Practice Parameter

Contact Dermatitis: A Practice Parameter—Update 2015

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Key words: *Allergic contact dermatitis; patch testing; allergen; parameter; guideline; contact dermatitis; occupational; sensitizer*

PREFACE

The Practice Parameter on Contact Dermatitis (CD) was last updated in 2006, and focused primarily on the basics of CD and patch testing for the allergist. In the ensuing years, there has been considerable interest by the allergist in allergic skin diseases due to increasing numbers of referrals for CD. With the ease of application, the use of the preloaded commercially available T.R.U.E. Test patch testing method has increased among allergists, as has the use of patch testing with individually loaded chambers. The T.R.U.E. Test has also been expanded to include 35 antigens and a negative control, improving their sensitivity to detect inclusive allergens. There have also been advances in the field in many areas including our basic understanding of type IV hypersensitivity reactions, emerging contact allergens, irritant contact dermatitis (ICD), systemic contact dermatitis (SCD), patch testing in children, occupational dermatitis, and reactions to biomedical devices. Improved diagnosis and management of CD and availability of more comprehensive databases of causative contact allergens enable physicians to manage allergic contact dermatitis (ACD) with avoidance of allergens the patient is sensitized to and availability of lists of safe products that do not contain these allergens. Given the many advances in the field, the Joint Task Force on Practice Parameters (JTF) appointed a working group to review and update the standing practice parameters.

The Contact Dermatitis: A Practice Parameter—Update 2015 workgroup was commissioned by the JTF to develop a practice parameter that addresses recent advances in the field of CD and the optimal methods of diagnosis and management based on an assessment of the most current literature. The Chair (Luz Fonacier, MD) invited workgroup members to participate in the parameter development who are considered to be experts in the field of CD. Workgroup members have been vetted for conflict of interest (COI) by the JTF and their COIs have been listed in this document and are posted on the JTF web site at http://www.allergyparameters.org.

The charge of the workgroup was to develop current practice guidelines based on an up-to-date systematic literature review. Consensus expert opinion and workgroup-identified supplementary documents were utilized when published evidence was lacking.

A search of the medical literature on PubMed was performed for a variety of terms that were considered to be relevant to this

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See Appendix A for members of the Joint Task Force Contact Dermatitis Parameter Workgroup, reviewers of this Practice Parameter, and members of the Joint Task Force on Practice Parameters.

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The Joint Task Force recognizes that experts in a field are likely to have interests that could come into conflict with the development of a completely unbiased and objective practice parameter. To take advantage of that expertise, a process has been developed to prevent potential conflicts from influencing the final document in a negative way.

At the workgroup level, members who have a potential conflict of interest either do not participate in discussions concerning topics related to the potential conflict or if they do write a section on that topic, the workgroup completely rewrites it without their involvement to remove potential bias. In addition, the entire document is then reviewed by the Joint Task Force and any apparent bias is removed at that level. Finally, the practice parameter is sent for review both by invited reviewers and by anyone with an interest in the topic by posting the document on the web sites of the ACAAI and the AAAAI.

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Abbreviations used
AA- Amidoamine
AAAAI- American Academy of Allergy, Asthma and Immunology
ACAAI- American College of Allergy, Asthma and Immunology
ACC- Allergic contact cheilitis
ACD- Allergic contact dermatitis
ACDS- American Contact Dermatitis Society
AD- Atopic dermatitis
AGEP- Acute generalized exanthematous pustulosis
APT- Atopy patch test
BOP- Balsam of Peru
BTM- Betamethasone
CAMP- Contact Allergen Management Program
CAPB- Cocoamidopropyl betaine
CARD- Contact Allergen Replacement Database
CD- Contact dermatitis
CLO- Clobetasol
COI- Conflict of interest
CS- Corticosteroid
CU- Contact urticaria
DMAPA- Dimethylaminopropylamine
DRESS- Drug rash with eosinophilia and systemic symptoms
ELISA- Enzyme-linked immunosorbent assay
EliSPOT- Enzyme-linked immunospot
ENDA- European Network on Drug Allergy
ESCD- European Society of Contact Dermatitis
FDA- Food and Drug Administration
FM- Fragrance mix
FM I- Fragrance mix I
FM II- Fragrance mix II
GCDG- German Contact Dermatitis Group
HC- Hydrocortisone
ICD- Irritant contact dermatitis
IM- Intramuscular
IPPD- Isopropyl-para-phenylenediamine
IUDs- Intrauterine devices
IV- Intravenous
LPTs- Lymphocyte proliferation tests
MCI- Methychloroisothiazolinone
MELISA- Memory Lymphocyte Immuno Stimulation Assay
MI- Methylisothiazolinone
MPL- Methylprednisolone
MSDS- Material safety data sheets
NACDG- North American Contact Dermatitis Group
NHIS- National Health Interview Survey
NS- Nasal spray
NSAIDs- Nonsteroidal anti-inflammatory drugs
OCD- Occupational contact dermatitis
OHS- Occupational health supplement
PABA- Para-aminobenzoic acid
PPD- Para-phenylenediamine
PT- Patch test
PTDS- Para-toluenediamine sulfate
ROAT- Repeated open application test
SCD- Systemic contact dermatitis
SJS- Stevens Johnson syndrome
TCI- Topical calcineurin inhibitors
TCL- Triamcinolone
TCS- Topical corticosteroids
TEN- Toxic epidermal necrolysis
UK- United Kingdom
UVA- Ultraviolet A
UVB- Ultraviolet B

practice parameter. All reference types were included in the results. References identified as being relevant were searched for other relevant references. Published clinical studies were rated by category of evidence and utilized to establish the strength of the recommendations (see Appendix B). The parameter was subsequently appraised by reviewers designated by the AAAAI and ACAAI. Based on this process, this parameter represents an evidence-based, broadly accepted consensus document.

Search terms include contact dermatitis, eczema, cosmetic allergy, contact allergen, patch testing, and each of the specific conditions reviewed in this parameter.

GLOSSARY

"Angry back" syndrome or "excited skin" syndrome: defined as false-positive patch test (PT) reactions usually adjacent to large true-positive reactions that induce contiguous skin inflammation and irritability.

Ectopic allergic contact dermatitis: contact allergy lesions manifested in locations distant from or indirectly in contact with the original skin sites directly exposed to allergens due to inadvertent transfer by the patient (eg, transfer of sensitizers in nail polish to the eyelids) or others (eg, mother transferring allergen to the child or a partner transferring the allergen by contact).

Contact sensitization: evidence of sensitization such as positive PT reaction is not definitive of an "allergy" but simply a confirmation of immunologic sensitization that must then be confirmed as clinically relevant by history and clinical findings analysis.

Contact urticaria: defined as the development of a wheal-and-flare reaction at a site where an external agent contacts the skin or mucosa.

Late patch test reading: late PT reading is performed at or after 7 days after application of a PT as opposed to the standard of care reading that is performed between day 3 and 7.

Photo-allergic contact dermatitis: it is a delayed contact hypersensitivity reaction to an allergen activated by exposure to UV radiation.

Repeated open application test (ROAT): several open PT techniques have been used to test substances with the potential for irritation, and are especially suitable for cosmetics and other personal care products such as makeup foundation and skin lotions. The more commonly used provocative open use test involves the repeated application of a suspected allergen to the antecubital fossa twice daily for up to 1 to 2 weeks, and observation for the local development of dermatitis at the application site.

Usage test: use of a product highly suspected of containing a sensitizer under *real world* conditions to prove causation. An example is for a patient to use eye mascara daily on 1 eye and not the other to observe for the development of local dermatitis at the exposed site. This is often used when PT with suspected commercial allergens is negative but the suspicion of ACD is high.

Systemic allergic contact dermatitis: a generalized ACD rash from systemic administration of a drug, chemical, or food to which the patient previously experienced ACD.

INTRODUCTION

Contact dermatitis (CD) is defined as any skin disorder caused by contact with an exogenous substance that elicits an allergic

and/or irritant response. The vast majority of cases are attributable to irritant ICD. CD is also a significant cause of workplace disability.

Contact urticaria (CU) is defined as the development of a wheal-and-flare reaction, or hives, at a site where an external agent contacts the skin or mucosa. CU can be divided in 2 broad categories: nonimmunologic CU and immunologic CU (caused by an IgE-mediated hypersensitivity reaction). Symptoms of CU range from pruritic, localized wheal-and-flare reactions to generalized urticaria and anaphylaxis. Aside from the need to differentiate between ACD and CU, this parameter will not discuss CU in detail.

This CD practice parameter, updated from the original document published in 2006, is intended as a useful guide for the practicing allergist in the evaluation and management of ACD in adults and children. This updated parameter has been restructured around action-based and patient-centered summary statements that provide specific evidence-based recommendations for assessing and treating ACD. In contrast to the original 2006 parameter, the pathophysiology, susceptibility, and clinical background are not reviewed here. The evidence-based summary statements in this document provide specific recommendations pertaining to the approach to medical history, physical examination, patch testing, and management of patients suspected of ACD.

As in the 2006 parameter, action-based summary statements provide guidance for identification of potential causative sensitizers based on clinical presentation in specific geographical skin locations. Patch testing is emphasized in this updated parameter, with action-based statements that address selection of PT antigens; testing to personal products when necessary; different patch testing devices; timing of readings; late PT reactions; false-positive, false-negative, and true-negative responses; and photo-patch testing. Lists of sensitizers encountered in different settings or in specific types of products (eg, cosmetics, sunscreens, joint prostheses) are presented as tables in the appendices.

Since the publication of the original parameter, new questions have been addressed in summary statements related to emerging clinical problems including preoperative screening for and post-implantation patch testing for metal allergy in patients who have undergone joint replacement surgery. In this updated practice parameter, summary statements have been added that more comprehensively address evaluation and management of occupational contact dermatitis (OCD). The potential benefits and limitations of drug patch testing in patients with maculopapular rashes, erythroderma, and nonimmediate cutaneous reactions are addressed in a summary statement. New summary statements have been included that make recommendations pertaining to the overall management of CD, focusing on avoidance and prevention.

The majority of summary statements in this document are based on descriptive and retrospective studies, representative of the current published CD literature. Because the treatment of choice for CD is avoidance, there are limited numbers of published placebo-controlled studies of other therapeutic interventions (eg, drugs). The absence of a validated positive control to confirm a diagnosis of ACD is a major limitation of studies reporting patch testing data. For these reasons, the categories of evidence supporting the summary statements in this document are relatively low. Therefore, the strength of recommendation for most of the statements in this parameter is "Moderate" even if in some clearly identified circumstances, "Strong" recommendations may be made based on lesser evidence because high-quality evidence is impossible to obtain, and the anticipated benefits strongly outweigh the harms.

Overall, this is a practical, clinically pertinent, and user-friendly parameter that has attempted to address important clinical questions pertaining to the evaluation and management of ACD. This document, although not intended to replace an authoritative textbook, is a valuable updated evidence-based resource for the practicing allergist.

COMPILATION OF SUMMARY STATEMENTS

Summary Statement 1: Consider ACD in the differential diagnosis of patients with chronic eczematous or noneczematous dermatitis. [Strength of Recommendation: Strong; C Evidence]

Summary Statement 2: In patients suspected of ACD, patch testing is the gold standard to confirm the diagnosis. [Strength of Recommendation: Strong; C Evidence]

Summary Statement 3: In addition to personal products used by a patient suspected of ACD, review the home and workplace for other sources of contact allergens. [Strength of Recommendation: Moderate; D Evidence]

Summary Statement 4: Evaluate patients for both irritant and allergic causes, especially in those presenting with hand dermatitis. [Strength of Recommendation: Strong; C Evidence]

Summary Statement 5: Allergic CD should be suspected and evaluated in the patient with both generalized and anatomically localized skin eruptions (such as the hands, face, eyelids) that come in contact with the substances in the environment. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 6: In a patient with a facial rash involving the periorbital areas (eg, eyelids), evaluate for ACD caused by components of cosmetics, such as fragrances, preservatives, and excipients, because these are common sensitizers of the facial skin. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 7: Evaluate patients presenting with lip dermatitis (cheilitis) and perioral dermatitis for both irritant and allergic causes of contact dermatitis. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 8: Evaluate patients with chronic oral mucosal inflammatory conditions for disorders other than ACD. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 9: In patients presenting with dermatitis that involves the scalp and neck, consider patch testing for common causative sensitizers in cosmetics, hair products, and jewelry. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 10: Consider irritant and ACD in all patients presenting with acute or chronic hand eczema. All such patients suspected of CD should undergo patch testing. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 11: Evaluate patients with axillary dermatitis for ACD caused by local contact sensitivity to allergens in topically applied products found in deodorants and textiles. In some cases, axillary dermatitis could be a manifestation of systemic contact dermatitis (SCD) (ie, "the baboon syndrome"). [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 12: Evaluate patients presenting with anogenital dermatitis for possible ACD to antigens contained in topically applied products. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 13: Consider a diagnosis of SCD following systemic exposure (eg, ingestion, infusion, or

transcutaneous exposure) to a known contact sensitizer in a patient who presents with generalized dermatitis, intertriginous and flexural exanthema (Baboon syndrome), and/or a flare at previous cutaneous sites of exposure [Strength of Recommendation: Moderate; C Evidence].

Summary Statement 14: Consider PT to rubber chemicals, adhesives, and leather components of footwear in patients presenting with unexplained chronic dermatitis involving the lower extremities, feet and/or soles. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 15: In addition to avoiding irritants in patients with atopic dermatitis (AD), evaluate for ACD, if suspected, as the 2 dermatologic conditions often coexist in the same patient. [Strength of Recommendation: Moderate; C Evidence]

Patch testing recommendations

Summary Statement 16: Avoid or reduce doses of immunosuppressant medications such as systemic corticosteroids (CS) and systemic immunosuppressants before patch testing. Avoid application of topical corticosteroids (TCS), topical calcineurin inhibitors (TCI), or ultraviolet radiation to the PT site, because these may reduce allergic PT responses. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 17: In addition to using a core or baseline series of PT allergens in evaluating ACD, consider using supplemental series of PT allergens based on specific patient exposures, and the patient's personal products to increase the probability of identifying relevant sensitizers. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 18: Patch testing can be performed either using a preloaded thin-layer rapid use epicutaneous testing kit of 36 chambers or with a panel of antigens loaded individually in a chamber system recommended by the North American Contact Dermatitis Group (NACDG) Research Group or the American Contact Dermatitis Society (ACDS). [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 19: Read and interpret PT conforming to the scoring system developed by the International Contact Dermatitis Research Group. [Strength of Recommendation: Moderate; D Evidence]

Summary Statement 20: Remove and read PT at approximately 48 hours after application. A second reading should be done between 3 and 7 days after application. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 21: Consider that a possible false-positive reaction can result with the use of irritants or allergic substances at potentially irritating higher concentrations, pressure reaction from the filling chamber, an "angry back syndrome," or patch testing on skin with active dermatitis. [Strength of Recommendation: Moderate; D Evidence]

Summary statement 22: Recognize the possibility that false-negative reactions could be due to inadequate allergen concentration needed to elicit a response; inability of the vehicle to release sufficient allergen; reduced skin responsiveness because of prior ultraviolet light exposure (ie, sun, tanning bed); concomitant immunosuppressive therapies; or methodological testing errors such as insufficient occlusion, failure to perform delayed readings, and failure to perform a photo PT. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 23: Determine the relevance of a PT result based on the clinical and exposure history when interpreting the PT. [Strength of Recommendation: Moderate; D Evidence]

Summary Statement 24: Consult physicians with expertise in patch testing to household cleaning or industrial products if testing to the actual product suspected of containing the relevant allergen(s) is necessary, because false-positive and severe irritant reactions can occur. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 25: Consult physicians with expertise in UV radiation and photo-patch testing to confirm a suspected diagnosis of photo-allergic CD. [Strength of Recommendation: Strong; C Evidence]

Summary Statement 26: Although *in vitro* tests for delayed hypersensitivity to contact allergens (ie, metals and bone cement) are available, routine use of such assays is not currently recommended as their sensitivity and specificity for diagnosing ACD has not been determined and should be considered investigational. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 27: Use the repeated open application test (ROAT) to further evaluate a patient suspected of ACD who exhibits doubtful or negative PT responses, to confirm that the patient is reacting to that particular product or to determine clinical tolerability to new cosmetic products. [Strength of Recommendation: Moderate; C Evidence]

Sources of exposure to clinically relevant allergens

Summary Statement 28: Evaluate patients who present with recurrent dermatitis on exposed skin surfaces during airborne pollen seasons for contact sensitization to seasonal pollen allergens. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 29: The clinician should consider cosmetics and personal hygiene products that are directly applied to involved skin or ectopically transferred from uninvolved skin as potential sources of allergens in patients with ACD. [Strength of Recommendation: Strong; C Evidence]

Summary Statement 30: When evaluating ACD from cosmetics and personal care products that contain many different chemical ingredients, consider that the most common causes are due to a few important chemical classes, including fragrances, preservatives, excipients, nickel, and sun screening agents. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 31: Patients suspected to have allergy to hair products should be evaluated for PT reactions to cocoamidopropyl betaine (CAPB), para-phenylenediamine (PPD), fragrances, preservatives, and glycerol thioglycolate. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 32: Suspect allergy to nail products when the dermatitis presents locally at the distal digit or ectopically on the eyelids and face. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 33: Suspect the diagnosis of photo-allergic CD to cosmetics when eczema occurs in a light-exposed distribution following the use of a skin care product or cosmetic, including sunscreens. [Strength of Recommendation: Strong; C Evidence]

Topical medicinal CD

Summary Statement 34: If an eruption worsens, rather than improves, after the topical application of certain medications, or fails to respond to TCS, PT should be performed to the

suspected product and/or ingredients known to be contact sensitizers. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 35: The clinician may use the drug PT for the diagnosis of some drug hypersensitivity reactions, recognizing that there is no standardized approach to define the population, clinical manifestation, drug to PT, and PT materials to make patch testing to drugs a standard of care. [Strength of Recommendation: Weak; D Evidence]

Summary statement 36: Consider preoperative patch testing for metal sensitization in patients with a significant history of metal allergy. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 37: In patients with joint replacement failure, patch testing to components of the implant may be helpful after infection and biomechanical causes have been excluded. [Strength of Recommendation: Moderate; C Evidence]

Special populations

Contact dermatitis in children. Summary Statement 38: ACD and ICD are significant clinical problems in children. Patch testing should be performed and remains the gold standard for the diagnosis of ACD in children. [Strength of Recommendation: Strong; C Evidence]

Occupational contact dermatitis. Summary Statement 39: In a patient who presents with dermatitis associated with workplace exposures (ie, OCD), consider ICD as well as ACD. [Strength of Recommendation: Strong; C Evidence]

Summary Statement 40: In patients with suspected occupation-related CD, the examining physician should verify the diagnosis by confirming that the dermatitis was caused or aggravated by workplace exposures. [Strength of Recommendation: Moderate; C Evidence]

Summary Statement 41: Consider botanical-related ACD in outdoor workers, or others exposed to plants, including florists, gardeners, landscapers, maintenance workers, park, and wildlife officials. [Strength of Recommendation: Moderate; C Evidence]

Treatment of contact dermatitis. Summary Statement 42: Once the allergen or irritant has been identified, the patient should be counseled on avoidance of contact with the offending agent and informed of any cross-reactivity concerns. [Strength of Recommendation: Strong; B Evidence]

Summary Statement 43: In addition to avoidance of exposure, the physician should prescribe appropriate adjunct medical treatment. [Strength of recommendation: Strong; B Evidence]

Summary Statement 44: To prevent CD, avoid exposure to irritants and allergens and use appropriate skin protection. [Strength of Recommendation: Strong; B Evidence]

Summary Statement 45: Education of the workers with ACD or ICD should include prognosis, and information that their disease may persist and need long-term management even after treatment and workplace modifications. [Strength of Recommendation: Moderate; C Evidence]

EXECUTIVE SUMMARY

Contact dermatitis may be suspected on the basis of the clinical appearance of the cutaneous lesions, the distribution of the dermatitis, and the absence of other etiologies. Acute CD is characterized by erythematous papules, vesicles, and crusted lesions. There are other dermatological conditions that may resemble the clinical and/or histological appearance of CD, and these should be considered in the differential diagnosis. The suspicion of ACD is the first step in making the diagnosis. Patch testing is indicated in any patient with acute or chronic, often pruritic, dermatitis if underlying or secondary ACD is suspected.

