Wound-Related Allergic/Irritant Contact Dermatitis

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PURPOSE:
To provide information from a literature review about the prevention, recognition, and treatment for contact dermatitis.

TARGET AUDIENCE:
This continuing education activity is intended for physicians and nurses with an interest in skin and wound care.
OBJECTIVES:
After participating in this educational activity, the participant should be better able to:
1. Identify signs and symptoms of and diagnostic measures for contact dermatitis.
2. Identify causes and risks for contact dermatitis.
3. Select appropriate treatment for contact dermatitis and its prevention.

INTRODUCTION
Contact dermatitis can be divided into irritant and allergic subtypes. Irritant contact dermatitis (ICD) can occur on initial exposure and is a result of excessive moisture or irritation on the skin surface. This form of contact dermatitis is often red and scaly with poorly defined borders. If moisture is associated, the hydration of keratin leads to a white macerated surface, especially if occlusive or moisture-balance dressings are applied locally.

The allergic form of contact dermatitis occurs after an initial sensitizing exposure is associated with reexposure of the responsible allergen. Allergic contact dermatitis is often more acute with bright red erythema in the pattern of skin contact with the responsible allergen. Acute contact dermatitis presents with small blisters (vesicles that are fluid-filled <1 cm) or larger bullae (blisters >1 cm). Allergic contact dermatitis is common in patients with chronic ulcers because of allergenic properties of frequently utilized wound care products. Up to 80% of patients with venous leg ulcers have 1 or more positive patch test reactions, with most of the identified allergens relating to previous exposure or a history of contact dermatitis. The allergic sensitization typically results from long-term exposure to allergens under occlusion from dressings and compression wraps combined with the impaired barrier function of the ulcerated skin.

There are many sources of allergens, from topical dermatological preparations to wound care products designed as wraps (Figure 1) or modern occlusive dressings with autolytic debridement and anti-inflammatory, antimicrobial, or moisture-balancing properties. Clinically, wound-associated contact dermatitis presents with localized itching, pain, and discrete or diffuse periwound dermatitis of varying severity that may delay healing or worsen the wound base and margin despite appropriate treatment (Figure 2). Early recognition of allergic contact dermatitis (ACD) and removal of the suspected allergen are critical to minimize patient suffering, curtail topical suspected allergen overuse, and optimize the healing environment.

METHODS
A PubMed English-language literature review was conducted to identify relevant articles published between January 2000 and December 2015. The search terms included “wound care,” “irritant contact dermatitis,” and “allergic contact dermatitis.” The commonly reported wound product–related irritant and allergen ingredients were identified and summarized. These allergens were subsequently used as search terms for additional PubMed literature searches. References were also reviewed and evaluated for relevance.

REVIEW OF THE CURRENT LITERATURE
Treatment of minor wounds includes local application of creams, ointments, dressings, and wraps. Multiple potential allergens in these products may result in sensitization (Table 1). A direct relationship between ulcer duration and number of multiple positive allergen sensitivities has been documented. A change in the most common allergens has occurred since the authors’ previous work (Table 2).

A prospective multicenter study of 423 patients with chronic leg ulcers (CLUs) demonstrated that Myroxylon pereirae (balsam of Peru) (41%), fragrance mix (26.5%), antiseptics (26.5%), and topical corticosteroids (8%) were the most common allergens. The North American Contact Dermatitis Group identified that 1.5% to 9.1% of patch-tested patients older than 20 years are
allergic to bacitracin, and 7.2% to 13.1% of patch-tested patients older than 20 years have allergic sensitization to neomycin.\textsuperscript{3–5}

In a recent study on 354 patients with CLUs, the percentage of positive patch test to modern wound-related materials was reported as high as 59.6%.\textsuperscript{6} The number of positive patch test was correlated with the duration of ulcerative disease and independent of ulcer etiology (venous, arterial, or mixed arteriovenous).\textsuperscript{6} The top 5 common allergens in 5 studies from 2009 to 2015 include balsam of Peru, lanolin, amerchol, fragrance mix, and benzocaine (Table 2).

