Practice parameter

Contact dermatitis: a practice parameter

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PREFACE

Contact dermatitis (CD) encompasses all adverse cutaneous reactions that result from the direct contact of an exogenous agent (a "foreign" molecule, UV light, or temperature) to the surface of the skin or mucous membranes. The skin can react immunologically and/or nonimmunologically to such exogenous agents. The inflammatory process that results from an allergic substance is mediated through immunologic mechanisms, whereas irritant reactions result from direct tissue damage, which initiate alternative inflammatory reactions. However, the distinction between allergic contact dermatitis (ACD) and irritant contact dermatitis (ICD) has become increasingly blurred. Often these exogenous forms of dermatitis must be distinguished from endogenous dermatitis (eg, atopic dermatitis, nummular eczema, dyshidrosis).[1] It is not unusual for an exogenous dermatitis to be superimposed on an endogenous eruption, most commonly encountered when compresses or topical antibiotics are used too long on barrier impaired skin.

Based on several studies, the bulk of exogenous cases are diagnosed as ICD. The appropriate diagnosis is made by evaluating the location and evolution of the inflammation, together with morphologic nuances, to arrive at a probable diagnosis. Patch testing remains the most useful method for confirming ACD. ICD is a diagnosis of exclusion without firm criteria or when patch test results for ACD are negative. However, if patch tests fail to test for the appropriate substance, an ICD diagnosis could be incorrect.

Several recent surveys sponsored by both allergy and dermatology national societies revealed that 57% and 53% of American Academy of Allergy, Asthma and Immunology (AAAAI) and American College of Allergy, Asthma and Immunology (ACAAI) fellows, respectively, perform patch testing,[2,3] compared with 83% of dermatologists in a separate survey.[4] The patch testing methods used by both groups were similar.[2] A noteworthy aspect of the ACAAI survey was that fellowship- or contact workshop–trained allergists not only

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The American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) have jointly accepted responsibility for developing Contact Dermatitis: A Practice Parameter. This is a complete and comprehensive document according to current scientific standards. Medicine is a constantly changing discipline, and not all recommendations will be appropriate for all patients. Because this document incorporates the efforts of many participants, no single individual, including those who served on the Joint Task Force, is authorized to provide an official AAAAI or ACAAI interpretation of these practice parameters. Any request for information about or an interpretation of these practice parameters by the AAAAI or ACAAI should be directed to the Executive Offices of the AAAAI, the ACAAI, and the Joint Council of Allergy, Asthma and Immunology. These parameters are not designed for use by pharmaceutical companies in drug promotion.

performed patch testing more frequently than physicians without CD training but also were more confident about the clinical relevance of such testing, especially in the differential diagnosis of the common eczematous diseases.[2] The emergent professional role of the allergist/clinical immunologist in the diagnosis and treatment of CD is a major impetus for this Practice Parameter on Contact Dermatitis.[5]

This guideline was developed by the Joint Task Force on Practice Parameters, which has published 20 practice parameters for the field of allergy/immunology (see list of publications). The 3 national allergy and immunology societies—the ACAAI, the AAAAI, and the Joint Council of Allergy, Asthma and Immunology (JCAAI)—have given the Joint Task Force the responsibility for both creating new and updating existing parameters.

The major goal of these guidelines is to ensure that CD patients benefit from the best available diagnostic and therapeutic applications by consultant allergists/clinical immunologists. In achieving this balance, allergists/clinical immunologists may choose to develop a collegial working relationship with a CD-oriented dermatologist subspecialist for assistance with diagnosis, differential diagnosis, and management of unusual clinical presentations or refractory CD.[5] The general principles in this Practice Parameter should also help to develop improved understanding of CD among other health care professionals, students, residents, and fellows.

As was the case with other Practice Parameters previously published by the Joint Task Force, the initial phases of this Practice Parameter were developed by a Work Group in direct liaison with a Joint Task Force member. Ten years ago, dermatologic members of the Work Group with special interests in CD were recruited in a joint collaboration with allergists having a similar interest. This collegial effort produced an initial draft that was redacted and enhanced by Joint Task Force members to fulfill the Joint Task Force prerequisites of basing all decisions and recommendations on evidence-based analysis of the pertinent published literature, insofar as that is currently possible. The working draft of the Practice Parameter was then reviewed by a number of experts on CD selected by the supporting organizations. This document therefore represents an evidence-based, broadly accepted, consensus opinion.

Objective evidence for major content listings was obtained by searching PubMed MEDLINE. Wherever possible, references were selected according to the following priority scale: (1) meta-analyses; (2) randomized controlled trials; (3) controlled trials without randomization; (4) other quasi-experimental studies; (5) nonexperimental descriptive studies, such as comparative, correlation, or case-controlled studies; (6) committee reports or opinions, clinical experience of respected authorities, or both; and (7) laboratory-based studies. Both references and summary statements are graded by this evidence profile (see below).

This Practice Parameter is divided into 2 main sections: (1) a synopsis that includes a glossary, an executive summary, an algorithm with annotations, and a collation of summary statements and (2) a narrative text with graded references and appendices. The synopsis sections are intended to provide a practical, ready-to-use reference guide, whereas the narrative is a more detailed discussion of the best available evidence for each graded summary statement.

The evidence-based narrative section is considered in the context of several major aspects of CD: (1) pathophysiology, genetic, and susceptibility factors; (2) clinical diagnosis; (3) differential diagnosis; (4) special contact exposures; (5) ACD in children; and (6) management. Special emphasis is placed on the difficulty in separating ICD from ACD. The most frequent sources of exposure to contactant allergens are summarized in the special contact exposures category with emphasis on the leading causes of occupational contact dermatitis (OCD). The diagnosis section contains a detailed discussion of proper performance, interpretation, and clinical relevance of patch testing.

In summary, the Practice Parameter has been prepared for allergists (with the assistance of dermatologists) on behalf of the AAAAI, ACAAI, and JCAAI. As in any specialized area of medical expertise, some exceptions to the guidelines can be expected to occur as future research modifies and/or expands the current body of knowledge about CD. Further, in recognition of the fact that total adherence to these parameters is not always possible, a divergent approach in exceptional patients beyond the framework of these guidelines should not necessarily be construed as substandard, provided that such methods are necessitated by unusual circumstances and are based on validated medical principles.

GLOSSARY

- *Acantholysis*—A histologic finding occurring in vesiculobullous and pustular diseases describing the loss of cohesion between keratinocytes due to breakdown of intercellular bridges.
- *Allergic contact dermatitis*—A cutaneous reaction caused by cell-mediated sensitization to a contactant allergen(s) (ie, chemical or rarely a protein) and a subsequent delayed hypersensitivity-mediated proinflammatory response after reexposure to the same or cross-reacting sensitizer(s).
- *"Angry back" syndrome*—A strongly positive inflammatory patch test response(s) that nonspecifically increases the percentage of false-positive reactions to contactants placed on the back at the same time.
- *Berloque dermatitis*—A phytophotodermatitis causing pigmentation at the site of application of perfumes or colognes containing oil of bergamot.
- *Contact dermatitis*—An inflammation of the skin caused by irritants or allergic sensitizers.
- *Cosmetics, leave-on*—A term to denote cosmetics that persist on the skin for varying periods.
- *Cosmetics, wash-off*—Cosmetic formulations that are readily removed from the skin by simple washing or rinsing.
- *Cross sensitization*—ACD induced by a secondary sensitizer chemically related to the primary sensitizer.
- *Dermatophytid*—An eczematous eruption as a manifestation of allergy to a dermatophyte infection elsewhere on the skin.

- *Ectopic ACD*—ACD occurring in location(s) distant from the original contact skin site.
- *Formaldehyde-releasers*—Chemicals that, on degradation or catabolism, lead to the presence of active formaldehyde.
- *Grenz ray*—An "ultra-soft" or superficial x-ray examination that only penetrates the top 0.5 mm of the skin (ie, the thickness of paper). It should not be confused with "superficial radiation therapy," which requires lead shielding.
- *Irritant contact dermatitis*—A nonimmunologic inflammatory response to a toxic agent coming in direct or prolonged contact with the skin.
- *Hapten*—A small-molecular-weight chemical that is antigenic but not immunogenic. It may become immunogenic after in vitro and/or in vivo conjugation with protein.
- *Likelihood ratio*—The likelihood that a given test result would be expected in a patient with a disorder compared with the likelihood that the same result would be expected in a patient without the disorder.
- *Melkersson-Rosenthal syndrome*—A genetic condition associated with cheilitis, labial edema, recurrent facial palsy, orofacial granulomata, and scrotal tongue.
- *Pompholyx*—A vesicular and/or bullous dermatitis of the hands and feet. It is also referred to as dyshidrotic eczema.
- *Predictive value*—The proportion of persons with a positive test result who have a disorder (positive predictive value) or the proportion of those with a negative test result without the disorder (negative predictive value).
- *Primary irritant*—An agent that directly damages the skin without allergic sensitization.
- a) *Absolute primary irritant*—A corrosive agent (eg, strong acids or alkalis) that immediately damages the skin.
- b) *Relative primary irritant*—A less toxic agent (eg, detergent) that damages the skin for longer periods.
- *Sensitivity*—The proportion of patients with an illness who test positive for it.
- *Specificity*—The proportion of patients without a disorder who test negative for it.
- *Spongiosis*—Intercellular epidermal edema, which leads to stretching and eventual rupture of intercellular attachments with formation of microvesicles.

CLASSIFICATION OF RECOMMENDATIONS AND EVIDENCE CATEGORY

Categories

Ia—Evidence from meta-analysis of randomized controlled trials.

Ib—Evidence from at least 1 randomized controlled trial.

IIa—Evidence from at least 1 controlled study without randomization.

IIb—Evidence from at least 1 other type of quasi-experimental study.

III—Evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-controlled studies.

IV—Evidence from expert committee reports, the opinions or clinical experience of respected authorities, or both.

LB—Evidence from laboratory-based studies.

Strength of Recommendation

A—Directly based on category I evidence.

B—Directly based on category II evidence or extrapolated from category I evidence.

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

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

E—Directly based on category LB evidence.

F—Based on consensus of the Join Task Force on Practice Parameters.

EXECUTIVE SUMMARY

CD is a common skin problem for which 5.7 million physician visits per year are made. There are more than 85,000 chemicals in the world environment today. Almost any substance can be an irritant, whereas more than 3,700 substances have been identified as contact allergens. All age groups are affected, with a slight female preponderance based on a large population-based survey of public health issues. The clinical expression of CD is most commonly recognized as eczematous inflammation. The severity of this dermatitis ranges from a mild, short-lived condition to a severe, persistent, but rarely life-threatening, disease.

Cutaneous immunologic reactions associated with ACD are noted almost exclusively at the site of contact with a putative antigen. Most ACD antigens are small-molecular-weight molecules that become immunogenic after conjugation with proteins in the skin. After a complex series of interactions with antigen-presenting Langerhans and/or other dendritic cells and $CD4^+$ and $CD8^+$ T cells, both regulatory and cytotoxic, an intense inflammatory response ensues, leading to spongiosis and perivascular infiltration.

ICD is generally a multifactorial response that involves contact with a substance that chemically abrades, irritates, or damages the skin. The cellular damage in ICD occurs because proinflammatory cytokines are released by T cells activated by irritant or innate mechanisms. The gross and microscopic appearances of ACD and ICD are often similar and at times cannot be specifically distinguished.

Susceptibility of CD has been shown to be slightly increased in women, presumably due to exposure to specific contactants in jewelry and cosmetics. In recent years, certain cytokine gene polymorphisms (eg, tumor necrosis factor α [TNF-α]) have been demonstrated to be more common in polysensitized individuals.

The suspicion of ACD constitutes the first step in making a diagnosis. For ACD to occur, the site of inflammation must have come in contact with the offending agent in a sensitized individual. Initially, the area might itch, burn, or sting, but later pruritus is a major symptom. The evolution and severity of the ACD lesion depend on multiple factors, including the

constitutive allergenicity/irritancy of the agent, the integrity of the involved skin, environmental conditions, a history of prior reactions, and the immunocompetency of the patient. Work history must be carefully reviewed. Hobbies and nonwork activities, such as gardening, painting, music (ie, playing stringed instruments), and photography, may also be sources of exposure to a number of contactants. The location and clinical appearance of the lesion may also suggest a possible ACD. Particular attention should be given to certain anatomical sites, which include eyelids, face, neck, scalp, hands, axillae, lower extremities, and the anogenital region. Although history can strongly suggest the cause of ACD, it has been reported that experienced physicians accurately predict the sensitizer in only 10% to 20% of patients with ACD when relying solely on the history and physical examination.

Patch testing is the gold standard for identification of a contact allergen. The number of appropriate patch tests required to diagnose ACD may vary, depending on the nature of the clinical problem and the potential for significant allergen exposure. Because it is impractical to test an unlimited number of allergens, standardized panels of allergens have been designed and validated by collaborative research dermatologic societies. Although standardized panels, which include relatively few of all known allergens, perform robustly and may account for 25% to 30% of the most relevant contactant allergens, many patients need additional testing. Patch tests are indicated in any patient with a chronic pruritic, eczematous lichenified dermatitis if underlying or secondary ACD is suspected. Patch test results cannot be interpreted reliably in patients who are taking therapeutic doses of systemic corticosteroids or topical and calcineurin inhibitors applied on or near patch test sites. Patch test results should be read at 2 days unless discomfort occurs earlier. Since 30% of reactions are negative at 2 days, additional reading(s) should be performed at 3, 4, and sometimes 7 days after the initial application, depending on the allergen. Interpretation of patch test results is based on a nonlinear, descriptive scale that was developed and validated by an International Contact Dermatitis Research Group. Interpretation of patch test results must also consider the fact that there may be false-negative or false-positive reactions. Customized patch tests may be required, depending on the patient's exposure history.

If results of patch tests with the appropriate antigens are negative, ICD or another underlying condition (dermatologic or systemic) should be considered. The differential diagnosis of CD is extensive in that virtually any disease with histologic evidence of spongiosis or inflammation may have to be considered.

Certain occupational and nonoccupational exposures are frequently associated with CD. The most common occupations associated with OCD are the health professions, food processors, beauticians, hairdressers, machinists, and construction workers. In the nonwork environment, plant dermatitis is the most commonly recognized form of ACD in the world. For example, *Toxicodendron* (formerly referred to as *Rhus*) varieties of plants grow practically everywhere in the United States and affect up to 50 million Americans every year. A number of other plant families (eg, *Ambrosia*) are also known to induce ACD. Exposure to metals, cosmetics, and personal hygiene products is another common cause of ACD. Many topically applied medications may ultimately become potent sensitizers. Allergic contact cheilitis (ACC) and mucositis have been reported to occur after exposure to chemicals in oral products, including lipsticks, lip balms, dentifrices, chewing gum, and chemicals applied during dental treatments. In patients with contact sensitivity to certain chemicals, such as ethylenediamine, systemic eczematous dermatitis is possible after intravenous or oral ingestion of drugs (eg, aminophylline) having the same chemical moiety. Simultaneous exposure to allergens and irritants tends to lower the irritant threshold of patients with ACD and thus creates a greater susceptibility to skin irritation after subsequent exposures. ICD appears to be the major factor in chronic detergent hand dermatitis, because liquid detergents have a known propensity to injure the skin barrier mechanisms.

Although rare in the first years of life ($<$10 years), the rate of occurrence of ACD in older children attains and even exceeds that observed in adults. The order of prevalence of ACD to individual allergens in children is generally comparable to the general adult population, with occurrences of nickel, fragrances, *Toxicodendron,* and rubber chemicals being similar.

