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OCTOBER 2008

A SUPPLEMENT TO

cutis®

CHRONIC HAND ECZEMA:

Diagnosis, Management, and Prevention
of a Challenging Condition



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cutis[®]

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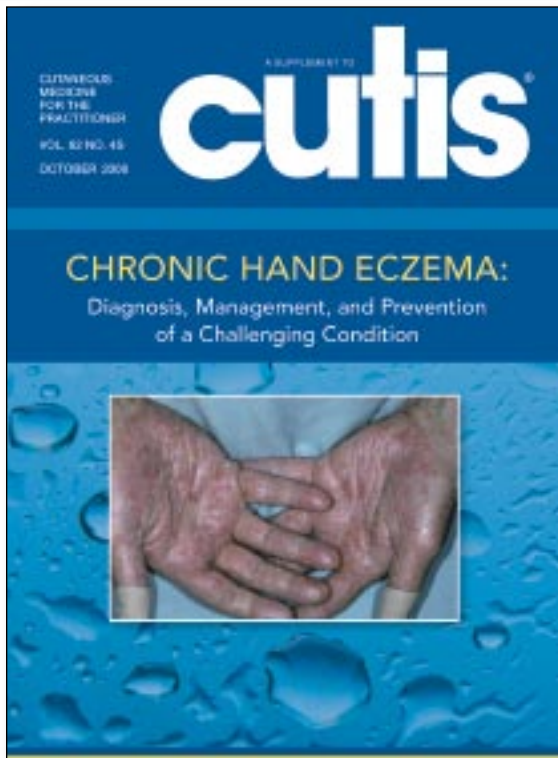


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Chronic Hand Eczema: Diagnosis, Management, and Prevention of a Challenging Condition

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Chronic Hand Eczema: Diagnosis, Management, and Prevention of a Challenging Condition

Joseph Fowler, MD

Hand eczema, the most common occupational skin disorder, remains a challenging condition for numerous reasons. Overlapping disease entities and multifactorial etiologies are common. The 2 most common forms of hand eczema—irritant contact dermatitis and allergic contact dermatitis—can be difficult to accurately diagnose. Endogenous factors such as atopy also contribute to the occurrence of hand eczema, especially in individuals involved in wet work (activities that cause one or both hands to become wet from contact with detergents or other skin irritating substances). The persistent and recurring nature of the condition is frustrating for the patient and physician alike. As one's hands are not only used as "tools" but for social expression as well, it is not surprising that chronic hand eczema has a negative impact on quality of life. In fact, the Dermatology Life Quality Index was reported to be just below psoriasis and atopic dermatitis for impairment of quality of life.¹ For some individuals with chronic hand eczema, the ability to work in the profession they have chosen becomes no longer viable, thus affecting their livelihood. Hand eczema has a substantial economic consequence. Monetary figures released in 2004 for the United States estimated that annual direct costs for physician and clinic services as well as prescription drugs were \$1.6 billion, with indirect costs of approximately \$566 million for lost productivity.² Clearly, it is a medical condition with considerable monetary and psychosocial consequences.

Management of chronic hand eczema requires a multipronged approach. Topical corticosteroids for the relief of inflammation and moisturizers to repair the barrier function of the skin are mainstays of therapy. The

physician's armamentarium has increased with therapeutic options to treat the inflammation and repair the barrier function of the skin, while the reoccurring nature of hand eczema from continual exposure to irritants remains a challenge. Identification and avoidance of the responsible irritant is the ultimate goal in breaking the cycle of hand eczema; however, a substantial number of patients with occupational chronic hand eczema are unable to avoid contact with irritants. In these situations, the strategy is to minimize exposure to the irritant through protective measures such as gloves or barrier protection creams; however, effective protection from the culprit irritants and allergens remains elusive.

It is the purpose of this supplement to review the topic of hand eczema, including prevalence, diagnosis, management, and prevention.^{3,4} Slade et al^{5,6} address the need for prevention in the dermatologist's armamentarium and review the safety and efficacy of a novel barrier protection cream that offers the opportunity to break the ongoing cycle of hand eczema.

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Chronic Hand Eczema: A Prevalent and Challenging Skin Condition

Joseph Fowler, MD

Hand eczema is a common condition in the industrialized world and the most common occupational skin disorder. The economic impact of hand eczema is daunting, with both direct and indirect costs. The former include medical costs, as well as costs associated with disability, workers' compensation, and rehabilitation, while the latter include absence from work, loss of productivity, job changes, and even job loss. Individuals with more severe, recurrent, or protracted hand eczema can endure serious psychosocial repercussions and a substantially impaired quality of life (QOL). In some cases, hand eczema adversely affects patients' social lives. Individuals with hand eczema also may experience emotional distress, including depression, mood disorders, and disrupted sleep. Because of these potentially deleterious economic and psychosocial consequences, hand eczema should be regarded as an important public health challenge.

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Although it is difficult to establish the precise prevalence of hand eczema, most evidence suggests that it is a common disorder, with substantial economic and psychosocial ramifications. It is difficult to obtain even an estimate of the prevalence of hand eczema because few relevant population studies have been conducted. The lack of consistency in defining eczema versus dermatitis makes it difficult to compare prevalence studies. Specifically, eczema involves an inflammatory response of the skin, with distinctive features caused by various endogenous

and/or exogenous factors, whereas dermatitis is a broader term used to define all conditions involving skin inflammation. Not all forms of dermatitis are eczematous, but because the 2 terms often are used interchangeably and no universal definitions of hand eczema or hand dermatitis exist, they tend to be regarded as synonymous and further obscure estimates of prevalence. In addition, many of those patients affected by hand eczema do not seek medical attention. A review of the literature, however, indicates that an estimated 2% to 10% of the general population is affected by hand dermatitis, and 20% to 35% of all cases of dermatitis involve the hands.¹

Prevalence of Hand Eczema

Several studies conducted in Sweden in the latter part of the 20th century have sought to determine the exact prevalence of hand eczema. In one of the most extensive and widely known cross-sectional studies, 20,000 individuals aged 20 to 65 years randomly drawn from the 1982 register of Gothenburg, Sweden, received a questionnaire by mail inquiring about the occurrence of hand eczema at some time in the past 12 months.² Of 16,584 individuals who responded to the questionnaire, 71% underwent dermatologic examination, including patch testing. Of the total respondents, 11.8% reported having hand eczema at some point in the past 12 months. The 1-year prevalence was estimated to be 10.6%, while the point prevalence was 5.4%. Hand eczema was found to be a persistent disease, with a mean duration of 12 years from the initial appearance to the time of the examination. Eczema-free intervals were reported in 77% of respondents; therefore, it can be inferred that approximately 1 of 4 respondents did not have disease-free periods.² These findings suggest that individuals with eczema have an unfavorable prognosis with regard to achieving complete remission of their disease. A follow-up survey was conducted in 1996 to study changes in the prevalence of hand eczema in this group of Swedish adults over time.³ Based on these more recent findings, the reported 1-year prevalence of hand eczema was found to have decreased to 9.7% in 1996, a

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Dr. Fowler prepared this article after attending a roundtable on hand eczema sponsored and supported by Alpha & Omega Worldwide, LLC. Alpha & Omega is a consultant of Coria Laboratories, Ltd, and assisted with the preparation of the article. Dr. Fowler is a consultant and investigator and is on the speakers bureau for Coria Laboratories, Ltd.

statistically significant decrease ($P < .01$) that was attributed to an increase in the unemployment rate as well as a decrease in the percentage of respondents employed in high-risk occupations for hand eczema. The greatest increase in the prevalence of hand eczema was observed in the youngest age group, namely those individuals aged 20 to 29 years.³

Fowler et al⁴ conducted the first epidemiologic study specifically designed to assess the prevalence of chronic hand dermatitis, as well as its impact on patient-reported outcomes and economic costs, in a US managed care population. In this survey, a 13-item validated self-assessment questionnaire was mailed to a random sample of 1380 members of a Massachusetts managed care organization who had been continuously enrolled from January 1, 2001, to November 30, 2003. To estimate the prevalence of chronic hand dermatitis in both the general and dermatitis populations at this healthcare organization, the sample was divided into 502 members from the general population and 878 members from the dermatitis population. The latter group was defined as individuals with 2 or more medical claims for nonspecific dermatitis or eczema between April 1, 2001, and August 31, 2003. A total of 507 (37%) of 1380 individuals surveyed responded to the questionnaire, of which 140 (28%) were identified as having chronic hand dermatitis.⁴

Of 183 respondents from the general population, 32 met the definition for chronic hand dermatitis, resulting in a point prevalence of 17%.⁴ Among 324 respondents in the dermatitis population, chronic hand dermatitis was diagnosed in 108 respondents, yielding a point prevalence of 33%. Approximately one-third of all cases of nonspecific dermatitis involved the hands. Approximately 45% of members from the general population had mild to moderate symptoms compared with only 24% of the dermatitis population, which was a statistically significant difference between groups ($P = .016$). As might be expected, members of the dermatitis population had a higher incidence of moderate to severe symptoms compared with the general population.⁴

Although chronic hand dermatitis was diagnosed based on the questionnaire in 32 respondents from the general population, no dermatitis-related medical services were recorded in the claims database.⁴ These findings indicate that approximately 17% of respondents from the general population did not seek medical attention for their condition. The projected prevalence of chronic hand dermatitis in the United States was estimated to be approximately 16% after standardization against the US general population with regard to distributions for age, gender, and race.⁴

Economic Impact of Hand Eczema

It is widely acknowledged that hand eczema can have profound economic consequences, both direct and indirect.¹ Direct expenses may include medical costs, as well as costs associated with disability, workers' compensation, and rehabilitation. Among the indirect consequences are absence from work (eg, sick leave), loss of productivity, and the possible need for a change of jobs. The psychosocial consequences of hand eczema also may have an indirect economic impact, as emotional distress, disrupted sleep, and compromised interpersonal relations may further contribute to absence from work and reduced productivity.¹

Monetary figures released in 2004 indicated that the direct costs associated with occupational contact dermatitis in the United States were estimated to be \$1.6 billion, of which \$870 million were attributed to physician and clinic services and \$747 million to prescription drugs.⁵ However, these statistics were undoubtedly underreported because they did not include the purchase of over-the-counter products used by many patients with contact dermatitis. Based on this survey, the indirect costs of lost productivity were estimated to be approximately \$566 million.⁵

As previously noted, Fowler et al⁴ conducted the first epidemiologic study to evaluate the impact of chronic hand dermatitis on patient-reported outcomes and economic costs. In a separate report, the data generated by a 14-page, 102-item survey were analyzed to determine the impact of chronic hand dermatitis on work productivity and healthcare costs in the same cohort of respondents described earlier.⁶ After adjusting for significant covariates, a multivariate analysis revealed that chronic hand dermatitis significantly impaired overall work productivity by approximately 23% and functionality at work by approximately 14% ($P < .001$ for both). Overall, the total healthcare costs of respondents with chronic hand dermatitis were approximately 25% greater than the general population, which was a statistically significant difference between groups ($P < .001$). For respondents with chronic hand dermatitis, prescription drugs accounted for the largest percent cost increase, followed by outpatient services. When translated into monetary figures, it was found that the average incremental monthly cost for the dermatitis population relative to the general population was approximately \$71 per patient.⁶

Hand Eczema: The Most Common Occupational Skin Disease

According to a review of the published literature by Elston et al,¹ hand eczema appears to be the most common occupational skin disease, comprising 9% to 35% of all cases of occupational disease and 80% or

more of all cases of occupational contact dermatitis. A number of populations at risk have been identified; individuals employed in occupations requiring frequent hand washing or interaction with irritants are at highest risk, including not only nurses and other hospital workers but manual workers in chemical companies, workers in electric or metalworking companies, and individuals in service and production jobs. In addition, a history of atopy predisposes patients to develop hand dermatitis, particularly individuals involved in wet work (activities that cause one or both hands to become wet from contact with detergents or other skin irritating substances). It is estimated that 7% to 23% of patients with hand dermatitis have associated atopic disease.¹