Prolonged topical antibiotic use, impaired skin barrier, and occlusion for extended periods increase the risk of developing allergic contact dermatitis (ACD) from topical antibiotics.\textsuperscript{4} Topical antibiotics often require only 1 mutation to induce resistance to bacteria, and they do not provide the wound bed preparation components of moisture balance provided by some antiseptic dressings containing silver (calcium alginate, foam, hydrofibers, gel), iodine (cadoxomer), chlorhexidine derivatives (PHMB [polyhexamethylene biguanide] foam), or methylene blue/crystal violet foam. Allergic contact dermatitis is more common in patients with chronic venous insufficiency, chronic otitis externa, postoperative or posttraumatic wounds, chronic eczematous conditions (eg, atopic dermatitis, nummular eczema, stasis eczema), and in certain occupations (nurses, farmers, veterinary surgeons, and pharmaceutical workers who handle antibiotics) involving skin contact with topical or systemic antibiotics.\textsuperscript{4}

A 2011 double-blind randomized study investigated the allergy and irritancy potential of 5 topical wound care products\textsuperscript{7}:

- Topical healing ointment composed of petrolatum (41%), mineral oil, caresin (a white wax extracted from ozokerite, also called earth wax), lanolin alcohol, panthenol, glycerin, and bisabolol
- Topical emulsion\textsuperscript{8} with ingredients that include liquid paraffin, ethylene glycol monostearate, propylene glycol (PG), paraffin wax, methylparaben, propylparaben, and fragrance.

The results did not identify induction ACD with the tested products. The topical emulsion caused the most irritation, and the topical healing ointment caused the least. The topical triple antibiotic combination ointment and the topical healing ointment had similar irritation potential on normal skin; however, on tape-stripped “wounded” skin, the topical triple antibiotic combination ointment with polymyxin B sulfate/bacitracin/neomycin appeared to cause the most irritation of the 3 topical preparations in the study.\textsuperscript{8} Allergic contact dermatitis may not have occurred because of the relatively short duration of the study compared with the longer duration of potential allergen application to chronic wounds.

A 2007 study\textsuperscript{9} of 30 disease-free participants compared trans-epidermal water loss and irritancy from 6 common wound care dressing products applied to the same area of skin, 6 times over a 14-day period. The dressings with lower irritancy in this study were soft silicone-faced polyurethane foam dressing, polyurethane foam self-adhesive island dressing, soft hydrophilic polyurethane foam dressing, polyurethane foam dressing, hydrocolloid semipermeable polyurethane dressing, and hydrocolloid semipermeable dressing. Also, soft silicone-faced polyurethane foam dressings, polyurethane foam self-adhesive island dressings, and soft hydrophilic polyurethane foam dressings had low mean transepidermal water loss values closer to that of normal skin. Based on this study, those 3 foam dressings may...
also be better tolerated for wound care applications where patients are susceptible to ICD. Colophony or resin is extracted from conifer trees, usually pine species. Its manufactured use includes adhesives in hydrocolloid dressings along with violin and baseball resin, soldering flux, chewing gum, and printing/paper processing. Colophonium derivative is an adhesive adjunct used as tackifying agent (adhesive) in some hydrocolloid dressings, and this ingredient is often responsible for allergic sensitization to hydrocolloid dressings that contain this ingredient. Sensitization to hydrocolloid dressings is observed in 11% to 52% of patients with chronic wounds. The reported allergen may be listed as pentalyn H, which is the derivative of colophony (the pentaerythritol ester of the hydrogenated resin), originally believed to be a purified resin that would not act as an allergen, and other ester gum resins. Patients with hydrocolloid dressing allergy may also show cross sensitization to unmodified colophony, but unfortunately, patients with sensitization to pentaerythritol ester of the hydrogenated resin may have a negative patch test to colophony. Patients with hydrocolloid dressing allergy may also show cross sensitization to unmodified colophony, but unfortunately, patients with sensitization to pentaerythritol ester of the hydrogenated resin may have a negative patch test to colophony.