Considering the management of ACD, 2 phases are of prime importance. The acute treatment phase involves identification, withdrawal, and avoidance of contact to offending agents. This is the key to successful treatment. Treatment of ongoing dermatitic lesions includes both palliative and other therapeutic measures. Cold compresses and other measures to hydrate and soothe the skin may be helpful. The use of topical corticosteroids (TCs) is the mainstay of treatment. Traditionally, physicians prescribe higher-potency corticosteroids initially and then gradually switch to medium or lower-potency corticosteroids as improvement becomes evident. ICD does not respond as well to TCs as ACD.

The second phase of management concerns prevention. Primary prevention is chiefly applicable to the workplace, where it is often possible to initiate surveillance programs that are successful in bringing attention to proper skin care and helping workers avoid undue exposure to highly sensitizing chemicals. Secondary prevention methods are undertaken to prevent dryness and fissuring of the skin and involve the use of emollients and moisturizers. The efficacy of protective barrier creams is controversial. Unfortunately, none of these secondary measures appear to be totally effective, especially in occupations with high exposure to skin irritants.

Prognosis is only well established for OCD, where improvement ranges from 70% to 84%. Rarely, some workers have persistent, ongoing dermatitis precipitated by prior OCD despite removal of exposure at work. Persistent ACD has an appreciable effect on quality of life in a small number of

workers who have to change jobs because of severe recalcitrant OCD.

COLLATION OF SUMMARY STATEMENTS

Clinical Background

Summary statement 1. CD is a common skin disorder seen by allergists and dermatologists and can present with a spectrum of morphologic cutaneous reactions. (C)

Pathophysiology of CD

Summary statement 2. The inflammatory lesions of CD may result from either allergic (ACD) or nonallergic, irritant (ICD) mechanisms. Factors that affect a response to the contact agent include the agent itself, the patient, the type and degree of exposure, and the environment. (A)

Summary statement 3. Tissue reactions to contactants are attributable primarily to cellular immune (delayed hypersensitivity) mechanisms, except for contact urticaria. (A)

Summary statement 4. ICD is usually the result of nonimmunologic, direct tissue reaction and yet may at times be difficult to differentiate from ACD. (A)

Summary statement 5. Spongiosis is the predominant histologic feature of CD. (A)

Susceptibility and Genetics of CD

Summary statement 6. Age- and sex-specific, but not race-specific, differences in patch test responses have been observed in several large patch test surveys. (B)

Summary statement 7. In recent years, several cytokine gene polymorphisms have been described, but their functional significance is not yet clear. (A)

Clinical Diagnosis of ACD

Historical features

Summary statement 8. The diagnosis of ACD is suspected from the clinical presentation of the rash, which then must be supported by a history of exposure to a putative agent and subsequently confirmed by patch testing whenever this is possible. (C)

Physical examination

Summary statement 9. Location. The skin site of the dermatitis is important in the diagnosis of ACD, because the area of predominant involvement and the regional distribution of the lesions often reflect the area of contact with the allergen. (A)

Summary statement 10. Eyelids. ACD is a common cause of eyelid dermatitis induced not only by locally applied cosmetics but also by agents applied to other parts of the body (ie, nail polish) that may come into contact with the eyelids. (A)

Summary statement 11. Face. Cosmetics (including vehicles and preservatives) and fragrances are the most common sensitizers of the facial skin. (B)

Summary statement 12. Scalp. Paraphenylenediamine is a common sensitizer of scalp skin. (B)

Summary statement 13. Hands. Hand dermatitis is extremely common (10% of women and 4.5% of men, aged 30–40 years). In this location, ICD and ACD are often indistinguishable. (B)

Summary statement 14. Neck. Vehicles, preservatives, drippings from permanent wave preparations, hair dyes, shampoos, conditioners, fragrances, and nickel in jewelry may produce ICD or ACD on the neck. (A)

Summary statement 15. Axilla. Contact to topically applied agents may involve the entire axillary vault, whereas allergy due to clothing leachates usually spares the apex of the vault. (B)

Summary statement 16. Lower extremities. Drug- or excipient-induced ACD of the lower extremities often occurs in patients with chronic stasis dermatitis due to increased exposure to topical medications. Less commonly, other sensitizing agents, such as shaving agents, moisturizers, and, rarely, stocking materials or dyes, should be considered. (B)

Summary statement 17. Anogenital area. Topical medications, suppositories, douches, latex condoms and diaphragms, spermaticides, lubricants (used during coitus), sprays, and anogenital cleansers are potential causes of CD in the anogenital area. (B)

Patch Tests

Summary statement 18. Epicutaneously applied patch tests are the standardized diagnostic procedures to confirm ACD. (A)

Summary statement 19. The clinical diagnosis of ACD can be complicated by atopic susceptibility. (B)

Summary statement 20. Although clinical relevance is still evolving with regard to the atopic patch test (APT), several European investigative groups have reported that this test may be an adjunct in the detection of both inhalant and food allergy in atopic dermatitis patients. (B)

Summary statement 21. Patch tests are indicated in any patient with a chronic, pruritic, eczematous, or lichenified dermatitis if underlying or secondary ACD is suspected. (C)

Summary statement 22. Patch test results are affected by oral corticosteroids, TCs, and calcineurin inhibitors but not by oral antihistamines. (A)

Summary statement 23. A screening battery of patch tests is best developed by using standardized sets of allergens previously calibrated with respect to nonirritant concentrations and compatibility with the test vehicle. (A)

Summary statement 24. Reading and interpretation of patch tests should conform to principles developed by the International Contact Dermatitis Research Group and the North American Contact Dermatitis Research Group. (A)

Summary statement 25. A 96-hour reading may be necessary, because 30% of relevant allergens that are negative at the 48-hour reading become positive in 96 hours. (A)

Summary statement 26. Interpretation of patch test results must include the possibilities of false-positive and false-negative reactions. (A)

Summary statement 27. Nonstandard and customized patch testing is often required, depending on the patient's exposure history. (C)

Summary statement 28. Several in vitro procedures are being investigated for the diagnosis of ACD. (A)

Summary statement 29. Several other tests are available for (1) identification of allergens, (2) improving the reliability of interpreting test results for leave-on products, or (3) distinguishing CD from morphologically similar diseases. (B)

Summary statement 30. Although systemic ACD after patch testing is rare, reactivation of patch test reactions may occur after oral ingestion of related allergens or even by inhalation of budesonide in patients with sensitization to topical steroids. (B)

Summary statement 31. Patch testing can sensitize a patient who had not been previously sensitized to the contactant being tested, particularly to poison ivy/oak. (B)

Differential Diagnosis of CD

Summary statement 32. The differential diagnosis for CD is influenced by many factors, such as clinical appearance of the lesions, distribution of the dermatitis, and associated systemic manifestations. (B)

Special Exposures Associated With CD

Occupational CD

Summary statement 33. OCD is an inflammatory cutaneous disease caused or aggravated by workplace exposure. (B)

Summary statement 34. There are 7 generally acceptable criteria for establishing causation and aggravation of OCD. (C)

Summary statement 35. The most common occupations associated with OCD are health professionals (especially nurses), food processors, beauticians and hairdressers, machinists, and construction workers. (A)

Summary statement 36. Among health professionals, ACD may occur as part of the spectrum of immunoreactivity to natural rubber latex (NRL) in latex gloves. (A)

Plant dermatitis

Summary statement 37. ACD from exposure to plants is the result of specific cell-mediated hypersensitivity induced by previous contact with that family of plants. (A)

Summary statement 38. Toxicodendron (Rhus) dermatitis (poison ivy, poison oak, and poison sumac) is caused by urushiol, which is found in the saps of this plant family. (A)

Summary statement 39. Sesquiterpene lactones and tuliposides are large, diverse groups of chemicals found in several plant families that cause ACD in florists, bulb growers, and others working in the floral industry. (A)

Summary statement 40. Seasonal recurrence of ACD on exposed skin surfaces may be due to airborne pollen. (B)

Summary statement 41. Since there are not standardized test antigens for all plants, the incidence of sensitivity in the general population is largely unknown but is likely to be much more common than currently recognized. (D)

Cosmetics

Summary statement 42. Cosmetics and personal hygiene products contain a variety of potential allergens that are common causes of CD, which can occasionally manifest in sites distant from the original application of the product. (B)

Summary statement 43. Although routinely used cosmetics and personal care products contain considerable numbers of chemical ingredients, the most common causes are due to a few important chemical classes. (B)

Summary statement 44. Fragrances are among the most common causes of CD in the United States. (A)

Summary statement 45. Preservatives and antibacterials are present in most aqueous-based cosmetics and personal hygiene products to prevent rancidity and microbial contamination. (A)

Summary statement 46. Formulation excipients other than preservatives and fragrances are typically defined as inert substances that serve to solubilize, emulsify, sequester, thicken, foam, lubricate, or color the active component in a product. They can be responsible for ACD or, when used in higher concentrations, can act as irritants. (A)

Summary statement 47. Hair products are second only to skin care products as the most common cause of cosmetic allergy. Cocamidopropyl betaine, paraphenylenediamine, and glycerol thioglycolate have been reported to cause ACD from hair products. (A)

Summary statement 48. Allergy to acrylics in nails can present locally at the distal digit or ectopically on the eyelids and face. (A)

Summary statement 49. Sunblocks or sunscreens, common causes of photoallergic ACD, are frequently present in cosmetics such as moisturizers, "night" creams, lip and hair preparations, and foundations. (A)

Medicinal CD

Summary statement 50. CD commonly develops after exposure to topical medications, including lanolin, para-aminobenzoic acid, "caine" derivatives, antibiotics, antihistamines, iodochlorhydroxyquin, nonsteroidal anti-inflammatory drugs (NSAIDs), and corticosteroids. (A)

Summary statement 51. ACD due to TCs may occur in up to 5% of patients presenting with suspected CD. (A)

Summary statement 52. Topical NSAID preparations that are generally available in over-the-counter preparations can frequently induce ACD. (B)

Summary statement 53. Drug APTs are being investigated as possible diagnostic adjuncts for mixed (T_H1 and T_H2) allergic cutaneous drug reactions. (C)

Allergic contact cheilitis

Summary statement 54. ACC is a common form of ACD, because the epithelium of the lips is similar to the skin. (C)

Summary statement 55. Allergic contact mucositis may be a cause of recurrent oral ulcerations. (B)

Summary statement 56. Cinnamon and peppermint flavorings are probably the most common causes of allergic stomatitis from dentifrices and chewing gum. (C)

CD due to surgical implant devices

Summary statement 57. CD to surgical implants is at times suspected, but definitive association of the reaction with the implant material is only rarely documented. (D)

Systemic CD

Summary statement 58. Allergic systemic CD is a generalized ACD rash from systemic administration of a drug, chemical, or food to which the patient previously experienced ACD. (A)

Concurrent exposure to irritants and contactant allergens

Summary statement 59. Simultaneous exposure to allergens and irritants may produce both additive and synergistic ACD responses due to their interaction. (A)

Summary statement 60. The role of detergents in hand dermatitis is a reflection of their ability to disrupt the skin barrier. (A)

ACD in Children

Summary statement 61. ACD is a significant clinical problem in children. (A)

Management and Prognosis of ACD

Acute treatment

Summary statement 62. The identification and avoidance of contact with the offending agent(s) are key to the success of ACD treatment. (A)

Summary statement 63. Topical palliative treatment may offer transient relief during the acute phases of ACD and ICD. (C)

Summary statement 64. TCs are first-line treatment for localized forms of ACD. (A)

Summary statement 65. Systemic corticosteroid therapy offers relief within 12 to 24 hours. (A)

Summary statement 66. Although TCs have been advocated for the treatment of ICD, several recent studies demonstrated that they are ineffective in suppressing experimental ICD induced by known irritants. (A)

Summary statement 67. Several topical T-cell selective inhibitors of inflammatory cytokines have been used successfully in treatment of atopic dermatitis, but their efficacy in ACD or ICD has not been established. (A)

Summary statement 68. Topical, and occasionally systemic, antibiotics should be used for secondary infections of ACD or ICD. (D)

Summary statement 69. Although antihistamines have been used for relief of pruritus associated with ACD, they are generally ineffective for this indication. (C)

Summary statement 70. Several nonspecific alternative treatment modalities are available for immunosuppression and/or long-term, refractory ACD. (C)

Summary statement 71. Patients should be instructed carefully about the causes and future risks of potential exposures to specific contactants. (D)

Prevention

Primary prevention

Summary statement 72. In high-risk industries and professions, preventive surveillance programs are possible, especially for apprentices or newly hired workers. (A)

Secondary prevention

Summary statement 73. Once the diagnosis of ACD or ICD is established, emollients, moisturizers, and/or barrier creams may be instituted as secondary prevention strategies for continued exposure. (C)

Prognosis

Summary statement 74. Long-term prognosis of ACD or ICD has only been adequately investigated in OCD. (C)

Summary statement 75. Persistent ACD has an appreciable effect on quality of life. (C)

ALGORITHM AND ANNOTATIONS:

Annotation 1: Patient presents with localized or generalized manifestations of an eczematous pruritic dermatitis.

CD is a common skin problem. All age groups are affected with a slight female preponderance. The most common presentation consists of a papulovesicular eruption, which may evolve into a pleomorphic dermatitis with hyperkeratosis, lichenification, fissuring, and scaliness. The lesions may be localized or generalized. Exposure to a putative agent may be evident. If the lesion is associated with exposure to sunlight, a photoallergic CD or a phototoxic reaction is possible. Pruritus is a prominent symptom.

Annotation 2: Evaluation of history and physical examination consistent with CD (allergic vs irritant)?

The history should elicit the suspicion that CD, either ACD or ICD, is the cause of the symptoms. The site of inflammation must have come in direct contact with the offending agent. Initially, the area may itch, burn, or sting, but as the lesion evolves, pruritus is the major symptom. Identifying the putative agent requires meticulous exploration of the history. Work and hobby history must be carefully reviewed. Careful examination of the skin may yield important clues as to what

contactants are involved. This is particularly germane to skin areas, such as eyelids, face, neck, scalp, hair, axillae, lower extremities, and the anogenital region.

Annotation 3: CD not the likely cause.

If CD is not probable based on history and physical examination, many dermatologic and/or systemic diseases should be considered. Additional evaluation should include a skin biopsy interpreted by a dermatopathologist and skin scrapings for the presence of hyphal fragments. For further delineation of the problem, the patient may be referred to a dermatologist.

Annotation 4: Is the dermatitis active or widespread?

Acute vesiculobullous ACD (eg, *Toxicodendron* dermatitis) may become widespread within a short time and may also be associated with considerable soft tissue swelling. The evolution of CD caused by other agents is usually more gradual. If the symptoms are disabling or the lesions are widespread, immediate treatment is required. Patch testing should be delayed until the acute phase is resolved because of the potential for worsening of the dermatitis and the possibility of false-positive reactions due to hyperirritability of the skin.

Annotation 5: Consider diagnostic testing. Patch test result positive?

Under ordinary circumstances, patch tests to *Toxicodendron* are not indicated. For other suspected presentations, patch testing should be offered to confirm the specific agent that is responsible for ACD. Patch testing with appropriate antigens is the gold standard for confirming ACD. Even though this is the best way to identify specific contactants, patients may not desire patch testing, particularly when avoidance of the suspected contactant is effective.

If the history is consistent with a potential contactant and patch test results to a standard battery of screening allergens (eg, TRUE Test) are negative, patch testing patients with their own products at nonirritant concentrations may be required. In some cases, contacting the manufacturer of a suspected product may be necessary to identify the ingredient(s) responsible for the ACD. If this is contemplated, toxicity and irritant reactions should be excluded by using suitable controls.