Investigators in the Netherlands conducted a series of surveys designed to determine the prevalence of eczema in the general population compared with individuals employed in a variety of different occupations (N=2185).⁷ The latter group included nurses and surgical assistants, as well as individuals who worked at a chemical company, a municipal electrical company, and a municipal public works company. Responses to a standardized questionnaire revealed dramatic differences in the prevalence of hand dermatitis based on the respondents' occupation. For example, in the general population consisting of 290 men and 380 women, approximately 5% of men and 11% of women had hand dermatitis compared with approximately 30% of nurses (men and women)(men, n=34; women, n=153). There was a higher prevalence of hand eczema among nurses than surgical assistants, suggesting that frequent washing of the hands is more harmful to the skin than the less frequent but more intensive exposure experienced by surgical assistants. In addition, the prevalence was high among manual workers who had low to moderate exposure to irritants in combination with mechanical stress (repeated friction). Approximately 15% to 35% of workers sought medical attention and approximately 3% to 9% required a sick leave because of their condition.⁷

The 1238 respondents with a confirmed diagnosis of hand eczema in the aforementioned cross-sectional study conducted in Gothenburg, Sweden, also were queried regarding any changes in occupation that had occurred because of their skin disease in a separate report.⁸ Approximately 21% of the respondents with hand eczema reported that their condition had required a sick leave from work of 7 days or more on at least one occasion, while approximately 4% reported sick leave on more than 5 occasions. The mean total sick leave time due to hand eczema was 4 weeks. As might be expected, allergic contact dermatitis resulted in more frequent

and more prolonged sick leave than any other type of hand eczema. Interestingly, the number of times on sick leave was significantly higher among patients in service work than any other occupations ($P<.001$). In addition, the survey revealed that many of the respondents had changed jobs because of hand eczema. This trend was observed most often among hairdressers—18% of whom abandoned their occupation because of their condition—followed by bakers, dental nurses, cleaners, kitchen maids, cooks, machine tool operators, and nurses.⁸ Consistent with the findings reported by Smit et al,⁷ the survey results indicated that job changes were significantly more common among respondents in service work, production, and medical or nursing work compared with administrative work, education, or engineering ($P<.001$). Furthermore, those respondents who changed jobs sought a significantly higher number of medical consultations ($P<.001$) in addition to taking more frequent and prolonged sick leave.⁸

A retrospective analysis of workers' compensation claims in Oregon from 1990 to 1997 was performed to elucidate the incidence rates, costs, severity, and work-related factors associated with occupational dermatitis.⁹ All dermatitis-related claims were merged with the US census data to provide estimates of the rate of dermatitis according to age, gender, occupation, and industry. Associated claims costs and duration of disability also were calculated from these data. A total of 611 individuals with accepted dermatitis claims were included in the analyses. The average claim rate of individuals with occupational dermatitis was estimated to be 5.73 per 100,000 workers (95% confidence interval [CI], 5.66-5.80). The most affected part of the body was the hands, accounting for approximately 38% of the accepted claims. There were statistically significant differences in claim rates according to age, gender, occupation, and industry ($P<.001$), with the highest claim rates reported for employees in the farming, fishing, and forestry industries. The average cost per claim was \$3552, while the average period of disability was 23.9 days.⁹ These findings indicate that occupational dermatitis remains a substantial problem, particularly in certain occupational settings.

To identify prognostic risk factors in patients with occupational hand eczema (OHE), a cohort study with a 1-year follow-up was conducted by investigators in Denmark in all patients with newly diagnosed OHE who were 18 years or older at the time they registered in the Danish National Board of Industrial Injuries (DNBII) Registry from October 1, 2001, through November 10, 2002.¹⁰ All of the 758 eligible patients received a baseline

questionnaire by mail within 1 to 2 weeks of registering with the DNBII. Of the 621 patients who responded, 564 returned the follow-up questionnaire 1 year later. The assessment of disease severity was based on medical certificates from dermatologists and a patient visual analogue scale, and the respondents were requested to provide information regarding any sick leave or job losses due to OHE that had occurred in the past year.¹⁰

The presence of atopic dermatitis and an age of 25 years or older appeared to be associated with a poor prognosis in this cohort.¹⁰ Specifically, patients with atopic dermatitis had a 1.5 times higher risk for exacerbated or persistently severe OHE when compared with patients without atopic dermatitis. Patients with severe OHE at baseline also had a substantially higher risk for taking a sick leave in the following year. In addition, severe impairment of quality of life (QOL) at baseline was a strong predictor of prolonged (ie, >5 weeks) sick leave, independent of the severity of OHE, underscoring the importance of measuring patients' perceived health-related QOL. There also was a strong association between severe OHE at baseline and job loss during the following year.¹⁰

Psychosocial Impact of Hand Eczema

While many patients with minor hand eczema are minimally affected by their condition, patients with more severe, recurrent, or protracted conditions can endure serious psychosocial repercussions. In the previously mentioned cross-sectional study conducted in Gothenburg, Sweden, the respondents were queried about any changes in occupation that had occurred because of their skin disease as well as the psychosocial impact of their condition.⁸ Specifically, the respondents were asked to identify any changes in their occupation or leisure activities, changes in their daily activities, the need to give up hobbies, any sleep or mood disturbances, the avoidance of social contact, and their perception that people kept distance from them. Overall, 81% of respondents—mostly females—reported that their condition had produced some type of emotional or social disturbance. Approximately half of the respondents described their hand eczema as a handicap with regard to their occupational and leisure activities, and about one-third reported that it required a change of daily activities. More than 1 of every 3 respondents reported mood and sleep disturbances attributed to their condition and stated that they avoided social contact and people kept distance from them. The authors concluded that these findings demonstrate that physicians caring for patients with hand eczema should focus not only on the physical manifestations of the disease but also on the impact on the patient's overall well-being.⁸

Poor QOL and Depressive Symptoms in Patients With OHE—These observations are supported by additional findings¹¹ based on the previously mentioned cohort of Danish patients with OHE.¹⁰ In addition to examining prognostic risk factors,¹⁰ the investigators sought to determine risk factors for low QOL, the frequency and severity of depression, and changes in both QOL and depression at baseline and after 12 months of follow-up.¹¹ The respondents were asked to complete 2 questionnaires: the Dermatology Life Quality Index (DLQI) and the Beck Depression Inventory (BDI-II). The DLQI is a 10-item questionnaire that addresses 6 aspects of daily life experienced during the past week, including symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. Each item is assigned a score of 0 (not at all) to 3 (very much), with the total scores calculated by adding the score of each question. The maximum score is 30 (reflecting the greatest impairment of QOL) and the minimum score is 0 (indicating no impairment of QOL). The BDI-II is a 21-item questionnaire measuring depressive symptoms during the past 2 weeks; each item is assigned a score of 0 (no symptoms) to 3 (most severe symptoms). A cumulative score is attained by adding the scores of the individual items. Responders are classified as having no or minimal depression (score, 0–13), mild depression (score, 14–19), moderate depression (score, 20–28), or severe depression (score, 29–63). The results of the survey indicated that the mean (SD) total DLQI score of the respondents was 5.5(4.8)(range, 0–26). However, approximately one-third of the patients no longer had active eczema or had only minimal disease at the time they responded to the questionnaire. Based on the 6 DLQI category scores, it was found that “symptoms and feelings” and “work and school” were most severely affected at baseline. In addition, there were strong associations between mild to moderate OHE (prevalence ratio [PR], 3.5; 95% CI, 1.8-7.0) and severe OHE (PR, 3.7; 95% CI, 1.7-7.7) and a low QOL at baseline compared with patients with no to minimal OHE.¹¹ Interestingly, the risk for a low QOL at baseline was 2 times higher among patients with a lower socioeconomic status, independent of disease severity. Depressive symptoms also were strongly associated with a low QOL (PR, 3.8; 95% CI, 2.5-5.6). In addition, the mean total DLQI scores increased in association with increasing disease severity. In patients with severe OHE, the mean DLQI total score at baseline was 7.8, which ranks the disease just below psoriasis and atopic dermatitis with respect to impairment of QOL.¹¹

A total of 9% of respondents showed signs of moderate to severe depression, both at baseline (46/564) and 1-year follow-up (50/564).¹¹ The mean (SD) BDI-II total score at baseline was 7.1 (7.4)(range, 0–41). There was a significantly higher incidence of depressive symptoms among respondents aged 30 to 39 years compared with other age groups ($P=.05$). While a low QOL appeared to be strongly associated with a high BDI-II score (PR, 4.5; 95% CI, 2.6-7.9), there were no significant associations between a high BDI-II score and socioeconomic status, gender, diagnosis, disease severity, or disease duration. According to the investigators, because only minor changes in both QOL and depressive symptoms were observed after 12 months of follow-up, it is important to recognize hand eczema as a chronic disease.¹¹

Obsessive-Compulsive Disorder and Hand Eczema— There also appears to be a subgroup of patients whose skin conditions are self-induced and reflect underlying psychopathologic conditions, such as patients whose hand dermatitis results from excessive hand washing typically associated with obsessive-compulsive disorder (OCD). Several studies have demonstrated that a surprisingly high number of patients seen in dermatology clinics have unrecognized OCD.¹²⁻¹⁴ A study conducted in the United Kingdom found that 18 of 92 (20%) consecutive patients screened for OCD at an outpatient dermatology clinic fulfilled the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) criteria for this diagnosis; only 1 patient had been previously diagnosed. The majority of patients had more than 1 symptom, most commonly checking, cleaning or washing, and symmetry.¹²

Conclusion

Hand eczema is a common and often chronic clinical condition that afflicts up to 10% of the general population, mostly women.¹ However, these figures are substantially higher among individuals employed in certain occupations, such as nurses and other healthcare workers, hairdressers, food service workers, and construction workers. Indeed, hand eczema is the most common occupational disease, accounting for up to 80% of all cases of occupational contact dermatitis.¹ Individuals with an atopic skin diathesis are at greatest risk for developing hand eczema or chronic hand eczema. The economic consequences of hand eczema are far-reaching and include both direct costs (eg, medical costs, workers' compensation, rehabilitation) and indirect costs (eg, absence from work, loss of productivity). In addition, hand eczema has a substantial impact on patients' psychosocial well-being as well as on their occupations. In many cases, patients' QOL is adversely affected, and some patients

even withdraw from social contact. Hand eczema also affects patients' occupations, often resulting in sick leave, job change, and even job loss. For this reason, there is an urgent need to identify patient populations at highest risk and to institute measures that will mitigate the toll that this often disabling condition has on patients, both short-term and long-term.

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Hand Eczema: Diagnosis and Management

Joseph B. Bikowski, MD

The most common clinical presentations of hand eczema are atopic hand dermatitis, pompholyx, and contact dermatitis (irritant contact dermatitis [ICD], allergic contact dermatitis [ACD]). The diagnosis of hand dermatitis is determined by a review of the patient's medical history, a physical examination including other body sites as well as the hands, and a thorough overview of the patient's daily activities with emphasis on occupation and hobbies. Irritant contact dermatitis usually is diagnosed by the absence of a positive patch test result; however, patch testing is essential in confirming a clinical diagnosis of ACD by identifying the allergens to which the patient has been sensitized. Treatment includes topical and/or systemic corticosteroids to reduce inflammation and ceramide-containing moisturizers to repair the skin's barrier function. Topical calcineurin inhibitors may be alternatives to topical corticosteroids. The most important step in the management of hand eczema is prevention with physical protective products (eg, gloves) or barrier protection creams.

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Numerous challenges confront clinicians when diagnosing and managing hand eczema. For example, there is no universally accepted classification for hand eczema,¹ overlapping disease entities and multifactorial etiologies are common,¹ multiple therapies are required for the relief of symptoms and clinical improvement, avoidance of the identified irritant or allergen is not always feasible, and the relapsing nature of the condition creates an ongoing cycle of chronic disease. Hand eczema is inflammation characterized by signs of erythema, papules, vesicles, scaling, weeping, oozing, fissures, and lichenification, and is associated with pain and itching.¹ Primary hand eczema is endogenous, whereas secondary hand eczema involves exogenous factors. Hand eczema can be classified as an acute, subacute, or chronic itchy rash. Patients with acute eczema experience intense pruritus associated with a red, scaling, weeping, and oozing skin rash (Figure 1), while patients with subacute eczema have the same clinical presentation but experience only moderate pruritus (Figure 2). Patients with chronic hand eczema experience moderate to intense pruritus associated with hyperpigmented, dry, scaling, and lichenified skin (Figure 3).² Although there are numerous clinical variants of hand eczema, atopic hand dermatitis, pompholyx (dyshidrotic eczema), and contact dermatitis are the most common clinical presentations.

