

#### **Steroids**

Topical steroids are the mainstay of the dermatologic armamentarium for ACD. Potent topical steroids (classes 1 and 2) are a reasonable approach for initial treatment of hand, foot, and scalp allergic dermatitis. Because of possible skin atrophy, striae, and dyspigmentation, use should be limited to weeks rather than months. Mid-potency steroids (classes 3–5) can be used on thicker areas of the limbs for a similar period of time. Lower-potency steroids can be considered for intertriginous and facial areas (avoiding eyes), again decreasing dosage as soon as possible to avoid local side effects.

# Other topical agents

- Topical calcineurin inhibitors such as tacrolimus or pimecrolimus are suitable alternatives to topical steroids. These may be preferred for use in intertriginous, facial, periocular, or groin areas. Topical calcineurin inhibitors carry a black box warning regarding rare occurrence of skin malignancies and lymphoma.
- Hyperkeratotic hand and foot dermatitis may require a mild keratolytic such as topical urea or ammonium lactate.

#### Systemic medications

#### **Immunosuppressants**

- Oral steroids such as prednisone can be considered in cases of severe or widespread ACD. It is imperative to treat with a slow, long taper of at least 3 weeks to avoid a rebound flare.
- A recent study suggests that oral cyclosporine can cause alterations in epidermal cell gene expression and can modify cytokine activation [55]. We recommend judicious use of cyclosporine for occupational contact dermatitis due to potential risks associated with treatment.
- Other systemic immunosuppressant medications can be used in recalcitrant cases of occupational contact dermatitis including methotrexate, mycophenolate mofetil, dapsone, and

azathioprine. These are considered last resorts given their medical risk profiles. A recent article by Sheehan is an excellent reference for further review  $[56\bullet]$ .

#### Retinoids

 In cases of hyperkeratotic hand and/or foot dermatitis recalcitrant to topical treatment, a systemic retinoid such as acitretin can be considered. Because of its possible teratogenicity, acitretin should not be prescribed for women of childbearing potential.

#### **Antihistamines**

Antihistamines are a somewhat effective method for symptom control with minimal side effects. In fact, sedation may be a desired outcome for patients unable to sleep due to pruritus  $[56\bullet]$ .

### **Interventional procedures**

### Public health approach

The preferred preventive approach to minimizing occupational exposure is as follows:

- 1. Elimination
- 2. Substitution
- 3. Isolation
- 4. Engineering controls
- 5. Safe work practices
- 6. Personal protection

Quite often in the medical treatment of patients, we overlook options 1 through 5 and focus on the last option (6), personal protective equipment.

#### Personal protection

The US Department of Labor's Occupational Safety and Health Administration (OSHA) requires employers to "institute all feasible engineering and work practice controls to eliminate and reduce hazards before using PPE to protect against hazards" [57]. However, personal protection is still required in many industries where there remains a risk of exposure. OSHA provides employers with a guide to establishing a personal protective equipment (PPE) program. The appropriate equipment necessary is highly dependent on the occupation and type of exposure. Commonly used protective gear includes goggles, face shields, gloves, gowns, aprons, and full body suits.

# **Phototherapy**

- Around 2–4 % of patients with dermatitis will require UV therapy after failing avoidance measures and other medical therapies [58]. Psoralen photochemotherapy with ultraviolet light A (PUVA) penetrates more deeply than other modalities and thus may be used in cases of hand dermatitis. However, it is only occasionally used due to risk of phototoxic reactions and requirement of topical or systemic psoralen.
- UVA therapy is generally utilized in cases of acute dermatitis [59], but UVA may not be widely available.
- Narrow band UVB (NBUVB) therapy is well established in managing moderate to severe allergic and chronic contact dermatitis. It is the preferred modality due to better safety profile, accessibility, and lower cost than other modalities.
- Excimer laser therapy is a specific wavelength (308 nm) that decreases inflammatory infiltrate with low risk of side effects [60]. Its use is limited to small areas of skin involvement.
- Other modalities capable of treating chronic dermatitis include Grenz ray therapy, which is ionizing radiation with a low adverse event profile [61].
   Lack of availability of equipment limits the use of this therapy.
- Additionally, novel use of intensity-modulated radiotherapy and megavoltage low-dose external beam radiotherapy also shows some promise in treating recalcitrant dermatitis [62].

### **Programmatic**

- Multidisciplinary teams focusing on both intensive treatment and education may represent the *best* practice model for the rehabilitation and return to work of employees with occupational contact dermatitis.
- A German model included inpatient and outpatient care, and this group reported that of the involved employees, 87 % remained in workforce [63•].
- A report from the Netherlands included a successful multidisciplinary team composed of a dermatologist, education nurse, and an occupational medicine physician [64•].
- A Canadian model studied 100 workers assessed for occupational health complaints and found that 78 % of diagnosis was related to skin disease.
   Follow-up of these patients showed variable exposure to occupational hazard training related to chemicals, skin care, and gloves and that unionized workers were most likely to receive training in these areas [65].

# **Primary intervention**

#### Avoidance of allergen and associated education

Avoidance of allergens is the mainstay of treating occupational contact dermatitis.