The history is important for the diagnosis and subsequent management of this disease. Although medical history can strongly suggest the cause of ACD, it has moderate sensitivity (76%) and specificity (76%) in establishing the diagnosis. In addition, the occupational, avocational, and environmental history must all be carefully reviewed. Chronologic exposure histories that include hobbies and specific activities relative to onset of the dermatitis should be obtained. Because the worker may be unaware of specific chemicals to which he or she is exposed, material safety data sheets (MSDS) obtained from the manufacturer may be helpful. Hobbies and nonwork activity such as gardening, macramé, painting, ceramic work, carpentry, and photography may be sources of exposure to culprit contactants. In addition to exposure to a single agent, simultaneous exposure to multiple irritants and contact allergens may produce additive, synergistic, or antagonistic responses. Simultaneous exposure to both an irritant and a contact allergen or 2 contact allergens can reduce the clinical threshold concentration for elicitation of response to a given allergen due to irritant disruption of the skin barrier and immunologic activation of the skin.

There is conflicting evidence as to whether patients with AD are at heightened overall risk of contact sensitization compared with nonatopic individuals. Because AD is associated with an impaired skin barrier, it is plausible that this impairment is likely to increase absorption of topically applied chemicals and enhance the risk of subsequent sensitization, resulting in ACD and worsening of the underlying dermatitis. In children with severe recalcitrant AD and concomitant ACD, avoidance of offending allergens in topically applied products can result in marked improvement of eczema.

The latest NACDG lists the top 3 most common body locations of contact dermatitis as scattered and/or generalized distribution, the hands, and the face. In addition, attention should be given to specific anatomical sites, particularly the eyelids, neck, scalp, axillae, lower extremities, and anogenital area. Facial ACD may present as a generalized facial eruption or in specific regions such as the forehead, periorbital, or perioral areas. Sensitizers in commercial facial products that are in direct skin contact are the most common causes of facial ACD.

Patients presenting with acute or chronic hand eczema should undergo patch testing. Although most cases of CD involving the hands are caused by irritants, allergic contact sensitization is a common cause of chronic hand dermatitis. The prevalence of ACD in patients presenting with hand dermatitis or hand eczema varies according to exposure history and occupation. Thus, it is strongly recommended to evaluate all patients with chronic hand eczema for ACD by obtaining a medical history of contact allergy and performing patch testing.

Acute or chronic inflammation of the lips manifested as eczematous cheilitis can be characterized by itching, burning, redness, edema, and fissuring. This is most commonly caused by physical (eg, cold, dryness, wind) or chemical irritants (eg, saliva, lip cosmetics, or other oral products). Fragrance mix (FM), balsam of Peru (BOP, *Myroxylon pereirae*), and nickel are the most common positive allergens on PT. Sources of fragrances include oral hygiene products (eg, toothpastes, mouthwashes, flavorings, compounds used for dental impressions), cosmetics,

and lip products (including lipsticks, glosses, and lip balms). Oral contact sensitization is considered to be uncommon. Persistent oral complaints or gingivitis has been associated with positive PT reactions to allergens in dental components, including mercury, methacrylate, and beryllium. Chemical and traumatic injury may be the most common causes of contact reactions involving mucous membranes. Other conditions that should be considered in patients with oral mucosal inflammation include burning mouth syndrome, lichenoid tissue reactions, stomatitis, gingivitis, orofacial granulomatosis, recurrent aphthous stomatitis, precancerous and cancerous lesions, viral and fungal infections and lichen planus.

In patients presenting for patch testing for evaluation of CD, nickel remains the most common contact sensitizer and is found more frequently in women than it is in men. The gender difference is likely due to greater exposure of the neck, hands, and ears to nickel in jewelry and body piercing practices. Females are twice as likely as males to have ACD involving the head and neck due to cosmetics. Among patients with cosmetic allergies, fragrances, preservatives, and emulsifiers are the most common causative allergens. In addition to the most common hair dye sensitizer, PPD, there are sensitizers in shampoos, including fragrances, CAPB, and preservatives. ACD involving the scalp is frequently caused by allergens in personal hygiene and medical products (eg, neomycin, benzocaine), hair tint and/or dyes, hair cleansing products, and bleaches.

ACD involving the axillary region is often due to contact sensitivity to fragrance chemicals in deodorants; antiperspirant chemicals are uncommon causes of ACD. Allergic CD due to disperse dyes in clothing can elicit eczematous eruptions in the axillae, feet, and groin. Axillary dermatitis may be a manifestation of SCD, specifically the "baboon syndrome," a diffuse eruption involving flexural and intertriginous areas following oral, intravenous, or transcutaneous exposure to the allergen in a contact-sensitized individual. Three groups of allergens are most common causes of SCD: (i) metals such as mercury, nickel, and gold; (ii) medications including aminoglycoside antibacterials, CS, and aminophylline; and (iii) plants and herbal products including Compositae and Anacardiaceae families and BOP (also known as *Myroxylon pereirae*).

Patients presenting with anogenital dermatoses have been diagnosed with confirmed ACD to allergens contained in topically applied products such as cosmetics, medications, feminine hygiene and contraceptive products. The most common sources of antigens were topical medications, including TCS, fragrances, BOP, nickel sulfate, cinnamic aldehyde, and neomycin sulfate. The preservative methylisothiazolinone (MI) and benzocaine were frequently identified as contact allergens in patients with anogenital complaints.

The pattern of foot dermatitis due to ACD varies according to the type of footwear used. Para-tertiary butylphenol formaldehyde resin (in adhesives), potassium dichromate, cobalt chloride, and carbamates are among the most common allergens. Allergic CD involving the feet is commonly caused by sensitization to common rubber allergens (carbamates, thiurams, and mercaptobenzothiazole). Children presenting with sole dermatitis should be evaluated by patch testing to rule out ACD caused by rubber additives, adhesives, and/or chromates. The majority of patients with chronic leg ulcers and leg dermatitis have contact sensitization to chemical sensitizers found in topically applied preparations including BOP, FMs, antibacterial agents, CS, and lanolin.

Patch testing is indicated in any patient suspected of ACD. Patch testing can be performed using either a preloaded thin-layer rapid use epicutaneous testing kit of 36 chambers or with a panel of antigens individually loaded in a chamber system recommended by the NACDG Research Group or the ACDS. The T.R.U.E. Test (panel of 35 antigens and a negative control) (see Appendix H) is standardized across lot numbers and is highly reproducible. Depending on the test antigen, the T.R.U.E. Test method has moderate concordance (62% to 63%) with individually loaded chamber systems (eg, Finn chamber system). Reliance on a core or baseline series of PT antigens such as those used by the NACDG Research Group or in the T.R.U.E. Test panel for assessing all patients is likely to lead to underdiagnoses of ACD. Selection of allergens to be patch tested will be more accurate when selection is based on the clinical history. One can use PT panels based on the specific industry or exposure group. Frequently, especially in the eyelid, lip, and facial dermatitis, it may be necessary to include personal products and substances specific to the patient's exposure history.

Commercially available panels of supplemental allergens that are constituents of personal care products or encountered in specific occupational environments are listed in the Appendices B, C, and D.

The International Contact Dermatitis Research Group's scoring system listed below is widely used:

(-) Negative reaction

(?+) Doubtful reaction with faint erythema only

(1+) Weak positive reaction with nonvesicular erythema, infiltration, possibly papules

(2+) Strong positive reaction with vesicular erythema, infiltration, and papules

(3+) Extreme positive reaction with intense erythema and infiltration, coalescing vesicles, bullous reaction

(IR) Irritant reaction

(NT) Not tested

In the evaluation of delayed hypersensitivity reactions, the initial reading of PT should be done approximately 48 hours after their application following patch removal. Tests may need to be read 30 minutes after removal of the patches to allow erythema from the occluding pressure of the tape and/or chamber to resolve. A second reading must be done; this is often done at day 3 to 7 after the initial application. A collaborative study demonstrated that 30% of relevant allergens were positive at 96 hours and were negative at the 48-hour reading, which suggests that 96 hours may be optimal for a second reading. Occasionally, an additional late reading after 7 days may be needed for certain contactants such as metals, some antibiotics, and TCS that may yield late reactions. Oral CS exceeding 20 mg/day of prednisone or its equivalent have been shown to diminish skin test reactivity to 5% nickel sulfate at 48 hours. There is minimal evidence to guide the duration of steroid reduction or withdrawal before performing patch testing. If the clinical suspicion is high despite a negative PT in a patient receiving immunosuppressive medications, consider repeat testing when the immunosuppressant doses are lowered or discontinued. The test site where the PT are applied should have no topical potent CS or TCI applied for 5 to 7 days before testing. UV irradiation of PT sites before testing can suppress PT responses.

Doubtful (?+) or weakly positive (1+) questionable or irreproducible reactions on PT can be easily misinterpreted. The timing of the response may also affect its clinical significance,

with a weak reaction at day 7 more likely to be clinically relevant than one at day 3. The inability to separate nonspecific from true allergic responses may be due to the "angry back" or "excited skin" syndrome, which is defined as false-positive reactions adjacent to large true-positive reactions that induce contiguous skin inflammation and irritability. The frequency of false-negative results is not known, but has been estimated to occur in up to 30% of patch-tested patients. The ROAT is used to further evaluate a patient suspected of ACD who exhibits doubtful or suspected false-negative PT responses, to confirm that the patient is reacting to that particular product or to determine clinical tolerability to new cosmetic products. The threshold concentration for a positive reaction for the ROAT is lower than the threshold concentration for a positive PT, although the accumulated ROAT dose was very similar to the PT.

The clinical relevance of positive PT reactions to ACD can only be established by carefully correlating the history, which includes exposure to the allergen, with the PT results. A positive PT may be clinically relevant depending on current or past exposures. Current relevance is defined as *definite* if the PT or use test with the suspected material is positive; *probable* if the PT is positive and the antigen is present in known skin contactants and the clinical presentation is consistent with that exposure; or *possible* if the PT is positive, and skin contact with materials known to contain the allergen was likely.

If photo-allergic CD is suspected, physicians should be consulted with expertise in UV radiation and photo-patch testing to confirm a suspected diagnosis. Photo-allergic CD typically affects sun-exposed areas such as the face, the "V" of the anterior neck, the dorsal hands, and forearms. It typically spares the upper eyelids, upper lip, and submental and postauricular areas. The more common cause of sunscreen sensitization is the chemical sunscreens. Titanium dioxide and zinc oxide (physical UV blockers) have not been reported to cause ACD or photo-allergy, although there are a few reports of titanium in implants causing ACD. Testing requires duplicate application of allergen with subsequent occlusion, and irradiation of one side to compare to the other, nonirradiated application.

Although *in vitro* tests for delayed hypersensitivity to contact allergens (ie, metals and bone cement) are available, routine use of such assays is not currently recommended as their sensitivity and specificity for diagnosing ACD has not been determined and should be considered investigational. *In vitro* tests for assessing antigen specific sensitization are based on measuring lymphocyte proliferation (lymphocyte proliferation tests—LPTs) or cytokine production (ELISA or EliSPOT) after incubation with antigens. Some *in vitro* tests have been validated against patch testing, whereas others have not. The clinical relevance of *in vitro* testing to the diagnosis of CD has not been established and is still investigational.

Identifying sources of exposure to clinically relevant allergens is challenging. Dermatitis present on the face, hands, and exposed chest may be triggered by airborne protein allergens such as grass pollen, house dust mite, and cat dander; and diagnosed by the application of the allergen by patch testing. CD caused by cosmetics is noted predominantly at the site of application; however, occasionally personal care products and cosmetics manifest the contact allergy lesions in locations distant from the original skin sites. This phenomenon termed *ectopic CD* can be caused by nickel transferred to the eyelid by fingers that have been exposed to a nickel source or toluene sulfonamide formaldehyde resin in nail polish.

When evaluating ACD from cosmetics and personal care products that contain many different chemical ingredients, consider that the most common causes are due to a few important chemical classes, including fragrances, preservatives, excipients, nickel, and sun blocks. Fragrances are complex substances and are the most common cause of ACD from cosmetic in the United States. Previous studies suggest that the standard FM and BOP will detect approximately 60% to 70% of fragrance-allergic individuals. The addition of other commonly used fragrance ingredients (FM II, lyral, ylang ylang oil, narcissus oil, and sandalwood oil) may increase the yield up to 96%. However, it should be noted that fragrances in PT have marginal irritant potential and weak positive reactions may not be regarded as proof of contact sensitization (low specificity of the test).

Preservatives and antibacterials are used to prevent rancidity and microbial contamination. Preservatives tend to be grouped into 2 broad categories: formaldehyde releasers (products that emit formaldehyde) and nonformaldehyde releasers. It is recommended that patients allergic to formaldehyde be advised to avoid stay-on cosmetics preserved with formaldehyde releasers. Among nonformaldehyde releaser preservatives, methlydibromo gluteronitrile and methychloroisothiazolinone/methylisothiazolinone (MCI/MI) (trade name: Kathon CG) have emerged as an important cosmetic and toiletry allergen with increasing prevalence. The use of MI alone as a preservative in personal care and cosmetic products has increased in the past few years especially in rinse-off products such as shampoos, conditioners, baby soaps and detergents, and wet wipes. Although parabens formulated in cosmetics are infrequent causes of ACD, they can induce ACD when used as antibacterial in topical medications especially those used on damaged skin, such as in long-standing dermatitis and stasis ulcers. The rate of sensitization to parabens in patients with chronic leg ulcers is higher than that of the general population.

"Botanicals" (such as tea tree oil, propolis, and other essential oils) are plant extracts that are increasingly used as additives to skin care products and are potential causes of CD. It is important that patients who are allergic to fragrance also be made aware of the potential dangers of cosmetic products that may contain plant extracts and patients should also be counseled that "natural products" does not equate with safety.

In patients suspected to have allergy to hair products, CAPB, PPD, fragrances, preservatives and glycerol thioglycolate should be considered. CAPB is an amphoteric surfactant that is often found in shampoos, bath products, and cleaners. Allergy to CAPB typically presents as eyelid, facial, scalp, and/or neck dermatitis. Paraphenylenediamine is the active ingredient in many hair dyes, and is a very common cause of CD in hairdressers. Other routes of exposure include body painting and temporary tattooing. ACD from PPD can be severe, sometimes mimicking angioedema. Cross-reactivity of PPD with other para-amino compounds, such as benzocaine, para-aminobenzoic acid (PABA), sulfa drugs, aminoazobenzene, isopropyl-para-phenylenediamine (IPPD), and azo dyes has been reported and may require avoidance. Glycerol thioglycolate is the active ingredient in permanent wave solution and tends to cause more occupational dermatitis in hair dressers than consumers. Thioglycolates may remain allergenic in the hair long after it has been rinsed out.

Allergy to nail products is suspected when dermatitis presents locally at the distal digit or ectopically on the eyelids and face.

Most allergic reactions to nail polish and artificial nail products are to tosylamide and/or formaldehyde resin found in nail polish enamel, in addition to nail hardeners and setting lacquers. Up to 80% of the reactions appear on the neck, face, lips, and eyelids. Alkyl polyester resin may be a suitable alternative for sensitive patients.

Topical medicinal CD commonly develops after exposure to topical medications, including lanolin, para-aminobenzoic acid (in sunscreens), "caines" (anti-itch preparations), topical antibiotics (neomycin, bacitracin), topical antihistamines, nonsteroidal anti-inflammatory drugs (NSAIDs), and/or TCS. Lanolin is used as the base of many topical medications, including TCS and moisturizers. Allergy to TCS affects 0.5% to 5.8% of patients suspected of ACD. PT to CS is complicated by the inherent, anti-inflammatory nature of the drug itself, which results in frequent false-negative results if tested at too high concentration or late PT readings (7-10 days following application) are not done. Coopman et al classified 4 major groups of CS preparations based on 2 immune recognition sites with considerable cross-reactivity within the groups. Testing should include tixocortol pivalate, budesonide, triamcinolone, the patient's commercial steroid, the vehicle, and the preservatives in the preparations. Although rare, patients sensitized to TCS can develop SCD with administration of the CS by an oral, IV, IM, or inhalation route.

PT to drugs may have a role in delayed hypersensitivity drug reactions and have a higher positivity in patients presenting with maculopapular rashes, erythroderma, and nonimmediate cutaneous reactions including drug rash with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), Stevens Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), and fixed drug eruptions. The utility of the PT depends on various factors including the type and formulation of the drug being tested, the vehicle used, as well as the immunopathogenesis eliciting the eruption. Currently, there is no standardized approach to define the population likely to benefit and validated PT materials to make PT to drugs a standard of care.

Indications for pre-operative patch testing in patients with a history of metal allergy are still being studied. However, preoperative PT may help guide the selection of implant alloys in patients with a high suspicion of metal allergy, and such patients demonstrate improved outcomes. This testing is not recommended for patients without such a history of metal sensitivity. There is no information regarding pre-operative PT in patients with a prior history of methacrylate or antibiotic sensitivity.

The clinician should recognize that contact sensitization to metals or bone cement that are used in orthopedic, cardiac, dental, and gynecological implants have been associated with both dermatitis and noncutaneous complications. These complications may include localized pain, swelling, erythema, warmth, implant loosening, decreased range of motion, stent stenosis, and pericardial effusions in the case of cardiac implants. Patch testing to implant or device components is recommended to help determine the etiology of the postimplantation adverse reaction.

Patients who experienced failed joint replacements and underwent revision using components dictated by a positive metal PT reported resolution of their joint symptoms, most frequently joint pain, joint loosening, and localized dermatitis. Those patients with a positive metal PT who were not revised continued to experience the same symptoms. Similarly, a group of patients with implant-related eczema who were metal sensitized, and then underwent revision with a different metal alloy implant, had a higher incidence of eczema resolution. Anecdotal case reports suggest that patients with skin or systemic manifestations of sensitization to components of implantable defibrillators, pacemakers, arterial stents, dentures, and intrauterine devices (IUDs) appeared to improve once the sensitizing agent was replaced.

There are no current guidelines or recommendations for symptomatic patients with positive PT to metals or bone cement components. The decision regarding implant revision following positive PT results can only be made after a thorough discussion between the patient, the allergist or dermatologist, and the orthopedic surgeon. In addition to the possibility of metal sensitization as a potential cause of joint replacement failure, there are also reports of implant failure related to bone cement or its components including benzoyl peroxide, hydroquinone, methyl methacrylate, and *n*,*n*-dimethyl para-toluidine.

In considering special populations, both ACD and ICD are significant clinical problems in children. Patch testing should be performed and remains the gold standard for the diagnosis of ACD in children. In children, a careful, age-appropriate history should include exposure to diapers, hygiene products, personal care products, cosmetics, sunscreens, textiles with dyes and fire retardant materials, medications, pets and pet products, school projects, sports, and so on. A US-based study showed nickel, fragrance, cobalt, thimerosal, BOP, potassium dichromate, neomycin, lanolin, thiuram mix, and PPD to be common allergens in children. In addition, there are highly relevant allergens that have significant frequency in children because of their unique exposure such as MCI/MI, dialkyl thiourea, p-tert-butyl formaldehyde resin, CAPB, and disperse dyes.

Contact dermatitis is one of the most common types of occupational illness, with estimated annual costs exceeding $1 billion. OCD is classically divided into ICD and ACD. ICD represents approximately 80% of all cases of OCD and most commonly involves the hands. Common irritant exposures include wet work, solvents and alcohols, cutting oils, coolants, degreasers, soaps, detergents, and other cleaning agents and disinfectants. The major chemical groups associated with ACD include metals, rubber-related materials, epoxies, resins and acrylics, organic dyes, plants, foods, medications, biocides, and germicides. The most common causes of plant dermatitis in outdoor workers include poison ivy, poison oak, and poison sumac. Patch testing is not recommended to poison ivy because it can cause sensitization or large bullous reactions.