Atopic Dermatitis

Individuals with a history of atopic dermatitis are prone to developing hand dermatitis, especially if their occupation involves wet work (activities that cause one or both hands to become wet) or exposure to irritants.^{3,4} Although atopic hand eczema has no uniform clinical presentation, typically the fingers and dorsal aspects of the hands are involved. The clinical presentation, which usually is symmetric, includes dryness, mild erythema, and lichenification.⁵ Patients with atopic dermatitis of the hands frequently report pruritus and pain.³ There often is involvement of other body areas, such as the neck, flexural surfaces (antecubital space, popliteal fossa), and dorsal aspects of the feet.⁶



Figure 1. Acute eczema of the hand.

Pompholyx

Pompholyx is characterized by recurrent vesicles on the lateral aspects of the fingers, palms, and periungual area. Eruption of the vesicles usually is preceded by severe pruritus; in some patients, there also is a burning sensation.⁷ Unless there are repeated eruptions, there usually is no or minimal inflammation.⁴ Often there is a patient history of atopy and reported flares

with stress, exposure to irritants, or wearing occlusive gloves.⁸ Patients frequently experience palmoplantar hyperhidrosis and may complain of pruritus or pain.

Contact Dermatitis

The 2 most common forms of hand eczema are irritant contact dermatitis (ICD) and allergic contact dermatitis (ACD), which are the focus of this article.

Irritant Contact Dermatitis—Irritant contact dermatitis, initially referred to as “housewives’ eczema” or “dishpan hands,” is the most common occupational skin disease, constituting 70% to 80% of all occupational skin disorders.⁹ It is a localized, nonimmunologically initiated inflammatory reaction with polymorphous clinical characteristics, and it develops when the healthy epidermal barrier is disrupted and secondary inflammation develops. Most cases are caused by long-term cumulative exposure to one or more irritants, including inorganic and organic acids, alkalis or bases, common solvents, alcohols, detergents, cleansers, and disinfectants, though severe irritants can cause toxic reactions even after a short exposure. In addition, friction, trauma, pressure, and vibration can be considered irritants.

The clinical spectrum of ICD is as varied as the irritants themselves and may present as sensations such as stinging, burning, pain, and itching, or as clinical signs of erythema, scaling, fissures, vesicles, blisters, and necrosis.⁴ Acute ICD develops in response to a single exposure to an irritant. The clinical presentation is determined by the characteristics of the skin involved and the nature of the irritant, but typically erythema, edema, pustules, blisters, or necrosis appear. A stinging, burning, or painful sensation may accompany the clinical signs. Lesions are demarcated and usually limited



Figure 2. Subacute eczema of the hand.

to the area of the hand that came in contact with the irritant.⁴

Chronic ICD may develop by repetitive exposure to an irritant or by a cumulative effect of several irritants. Slight erythema with fine scaling, often the first visible sign of ICD, rapidly can change to redness, edema, scaling, fissures, and chapping when an additional insult to the skin moves from subclinical damage to visible dermatitis.⁴ In long-standing chronic ICD, the clinical presentation may include erythema, edema, eczematous vesicles, itch, and lichenification.

The clinical presentation depends on the nature of the irritant and location of contact. For example, dermatitis will occur on the hand exposed to the irritant, which may or may not be the dominant hand. Fingertip fissures and cracks occur in individuals with occupations involving prolonged exposure to organic solvents, while finger web dermatitis occurs in individuals with wet work occupations.⁴ Nail involvement often occurs in chronic ICD.⁵ Individuals with atopic dermatitis are particularly susceptible to developing ICD of the hand.⁴

Allergic Contact Dermatitis—Allergic contact dermatitis, which is typically more acute and inflammatory than ICD, is a type IV, T-cell-mediated, delayed-type hypersensitivity reaction that occurs when the skin comes into contact with an allergen to which a patient has been previously sensitized. The appearance of ACD depends on the location, severity, and duration of the skin lesions, which present as pruritic eczematous eruptions that usually are localized. The clinical presentation of acute ACD includes erythema, vesicles, and bullae; chronic ACD presents as plaques with scaling, fissures, and lichenification.⁸

Thousands of substances can cause ACD; however, the most common allergens associated with this condition are certain metals (eg, nickel), preservatives, topical antibiotics, and fragrance components, as well as various chemicals used in manufacturing.¹⁰ A patient sometimes can be sensitized by only one exposure to one of these substances; at other times, sensitization occurs after multiple exposures. Once sensitized, the next exposure causes symptoms within 24 to 72 hours.⁸ Wet work may potentiate the development of ACD.³ The list of occupations associated with an increased risk for ACD is extensive and includes concrete workers, housepainters, shoemakers, healthcare workers, mechanics, printers, hairdressers, housekeepers, machinists, farmworkers, bakers, and other food handlers.¹¹

Diagnosis of Hand Eczema

When diagnosing hand eczema, it is important to note that certain predictive factors should be taken



Figure 3. Chronic hand eczema.

into account when first assessing a patient, including a history of childhood eczema (the most important predictive factor); occupational exposure; a history of asthma and/or hay fever; and employment in a service occupation, such as nursing, hairdressing, or food handling. The overall clinical history should include a thorough overview of the patient's daily activities, both at home and in the workplace, with special emphasis on the patient's occupation and hobbies. A number of issues should be addressed, such as whether or not the patient uses latex, vinyl, lined, or cotton gloves; how long they are worn; and how frequently they are changed. Patients also should be asked about what skin care products they use and if there have been any changes in the products used, and about how often they wash their hands or are exposed to water. Hand washing more than 35 times per shift was linked with occupational hand dermatitis in intensive care workers.¹² It also is important to determine what prescription and over-the-counter medications the patient uses, both currently and in the recent past, as the use of certain treatments may be linked to a diagnosis of ACD. In addition, patients should be queried as to whether they have observed any relationship between their activities and any

Table 1.

Key Characteristics Differentiating ICD From ACD

Cumulative ICD	ACD
Clinical Lesion	
Redness, scaling, chapping	Polymorphic: redness, papules, vesicles, crusts, exudation, erosions, lichenification
Demarcation	
Patchy, relatively unsharp	Interdigital, fingers, palmar or dorsal aspect of the hand
Localization	
Fingertips, finger web, dorsal aspect of the hand	Interdigital, fingers, palmar or dorsal aspect of the hand
Clinical Course	
Chronic; aggravated by climatic changes, wet work (activities that cause one or both hands to become wet), detergents, gloves	Relapsing, resolving on weekends or holidays
Epidemiology	
Multiple persons affected in environment	One person affected in environment
Patch Testing Results	
Negative	Negative, allergen missed
Positive, nonrelevant	Positive, relevant

Abbreviations: ICD, irritant contact dermatitis; ACD, allergic contact dermatitis.

Adapted with permission from van der Walle.⁴

improvement or relapse in their condition. Because a series of cumulative irritant episodes may belatedly lead to ICD, it is important to recognize that patients with this condition often fail to make a connection between their hand dermatitis and exposure to the causative irritant, a possible correlation that must be carefully explored.

There also are a number of points to consider when evaluating the patient’s occupational history. The period over which the condition has developed (ie, days, weeks, months) should be noted, and the clinician should consider if dermatitis is consistent with work exposure and if time off from work results in any improvement. Various materials that the patient handles can have an irritant, corrosive, or sensitizing effect, raising the question of whether an allergic reaction to protective equipment may have

occurred, if used. According to an analysis of contact dermatitis of the hands by the North American Contact Dermatitis Group, common occupations in individuals with ICD are healthcare worker, machine operator, fabricator, and laborer with exposure to irritants including solvents, oils, lubricants, fuels, soaps, detergents, cleansers, and hair care products.¹⁰ Thiuram and carba mixes were the most common allergens associated with occupational ACD. The most commonly associated source of these allergens—gloves—was observed in individuals whose occupations required regular use of gloves and other rubber products, including healthcare workers, machine operators, mechanics, welders, cutters, technicians, and cleaning service providers.¹⁰

The physical examination should include a thorough examination of the patient’s hands as well as

Table 2.

Management of Chronic Hand Eczema^{13,14}

Eliminate or avoid the cause

Therapy

Reduce inflammation

Topical corticosteroids

Topical calcineurin inhibitors

Restore the skin barrier

Ceramide-containing moisturizer

Provide skin protection

Physical protection (eg, gloves)

Protective barrier cream

a close inspection of other key body sites because the presence of lesions at other locations (eg, nails, feet, elbows, knees, mouth, genital area) may provide important diagnostic clues. In forming an overall impression of the patient's condition, it is essential to distinguish between primary and secondary lesions.

Table 1 summarizes the key characteristics differentiating ICD from ACD. Irritant contact dermatitis usually is localized to the fingertips, finger web, and dorsal aspect of the hand; ACD usually occurs interdigitally, on the fingers, and on the palmar or dorsal aspect of the hand. Irritant contact dermatitis typically is chronic and is aggravated by factors such as climatic changes, wet work, and exposure to detergents or gloves; ACD is relapsing, often resolving on weekends or holidays.⁴ Patch testing, regarded as the gold standard for the diagnosis of ACD, is essential in determining to which allergen(s) the patient has been sensitized. Irritant contact dermatitis often is diagnosed by the absence of a positive patch test result.

Management of Contact Dermatitis

Management of chronic hand eczema due to contact dermatitis requires a multipronged approach (Table 2). Topical corticosteroids are the mainstay of therapy.^{13,14} Active inflammation disrupts the skin barrier and predisposes the skin to irritants in soaps and detergents that generally would not be able to penetrate the epidermis.¹⁵ However, topical

corticosteroids are not completely benign in patients with hand eczema, as they may develop a contact allergy to the prescribed agent.¹⁶ The topical calcineurin inhibitors tacrolimus and pimecrolimus have been studied in hand eczema and shown to lead to improvements in the condition of the skin. These agents can be alternatives to low- or mid-potency topical corticosteroids in patients with chronic irritant dermatitis and mild inflammatory changes.¹³ However, there have been reports of allergic contact dermatitis from topical calcineurin inhibitors.¹⁷⁻²¹

Moisturizers are essential in the management regimen to repair the barrier function of the skin. In a review of the literature on the treatment and prevention of contact dermatitis, Saary et al²² found evidence that lipid-rich moisturizers are effective in the short-term treatment of experimentally induced ICD. di Nardo et al²³ observed that participants with low baseline levels of ceramide 1 were more prone to develop a barrier impairment after acute irritation than individuals with ceramide 1 levels within reference range. Although a more recent study was not specific to hand eczema, the addition of a ceramide-containing (ceramides 1, 3, and 6) liquid cleanser and moisturizing cream to therapy with a high-potency corticosteroid enhanced the treatment outcome of mild to moderate eczema compared with a bar cleanser and high-potency corticosteroid. Reductions in disease duration, time to disease clearance, and symptoms were reported for groups receiving the ceramide-containing liquid cleanser and moisturizing cream.²⁴ Because barrier repair must occur concomitantly with inflammation reduction for complete healing, moisturizers containing ceramides are a logical choice when recommending a moisturizer for hand eczema.

Treatment of hand eczema is frustrating for both the patient and clinician when the patient responds to therapy and relapses on reexposure to the culprit irritant or allergen or on exposure to a different irritant. Therefore, the most important step in the management of hand eczema is prevention. If the hand eczema is the result of contact dermatitis, identifying and avoiding further contact with the responsible irritant is key. However, a substantial number of patients with occupational chronic hand eczema will not be able to avoid contact with irritants. In these situations, the strategy is to minimize exposure to the irritant. Patient education is essential for an understanding of proper skin care to restore and maintain the barrier function of the skin and protective measures that may be applicable to each patient's situation. Educational programs conducted in the workplace on skin care and protectant products have been shown to improve the employees' skin

Table 3.