Patches should be applied to the skin of the back 2.5 cm lateral to the midspinal column. The patches are removed and results read at 48 hours. Patients should be instructed to remove patches from the irritable site(s) before 48 hours should the site of application become uncomfortably pruritic. Since 30% of reactions are negative at 48 hours, additional reading(s) should be performed at 3 or 4 and sometimes 7 days after the initial application, depending on the allergen. Patches are read according to a special scale recommended by the International Contact Dermatitis Research Group. Correct interpretation of the test result is critical, because both false-negative and false-positive test results are possible. Reactions graded as 2+ and 3+ strongly suggest the presence of prior or present sensitization to a contactant. The relevance of these test results should be interpreted by considering historical probability of exposure and the area of involved skin.

Annotation 6: Initial management.

If presenting symptoms are severe or lesions are generalized, palliative methods to control the itching and skin hydration should be instituted. Cold compresses, colloidal baths, and emollients may be helpful. Antihistamines may partially control pruritus. The mainstay of treatment is TCs. Traditionally, treatment begins with high-potency corticosteroids that may be switched to medium- or even lower-potency preparations as symptoms improve. For unusually severe or widespread ACD, systemic corticosteroids may be required. If the history is suggestive of a particular contactant, avoidance should be started immediately at this stage of treatment. Rarely, CD may be secondarily infected with staphylococcal or streptococcal bacteria, which ultimately may act as superantigens. Systemic antibiotics should be used if this is suspected. Since topical irritants such as detergents are known to augment the effects of contact allergens, they should be avoided.

Annotation 7: Avoidance of proven contact allergens.

Known contact allergens should be avoided. Patients therefore should be given complete instructions on how to avoid allergens that were detected by patch tests. This is often difficult for cosmetics, since many of the contact allergens are used in all cosmetic products even though they are purported to be nonallergenic. There are also specific circumstances where ingestion of a cross-reacting food or drug could lead to a serious systemic flare of the ACD. OCD may require counseling for not only the worker but also the responsible industrial health professional. Material safety data sheets may provide clues regarding the offending agent. Sometimes a work site visit may be helpful in determining whether a worker can continue to work in a particular job or work site.

Annotation 8: Perform additional patch tests.

If test results to standard sets of validated contact allergens are negative, it may be necessary to obtain expanded patch test kits that contain the relevant contact allergens in certain occupations or activities. At times it also may be necessary to prepare customized test reagents. Indeed, this is most productive if cosmetics are suspected. Once the suspected product produces a positive patch test result, further tests for the active or inert ingredients in the preparation can then be done. In some cases, especially with substances causing CD around the eyelids or other areas of thin skin, an open application test may be helpful. This involves applying the patch to more sensitive skin areas, such as antecubital fossae or behind the ear. Repetitive challenges are then applied to the same site daily for 1 to 2 weeks.

Annotation 9: If screening and additional test results are negative, the probable diagnosis is ICD.

ICD is generally a multifactorial response that occurs after contact with a substance that chemically abrades, physically irritates, or damages the skin. It is usually a direct cytotoxic reaction produced by a wide variety of agents and by contributory physical factors that include scrubbing, washing, overhydration, perspiration, and temperature extremes. The inflammatory reaction that results from these irritants is dose

dependent. The evolution and resolution of ICD are less predictable than ACD.

Annotation 10: Management of ICD.

Although palliative relief after use of skin hydrating and emollient agents may be helpful, avoidance of the involved irritants should be implemented whenever this is possible. The use of topical or systemic corticosteroids does not appear to offer as much relief in ICD as in ACD.

Annotation 11: Management successful?

If there is complete clearance of ACD, the patient is less likely to have a recurrence provided there is avoidance of the proven contact allergen. In occupational settings, however, clearance rates vary between 18% and 40%. Partial improvement ranges from 70% to 84%. Rarely, some workers continue to have persistent, ongoing dermatitis despite removal of exposure at work.

Annotation 12: Follow-up after initial successful treatment.

Prevention of skin dryness in patients with a proven diagnosis of CD can be attempted with the long-term use of emollients and moisturizers. The efficacy of protective barrier creams is debatable. Unfortunately, none of these secondary measures appears to be effective, especially after large amounts of exposure to skin irritants. If symptoms recur, further treatment options in Annotation 15 may be considered.

Annotation 13: Is diagnosis of CD correct?

If no improvement in symptoms or appearance of the lesions is evident, reassessment is appropriate at this stage of management. This is essential to prevent further complications, such as superinfection of the skin, excess keratinization, or, rarely, exfoliative dermatitis.

Annotation 14: Other consultation?

A dermatologist's opinion should be sought to determine whether other possible dermatologic or systemic diseases are masquerading as CD. In some cases, there is underlying dermatologic disease with secondary contact sensitization. A dermatologist can be of help in making this judgment. If other diagnostic studies, such as skin biopsy or skin scrapings for dermatophytosis, have not yet been done, the dermatologist may wish to pursue these possibilities.

Annotation 15: Additional treatment possibilities.

Further stepwise treatment options should be considered for recalcitrant CD. Several new immunophilin (calcineurin inhibitors) T-cell suppressants have been approved by the Food and Drug Administration (FDA) for atopic dermatitis. Some early studies indicate that they may also be effective in CD. Thus, a trial of one or both of these topical agents could be considered for refractory CD. If these treatments are unsuccessful, systemic corticosteroids in sufficient doses (1 mg/kg daily) should be considered. For particularly severe treatment failures, phototherapy with or without psoralen may be attempted by physicians experienced in this technique. In the case of widespread CD evolving into generalized exfoliative dermatitis, hospitalization may be required. If large areas of the skin are denuded by the exfoliative process, transfer to a burn unit for appropriate treatment is mandatory.

CLINICAL BACKGROUND

Summary statement 1. CD is a common skin disorder seen by allergists and dermatologists and can present with a spectrum of morphologic cutaneous reactions. (C)

CD is a common skin problem for which 5.7 million physician visits per year are made.[6,7] All age groups are affected, with a slight female preponderance based on a large population-based survey of public health issues.[8] The acute clinical expression of CD is characterized by redness, edema, papules, vesiculation, weeping, crusting, and pruritus most commonly recognized as eczema, a nonspecific term applied to a number of dermatides, including atopic dermatitis. Prolonged persistence of this dermatitis may be associated with acneiform eruptions secondary to irritation of follicular function, hypopigmentation or hyperpigmentation due to alterations in melanocytic biology, skin thickening, lichenification, and fissuring. Exposure to UV light most commonly causes a phototoxic or sunburn type of reaction and less commonly a photoallergic reaction when the UV light interacts with chemical agents (ie, fragrances, para-aminobenzoic acid, plants, parsnips, figs, or several ingested drugs), inducing photosensitization of various forms.

PATHOPHYSIOLOGY OF CD

Summary statement 2. The inflammatory lesions of CD may result from either allergic (ACD) or nonallergic, irritant (ICD) mechanisms. Factors that affect a response to the contact agent include the agent itself, the patient, the type and degree of exposure, and the environment. (A)

There are more than 85,000 chemicals in the world environment today. Almost any substance can cause CD, depending on circumstances, whereas more than 3,700 agents have been identified as contact allergens.[9] The potential for these substances to cause either ICD or ACD is variable. Thus, both water and detergents have a high irritancy index, whereas nickel is a major allergenic contactant chemical. The severity of the CD ranges from a mild, short-lived condition to a severe, persistent, but rarely life-threatening, disease. The thickness and integrity of the skin influence the potential for developing ICD or ACD. Thinner skin sites, such as the eyelids, ear lobes, and genital areas, are most vulnerable, whereas the thicker palms and soles are more resistant to injury induced by irritation or sensitization. Exposure time to allergenic contactants, which usually defines both induction and elicitation phases of ACD, varies from being brief (eg, poison ivy) to protracted (eg, nickel in jewelry or other chemicals in the work environment). Similarly, irritant substances may damage the skin in the short or long term.

Summary statement 3. Tissue reactions to contactants are attributable primarily to cellular immune (delayed hypersensitivity) mechanisms, except for contact urticaria. (A)

CD reactions are noted almost exclusively at the site of exposure with the putative antigen. Most ACD antigens are small-molecular-weight molecules or haptens that become immunogenic after conjugation with proteins in the skin. Less commonly, larger-molecular-weight peptides or proteins (eg,

latex, cashew nuts) may both induce and elicit the classic inflammatory lesions of ACD. The immune response in ACD requires participation of both afferent and efferent limbs.[10] The afferent limb consists of an appropriate allergen gaining entrance to the epidermis, activating keratinocytes, which release proinflammatory cytokines (interleukin [IL] 1, IL-6, IL-8, and granulocyte-macrophage colony-stimulating factor [GM-CSF]) and sequential expression of monocyte chemoattractant protein-1, RANTES, and interferon-inducible protein 10.[11] In the appropriate cytokine-chemokine milieu, the hapten-protein conjugate or protein alone is then endocytosed by special antigen-presenting, Langerhans, and/or other dendritic cells, which process and combine specific hapten peptides with HLA class I or class II presentation molecules and then migrate (within 24 hours) to draining regional lymph nodes. Dendritic cell surface bound HLA molecules that contain the specific haptenic epitope then activate and sensitize naïve $CD4^+$ T cells (T_H0 cells) in the lymph node. Once activated, these $CD4^+$ T helper cells proliferate and generate hapten-specific $CD4^+CD25^+$ regulatory and $CD8^+$ effector clones, which subsequently become either memory or effector cells. At times $CD4^+$ lymphocytes may also function as effector delayed hypersensitivity cells.[12] The $CD4^+$ regulatory/effector and $CD8^+$ effector cells then "home" to the original induction skin site and there function as the efferent limbs of the immune reaction wherein specifically sensitized effector cells (both $CD4^+$ and $CD8^+$) release their proinflammatory cytokines or cytotoxins (interferon-γ, TNF-α, GM-CSF, IL-2, perforin, granzyme), leading to spongiosis and an intense perivascular inflammatory infiltrate. This sequence of events accounts for the latency period (18–96 hours) from initial contact to the emergence of the rash. During the effector phase, considerable numbers of plasmacytoid dendritic cells also appear in close proximity to $CD56^+$ natural killer cells.[13] Subsequent exposure to sensitizing agents shortens the latent period (anamnesis). The anamnestic reaction occurs more rapidly, because certain $CD4^+$ cells are retained for long periods in the original ACD skin sites.[14] These $CD4^+$ retention or memory lymphocytes are unique in that they express the CCR10 chemokine. These persisting cells are responsible for the accelerated inflammatory response after additional allergen challenge. Resident mast cells at the site of ACD may recruit polymorphonuclear leukocytes cells to the site by the release of 2 mediators, TNF-α and IL-8.[15] A hypothesis is emerging that ACD may require interaction between irritant and antigenic properties of sensitizing chemicals. This implies that a requisite irritant domain of chemicals may be mediated through the cutaneous innate immune system.[16]

Summary statement 4. ICD is usually the result of nonimmunologic, direct tissue reaction and yet may at times be difficult to differentiate from ACD.

ICD is generally a multifactorial response that involves contact with a substance that chemically abrades, physically irritates, or damages the skin.[17] Irritation is usually a direct cytotoxic reaction produced by a wide variety of agents (eg, chemicals, detergents, solvents, alcohol, creams, lotions, ointments, and powders) and by contributory physical factors that include excessive scrubbing, washing, overhydration, improper drying, perspiration, and temperature extremes. The cellular damage of ICD may occur because inflammatory cytokines (TNF-α, IL-1, IL-8, GM-CSF) are released by T cells activated by nonimmune, irritant, or innate mechanisms. How this interaction occurs is unknown. It is hypothesized that irritants act as "danger" signals that stimulate host innate components (eg, macrophages, neutrophils, NK or NKT cells) that contribute to the inflammatory response.[18] This inflammatory reaction is dose dependent. Many allergens can also act as irritants at high concentrations.[16] Any impairment to the epidermal barrier layer (eg, fissuring, superhydration) increases skin susceptibility to an irritant defect. The evolution and resolution of ICD are less predictable than ACD. The clinical presentation of ICD is more limited to the skin site directly in contact with the offending agent(s), with little or no extension beyond the site of contact.

Summary statement 5. Spongiosis is the predominant histologic feature of CD. (A)

Spongiosis is edema of the intercellular epidermal cells that may lead to stretching and eventual rupture of the intercellular attachments and vesicle formation.[19] These vesicles may coalesce and become large or, in more severe cases, lead to disintegration of the suprapapillary epidermis. Secondary changes from scratching may cause superficial erosions, hemorrhage, or fibrinoid changes. Histopathologically, there are certain features that suggest ICD rather than ACD.[20] In general, there is more spongiosis in ACD than in ICD. Irritants tend to cause more necrosis, acantholysis, and pustulosis. However, despite these features that suggest one or the other diagnosis, there is no distinct dermatopathologic feature that is diagnostic of either ICD or ACD.[21] This may be complicated by the fact that some allergens are also potential irritants.

Noninvasive reflectance, confocal microscopy is a novel method of visualization of human skin and the histopathologic features of CD.[20] Compared with patch tests alone without specific allergen or irritant, ICD was demonstrated to be associated with increased epidermal thickness, whereas ACD showed microvesicle formation, peaking at 96 hours after patch removal. Both ACD and ICD showed exocytosis and a similar degree of spongiosis. From previous animal studies, it was thought that cytotoxic T cells were critically involved in the mononuclear cell infiltrate of ACD. In support of these data, a recent investigation of patients with ACD revealed that perforin and granzyme B in the cytoplasm of both $CD4^+$ and $CD8^+$ lymphocytes were located not only in the perivascular infiltrate but also at sites of marked spongiosis in the epidermis.[22]

SUSCEPTIBILITY AND GENETICS OF CD

Summary statement 6. Age- and sex-specific, but not race-specific, differences in patch test responses have been observed in several large patch test surveys. (B)

The prevalence of CD is slightly increased in women, presumably due to frequent exposure to specific contactants (eg, cosmetics).[8] A cross-sectional study in adolescents (12–16 years of age) demonstrated similar sexual predominance.[23] There is age variability, with peaks at the age of 10 years through the teen years and at the ages of 40 to 60 years, and a subsequent study demonstrated decreased prevalence in patients older than 70 years.[24,25] There are no overall differences in either irritant or allergic thresholds (including poison ivy) in blacks vs whites except for differences in the use of specific sensitizers (eg, paraphenylenediamine).[26,27] Once dermatitis occurs in blacks, it is often complicated by hyperpigmentation and lichenification unless treated early and vigorously with TCs.[28] Irritant thresholds for ICD were reported to be lower in Japanese than white women, but subsequently this finding was not confirmed.[29–31] The latter study demonstrated that Japanese women have a higher rate of self-reported skin sensitivity compared with German women, as evaluated by a lactic acid stinging test.[31]

Summary statement 7. In recent years, several cytokine gene polymorphisms have been described, but their functional significance is not yet clear. (A)

Certain cytokine gene polymorphisms (TNF-α and IL-16 genotypes) tend to be more common in polysensitized individuals.[32,33] Recently, keratinocyte CD80 gene up-regulation was found to be useful in predicting ACD for specific sensitizers.[34] A preliminary study using Affymetrix gene chip analysis suggested that as many as 26 differentially expressed genes may function as potential diagnostic markers for ACD.[35] Interestingly, a TNF-α gene polymorphism at position 308 appears to confer increased irritant susceptibility in healthy persons.[36]

CLINICAL DIAGNOSIS OF ACD

Historical Features

Summary statement 8. The diagnosis of ACD is suspected from the clinical presentation of the rash, which then must be supported by a history of exposure to a putative agent and subsequently confirmed by patch testing whenever this is possible. (C)

The suspicion of ACD is the first step in making the diagnosis. Thus, the history remains an essential part of the diagnosis and subsequent management of this disease. Although history can strongly suggest the cause of ACD, it has been reported that experienced physicians accurately predict the sensitizer in only 10% to 20% of patients with ACD when relying solely on the history and physical examination.[19]

For ACD to occur, the site of inflammation must have come in direct contact with the offending agent. Initially, the area may itch, burn, or sting. The evolution of the lesion depends on multiple factors, including the innate allergenicity or irritancy of the agent, the integrity of the involved skin, environmental conditions, a history of prior reactions, and immunocompetency status. Activities that involve exposure to sun, water, or airborne allergens may affect the skin distribution. Remissions and exacerbations may be related to weekends, vacations, and work schedule.