- Traditional education and patient counseling typically occur after patch testing is completed. This usually includes handouts on specific allergens and their sources of exposure.
- A "safe list" is generated for patients when the allergen relates to topical products.
- Provider knowledge of the workplace and exposures is paramount for successful patient allergen avoidance. MSDS may be helpful as is communication with the employer.
- As the use of personal electronic devices is becoming more widespread, so are the numbers of applications ("apps") and databases available to help patients avoid allergens and irritants.
- The ACDS offers an electronic database called the Contact Allergen Management Program (CAMP), which allows patients and providers to easily access a list of "safe products" based on patch test results [66].
- The Contact Allergen Replacement Database (CARD) is another similar database available on mobile and web access which helps patients find safe products based on known allergens [67].
- A major barrier to effective avoidance practice as well as protective skin care is patient education [68]. Within the cohort of patients with occupational skin dermatitis, males and those over the age of 50 had the least knowledge about protective practices [69].
- In a study of full-time hospital cleaners, a 1-h educational session on hand protective behavior was found to improve rates of hand dermatitis after 3 months [70•].
- In 2013, the Prevention of Hand Eczema (PREVEX) trial was initiated to study the effects of education on patients with occupation hand eczema [71•]. Results of this trial have not been published at the time of writing this manuscript.

#### Avoidance of wet work

- There is a well-established link between dermatitis and duration and frequency of wet work; wet work is defined as workers who wash hands
   20 times per shift, have hands immersed in liquids for at least 2 h per shift, or wear occlusive gloves for at least 2 h [10].
- While some findings of the negative effects of occlusive gloves have been equivocal [72], it is currently standard of care in the UK to provide cotton liners under gloves to reduce rates of hand dermatitis [73]. This helps ameliorate the moisture which accumulates under gloves during use.

We recommend that the approach to treating occupational contact dermatitis be stepwise in the following order: elimination, substitution, isolation, engineering controls, safe work practices, and, then, personal protection. In rare circumstances, occupational contact dermatitis may be refractive to all avoidance practices and treatment options and a job change may be required.

### Regulatory

- Guidelines including the 2010 British Occupational Health Research Foundation (BOHRF) have outlined non-legal standards of practice for employers and health professionals.
- In addition, there is now increased interest in limitation of allergen from a regulatory perspective.
- Chromium compounds are commonly used in chrome plating, leather, and wood preservation among other manufacturing processes. Chromium is a known carcinogen and can cause acute epidermal irritation and chronic dermatitis in addition to respiratory, GI, and neurological impairments [74]. The European Union has implemented tighter control on hexavalent chromium in an effort to reduce allergy and dermatitis [75, 76].
- The European Union (EU) has already demonstrated success with the 2001 EU Nickel Directive which regulates nickel content in consumer products. Within a decade of implementation, there was a statistically significant reduction in the prevalence of nickel allergy in young men and women in Germany and the UK [77••].
- In the USA, the National Institute for Occupational Safety and Health (NIOSH) is a branch of the Centers for Disease Control and Prevention (CDC) aiming to prevent workplace illness and injury. However, despite a clear need for similar nickel regulation policies, no such legislation has been set in the USA [78]. There is a recent push from dermatologists to establish such a directive [79•].

# **Emerging therapies**

New therapies for contact dermatitis may soon be available.

- Alitretinoin shows promise for patients with severe chronic dermatitis refractive to steroids. A phase 3 randomized controlled trial, the Benefit of Alitretinoin in Chronic Hand Dermatitis (BACH) study, found that daily oral alitretinoin results in greater and faster improvement of severe chronic hand eczema as measured by physician global assessment scale and modified total lesion score [80].
- In 2013, E6005, a topical phosphodiesterase (PDE) 4 inhibitor, demonstrated reduction in atopic dermatitis skin lesions as well as inflammatory cytokines in murine models [81]. In mice, PDE4 inhibitors decrease pruritus by increasing cutaneous concentrations of cAMP to suppress mast cell degranulation [82].
- Dupilumab, a human monoclonal antibody against IL-4 receptor alpha, modulates anti-inflammatory response with the potential for reversing atopic dermatitis [83, 84]. In November 2014, the US Food and Drug Administration (FDA) granted Breakthrough Therapy designation to dupilumab to allow for expedited development and review of the drug.

Most of the available treatment that we have described targets reduction of the cutaneous inflammation in ACD. While there are currently no biologic agents approved for treatment of atopic dermatitis, there is increasing research toward this area of study. Targeting the underlying immuno-pathophysiology shows great promise in other inflammatory conditions such as psoriasis, and we are hopeful that our treatment armamentarium for occupational contact dermatitis will continue to grow.

# **Compliance with Ethical Standards**

#### **Conflict of Interest**

Heather Lampel reports working on the IntraDerm Advisory Board. Rosie Qin declares that she has no conflict of interest.

#### **Human and Animal Rights and Informed Consent**

This article does not contain any studies with human or animal subjects performed by the author.

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No pharmaceutical, industry, or other support was used in the writing of this paper.

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