Alternatives to Latex Gloves²⁶

Neoprene
Nitrite
Styrene-butadiene
Styrene-ethylene-butylene-styrene
Vinyl

condition.²² The use of protective products (eg, gloves, barrier creams) has been shown to be effective in reducing exposure to irritants. In a review of the value of several prevention approaches to hand eczema, Saary et al²² concluded that the use of cotton liners under occlusive gloves to prevent ICD was effective. Because atopy is a risk factor for latex allergy, individuals with a history of atopy who must use rubber products should be advised to substitute synthetic rubber for natural rubber latex gloves (Table 3).^{25,26}

Although there is evidence that barrier creams are effective in the prevention of contact dermatitis, their use has been controversial. Numerous products have been formulated with the specified concentrations of the 13 ingredients identified by the US Food and Drug Administration as skin protectants (Table 4), but supporting studies of their ability to provide protection against known irritants or allergens often are limited or lacking.^{22,27} In a review by Saary et al,²² some investigators have reported satisfactory protective action of specific formulations of barrier protection creams, while others have reported no protection with the products tested²² or even aggravation of irritant dermatitis.²⁶ Slade et al^{28,29} summarize safety and efficacy studies with a new barrier protection cream (Tetrix™ Cream) formulated using a unique patented technology.

Most patients with hand eczema can be managed with topical corticosteroids, moisturizers, and skin protection measures; recalcitrant cases may require systemic therapies or phototherapy. Systemic therapies include azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate mofetil, and retinoids.¹⁴ Phototherapy with UVB, psoralen plus UVA, and grenz ray have been reported to improve chronic hand eczema.^{1,3,14}

Conclusion

Although ICD and ACD constitute most hand skin diseases, an accurate diagnosis can be difficult. The

Table 4.

US Food and Drug Administration-Identified Skin Protectants and Concentrations

Ingredient	Concentration
Allantoin	0.5%–2.0%
Aluminum hydroxide gel	0.15%–5.0%
Calamine	1%–25%
Cocoa butter	50%–100%
Dimethicone	1%–30%
Glycerin	20%–45%
Kaolin	4%–20%
Petrolatum	30%–100%
Shark liver oil	3%
White petrolatum	30%–100%
Zinc acetate	0.1%–2.0%
Zinc carbonate	0.2%–2.0%
Zinc oxide	1%–25%

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etiology of hand eczema rarely is obvious and leads clinicians to determine if the disease is a primary or secondary condition and if it could resemble other hand skin diseases. For this reason, a complete clinical examination, specifically checking the feet, elbows, scalp, and genitals for signs of other primary skin diseases, should be performed. A patch test is essential to diagnose ACD; however, screening often is inconclusive, which is one reason why a complete patient history may be the clinician’s most valuable diagnostic tool. Childhood diseases such as hay fever are strong predictors of ACD; an occupational history as well as knowledge of the patient’s hobbies helps pinpoint a diagnosis of ICD.

Although numerous treatment options are available, the recurring nature of hand eczema from reexposure to irritants makes it a challenging condition for both the patient and clinician. Prevention by minimizing exposure to irritants is needed to help break the cycle of hand eczema. Although several treatment modalities are available for the

management of hand eczema, prevention through the use of gloves or barrier creams is needed to reduce exposure to irritants and allergens. New additions to the clinician's armamentarium in this area will help manage this challenging skin condition.

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Clinical Safety Evaluation of a Novel Barrier Protection Cream

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Patients with contact dermatitis require both preventive and therapeutic interventions to minimize their burden of disease. The ideal product would support resolution of inflamed skin without the use of glucocorticoids while protecting undamaged skin against further contact with irritants and antigens. COR806.805 (Tetrix™ Cream) is a novel barrier cream formulated for use on both lesional and nonlesional skin. Three clinical trials were conducted to evaluate the safety of this new product by studying sensitization, cumulative irritation, and effect on healing; a combined total of 265 participants completed the studies (210, 45, and 10, respectively), with no serious adverse events considered to be related to the product. Six mild adverse events were considered related or potentially related. As tested, COR806.805 is neither sensitizing nor irritating when applied to intact or lesional skin. Testing indicates that COR806.805 does not inhibit healing of allergic contact dermatitis lesions.

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Irritant contact dermatitis of the hands, or hand eczema, is a common problem associated with repeated occupational exposure. Detergents and solvents that remove lipids from the skin are major contributing factors to the barrier dysfunction that allows irritants to gain entry and cause damage to the skin. Workers in industrial settings, healthcare providers, hairdressers, and food handlers are most

frequently affected. Management of irritant contact dermatitis is straightforward in principle but challenging in practice. Topical glucocorticoids can be used to reduce inflammation; afterward, identification and avoidance of the irritants, combined with restoration of the stratum corneum barrier, are essential to achieve resolution.

When contact with irritants is unavoidable, the use of appropriate protective gloves may be helpful but often is inconvenient or unacceptable. An alternative skin-protection approach is to apply a barrier product that has low inherent irritancy, emollient properties, and good persistence. A clinical comparison of 6 different skin protectant products revealed that formulation is critical to performance. In the study, petroleum-based products protected against irritation and maceration and provided some degree of skin moisturization, while dimethicone-based products varied in their ability to protect against irritants and had low barrier efficacy in preventing maceration but provided good skin hydration.¹

COR806.805 (Tetrix™ Cream) is a new product that is designed to create a protective barrier against environmental irritants and antigens while also incorporating a skin conditioner, thus allowing the product to be used on chafed, chapped, cracked, and dry skin. The product is a water-based, water-resistant, water-in-oil emulsion that was formulated using patented technology blending cyclomethicone and aluminum-magnesium hydroxide stearate. When applied to a synthetic nylon membrane in vitro, COR806.805 prevented any substantial diffusion of dimethyl sulfoxide, nickel sulfate, and balsam of Peru (major components are benzyl cinnamate and benzyl benzoate) into the membrane, indicating a potential clinical benefit in preventing contact with known irritants and antigens. Preclinical toxicology studies have shown that the product does not cause delayed contact sensitization and is not associated with systemic toxicity; additionally, it showed no evidence for subacute toxicity.² The product was found to cause mild cytotoxicity in

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Drs. Slade and Cargill are full-time employees of DFB Pharmaceuticals, Inc, an affiliate of Coria Laboratories, Ltd. Dr. Fowler is a consultant and investigator and is on the speakers bureau for Coria Laboratories, Ltd. Mr. Reece reports no conflict of interest.

vitro, consistent with products containing the same preservative system. Results for mutagenicity were negative. Prior to being submitted for US Food and Drug Administration 510(k) clearance, 3 human trials were conducted to further characterize the safety of COR806.805 for topical use.

Methods

Each trial was conducted following good clinical practices and conformed to the Declaration of Helsinki ethical principles. Each protocol and informed consent document was approved in advance by a properly constituted institutional review board, and written informed consent was obtained from each study participant prior to screening.

Contact Sensitization Potential—Trial no. 9320-009-001 was a standard single-center human repeat insult patch test consisting of induction, rest, and challenge phases using COR806.805 alone. During the induction and challenge phases, 0.2 mL of product was placed on the skin under occlusion using ready-cut gauze bandages (Parke-Davis Readi-Bandages®). The induction phase consisted of 9 applications of product at the same placement sites for periods of 48 or 72 hours over 3 weeks. Following the induction phase, participants did not treat the sites for 2 weeks (rest phase). The participants then took part in the challenge phase, which consisted of 48-hour occluded application of product at a site that had not been previously patched. The patches were removed and the sites were scored immediately (\approx 48 hours post-challenge patch applications) as well as 72 and 96 hours post-challenge patch applications. A standard system of scoring (0=no visible reaction; +=slight, confluent or patchy erythema; 1=mild erythema [pink]; 2=moderate erythema [definite redness]; 3=marked erythema [very intense redness]; 4=severe erythema [deep red]) plus 22 additional modifiers such as glazing, erosion, induration, and edema were used to determine if sensitization was evident.

Participants who fulfilled all of the inclusion and none of the exclusion criteria were eligible for participation in the study. Inclusion criteria included the following: individuals who were ambulatory, aged 18 to 65 years, and in reasonably good health; of any ethnicity or skin type, provided skin pigmentation did not interfere with evaluations; if female, were surgically sterile, postmenopausal, or using an acceptable method of birth control; willing to refrain from sunbathing, using tanning salons, swimming, or using hot tubs during the entire study; agreeable to try and keep the patch test site as dry as possible; and able to read and sign the informed consent form.

Exclusion criteria included the following: individuals who had any systemic disease or disorder, complicating factors, or structural abnormality that would have negatively affected the conduct or outcome of the study; used a prescribed anti-inflammatory drug, immunosuppressive drug, antihistamine medication, or any over-the-counter pain medication that was ingested in quantities exceeding label instructions; received an investigational drug; participated in a Draize-type patch test within 28 days prior to enrollment or were currently participating in or planned to enter a clinical trial; a history of noncompliance or considered potentially unreliable; a history of skin allergies, including known sensitivities or strong reactions to any topical preparations, medical dressings, tapes, or adhesives; a history of clinically significant skin diseases that might have contraindicated participation, even if currently controlled through medication; used topical or oral antibiotics; used topical medications at the test area 2 weeks prior to enrollment or any body lotions/oils/creams at the test area 48 hours prior to enrollment; women who were pregnant, stopped contraceptive measures, expected to become pregnant, or were breastfeeding; any condition known to interfere with the absorption, distribution, metabolism, or excretion of drugs; hematologic or immunologic disorders; any significant organ abnormality or disorder; any clinically significant illness (eg, sought medical attention, fever, took prescription medication) within 4 weeks prior to study entry; a history of asthma, chronic bronchitis, or any other bronchospastic condition that required medication; anticipated a change in the use of a systemic medication during the study that would have affected the conduct or outcome of the study (participants must have been stabilized on these medications for at least 1 month prior to receiving the test product and were expected to continue the same regimen throughout the study); bilateral mastectomy for cancer involving removal of lymph nodes; treatment for any type of cancer 6 months prior to enrollment; or declared ineligible by the medical investigator for a sound medical reason. The target was to have 200 evaluable participants.

Cumulative Irritation Potential—Trial no. 9320-009-012 was a single-center 21-day study involving daily consecutive applications of test products under both occlusive and semioclusive patches. In this trial, COR806.805 was compared with both a negative control (Johnson's® Baby Oil) and a positive control (sodium lauryl sulfate 0.2%). Each test product remained in contact with the skin continuously for a total of 21 applications, except when wiped off during evaluations. Patches were removed daily by study site personnel at

approximately 24 hours after application, and test sites were evaluated approximately 10 minutes after each patch removal. If a dermal reaction of 3 or greater (0=no visible reaction; 0.5=slight, confluent or patchy erythema; 1=mild erythema [pink]; 2=moderate erythema [definite redness]; 3=marked erythema [very intense redness]; 4=severe erythema [deep red]) occurred with any test product at any point during the study, further application of the test product at the test site involved was terminated and the observed score was assigned to that site for the remainder of the study (ie, score carried forward). At the conclusion of the study, cumulative irritation scores for the occluded patches were calculated for each test product by adding the numerical irritation grades assigned daily during the 21-day application period using the Berger and Bowman³ classification system (valid only for test products evaluated under occlusive conditions).