Work history must be carefully reviewed. The exact nature of the work duration of each activity and similar skin effects in coworkers may be relevant. Recent changes in procedure or chemical exposures, including vapors and fumes, must be probed. Protective wear and compliance with its use may give a clue as to the nature of the suspected allergen. Certain jobs require frequent hand washing and the use of special cleansing agents that not only may impair skin barrier but also may cause irritant hand dermatitis. Although moisturizers after hand washing may prevent dehydration, they may expose the patient to unsuspected allergens in the moisturizer preparation. Since the worker may be unaware of specific chemicals to which he or she is exposed, material safety data sheets may have to be obtained from the manufacturer.[37] Chronologic exposure histories and other activities must be obtained.

Hobbies and nonwork activity, such as gardening, macramé, painting, ceramic work, carpentry, and photography, may be sources of exposure to other contactants. Obtaining a detailed history of animal exposure is essential. Pet dander, products used on pets, and traces of outdoor allergens all can cause ACD. The history should also include response to previous treatment. Many patients will have tried to eliminate multiple agents or have used various remedies before seeing a physician.

Physical Examination

Summary statement 9. Location. The skin site of the dermatitis is important in the diagnosis of ACD, because the area of predominant involvement and the regional distribution of the lesions often reflect the area of contact with the allergen. (A)

All inflammatory and spongiotic clinical reactions should include ACD as a possibility. Each lesional site usually corresponds to the site of contact with the putative allergen and the physical appearance of the lesion may also suggest the potential for ACD. Particular attention should be given to certain anatomical sites, which include eyelids, face, neck, scalp, hands, axillae, lower extremities, and the anogenital area. Each of these anatomical areas will be described in greater detail in summary statements 10 to 17.

Summary statement 10. Eyelids. ACD is a common cause of eyelid dermatitis induced not only by locally applied cosmetics but also by agents applied to other parts of the body (eg, nail polish) that may come into contact with the eyelids. (A)

ACD is the most common identifiable cause of eyelid dermatitis.[38] Because of constant aerogenic exposure and access to irritants (volatile agents) and allergens (eg, pollens), minimal barrier protection, and a tendency to be touched often, eyelids are particularly susceptible to ACD.[39,40] One study of patients with CD on their eyelids revealed ACD in 151 (74%) of 203 patients.[41] Chronic eyelid dermatitis is more often due to cosmetics applied to the hair, face, or fingernails than to agents applied directly to the eyelid.[42] For

example, fingernail hardeners such as sulfonamide-formaldehyde resins, fingernail coatings that polymerize (ie, acrylates), and artificial nails are frequent causes of eyelid ACD.[42,43] Exposure history should include not only cosmetics but also methods of application and removal (eg, rubber sponges).[44–46] The use of eyelash curlers can be a source of contact with nickel or rubber. Facial tissues may be perfumed or contain formaldehyde or benzalkonium chloride.[47] Neomycin and TCs are commonly used by many patients and rank high as suspected sensitizers. Shampoos, conditioners, hair sprays, gels, and mousse may cause eyelid dermatitis without scalp or forehead involvement with allergens, with cocamidopropyl betaine/amidoamine leading the list. Paraphenylenediamine and ammonium persulfate applied to the scalp may cause symmetrical eyelid edema with or without urticaria.[48] Periorbital dermatitis due to the external use of ophthalmic drugs is also a more obvious cause at times.[49] Chronic, "irritant" eyelid dermatitis may have started from rubbing the eyes in 25% of patients with IgE-mediated allergic conjunctivitis.[6] Many important eyelid dermatitis allergens are typically not found in standard allergen batteries and require supplemental testing to the product itself or component chemicals in the product.

Summary statement 11. Face. Cosmetics (including vehicles and preservatives) and fragrances are the most common sensitizers of the facial skin. (B)

Similar to eyelid dermatitis, facial ACD often occurs secondarily when contactants are brought to the face from other regions of the body. Direct contact with the product can also cause facial ACD, as can, rarely, skin exposure to airborne allergens (eg, tree, weed pollens).[40–45,50,51] According to a ruling of the Federal Food, Drug, and Cosmetic Act, all cosmetics to be used around the eyes are placed in a special category wherein no recognized highly allergic substance (including vehicles and preservatives) may be used in the periorbital vicinity.[52] Nevertheless, products labeled "hypoallergenic" include the most common sensitizers found in products that do not claim to be hypoallergenic.[53] Highly sensitive individuals may react to rubber sponges, masks, balloons, and children's toys if these come in contact with the face.[46] A partner's fragrance and cosmetics also may be causes of a localized facial lesion.[54] Patients who complain of stinging, burning, or itching without objective findings may be experiencing irritant-type reactions to topical agents (eg, aftershave lotions), which include benzoic acid, formaldehyde, lactic acid, sorbic acid, propylene glycol acid, and urea. A number of relevant sensitizing preservatives and vehicle ingredients are not included in standard allergen batteries and require supplemental testing to detect possible sensitization.

Summary statement 12. Scalp. Paraphenylenediamine is a common sensitizer of scalp skin. (B)

Scalp skin is relatively resistant to allergic sensitization despite the many agents applied to this area. Hair dye that contains paraphenylenediamine is the most common sensitizer in scalp skin.[55] In fact, the manufacturer's instructions for hair dyes recommend patch testing before each application. Irritant reactions to hair straighteners and relaxers are not uncommon and may result from improper use. Periorbital edema or dermatitis of the forehead and neck may often be the presenting symptoms of scalp reactions.

Summary statement 13. Hands. Hand dermatitis is extremely common (10% of women and 4.5% of men, aged 30–40 years). In this location, ICD and ACD are often indistinguishable. (B)

Both ICD and ACD occur chiefly on the dorsa of both hands, because the thickness of palmar skin is protective.[56] Hand dermatitis, both ICD and ACD, occurs frequently after occupational exposure. "Wet" occupations (eg, food processors, housewives, health professionals) and the handling of solvents often establish an absolute or irritant template for subsequent ACD. The physical appearance of ICD and ACD of the hands is similar, although the presence of vesicles is less commonly observed in ICD.[57] Appropriate designation of patch test materials for the evaluation of hand dermatitis depends strongly on determining occupational and recreational exposures.

Summary statement 14. Neck. Vehicles, preservatives, drippings from permanent wave preparations, hair dyes, shampoos, conditioners, fragrances, and nickel in jewelry may produce ICD or ACD on the neck. (A)

Similar to the eyelids and genitalia, the skin of the neck is very reactive, making it more susceptible to both induction and elicitation of contact sensitization. Nickel dermatitis usually corresponds to the areas of the neck in contact with jewelry and appliances (zippers) that contain this material. Permanent wave preparations, hair dyes, shampoos, and conditioners may produce either ICD or ACD. Vehicles, excipients, and preservatives in these agents must also be suspected. Dermatitis from perfumes (berloque dermatitis) or nail polish may produce a localized area of involvement where these agents have been applied.

Summary statement 15. Axilla. Contact to topically applied agents may involve the entire axillary vault, whereas allergy due to clothing leachates usually spares the apex of the vault. (B)

The agents that come in contact with the axilla of the skin include antiperspirants (with or without deodorants), dyes, and resin systems that leach out of clothing in sweat. The chief ingredient in most antiperspirants is aluminum hydroxide, which may be irritating but rarely causes ACD. However, cutaneous granulomata and skin sensitivity have been reported when it is complexed with zirconium and glycine.[58] Deodorants include fragrances and other common sensitizers that require patch testing for confirmation.[59] Leachates from permanent press, wash-and-wear apparel, which contain formaldehyde-based resin systems, and formaldehyde-releasing preservatives found in cosmetics may induce ACD. Use of shaving and depilatory agents for removal of axillary hairs is more likely to cause ICD. Textile-based resin systems and dyes and most cosmetic preservative systems are not present in standard allergen batteries and require supplemental testing.

Summary statement 16. Lower extremities. Drug- or excipient-induced ACD of the lower extremities often occurs in patients with chronic stasis dermatitis due to increased exposure to topical medications. Less commonly, other sensitizing agents, such as shaving agents, moisturizers, and, rarely, stocking materials or dyes, should be considered. (B)

The decreased barrier function of stasis dermatitis permits easy access for small-molecular-weight molecules. Occasionally, increased absorption of a topical medication through this site may cause systemic sensitization and a generalized eruption sometimes referred to as an ID reaction. Sensitization to topical treatments used for leg ulcers (eg, bacitracin, neomycin, corticosteroids, and excipients) is common.[60] A meta-analysis revealed sensitization rates of 75% and 57% to 1 or 2 agents, respectively. High sensitization rates of reports before 1990 persist in recent studies.[61]

Summary statement 17. Anogenital region. Topical medications, suppositories, douches, latex condoms and diaphragms, spermaticides, lubricants (used during coitus), sprays, and anogenital cleansers are potential causes of CD in the anogenital area. (B)

Patch tests on 1,008 patients evaluated for anogenital dermatitis revealed that 23% and 35% had ICD and ACD, respectively. The remaining patients were classified as having nonspecific dermatitis.[62] Active agents, preservatives, or other excipients in topical medications and popular remedies cause most ACD and ICD in the vulvar region.[63] Lanolin sensitization remains relatively low (1.7%), whereas sensitization to wool alcohols is more common (6%).[64] Hand-transferred agents, such as *Toxicodendron* alkaloids and nail polish, may also be causes. Fragrance dermatitis may be encountered in scented liners, diapers, toilet paper, soap, and bubble baths. Contraceptive methods, such as use of a diaphragm or condoms, may affect rubber-sensitive individuals.[46] Ammonia in the urine can cause an irritant dermatitis, especially in infants and incontinent patients. The ingestion of spices, antibiotics, or laxatives may cause or aggravate anal itching. The possibility of sensitization to a partner's seminal fluid can only be determined by direct questioning, because patients are frequently reluctant to consider this possibility.[65]

PATCH TESTS

Summary statement 18. Epicutaneously applied patch tests are the standardized diagnostic procedures to confirm ACD. (A)

Patch testing is the gold standard for identification of a contact allergen.[66] Although occlusive patch testing is the most common technique, open, prophetic (provocative), repeated insult, photopatch and APTs are also available if special situations indicate their use. For example, open patch tests are preferred for potential photosensitizers, volatile substances, mascara, antiperspirants, shaving creams, dentifrices, and strong topical medicaments that could act as relative primary irritants. If photosensitization is suspected, photopatch tests should be performed by a physician with expertise in UV radiation. Duplicate applications of the suspected photocontactant(s) are placed on each side of the upper back. One side is irradiated with 5 J cm^{-2} of UV-A 24 to 48 hours later and both radiated and unradiated sides are read 48 hours later.

The number of appropriate patch tests required to diagnose ACD may vary, depending on the nature of the clinical problem and the potential for significant allergen exposure. The value of a test depends on whether the clinical presentation warrants its use, the quality of reagents used, the timing of the application, an appropriate interpretation of the reaction, and establishing relevance for the benefit of the patient. Although the application of allergen patch testing is rather simple, allergen selection, the proper test concentration, and interpretation of the test require expertise. Clinical research defining the validity of each of these components has been extensive. Such data are well described in textbooks and a Practice Parameter for Allergy Diagnostic Testing.[38,67–69] These sources provide details for the purchase and/or preparation of allergens and materials for application, forms for record keeping, preparation of patch test sites, application of the allergens, times of reading, and interpretation according to internationally approved guidelines.[66,68] Because it is impractical to test an unlimited number of contactants, standardized sets have been designed and validated by collaborative dermatologic societies.[70–74] However, use of the FDA-certified antigen panel available in the United States can fully evaluate approximately 25% to 30% of patients with ACD, especially those patients who are allergic to rubber, metals, fragrances, cosmetics, and medicaments.[74] These vary somewhat to reflect differences in exposure patterns in different parts of the world. New allergens are added from time to time, depending on changes of product utilization and exposure patterns. Since 2001, the North American Contact Dermatitis Group has enlarged its standard panel to 65 allergens and/or allergen mixes.

Summary statement 19. The clinical diagnosis of ACD can be complicated by atopic susceptibility. (B)

It is estimated that atopic patients comprise 25% to 30% of the total population.[75] Clinical studies that compare rates of ACD between atopic and nonatopic patients are controversial.[38,76,77] Patients with atopic dermatitis have an impaired skin barrier that is thought to predispose them to greater risk of irritation and allergic sensitization.[77,78] It has been noted that occupational ICD occurs more commonly in atopic persons.[38] On patch testing, atopic individuals are more likely to develop deeper dermal reactions with minimal epidermal changes to some allergens. In particular, they may develop false-positive, pustular reactions to some allergens, particularly nickel. Patch testing a patient with active atopic dermatitis is more likely to produce an "angry back" reaction, resulting in a false-positive reading.[38]

Summary statement 20. Although clinical relevance is still evolving with regard to the APT, several European investigative groups have reported that this test may be an adjunct

in the detection of both inhalant and food allergy in atopic dermatitis patients. (B)

Evaluation of APTs as a diagnostic adjunct for IgE-mediated inhalant and food allergy in atopic dermatitis patients has occurred chiefly in non–North American international centers. Because these tests are as yet not standardized, attempts are ongoing to establish reliable systems for evaluation of clinical relevance. In patients being tested for aeroallergen reactivity, allergen specific concordance of APTs was compared with prick and puncture tests and Pharmacia UniCap tests with 2 different concentrations and using 2 different vehicles. Optimal concordance was obtained when petrolatum was the vehicle and allergy concentration was more than 1,000 PNU/g.[79] Reproducibility was also tested with the allergens from different commercial sources. Reproducibility was 56% using the same manufacturer's extracts but much less than when 2 different commercial extracts were compared.[80] An interesting insight into APTs was provided by a recent report that compared routine histologic analysis and in situ hybridization between involved and noninvolved skin of atopic dermatitis patients who exhibited positive APT results. A positive APT reaction required the presence of epidermal IgE on the surface of CD1a positive cells in both clinically involved and noninvolved skin.[81]

Although unicenter studies have disagreed about the overall reliability of APT for the diagnosis of inhalant allergy in atopic dermatitis patients,[82–86] a large multicenter European study concluded that APTs had a higher specificity (64%–91%), depending on the allergen, than skin prick and puncture (50%–85%) or in vitro IgE tests (52%–85%). Positive APT reactions were not seen in 10 nonatopic controls. The conclusion of this study was that the potential for aeroallergens as causes of AD may be evaluated by APTs in addition to prick and puncture and in vitro IgE tests.[87]

With respect to the diagnosis of food allergy by APT in atopic dermatitis patients, several European investigative groups have reported that APTs may be adjunctive diagnostic methods of evaluating food allergy in atopic dermatitis patients, especially those patients having nonimmediate, late-phase, or delayed reactions and in younger subjects (6 years).[88] In eosinophilic esophagitis, the combination of prick and puncture tests and APTs led to the discovery of causative foods in 8 of 26 cases.[89] However, it is unlikely that APTs will have wide applicability in North America until issues of standardization and reproducibility of these tests are more fully resolved.