<table>
<thead>
<tr>
<th>Table 1. CONTACT DERMATITIS TO WOUND PRODUCTS AND RELEVANT PRODUCTS</th>
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<tr>
<td><strong>Evidence/Comment</strong></td>
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<tr>
<td><strong>Topical antibiotics:</strong></td>
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<tr>
<td>Bacitracin: 1.5%–9.1% patients &gt;20 y old are allergic</td>
</tr>
<tr>
<td>Neomycin: 7.2%–13.1% patients &gt;20 y old are allergic</td>
</tr>
<tr>
<td>Neomycin was associated with greater local wound irritation compared with products in combination with polymyxin 10</td>
</tr>
<tr>
<td><strong>Preservatives:</strong></td>
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<tr>
<td>Propylene glycol (PG)</td>
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<tr>
<td>Formaldehyde-releasing preservatives including quaternium 15</td>
</tr>
<tr>
<td><strong>Fragrances:</strong></td>
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<tr>
<td>Balsam of Peru—can cross-react with fragrances</td>
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<tr>
<td>Stage 1–2 pressure ulcers treated with trypsin/balsam of Peru/castor oil combination product</td>
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<tr>
<td><strong>Hydrocolloids:</strong></td>
</tr>
<tr>
<td>Colophony 11,28,29 Carboxymethylcellulose 30</td>
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The concept of wound bed preparation dates back to ancient times when wounds were cleansed and covered by oils and topical products. Over the past decade, some wound care products have moved from passive to active treatment in order to promote healing. The use of topical preparations in the form of ointments, creams, and dressings is determined by the underlying wound characteristics. These externally applied topical preparations (potential irritant contacts and allergens), as well as wound fluids (potential contact allergens), have the potential to cause contact dermatitis of the periwound skin. Symptoms of itching and burning often accompany contact dermatitis and can cause considerable discomfort. In routine practice, products containing common allergens should be avoided. The integrity of periwound skin is an important concept of wound care. Early diagnosis of contact dermatitis is
critical to optimize local wound and skin care. Patients with chronic wounds may develop a sensitization to even weak allergens in wound care materials. Possible causes are intrinsic genetic predisposition, lipophilic galenic formulations (the compounding of medicines for optimum absorption), and the use of occlusive dressings combined with disrupted skin barriers.

Venous stasis dermatitis is associated with decreased venous return, local pitting edema, exudation of red blood cells, inflammatory cytokines, and the dermal fibril deposition (fibrin cuff) often associated with recurrent or chronic ulcers. The clinical relevance of this observation requires further study.

In a 2008 prospective study of 45 patients with chronic wounds and sensitization to wound dressings, the most common contact sensitizers identified were povidone-iodine, balsam of Peru, fragrance mix, colophony, and potassium dichromate. A 2004 prospective study of 54 patients with CLUs who underwent patch testing demonstrated a high incidence of positive patch test results; the most common allergens were balsam of Peru, fragrance mix, wood tar mix, PG, neomycin sulfate, benzalkonium chloride, carba mix, nickel sulfate, and control gel hydrocolloid. Propylene glycol is primarily a vehicle in topical medications, cosmetics, and topical corticosteroids and may cause allergic dermatitis or ICD. Lessmann et al demonstrated that PG exhibits very low sensitization potential, and the risk of sensitization to PG on uncompromised skin appears to be quite low but is likely higher in persons with leg ulcers. As previously mentioned, controlled gel hydrocolloids contain a purified derivative of colophony called the pentaerythritol tetranitrate ester of hydrogenated rosin. This is an adhesive in some hydrocolloid dressings that commonly cross-reacts with colophony. In the study by Saap et al, only 17% (1/6) of patients with a positive patch test result to the control gel hydrocolloid and 25% (1/4) of patients with a positive patch test result to thin polyurethane hydrocolloid were also allergic to colophony. In a 2008 case series, 100 patients with leg ulcers were patch tested, and 46% had at least 1 positive patch test with the most common sensitizers identified as fragrance, lanolin, antibacterial agents, and rubber allergens.

Wound hydrogels are common irritant/allergens in wound products, mainly due to ICD because 70% to 90% of hydrogels are water with a backbone to allow them to adhere to wounds called tack. The backbone of some hydrogel dressings is PG, which is generally a more common irritant than a common allergen. In studies on patients with chronic wounds, the rate of sensitization to hydrogels was common, ranging from 9% to 23%.