Accepted and validated criteria such as those proposed by Mathias should be used to confirm the diagnosis of OCD. These include (1) the clinical appearance that is consistent with CD; (2) potential culprit cutaneous irritants and/or allergens are present in the workplace; (3) the anatomic distribution of dermatitis is consistent with workplace skin exposure; (4) the temporal relationship between exposure and onset of symptoms is consistent with CD; (5) nonoccupational exposures are excluded as probable causes of the dermatitis; (6) the dermatitis improves when absent from work exposure, and re-exposure results in exacerbation; and (7) PT performed according to established guidelines demonstrates positive and relevant reactions.

Management of CD begins with avoidance of contact with the confirmed offending agent and the patient is informed of any cross-reactivity concerns. The identification and avoidance of

contact with the offending agent(s) is the key to successful treatment of ICD and ACD. For cosmetic products, the patients should be given not only a list of what they are allergic to but also a list of products that they can use, that are free of the suspected allergens. Several databases are currently available in the United States.

Components of medical management of ACD include TCS with second line therapies including phototherapy, oral retinoids, and immunosuppression. TCS are widely accepted as the treatment of acute and chronic dermatitis, and selection of the TCS for efficacy, potency, and acceptability is determined by many factors including the severity, the location, and the acuteness of the dermatitis. Key to the management of ACD is still the identification and avoidance of the allergen. Several topical T-cell selective inhibitors (topical tacrolimus and pimecrolimus) have been used successfully in the treatment of AD, but their efficacy in ACD or ICD has not been established. Other treatments including cyclosporin, azathioprine and psoralen plus ultraviolet A (UVA) have been used for steroid-resistant ACD such as chronic hand dermatitis.

Primary prevention of ICD and ACD involves avoidance of exposure to possible irritants and allergens and appropriate skin protection. Avoidance of exposure may be accomplished by several means including elimination of an irritant or an allergen, substitution, training, and rotation of job task. The use of personal protective equipment such as gloves, goggles and/or face shields, uniforms, and equipment to protect the skin from the exposure is important. The use of cotton liners under gloves can be useful. Skin care to protect the barrier function of the skin is important and involves the use of moisturizers, particularly lipid-rich moisturizers.

In a review of 15 studies reporting prognosis in OCD between 1958 and 2002, the range of complete clearance of the dermatitis was 18% to 72%. Atopic dermatitis is associated with poorer outcomes. The longer the duration between the onset and diagnosis of hand dermatitis, the poorer the outcome. There is significant job disruption for workers with CD. There are a small percentage of individuals with occupational hand dermatitis who do poorly even with removal from exposure.

CONTACT DERMATITIS: A PRACTICE PARAMETER—UPDATE 2015

Clinical evaluation

Summary Statement 1: Consider ACD in the differential diagnosis of patients with chronic eczematous or non-eczematous dermatitis. [Strength of Recommendation: Strong; C Evidence]

Contact dermatitis may be suspected on the basis of the clinical appearance of the lesions, the distribution of the dermatitis, and the absence of other etiologies or lack of associated systemic manifestations. Acute CD is characterized by erythematous papules, vesicles, and crusted lesions. Recurrent or persistent episodes of CD will change over time from acute skin inflammation to skin thickening, hardening, scaling, and fissuring, with exaggeration of the normal markings known as lichenification. Pruritus is characteristic of both acute and chronic CDs, and constant skin rubbing contributes to the lichenification. Histologically, CD demonstrates intercellular edema of the epidermis known as spongiosis, with varying degrees of acanthosis (thickening of the epidermal stratum basale and stratum spinosum) and superficial perivascular, lymphohistiocytic infiltrates. Features on physical examination or histological findings are unable to differentiate ACD from ICD. Patch testing and environmental history of exposure to contact allergens is required. There are other dermatological conditions that may resemble the clinical and/or histological appearance of CD, and these should be considered in the differential diagnosis (Table I)[1,2] that includes cutaneous T-cell lymphoma. The cutaneous biopsy, if needed to differentiate CD from other forms of dermatitis, should be interpreted by a pathologist with expertise in dermatopathology.

Summary Statement 2: In patients suspected of ACD, patch testing is the gold standard to confirm the diagnosis. [Strength of Recommendation: Strong; C Evidence]

The suspicion of ACD is the first step in making the diagnosis. Patch testing is indicated in any patient with acute or chronic, often pruritic, dermatitis if underlying or secondary ACD is suspected. The history is important for the diagnosis and subsequent management of this disease. Although medical history can strongly suggest the cause of ACD, it has moderate sensitivity (76%) and specificity (76%) in establishing the diagnosis.[3] Because the patient may be unaware of any relevant exposure, virtually any eczematous lesion could be aggravated by a contact sensitizer.[4-8] Noneczematous eruptions such a prurigo nodularis may also be associated with clinically relevant positive PT.[9] Studies have demonstrated the utility of patch testing in children with chronic dermatitis.[10]

The sensitivity and specificity of patch testing varies according to the allergen. For example, it has been reported that a positive PT to nickel sulfate is demonstrable in only 60% of patients with a positive history of nickel allergy (ie, positive predictive value 60%), whereas 12.5% to 15% of persons reporting a negative history of metal allergy had a positive PT response to nickel sulfate.[3,11]

Patch testing identifies contact sensitizers in nearly 50% of patients presenting with scattered generalized dermatitis.[12] The experienced clinician can misclassify ACD as nonspecific eczema or IgE-mediated CU if the assessment is based solely on the medical history without patch testing.[13,14]

Although sensitization occurring after patch testing is rare, this has been reported after testing to plant allergens such as poison ivy or poison oak, as well as to p-aminoazobenzene, p-phenylenediamine, diaminodiphenylmethane, cobalt, chromium,[15] and beryllium.[16] The possibility of active sensitization can be minimized by testing with dilute solutions.[17]

Patch testing has been shown to be cost effective if performed early in the course of the disease in patients with chronic ACD by reducing prediagnosis costs of treatment. Treated patients with CD confirmed by patch testing exhibit significantly greater improvement in dermatology-specific quality of life than those patients who were not patch tested.[18] Skin prick testing has no role in the evaluation of ACD but is often useful in patients presenting with allergic CU.

Summary Statement 3: In addition to personal products used by a patient suspected of ACD, review the home and workplace for other sources of contact allergens. [Strength of Recommendation: Moderate; D Evidence]

Work and environmental history must be carefully reviewed. Chronologic exposure histories that include hobbies and specific activities relative to onset of the dermatitis should be obtained.

The exact nature of the work duration of each activity and occurrence of similar skin effects in coworkers may provide clues

TABLE I. Differential diagnosis of allergic contact dermatitis (ACD)

Dermatologic condition	Differentiating features and clues to diagnosis
Irritant contact dermatitis	• Glazed, parched, or scalded appearance • Sharply circumscribed dermatitis • Healing begins promptly on withdrawal of the offending agent • Patch testing negative
Atopic dermatitis	• Personal or family history of atopy • Early age of onset • Chronic and recurrent • Dry, scaly very pruritic • Typical distribution Facial in infancy Extensors in early childhood Flexural areas in adolescence and adults
Seborrheic dermatitis	• Distribution: areas with sebaceous glands • Scalp, periauricular, face (medial eyebrows, glabella, nasolabial folds), presternal trunk, interscapular • Blepharitis common • Dandruff appears to be a precursor • Distinctive morphology: dull, yellowish-red, sharply demarcated lesions covered with greasy-looking scales
Dyshidrotic eczema	• Small (1-2 mm) vesicles, deep seated on nonerythematous base • Palms, soles, and/or lateral aspects of fingers, often symmetrical • Intensely pruritic and itching prodrome • Persists for 2-3 weeks and then resolves by involution and desquamation
Psoriasis	• Plaques typically have dry, thin, silvery-white, or micaceous scale • Auspitz sign: removing scale reveals a smooth, red, glossy membrane with tiny punctate bleeding
Dermatitis herpetiformis	• Genetic predisposition for gluten sensitivity • Intensely pruritic • Symmetrically grouped (herpetiform) papules and vesicles • Elbows, knees, buttocks, scapula, scalp • Direct immunofluorescence of the skin shows granular IgA at dermal papillae and occasionally along the dermo-epidermal border
Mycoses fungoides and cutaneous T-cell lymphoma	• Patches with thin, wrinkled quality, often with reticulated pigmentation • Pruritus varies from minimal or absent to common in premycotic phase and may precede MF by years • Often on lower trunk and buttocks • Cutaneous biopsy required for confirmation

as to potential causes of work-related ICD or ACD.[19,20] Relevant changes in work environments that result in new direct chemical exposures to the skin, including vapors and fumes, must be probed. Certain occupations (eg, hospital workers) require frequent hand washing, and the use of cleansing agents may compromise the skin barrier and cause irritant hand dermatitis.[21] Because the worker may be unaware of specific chemicals to which he or she is exposed, MSDS obtained from the manufacturer may be helpful; however, key sensitizing ingredients found at low concentrations are often omitted from product descriptions.[22]

Hobbies and nonwork activity such as gardening, macramé, painting, ceramic work, carpentry, and photography may be sources of exposure to culprit contactants. Obtaining a detailed history of animal and animal product exposure is essential.

Summary Statement 4: Evaluate patients for both irritant and allergic causes, especially in those presenting with hand dermatitis. [Strength of Recommendation: Strong; C Evidence]

In addition to exposure to a single agent, simultaneous exposure to multiple irritants and contact allergens may produce additive, synergistic, or antagonistic responses. Although most research related to irritant and allergic effects comes from studies of single agents, individuals are often exposed to multiple irritants and allergens. In some situations, accepted threshold concentrations for elicitation of an allergic cutaneous PT response to a specific contact allergen may not apply. Simultaneous exposure to both an irritant and a contact allergen or 2 contact allergens can reduce the clinical threshold concentration for elicitation of response to a given allergen. The 2 mechanisms have been suggested to explain the effect of exposure to an irritant on potentiation of contact sensitization, including effects on the immune response by upregulation of proinflammatory cytokines and/or enhanced penetration of the allergen.[23]

Detergents are common causes of hand dermatitis because of their disruption of the skin barrier and are frequently associated with ICD of the hand. Although there are some reports of ACD related to detergents, careful evaluation suggests that allergic responses are rare.[24] Irritants that disrupt the skin barrier may then penetrate into the epidermis resulting in injury to the keratinocyte membranes and release of inflammatory cytokines, and contribute to developing ICD. This disruption of the skin barrier also allows for allergen penetration and resultant induction of immunological responses.[25]

Physical examination

Summary Statement 5: Allergic CD should be suspected and evaluated in the patient with both generalized and anatomically localized skin eruptions (such as the hands, face, eyelids) that come in contact with the substances in the environment. [Strength of Recommendation: Moderate; C Evidence]

The latest NACDG lists the top 3 most common body locations of CD as scattered and/or generalized distribution, the hands and the face.[26] In addition, attention should be given to specific anatomical sites, particularly the face, eyelids, lips, oral mucosa, neck and scalp, hand, axillae, anogenital area, feet, and lower extremities. Each of these areas can be affected by ACD and will be described in greater detail in Summary statements 6 through 14. A diagnosis of ACD based on the physical examination and history alone, however, is not conclusive and should be confirmed by PT.[27]

Summary Statement 6: In a patient with a facial rash involving the periorbital areas (eg, eyelids), evaluate for ACD caused by components of cosmetics, such as fragrances, preservatives, and excipients, because these are common sensitizers of the facial skin. [Strength of Recommendation: Moderate; C Evidence]

Facial ACD may present as a generalized facial eruption or in specific regions such as the forehead, periorbital, or perioral areas. Sensitizers in commercial facial products that are in direct skin contact are the most common causes of facial ACD.[28] Facial ACD may also occur when contact allergens are transferred ectopically to the face by the hands from other regions of the body. Skin exposure to airborne plant-derived aeroallergens (eg, tree, weed pollens) may cause an eczematous dermatitis of the exposed areas of the face, neck, and arms. These reactions typically occur on a seasonal basis during the summer months.[29] Compositae sensitizers are also found in many "natural" cosmetic products and may cause facial ACD.

Allergic CD is the most common cause of isolated periorbital and eyelid dermatitis.[28] Risk factors include female gender, AD, and age over 40 years. In one study, the most common sources of causative allergens were found in cosmetic products (eg, facial cream, eye shadow) and ophthalmic therapeutics. The most commonly identified sensitizers were FM (19%), BOP (10%), thimerosal (10%), and neomycin sulfate (8%).[28] Nickel has also been identified as a very common sensitizer associated with periorbital CD.[30] Although it has been suggested that preservatives in topical ophthalmic medications are important sensitizers, benzalkonium chloride (the most frequently used today) has not been found to be a common sensitizer in patients with periorbital CD.[31] Thimerosal, a possible sensitizer, is less commonly used in ophthalmic products. A recent retrospective North American study of patients evaluated for periorbital dermatitis could not detect significant sensitizers related to ophthalmic products, and found that nickel and fragrances were still the most common sensitizers identified by PT.[32] ACD is responsible for 81% of cases of eyelid dermatitis. Common sensitizers included nail product chemicals (tosylamide and/or formaldehyde resin, acyrlates), botanicals in personal care products, and nickel.[33]

Summary Statement 7: Evaluate patients presenting with lip dermatitis (cheilitis) and perioral dermatitis for both irritant and allergic causes of contact dermatitis. [Strength of Recommendation: Moderate; C Evidence]

Eczematous cheilitis is an acute or chronic inflammation of the lips and is characterized by itching, burning, redness, edema, and fissuring. This is most commonly caused by physical (eg, cold, dryness, wind) or chemical irritants (saliva, lip cosmetics, or other oral products). Other causes include atopic cheilitis that is observed in patients with AD. In a series of more than 10,000 patients reported by the NACDG, 2% of patients presented with lip dermatitis and 85% of these cases were women.[34] Allergic contact cheilitis (ACC) often involves the lip vermillion border and extends to contiguous skin presenting with concomitant perioral dermatitis; with adjacent oral mucosa typically spared. In patients presenting to dermatologists with cheilitis, history combined with patch testing was able to confirm ACC in only 34% to 38% of patients.[34,35] FM, BOP, and nickel were the most common positive allergens on PT. Sources of fragrances include oral hygiene products (eg, toothpastes, mouthwashes, flavorings, compounds used for dental impressions), cosmetics, and lip products (including lipsticks, glosses, and lip balms). In another study, lipsticks and lip balms were identified as the most common sources of allergens for ACC in females and toothpaste was the most commonly implicated allergen[35] in males. In toothpastes, flavoring chemicals are most frequent relevant allergens, including mint derivatives such as spearmint, menthol, peppermint, carvone as well as cinnamal, and anethole.[36] In lip balms, propolis produced by bees, lanolin, coconut oil, almond oil, peppermint oil, and vitamin E are potential sensitizers.[37] Less common antigen sources of ACC are jewelry (ie, nickel by ectopic transfer) and topical medications (eg, neomycin, budesonide, tetracaine). Interestingly, relevant positive PT to allergens that were not part of the NACDG patch series have been identified in 36% of patients with ACC.[34] This suggests that a selected panel should be used that is based on the patient's personal products.

Summary Statement 8: Evaluate patients with chronic oral mucosal inflammatory conditions for disorders other than ACD. [Strength of Recommendation: Moderate; C Evidence]

ACD is often considered in the differential diagnosis of burning mouth syndrome, lichenoid tissue reactions, stomatitis, gingivitis, orofacial granulomatosis, recurrent aphthous stomatitis, precancerous and cancerous lesions, viral and fungal infections, lichen planus, especially in human immunodeficiency virus-infected patients and those with Melkersson-Rosenthal syndrome. Nevertheless, the oral mucosa is considered an immune privileged site and oral contact sensitization is considered to be uncommon. Persistent oral complaints or gingivitis has been associated with positive PT to allergens in dental components including mercury, methacrylate, and beryllium.[38]

In a large study of 331 patients presenting with oral symptoms, PT was conducted to a comprehensive panel of flavorings, preservatives, acrylates, medications, and metals.[39] The mean age in this study was 58 years and 81% were women. The most frequent positive PT was to potassium dicyanoaurate, nickel, gold sodium thiosulfate, FM, BOP, beryllium, cobalt, and acrylate. More than 50% of patients presenting with burning mouth syndrome, lichenoid tissue reaction, cheilitis, stomatitis, and gingivitis exhibited at least one positive reaction considered to be relevant by the reporting physician. However, the term "relevant positive" PT used in large retrospective PT studies is severely limited due to the lack of documentation of clinical improvement following avoidance to the suspected "relevant" allergens. Thus, based on available clinical data, there is insufficient evidence to confirm a causative role of contact allergy in the aforementioned oral syndromes.

Chemical and traumatic injury may be the most common causes of contact reactions involving mucous membranes. Many of these reactions are caused by caustic chemical agents inadvertently applied during dental treatment. Lastly, one should be aware that oral erosions and blistering lesions may be the initial

presenting symptoms of autoimmune blistering diseases such as pemphigus.

Summary Statement 9: In patients presenting with dermatitis that involves the scalp and neck, consider patch testing for common causative sensitizers in cosmetics, hair products, and jewelry. [Strength of Recommendation: Moderate; C Evidence]

Nickel remains the most common contact sensitizer and is found more frequently in women than it is in men. The gender difference is likely due to greater exposure of the neck, hands and ears to nickel in jewelry,[40,41] as well as piercing practices.

Females are twice as likely as males to have ACD involving the head and neck due to cosmetics.[42] Among patients with cosmetic allergies, fragrances, preservatives, and emulsifiers are the most common causative allergens. Specifically the most common in both genders are quaternium-15, FM and BOP. PPD (hair dye), glyceryl thioglycolate (permanent wave solutions), tosylamide and/or formaldehyde resin (nail enamel products), and methyl methacrylate (nail product adhesive) were common sensitizers in females. Sensitizers in hair care products affect 30% of females and 22% of male patients who were evaluated for CD.[42] In addition to the most common hair dye sensitizer, PPD, more than 20 other potential sensitizers have been identified in hair dye products.[43] Frequent sensitizers contained in shampoos include fragrances, CAPB (a surfactant), preservatives such as MCI/MI, and preservatives that are formaldehyde releasers (eg, quaternium-15, imidazolidinyl urea). Other ingredients that are potential sensitizers include propylene glycol, vitamin E, parabens, benzophenones, iodopropynyl butylcarbamate, and methyldibromo glutaronitrile/phenoxyethanol.[44] Allergic CD involving the scalp is most frequently caused by sensitization to medical products (eg, neomycin, benzocaine), hair tint, dyes, hair cleansing products, and bleaches.[45]

Summary Statement 10: Consider irritant and ACD in all patients presenting with acute or chronic hand eczema. All such patients suspected of CD should undergo patch testing. [Strength of Recommendation: Moderate; C Evidence]

Allergic contact sensitization is a common cause of chronic hand dermatitis. The prevalence of ACD in patients presenting with hand dermatitis or hand eczema varies according to exposure history and occupation. Hair dressers presenting with hand dermatitis had a high prevalence of ACD (75%) with 25% of the remaining cases being attributed to irritants.[40] In a multicenter collaborative study in Denmark, 508 consecutive patients who presented with hand eczema were evaluated. In these patients, ICD was diagnosed in 38%, ACD in 24%, AD in 19%, and in 22%, nonspecific dermatitis was the diagnosis.[46] Even in children, ACD is a common cause of hand dermatitis with one study reporting as high as 36% prevalence. Sensitizers deemed relevant to ACD involving the hands included the preservative quaternium-15 (16.5%), formaldehyde (13.0%), nickel sulfate (12.2%), FM (11.3%), thiuram mix (10.2%), BOP (9.6%), carba mix (7.8%) used in rubber products, neomycin sulfate (7.7%), bacitracin (7.4%), and methyldibromo glutaronitrile/phenoxyethanol 2.0% (7.4%). Thus, it is strongly recommended to evaluate all patients with chronic hand eczema for ACD by obtaining a medical history of contact allergy and performing patch testing. In addition to ACD, chronic hand eczema may be a presenting symptom of psoriasis and should be considered in the differential diagnosis.