Summary statement 21. Patch tests are indicated in any patient with a chronic, pruritic, eczematous, or lichenified dermatitis if underlying or secondary ACD is suspected. (A)

Virtually any eczematous lesion could be caused or aggravated by a contactant.[17,70–73,90,91] The decision to patch test under these circumstances is often independent of the history, because the patient may be unaware of any relevant exposure. Based on additional tests in patients with the "angry back" syndrome, it is recommended that patch testing should be deferred until the underlying dermatitis is no longer acute or severe.[92] Under such circumstances, the entire skin may be irritable and false-positive reactions may occur. There is always the possibility that a positive patch test result may trigger an exacerbation of the original dermatitis. In this situation, however, negative patch test results to a standard battery of allergens can be valuable in ruling out a suspected agent.

Summary statement 22. Patch test results are affected by oral corticosteroids, TCs, and calcineurin inhibitors but not by oral antihistamines. (A)

Immunocompromised adult patients, including those taking oral corticosteroids (≥20 mg/d of prednisone or its equivalent) or those undergoing cancer chemotherapy may show diminished or absent reactivity to the patch tests.[93,94] A multicenter, randomized, double-blind study revealed that systemic steroids in doses of 20 mg/d or less were not likely to suppress strongly positive patch test results, but they could suppress milder responses.[94] The same study concluded that equivalent doses of prednisone did not affect irritant responses.[94] The effect of systemic corticosteroids on the results of patch testing is less understood for children.

The skin site where the patch tests are to be applied should have had no topical potent corticosteroid or calcineurin inhibitor applied for 5 to 7 days before testing, since local anti-inflammatory effects of these agents can diminish or obliterate a possible positive test result. Systemic antihistamines do not affect the interpretation of patch tests. Surprisingly, patients who have late human immunodeficiency virus disease are still reactive to contact allergens.[95]

Summary statement 23. A screening battery of patch tests is best developed by using standardized sets of allergens previously calibrated with respect to nonirritant concentrations and compatibility with the test vehicle. (A)

Aluminum is the major substrate for current patch tests because of its low allergenicity.[96,97] The Finn chamber is the most popular system and uses small 8-mm (inner diameter) aluminum chambers that are occlusive and permit more accurate quantification of the dose of allergen per unit area of skin. Individual Finn chambers are filled with contactants and applied at the time of testing. The chamber is applied to the skin and held in place by hypoallergenic tape. The thin layer rapid use epicutaneous test (TRUE Test) is an FDA-approved method for screening contactant allergens. The TRUE Test is preloaded with 23 common contactants and vehicle control that have been previously incorporated into a dried-in-gel delivery system, which is coated onto a polyester backing to form a patch template. When the template is applied to the skin, the allergens are released as the gel becomes moisturized by transepidermal water. A recent retrospective survey recommended that standardized tests encompass at least 50 allergens, because an expanded group of allergens may more accurately identify positive and relevant allergens than the TRUE Test.[98]

Although many contact allergens have been identified and reported, most cases of ACD are due to only several dozen substances. Fewer than 40 allergens produce most cases of

ACD. A recent US patch test survey demonstrated that the 10 most frequent positive reactions were caused by nickel, balsam of Peru, neomycin, cobalt, fragrance mix, potassium dichromate, bacitracin, thimerosal, formaldehyde, and glutaraldehyde.[99] Identification of the actual sensitizer in a complex product can be daunting at times. Contaminating chemicals and minor ingredients may be the actual allergen(s), whereas the parent compound or major component(s) was originally considered to be the sensitizer. In some contactant tests, when mixtures such as balsam of Peru cause a positive reaction, it is difficult to determine the precise chemical antigen. In other cases, the hapten may be an altered product metabolized after contact of the substance to skin has occurred. The allergens formulated in the TRUE Test panel are likely to identify only a few clinically relevant ACD.[77,97,98,100] Selected panels of contactant allergens based on the patient's history may be required to supplement the screening panel of allergens and cover as completely as possible the range of exposures of the patient.[100] Although such screening panels are not FDA approved, they conform to standards of care recommended by CD experts.[77,100] Kits for specific occupations (eg, hairdressers, machinists) and exposures (eg, shoes, plants, photoallergens) permit identification of other significant contactant allergens. Each new antigen that is evaluated requires identification, validation, and determination of the minimal eliciting concentration, as well as the zero-level irritant concentration for appropriate patch testing. Smaller chamber sizes may be required for infants and children.

The chambers are applied to the upper or midback areas (2.5 cm lateral to a midspinal reference point), which must be free of dermatitis and hair. If shaving is required, an electric razor is preferable. Similar standard (but not FDA approved) test sets are available in Canada (Trolab-Pharmascience Inc, 8400 ch Darnley Road, CND-Montreal, Quebec H4T 1 M4; Chemotechnique, Dormer Lab, Toronto, Ottawa), Europe, China, and Japan.[6,73] The occlusive patches should be kept in place and dry for a period of 48 hours unless a severe reaction, such as significant discomfort at the site, to the patch ingredient occurs.

Summary statement 24. Reading and interpretation of patch tests should conform to principles developed by the International Contact Dermatitis Research Group and the North American Contact Dermatitis Research Group. (A)

Summary statement 25. A 96-hour reading may be necessary, because 30% of relevant allergens that are negative at the 48-hour reading become positive in 96 hours. (A)

The initial reading of patch tests should be done 48 hours after their application. Tests may need to be read 30 minutes after removal of the patch to allow resolution of erythema due to occluding pressure or the tape and/or chamber if present. Ideally, there should be an additional reading 3 to 4 days after the initial application and occasionally after 7 days for certain contactants.[101–103] A collaborative study documented that approximately 30% of relevant allergens that were negative at the 48-hour reading become positive at a 96-hour reading.[104] Conversely, some irritant reactions at 48 hours tended to disappear by 96 hours. The reading itself is based on a nonlinear, descriptive scale that was developed and validated by the International Contact Dermatitis Research Group.[76] The details of this rating system and corresponding clinical interpretation with a visual key are given in the Appendix. In general, there is good concordance of positive patch test results between individual Finn chamber tests and the True technology, as well as among different commercial manufacturers.[105–108] As shown in the Appendix, the relevance of positive reactions to clinical ACD can only be established by carefully correlating the history, including exposure to the allergen with the test results.[107,109] Laser Doppler perfusion imaging of cutaneous blood flow has been proposed as an alternative to visual reading.[110] This technique correlates with visual scoring but is not useful in distinguishing between allergic and irritant reactions.[111]

Summary statement 26. Interpretation of patch tests must include the possibilities of false-positive and false-negative reactions. (A)

The major cause of spurious outcomes is faulty technique, which is correctable by training. The greatest source of misinterpretation is due to questionable or irreproducible reactions in the equivocal $\pm$ or 1+ categories. Inability to separate irritant from allergic responses is often encountered in patients who exhibit the "angry back" or "excited skin" syndrome, presenting as generalized reactivity to most or all allergens in the test battery. A recent prospective study revealed that this occurred in 6.2% of tested patients and was more likely to develop in patients with a longer duration of the primary dermatitis.[92] The position of allergen in the multiple allergen template may also give rise to the false-positive results, especially if cross-reacting or cosensitizing substances are tested in too close proximity.[112]

Summary statement 27. Nonstandardized and customized patch testing is often required, depending on the patient's exposure history. (C)

When an agent not included in the "standard" set is suspected, kits for specific occupations (eg, beauty operators, machinists) and exposures (eg, shoes, plants, photoallergens) permit identification of many other significant allergens. At present, such kits can only be obtained from the manufacturers listed in Table 1. Not infrequently, it may be necessary to customize patch tests in accordance with a patient's specific exposure history. Leave-on cosmetics (eg, nail polish, lipstick, rouge, foundation), clothing, gloves, and foods may be applied as is. Wash-off cosmetics (eg, shampoo, conditioners, cleansers) should be diluted (10^{-2} or 10^{-3}) before application.[38,76] Other household and industrial products should only be tested after ascertaining their safety in material safety data sheet background information and in accord with an authoritative text on patch test concentrations.[9] Even after this research, nonirritant concentrations may need to be performed in unexposed controls if more precise toxic information cannot be obtained from recently developed in vitro dermal corrosion data bases (eg, Corrositex).[113] Corrositex is

Table 1. Commercial Sources of Special Kits and Customized Patch Testing

Sources of allergens	Finn chambers
Dormer Laboratories, Inc Chemotechnique Laboratories 91 Kelfield St (Unit 5) Rexdale, Ontario Canada Tel: 416-242-6167 Fax: 416-242-9487	Allerderm Laboratories, Inc. 3400 E McDowell Rd Phoenix, AZ 85008 USA Tel: 1-800-878-3837 Fax: 1-800-926-4568
Omniderm Inc Trolab Allergens 8400 Darnley Rd Montreal, Quebec Canada H4T 1M4 Tel: 514-340-1114 or 1-800-363-8805 ext 3038	

one of a series of in vitro irritancy tests currently being evaluated as alternatives to animal irritancy tests.[114,115]

Whenever possible, customized contactants should be incorporated into a petrolatum base, because aqueous vehicles are more likely to penetrate the stratum corneum and give consistently negative results. In performing customized patch testing, it is preferable to test 1 or 2 unexposed control subjects at the same time as the patient. Various standard sets of contactant allergens are constantly being updated by international CD research groups with the goal of eliminating agents being encountered less often and adding "new" more frequently used substances.[73,107,116,117] Recently, the question of proper pretesting probability evaluation has been raised with the purpose of discouraging random patch testing, which has a low pretest predictive probability.[118] It is postulated that pretest probabilities can be estimated by the data of large-scale prevalence studies of contact allergy in the general population. Using these data, likelihood ratios and post–patch test probability of contact allergy can be ascertained.[118]

If photosensitization is suspected, photopatch tests should be performed by a physician with expertise in UV radiation. Duplicate applications of the suspected photocontactant(s) are placed on each side of the upper back. One side is irradiated with 5 J cm^{-2} of UV-A 24 to 48 hours later and both irradiated and unradiated sides are measured 48 hours after irradiation.[119]

Summary statement 28. Several in vitro procedures are being investigated for the diagnosis of ACD. (A)

The potential for induction and elicitation of sensitization is augmented if the allergen also has the ability to induce irritant signals, presumably through the innate immune system.[120] Irritant signals may induce the synthesis and release of proinflammatory cytokines, such as TNF-α, IL-1, IL-8, and GM-CSF.[120] Thus, there is a rationale for developing alternative in vitro diagnostic tests. The lymphocyte transformation test is mostly used for research purposes.[69] Recently, an enzyme-linked immunospot assay, specifically designed to detect contactant-induced cellular release of cytokines (interferon-γ, IL-2, IL-4) by the patient's peripheral mononuclear cells, was compared with patch tests and lymphocyte transformation test. Overall, there was a statistically significant relationship ($P < .05$) among the 3 tests.[121] Several recent research methods for classifying allergenic potency of contact allergens could possibly facilitate the clinical utility and reliability of patch tests in the future.[122–125]

Summary statement 29. Several other tests are available for (1) identification of allergens, (2) improving the reliability of interpreting tests for leave-on products, or (3) distinguishing CD from morphologically similar diseases. (B)

Sometimes chemical analysis of a material may identify the presence of a contactant allergen. The most commonly used test of this nature is the dimethyl-glyoxime test for nickel.[126]

The repeat open application test is an exaggerated-use test that involves the application of a suspected allergen to the antecubital fossa twice daily up to 1 to 2 weeks and observing for dermatitis in the same area.[127] This is primarily indicated for leave-on products intended for use on the skin. Because eyelid skin is more reactive than skin in other locales, patch test responses may be negative on the skin of the back even to a known sensitizing agent. In such instances, repeat open application test can be performed by applying the patch test to the back of the ear or the antecubital fossa.

Skin biopsy may be helpful in differentiating ACD from other morphologically similar diseases. To exclude cutaneous fungal diseases, skin scrapings for culture and a potassium hydroxide preparation (for detection of hyphal fragments) may be considered.

Summary statement 30. Although systemic ACD after patch testing is rare, reactivation of patch test reactions may occur after oral ingestion of related allergens or even by inhalation of budesonide in patients with sensitization to topical steroids. (B)

Summary statement 31. Patch testing can sensitize a patient who had not been previously sensitized to the contactant being tested, particularly to poison ivy or poison oak. (B)

Systemic ACD occurring after patch testing is rare.[104] However, it is not uncommon for patients to experience local flares on patch test sites after peroral challenges with fragrance-containing foods, Chinese herbs, contactant chemicals (eg, nickel, gold), or drugs.[128–132] Reactivation of patch test reactions caused by budesonide have also been reported after inhalation of the same drug weeks after the positive patch test result.[133] Exaggerated local reactions may also be encountered if the concentration of the patch test is too strong, thereby causing both irritant and exaggerated allergic reactions. There is also the possibility of sensitizing a patient who had not been previously sensitive to the allergen being tested. This is particularly true of plant allergens, such as poison ivy or poison oak.[77] The possibility of active sensitization can be minimized by testing with dilute solutions of various materials. Foods that are prone to cause ACD and also have the ability to cause systemic CD include flavoring agents (eg, oil of cinnamon, vanilla, balsam of Peru), various spices, garlic, cashew nuts, and proteinaceous substances handled by grocers, meat and fish handlers, and bakers.[134–138]

DIFFERENTIAL DIAGNOSIS OF CD

Summary statement 32. The differential diagnosis for CD is influenced by many factors, such as clinical appearance of the lesions, distribution of the dermatitis, and associated systemic manifestations. (B)

Clinically, CD is an eczematous disease. Eczema encompasses a group of pleomorphic, cutaneous disorders (with or without identifiable exogenous causes) that present with an inflammatory tissue response. The diagnosis of CD is based on the clinical appearance and the presence of intercellular edema of the epidermis known as spongiosis with varying degrees of acanthosis and superficial perivascular, lymphohistiocytic infiltrate.[19,67] Clinically, the lesions of CD range from red clustered papules to vesicles and bullae. Scaling and pruritus are prominent features. There are many dermatologic entities that may simulate the clinical appearance of CD at various stages of their evolution. Table 2 summarizes this extensive differential diagnosis.

SPECIAL EXPOSURES ASSOCIATED WITH CD

OCD

Summary statement 33. OCD is an inflammatory cutaneous disease caused or aggravated by workplace exposure. (B)

According to the US Bureau of Labor Statistics, occupational skin diseases (chiefly ICD and ACD) rank second only to traumatic injuries as the most common type of occupational disease. In 1999, the incidence rate of occupational skin disorders was 49 cases per 100,000 (http://www.cdc.gov/niosh/ocdrm1.htm). The OCD rate tends to be highest in small plants (<500 workers), because they lack comprehensive health care programs. Chemical irritants such as solvents and cutting fluids account for most ICD cases.[139,140] More than 40% of Worker's Compensation cases involve the skin, and it is estimated that OCD constitutes 90% to 95% of all occupational skin diseases and that ICD is found in 70% to 80% of all OCD.[141,142] Of 5,839 patients tested in a collaborative study of the North American Contact Dermatitis Group, 1,097 (19%) were deemed to be occupationally related.[143] Sixty percent were allergic and 32% were irritant. Hands were primarily affected in 64% of ACD and 80% of ICD. Carba mix, thiuram mix, epoxy resin, formaldehyde, and nickel were the most common allergens.[143]

Reducing this cost to industry and preventing morbidity in workers should be the goal of occupational medical experts.[144] Unfortunately, distinction rarely is made between ICD and ACD, either retrospectively or in ongoing surveillance programs.