**IRRITANT CONTACT DERMATITIS**

Irritant contact dermatitis involves direct physical or chemical damage to the skin. Because it is not a cell-mediated response, previous sensitization exposure is not necessary. Acute irritant dermatitis has a rapid onset within 6 to 72 hours of

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**Table 2. COMPARISON OF 10 TOP ALLERGENS IN LEG ULCERS 2009–2015**

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<tbody>
<tr>
<td>Myroxylon pereirae resin (balsam of Peru)</td>
<td>8</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>10</td>
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<tr>
<td>Lanolin alcohol</td>
<td>—</td>
<td>6</td>
<td>1</td>
<td>8</td>
<td>7</td>
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<tr>
<td>Amerchol L101</td>
<td>6</td>
<td>—</td>
<td>5</td>
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<td>8</td>
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<tr>
<td>Fragrance mix I</td>
<td>—</td>
<td>—</td>
<td>9</td>
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<td>9</td>
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<tr>
<td>Benzocaine</td>
<td>—</td>
<td>10</td>
<td>—</td>
<td>5</td>
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<tr>
<td>Colophonium</td>
<td>—</td>
<td>9</td>
<td>—</td>
<td>—</td>
<td>5</td>
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<tr>
<td>Fragrance mix I and II</td>
<td>7</td>
<td>—</td>
<td>6</td>
<td>—</td>
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<tr>
<td>Fragrance mix II</td>
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<td>3</td>
<td>—</td>
<td>9</td>
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<tr>
<td>Benzalkonium chloride</td>
<td>—</td>
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<td>6</td>
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<td>6</td>
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<tr>
<td>Thiuram mix</td>
<td>—</td>
<td>—</td>
<td>7</td>
<td>3</td>
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Top 10 allergens in each study, given a score of 10 (most common allergen) to 1 (least common allergen).
exposure and is usually confined to the contact area. Chronic cumulative irritant dermatitis is also likely in patients with longstanding lower-extremity ulcers, especially with leakage of exudate to the surrounding skin. With a variable response threshold, anyone can develop ICD due to repeated application and removal of adhesive dressings or tape from the skin. Patients with sensitive skin, preexisting eczema, and use of occlusive dressings are more likely to develop ICD due to wound care products.

**MOISTURE-ASSOCIATED SKIN DAMAGE**

Moisture-associated skin damage is a form of ICD that is common in persons with chronic wounds (Figure 3). There are 4 types of moisture-associated skin damage:

- **Periwound-associated skin damage**. This is due to wound exudate that requires treatment of the cause (eg, venous edema with compression, superficial critical colonization with topical antimicrobial dressings, or deep and surrounding infections with systemic therapy).
- **Peristomal-associated skin damage** may be due to ileostomy, colostomy, or urostomy and associated stool or urine coming in contact with skin. This dermatitis requires containment of the stool or urine with a better fit of the collection bag or alteration of the stoma.
- **Incontinence of rectal stool or urethral urine (incontinence-associated skin damage)** requires a regular bowel routine or diversion for stool and intermittent or indwelling catheter for urine.
- **Intertrigo or moisture in the skin folds due to perspiration**. This is common in persons with chronic wounds as patients tend to be older and are often overweight or obese. The control of perspiration requires antiperspirants and local agents to absorb moisture.

**GENERAL RECOMMENDATIONS IN THE MANAGEMENT OF IRRITANT CONTACT DERMATITIS**

For the management of ICD, the causative agent must be identified and removed. If wound exudate is the cause, the surrounding skin can be protected with zinc paste, petrolatum, a film-forming liquid acrylate, or a windowed hydrocolloid or film dressing. If bandages are the cause, cotton tubular gauze can be applied, avoiding direct skin exposure of the primary bandages. Adhesive tape should be avoided, and tap water or saline compress used instead of antiseptics. Superimposed infection needs to be diagnosed and addressed. Uncontrolled edema of the lower extremities requires compression bandages to control edema after adequate blood supply has been determined with an ankle-brachial pressure index >0.9 for high-compression bandages, or an ankle-brachial pressure index between 0.65 and 0.9 for modified-compression bandages.

Local exudate management (moisture balance) of the wound requires choosing the appropriate moisture balance dressing. For exudative wounds, polyurethane foam dressings absorb exudate but also participate in fluid exchange, giving back moisture that can cause periwound margin maceration. Super-absorbent dressings (diaper technology) help to wick away moisture and lead to fluid lock. Periwound area is a common location for ICD.