Participants who fulfilled all of the inclusion and none of the exclusion criteria were eligible for participation in the study. Inclusion criteria included the following: individuals who were ambulatory, aged 18 to 65 years, and in reasonably good health; of any ethnicity or skin type, provided skin pigmentation did not interfere with evaluations; if female, either postmenopausal for at least 1 year or using an acceptable method of birth control and agreed to take a urine pregnancy test; willing to refrain from sunbathing, using tanning salons, swimming, and using hot tubs during the entire study; and agreeable to try and keep the patches as dry as possible. Exclusion criteria included the following: individuals who had any systemic disease or disorder, complicating factors, or structural abnormality that would have negatively affected the conduct or outcome of the study; used a prescribed anti-inflammatory drug, immunosuppressive drug, or antihistamine medication, or use of over-the-counter pain medications in quantities exceeding label instructions; received an investigational drug or participated in a patch test within the 28 days prior to starting this study or were participating in or planned to enter a clinical trial; a history of noncompliance or considered potentially unreliable; a history of skin allergies, including known sensitivities or strong reactions to any topical preparations, medical dressings, tapes, or adhesives; a history of clinically significant skin diseases that might have contraindicated participation, even if it was controlled through medication; used topical or oral antibiotics; used topical medications at the test area within 2 weeks prior to enrollment or any body lotions/oils/creams at the test area 48 hours prior to enrollment; women who

were pregnant, stopped contraceptive measures, expected to become pregnant, or were breastfeeding; any condition known to interfere with the absorption, distribution, metabolism, or excretion of drugs; hematologic or immunologic disorder; any significant organ abnormality or disorder; any clinically significant illness (eg, sought medical attention, fever, took prescription medication) within 4 weeks prior to study entry; a history of asthma, chronic bronchitis, or any other bronchospastic condition that required medication; a known history of either real or suspected allergy or sensitization to products being tested; anticipated a change in the use of a systemic medication during the study that would have affected the conduct or outcome of the study (participants must have been stabilized on these medications for at least 1 month prior to receiving the test product and continued the same regimen throughout the study); bilateral mastectomy for cancer involving removal of lymph nodes; treatment for any type of cancer within 6 months of study entry; or declared unreliable by the principal investigator for a sound medical reason. The target was to have 35 evaluable participants.

Resolution of Experimentally Induced Allergic Contact Dermatitis—Trial no. 806-805-09-003 explored the potential of COR806.805 to impede healing of allergic contact dermatitis in participants known to be sensitized to nickel sulfate when applied to lesional skin. Participants had 2 test sites marked on the volar aspect of one arm. Nickel sulfate was applied to both sites and the sites were occluded using a patch test device (Finn Chamber®). Forty-eight hours after antigen application, the chambers were removed and the sites were wiped clean of antigen and scored individually for signs of local skin reactions evoked by the antigen. The assessed signs consisted of ulceration, erythema, induration, excoriation, flaking, weeping, edema, and scabbing (crusting), which were evaluated using a 4-point scale (0=none; 3=severe). Immediately after assessment of the skin reactions, COR806.805 was applied as a thin film to one site only. Participants continued to apply COR806.805 twice daily (after showering in the morning and just before going to bed) for 10 days. On days 2, 4, 7, 9, and 11, participants returned to the study site to have both test sites evaluated and scored. Results were analyzed using the Wilcoxon signed rank test.

Participants who fulfilled all of the inclusion and none of the exclusion criteria were eligible for participation in the study. Inclusion criteria included the following: individuals who were 18 years or older, of either sex, and of any ethnicity or skin type, provided that the skin pigmentation, in the opinion

of the investigator, did not interfere with the study assessments; known to be sensitized to nickel sulfate; in good health as shown by medical history, a brief physical examination, and the judgment of the investigator; willing and able to make all required study visits; able to follow instructions; willing to refrain from sunbathing, using tanning salons, swimming, or using hot tubs during the entire study; agreeable to try to keep the test sites as dry as possible; and if female of childbearing potential, must have a negative pregnancy test and must agree to use contraception during the study. Exclusion criteria included the following: individuals who had a known contraindication or hypersensitivity to the use of the test product; received an investigational drug, other than COR806.805 or the antigens under study, or participated in a Draize-type patch test within the past 30 days; taken immunosuppressive therapy, including systemic corticosteroids, or other medications that could interfere with immune responses; a history of clinically significant active skin disease(s) that may impair the ability of the investigators to place and interpret patch tests; pregnancy; or used topical corticosteroids or calcineurin inhibitors at the test area within 1 week prior to enrollment or any body lotions/oils/creams at the test area 48 hours prior to enrollment. The target was to have 10 evaluable participants.

Results

Contact Sensitization—Actual enrollment was 266 participants, with 210 participants completing the study. A total of 15 adverse events were recorded, including 1 rash potentially related to the test product. The participant removed his patch after the second application in the induction phase because it was irritating him. After removal, he noticed a mild rash at the test site. No medications were taken. The participant subsequently failed to return telephone calls and was considered lost to follow-up. With respect to irritation, COR806.805 produced barely perceptible to mild patch test/irritant patch test responses (non-cumulative), occasionally accompanied by mild to moderate dryness, peeling, scabbing, pustules, erosion, or a mild to moderate papular response in 122 (58%) of 210 participants in the test population during the induction and/or challenge phases of the study. Additionally, 5 participants displayed barely perceptible (score, +) to moderate (score, 2) patch test/irritant patch test responses (cumulative and noncumulative), occasionally accompanied by mild to moderate dryness, mild edema, scabbing, pustules, erosion, vesicles, or a mild to moderate papular response during the induction and/or challenge phases of the study. Finally, although reactivity suggestive of irritation was observed, there was

no evidence that COR806.805 induced contact sensitization in any of the participants.

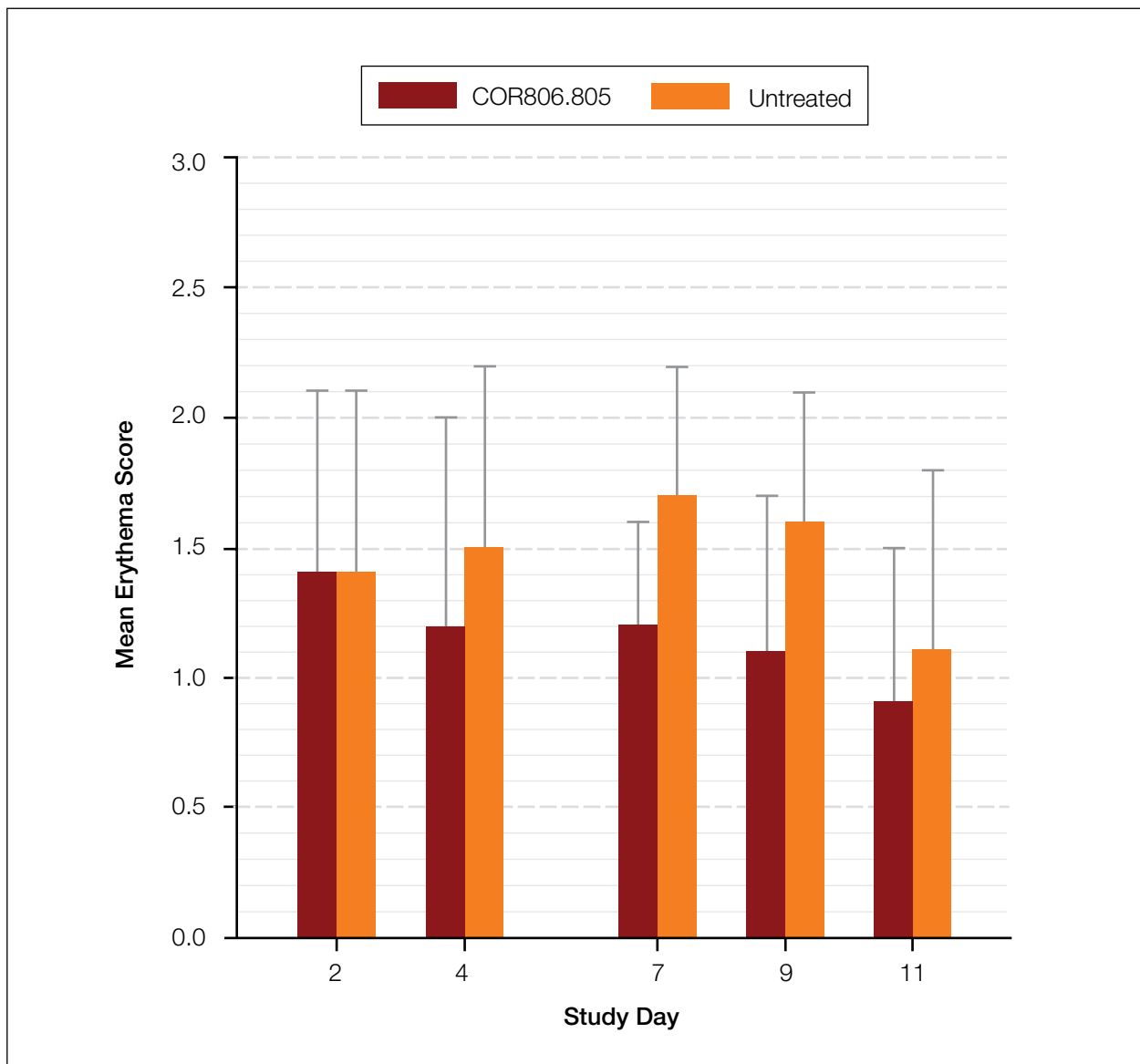
Cumulative Irritation—Actual enrollment was 58 participants, with 45 participants completing the study. A total of 6 adverse events (all tape dermatitis) were recorded, consisting of 5 mild reactions and 1 severe reaction. Compared with the negative and positive controls, COR806.805 was rated as probably mild and therefore not a cumulative irritant. Under semioclusive conditions, which are more closely matched to expected clinical use, COR806.805 produced less irritation than the negative control. As the Berger and Bowman³ classification system has not been validated under semioclusive conditions, no formal evaluation of these scores was undertaken.

Effect on Healing of Allergic Contact Dermatitis—Actual enrollment was 12 participants, with 10 participants completing the study. Overall, 6 adverse events were reported by 4 (33%) of 12 participants; none of the events were treatment related and none were associated with the skin. None of the participants experienced ulceration, weeping, or scabbing (crusting). One participant experienced mild exco-riation at the COR806.805-treated site at a single visit. The mean reaction scores for each test site at every visit indicated that the COR806.805-treated sites consistently evidenced the same or lower severity reactions than the untreated sites, with the exception of flaking at visit 6, which was slightly greater for the COR806.805 sites. The differences in scores generally were not statistically significant. Reaction scores for erythema (Figure) were typical of the scores for edema and induration. Overall, there was no evidence of inhibited healing with the product but rather some suggestion of improved healing.

Comment

The effectiveness of a barrier cream depends in large part on its formulation. Older hydrophilic barriers prevent grease and oil from contacting the skin but may be easily washed off with mild cleansing. Hydrophobic oil-based products provide good protection against irritation from water or water-borne irritants but limited barrier function against lipid-soluble irritants. The introduction of a new barrier cream requires a thorough evaluation of safety to be assured that it will not worsen the condition to be treated or serve as a new irritant.

The results of these safety studies indicate that COR806.805 does not produce sensitizing or irritating reactions and is not inhibitory with respect to healing of allergic contact dermatitis lesions. Each of the studies was appropriately powered and expected to be predictive of the performance of this new product in clinical practice.



Healing of allergic contact dermatitis was assessed in participants known to be sensitized to nickel sulfate, with one test site treated with COR806.805 (Tetrix™ Cream) and the other test site untreated. Mean erythema scores were similar to scores for edema and induration. Signs of local skin reactions evoked by the antigen were evaluated using a 4-point scale (0=none; 3=severe).

In particular, the number of participants in the standardized sensitization and irritation studies was considered to yield reliable estimates of effect. The study that explored effect on healing was limited to a specific antigen in a small number of participants. Further studies examining healing and protection will be reported separately.⁴

Conclusion

As tested, COR806.805 produced no untoward effects when applied to intact or lesional skin under various conditions.

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Clinical Efficacy Evaluation of a Novel Barrier Protection Cream

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COR806.805 (Tetrix™ Cream) is a new barrier cream formulated using a unique patented technology. As a water-in-oil emulsion, COR806.805 has a water-resistant outer surface and water-soluble inner surface. Clinical studies have demonstrated the safety of COR806.805 in healthy adults with respect to sensitization, irritation, and effect on the healing of existing skin lesions. We report the results of trials undertaken to explore the substantivity and barrier protection properties of this new product when applied to clinically normal skin, as well as the beneficial effects when applied to inflamed skin, including skin affected by eczema. The results indicate that the cream establishes a barrier against common irritants, with persistence over 6 hours. The product appears effective and well-tolerated as a barrier and also may provide benefit in managing the itching and burning associated with contact dermatitis.