Summary statement 34. There are 7 generally acceptable criteria for establishing causation and aggravation of OCD. (C)

Table 2. Major Conditions That May Be Investigated in the Differential Diagnosis of Contact Dermatitis

Primary skin diseases	Systemic diseases
Atopic dermatitis	Wiskott-Aldrich syndrome
Lichen simplex dermatitis;	X-linked agammaglobulinemia
Neurodermatitis; prurigo nodularis	Phenylketonuria
Nummular dermatitis	Acrodermatitis enteropathica
Dyshidrotic dermatitis	Hurler syndrome
Seborrheic dermatitis	Chronic granulomatous disease
Psoriasis	Hyper-IgE syndrome
Dermatophytosis	Drug reactions
Polymorphous light eruption	Dermatophytid ID reaction
Impetigo	Connective tissue diseases
Acne rosacea	(lupus erythematosus, dermatomyositis)
Factitial dermatitis	Porphyria cutanea tarda
Intertrigo	Mycosis fungoides
Erythrasma	
Lichen planus	
Scabies	
Pyoderma gangrenosum	

The responsibility for determining that dermatitis was caused or aggravated by employment is incumbent on the examining physician. As a practical guideline for this evaluation, Mathias[145] proposed 7 criteria for confirming this judgment. These include (1) the clinical appearance is consistent with CD; (2) potential cutaneous irritants or allergens are present in the workplace; (3) the anatomic distribution of dermatitis is consistent with skin exposure to chemicals in the course of various job tasks; (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) dermatitis improves away from work exposure and reexposure causes exacerbation; and (7) there are positive-reaction and relevant patch tests performed according to established guidelines.[94] Four of the 7 criteria must be positive to conclude that dermatitis is OCD. The validity of the Mathias criteria was recently confirmed in a 2- to 5-year prospective study.[146]

Summary statement 35. The most common occupations associated with OCD are health professionals (especially nurses), food processors, beauticians and hairdressers, machinists, and construction workers. (A)

In the United States, more than half of all proven OCD cases are seen in the manufacturing and service industries, with the highest incidence rate reported in agriculture, forestry, and fishing.[147–156] Included in the services category are health professions, food processors, and beauticians and hairdressers.

Several large prospective surveillance studies reported that more than half of all proven cases of OCD are included in these trades or professions.[148,149,153] When hand OCD was evaluated in Denmark, the most frequently recognized diagnosis was ICD, mainly occurring in "wet" occupations, and the prevalence was equal for males and females.[156] Occupational ACD was higher among males, with the most frequent causes being chromium (leather exposure), rubber additives (gloves), and nickel (work tools and metal working). In food processing workers, the prevailing factors were exposure to food ingredients (even intact proteins) and hand washing.[150–152] One smaller retrospective analysis of patch test data in 537 patients revealed that ACD occurred more often (16% of patients) than ICD.[153] In 132 farmers with suspected OCD, ACD induced by metals, disinfectants, rubber, and pesticides were chiefly noted.[157–161] Less commonly, they reacted to colophony, lanolin, and propolis (especially bee keepers).[161] The CD lesions in farmers were frequently aggravated by irritating chemicals in fertilizers and pesticides.[158–160]

Summary statement 36. Among health professionals, ACD may occur as part of the spectrum of immunoreactivity to NRL in latex gloves. (A)

With the advent of acquired immunodeficiency syndrome and consequent universal barrier control required for health professionals, the repetitive use of latex gloves eventuated in a progressive increase in the prevalence of both occupational and nonoccupational reactions, both immune mediated and irritant.[162–166] Clinical responses were chiefly IgE mediated, including contact urticaria, rhinitis, asthma, and/or anaphylaxis. In most cases, these clinical events could be confirmed by specific prick or in vitro tests.[167,168] However, a large multicenter, prospective study conducted by the British Contact Dermatitis Group revealed that 1% of patients with hand eczema had positive patch test results to NRL.[46] Health care workers may develop ACD to other chemicals in rubber gloves, including bisphenol A in vinyl gloves.[169,170] In such instances, patch tests to various rubber mix chemicals or the suspected article itself are appropriate. Patients with proven ACD may experience flares of generalized or localized dermatitis after ingestion of foods cross-reactive with NRL (see Practice Parameters on Food Allergy and Anaphylaxis).

Plant Dermatitis

Summary statement 37. ACD from exposure to plants is the result of specific cell-mediated hypersensitivity induced by previous contact with that family of plants. (A)

Toxicodendron dermatitis (poison ivy) is the most common form of ACD and can be readily identified by its streak-like or linear papulovesicular presentation (isomorphic Koebner reaction). Although the poison ivy group of plants (Anacardiaceae) causes most cases of plant dermatitis, other plants that are common sensitizers are given in Table 3. The sensitizing substances in most plants are present mainly in the oleoresin fraction; in some plants, the allergens are water-soluble glucosides. Most plants must be crushed to release the antigenic chemicals.

Table 3. Common Non-*Rhus* Plant Contactants

	Common names	Antigen
Ambrosia	Giant and dwarf ragweed	Sesquiterpene lactones
Compositae	Chrysanthemums and daisies	Sesquiterene
Liliaceae	Tulips, hyacinth, asparagus, garlic	Tuliposide
Amaryllidaceae	Daffodil and narcissus	Unknown
Primrose	Primula (a household plant)	Primin
Umbelliferae	Carrots, celery and parsnips	Unknown
Cannabinaceae	Nettles (hops)	Unknown
Rutaceae	Oranges, lemons, grapefruits	Unknown

Summary statement 38. Toxicodendron (*Rhus*) dermatitis (poison ivy, poison oak, and poison sumac) is caused by urushiol, which is found in the saps of this plant family. (A)

Toxicodendron-containing plants grow practically everywhere in the United States (except Hawaii, Alaska, and some of the desert country in Nevada) and affect up to 50 million Americans every year. Urushiol readily oozes from any cut or crushed part of the plant.[6] This oleoresin is invisible and spreads very easily. It can be carried on the fur of animals, garden tools, and sports equipment and can even be disseminated in the smoke of burning leaves. Urushiol rapidly penetrates the stratum corneum, and rinsing should be performed with great expediency to prevent clinical disease. Sensitivity to *Toxicodendron* usually develops after several repetitive encounters with the plants, which in some cases may only occur after many years of exposure. Studies have shown that approximately 85% of the population will develop a clinical reaction when exposed. Ten percent to 15% of the population is believed to be highly susceptible to poison ivy and poison oak. These people develop systemic sensitization manifested as rashes with accompanying swelling of the face, arms, and genitalia. Sensitivity changes with time and tends to decline with age. In sensitive individuals, the rash appears in the form of a line or a streak within 12 to 48 hours. Redness and swelling precede the vesiculation and pruritus. In a few days the vesicles rupture, form crusts, and then scale. The dermatitis will not spread due to touching or scratching at this stage, because the vesicle fluid does not contain urushiol. Resolution typically occurs in 2 to 4 weeks and occasionally may persist for 1 to 2 months.

The *Toxicodendron* dermatitis is similar whether caused by poison ivy, poison oak, or poison sumac. Interestingly, urushiol is also contained in mango skin,[134] cashew nut oil, ginkgo (female) leaves, Japanese lacquer, and Indian marking ink. Patch testing is not indicated for *Toxicodendron* dermatitis, because the dermatitis is self-limiting and usually readily diagnosable and there is a danger of exacerbating ACD.

Summary statement 39. Sesquiterpene lactones and tuliposides are large, diverse groups of chemicals found in several plant families that cause ACD in florists, bulb growers, and others working in the floral industry. (A)

In the United States, *Alstroemeria*, also called Peruvian lily, is the most frequent cause of hand eczema in flower workers.[171] This classic dermatitis is a chronic, lichenified eczematous and intensely pruritic eruption that affects the first 3 fingers and exposed areas of dorsal hands, forearms, the V-region of the neck and the face. Recurrent summertime flares during plant growing seasons and winter remissions are typical. The presentation often simulates a photodermatitis, although the upper eyelids and antecubital fossae may be involved, which would be somewhat unusual for photodermatoses.

Summary statement 40. Seasonal recurrence of ACD on exposed skin surfaces may be due to airborne pollen. (B)

Repetitive exposure to the oleoresins in airborne pollen may induce and elicit ACD in susceptible patients. This has been reported particularly for *Ambrosia* pollen, but sporadic instances of ACD to tree and grass pollen also occur.[42,50] Epidemic ACD occurs after exposure to *Parthenium* pollen in countries such as India and Australia.[172]

Summary statement 41. Since there are not standardized test antigens for all plants, the incidence of sensitivity in the general population is largely unknown but is likely to be much more common than currently recognized. (D)

Open patch testing with fresh plants or flowers is of value when the results are positive and may cause severe bullous reactions due to high allergen content in this type of exposure. The positive reaction must be differentiated from an irritant reaction by testing nonsensitized controls. Cross-reactivity with balsam of Peru and other fragrance materials is not uncommon. Negative reactions may be false negative, presumably because of the lack of standardized test antigens.

Cosmetics

Summary statement 42. Cosmetics and personal hygiene products contain a variety of potential allergens that are common causes of CD, which can occasionally manifest in sites distant from the original application of the product. (B)

It is not unusual for individuals to apply dozens of personal hygiene products to their skin on a daily basis. Such products can include aromatic soaps and cleansers, emollients for day and night use, hair care products (acrylic nails, 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.[6,38,76,77]

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 toluene sulfonamide formaldehyde resin in nail polish, which may cause an eyelid dermatitis yet leave the periungual skin and distal fingers clear.[173] Also, patients allergic to hair products that contain cocamidopropyl betaine, a surfactant in shampoo, can present with eyelid dermatitis without concurrent dermatitis on the scalp, neck, and ears.[48,174]

Summary statement 43. Although routinely used cosmetics and personal care products contain considerable numbers of chemical ingredients, the most common causes are due to a few important chemical classes. (B)

In aggregate, the number of chemical contactants used by an individual patient in a typical day can mount to 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, glues, and sun blocks.[143,175–177]

Summary statement 44. Fragrances are among the most common causes of CD in the United States. (A)

Fragrances are regularly present in cosmetics and personal hygiene products, either to achieve an appealing scent or to mask unpleasant odors, and the labeling of products with regard to fragrance can be confusing.[47,178–181] The use of the term *unscented* can erroneously suggest that a product does not contain fragrance when, in fact, a masking fragrance is present. For fragrance-allergic individuals, this type of product is not a suitable substitute. *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. The inclusion of these extracts may be for the purpose of improving odor characteristics rather than the overtly expressed use.[182]

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. Unfortunately, allergy to fragrances may be difficult to detect because of the wide variety of product vehicles that carry it. Hence, individuals may be exposed to fragrance chemicals in their shampoos, conditioners, cosmetics, moisturizers, soaps, laundry detergents, and fabric softeners.

It is necessary to patch test to appropriate screening chemicals for detection of delayed hypersensitivity to this group of allergens.[183–188] A fragrance mix that is popularly used for this purpose contains 9 difference fragrance ingredients that are tested as a single mix. This mix includes oak moss, absolute, cinnamic aldehyde, cinnamic alcohol, α-amyl cinnamic alcohol, geraniol, hydroxycitronellal, isoeugenol, and eugenol. Recent evidence suggests that this fragrance mix will detect approximately 85% of fragrance-allergic individuals. The addition of other commonly used fragrance ingredients (ylang ylang oil, narcissus oil, sandalwood oil, and balsam of Peru) increases the yield to 96%.[178]

The elucidation of fragrance allergy should result in advising an avoidance protocol that involves the elimination of all fragranced cosmetics and personal hygiene products. Since current labeling laws do not require manufacturers to label a specific fragrance present in a product, consumers may have to eliminate far more material from their daily living activities than would be necessary if this information was available. 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.

Summary statement 45. Preservatives and antibacterials are present in most aqueous-based cosmetics and personal hygiene products to prevent rancidity and microbial contamination. (A)

Many preservative systems have been developed in the hope of providing the broadest antimicrobial coverage with the lowest potential for contact sensitivity. These preservatives tend to be grouped into 2 broad categories: formaldehyde donors (products that emit formaldehyde) and nonformaldehyde donors.[189–191] Like fragrances, the clinical presentation of preservative allergy depends on the formulation vehicle. Testing to those allergens that have high rates of contact allergy determined by recent epidemiologic studies offers the best chance of detecting contact sensitivity.[189–192] Table 4 is a list of preservative systems commonly used in cosmetic and personal care products.[177]

Although parabens formulated in cosmetics are infrequent causes of ACD, they can induce ACD when they are used as antibacterials in topical medications.[76,193] This sensitization disparity is commonly known as the paraben paradox.

Summary statement 46. Formulation excipients other than preservatives and fragrances are typically defined as inert substances that serve to solubilize, emulsify, sequester, thicken, foam, lubricate, or color the active component in a product. They can be responsible for ACD or, when used in higher concentrations, can act as irritants. (A)

Contact allergy to formulation chemicals presents in locations of direct contact with the allergen-containing products.[177,190,191] However, given the omnipresence of these chemicals in almost every cosmetic product, predicting the precise allergen in suspected cosmetics is difficult. Table 5 is a collation of representative excipient ingredients that have been reported to cause ACD.

Summary statement 47. Hair products are second only to skin care products as the most common cause of cosmetic allergy. Cocamidopropyl betaine, paraphenylenediamine, and glycerol thioglycolate have been reported to cause ACD from hair products. (A)

Reports of allergy to cocoamidopropyl betaine, an amphoteric surfactant often found in shampoos, bath products, and

Table 4. Classification of Preservative Agents in Cosmetics

Formaldehyde releasers	Nonformaldehyde systems
• Diazolidinyl urea	• Parabens
• Imidazolindinyl urea	• Methylchloroisothiazolinone/methylisothiazolinone
• Quaternium-15	• Methyldibromoglutaronitrile/phenoxyethanol
• DMDM hydration	• PCMX/PCMC
• Bromonitropropane	• Benzalkonium chloride
	• Thimerosal

Table 5. The Chief Excipient Chemicals That Cause Allergic Contact Dermatitis

Antioxidants (sulfites)	Propylene glycol	Enzylkonium chloride
EDTA	Ethylenediamine	Cetrimide
Several FD&C colorants	Butylene glycol	Vegetable gums
Lanolin	Polyethylene glycol	Chlorocresol
Chloramine-T	Triethanolamine	Thimerosal
	Butyl alcohol	

eye and facial cleaners, are increasing.[71,194,195] Positive reactions to this allergen are often clinically relevant. In addition to routine hair care products, cosmetic hair products used intermittently as permanent and semipermanent hair dye (eg, henna) and permanent wave solutions are commonly used. The active ingredient in many hair dyes is paraphenylenediamine, which is currently the most common cause of CD in hairdressers.[48,55] Glycerol thioglycolate is the active ingredient in permanent wave solution. Unlike paraphenylenediamine, 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 permanent, and hairdressers allergic to it may be unable to cut or shape permanent waved hair.[196]

Summary statement 48. Allergy to acrylics in nails can present locally at the distal digit or ectopically on the eyelids and face. (A)

There are 3 main techniques for sculpting nails, an increasingly popular practice.[197] Nails can be molded using an acrylic monomer in the presence of an organic peroxide and accelerator. Photo-bonded, sculptured acrylate nails require exposure to UV radiation for polymerization and hardening to occur. Cyanoacrylates are used to bond a silk wrap or plastic tip to the nail. Since 1974, the FDA prohibited the use of methyl methacrylate in nail cosmetics because of reports of severe ACD, paronychia, or even onychia.

Currently marketed products contain various methacrylate ester monomers, dimethylacrylates, and trimethylacrylates, as well as cyanoacrylate-based glues. Patch testing to a variety of acrylates and nail polish resins may be necessary to delineate the causative agent. Ethylacrylate has been demonstrated to detect a higher number of acrylate allergic patients. Formaldehyde-based nail resins should also be suspected and tested when ectopic facial dermatitis is present.