The periwound skin also needs to be protected and similar to irritant contact dermatitis, there are 4 methods of protecting the periwound skin:

- **Film-forming liquid acrylates**. These products are applied as liquids that dry on skin contact, forming a protective film. They are translucent, allowing visualization of the wound margins. This type of preparation can be used under an ostomy appliance, on the periwound skin and around an area of incontinence.
- **Petrolatum (petroleum jelly)** provides an oleaginous translucent barrier around the wound, but with heat and moisture, the petrolatum can leak into the wound surface and create interference with moisture balance dressings.
Zinc oxide ointment is an ideal barrier for many patients with incontinence-associated dermatitis from urine or stool in the groin or perianal area. The zinc is incorporated into an ointment base to make it stiffer, but it can creep into the wound surface and interfere with the moisture balance, as well as partially inactivate the antibacterial action of ionized silver dressings. Zinc oxide ointment can be applied to the groin or perianal area with a tongue depressor to form an even layer of white ointment and act as a protectant against urine and stool to ICD from the urine and stool and secondary *Candida* yeast involvement. The red skin may require a topical steroid (eg, 1% hydrocortisone) or in the powder form combined with an antifungal agent, such as azoles, including clotrimazole, miconazole, ketoconazole, or econazole.

Windowed hydrocolloid or film dressings can be placed around the wound or ostomy margin to protect the periwound skin. For ostomies, there are rings that can minimize stool or urine leakage.

### Allergic Contact Dermatitis and Patch Tests

Patch tests are used to identify individual allergies to common potential contact allergens. They differ from the prick test that is initiated with scratching an area on the forearm and applying an allergen, with a reading in 15 to 20 minutes. This prick test is an immediate allergic response that relates to asthma or a type 1 immunoglobulin E reaction. Allergic contact dermatitis is a type 4 cellular delayed hypersensitivity reaction similar to a tuberculin test. The North American Contact Dermatitis Advisory Panel determines common allergens, and a North American series of allergens are updated on a regular basis. These allergens are supplied in a concentration that is most likely to produce an allergic response and not elicit an ICD. The tests are applied as a patch test in circular aluminum chambers and applied to the upper back for 48 hours. The patches are then removed and read as positive if there is local erythema, elevation of the skin response, or the presence of a blister. A final reading is made 96 hours after the patches are applied and 48 hours after the initial patch test removal and reading (Figure 4).

### Prevalence and Avoidance of Allergic Contact Dermatitis

Allergic contact dermatitis is more prevalent in individuals with leg ulcers than in individuals with any other dermatological condition. Common allergens in perfumes and their derivaties include colophony, balsam of Peru, and the perfume mix found in the patch test series. Other common contact allergens for persons with leg ulcers include preservatives such as formaldehyde, quaternium 15 (a formaldehyde releaser), and PG. For this reason, clinicians should consider using ointments rather than creams for peril ulcer care, but not for topical care of the ulcerated skin where wound dressings are a better option. Hydroxybenzoate or other preservatives found in creams and in some paste bandages are also potentially allergenic; thus, preservative-free zinc bandages are a suitable alternative.

Topical antibiotics should be avoided in most chronic wounds with antiseptic agents best suited for ulcer care. Antiseptic agents include ionized silver, iodine, PHMB (a chlorhexidine derivative), and a combination of methylene blue and crystal violet, all with a broader spectrum of antimicrobial coverage. Multiple mutations are often needed to cause resistance. Topical antibiotic agents have more limited coverage (eg, mupirocin covers only gram-positive bacteria, and chronic wounds are primarily colonized with gram-negative and anaerobic bacteria), and there is only a single mutation needed for resistance. Dressings can also help provide moisture balance and autolytic debridement. Other common allergens identified by patch testing in persons with leg ulcers include rubber accelerators, lanolin, wood alcohols, topical corticosteroids, and acrylic adhesives. Thiuram is a rubber accelerator that may be present in rubber products including rubber gloves, adhesive dressings, tapes, and compression bandages. Powdered rubber gloves can aerosolize latex, increasing the
risk of sensitization and increasing the risk for both healthcare providers and patients to experience a type 1 anaphylactic reaction. Thus, healthcare providers should wear vinyl non-powdered gloves for routine wound care.