Summary Statement 11: Evaluate patients with axillary dermatitis for ACD caused by local contact sensitivity to allergens in topically applied products found in deodorants and textiles. In some cases, axillary dermatitis could be a manifestation of SCD (ie, "the baboon syndrome"). [Strength of Recommendation: Moderate; C Evidence]

ACD involving the axillary region is often due to contact sensitivity to fragrance chemicals in deodorants, including hydroxyisohexyl-3-cyclohexene carboxaldehyde, isoeugenol, hydroxycitronellal, as well as cinnamic aldehyde and sensitizers in natural botanical deodorants.[47-52] Although ICD is more common, ACD has been rarely attributed to antiperspirants.[53] Isolated case reports of ACD causing axillary dermatitis have been attributed to propantheline bromide used as a treatment for hyperhidrosis.[54] Pretesting with a ROAT on the flexor surface of the forearm and axilla is advised in any patient with a history of a pre-existing axillary dermatitis before initiating use of a new product.

ACD due to disperse dyes in clothing can elicit eczematous eruptions in the axillae, feet, and groin.[55] In Sweden, 1.5% of all patients undergoing patch testing has positive reactions to a textile dye mix and the most common reactive dye was disperse orange 1, whereas a clinic in North America reported that disperse blue 106 and disperse blue 124 were the most frequent sensitizers.[56] Patients reacting to a textile dye mix more often reported dermatitis involving the axillary folds, arms, face, and neck.[57] In the axillae, the periphery is more often involved than the axillary vault due to greater contact of the garment to the skin in this area.

Axillary dermatitis may be a manifestation of SCD, specifically the "baboon syndrome", a diffuse eruption involving flexural and intertriginous areas following oral, intravenous, or transcutaneous exposure to the allergen in a contact-sensitized individual.[58] Allergens associated with SCD are listed in Appendix C.

Summary Statement 12: Evaluate patients presenting with anogenital dermatitis for possible ACD to antigens contained in topically applied products. [Strength of Recommendation: Moderate; C Evidence]

Allergic CD can cause anogenital dermatitis. A total of 17% to 74% of patients presenting with anogenital dermatoses have been diagnosed with confirmed ACD to allergens contained in topically applied products such as cosmetics, medications, and feminine hygiene and contraceptive products. In a recent large retrospective study, 44% of patients with anogenital dermatitis (including 41% of women and 50% of men) were identified with ACD. The most common sources of antigens were topical medications, including TCS, fragrances, BOP, nickel sulfate, cinnamic aldehyde, and neomycin sulfate. Cinnamic aldehyde, dibucaine, benzocaine, hydrocortisone-17-butyrate, and budesonide were more common sensitizers in patients presenting exclusively with anogenital dermatitis. A total of 21% patients were diagnosed with ICD; the most common irritants were cosmetics, soaps and cleansers, various health aides, and unknown agents.[59] In another patient series, the preservative MI and benzocaine were frequently identified as contact allergens in patients with anogenital complaints.[60] Methylisothiazolinone, used as a preservative in wet baby wipes has been identified as a sensitizer and cause of ACD involving the buttocks and perianal area in children.[61]

Summary Statement 13: Consider a diagnosis of SCD following systemic exposure (eg, ingestion, infusion, or

transcutaneous exposure) to a known contact sensitizer in a patient who presents with generalized dermatitis, intertriginous and flexural exanthema (Baboon syndrome), and/or a flare at previous cutaneous sites of exposure. [Strength of Recommendation: Moderate; C Evidence]

The most common causes of SCD consist of 3 groups of allergens: (i) metals such as mercury, nickel, and gold; (ii) medications including aminoglycoside antibacterials, CS, and aminophylline; and (iii) plants and herbal products including the Compositae and Anacardiaceae plant families and BOP.[58] Nickel sulfate is ubiquitous in steel devices, jewelry, clothing, and food. Systemic CD can result from ingestion of trace amounts of nickel in soy, chocolate, nuts, green beans, peas, and canned foods.[62] Other examples of systemic exposure to allergens that can trigger diffuse SCD include systemic administration of aminoglycoside antibiotics in a patient sensitized to topical neomycin; hydroxyzine ingestion or administration of IV aminophylline in patients with ACD to ethylenediamine, which cross-reacts with both medications; oral estrogen triggering a systemic dermatitis after sensitization to estrogen patches[63]; or flare of previously positive budesonide PT sites after inhalation of nebulized budesonide.[64] It is postulated that once the allergen has entered the blood stream, it encounters and reactivates specific memory T cells that then home to the site of the previous dermatitis.

Patients may also experience SCD after oral challenges with fragrance-containing foods, Chinese herbs, or drugs. Patients who are contact sensitive to BOP are prone to SCD with ingestion of foods or flavoring agents that are constituents of BOP (eg, citrus products, ice cream, cinnamon, chutney, cola, vanilla, curry, ketchup, or tomatoes) or cross-react with those constituent allergens. In addition, various spices, garlic, cashew nuts, and proteinaceous substances handled by grocers, meat and fish handlers, and bakers have been cited as causes of SCD.

Summary Statement 14: Consider PT to rubber chemicals, adhesives, and leather components of footwear in patients presenting with unexplained chronic dermatitis involving the lower extremities, feet and/or soles. [Strength of Recommendation: Moderate; C Evidence]

The pattern of foot dermatitis due to ACD varies according to the type of footwear used. ACD rarely localizes between the toes and typical sole involvement spares the instep and the toe's flexural creases. Patch testing studies have identified p-tertiary butylphenol formaldehyde resin (in adhesives), potassium dichromate, cobalt chloride, and carbamates as the most common allergens.[27,65-72] Allergic CD involving the feet is commonly caused by sensitization to common rubber allergens (carbamates, thiurams, and mercaptobenzothiazole). Patients suspected of rubber ACD should also be tested to mixed dialkyl thioureas (diethylthiourea and dibutylthiourea) because the majority of thiourea-sensitized patients do not react on PT to the more common rubber allergens.[67] Children presenting with sole dermatitis should be evaluated by PT to rule out ACD caused by rubber additives or chromates (from leather tanning).[68] All the aforementioned chemicals should be included in PT panels to evaluate patients with foot dermatitis.

The vast majority of patients with chronic leg ulcers have positive PT to chemical sensitizers found in topically applied preparations. The most common of sensitizers were BOP, FM I, antibacterial agents, CS, and lanolin.[69,70] In a recent prospective study of patients with leg ulcers, the number of positive PT correlated with duration of the leg ulcers. This suggests that topical preparations containing fragrances and antiseptics should be avoided in patients with leg ulcers and that they have the potential to become sensitized to components of products and medications that are used to treat leg ulcers.[70]

Summary Statement 15: In addition to avoiding irritants in patients with AD, evaluate for ACD if suspected, as the 2 dermatologic conditions often coexist in the same patient. [Strength of Recommendation: Moderate; C Evidence]

There is conflicting evidence as to whether patients with AD are at heightened overall risk of contact sensitization compared with nonatopic individuals. One recent study showed an inverse relationship between contact sensitization and severe AD.[73]

Because AD is associated with an impaired skin barrier, it is plausible that this impairment is likely to increase absorption of topically applied chemicals and enhance the risk of subsequent sensitization. Atopic dermatitis has been diagnosed in 34% of children with clinically relevant PT reactions, although children without AD are equally as likely as those with AD to exhibit clinically relevant positive PT.[74]

In a large population-based study of Danish adults, contact sensitization to at least one allergen was observed in 14% of patients who self-reported AD, whereas in 10% of those without AD had ACD. This overall difference between atopics and nonatopics in this study was primarily attributed to a higher frequency of allergy to fragrances that may reflect a greater cumulative skin exposure to topical treatments containing fragrances.[73] In this same study, the risks associated with filaggrin mutations were also evaluated. Self-reported hand dermatitis as well as AD combined with hand dermatitis was significantly associated with contact sensitization in patients with a filaggrin gene mutation (R501X, 2282del4), whereas AD alone combined with filaggrin mutations but without hand dermatitis was not significantly associated with contact sensitization.[75] In a North American study, PT results compared between 300 patients with AD and approximately 3000 patients without AD found that patients with AD were significantly more likely to exhibit contact sensitization and this difference was attributable to sensitization to metals.[76]

In a report by Jacob et al,[77] comprehensive PT played a key role in the identification of relevant chemical allergens in personal hygiene products and topical treatments used in management of 3 children with severe, recalcitrant AD. Avoidance of offending allergens resulted in marked improvement of eczema, which permitted reduction in TCS and subsequent discontinuation of systemic immunosuppressive therapy.

Patch testing recommendations

Summary Statement 16: Avoid or reduce doses of immunosuppressant medications such as systemic CS and other systemic immunosuppressants before patch testing. Avoid application of TCS, TCI, or ultraviolet radiation to the PT site, because these may reduce allergic PT responses. [Strength of Recommendation: Moderate; C Evidence]

The majority of adult patients treated with oral CS exceeding 20 mg/day of prednisone or its equivalent have been shown to diminish skin test reactivity at 48 hours to 5% nickel sulfate.[78] The effect of systemic CS on the results of PT is less understood for children. Patch tests in patients on low doses of prednisone and cyclosporine may still yield clinically relevant results.[79]

There are no supporting data that guide the duration of steroid reduction or withdrawal before performing PT. The

suppression is not absolute, and if necessary, PT should be performed while on the lowest possible dose of the immunosuppressant medication.[79,80] If the clinical suspicion is high despite a negative PT, consider repeat testing when the immunosuppressant doses are lowered or discontinued.

High/medium potency TCS (ie, betamethasone dipropionate 0.05%) applied topically to PT sites for 3 successive days suppress 48-hour responses to contact allergens.[81] The test site where the PTs are applied should have no topical potent CS or TCI applied for 5 to 7 days before testing.[82,83] Topical tacrolimus (0.1%) pre-applied to skin test sites for 48 hours suppressed 48-hour PT responses to 5% nickel sulfate.[84] Pretreatment of skin test sites with UV irradiation produced dose-related suppression of erythema measured at 48 hours after application of nickel sulfate PT in nickel-sensitized subjects.[85] Protection from UV-induced immunosuppression of allergic responses to nickel sulfate was achieved by application of sunscreen products blocking UVA and UVB wavelengths.[86]

Systemic antihistamines are generally not believed to interfere with the PT readings. A study showed that treatment with 10 mg loratadine for 4 days before patch testing was associated with a significant reduction in the size of the eczematous responses to nickel sulfate. Recently, desloratadine given for 4 days at twice the normal daily dose (5 mg po bid) did not significantly impact interpretation of positive patch responses to 10 contact allergens.[87] This would indicate that antihistamines do not need to be withheld for PT.

Summary Statement 17: In addition to using a core or baseline series of PT allergens in evaluating ACD, consider using supplemental series of PT allergens based on specific patient exposures and the patient's personal products, to increase the probability of identifying relevant sensitizers. [Strength of Recommendation: Moderate; C Evidence]

Reliance on a core or baseline series of PT antigens such as those used by the NACDG or in the T.R.U.E. Test panel for assessing all patients is likely to lead to underdiagnoses of ACD. A recent multicenter North American study of over 4300 patients published in 2013 revealed that 25% of patients exhibited a clinically relevant positive test to an antigen not included in a standard 70-antigen panel, and 25% reacted to an allergen that was not part of the T.R.U.E. TEST panel.[26] In 2009, the NACDG reported that 23% of 4454 patients in a multicenter study exhibited at least one relevant positive test to a supplementary allergen and 5% reacted to a clinically relevant occupational allergen not part of the standardized panel of 65.[88] Many PT companies provide kits with allergen panels selected for a specific industry such as machinists, cosmetologists, or dental workers (Appendix D). There are other standardized panels for exposure groups such as cosmetics, textiles, plastics, and glues (Appendix E), and medications and topical treatments (Appendix F). Currently, such kits can only be obtained from the manufacturers listed in Appendix G. Frequently, especially in the eyelid, lip, and facial dermatitis, it may be necessary to include personal products and substances specific to the patient's exposure history.

Summary Statement 18: Patch testing can be performed either using a preloaded thin-layer rapid use epicutaneous testing kit of 36 chambers or with a panel of antigens loaded individually in a chamber system recommended by the NACDG Research Group or the ACDS. [Strength of Recommendation: Moderate; C Evidence]

A study of the T.R.U.E. Test (panel of 35 antigens and a negative control) (Appendix H) showed that it is highly reproducible with only a 5% discordance between concomitant duplicate tests in individual patients.[89] Depending on the test antigen, the T.R.U.E. Test method has moderate concordance with individually loaded chamber systems. In separate studies, 62% to 63% overall positive concordance rates were reported between the Finn chamber system and T.R.U.E. Test methods.[90,91] The T.R.U.E. Test is widely used because of its ease of application. However, it lacks flexibility and has currently a limited number of allergens available. The NACDG series comprises 65-70 allergens and is used as a screening research tool to track trends in delayed-type contact sensitization. It also tests established and newly marketed chemicals to determine prevalence and relevance in causing ACD. Thus, the NACDG may contain allergens in different vehicles and concentrations. The ACDS has outlined a Core Allergen Series of suggested 80 allergens that can be scaled up or down depending on the needs of the physician and the patient being tested. The allergens are arranged with more likely allergens being higher in the tray.

Appendix I is an example of a PT form listing the NACDG series. Exclusive reliance on the T.R.U.E. Test antigen panel as opposed to an extended panel used by the NACDG or the standard series outlined by the ACDS and personal products can miss detection of sensitization to clinically relevant antigens.[26] Currently, there are different loading chambers available; however, none have shown superiority over another.

Summary Statement 19: Read and interpret PT conforming to the scoring system developed by the International Contact Dermatitis Research Group. [Strength of Recommendation: Moderate; D Evidence]

Patch testing techniques and scoring reactions by a grading scale were first standardized in the 1930s. The International Contact Dermatitis Research Group published the following nonlinear, descriptive grading scale in 1970,[92] which continues to be widely used.

(-) Negative reaction

(?+) Doubtful reaction with faint erythema only

(1+) Weak positive reaction with nonvesicular erythema, infiltration, possibly papules

(2+) Strong positive reaction with vesicular erythema, infiltration, and papules

(3+) Extreme positive reaction with intense erythema and infiltration, coalescing vesicles, bullous reaction

(IR) Irritant reaction

(NT) Not tested

The details of this rating system and corresponding clinical interpretation with a visual key are given in Appendix H and Figure 1.

Summary Statement 20: Remove and read PT at approximately 48 hours after application. A second reading should be done between 3 and 7 days following application. [Strength of Recommendation: Moderate; C Evidence]

In the evaluation of delayed hypersensitivity reactions, the initial reading of PT should be done approximately 48 hours after their application following patch removal.[93] However, if CU is considered, the PT has to be checked at 20-30 minutes after application. Tests may need to be read 30 minutes after removal of the patches to allow erythema from the occluding pressure or stripping of the tape and/or chamber to resolve. A second reading must be done, usually between day 3 and day 7

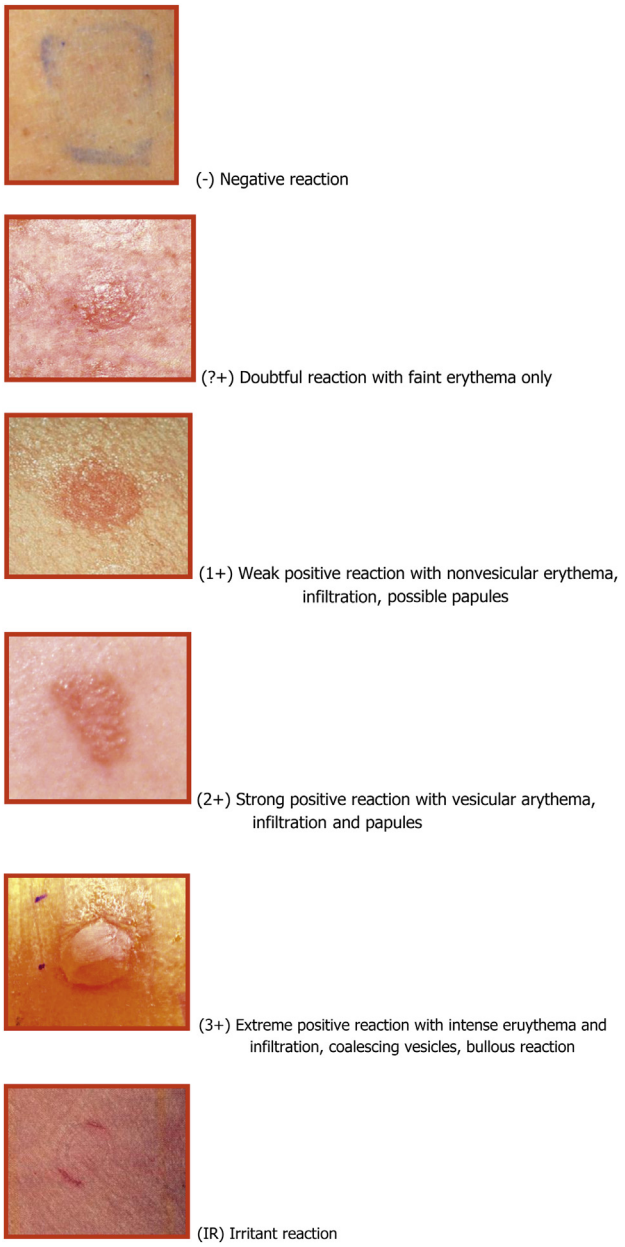

FIGURE 1. Visual key for scoring patch test reactions.

after the initial application.[94] Occasionally, an additional late reading after 7 days may be needed for certain contactants such as metals, some antibiotics, and TCS that may yield late reactions.[95] A collaborative study documented that approximately 30% of relevant allergens that were negative at the 48-hour reading became positive at a 96-hour reading, suggesting that 96 hours may be optimal for a second reading. Consider a late reading for allergens with negative early reactions, when the clinical history strongly supports sensitization. Four allergens with the highest frequencies of delayed-positive reactions were gold sodium thiosulfate 0.5% (delayed-positive reactions in 22/353 patients), dodecyl gallate 0.25% (6/105), palladium chloride 2% (8/194), and neomycin sulfate 20% (10/253). In contrast, reactions to certain preservatives and fragrance allergens dissipated after the day 5 reading.[96] With most allergens, however, the gain in positive reactions was biggest when a reading was performed at day 5.[95,97] Table II lists allergens with typical early and late reactivity. Reactions occurring even as late as days 10 to 14 may be due to a delayed irritant response and delayed allergic reactions such as for metals and TCS, and very rarely represent sensitization from the PT.[97-99] Conversely, some irritant reactions appearing within the first 48 hours tend to disappear (decrescendo effect) by 96 hours.[100] In rare situations where patient circumstances (ie, distance from the practice, insurance issues) do not permit 3 visits, the patches can be removed by the patient or local physician at 48 hours and read by the treating physician in 72-96 hours. Patients can be instructed to take a picture of the back before removing the patch (to help the clinician determine the integrity of the PT system, and to record any nonadherent or loose patches), and another picture after removing the patch. They should also re-label the PT sites after removal. However, this approach is considered suboptimal.