Summary statement 49. Sunblocks or sunscreens, common causes of photoallergic ACD, are frequently present in cosmetics such as moisturizers, "night" creams, lip and hair preparations, and foundations. (A)

Sunblocks are often overlooked as a cause of CD, since other excipients are more frequently implicated.[6] They are capable of causing ACD even in the absence of photoactivation. "Chemical-free" sun blocks use physical-blocking agents instead of photoactive chemicals. They include micronized titanium dioxide and zinc oxide and are rare sensitizers. Table 6 summarizes the most frequently used sunscreen agents.

Medicinal CD

Summary statement 50. CD commonly develops after exposure to topical medications, including lanolin, para-aminobenzoic acid, "caine" derivatives, antibiotics, antihistamines, iodochlorhydroxyquin, NSAIDs, and corticosteroids. (A)

If an eruption worsens, rather than improves, after the application of lanolin, para-aminobenzoic acid (in sunscreens), "caines" (anti-itch preparations), antibiotics, antihistamines, and/or corticosteroids, patch testing to the suspected topical agent should be considered.[198–203] Neomycin, bacitracin, and iodochlorhydroxyquin are well-known sensitizers. When a topical sensitizing agent is used systemically in sensitive individuals, CD can occur at the original site of sensitization.

Summary statement 51. ACD due to TCs may occur in up to 5% of patients with suspected CD. (A)

Corticosteroids are used extensively in all areas of medicine and are administered orally, parenterally, intralesionally, intra-articularly, intrathecally, by inhaled nasal/asthma dispensers. and topically to the skin.[204,205] Certain groups of diseases put patients at increased risk of corticosteroid ACD. These include treatment of refractory eczema, leg ulcers, and stasis dermatitis.[205] The patient usually notes a failure to improve or experiences a flare-up of the underlying dermatitis being treated with the TC. Patch testing to corticosteroids is complicated by the therapeutic, anti-inflammatory nature of the drug itself, which results in frequent false-negative results. Patch test readings should also be done 7 days after application because of the immunosuppressant nature of the test reagent itself.[206]

The most commonly used screening agents in patch testing for TC allergy are budesonide and 1% tixocortol

Table 6. The Most Common Cosmetic Sunscreen Agents

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

Table 7. Topical Corticosteroid Preparations Classified by Relative Potency

Brand name	Generic name	Vehicle
Group 1: superpotent		
Clobex	0.05% Clobetasol	Lotion, spray, shampoo
Cormax	0.05% Clobetasol	Cream, ointment, solution
Diprolene	0.05% Augmented betamethasone dipropionate	Ointment
Olux	0.05% Clobetasol	Foam
Psorcon	0.05% Diflorasone diacetate	Cream, ointment
Temovate	0.05% Clobetasol	Cream, ointment, solution
Ultravate	0.05% Halobetasol	Cream, ointment
Vanos	Fluocinonide	Cream
Group 2: High potency		
Cyclocort	0.1% Amcinonide	Ointment
Diprolene AF	0.05% Augmented betamethasone dipropionate	Cream
Diprosone	0.05% Betamethasone dipropionate	Ointment
Florone	0.05% Diflorasone diacetate	Ointment
Halog	0.1% Halcinonide	Cream, ointment
Lidex	0.05% Fluocinonide	Cream, ointment, gel
Topicort	0.05%–0.25% Desoximetasone	Cream, gel, ointment
Group 3: mid to high potency		
Aristocort	0.5% Triamcinolone acetonide	Cream, ointment
Cutivate	0.005% Fluticasone propionate	Ointment
Cyclocort	0.1% Amcinonide	Cream, ointment, lotion
Diprosone	0.05% Betamethasone	Cream
Elocon	0.1% Mometasone furoate	Ointment
Group 4: mid potency		
Cloderm	0.1% Clocortolone pivalate	Cream
Elocon	0.1% Mometasone furoate	Cream
Kenalog	0.1% Triamcinolone	Ointment
Luxiq	0.12% Betamethasone valerate	Foam
Pandel	0.1% Hydrocortisone probutate	Cream
Synalar	0.025% Fluocinolone	Ointment
Valisone	0.1% Betamethasone valerate	Ointment, cream, lotion
Westcort	0.2% Hydrocortisone valerate	Ointment
Group 5: mid to low potency		
Cordran	0.05% Flurandrenolide	Cream, lotion
Cutivate	0.05% Fluticasone propionate	Cream
Locoid	0.1% Hydrocortisone butyrate	Cream
Westcort	0.2% Hydrocortisone valerate	Cream
Westcort	0.1% Hydrocortisone butyrate	Cream
Group 6: low potency		
Aclovate	0.05% Alclometasone dipropionate	Cream, ointment
DesOwen	0.05% Desonide	Cream, ointment
Tridesilon	0.05% Desonide	Cream
Valisone	0.01% Betamethasone valerate	Cream
Group 7: low potency		
Hydrocortisone	1% and 2.5%	Cream, ointment, solution, lotion

tivalate in petrolatum.[207] Because these allergens do not detect all cases of sensitivity, other screening agents have been suggested. Coopman et al[208] have suggested that 4 major groups of corticosteroid preparations should suffice, because there is considerable cross-reactivity within groups and possible cross-reactivity between them. For budesonide testing, Rhinocort nasal formula can be sprayed onto a Finn chamber and used as a patch test.[209] Testing with the patient's own corticosteroid product may be required for definitive evaluation of possible corticosteroid allergy. Ferguson et al[207] have reported that intracutaneous tests demonstrate allergic reactivity when corticosteroid patch test results are negative. Sensitized patients must be instructed to avoid corticosteroid administration by nontopical (including inhalant and oral) routes, because such treatment may cause local and distant flare-up of ACD.

Summary statement 52. Topical NSAID preparations that are generally available in over-the-counter preparations can frequently induce ACD. (B)

Topical NSAID preparations are used chiefly in over-the-counter preparations. Numerous case reports indicate that these agents cause not only ACD but also several forms of allergic contact photodermatitis.[210–213] Changes may be barely visible or may vary from a mild erythema to a fiery red color with or without edema.

Summary statement 53. Drug APTs are being investigated as possible diagnostic adjuncts for mixed (T_H1 and T_H2) allergic cutaneous drug reactions. (C)

For a determination of possible mixed cutaneous drug allergy, drug patch tests are performed with high concentrations of the commercial form of the drug.[214] It has been determined that 30% is the highest concentration possible for preparation of homogenous dispersion in petrolatum, water, or ethanol. To avoid serious reactions, dilutions ranging from 1% to 10% may be preferable for specific drugs. If a commercial tablet is used, the coating must first be removed before the substance within the tablet is pulverized to a fine powder. The powder is then incorporated into white petrolatum at a concentration of 30% and also diluted at the same concentration in aqueous solvents. Powder contained in capsules is also tested at 30% in petrolatum or solvent. The jacket portion of the capsule is moistened and tested as is. Liquid formulations are tested both as is and diluted 30% in solvent. Various formulations are loaded into Finn chambers and placed on the upper back. Because some drugs can cause immediate positive reactions, drug patch test results have to be read in 20 minutes. For delayed hypersensitivity readings, it is necessary to read the patches at 48 and 96 hours and, if negative, on day 7.[214] An open topical provocation is also used for the diagnosis of mixed cutaneous drug eruptions. One modification of the open technique is to incorporate drug preparations into dimethylsulfoxide, which enhances absorption.[215] This method has been successful for the diagnosis of metamizol- and naproxen-induced fixed drug eruptions.[215]

Thus far, there have been no collaborative efforts to suggest standardizing of APTs for the diagnosis of drug allergies. Results are highly variable at present, and it is impossible to predict whether such testing will ultimately be generally useful in the diagnosis of mixed cutaneous allergic drug reaction. It should be emphasized that such tests are inappropriate and potentially life threatening if used for detection of IgE-mediated drug allergy.

AACC

Summary statement 54. ACC is a common form of ACD, because the epithelium of the lips is similar to the skin. (C)

Dryness and fissuring may be the first signs of ACC. Later edema and crusting appear.[76,77] Contactants to both oral mucosa and lips can induce ACC. Some of the common ACC contactants include dentifrices, lipsticks, lip balms, nail polish, cigarette paper, various essential oils, and mangoes (in *Toxicodendron*-sensitive patients). Many ingredients in lipsticks and lip balms can cause ACC. Lipstick dermatitis involves vermilion borders of the lips, and lesions range from mild redness to edema and crusting. Occasionally food-induced ACC (eg, orange peel) must be distinguished from the oral allergy syndrome. Since cheilitis has a broad differential diagnosis, care should be taken to rule out other diseases before a presumptive diagnosis of ACC is made.

Summary statement 55. Allergic contact mucositis may be a cause of recurrent oral ulcerations. (B)

Summary statement 56. Cinnamon and peppermint flavorings are probably the most common causes of allergic stomatitis from dentifrices and chewing gum. (B)

Itching and vesiculation are rare signs of contact mucositis.[216–220] Objectively, changes may be barely visible or may vary from a mild erythema to a fiery red color with or without edema. Allergic mucosal dermatitis is often accompanied by a periorificial CD manifesting as an eczematous eruption with pruritus and scaling.[221] Chemical and traumatic injury may be the most common contact reaction of mucous membranes. Many of these are caused by chemical caustic agents inadvertently applied during dental or vaginal treatment. Aspirin placed next to a sore tooth is a common cause of irritant dermatitis or mucosal ulcer.[222] Dental and mouth care products contain abrasives and sensitizing chemicals, including cinnamon and peppermint flavorings, which are probably the most common causes of allergic stomatitis.[223] Metals used in dentistry that have been responsible for CD include mercury, chromium, nickel, gold, cobalt, beryllium, and palladium. Contact hypersensitivity to mercury is not related to so-called amalgam disease, which has received extensive and probably inordinate coverage in the lay and medical media. The current literature on this issue provides no objective evidence of a role for amalgam in human disease other than as a possible cause of ACD.[177,224,225]

The differential diagnosis of mucous membrane disease includes precancerous and cancerous lesions, viral and fungal infections, aphthous ulcers, lichen planus, especially in human immunodeficiency virus–infected patients, and the Melkersson-Rosenthal syndrome. Patch testing for causes of allergic contact mucositis need not be applied to the mucous membranes directly, since skin is a reliable surrogate of allergic contact mucositis.[226]

CD Due to Surgical Implant Devices

Summary statement 57. CD to surgical implants is at times suspected, but definitive association of the reaction with the implant material is only rarely documented. (D)

The reported clinical manifestations of such reactions include rashes and implant loosening. True allergic delayed-type hypersensitivity reactions should be suspected if they occur in a temporal relationship with the surgery.[227] The criteria for diagnosis of a cutaneous implant–induced reaction are (1) dermatitis (localized or generalized) appearing after implant surgery, (2) persistent dermatitis that is resistant to appropriate therapies, (3) a positive patch test result proven history to a metallic component of the implant or to commonly used acrylic glues, and (4) resolution of the dermatitis

after removal of the implant.[228] Although patch testing to metals or other implanted materials will help to identify previously sensitized individuals, they are unreliable in predicting or confirming implant reactions.[229] Prior history of metal (eg, nickel in costume jewelry) ACD and/or preoperative testing to implant metals may be useful to screen patients who may have the potential for an implant reaction. In the event that there are temporally related cutaneous signs of a response, sensitivity to the implanted materials (eg, metals or acrylates) should be considered.[230] Gold-plated and stainless steel (which contains nickel and molybdenum) intracoronary stents that cause restenosis are associated with an increased prevalence of patch test reactivity to these metals.[231,232]

Systemic CD

Summary statement 58. Allergic systemic contact CD is a generalized ACD rash from systemic administration of a drug, chemical, or food to which the patient previously experienced ACD. (A)

Patients with ACD reactions to ethylenediamine may have a "systemic" eczematous dermatitis from intravenous aminophylline, which contains ethylenediamine, or from antihistamines having piperazine or ethanolamine groups.[177,233] Patients allergic to topical antihistamines (eg, Benadryl cream) may develop systemic CD after systemic administration of diphenhydramine. Diabetic patients previously sensitized to topical sulfanilamide and benzocaine drugs can have widespread systemic ACD from orally administered hypoglycemic drugs, such as tolbutamide or chlorpropamide, which contain a paraminosulfonamide moiety. Reactions have also occurred after systemic and intra-articular use of corticosteroids to which a patient had been topically sensitized. Extremely sensitive nickel patients may develop a systemic reaction from ingestion of nickel in tap water or foods cooked in nickel-containing cooking utensils.[234,235] Local and systemic flares of gold ACD have been reported after intramuscular injection of gold sodium thiomalate.[236] There are anecdotal reports that citrus (oranges, lemon, grapefruit), spices (cinnamon, cloves, vanilla, curry, allspice, anise, ginger), spicy condiments (chili), chocolate, cola, and tomatoes cause systemic ACD reactions in patients with documented fragrance-related ACD.[237] Unusual cases of systemic ACD to ingested nutrients have also been reported.[238,239]

Concurrent Exposure to Irritants and Contactant Allergens

Summary statement 59. Simultaneous exposure to allergens and irritants may produce both additive and synergistic ACD responses due to their interaction. (A)

Up-regulation of TNF-α, IL-1, IL-8, and GM-CSF by an irritant or the irritant domain of an allergen is important for initiation of ACD.[18] Another possible interaction is that the irritant may facilitate penetration of the allergen. Conversely, patients with positive patch test results tend to have a lower irritant threshold and thus greater susceptibility to skin irritation.[240] Several investigations have documented that exposure to irritants before or at the same time as allergen patch tests significantly decreased elicitation thresholds and concentration required for patch test reactivity.[241,242]

Summary statement 60. The role of detergents in hand dermatitis is a reflection of their ability to disrupt the skin barrier. (A)

In a prospective, controlled study of consumers for evaluation of potential ACD to granular and liquid detergents, 0.7% had a positive patch test result.[243] On further testing, these reactions either could not be replicated or were identical to control patch test sites. These findings suggest that this was an irritant rather than an allergic response. By contrast, other investigators have found evidence of ACD hand dermatitis. In a separate investigation of ACD in patients with hand dermatitis vs nonhand ACD, ACD was less common in hand dermatitis (47%) than nonhand dermatitis (63%).[177] However, ACD was more common in vesicular and fissured forms than hyperkeratotic and pompholyx-like hand dermatitis. Taken together, these studies emphasize the important role of barrier injury as a prerequisite to ACD.

ACD IN CHILDREN

Summary statement 61. ACD is a significant clinical problem in children. (A)

Although less frequent in the first years of life (ie, before the age of 10 years), the rate of occurrence beginning at this age and through the teen years attains and even exceeds that observed in adults.[244,245] The order and prevalence of ACD to individual allergens are generally comparable to a general adult population, with nickel, fragrances, and rubber chemicals being similar in occurrence in the 2 groups of patients.[246] The influence of fashion trends, hobbies, and lifestyle activity, such as body piercing, decorative skin paintings (eg, black henna tattoo), natural remedies, and cosmetics (eg, tea tree oil), or the use of products with fragrances and herbal ingredients are important determinants for ACD in this age group.[246–248]

MANAGEMENT AND PROGNOSIS OF ACD

Acute Treatment

Summary statement 62. The identification and avoidance of contact with the offending agent(s) is key to the success of ACD treatment. (A)

When the agent(s) causing the dermatitis is identified, successfully withdrawn, and avoided, recovery can be anticipated. If contact continues (as in OCD), the dermatitis may become chronic, disabling, generalized, and a serious threat to continued employment and quality of life in patients. Despite these admonitions, some patients choose to continue working where their exposure to contactants persists.[142] On occasion, a visit to the site of exposure may help to identify the patient's allergen and whether it would be possible to avoid contact. Avoidance of contact with sensitizing plants may be difficult due to their widespread prevalence in nature

and their frequent presence in herbal medicines, toiletries, and cosmetics.