Cutis. 2008;82(suppl 4):21-28.

As a primary interface between the body and the environment, the skin is endowed with remarkable immunologic capabilities. Substances that pass through the stratum corneum are surveyed and analyzed and then a tailored response occurs. The response may be to ignore the substance or to sequester it in the form of a foreign-body granuloma. When the substance is damaging, a more vigorous response takes

place. Normally sensitive individuals tend to respond to primary irritants and certain potent allergens (eg, urushiol, 1-chloro-2,4-dinitrobenzene). Hypersensitive individuals develop reproducible symptoms or signs on exposure to a defined stimulus at a dose tolerated by healthy individuals.

A common feature across the spectrum of immune-mediated skin disorders is the involvement of substances from the environment. When barrier dysfunction is a contributing factor, as in atopic dermatitis, the inciting environmental substances may be as benign as hard water and lipid solvents. Substances such as nickel sulfate serve as both irritants and antigens, while larger molecules such as parabens and neomycin serve as allergens without primary irritancy. A related problem, termed *status cosmeticus*, involves stinging reactions in susceptible individuals; benzoic acid, formaldehyde, lactic acid, and propylene glycol are among the many agents associated with this nonimmunologic response.

COR806.805 (Tetrix™ Cream) is a new product that is designed to create a protective barrier against environmental irritants and antigens. It is formulated for use on both lesional and nonlesional skin. Labeling for the product cleared by the US Food and Drug Administration is based on safety and efficacy trials in both healthy volunteers and participants with contact dermatitis. We report the results of 4 clinical trials designed to assess the barrier properties of this novel cream as well as its ability to control the itching and burning associated with contact dermatitis when used on lesional skin.

Methods

Each trial was conducted following good clinical practices and conformed to the Declaration of Helsinki ethical principles. Each protocol and informed consent document was approved in advance by a properly constituted institutional review board, and written informed consent was obtained from each study participant prior to screening.

Drs. Slade and Cargill are from DFB Pharmaceuticals, Inc, and the University of North Texas Health Science Center Graduate School of Biomedical Sciences, both in Fort Worth. Dr. Fowler is from the Department of Medicine, University of Louisville, Kentucky, and private practice, Louisville. Dr. Draelos is from Dermatology Consulting Services, High Point, North Carolina. Mr. Reece is from Reliance Clinical Testing Services, Inc, Irving, Texas. Drs. Slade and Cargill are full-time employees of DFB Pharmaceuticals, Inc, an affiliate of Coria Laboratories, Ltd. Dr. Fowler is a consultant and investigator and is on the speakers bureau for Coria Laboratories, Ltd. Dr. Draelos received research support from Coria Laboratories, Ltd. Mr. Reece reports no conflict of interest.

Substantivity Test—Trial no. 806-805-09-001 was a comparison study of the substantivity of COR806.805 versus Vaseline® Intensive Care hand cream following a single controlled hand wash.¹ A cosmetic face foundation (CoverGirl® Queen Collection; shade, true ebony) was mixed with each product to a uniform color and the products were applied to the dorsal aspect of the left or right hand according to a randomization scheme. Because the pigment is unlikely to penetrate the skin, visualization after hand washing is indicative of the presence of residual product. The study enrolled 10 healthy white women (mean age, 42.7 years) with normal hand skin. Fifteen minutes after application of COR806.805 and the control, the investigator performed a controlled wash on each participant's hands using lukewarm tap water and Dove® soap. The amount of residual pigment on the skin then was rated on a 5-point scale (0=none; 4=significant pigment). Digital photographs were taken of both hands prior to and after washing to provide documentation of the results.

Closed Patch Barrier Test—Trial no. 806-805-09-002 was a nonrandomized, investigator-blinded, single-site, controlled trial of the barrier effect of COR806.805 in closed patch testing with 3 antigens: nickel sulfate, neomycin, and a fragrance mixture. Potential participants must have had a known sensitivity to 1 of 3 antigens. After providing consent, participants were screened against the inclusion/exclusion criteria. Inclusion criteria included the following: individuals who were 18 years or older, of either sex, and of any ethnicity or skin type, provided that the skin pigmentation did not interfere with the study assessments; previously sensitized to one of the antigens; in good health as shown by medical history plus a brief physical examination; willing to make all required study visits; able to follow instructions; willing to refrain from sunbathing, using tanning salons, swimming, or using hot tubs during the entire study; and if female of childbearing potential, must have a negative pregnancy test and must agree to use contraception during the study. Exclusion criteria included the following: individuals who had a known contraindication or hypersensitivity to the use of the test products or their components; have received an investigational test article, other than COR806.805 or antigens used in this study, or participated in a Draize-type patch test within the past 30 days; are taking immunosuppressive therapy, including systemic corticosteroids, or other medications that could interfere with immune responses; have a history of clinically significant active skin disease(s) that may impair the ability of the investigator to place and interpret patch tests;

are pregnant; have used topical corticosteroids or calcineurin inhibitors at the test area within 1 week prior to enrollment or any body lotions/oils/creams at the test area for 48 hours prior to enrollment; or are declared ineligible by the medical monitor for a valid medical reason. Eligible participants had 4 pairs of test sites marked on clinically normal skin on their upper backs; COR806.805 was applied to 1 site in each of the 4 test pairs. After allowing the cream to dry, the antigen (dispersed in petrolatum) to which the participant had a known sensitivity was applied to both sites using a patch test device (Finn Chamber®) for 3 test pairs. The fourth pair was used as a control and included only COR806.805 on 1 site and white petrolatum on the contralateral site; both control sites were covered with empty patch test devices. Additionally, a 16-cm² site was marked on the volar aspect of 1 forearm on each participant and coated with a thin film of COR806.805 followed by the appropriate antigen; this open test site was allowed to air-dry and was not occluded. Six hours after application, the participants had the first pair of patch test devices removed and the site on the volar aspect of the forearm was wiped clean (visit 2). Signs of delayed-type hypersensitivity (DTH) reactions were recorded for the pair of sites on the back and 1 site on the forearm using the North American Contact Dermatitis Group (NACDG) scale. The forearm site was placed only to establish concordance with the test sites. At visit 3 (24 hours after visit 1), participants had the second pair of patch test devices removed from the back and these test sites, together with the test sites evaluated at 6 hours, were evaluated/reevaluated. At visit 4 (48 hours after visit 1), participants had the third and fourth pairs of patch test devices removed from the back and all 8 test sites were evaluated/reevaluated. Finally, participants returned 96 hours after visit 1 to have all test sites reevaluated. After this last assessment (visit 5), participants exited the study. At all visits, participants were queried regarding adverse events, changes in medical histories, and concomitant medication use.

The trial was designed to statistically evaluate product barrier performance under artificially harsh conditions that are unlikely to be encountered during clinical use of the product. In actual use, the product is likely to be applied several times daily and the antigen would not be held against the skin continuously for up to 48 hours under an occlusive aluminum disc.

An evaluation of DTH reactions at each test site was conducted during the study visits using the NACDG scale. The sensitization scale enabled documentation of negative reactions (0) as well as weak (1+), strong (2+), and extreme (3+)

reactions. Using the McNemar test for paired comparisons, the NACDG scores for the test sites exposed to COR806.805 and antigen were compared with the scores for the test sites exposed to antigen alone for each antigen sensitivity group at each time point after removal of the patch test device. The primary efficacy analysis examined if application of COR806.805 provides protection against exposure to sensitizing antigens and over what period the protection is maintained. Barrier protection was defined as COR806.805 test sites having fewer positive DTH reactions than untreated sites under identical periods of occlusion. Evaluations of the open site on the forearm were made to establish concordance with the test sites, not as independent analyses of efficacy.

Thirty-six participants were enrolled to obtain at least 30 evaluable participants (10 participants sensitive to each antigen).

Lactic Acid Barrier Test—Trial no. 806-805-09-005 was a single-center evaluation of the effectiveness and duration of COR806.805 as a barrier to the stinging effect induced by a solution containing lactic acid 10% when applied to the nasolabial fold of participants with a predetermined sensitivity.² Prior to study initiation, women were screened to ensure they met all of the inclusion and none of the exclusion criteria. Inclusion criteria included the following: females aged 18 to 65 years, in good general health, and sensitive to lactic acid (10% vol/vol) as determined at the screening visit; faces must be free of abrasions or other skin conditions that would exclude participation in the study; individuals free of any systemic or dermatologic disorder, including a known history of allergies or other medical conditions, which, in the opinion of the investigator, could interfere with the conduct of the study, interpretation of results, or increase the risk of adverse reactions; ability to complete the course of the study and to comply with instructions; agreement to not use or introduce any new personal care products, including cosmetics, skin care, hand care, body care, hair care, personal hygiene, and others, during the course of the study; agreement to avoid sun exposure during the course of the study; agreement to not apply any lotions, creams, oils, gels, or moisturizing cleansers to the face 10 hours prior to visits; females who are of childbearing potential must submit to a urine pregnancy test; and individuals must be able to read, understand, and provide written informed consent. Exclusion criteria included the following: individuals with any visible skin disease or skin condition (eg, eczema, psoriasis) that could interfere with the evaluations; abnormal skin pigmentation or body art (tattoos) at the test sites that could interfere with subsequent evaluations of dermal responsiveness; excessive dryness or redness at the test sites; known allergic

hypersensitivity to personal care products including those products containing lactic acid; pregnancy, planning a pregnancy, or nursing a child; currently participating or have participated in a clinical study involving the face within the past 14 days; currently under treatment for asthma or diabetes; and/or taking prescription or over-the-counter anti-inflammatory medications, nonsteroidal anti-inflammatory drugs, and/or steroids (topical, oral, and systemic).

Participants continuing into the prequalification phase were directed into an environmentally controlled room ($70^{\circ}\pm 3^{\circ}\text{F}$; relative humidity, $35\%\pm 15\%$) where they underwent environmental equilibration for at least 15 minutes. Following equilibration, a technician applied 2 strokes of a cotton applicator saturated with a solution containing lactic acid 10% to each side of the face, ensuring that the applicator passed along the nasolabial fold and terminated at the cheek midpoint. Approximately 2.5 minutes after application, participants were asked to assess the degree of stinging and/or burning according to a 4-point scale (0=no discomfort [ignoring sensations such as wet or cold]; 1=slight discomfort [barely perceptible stinging and/or burning]; 2=moderate discomfort [uncomfortable stinging and/or burning; participant is always aware of the discomfort]; 3=severe discomfort [intensely uncomfortable stinging and/or burning; would interfere with the participant's daily routine]). At the conclusion of the prequalification assessment, participants were instructed to wash their faces with soap and a washcloth at the testing facility. Participants who perceived at least slight discomfort (barely perceptible stinging and/or burning sensations) were enrolled in the study and scheduled to return to the testing facility within 7 days for the test product application phase. In this phase, following environmental equilibration, a technician applied the COR806.805 to each side of the participant's face (≈ 0.5 g on each side of the face). To determine the longest time point for which the COR806.805 appeared effective in preventing lactic acid-induced stinging, 3 groups containing 5 participants each were assigned to be evaluated at 2 different time points (one time point for each side of the face/nasolabial fold). The time points were immediately and 30 minutes after test product application (5 participants), 1 and 2 hours after application (5 participants), and 4 and 6 hours after application (5 participants). At each post-test product application time point, a technician applied 2 strokes of a cotton applicator saturated with a solution containing lactic acid 10% to one side of the face along the nasolabial fold. The side of the face was randomized as to the application sequence. Approximately 2.5 minutes after application of the

solution containing lactic acid 10%, participants were asked to assess the degree of stinging and/or burning according to the same 4-point scale (0–3) administered during the prequalification phase. An additional 25 participants then were evaluated at the time point showing the maximum duration of protection.