A common sensitizer in moisturizing creams and ointments is lanolin or wood alcohols. The greater the hydrogenation of lanolin (combine hydrogen in the unsaturated sites), the less effective it is as a moisturizer, but it is also a less potent allergen. Lanolin is a weak sensitizer in general, but sensitization is more common in persons with atopy (eczema, asthma, and/or allergic rhinitis) and leg ulcers.

Topical corticosteroids are a frequently missed sensitizer. There are 4 groups of topical corticosteroids with representative allergens for testing (groups A-D). Positive patch test reactions to topical corticosteroids are often delayed, appearing only at the 96-hour reading, and the erythema under a positive test is often less pronounced (1+ or 2+) than the result from most other allergens. In the miscellaneous category, several allergens should be avoided in persons with leg ulcers including propolis (component of beeswax) extract in honey.

**GENERAL RECOMMENDATIONS IN THE MANAGEMENT OF ALLERGIC CONTACT DERMATITIS**

Ideally, healthcare providers should avoid potential wound care product allergens, especially when treating patients with leg ulcers. Once contact dermatitis develops, treatment typically includes corticosteroid creams, oral antihistamines, topical immune response modifiers (e.g., tacrolimus, pimecrolimus), and moisturizers. Some patients may require systemic corticosteroids with a moderate to severe local reaction leading to autosensitization/generalization of the skin rash over the entire body because lymphocytes from the primary skin reaction site migrate to the regional lymph nodes and then traffic to other skin sites spreading the reactions (often called an autosensitization or IgE-like reaction).

Practitioners should suspect ACD if there are eczematous changes surrounding the wound where topical medications and dressings were applied, if the wound does not respond to treatment, or if there is recurrent eczema around the wound with minimal improvement from topical corticosteroids. To diagnose ACD, patch testing to standard allergens should be performed after a detailed review of potential exposures. In addition, skin testing including small pieces of the wound care products (bandages and dressings) moistened with a small amount of water if necessary, covered and left on for the 48-hour similar duration of the patch test, can help identify ingredients that are potential allergens but not in the standard patch test series.

If ICD and ACD cannot be distinguished clinically, patch testing (Figure 4) should be used to determine the potential contact allergen. When a cream or ointment is suspected as the allergen, a repeat open application test to normal skin on the forearm twice daily for 2 to 4 days can be used to screen products for potential allergens. A testing circle about the size of a silver dollar should be outlined, with the test substance applied on the area twice a day and observed for 2 to 4 days for the presence of local erythema. For suspected allergies to ostomy appliances, the other side of the abdomen can be used to screen appliances (application for 48 hours) to detect an allergic response.

For a potential allergy to a component in a wound dressing, the product is applied to normal skin with a 1-cm² size for 48 hours and then removed to detect underlying erythema and edema. For leg ulcers, dressing samples can be applied to normal skin on the other leg or above compression bandaging on the ulcerated extremity. Any positive repeat open application test to a dressing or appliance screen should be followed up if required with patch testing to identify the specific allergen that needs to be avoided in other topical products.

**CONCLUSIONS**

Allergic and irritant contact dermatitis to wound products or moisture-associated ICD on the skin surface is common. Clinicians should be cognizant of the allergens in wound and ostomy-related products and the potential for sensitization. With the increasing incidence of ACD to wound and ostomy products, all medical devices, including dressings, ostomy appliances, adhesives, and bandages, should be labeled with their complete ingredients. Manufacturers should be encouraged to remove common allergens from wound care and ostomy products, including topical creams, ointments, dressings, and ostomy appliances.

**PRACTICE PEARLS**

- Common wound and ostomy-related allergens to avoid include fragrances, PG, colophony, and topical antibiotics.
- Both ACD and ICD occur in patients with wounds and ostomies, particularly patients with leg ulcers.
- Patch testing for patients with chronic wounds to the North American standard series and their wound care products is a useful adjunct for patients with clinical symptoms or signs of ACD.
- Early recognition and treatment of contact dermatitis including removal of contact allergens and irritants are important as contact dermatitis can delay healing.
- The differentiation of allergic or irritant-related contact dermatitis from critical colonization or deep and surrounding infection is often difficult, with incorrect diagnoses leading to inappropriate management and potential delayed healing.
REFERENCES


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