Summary statement 63. Topical palliative treatment may offer transient relief during the acute phases of ACD and ICD. (C)

For topical palliation, cold compresses with water alone are usually effective for both ACD and ICD. At times, saline, Burrow solution (aluminum subacetate), or other soothing agents (eg, Aveeno) may be used. Calamine and colloidal oatmeal baths may help to dry and soothe acute, oozing lesions. Since ICD is more apt to manifest itself immediately after contact, thorough rinsing with water or neutralizing nonirritating acids or bases is recommended. For hand dermatitis, excessive handwashing should be discouraged and instead the patient should be instructed to use emulsions as substitutes and moisturizing after washing.[249]

Summary statement 64. TCs are first-line treatment for localized forms of ACD. (A)

Since the introduction of TCs, ACD has provided a propitious model for investigating different TC potencies.[250,251] Surprisingly few long-term randomized clinical trials of high- or ultrahigh-potency TCs have been published in recent years.[252,253] More recent assays of efficacy and potency have been conducted in experimental human nickel CD.[254,255]

Selection of TC for efficacy and potency is determined by the size of the lesion, the location of the dermatitis, and the phase of evolution (ie, acute or chronic). Table 7 classifies the 7 major groups of corticosteroids by relative potency compared with vasoconstrictor responses. However, a recent investigation demonstrated that the vasoconstrictor assay is likely to be equivalent to the steroid anti-inflammatory effects.[256]

When lesions are localized in small areas of the body, TCs may suffice, but when more than 20% of the body is involved, systemic therapy is warranted. Ointments and potent fluorinated corticosteroids should be avoided on areas of thinner skin (eg, flexural surfaces, eyelids, face); lower-potency products are best in these areas. Patients should be instructed to apply topical steroids sparingly and after hydration (ie, a bath or shower), when they are most effective. Application of the medication more frequently than indicated (ie, twice daily) is not more effective. Localized acute lesions respond best with midpotency to high-potency TCs.[255]

Summary statement 65. Systemic corticosteroid therapy offers relief within 12 to 24 hours (A)

If ACD involves extensive skin areas (>20%), systemic corticosteroid therapy is often required and offers relief within 12 to 24 hours. The recommended dose is 0.5 to 1 mg/kg daily for 5 to 7 days, and only if the patient is comfortable at that time is the dose reduced by 50% for the next 5 to 7 days. Thereafter, the rate of reduction of steroid dosage depends on factors such as severity, duration of ACD, and how effectively the contactant can be avoided. The anti-inflammatory effects of these drugs do not change the natural history of ACD, but they offer the patient relief from the inflammatory reaction. Rarely, ACD may persist for up to and beyond 28 days even after removal of the causative agent.[257] If the lesions are generalized, there is danger of exfoliative dermatitis, which could evolve into a serious loss of skin barrier protection. It is not prudent to continue giving patients prophylactic systemic corticosteroids or TCs when the sensitizing agent cannot be avoided. Examples of indications for systemic corticosteroid therapy include severe *Toxicodendron* dermatitis, systemic CD, and widespread ACD from any cause.[258]

Summary statement 66. Although TCs have been advocated for the treatment of ICD, several recent studies demonstrated that they are ineffective in suppressing experimental ICD induced by known irritants. (A)

Using objective measurements, including histology, transepidermal water loss, visual grading, and squamometry, 2 recent studies reported that corticosteroids were ineffective in treating surfactant-induced irritant dermatitis.[259,260] However, in one of the studies, a significant reduction in the number of cycling keratinocytes was associated with corticosteroid treatment. Even in this study, there was no change in erythema scoring or transepidermal water loss.[259] Since it is difficult to distinguish clinically between ACD and ICD, the overall efficacy of TCs cannot be defined until appropriate studies are done.

Summary statement 67. Several topical T-cell selective inhibitors of inflammatory cytokines have been used successfully in treatment of atopic dermatitis, but their efficacy in ACD or ICD has not been established. (A)

Tacrolimus is an immunophilin ligand with similar blockage effects of T-cell activation demonstrated by parenteral cyclosporine. Several early studies suggest that it may be effective in ACD, but thus far there are no published randomized, double-blind studies to verify these preliminary results.[261] Pimecrolimus is an azomycin macrolactam developed for the treatment of inflammatory skin diseases.[262] In a murine model, it appears to exert a more selective immunomodulatory effect by inhibiting the elicitation phase without affecting the sensitization phase of ACD.[263] Although several preliminary studies suggest that pimecrolimus may be effective in the treatment of ACD, one controlled study reported

Table 8. Supplementary Textbook References on Contact Dermatitis

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that it was ineffective in the treatment of ongoing *Toxicodendron* ACD in humans.[261,262,264]

Summary statement 68. Topical, and occasionally systemic, antibiotics should be used for secondary infections of ACD or ICD. (D)

Rarely, CD may become secondarily impetiginized. Some cases of sudden aggravation of ACD or ICD can be explained in this manner. If this is suspected, topical antibiotics may be indicated.[265–267] Both should be used primarily for superficial infections of limited extent and for the prevention of recurrent or more serious infections. Disinfectants are more often used to abolish chronic infectious colonizations.[267] If staphylococcus or β-hemolytic streptococcus bacterial infections supervene, proteins from these organisms may act as superantigens and cause polyclonal T-cell activation by binding directly to T-cell receptor major histocompatibility class 2 complex. This circumstance warrants systemic antibiotics, primarily antistaphylococcal agents.[265]

Summary statement 69. Although antihistamines have been used for relief of pruritus associated with ACD, they are generally ineffective for this indication. (D)

Although antihistamines generally are not effective for pruritus, they are commonly used. Anecdotally, sedation from more soporific antihistamines may offer some degree of palliation.[76] However, oral diphenhydramine (Benadryl) may be contraindicated in patients with CD to Caladryl (diphenhydramine in a calamine base). The same caveat applies to administration of hydroxyzine hydrochloride (Atarax) in a ethylenediamine-sensitive patient.[77]

Summary statement 70. Several nonspecific alternative treatment modalities are available for immunosuppression and/or long-term, refractory ACD. (C)

Immunomodulatory agents, such as azathioprine, cyclosporine, and thalidomide, have been used in refractory ACD.[257,268]

UV-B radiation may be tried initially.[269,270] If this fails, psoralen combined with UV-A phototherapy may be attempted. These procedures are usually performed under the supervision of a dermatologist. For refractory chronic hand dermatitis, several types of ionizing radiation (conventional superficial and Grenz) x-ray examinations may be used.[271]

Summary statement 71. Patients should be instructed carefully about the causes and future potential risks of exposures to specific contactants. (D)

As is the case for OCD, patient education about avoiding possible triggers and irritant factors is crucial. Self-management plans for preventing dehydration and treating recurrent lesions properly should be advised to prevent subacute or chronic ACD or ICD. Patient information sheets are available from a variety of sources (see Appendix).

Prevention

Primary prevention

Summary statement 72. In high-risk industries and professions, preventive surveillance programs are possible, especially for apprentices or newly hired workers. (A)

Surveillance of Worker's Compensation claims can identify occupational causal agents and occupational risk rankings.[272] Thus, it is possible for employers that use common contactants in their workplace to develop a long-term OCD preventive program. This could include employee seminars and information about individual protection regimens.[151,273] It would be helpful for the OCD specialist to assist in designing this preventive program.

Secondary prevention

Summary statement 73. Once the diagnosis of ACD or ICD is established, emollients, moisturizers, and/or barrier creams may be instituted as secondary prevention strategies for continued exposure. (C)

Prevention of dryness in ACD can be attempted with the use of emollients and moisturizers. It is claimed that topical medications that contain ceramide or urea may have salutary effects by decreasing transepidermal water loss.[274] The efficacy of protective barrier creams may be overrated.[275] However, controlled studies indicated that soap substitutes and after-work creams may reduce the incidence and prevalence of CD.[276,277] Unfortunately, none of these secondary measures appear to be totally effective, especially in situations where there is high exposure to skin irritants.[278]

To prevent ICD diaper rashes, some clinicians advocate gentle cleansing with warm water, the use of superabsorbent diapers, and the application of a barrier preparation at every diaper change.[279]

Prognosis

Summary statement 74. Long-term prognosis of ACD or ICD has only been adequately investigated in OCD. (C)

Most of the reviewed studies in this category reveal a complete clearance rate between 18% and 40%.[280] The degree of partial improvement ranges from 70% to 80%. Rarely, some workers have persistent, on-going dermatitis precipitated by prior OCD despite removal from exposure at work.[281,282] It is not known whether ACD or ICD has a better prognosis.[283–285] Atopic dermatitis may predispose an individual to develop ICD or ACD and may affect the outcomes and prognosis adversely.[286]

Summary statement 75. Persistent ACD has an appreciable effect on quality of life. (C)

Investigation of quality-of-life effects was evaluated by previously validated skin quality-of-life instruments (ie, Skindex) plus additional factors related to occupation.[287] Patients patch tested later in their dermatitis and who had to change jobs demonstrated the most severe quality-of-life impairment scores. The emotional domain of the quality-of-life instrument was particularly affected in patients with ACD on the face and hands.

APPENDIX

Descriptive Interpretation Scale Recommended by the International Contact Dermatitis Research Group, Visual Key, Instruction Sheet for Patients, and Standard Patch Test Record Form

No.	Grade	Meaning/appearance	Clinical relevance*
1	−	Negative reaction	Excludes ACD. If ACD is still suspected, recheck technique or do ROAT.
2	R	Irritant reaction	Controls show similar response or there was an excited skin response.
3	± + or ?	Doubtful reaction	Negative test result. Repeat readings at 3, 4, and 7 days after patch removed. If ACD still suspected, recheck technique or do ROAT.
4	1+	Light erythema, nonvesicular	Equivocal test result. Could either be negative or indicative of waning prior sensitization. False-positive test result or excited skin syndrome must be ruled out by test in control subject. Repeat steps in 3.
5	2+	Edema, erythema, discrete vesicles	Positive test result. Indicative of prior or current sensitization. Should correlate with history and physical findings. False-positive test result or excited skin syndrome must be ruled out by test in control subject
6	3+	Coalescing vesiculobullous papules	Strongly positive result. Same conditions in 5 apply.

Abbreviations: ACD, allergic contact dermatitis; ROAT, repeat open application test.

* Clinical relevance is based on the Joint Task Force's appraisal of current literature

INSTRUCTION SHEET FOR PATIENTS
PATCH TESTING

What is Patch Testing?

Patch testing helps to confirm a diagnosis of an allergic contact dermatitis, which is a type of skin rash that occurs when certain substances come in contact with the skin. Examples of these substances, known as allergens, may include fragrance in perfume, adhesives used in bandages, metals found in jewelry, and glues used in shoes, just to name a few.

Anyone can develop skin irritation (also called an *irritant* contact dermatitis) when exposed to harsh chemicals like strong detergents, household cleansers, solvents, and acids. However, reactions to allergens are different. Only some people will develop an *allergic* contact dermatitis when exposed to allergens. That's why you may be the only person you know that experiences a rash when coming in contact with a particular allergen. Allergic contact dermatitis can only occur after the immune system cells in the skin learn to recognize the allergen and become activated to cause inflammation. In some cases it may take just a few exposures to the allergen for this sensitization to occur. In other cases, sensitization occurs only after years of repeated exposure, which explains why a new allergy can develop to a product that you have used for months or years without any previous difficulty.

A patch test is not the same as a scratch or prick test (often performed by an allergist). Patch testing cannot identify allergies to foods, inhaled substances, or oral medications.

How is Patch Testing Performed?

Strips of tape containing small quantities of common allergens will be applied to the skin of your back during your first visit, which may last about 45 minutes. The allergens must remain in place and be kept dry for 48 hours.

After the 48 hours, the patches will be removed and an initial reading will be performed. The patch sites w/ill be outlined with a marker, and you will be asked to return for a final reading on another day.

A positive test will show a red, raised area of skin, often with itching. A strong reaction could cause blistering and, very rarely, a prolonged reaction (lasting several weeks) or scarring.

How Can I Increase the Reliability of the Test?

1. Keep the skin of your back dry until the patches are removed 48 hours after applied. Until then, no showering, bathing (except for sponge baths), or swimming.
2. Avoid any activity that may cause you to sweat heavily (examples: exercising, shoveling). Excessive perspiration could cause the patches to fall off.
3. If any of the patches begins to peel loose, reinforce it with adhesive tape.
4. Do not remove the magic marker marks until instructed to do so. Some of the ink sometimes does come off on clothing, so it may be a good idea to wear a dark undershirt.

PATCH TEST REPORT

Name:_____ Date Applied:_____

Occupation:_____ 1° reading by:_____

Working Diagnosis:_____ 2° reading by:_____

Referring MD:_____ 3° reading by:_____

	ALLERGEN Date	1° reading 48 hr	2° reading hr	3° reading dy
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38				

Guide to Morphology
(- negative*)
+/- slight=erythema alone
1+ erythema, infiltration
2+ edema +/- vesicles2
3+ bulla or ulcer

*All allergens listed were applied, except where otherwise noted.
Only positive reactions Are shown here

No.		1° reading	2° reading	3° reading
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40				
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70				
71				
72				
Supplemental Allergens				

Name:_____

Positive Tests Summary		
Allergens	**Interpretation**	**Relevance**

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Published Practice Parameters of the Joint Task Force on Practice Parameters for Allergy & Immunology include the following:

1. Practice parameters for the diagnosis and treatment of asthma. *J Allergy Clin Immunol.* 1995;96:S707–S870.
2. Practice parameters for allergy diagnostic testing. *Ann Allergy.* 1995;75:543–625.
3. Practice parameters for the diagnosis and management of immunodeficiency. *Ann Allergy.* 1996;76:282–294.
4. Practice parameters for allergen immunotherapy. *J Allergy Clin Immunol.* 1996;98:1001–1011.
5. Disease management of atopic dermatitis: a practice parameter. *Ann Allergy.* 1997;79:197–211.
6. The diagnosis and management of anaphylaxis. *J Allergy Clin Immunol.* 1998;101:S465–S528.
7. Algorithm for the diagnosis and management of asthma: a practice parameter update. *Ann Allergy.* 1998;81:415–420.
8. Diagnosis and management of rhinitis: parameter documents of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology. *Ann Allergy.* 1998;81: S463–S518.
9. Parameters for the diagnosis and management of sinusitis. *J Allergy Clin Immunol.* 1998;102:S107–S144.
10. Stinging insect hypersensitivity: a practice parameter. *J Allergy Clin Immunol.* 1999;103:963–980.
11. Disease management of drug hypersensitivity: a practice parameter. *Ann Allergy.* 1999;83:S665–S700.
12. Diagnosis and management of urticaria: a practice parameter. *Ann Allergy.* 2000;85:S521–S544.
13. Allergen immunotherapy: a practice parameter. *Ann Allergy.* 2003;90:SI–540.
14. Symptom severity assessment of allergic rhinitis: part I. *Ann Allergy.* 2003;91:105–114.
15. Disease management of atopic dermatitis: an updated practice parameter. *Ann Allergy.* 2004;93:S1–S21.
16. Stinging insect hypersensitivity: a practice parameter update. *J Allergy Clin Immunol.* 2004;114;4:869–886.
17. The diagnosis and management of anaphylaxis: an updated practice parameter. *J Allergy Clin Immunol.* 2005; 115:S483–S523.
18. Immunodeficiency update. *Ann Allergy.* 2005;94:S1–S63.
19. Attaining optimal asthma control: a practice parameter. *J Allergy Clin Immunol.* 2005;116:S3–S11.
20. Food allergy: a practice parameter. *Ann Allergy.* 2006; 96:3:S1–S68.

These parameters are also available on the Internet at: http://www.jcaai.org

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