Summary Statement 21: Consider that a possible false-positive reaction can result with the use of irritants or allergic substances at potentially irritating higher concentrations, pressure reaction from the filling chamber, an "angry back syndrome," or patch testing on skin with active dermatitis. [Strength of Recommendation: Moderate; D Evidence]

Many variables contribute to the strength of the PT reaction, including the concentration and potency of the allergen, the degree of subject sensitization, the length of application time, and the timing of the readings.[103] The greatest source of misinterpretation is due to questionable or irreproducible reactions in the doubtful (?+) or weakly positive (1+) categories. The timing of the response may also affect its clinical significance; for example, a weak reaction at day 7 is more likely to be clinically relevant than one at day 3. The inability to separate nonspecific from true allergic responses may be encountered in patients who exhibit the "angry back" or "excited skin" syndrome, which is defined as false-positive reactions adjacent to large true-positive reactions that induce contiguous skin inflammation and irritability. The longer the duration of the primary dermatitis, the greater the risk for the excited skin syndrome to occur with patch testing.[104] This should be suspected in cases with more than 5 reactions in close proximity to each other. The underlying mechanisms are not fully understood.

A pustular patch reaction should not be misinterpreted as a positive reaction in PT. A pustular reaction is common in atopic individuals and in response to test of metals such as nickel, copper, arsenic, and mercuric chloride. The test site is only minimally pruritic and this type of pustular reaction is frequently an irritant reaction.

The position of the allergen in a multiple allergen template may give rise to the false-positive results, especially if cross-reacting or co-sensitizing substances are tested in too close proximity.[105] Marginally irritating allergens may also trigger false-positive reactions.[106] Repeat the PT with greater separation of allergens or sequentially if the initial reactions are not clinically relevant, because false-positive reactions are not reproducible when the triggering allergens are removed.[106]

Summary Statement 22: Recognize the possibility that false-negative reactions could be due to inadequate allergen concentration needed to elicit a response; inability of the vehicle to release sufficient allergen; reduced skin

TABLE II. Allergens associated with early and late reactions

Allergens associated with early peak reactions (at 48 h)
Balsam of Peru resin (*Myroxylon pereirae*)[95,101,102]
Benzoyl peroxide[102]
Carba mix[102]
Cinnamic alcohol[102]
Cocamidopropyl betaine[95]
Fragrance mix[95]
Imidazolidinyl urea[102]
Thiuram mix[102]
Wool alcohols[102]
Allergens associated with reaction on day 5, resolved day 7
Fragrance mix[101]
Methyl dibromo glutaronitrile phenoxy ethanol[101]
Octyl gallate[101]
Balsam of Peru[101]
Benzalkonium chloride[101]
Benzoic acid[101]
Disperse blue #124[101]
Allergens associated with late peak reactions (days 6-7)
Dyes
Para-phenylenediamine[95,102]
Medications
Neomycin[95,101,102]
Caine mix[95]
Topical corticosteroids
Tixocortol-21-pivalate[95]
Budesonide[95,101]
Metals
Nickel sulfate[95,101]
Gold sodium thiosulfate[101]
Palladium chloride[101]
Potassium dichromate[95]
Cobalt chloride[95]
Preservatives and glues
Dodecyl gallate[101]
p-Tert-butyl phenol formaldehyde resin[95,102]
Methylchloroisothiazolinone[95]
Epoxy resin[95]
Ethylenediamine dihydrochloride[102]
Mercapto mix[95,102]
Thimerosol[95,101,102]

responsiveness because of prior ultraviolet light exposure (ie, sun, tanning bed); concomitant immunosuppressive therapies; or methodological testing errors such as insufficient occlusion, failure to perform delayed readings, and failure to perform a photo PT. [Strength of Recommendation: Moderate; C Evidence]

The strength of the reaction on the skin does not necessarily correlate with clinical relevance. For example, aminoglycosides may cause weak reactions on PT that are nonetheless clinically relevant.[107] The frequency of false-negative results is not known, but has been estimated to occur in up to 30% of patch-tested patients.[108] Potential causes of false-negative reactions include too low a concentration of the allergen in the extract, use of the wrong carrier vehicle that resulted in insufficient penetration of the allergen, or inclusion of the wrong salt or version of the allergen. UV sunlight (eg, tanning), TCS, and TCI on the area of PT and systemic CS (ie, >20 mg/day prednisone)[78] and other immunosuppressives can all inhibit a positive patch response. Also, the patient may need photo-patch testing if photo-allergic CD is suspected.

Summary Statement 23: Determine the relevance of a PT result based on the clinical and exposure history when interpreting the PT. [Strength of Recommendation: Moderate; D Evidence]

The clinical relevance of positive PT reactions to ACD can only be established by carefully correlating the history, which includes exposure to the allergen, with the PT test results. A positive PT may be clinically relevant depending on current or past exposures. Current relevance is defined as *definite* if the PT or use test with the suspected material is positive; *probable* if the antigen is present in known skin contactants and the clinical presentation is consistent with that exposure; or *possible* if skin contact with materials known to contain the allergen was likely. Past relevance is considered if the PT is positive but the exposure was in the past, and not the present.[109,110]

Summary Statement 24: Consult physicians with expertise in patch testing to household cleaning or industrial products if testing to the actual product suspected of containing the relevant allergen(s) is necessary, because false-positive and severe irritant reactions can occur. [Strength of Recommendation: Moderate; C Evidence]

Household and industrial products should only be tested by physicians with expertise on this type of testing after determination of safety from MSDS information and using nonirritating PT based on an authoritative text.[111] Some of these chemicals can be extremely toxic to the skin and on rare occasions even produce systemic effects. The PT concentration of these products must be based on established protocols when available. Nonirritant concentrations are established by testing groups of unaffected volunteer control subjects. Whenever possible, customized contactants should be incorporated into a petrolatum base, but in some instances, a different vehicle should be used to increase exposure to the relevant antigen.[112,113] It may be difficult to distinguish an irritant from an allergic reaction. Examples of direct PT to products at nonirritating concentrations found in Patch Testing 3rd Ed.,[112] are bath products 1% aqua, shampoo 5% aqua, synthetic detergents 2% aqua, soap 1% or 2% aqua, and glues 1% to 20% in aqua, acetone, alcohol, or petrolatum. Antiperspirant, eau de cologne, cosmetics that are leave on, and insect spray may be PT without dilution. Agents that should *not* be patch tested include benzene, toluene, and other solvents, such as gasoline, kerosene, lime, floor wax and polish, diesel oil, rust removers, and others. Furthermore, unknown substances should not be tested.

Summary Statement 25: Consult physicians with expertise in UV radiation and photo-patch testing to confirm a suspected diagnosis of photo-allergic CD. [Strength of Recommendation: Strong; C Evidence]

Photo-patch testing should be done in clinical settings with the expertise, materials, and equipment to perform the procedure. In brief, duplicate applications of the suspected photo-sensitizer(s) are placed on either side of the upper back, and occluded for 24 to 48 hours. A recent study suggests that 2 days of occlusion before irradiation of allergens is more sensitive at detecting photo-allergy.[114] After PT removal, one side of the back is then irradiated

with 5 J cm^{-2} of UVA and the other side is left open but untreated as the control. Both irradiated and unirradiated sides are then measured 48 hours after irradiation for a response. If the patient has persistent photosensitivity, the minimum erythema dose (MED) must be determined first and reduced to 1/2 of the MED for the photo-patch test. Readings are recorded pre-irradiation, immediately postirradiation, and 48 hours post-irradiation. Additional readings have been recommended.[115]

Summary Statement 26: Although *in vitro* tests for delayed hypersensitivity to contact allergens (ie, metals and bone cement) are available, routine use of such assays is not currently recommended as their sensitivity and specificity for diagnosing ACD has not been determined and should be considered investigational. [Strength of Recommendation: Moderate; C Evidence]

In vitro tests for assessing antigen-specific sensitization are based on measuring lymphocyte proliferation (LPTs) or cytokine production (ELISA or EliSPOT) after incubation with antigens. Some *in vitro* tests have been validated by patch testing to nickel,[116,117] chromium,[118] cobalt,[119] and beryllium.[120] Several other *in vitro* tests are available, including the MELISA (Memory Lymphocyte Immuno Stimulation Assay), and LPTs from Orthopedic Analysis, but have not been validated against patch testing. The clinical relevance of *in vitro* testing in the diagnosis of contact dermatitis has not been established and is still considered investigational.

Summary Statement 27: Use the ROAT to further evaluate a patient suspected of ACD who exhibits doubtful or negative PT responses, to confirm that the patient is reacting to that particular product or to determine clinical tolerability to new cosmetic products. [Strength of Recommendation: Moderate; C Evidence]

Several open PT techniques have been used to test substances with the potential for irritation, and are especially suitable for cosmetics and other personal care products such as make-up and skin lotions. The ROAT involves the repeated application of a suspected allergen to the antecubital fossa twice daily for up to 1 to 2 weeks, and observing for the development of dermatitis. To replicate the reactivity of the eyelid skin, the ROAT can also be performed on the back of the ear. Another provocative open use test involves the application of the product to the skin of the forearm, which is then left untouched and observed for 5 to 10 days for a reaction. A comparison of the ROAT with the PT for nickel demonstrated that although the threshold concentration for a positive reaction for the ROAT per application was significantly lower than the threshold concentration for a positive PT, the accumulated ROAT dose was very similar to the PT.[121] A usage test involves the daily direct application, under real world conditions, of an undiluted product highly suspected of containing a sensitizer, to prove causation. An example is for a patient to apply mascara to one set of eyelashes and to leave the other eye bare, to observe for dermatitis. This is often used when PT with suspected commercial allergens is negative but the suspicion of contact allergy is high.[122]

Sources of exposure to clinically relevant allergens

Summary Statement 28: Evaluate patients who present with recurrent dermatitis on exposed skin surfaces during airborne pollen seasons for contact sensitization to seasonal pollen allergens. [Strength of Recommendation: Moderate; C Evidence]

Patients with AD presenting in a pattern of airborne exposure (ie, present on face, hands, and exposed chest) may be triggered by airborne protein allergens such as grass pollen, house dust mite, and cat dander. Although currently not standardized, this can be diagnosed by the atopy patch test (APT), involving the application of intact protein allergens by PT and reading the site after 24 to 72 hours. An APT reaction correlates frequently with the skin prick test and serum IgE, but not always.[123,124]

For some plants, both plant parts and pollen may contain the same allergen, and have been reported to cause airborne CD. These include the weed *Parthenium hysterophorus* L. (a member of the Compositae family) in India and Australia,[125,126] Japanese cedar pollen confirmed by a positive scratch-patch test,[127] and *Ambrosia deltoidea*, or triangle-leaf bursage, confirmed by PT with an oleoresinous extract of *A. deltoidea* leaves.[128]

Mulberry pollen[129] and Compositae pollen from dandelions, blazing star, golden rod, yarrow, Aster ssp, chrysanthemums, or marguerite[130] are reported to cause airborne CU that can be confirmed by prick skin testing.

Summary Statement 29: The clinician should consider cosmetics and personal hygiene products that are directly applied to involved skin or ectopically transferred from uninvolved skin as potential sources of allergens in patients with ACD. [Strength of Recommendation: Strong; C Evidence]

The US Food and Drug Administration (FDA) defines "cosmetic" as articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and articles intended for use as a component of any such articles except soap (US FDA. The Federal Food, Drug, and Cosmetic Act, Sec. 201 [21 U.S.C. 321]; Chapter II, Definitions 1: www.fda.gov). Thus according to this broad definition, it is not unusual for individuals to apply dozens of personal hygiene products to their skin on a daily basis including a plethora of cosmetics, each with a unique formulation of synthetic or natural ingredients. Such products can include emollients for day and night use, hair care products (shampoos, conditioners, pomade, relaxers, sprays, gels, mousses, foams), nail products (acrylic nails, polishes, hardeners, repair agents, extenders, wraps), traditional cosmetics (eye liners, mascara, eye shadow, foundation, lipstick, lip liners), concealers, shave creams and gels, antiperspirants and deodorants, toothpastes, dentifrices, hand creams, and barrier creams.

Although ACD caused by cosmetics is noted predominantly at the site of application, occasionally personal care products and cosmetics will manifest the contact allergy lesions in locations distant from the original skin sites. This phenomenon is termed *ectopic CD*. Typical causes of ectopic ACD are allergens such as nickel transferred to the eyelid by fingers, toluene sulfonamide formaldehyde resin in nail polish (which may cause eyelid dermatitis yet spare the periungual skin and distal fingers), and gold[131] (where dermatitis is reported in women who wear facial cosmetics that contain titanium dioxide that may adsorb or abrade the gold released from jewelry and make occasional contact with facial skin).[132] In addition, patients allergic to hair products that contain CAPB, a surfactant in shampoo, can present with eyelid dermatitis without concurrent dermatitis on the scalp, neck, or ears. Consideration must also be given to dermatitis where the allergen is transferred between partners, parent or child.

Summary Statement 30: When evaluating ACD from cosmetics and personal care products that contain many

different chemical ingredients, consider that the most common causes are due to a few important chemical classes including fragrances, preservatives, excipients, nickel, and sun screening agents. [Strength of Recommendation: Moderate; C Evidence]

In aggregate, the number of chemical contactants used by an individual patient in a typical day can be more than 100. Despite this extensive use, typical contact allergens contained in these products tend to be clustered in a few important classes, including fragrances, preservatives, formulation excipients, nickel, and sun blocks. The 15 most frequently positive allergens of the NACD 2009-2010 PT were nickel sulfate (15.5%), neomycin (8.7%), FM I (8.5%), bacitracin (8.3%), BOP (7.2%), cobalt chloride (8.2%), formaldehyde (5.8%), quaternium-15 (5.8%), PPD (5.5%), FM II (4.7%), carba mix (4.6%), iodopropynyl butylcarbamate (4.3%), methyldibromo glutaronitrile/phenoxyethanol (3.8%), propylene glycol (3.2%), and thiuram mix (3.1%).[26]

Fragrances are complex substances that contain hundreds of different chemicals and are the most common cause of ACD from cosmetic in the United States. Fragrances are regularly present in cosmetics and personal care products, household products, and medicaments, either to achieve an appealing scent or to mask unpleasant odors. However, the labeling of products with regard to fragrance can be confusing.[133-137] The use of the term *unscented* can erroneously suggest that a product does not contain fragrance when, in fact, a masking fragrance is present. *Fragrance-free* products are typically free of classic fragrance ingredients and are generally acceptable for the allergic patient. Caution should be exercised when substitute products, which are labeled *fragrance free*, contain large numbers of botanical extracts used for the purpose of improving odor characteristics.[138] Allergy to fragrances can be detected clinically when obvious contact sites of perfume are involved. Clear demarcation of eczematous dermatitis on the neck where perfume is sprayed may be an obvious indication of fragrance allergy.

It is necessary to PT to appropriate screening chemicals for detection of delayed hypersensitivity to this group of allergens.[139-143] The fragrance antigens in the current T.R.U.E. Test include BOP (a fragrant resinous natural product containing a mixture of many substances), and FM I (cinnamyl alcohol, cinnamaldehyde, α-amyl cinnamaldehyde [amyl cinnamal], hydroxycitronellal, geraniol, isoeugenol, eugenol, oak moss). Although there is a strong association between these fragrances, separated PT may still be warranted to identify the specific offending fragrance so that not all fragrances need to be avoided.

Previous studies suggest that the standard FM and BOP will detect approximately 60% to 70% of fragrance-allergic individuals. The addition of other commonly used fragrance ingredients (ylang ylang oil, narcissus oil, and sandalwood oil) may increase the yield up to 96%.[141] In a recent study of patients with eyelid dermatitis, PT to fragrance markers within the standard series (ie, FM I, FM II, *Myroxylon pereirae*, and cinnamic aldehyde) detected 73.2% of cases of fragrance allergy.[144] The elucidation of fragrance allergy should result in advising an avoidance protocol that eliminates all culprit fragranced cosmetics and personal hygiene products. However, it should be noted that fragrances in PT have marginal irritant potential and weak positive reactions may not be regarded as proof of contact sensitization (low specificity of the test). The increased strength of the test reaction, a positive reaction on retest to FM (repeated positive reactions), and a positive PT to individual ingredients adds significantly to the probability of a relevant test.

Current labeling laws do not always require manufacturers to label a specific fragrance present in a product and regulation of fragrance ingredients in cosmetics exempts fragrance formulas as "trade secrets." Therefore, some manufacturers do not list essential oils that can also cause ACD such as tea tree oil (*Melaleuca alternifolia*), ylang-ylang oil (*Cananga odorata*), jasmine flower oil (*Jasminum officinale*), peppermint oil (*Mentha piperita*), lavender oil (*Lavandula angustifolia*), and citrus oil (limonene). "Covert fragrances" that may be used for purposes other than for aroma, ie preservatives, may be added to "fragrance free" products (benzaldehyde, benzyl alcohol, bisabolol, citrus oil, unspecified essential oils) and may be problematic. In addition, new fragrance chemicals are constantly introduced. Use testing and slow reintroduction of some fragrance products may allow for the detection of intolerance to specific cosmetic agents. It may be possible to identify the presence of specific fragrance ingredients by communicating directly with product manufacturers.

Preservatives and antibacterials are present in most aqueous-based cosmetics and personal hygiene products to prevent rancidity and microbial contamination. These preservatives are important cosmetic allergens. Preservatives tend to be grouped into 2 broad categories: formaldehyde releasers (products that emit formaldehyde) and nonformaldehyde releasers.[145-148] Table III is a list of preservative systems commonly used in cosmetic and personal care products.

In the United States, approximately 20% of cosmetics and personal care products (stay-on and rinse-off products) contain a formaldehyde releaser.[149] The most recent data from the FDA Voluntary Cosmetic Registration Program Database[150] approximate that 1 in 6 stay-on cosmetics and 1 in 4 rinse-off products contain a formaldehyde releaser, the most frequent of which is imidazolidinyl urea (7%), followed by DMDM hydantoin (5.4%), diazolidinyl urea (4.5%), and quaternium-15 (1.4%).

De Groot et al[149] recommend that patients allergic to formaldehyde be advised to avoid stay-on cosmetics preserved with quaternium-15, diazolidinyl urea, DMDM hydantoin, or imidazolidinyl urea. Provocation tests may also be performed to determine relevance to this particular patient.

Among nonformaldehyde releaser preservatives, methlydibromo gluteronitrile (also known as 1,2-dibromo-2,4-dicyanobutane and is the sensitizing ingredient in Euxyl K 400) has emerged as an important cosmetic allergen in recent years.[151] In North America, the prevalence of positive PT reactions to Euxyl K 400 increased from 1.5% between 1992 and 1994 to the current rate of 5.5% for 2007 and 2008.[109] A total of 11.8% of hand dermatitis cases associated with Euxyl K 400 were occupation related and were linked to solvents, oils, lubricants, fuels, and cosmetics.[152] In cosmetics, ACD from Euxyl K 400 or its components is most commonly reported in hand and face lotions, hair products, and ultrasonic gels.[152]

Another nonformaldehyde releaser preservative MCI/MI (trade name: Kathon CG) is commonly used in cosmetics and toiletries in the United States. The NACDG data from 2009 to2010[26] show that MCI/MI had a 2.5% frequency of positive PT reactions, ranking it the fifth most commonly positive preservative. The combination of MCI/MI is tested at a 3:1 combination. Both MCI and MI can cause contact allergy with MCI as the more potent allergen in this combination.[153] However, the use of MI alone as a preservative in personal care and cosmetic

TABLE III. Cosmetic preservatives

Formaldehyde releaser	Nonformaldehyde releaser
Formaldehyde	Iodopropynyl butylcarbamate
Quaternium-15	Methychloroisothiazolinone/ methylisothiazolinone (MCI/MI)
Diazolidinyl urea	Parabens
Imidazolidinyl urea	Methyldibromo glutaronitrile
Bromonitropropane	Chloroxylenol
DMDM hydantoin	Benzalkonium chloride
	Thimerosal
	Phenoxyethanol

products has increased in the past few years. According to the US Food and Drug Administration Voluntary Cosmetic Ingredient Registration Program, MI was used in a total of 1125 cosmetic products in the United States in 2007.[154] Of these, the majority are in rinse-off products: 24% were shampoos, 18% were conditioners, and 10% were baby soaps and detergents. Wet wipes (baby wipes, moist towelettes, and moist toilet paper) are a well-identified sensitization source for MI.[155]

The MCI/MI mix misses approximately 40% of allergy to MI likely because of the low concentration of MI in the MCI/MI combination in the PT. In Europe, several groups have documented frequency of allergy to this preservative of approximately 1.5%.[156] Patch testing to MI alone will likely diagnose more cases of MI contact allergy.