Therapeutic Effects in Irritant and Allergic Contact Dermatitis—Trial no. 806-805-09-004 was a randomized open-label study to determine the therapeutic effect of COR806.805 compared with no treatment on participant-assessed symptoms of itching and burning associated with irritant and allergic contact dermatitis. To qualify for the study, after providing consent, participants with hand eczema had to assess each of the eczema-associated symptoms of itching and burning as being greater than 50 mm on a visual analogue scale (VAS) of 0 (none) to 100 mm (worst possible). An additional group of participants with sensitivity to nickel sulfate underwent a run-in period during which they were exposed to the antigen under a patch for 48 to 96 hours to create DTH lesions. To be eligible for the study, by the end of the run-in period, participants had to have a DTH reaction of at least 1+ (weak) and have assessed their scores for itching and burning individually as being greater than 50 mm on the VAS. Forty-four participants (22 with hand eczema; 22 with sensitivity to nickel sulfate) were enrolled. Participants treated the test site on one arm/hand with COR806.805 twice daily for a total of 14 days, leaving the other arm/hand as an untreated control. Participants scored their perceived itching and burning based on the VAS at each of 6 subsequent visits, which occurred during the following ranges of days:

visit 2 (days 1–3), visit 3 (days 4–5), visit 4 (days 6–7), visit 5 (days 8–10), visit 6 (days 11–13), and visit 7 (days 14–15). At the same visits, the investigator scored the sites for ulceration, erythema, induration, excoriation, flaking, weeping, edema, and scabbing (crusting) based on a 4-point scale (0=none; 3=severe).

The primary efficacy evaluation was a comparison of the changes in participant-assessed VAS scores for itching and burning between the COR806.805-treated sites and the nontreated sites at each study visit.

Results

Substantivity Test—All 10 participants completed the study. The mean assessment score for residual pigment on hands exposed to COR806.805 was 3.4 (range, 2–4) compared with 0 for participants exposed to Vaseline Intensive Care hand cream ($P<.001$; Wilcoxon signed rank test)(Figure 1).

Closed Patch Barrier Test—Thirty-five participants completed the trial and were evaluable for analysis. Overall, only 3 adverse events were reported by 3 (8%) of 36 enrolled participants. One event (dermatitis on the anterior trunk) was considered related to exposure to the study treatment (the antigen). One participant discontinued participation because of a nonserious unrelated adverse event (bronchitis). Of the 35 evaluable participants, 12 each had nickel sulfate and neomycin sensitivities, while the other 11 participants were sensitive to the fragrance mixture. Thirty-four of 35 participants showed a positive response to antigen alone under the standard patch test conditions of 48 hours' exposure with evaluation at 96 hours, thus validating the selection of participants.

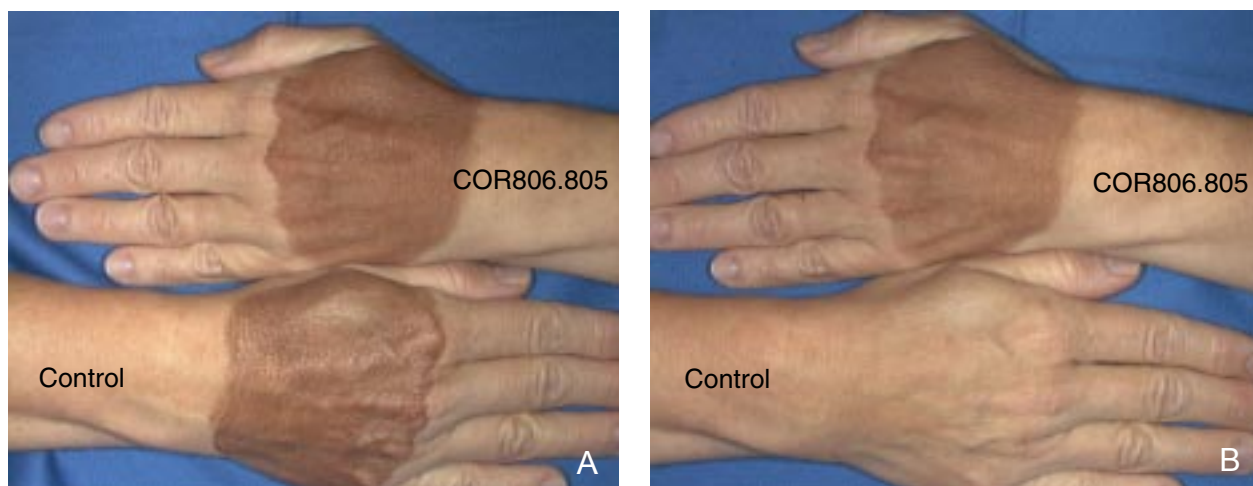


Figure 1. Substantivity of COR806.805 (Tetrix™ Cream) was evaluated in comparison with Vaseline® Intensive Care hand cream (control). Both products were blended with a pigmented cosmetic face foundation and applied to separate hands (A). Fifteen minutes after application of COR806.805 and the control, the hands were gently washed with Dove® soap and visually evaluated (B). In each of 10 participants, COR806.805 showed substantial residual presence of the added pigment.

Median Scores for Combined DTH Reactions to Nickel Sulfate, Neomycin, and Fragrance Mixture^a

Total Occlusion	Test Site	Median Postocclusion Assessments			
		Visit 2 (6 h)	Visit 3 (24 h)	Visit 4 (48 h)	Visit 5 (96 h)
6 Hours	COR806.805 + antigen	0.00	0.00	0.00	0.00
	Antigen alone	0.00	0.00	0.00	0.00
	<i>P</i> value	.0831	.3244	.5394	.1979
24 Hours	COR806.805 + antigen		0.00	0.00	1.00
	Antigen alone		0.50	0.50	1.50
	<i>P</i> value		.0007	.0413	.0144
48 Hours	COR806.805 + antigen			0.50	1.00
	Antigen alone			1.00	2.00
	<i>P</i> value			.5349	.0268

Abbreviation: DTH, delayed-type hypersensitivity.

^aAntigens dispersed in petrolatum either were placed over a single application of COR806.805 (Tetrix™ Cream) or directly onto the skin (antigen alone) for 6, 24, or 48 hours. Reactions were scored as negative (0), weak (1+), strong (2+), or extreme (3+). Midpoint values are calculated by the statistical method.

In the primary efficacy analysis, which compared pooled COR806.805 sites versus pooled antigen sites, a smaller proportion of COR806.805 test sites exhibited positive DTH reactions at all time points examined compared with antigen-only test sites (Table)(Figure 2). Within each individual antigen group, a smaller or identical proportion of test sites exhibited positive DTH reactions after application of COR806.805 plus antigen compared with test sites exposed to the individual antigen alone. Little difference could be observed between the 6-hour treated sites and the control sites, which indicates that a 6-hour antigen exposure under the test conditions was inadequate to create substantial DTH reactions.

Statistically favorable differences were observed between COR806.805 plus all antigens versus all antigens alone regarding the median skin reaction scores. For test sites that had been occluded for 24 hours, the immediate, 48-hour, and 96-hour evaluations revealed significant differences ($P=.0007$,

.0413, and .0144, respectively; Wilcoxon signed rank test). Test sites that had been occluded for 48 hours did not show a significant difference immediately but did so at 96 hours ($P=.0268$). A statistically favorable difference between COR806.805 plus fragrance mixture versus fragrance mixture alone was observed for test sites that had been occluded for 24 hours and evaluated immediately ($P=.0253$). Results for nickel sulfate and neomycin individually were directionally similar in terms of the proportion of participants showing reactions but did not reach statistical significance in this small study. Protection was best against the fragrance mixture and worst against nickel sulfate.

Lactic Acid Barrier Test—Baseline stinging scores for the first cohort of 15 participants were 1 (slight discomfort), with the exception of a single participant who reported a score of 2 (moderate discomfort). At each time point tested, COR806.805 pretreatment resulted in a substantially decreased

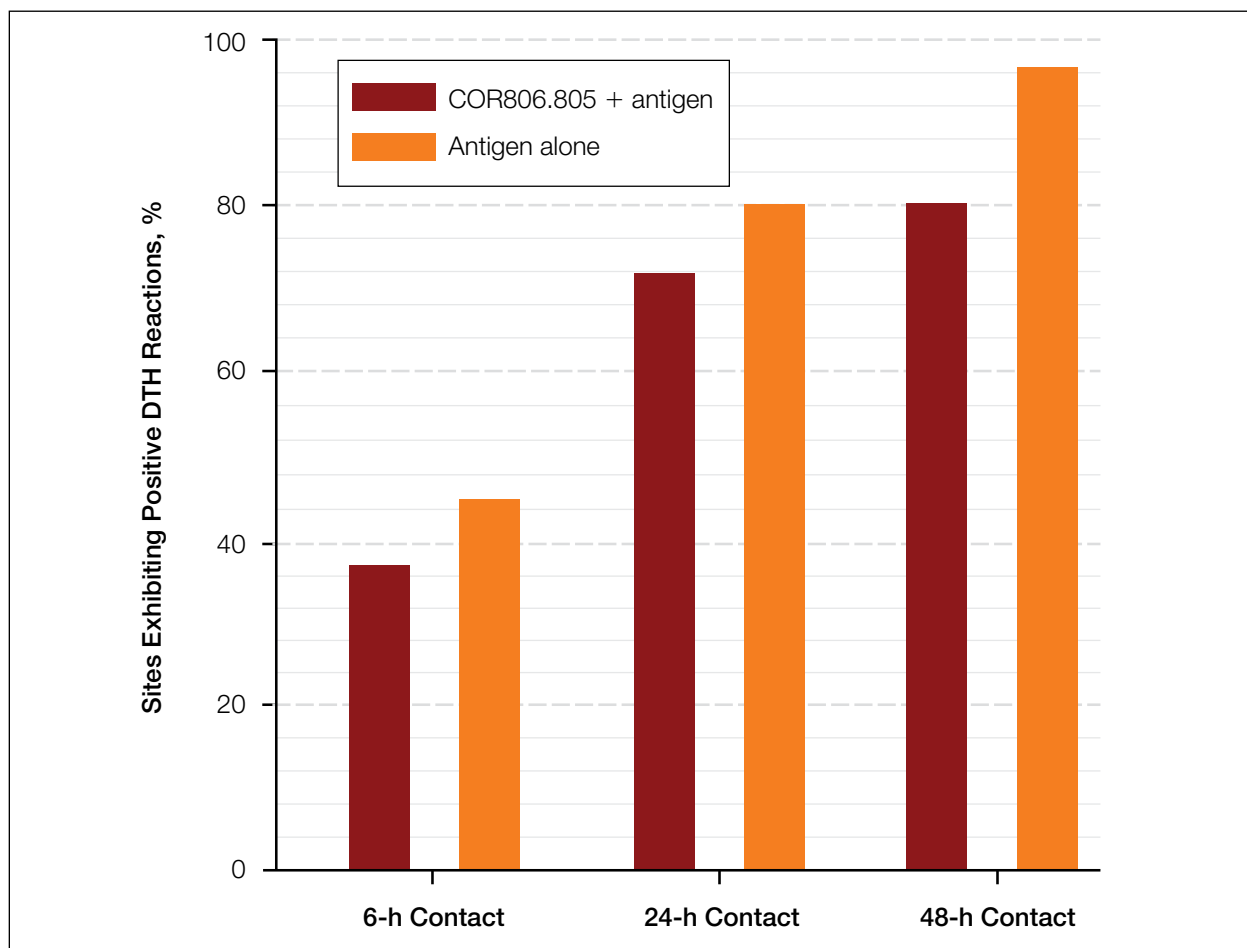


Figure 2. Delayed-type hypersensitivity (DTH) reactions evaluated at the 96-hour time point following 6, 24, or 48 hours of closed patch contact with nickel sulfate, neomycin, or a fragrance mixture dispersed in petrolatum. Antigen either was placed over a single application of COR806.805 (Tetrix™ Cream) or directly onto the skin (antigen alone).

mean stinging score. The mean of within-participant decreases from baseline varied from -0.4 at 1 hour to -1.0 at 2 and 6 hours (Figure 3). Variability in the scores was anticipated, as the groups consisted of only 5 participants each. Protection against stinging was as great at 6 hours as at any earlier time point; therefore, 6 hours was determined to be the longest duration of effect within the limits of the study. Because each participant could be tested twice, once on each nasolabial fold, the confirmatory group of 25 additional participants was tested at both 4 and 6 hours following application of product. Results then were combined with the first groups of 5 to give $N=30$, with an overall mean (SD) baseline score of 1.43 (0.50). As analyzed using the Wilcoxon signed rank test, barrier effectiveness was substantiated at both 4 hours (mean [SD] score, 0.87 [0.78]; $P<.001$) and 6 hours (mean [SD] score, 0.83 [0.76]; $P<.001$).