Although parabens formulated in cosmetics are infrequent causes of ACD, they can induce ACD when used as antibacterials in topical medications. ACD has most commonly been reported when paraben-containing products are used on damaged skin such as in long-standing dermatitis and stasis ulcers. The rate of sensitization to parabens in patients with chronic leg ulcers is higher than that of the general population.[157]

"Botanicals" are plant extracts that are increasingly used as additives to skin care products either for their medicinal properties or as fragrances (such as essential oils). Unfortunately, in cosmetics, product labeling may not list essential oils as fragrances. These natural botanicals, plant extracts, and herbal remedies are potential causes of CD. One study showed a sensitivity rate of 2.4% to testing with pure tea tree oil.[158] Other studies showed that 1.2% to 6.6% of patients patch tested for dermatitis are sensitive to propolis,[159] which is commonly used in cosmetic and medicinal preparations because of its antiseptic, anti-inflammatory, and anesthetic properties. Propolis is found in many "all natural" products, including lip balms, cosmetics, lotions and ointments, shampoos, conditioners, and toothpastes. Synonyms for propolis include bee glue, bee bread, hive doss, propolis balsam, propolis resin, and propolis wax.

Thus, PT should be considered for propolis, tea tree oil, and other essential oils in patients with cosmetic dermatitis. It is important that patients who are allergic to fragrance also be made aware of the potential dangers of cosmetics containing plant extracts and patients should be counseled that "natural products" does not equate with safety.[160]

Summary Statement 31: Patients suspected to have allergy to hair products should be evaluated for PT reactions to CAPB, PPD, fragrances, preservatives, and glycerol thioglycolate. [Strength of Recommendation: Moderate; C Evidence]

CAPB is an amphoteric surfactant that is often found in shampoos, bath products, eye and facial cleaners, liquid detergents, surface cleaners, pet care products, and other skin and hair care products, and the incidence of sensitization is increasing. Although it is less irritating than the older polar surfactants such as sodium lauryl sulfate,[161,162] it is more sensitizing. CAPB allergy typically presents as eyelid, facial, scalp, and/or neck dermatitis.[163] Consumers were sensitized mainly through shampoos (including baby shampoo) and other toiletry products that include liquid shower gels, roll-on deodorants, and facial cleansers.

According to the NACDG data for 2007-2008, 1.1% of patients tested had a positive reaction to CAPB[109] and positive PT reactions to this allergen are often clinically relevant.

Commercial bulk production of CAPB may result in contamination of the final product with 2 chemicals that are used in the synthesis of CAPB, such as amidoamine and dimethylaminopropylamine.[163]

Paraphenylenediamine is the active ingredient in many hair dyes, both permanent and semipermanent, and is a very common cause of CD in hairdressers. Although hair dye is the main source of exposure,[164] other routes of exposure include body painting and temporary tattooing. ACD from PPD can be severe, sometimes mimicking angioedema. The "skin sensitivity test" recommended in the package insert of hair dyes has been validated as an effective method to predict a type IV hypersensitivity reaction and should be used by hairdressers.[165] Nevertheless, PT may be needed to identify the active allergen in the consumer product.

It is difficult to find alternative hair dyes for PPD-allergic individuals. Alternatives include henna (giving a reddish tint for any hair color), lead oxide (which oxidizes to darken gray hair but has not been adequately evaluated for its toxicity), and temporary coloring agents (which only last for a few washes). Semipermanent hair dyes containing F, D & C and D & C dyes appear to have very low cross-reactivity with PPD (examples: Elumen Hair Color from Goldwell Cosmetics, Linthicum Heights, MD, and Clairol Basic Instincts-Loving Care from the Proctor & Gamble Company, Cincinnati, Ohio). However, semipermanent dyes may not be as cosmetically elegant and require more frequent application. Scheman et al reported that PPD-sensitive individuals who test negative to para-toluenediamine sulfate (PTDS) will very likely tolerate the newer permanent and demi-permanent PPD-free hair-dye products.[166] However, this study suggests that patients be tested for PTDS before using PPD contacting dyes. Examples of PPD-free hair dyes include Wella Koleston Perfect (permanent), Wella Color Charm (demi-permanent), Schwarzkopf Igora Royal (permanent), Goldwell Color Chic (permanent), Goldwell ReShade for Men (demi-permanent), Sanotint Light (demi-permanent), and L'Oreal Paris Excellence To-Go 10-Min. Crème Colorant (demi-permanent).[26,167] Both physicians and patients should consult available databases like Contact Allergen Management Program (CAMP) and Contact Allergen Replacement Database (CARD) regularly for updates.

Other sources of exposure to PPD include leather, fur, textiles, industrial rubber products, and black henna tattoos.[167] Cross-reactivity with other para-amino compounds, such as benzocaine, PABA, sulfa drugs, aminoazobenzene, IPPD, and azo dyes has been reported and may require avoidance.[168]

Glycerol thioglycolate is the active ingredient in permanent wave solution. ACD to this chemical tends to cause more occupational dermatitis in hair dressers than consumers. Unlike PPD, thioglycolates may remain allergenic in the hair long after it has been rinsed out. Hence, those individuals who are allergic to it may continue to have skin eruptions weeks after application of the perm, and hairdressers allergic to it may be unable to cut or shape permanent waved hair.[169]

Summary Statement 32: Suspect allergy to nail products when the dermatitis presents locally at the distal digit or ectopically on the eyelids and face. [Strength of Recommendation: Moderate; C Evidence]

Most allergic reactions to nail polish and artificial nail products are to tosylamide/formaldehyde resin[105] found in nail polish enamel, in addition to nail hardeners and setting lacquers. Up to 80% of the reactions appear on the neck, face, lips, and eyelids, although unusual locations including the gluteal, perianal, and genital areas have been reported. Only 27% of reactions were reported in the periungual region of the hands and feet. Some patients react to the polish when it is still wet, but the majority of patients appear to react to the water-soluble components (including monomers and dimers) of tosylamide/formaldehyde resin found in dry polish.[160]

As an alternative, some manufacturers may use an alkyl polyester resin and label their products as "hypoallergenic." These products would be suitable alternatives for sensitive patients.[170]

Artificial nails are increasingly used and are available as sculptured nails, photobonded nails, and preformed nails. Reactions to artificial nails have included paronychia, onychodystrophies, and dermatitis at contact areas and at distant sites. Acrylate monomers used for sculpting artificial nails are important sensitizers for contact and occupational dermatitis. Preformed plastic nails may be glued over the natural nail plate using ethyl cyanoacrylate, a potential sensitizer.

Certain guidelines for testing nail cosmetics are as follows: (1) Nail polish should be tested as is—undiluted. (2) Acrylate allergy should be screened with an acrylate test panel, including 2% methyl methacrylate, 1% bisphenol A, 2% tetraethylene glycol dimethacrylate, 2% bisphenol A dimethacrylate, 2% ethylene glycol dimethacrylate, 2% dimethyl-p-toluidine, and 1% benzoyl peroxide has been advocated.[171] (3) Patch testing for nail polish removers should be an open PT, at a concentration of 10% in olive oil. (4) Cuticle removers are tested as an open PT at a 2% aqueous concentration.[172]

Summary Statement 33: Suspect the diagnosis of photoallergic CD to cosmetics when eczema occurs in a light-exposed distribution following the use of a skin care product or cosmetic, including sunscreens. [Strength of Recommendation: Strong; C Evidence]

Some cosmetic ingredients may only cause an ACD after exposure to UV radiation. Photo-allergic CD typically affects sun-exposed areas such as the face, the "V" of the anterior neck, the dorsal hands, and forearms. It typically spares the upper eyelids, upper lip, and submental and postauricular areas. Before evaluation for photo-allergic CD, one should rule out phototoxic drug eruption, photo-allergic drug eruption, and systemic disease such as lupus erythematosus.

The prevalence of allergic reactions to sunscreens may continue to increase as the use of sunscreen continues to become more widespread. Allergic and photo-allergic reactions have been reported with several chemical sunscreen families.[173,174]

Sunscreens have traditionally been divided into chemical absorbers (UVB [290-320 nm], UVA II [321-340 nm], and UVA I [341-400 nm]) and physical blockers.

Sunscreens are often overlooked as a cause of CD, because other excipients (fragrances, formaldehyde releasers, preservatives, vitamin E, and lanolin alcohol)[175] are more frequently implicated. Sunscreen sensitization is much higher in individuals referred for evaluation of photosensitivity.[176] The most common cosmetic sunscreen agents used are listed in Table IV.

Physical ultraviolet light blockers

Titanium dioxide and zinc oxide are the most common physical UV blockers used today and have not been reported to cause contact dermatitis or photo-allergy.

Topical medicinal CD

Summary Statement 34: If an eruption worsens, rather than improves, after the topical application of certain medications, or fails to respond to TCS, patch testing should be performed to the suspected product and/or ingredients known to be contact sensitizers. [Strength of Recommendation: Moderate; C Evidence]

CD may develop after exposure to topical medications, including lanolin, para-aminobenzoic acid (in sunscreens), "caines" (anti-itch preparations), topical antibiotics, topical antihistamines, NSAIDs, and/or TCS.[177-182] Neomycin, bacitracin, and iodochlorhydroxyquin are well-known sensitizers. Lanolin is used as the base of many topical medications including TCS and moisturizers.

Allergy to TCS affects 0.5% to 5.8% of patients[183] suspected of ACD. Sensitization can occur by skin, airborne, oral, and IV routes.[184,185] Certain disorders predispose patients to an increased risk of CS ACD. These include treatment of refractory eczema, chronic venous leg ulcers, stasis dermatitis, and CD (in particular, patients with a history of 2 or more positive PT results and multiple medicament sensitivities).

Patch testing to CS is complicated by the inherent, anti-inflammatory nature of the drug itself, which results in frequent false-negative results if tested at too high concentration. Accordingly, PT readings should also be done 7-10 days following application because approximately 30% of ACD to TCS could be missed by conventional readings.[186,187]

Patch testing substances for TCS allergy that are commercially available include amcinonide, betamethasone-17,21-dipropionate, betamethasone-17-valerate, budesonide, clobetasol-17-propionate, desoximetasone, dexamethasone, hydrocortisone, hydrocortisone 17-butyrate, prednisolone, tixocortol-21-pivalate, and triamcinolone acetonide. The patient's own commercial steroid,[184] as well as the vehicle and preservatives in the preparations,[188,189] must also be tested. Coopman et al[190] suggested that 4 major groups of CS preparations should suffice, because there is considerable cross-reactivity within the groups and possible cross-reactivity between them. Ninety percent of ACD to CS should be detected by using tixocortol pivalate, budesonide, triamcinolone, and the patient's commercial steroid.[191,192] Although rare, patients sensitized to CS by skin contact can develop SCD with administration of the CS by an oral, IV, IM, or inhalation

TABLE IV. The most common cosmetic sunscreen agents

Cinnamates	Octyl dimethyl para-aminobenzoic acid
Salicylates	Benzophenones
Titanium dioxide	Anthranilates
Butyl methoxydibenzoylmethane or avobenzone (Parsol 1789)	Zinc oxide

route.[193] Cross-reactivity based on 2 immune recognition sites has been reported,[194] and the avoidance of TCS within each class is recommended once allergy to TCS has been confirmed by PT (Appendix J).

Summary Statement 35: The clinician may use the drug PT for the diagnosis of some drug hypersensitivity reactions, recognizing that there is no standardized approach to define the population, clinical manifestation, drug to PT, and PT materials to make patch testing to drugs a standard of care. [Strength of Recommendation: Weak; D Evidence]

Patch testing to drugs may have a role in delayed hypersensitivity drug reactions[177] and have a higher positivity in patients presenting with maculopapular rashes, erythroderma, and non-immediate cutaneous reactions,[195] including DRESS,[196] AGEP,[197] SJS/TEN, and fixed drug eruptions. The utility of the PT depends on various factors including the type and formulation of the drug being tested, the vehicle used, as well as the immunopathogenesis eliciting the eruption.

PT may be helpful with aromatic anticonvulsants and various antibiotics, but it is not consistently helpful for a wide range of drugs. Patients with a history of drug exanthem from antibiotics are more likely to have a positive PT (10% to 46%) compared with those with a history of a drug exanthem from nonantibiotic medications (~10% to 11%).[198-200]

Within antibiotic classes, there are higher rates of positive PT reactions to aminopenicillins, cephalosporins, pristinamycin, and clindamycin compared with macrolides, tetracyclines, and quinolones.[195]

PT can be performed for a wide variety of medications in multiple concentrations and vehicles.[201] The European Society of Contact Dermatitis (ESCD) and the European Network on Drug Allergy (ENDA) have guidelines for performing PT for medication-induced cutaneous eruptions.[202,203] However, the limitations of these studies include the lack of standardized test materials, the absence of information as to the ideal test concentration and vehicle to use, and the differences in the interpretation of the tests.

Summary Statement 36: Consider pre-operative patch testing for metal sensitization in patients with a significant history of metal allergy. [Strength of Recommendation: Moderate; C Evidence]

Indications for pre-operative PT in patients with a history of metal allergy are still being developed. However, pre-operative PT may help guide the selection of implant alloys in patients with a high suspicion of metal allergy, and such patients demonstrate improved outcomes.[204-207] This testing is not recommended for patients without such a history of metal sensitivity. There is no information regarding pre-operative PT in patients with a prior history of methacrylate or antibiotic sensitivity.

Summary Statement 37: In patients with joint replacement failure, patch testing to components of the implant may be helpful after infection and biomechanical causes have been excluded. [Strength of Recommendation: Moderate; C Evidence]

The clinician should recognize that contact sensitization to metals or bone cement that is used in orthopedic, cardiac, dental, and gynecological implants has been associated with both dermatitis and noncutaneous complications. These complications may include localized pain, swelling, erythema, warmth, implant loosening, decreased range of motion, stent stenosis, and pericardial effusions in the case of cardiac implants. Patch testing to implant or device components has been recommended to help determine the etiology of the adverse reaction (Tables V and VI).[208-210]

In a meta-analysis, the rates of sensitization to metals were significantly higher in patients with a failed implant than in patients with a well-functioning implant ($P = .002$) or without an implant ($P < .001$).[209] Patients who experienced failed joint replacements and underwent revision using components dictated by a positive metal PT reported resolution of their joint symptoms, most frequently joint pain, joint loosening, and localized dermatitis. Those patients with a positive metal PT who were not revised continued to experience the same symptoms.[204] Similarly, a group of patients with implant-related eczema who were metal sensitized, and then underwent revision with a different metal alloy implant, had a higher incidence of eczema resolution.[211] Anecdotal case reports suggest that skin or systemic manifestations of sensitization to components of implantable defibrillators,[212] pacemakers,[213] arterial stents,[214] dentures,[215] and IUDs,[216] appeared to improve once the sensitizing agent was replaced.

At present, the recommendation for implant removal remains controversial. Indeed there are reports of individual patients with documented metal allergy who have tolerated implants of the same metal without adverse reactions. An older study reported that 18 patients with documented metal allergy did well for over 6 years following a joint replacement that contained the allergenic metal.[217] Gawkrodger stated in 1993 that there was no evidence that nickel-sensitive patients, when given a plastic-to-stainless-steel hip implant, developed cutaneous reactions or loosening of their prostheses,[218] although he has since identified an association between metal sensitization, peri-implant hypersensitivity reactions, and implant loosening and failure. The overall risk, however, was low.[219] Other patients with documented metal sensitization have tolerated cardiac implants with the same metal without adverse reaction.[220]

As in all cases of PT, results must be interpreted within the clinical history and physical examination. If an implant is functioning well, then a positive PT to an implant component is not clinically relevant.[210] The likelihood that an allergy to implant components is the cause of implant failure is higher when other causes of implant failure (infection and biomechanical issues) have been ruled out. There are no current guidelines or recommendations for symptomatic patients with positive PT to metals or bone cement components. The decision regarding implant revision following positive relevant PT results can only be made after a thorough discussion between the patient, the allergist or dermatologist, and the orthopedic surgeon.

In addition to the possibility of metal sensitization as a potential therapeutic cause of joint replacement failure, there are also reports of implant failure related to bone cement or its components, including benzoyl peroxide, hydroquinone, methyl methacrylate, and n,n-dimethyl para-toluidine.[221-223]

TABLE V. Components of selected alloys used in metal implants

Alloy	316L Stainless Steel ~% content	Cobalt-chromium-molybdenum steel (ASTM F75) ~% content	Vitallium ~% content	Titanium ~% content	Nitinol ~% content	Oxinium ~% content
Nickel	8.3-35	<0.5		Trace	45	None
Chromium	20	27-30				
Manganese	2	<1	0.5			
Molybdenum	2-3	5-7	5.6			
Nitrogen	0.1	<0.25				
Carbon	0.003	<0.35	0.02			
Sulfur	0.03	<0.01				
Silicon	0.75	<1	0.5			
Phosphorus	0.045	<0.02				
Iron	Balance	<0.75	None			
Tungsten		<0.2				
Aluminum		<0.1		5.5-6.5		
Titanium		<0.1		89.9	55	
Boron		<0.01	0.1			
Cobalt		Balance	61			
Chromium			32			
Vanadium				3.5-4.5		
Zirconium (oxidized)						97.5
Niobium						2.5

Special population

ACD in children. Summary Statement 38: ACD and ICD are significant clinical problems in children. Patch testing should be performed and remains the gold standard for the diagnosis of ACD in children. [Strength of Recommendation: Strong; C Evidence]

Although ACD was historically considered to occur less frequently in children, recent studies show that positive PT reactions range from 14% to 70% of children patch tested.[224] ACD is considered rare in the first few months of life with increased reports suggesting an early peak around age 3, and an increasing rate of occurrence through the teen years, attaining and even exceeding that observed in adults.[225-227]

In children, a careful, age-appropriate history should include exposure to diapers, hygiene products, cosmetics, sun blocks, textiles with dyes and fire retardant materials, medications, pets and pet products, school projects, sports, and so on. The influence of fashion trends, hobbies, and lifestyle activity such as body piercing, decorative skin paintings (eg, PPD-laced black henna tattoos), natural remedies, and cosmetics (eg, tea tree oil), or products with fragrances and herbal ingredients have all been associated with ACD in this population.

Perioral dermatitis in children is associated with lip licking, lip chewing, thumb sucking, or excessive drooling. Metals including mercury, chromate, nickel, gold, cobalt, beryllium, and palladium are important allergens in patients with dental implants, orthodontic devices, or who play an instrument. ICD is the most common cause of diaper dermatitis in infancy because of friction, occlusion, maceration, and increased exposure to water, moisture, urine, and feces. Allergic CD to rubber chemicals (mercaptobenzothiazole, cyclohexyl thiophathalimide) or glues (p-tertiary-butylphenol-formaldehyde resin) has been reported to cause CD,[228] a dermatitis that is predominantly on the outer buttocks and on the hips in toddlers. This is frequently caused by the elastic bands that hold tightly on the thighs to prevent leaking.

The NACDG compared results of PT in children and adults and found no significant difference in the overall frequency of at least one relevant positive PT reaction in children (51.2%) compared with adults (54.1%).[34] Additionally, there are highly relevant allergens that have significant frequency in children because of their unique exposure such as MCI/MI, a preservative in infant wet wipes, liquid soaps, and shampoos. Also, exposures to dialkyl thiourea and p-tert-butyl formaldehyde resin in rubber products are seen in shin guards, wet suits, and protective pads.