Therapeutic Effects on Itching and Burning of Irritant and Allergic Contact Dermatitis—Forty-two participants completed the study (21 participants

in each group). There were no significant differences between the 2 groups in baseline VAS scores. Following the initiation of therapy, the treated hand eczema sites consistently showed a lower score at each visit compared with the control sites. This difference became significant by visit 3 ($P<.05$) and remained so through visit 7. In the participants with ongoing hand eczema, the VAS scores for itching fluctuated from 67.4 mm at baseline to 48.7 mm at visit 7 for the control sites compared with a consistent decrease from 65.8 mm at baseline to 25.8 mm at visit 7 for the COR806.805-treated sites. The VAS scores for burning fluctuated from 68.8 mm at baseline to 48.1 mm at visit 7 for the control sites compared with a decrease from 66.2 mm at baseline to 22.0 mm at visit 7 for the COR806.805-treated sites. Excoriation and flaking somewhat improved on the untreated hands, while erythema, induration, and edema worsened on average. On the COR806.805-treated hands, induration remained

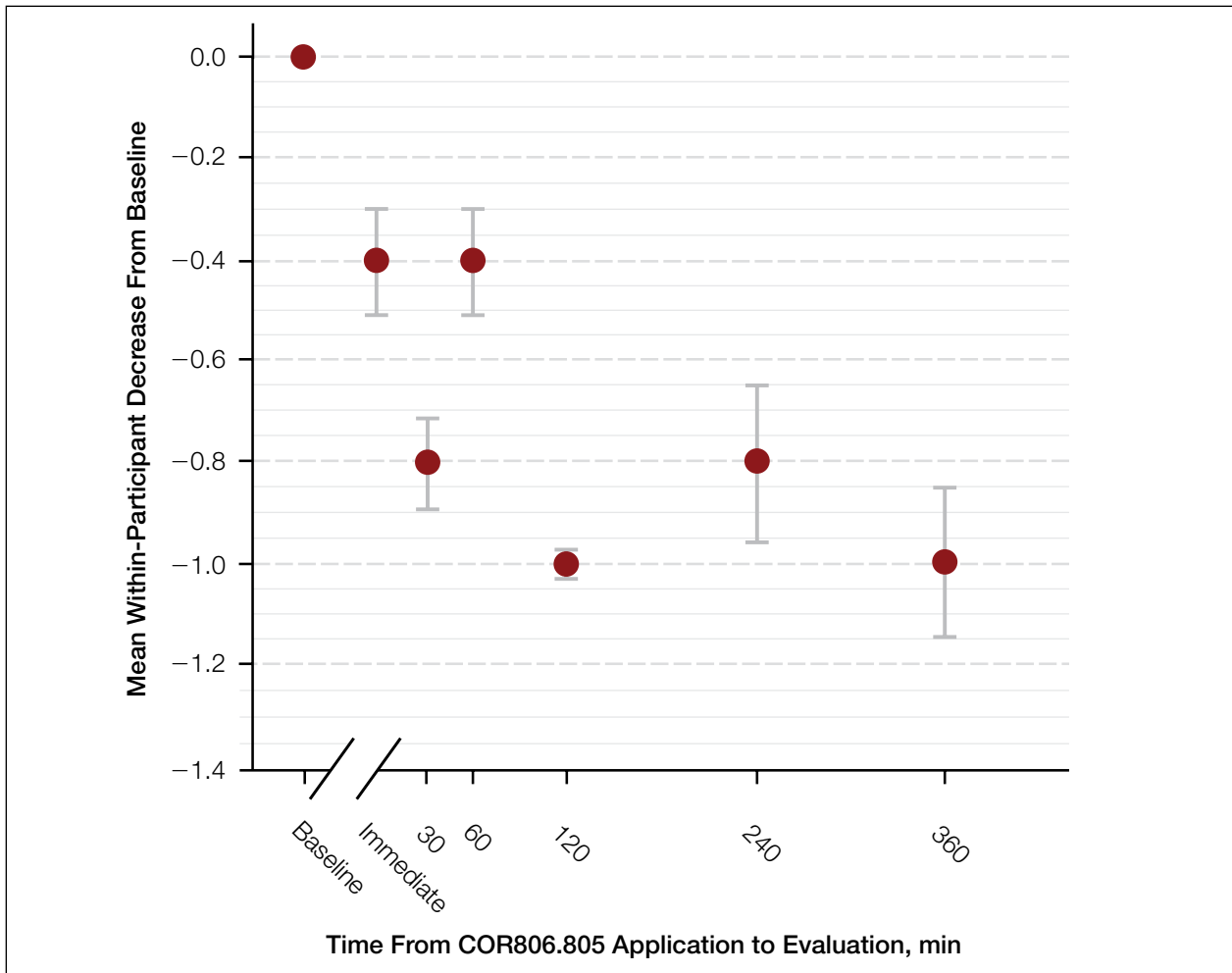


Figure 3. Mean differences from baseline in stinging scores for the first cohort of 15 participants. Following application of COR806.805 (Tetrix™ Cream), participants were tested immediately and at 30 minutes (5 participants), 1 and 2 hours (5 participants), and 4 and 6 hours (5 participants). Mean change in stinging score from baseline was used to determine the maximum duration of protection, which was 6 hours. Plot of mean (SEM).

unchanged on average, while erythema, excoriation, flaking, and edema all showed improvement.

Following the induction of a DTH reaction in participants sensitive to nickel sulfate, the itching and burning scores steadily declined over the duration of the study. This reduction in severity occurred more quickly in the sites treated with COR806.805. The differences between the treated and control sites did not reach statistical significance, but from visit 4 onward, the scores for the treated sites were consistently less than for the untreated control sites. Investigator-evaluated signs showed equivalent improvement between the treated and control sites.

Combining the data, COR806.805 was found to provide benefit in resolving the itching and burning associated with both irritant and allergic contact dermatitis, though the greatest benefit was seen in participants with hand eczema (Figure 4).

Comment

COR806.805 was effective and well-tolerated, with the study results demonstrating barrier protection properties against immediate reactions to a water-soluble substance (lactic acid) and against DTH reactions to 3 of the most common contact antigens: nickel sulfate, neomycin, and a fragrance mixture. These allergens were selected for testing not only because they are common but also because each is dissimilar in terms of chemical structure and molecular weight. The closed patch testing for DTH reactions was particularly stringent in that structurally different antigens were held in contact with barrier cream-treated skin for as long as 48 hours, a duration far in excess of what would be expected in actual clinical use. The findings were consistent with prior *in vitro* experiments conducted using a Franz cell.³

Good substantivity is an important characteristic of any skin barrier product because it gives

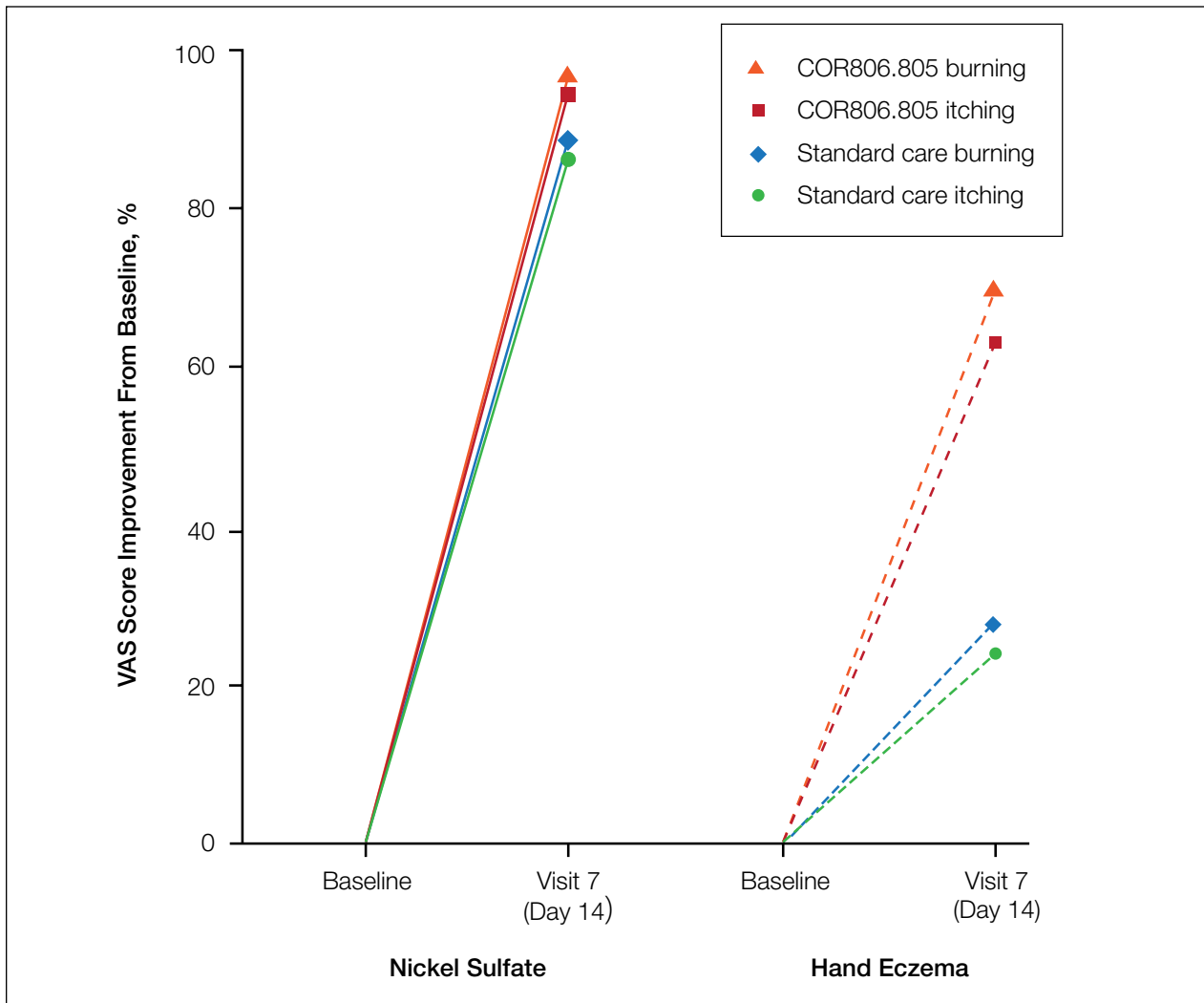


Figure 4. Improvement from baseline in visual analogue scale (VAS) scores for itching and burning. Improvements seen with the test product (COR806.805 [Tetrix™ Cream]) were most pronounced in participants with ongoing hand eczema.

patients—who often do not have the time or ability to apply a product after each hand washing—greater flexibility as well as confidence that they are using a product that provides maximum protection. COR806.805 is formulated to provide a hydrophobic barrier on the skin surface. Hence, it would be expected to remain on the hands and provide barrier protection after hand washing. One of the frustrations both dermatologists and patients encounter is the ongoing cycle of improvement of hand eczema following a prescribed course of a mild cleanser, corticosteroids, and moisturizer, only to recur when patients are reexposed to the culprit irritant or antigen. What has been lacking in the dermatologists’ armamentarium is a product with demonstrated barrier protection function against irritants and antigens. The addition of this novel barrier cream product may improve treatment outcomes by

providing long-lasting skin barrier protection from outside irritants.

Conclusion

COR806.805 gives barrier protection against a range of irritants and antigens. By controlling symptoms and providing a barrier against further contact with antigens, this novel barrier cream appears to be a product that offers the opportunity to break the ongoing cycle of hand eczema.

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