A US-based study showed nickel, fragrance, cobalt, thimerosal, BOP, potassium dichromate, neomycin, lanolin, thiuram mix, and PPD to be common allergens in children.[77] Eight of these are also in the top 10 allergens in adults suggesting that the sensitization profile for children does not differ significantly from that of adults. An allergen found in higher frequency in children than in adults is lanolin/wool alcohols that can be found in healing ointments, aftershave, baby and bath oil, hand sanitizers, and creams, reflecting the frequency of use of the products containing this contactant. Thimerosal positive PT has been reported in both adults and children, with the main source of sensitization likely due to previous vaccination and may not be a clinically relevant allergen. There are additional highly relevant allergens in children that correlate with unique exposures such as (1) MCI/MI, a preservative found in infant products (wet wipes, liquid soaps, shampoos); (2) CAPB, a surfactant in cleansing products (eg, No More Tears formulations); (3) disperse dyes in diaper material and colored garments (school and athletic uniforms); (4) carbamates and thiuram used in rubber (gloves, garments, shoes, and toys); (5) dialkyl thioureas; and (6) p-tert-butyl formaldehyde resin found in rubber and neoprene (shin guards, protective pads, and wetsuits).

The same test concentrations used in adults can be used in children.[229] However, it has been suggested that in very young children (<6 years of age), allergens such as formaldehyde, formaldehyde releasing preservatives, mercaptobenzothiazole, and

TABLE VI. Substances that may be present in different types of implant or device and that potentially should be considered for diagnostic patch testing

	Implant or device					
		Orthopedic				
Substances or alloy[3]	Dental	Pre-implant	Post-implant	Intravascular	Pacemaker and ICD	Gynecological
Aluminum	X	X	X	-	X	-
Beryllium	X	-	-	-	-	-
Cadmium	X	-	-	-	-	-
Chromium	X	X	X	X	X	X
Cobalt	X	X	X	X	X	-
Copper	X	-	-	-	-	X
Gold	X	-	-	X	-	-
Indium	X	-	-	-	-	-
Iridium	-	-	-	-	X	X
Iron	X	X	X	X	-	-
Manganese	X	X	X	X	-	X
Mercury	X	-	-	-	X	-
Molybdenum	X	X	X	X	X	-
Nickel	X	X	X	X	X	X
Niobium	X	X	X	-	-	-
Palladium	X	-	-	-	-	-
Phosphorus	X	X	X	-	-	-
Platinum	X	-	-	-	X	X
Rhodium	X	-	-	-	-	-
Ruthenium	X	-	-	-	-	-
Silicon	-	X	X	-	-	-
Silver	-	-	-	-	X	X
Tantalum	-	X	X	-	X	-
Tin	X	-	-	-	-	X
Titanium	X	X	X	X	X	X
Tungsten	-	X	-	X	-	-
Vanadium	X	X	X	-	X	-
Zinc	X	-	-	-	-	X
Zirconium	X	X	X	-	-	-
Custom-made disk of relevant alloy	X	X	X	X	X	-

ICD, irritant contact dermatitis.
Used with permission from *Contact Dermatitis* 2011;66:4-19.

thiuram be diluted 50%, and potassium dichromate diluted 25% in petrolatum, to avoid irritant false-positive reactions.[230,231]

The German Contact Dermatitis Group (GCDG)[232] recommends that children under 6 years should only be PT if there is a high degree of clinical suspicion and only to the suspected allergens. Children over the age of 12 can be tested in the same manner as adults.

The ideal number of PT to be applied depends on the patient and could be limited by the surface available for testing and the potential risk of active sensitization. Thus, Jacob et al.[233] recommend a basic North American Standard Series for children aged 6-12 years to include 20 selected allergens that are the most prevalent in the pediatric population with the highest clinical relevance and therefore would be the highest yield as a basic series. These are bacitracin, budesonide, carba mix, cobalt chloride, cocamidopropyl betaine, colophonium, Compositae mix/dandelion extract, disperse blue, ethylenediamine, formaldehyde, FM I, FM II, lanolin alcohol, MCI/MI, BOP, neomycin sulfate, nickel sulfate, potassium dichromate, quaternium-15, and tixocortol-21-pivalate. Additional allergens can also be tested for if there is a relevant exposure history, for example, black rubber mix, dialkyl thioureas, mercaptobenzothiazole, PPD, and p-tert-butylphenol formaldehyde resin. In conclusion, PT can and should be performed in children and remains the gold standard for the diagnosis of ACD with appropriate parental informed consent.

Occupational contact dermatitis. Summary Statement 39: In a patient who presents with dermatitis associated with workplace exposures (ie, OCD), consider ICD as well as ACD. [Strength of Recommendation: Strong; C Evidence]

Contact dermatitis is one of the most common types of occupational illness, with estimated annual costs exceeding $1 billion (http://www.cdc.gov/niosh/topics/skin). An occupational health supplement (OHS) to the 2010 National Health Interview Survey (NHIS) noted that 10%, or approximately 15.2 million US current or recent workers reported the presence of *dermatitis*. There was a higher prevalence rate in women (11.2%; 95% CI 10.4-12.0) than in men (8.5%; 95% CI 7.8-9.3). The estimate of *work-related dermatitis* was 7.4% or 1.12 million.[234]

Occupational CD is classically divided into ICD and ACD. Although the mechanisms differ between the two, the clinical and histologic appearance may be similar.

Irritant CD represents approximately 80% of all cases of OCD. Common irritant exposures include wet work, solvents and alcohols, cutting oils, coolants, degreasers, soaps, detergents, and other cleaning agents and disinfectants. The major chemical groups associated with ACD include metals, rubber-related materials, epoxies, resins and acrylics, organic dyes, plants, foods, medications, biocides, and germicides.[235]

A worker's skin may be exposed through direct contact with contaminated surfaces, deposition of aerosols or vapors, skin immersion, or splashes. The hands are most commonly affected by OCD and followed by the wrists, arms, and face. OCD can present at any stage in a worker's career, including apprenticeship.[236] The common agents that cause ICD and ACD in OCD as reported by the NACDG in the United States include carba mix, cobalt chloride, epoxy resin, formaldehyde, glutaraldehyde, glyceryl thioglycolate, mercaptobenzothiazole, nickel sulfate, potassium dichromate, quaternium-15, and thiuram. In addition, The Health and Occupation Reporting System, the European Prevention Initiative for Dermatological Malignancies, and the Occupational Physicians Reporting Activity in the UK reported chromes and/or chromates, foods, latex, rubber chemicals, PPD, preservatives, resins and acrylics, soaps and cleansers, wet work, cutting oils and coolants, petroleum products, solvents, and alcohols.

Summary Statement 40: In patients with suspected occupation-related CD, the examining physician should verify the diagnosis by confirming that the dermatitis was caused or aggravated by workplace exposures. [Strength of Recommendation: Moderate; C Evidence]

Accepted and validated criteria should be used to establish causation and aggravation of OCD. Mathias[237] proposed 7 criteria as a practical guideline for confirming this diagnosis: (1) the clinical appearance that is consistent with CD; (2) potential culprit cutaneous irritants and/or allergens are present in the workplace; (3) the anatomic distribution of dermatitis is consistent with workplace skin exposure; (4) the temporal relationship between exposure and onset of symptoms is consistent with CD; (5) nonoccupational exposures are excluded as probable causes of the dermatitis; (6) the dermatitis improves when absent from work exposure, and re-exposure results in exacerbation; and (7) PT performed according to established guidelines demonstrates positive and relevant reactions.[237] Of these 7 criteria, 4 must be present to conclude that the dermatitis is OCD. The validity of the Mathias criteria for establishing occupational causation and aggravation of CD was recently confirmed in a 2- to 5-year prospective study.[238]

Industries and jobs that pose a high risk for development of OCD are as follows:

1. Food service and food processing (cooks and caterers)
2. Cosmetology (beauticians and hairdressers)
3. Health care (personnel)
4. Agriculture, forestry, and fishing
5. Cleaning
6. Painting
7. Mechanics, metal working, and vehicle assembly
8. Electronics industry
9. Printing and/or lithography
10. Construction.

In food processing workers with OCD, the prevailing factors are exposure to food ingredients, even intact proteins, and hand washing. A review of NACDG results for hairdressers and cosmetologists demonstrated that glyceryl thioglycolate in permanent wave solutions, PPD in hair dyes, nickel sulfate, 2-hydroxyethyl methacrylate, and quaternium-15 are common sources of allergens.[239]

Among health professionals, hand dermatitis may be due to ICD, ACD, and IgE-mediated CU. With the advent of increased barrier control recommended for health professionals, the rapidly increased need for latex gloves resulted in a spike in the prevalence of both immune-mediated and irritant skin reactions. IgE-mediated responses include CU, rhinitis, asthma, and/or anaphylaxis, and sensitization can be confirmed by specific prick or *in vitro* tests. Health care workers may also develop ACD to rubber accelerants and other chemicals in gloves, which include bisphenol A in vinyl gloves. In one study of 3448 patients (1058 health care workers) with occupational dermatitis due to suspected glove allergy, 13% were sensitized to thiurams, 3.5% to dithiocarbamates, 3% to mercaptobenzothiazole and/or its derivatives, 0.4% to thioureas, and 3% to 1,3-diphenylguanidine.[240] Patch testing to rubber chemical mix or the suspected article itself is appropriate.

In 132 farmers with OCD, metals, disinfectants, rubber, and pesticides were the most important allergens. Less commonly, they reacted to colophony, lanolin, and propolis (especially bee keepers). Contact dermatitis lesions in farmers are frequently aggravated by irritant chemicals in fertilizers and pesticides.

A survey of Danish cleaners and/or housekeepers who had OCD showed significantly increased rates of sensitization to formaldehyde and rubber additives such as thiurams, zinc diethyldithiocarbamate and mercaptobenzothiazole compared with controls.[241]

In the military, common causes of ACD include exposure to plants and insects, formaldehyde resins, disperse dyes, and chromate-containing dyes in uniforms, methylchloroisothiazolinone/methylisothiazolinone in coolants and cutting oils, metal allergy to embedded shrapnel, and phenoxyethanol, formaldehyde, neomycin, aluminum, and thimerosal in vaccines.[242]

Summary Statement 41: Consider botanical-related ACD in outdoor workers, or others exposed to plants, including florists, gardeners, landscapers, maintenance workers, and park and wildlife officials. [Strength of Recommendation: Moderate; C Evidence]

The most common causes of plant dermatitis in outdoor workers are plants within the genus *Toxicodendron*, still identified as *Rhus* in the dermatological literature. These include poison ivy, poison oak, and poison sumac. The allergenic substance, *urushiol*, derives its name from the Japanese word for the sap found in the Japanese lacquer tree. It contains a mixture of catechols (1,2-dihydroxybenzenes) and resorcinols (1,3-dihydroxybenzenes). Urushiol avidly binds to skin, but it is readily degraded in the presence of water. Therefore, soak exposed skin with cool water as soon as contact is suspected. Interestingly, the nonleaf portions of the plant can also induce dermatitis, even in the winter (http://telemedicine.org/botanica/bot6.htm). The diagnosis is made on the basis of the history. Patch testing to Toxicodendron is generally not recommended because it can cause sensitization in an otherwise nonsensitized person and also large bullous reactions.

Alstroemeria (Peruvian lily) is the most frequent cause of hand dermatitis in floral workers. Lily and tulip sensitivity is caused by

sensitivity to alpha-methylene-gamma-butyrolactone or tulipalin A, which is derived from the glycoside tuliposide A. The allergenic chemical is found in several of the lily florae, including *Alstroemeria* (Peruvian or Inca lily), *Bomarea* (restios or grasses from South Africa), *Erythronium* (dog tooth violet, trout lily, adder's tongue), and *Tulipa*. It is present in less amount in *Dioscorea hispida* (water yam), *Fritillaria* (snake's head, chess flower, frog-cup, guinea-hen flower, checkered lily), and *Gagea* (Yellow Star-of-Bethlehem), and in at least one species of onion, *Allium triquetrum*. The allergen is present in both the flower and the bulb. Because the allergen penetrates latex and vinyl gloves, nitrile protective gloves should be used by allergic individuals when handling tulips and *Alstroemeria*.[243] Calcium oxalate crystals in the plant sap may also cause an irritant dermatitis.[244]

There are few standardized testing extracts available for plant allergens, although some companies do offer a limited plant series that includes alpha-methylene-gamma-butyrolactone and a few other flower allergens. In the absence of commercially available extracts, PT may be performed with caution by using small amounts of the fresh plant or bulb, as severe bullous reactions may result from their high allergy content.[245,246] Because of the potential for severe bullous reactions, it is recommended that an open test without occlusion be done.

Treatment of contact dermatitis. Summary Statement 42: Once the allergen or irritant has been identified, the patient should be counseled on avoidance of contact with the offending agent and informed of any cross-reactivity concerns. [Strength of Recommendation: Strong; B Evidence]

The identification and avoidance of contact with the offending agent(s) is the key to successful treatment of ICD and ACD. Recovery is possible if the agent is identified and avoided.

For cosmetic products, if PT identifies specific allergens, the patient should be informed of these allergens and counseled regarding avoidance. However, typical allergen names are long, difficult to spell, commonly have numerous complex synonyms, and are often intimidating for patients making compliance with allergen avoidance difficult. To improve compliance,[247,248] there are currently 2 computer-generated databases available in the United States. These databases list of products that are free of the suspected allergens. One database is the CAMP that is available for members of the American Contact Dermatitis Society (www.contactderm.org) and the other is Mayo Clinic's *SkinSAFE Database* (www.SkinSAFEapp.com) that is available for physicians for purchase, and patients of enrolled providers.

The dimethyl-glyoxime test (nickel spot test) can be used to detect nickel released from metal objects. It has a limit of detection of 0.13 mcg/cm^2.[249] The sensitivity of the test has been estimated at 59%, and a specificity of 97%.[250] The cobalt spot test is based on disodium-1-nitroso-2-naphthol-3,6-disulfonate[251] and may serve to detect dermal exposure.[252] There are wipe tests that can detect nickel, cobalt, and chromium on the skin.[253,254] Detection of these metals can aid in avoidance of exposure.

If contact with the culprit allergen or irritant continues, the dermatitis may become chronic, more generalized, disabling, and become a problem with continued employment and quality of life. There is some evidence that the use of conditioning creams may improve the skin condition. However, even with removal from exposure and avoidance of contact, the dermatitis may persist in some patients. On occasion, partnering with an occupational health professional may help with patient management.

Summary Statement 43: In addition to avoidance of exposure, the physician should prescribe appropriate adjunct medical treatment. [Strength of recommendation: Strong; B Evidence]

A number of professional organizations provide guidelines and consensus statements related to medical treatment. Several recent reviews provide guidelines for the medical management of hand dermatitis.[255,256] Key components of medical management include TCS with second line therapies including phototherapy, oral retinoids, and immunosuppression.

TCS are widely accepted as the treatment of acute and chronic dermatitis.[257] The selection of TCS for efficacy, potency, and acceptability is determined by many factors including the severity, the location, and the acuteness of the dermatitis. TCS may be sufficient for localized lesions, but acute extensive and severe dermatitis such as extensive *Toxicodendron* dermatitis may need systemic therapy. The clinician should avoid the prolonged use of systemic steroids for management of chronic dermatitis. Ointments and potent fluorinated CS should be avoided on areas of thinner skin such as the intertrigenous areas, eyelids and face, and in young children. The use of TCS over prolonged periods of time should be avoided and should not be a substitute for defining the etiology of the dermatitis. If symptoms worsen, the possibility of contact sensitization to the CS itself, the vehicle, or other ingredients in the TCS should be considered.[258-260]

Several topical T-cell selective inhibitors have been used successfully in the treatment of AD, but their efficacy in ACD or ICD has not been established. Topical tacrolimus has been shown to be effective in the murine model of nickel ACD.[261] However, there are no published randomized, double-blind studies to verify these preliminary results. Pimecrolimus has been shown to inhibit the elicitation phase but has no demonstrable effect on the sensitization phase of ACD in the murine model. Several preliminary studies suggest that pimecrolimus may be effective in the treatment of ACD.[262,263]

Other treatments including cyclosporin, azathioprine, and psoralen plus UVA have been used for steroid-resistant ACD such as chronic hand dermatitis.[255,264-266] The risks and benefits of these treatment options need to be considered; informed consent before use is necessary.

Prevention. Summary Statement 44: To prevent CD, avoid exposure to irritants and allergens and use appropriate skin protection. [Strength of Recommendation: Strong; B Evidence]

Primary prevention of ICD and ACD involves avoidance of exposure to possible irritants and allergens and appropriate skin protection.

Avoidance of exposure may be accomplished by several means. Elimination of an irritant or an allergen from exposure may not always be possible. Nevertheless, removal of chromium from cement in Europe is an example of successful elimination.[236] Substitution of a potential allergen with another agent in the workplace that is less allergenic may be effective.[236] Training is an important component of avoiding exposure in the workplace.[236,267] Rotation of job task may also reduce irritant exposure but may not eliminate the risk of sensitization. Examples of methods of reducing exposure include using long handled

cleaning tools (brush with a handle), vacuuming, or wet sweeping.

Skin protection remains the primary goal of prevention of occupational dermatitis. This should include the use of personal protective equipment such as gloves, goggles and/or face shields, uniforms, and equipment to protect the skin from the exposure. The use of cotton liners under gloves can be useful.[236] In some instances, this may also involve the use of specialized skin creams such as barrier creams containing quaternium-18 bentonite (organoclay) to prevent *Rhus* dermatitis or creams containing chelators such as pentaacetic acid to prevent nickel, chrome, or copper dermatitis.[268] In general, pre-work creams have not been demonstrated to be useful, but skin care to protect the barrier function of the skin is important. This involves the use of moisturizers, particularly lipid-rich moisturizers.[236,268]

Screening, to detect disease at an early stage when the disease is still reversible, is used in the occupational setting. Although screening for early detection appears to be feasible, there is little information available on its effectiveness.

Given the visual nature of dermatitis, screening for hand dermatitis seems feasible and has been recommended in the occupational setting.[269] Other than a program in Germany focused on dermatologists[270] and several research studies focused on the intervention,[271,272] there are no reports of its general use in workplaces with a high risk of OCD. As such, there is no evidence of the effectiveness of surveillance programs or particular methods for screening.[236]

Prognosis. Summary Statement 45: Education of the workers with ACD or ICD should include prognosis and information that their disease may persist and need long-term management even after treatment and workplace modifications. [Strength of Recommendation: Moderate; C Evidence]

In a review of 15 studies reporting prognosis in OCD between 1958 and 2002, the range of complete clearance of the dermatitis was 18% to 72%.[273] Two Australian studies from the 1980s documented ongoing problems in a significant proportion of affected workers. In one study, 55% had ongoing problems from between 6 months and 8 years following diagnosis, and the other study documented that 29% were unchanged or worse on average of between 1 and 5 years postdiagnosis.[274,275] A Toronto study that evaluated outcomes at a minimum of 2 years postdiagnosis found that 63% were clear of disease, 28% had mild disease, 15% had moderate disease, and 5% had severe disease.[108] Seventy-eight percent of the patients noted improvement, 17% were unchanged, and 5% reported it to be worse than at diagnosis. Two recent studies provide prognostic information in workers with occupational hand dermatitis. A 1-year follow-up study found that 41% had improved, but 25% had persistent, aggravated, or severe disease.[276] A longer term study with a follow-up between 7 and 14 years found that 40% had not experienced any dermatitis in the past year.[277] Atopic dermatitis was associated with poorer outcomes, whereas contact allergy was not. The longer the duration of the hand dermatitis before diagnosis, the poorer the outcome.

A number of studies have examined work outcomes in workers with OCD. These studies demonstrate that there is significant job disruption for workers with CD. Some studies report work absence at the time of assessment and others report the results of a follow-up study. Status at the time of assessment from the British reporting system EPIDERM found that 7% had been unemployed and 17% had taken time off work.[278]

A Danish study found similar results with prolonged sick leave reported by 20% of patients.[276] A recent study reported work status at 6 months postdiagnosis found 38% unemployed because of their skin disease.[279] Another Toronto follow-up study—at least 2 years postdiagnosis—found that 78% were working, but 57% had changed jobs and 35% had lost time of at least 1 month.[280] Two recent studies have also reported on job change many years after the diagnosis of OCD. Meding et al, in a 12-year follow-up, found that 82% had some change in their work, with 44% changing jobs.[281] In a Finish follow-up study at 7-14 years postdiagnosis, 54% had job modifications, 34% had changed jobs, 20% were re-trained, and 25% were not working.[277] Only 8% had no change in their work.

There are a small percentage of individuals with occupational hand dermatitis who do poorly even with removal from exposure. In a recent Australian study,[282] 18% of those with OCD dermatitis had persistent dermatitis.

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APPENDIX B. CLASSIFICATION OF RECOMMENDATIONS AND EVIDENCE

Recommendation Rating Scale

Statement	Definition	Implication
Strong recommendation (StrRec)	A strong recommendation means the benefits of the recommended approach clearly exceed the harms (or that the harms clearly exceed the benefits in the case of a strong negative recommendation) and that the quality of the supporting evidence is excellent (Grade A or B)*. In some clearly identified circumstances, strong recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Moderate (Mod)	A recommendation means the benefits exceed the harms (or that the harms exceed the benefits in the case of a negative recommendation), but the quality of evidence is not as strong (Grade B or C)*. In some clearly identified circumstances, recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits outweigh the harms.	Clinicians should also generally follow a recommendation but should remain alert to new information and sensitive to patient preferences.
Weak (Weak)	A weak recommendation means that either the quality of evidence that exists is suspect (Grade D)* or that well-done studies (Grade A, B, or C)* show little clear advantage to one approach vs another.	Clinicians should be flexible in their decision making regarding appropriate practice, although they may set bounds on alternatives; patient preference should have a substantial influencing role.
No recommendation (NoRec)	No recommendation means there is both a lack of pertinent evidence (Grade D)* and an unclear balance between benefits and harms.	Clinicians should feel little constraint in their decision making and be alert to new published evidence that clarifies the balance of benefit vs harm; patient preference should have a substantial influencing role.

*Refer to the next column.

Category of Evidence

Ia Evidence from meta-analysis of randomized controlled trials

Ib Evidence from at least one randomized controlled trial

IIa Evidence from at least one controlled study without randomization

IIb Evidence from at least one other type of quasi-experimental study

III Evidence from nonexperimental descriptive studies, such as comparative studies

IV Evidence from expert committee reports or opinions or clinical experience of respected authorities or both

Strength of Recommendation*

A Directly based on category I evidence

B Directly based on category II evidence or extrapolated recommendation from category I evidence

C Directly based on category III evidence or extrapolated recommendation from category I or II evidence

D Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence

LB Laboratory based

NR Not rated

APPENDIX C. ALLERGENS ASSOCIATED WITH SYSTEMIC CONTACT DERMATITIS

Contact sensitizer	Systemic reaction to
Glucocorticoids	Oral corticosteroids
Benadryl cream	Oral diphenhydramine
Neomycin	Oral neomycin
Penicillin	Oral penicillin
Sulfonamide	Para-amino sulfonamide hypoglycemics (tolbutamide, chlorpropamide)
Thiuram	Antabuse
Colophony, balsam of Peru, fragrance mix	Spices: clove, nutmeg, cinnamon, cayenne pepper
Ethylenediamine	Aminophylline Piperazine and ethanolamine (Atarax, Antivert)
Nickel	Nickel in tap water, utensils, and food

APPENDIX D. SPECIAL OCCUPATIONAL PATCH TEST ALLERGEN PANELS

- Bakery
- Dental screening—health care providers
- Dental screening—patients
- Hairdressing
- Machinists—oil & cooling fluids and/or metalworking
- Photographic chemicals

APPENDIX E. ALLERGEN PANELS BASED ON SPECIFIC EXPOSURES

- Cosmetics
- Epoxy series
- Eyelid dermatitis
- Footwear and/or shoes
- Fragrance and/or perfumes
- Isocyanates
- Methacrylate series: adhesives, dental, nails, and others
- Photoallergens
- Photochemicals and/or photopatch
- Plastics and glues
- Rubber additives and/or chemicals
- Sunscreens
- Textile colors and finish

APPENDIX F. MEDICATIONS, TREATMENTS, AND FOOD PANELS

- Antibiotics and/or antimycotics
- Corticosteroids
- Local anesthetics
- Medicinal substances
- Antimicrobials and/or preservatives
- External agents and/or emulsifiers
- Food additives
- Leg ulcer
- Metal compounds and implants
- Plants and/or compounds of natural origin

APPENDIX G. SOURCE OF PATCH TEST ALLERGENS

Sources of Patch Test Allergens
AllergEAZE by Smart Practice Canada SmartPractice Canada 2175 29th Street NE, Unit 90 Calgary, AB T1Y 7H8 Phone: 866-903-2671 Fax: 866-903-2672 E-mail: info@allergeaze.com
Dormer.com: http://www.dormer.com/Allergens/ReimCan.aspx 91 Kelfield, Suite 5 Rexdale, Ontario M9W 5A3 Phone: (416) 242 6167 Fax: (416) 242 9487 or 1-877-436-7637
True Test (Smart Practice): http://www.truetest.com/ Allerderm—*a SmartPractice affiliate* 3400 E. McDowell Rd. Phoenix, AZ 85008-7899 Customer Service: 1-800-878-3837 E-mail: info@allerderm.com

APPENDIX H. TRUE TEST PANEL ALLERGENS

Panel 1.2
Nickel sulfate
Wool alcohols
Neomycin sulfate
Potassium dichromate
Caine mix
Fragrance mix
Colophony
Paraben mix
Negative control
Balsam of Peru
Ethylenediamine dihydrochloride
Cobalt dichloride

Panel 2.2
p-tert-Butylphenol formaldehyde resin
Epoxy resin
Carba mix
Black rubber mix
Cl^{+} Me^{-} isothiazolinone (MCI/MI)
Quaternium-15
Methyldibromo glutaronitrile
p-Phenylenediamine
Formaldehyde
Mercapto mix
Thimerosal
Thiuram mix

Panel 3.2
Diazolidinyl urea
Quinoline mix
Tixocortol-21-pivalate
Gold sodium thiosulfate
Imidazolidinyl urea
Budesonide
Hydrocortizone-17-butyrate
Mercaptobenzothiazole
Bacitracin
Parthenolide
Disperse blue 106
2-Bromo-2-nitropropane-1,3-diol (Bronopol)

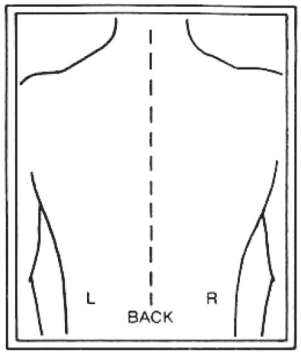
APPENDIX I. EXAMPLE OF A PATCH TEST FORM

Practice Name: _____

Patient Name: _____

Date of Birth:_____ Gender: _____Race _____

Date Test Applied: _____ By: _____



Patch #	Contact Allergen		1st Read	2nd Read	3rd Read	Interpretation	Relevance
	DATE						
1	2,5-diazolidinylurea (Germall II)	1.0% pet					
2	bisphenol A epoxy resin	1.0% pet					
3	2-bromo-2-nitropropane-1,3-diol (Bronopol)	0.5% pet					
4	2-hydroxy-4-methoxy-benzophenone	10.0% pet					
5	2-mercaptobenzothiazole	1.0% pet					
6	4-chloro-3,5-xylenol (PCMX)	1.0% pet					
7	4-phenylenediamine base	1.0% pet					
8	4-tert-butylphenol formaldehyde resin	1.0% pet					
9	methychloroisothiazolinone/methylisothiazolinone	0.1% water					
10	amidoamine (stearamidopropyl dimethylamine)	0.1% water					
11	bacitracin	20.0% pet					
12	balsam of Peru	25.0% pet					
13	benzocaine	5.0% pet					
14	bisphenol F	1.0% pet					
15	black rubber mix	0.6% pet					
16	budesonide	0.1% pet					
17	budesonide	0.01% pet					
18	carba mix	3.0% pet					
19	cinnamic aldehyde	1.0% pet					
20	clobetasol-17-propionate	1.0% pet					
21	cobalt (II) chloride hexahydrate	1.0% pet					
22	cocamidopropyl betaine	1.0% water					
23	coconut diethanolamide (cocamide DEA)	0.5% pet					
24	colophony	20% pet					
25	petrolatum						
26	dibucaine (cinchocaine-HCl)	2.5% pet					
27	dimethylol dihydroxyethyleneurea	4.5% water					
28	disperse blue 106	1.0% pet					
29	dl alpha tocopherol acetate	100%					
30	DMDM hydantoin	1.0% pet					
31	ethyl acrylate	0.1% pet					
32	ethylenediamine dihydrochloride	1.0% pet					
33	ethyleneurea, melamine formaldehyde mix	5.0% pet					
34	formaldehyde	1.0% water					
35	fragrance mix	8.0% pet					

(Continued)

APPENDIX I. *(Continued)*

Patch #	Contact Allergen		1st Read	2nd Read	3rd Read	Interpretation	Relevance
36	glutaraldehyde	0.3% pet					
37	glyceryl monothioglycolate	1.0% pet					
38	Hydrocortisone	1.0% pet					
39	imidazolidinyl urea (Germall 115)	2% pet					
40	iodopropynyl butyl carbamates	0.5% pet					
41	iodopropynyl butyl carbamates	0.1% pet					
42	jasmine abs	2.0% pet					
43	llidocaine-HCl	15.0% pet					
44	mercapto mix A	1.0% pet					
45	methyl methacrylate	2.0% pet					
46	methyldibromo glutaronitrile phenoxyethanol(MDGN/PE)	2.0% pet					
47	neomycin sulphate	20.0% pet					
48	nickel sulfate hexahydrate	2.5% pet					
49	paraben mix	12% pet					
50	potassium dichromate	0.25% pet					
51	propylene glycol	5% pet					
52	quaternium	15 2.0% pet					
53	sesquiterpenelactone mix	0.1% pet					
54	tea tree oil, oxidized	5% pet					
55	thiourea	1.0% pet					
56	thiuram mix	1.0% pet					
57	tixocortol-21-pivalate	1.0% pet					
58	tosylamideformaldehyde resin	1.0% pet					
59	Triamcinoloneacetonide	1.0% pet					
60	wool alcohols (lanolin)	100%					
61	ylang ylang oil	2.0% pet					
62	benzyl alcohol	1.0% pet					
63	desoximetasone	1.0% pet					
64	fragrance mix II	14.0% pet					
65	propolis	10.0% pet					
66	(2-hydroxyethyl)-methacrylate	2.0% pet					

Patch #	Personal products

Physician Signature Date

PATCH TEST MORPHOLOGY CODES

(−) = Negative reaction
(?+) = Doubtful reaction with faint erythema only
(1+) = Weak positive reaction with non vesicular erythema, infiltration, possible papules
(2+) = Strong positive reaction with vesicular erythema, infiltration and papules
(3+) = Extreme positive reaction with intense erythema and infiltration coalescing vesicles, bullous reaction
(IR) = Irritant reaction

PATCH TEST INTERPRETATION CODES

N = Negative
A = Allergic
U = Unknown
I = Irritant

RELEVANCE

Definite: if a use test with the putative item containing the suspected allergen is positive or positive patch to object/product
Probable: if the substance identified by patch testing can be verified as present in the known skin contactants of the patient.
Possible :if the patient is exposed to circumstances in which skin contact with materials known to contain the putative allergen will likely occur
Past
Unknown

APPENDIX J. STRUCTURAL GROUPS OF CORTICOSTEROIDS AND POTENCY CLASSIFICATION WITH EXAMPLES OF COMMERCIALLY AVAILABLE PREPARATIONS

Steroid group	A: Hydrocortisone Hydrocortisone & tixocortol pivalate: has C17 or C21 short chain ester	B: TCL acetonide Acetonides: has C16 C17 cis-ketal or -diol additions	C: BTM nonesterified Betamethasone: has C16 methyl group	D1: BTM-dipropionate has C16 methyl group & halogenated B ring	D2: MPL aceponate labile esters w/o C16 methyl nor B ring halogen substitution
Prevalence	**2.7%**	**1.5%**	**<0.2%**	**0.8%**	**0.8%**
Class 7: Least Potent	**HC** [*Hytone* C/L (1%/2.5%)] [*Cortaid*, C/O/Sp] [*Egocort* C 1%] **HC Acetate** [*Cortisone, Lanacort, Wellcortin, Gynecort, Lanacort*]				
Class 6: Low		**Desonide** [*DesOwen* (0.05%) C/L] **FLU acetonide** [*Capex Sh, Dermasmooth* F/S/ oil (0.01%)] **TCL acetonide** [Aristocort A C, Kenalog L (0.025%)]		**Aclometasone dipropionate** [*Aclovate* C/O (0.05%)]	
Class 5: Lower Mid		**Desonide** [*Tridesilon, DesOwen* O (0.05%)] **FLU acetonide** [*Synalar, Synemol* C (0.025%)] **Flurandrenolide** [*Cordran* C/L/Tape (0.05%)]		**Fluticasone propionate** [*Cutivate* C (0.05%)]	**HC-17-valerate** [*Westcort* C (0.2%)] **Prednicarbate** [*DermAtop* C (0.1%)]
Class 4: Mid		**FLU acetonide** [*Synalar, Synemol* (0.01%-0.2%)] **Flurandrenolide** [CordranO (0.05%)] **TCL acetonide** [*Kenalog, Aristocort A* O (0.1%)]	**Desoximetasone** [*Topicort LP* C/O (0.05%)]	**Mometasone Furorate** [*Elocon* C/L (0.1%)]	**HC 17-butyrate** [*Locoid* C/L/O (0.1%)] **HC-17-valerate** [*Westcort* O (0.2%)]
Class 3: Upper Mid		**TCL acetonide** [*Kenalog, Aristocort* C (0.5%)] **Triamcinolone Diacetate** [*Amcort, Aristocort* C/O (0.025%-0.1%)]	**Halometasone** [*Halometasone* (0.05%)]	**BTM 17 valerate** [*Luxiq* F (0.12%)] [Valisone O (0.1%)] **BTM dipropionate** [*Diprosone* C (0.05%)] **Clobetasone 17 butyrate** [*Eumovate* C (0.05%)] **Fluticasone propionate** [*Cutivate* O (0.005%)] **Mometasone Furorate** [*Elocon* O (0.1%)]	

(Continued)

APPENDIX J. *(Continued)*

Steroid group	A: Hydrocortisone Hydrocortisone & tixocortol pivalate: has C17 or C21 short chain ester	B: TCL acetonide Acetonides: has C16 C17 cis-ketal or -diol additions	C: BTM nonesterified Betamethasone: has C16 methyl group	D1: BTM-dipropionate has C16 methyl group & halogenated B ring	D2: MPL aceponate labile esters w/o C16 methyl nor B ring halogen substitution
Class 2: High		**Amcinonide** [*Cyclocort* O/L/C (0.05%-0.1%)] **Fluocinonide** [*Lidex* C/G/O/S (0.05%)] Halcinonide [*Halog* C/O/S (0.05%-0.1%)]	**Desoximetasone** [*Topicort* C/O (0.25%)] [*Topicort* G (0.05%)] **Clocortolone** [*Cloderm* C (0.1%)]	**BTM 17 valerate** [Betnovate C/O (0.1%)] **BTM dipropionate** [*Diprolene* AF C (0.05%)] [*Diprosone* O (0.05%)]	
Class 1: Super		**Fluocinonide** [*Vanos* C (0.1%)]		**BTM dipropionate** [*Diprolene* O/G/L (0.05%)] **Clobetasol propionate** [*Clobex* L/spray/sh, *Dermovate* C/O, *Olux* F, *Temovate* C/O/S/G (0.05%)] [*Olux* F (0.05%)] **Diflorasone Diacetate** [*ApexiCon, Psorcon* C/O, *Florone* O (0.05%)] **Halobetasol** [*Ultravate* C/O (0.05%)]	
Oral/Systemic Preparation	**Cortisone acetate** **HC-21-acetate** **MPL acetate** [*Medrol*] intra-articular, intralesional, intrasynovial **Prednisone** [*Cortan, Deltasone, Meticorten, Orasone*] **Prednisoloneacetate** [*Prediapred, Prelone syrup*] **Cloprednol** **Fludrocortisone Acetate** [*Florinef*] **HC sodium** [Solucortef]	**Budesonide** **TCM** [*Atolone* Tablets (I)] **TCM benetonide** **TCM diacetate** **TCM hexacetonide**	**BTM sodium phosphate** Injectable Suspension [*Celestone*] **Dexamethasone acetate** **Dexamethasone-sodium phosphate** Injection [*Decadron*] **Paramethasone acetate**	**BTM Oral/IM BTM dipropionate**	**HC Oral/IV**
Cross Reactions	**Cross reacts with D2**	**Budesonide specifically cross-reacts with D2**			**Cross reacts with Class A & Budesonide**
Patch Test Substance	**Tixocortol 21-pivalate**	**Budesonide** **TCL acetonide**		**Clobetasole-17-propionate**	**HC-17-butyrate**

(Continued)

APPENDIX J. *(Continued)*

Steroid group	A: Hydrocortisone Hydrocortisone & tixocortol pivalate: has C17 or C21 short chain ester	B: TCL acetonide Acetonides: has C16 C17 cis-ketal or -diol additions	C: BTM nonesterified Betamethasone: has C16 methyl group	D1: BTM-dipropionate has C16 methyl group & halogenated B ring	D2: MPL aceponate labile esters w/o C16 methyl nor B ring halogen substitution
International and other noncutaneous preparations	**Cloprednol** [*Syntestan* (Germany)] **Dichlorisone Acetate** [*Dermaren* (Spain)] **Fluprednisolone acetate** [*Medinost* (Georgia)] [*Prednisolon STADA* (Germany)] **Meprednisone** [*Cortipyren* (Argentina)] [*Deltisona B* (Argentina)] [*Meprednisona All Pro*, (Argentina)] **Tixocortol** [*Pivalone*] [*Thiovalone*] **Fluorometholone** [*FML Oph O*] **Medrysone** [*HMS* 1.0%] [*LIQUIFILM* Oph Su] **Prednisolone acetate** [*Pred Forte*, *Blephamide* Oph]	**Flucoronide procinonide** [*Topilar*] **Budesonide** [*Naricort* C 0.025%] [*Pulmicort INH, Rhinocort NS Butacort, Entocort*] **Fluocinonide** [*Aerobid INH*] **Flunisolide** [*Aerospan*] [*Nasalide NS*] **Triamcinalone acetonide** [*Azmacort* INH]	**Difluocortolone (pivalate, valerate)** [*Nerisone C* C/O] **Flumethasone** (Vet use) **Fluocortin butyl** [*Vaspit* (Spain)] **Fluocortolone (hexanoate, pivalate, caproate)** [*Ultralan*] [*Ultraproct*] **Fluprednidene acetate** [*Decoderm*]		**HC aceponate** [*Efficort*] **MPL aceponate** [*Advantan* C/O]

HC, hydrocortisone; *MPL*, methylprednisolone; *BTM*, betamethasone; *FLU*, fluocinolone; *TCL*, triamcinolone; *CLO*, clobetasol; *C*, cream; *O*, ointment; *L*, lotion; *F*, foam; *G*, gel; *S*, solution; *Su*, suspension; *Sp*, spray; *Sh*, shampoo; *Inh*, inhaler; *Oph*, ophthalmic; *NS*, nasal spray.
In parenthesis are examples of products available. For this manuscript the allergenicity is classified as Groups A, B, C, D1, and D2 and the potency is from Class 1-7; 1 being the most potent and 7 being the weakest class. The classification of potency may vary depending on factors such as the vehicle and reference source.