authors used multivariate logistic regression to analyze the association between atopic dermatitis subtypes and other allergic diseases.

RESULTS. Four subtypes of atopic dermatitis were identified. These phenotypes were identified as early transient (n = 96; 9.2%), early persistent (n = 67; 6.5%), late (n = 50; 4.8%), and never/infrequent (n = 825; 79.5%). The early transient and early persistent phenotypes had onset before 2 years of age, while the late phenotype had onset at or after 2 years of age. Multivariate logistic regression demonstrated a strong association between the early transient (adjusted odds ratio [aOr], 3.69; 95% confidence interval [CI], 1.93–7.035) and early persistent (aOR, 7.08; 95% CI, 3.59–13.975) subtypes with food allergy up to age 6 years, in addition to an association between the early persistent subtype and asthma up to age 6 (aOR, 2.87; 95% CI, 1.31–6.31). The late subtype had a positive association with allergic rhinitis. Parental history of allergy was a risk factor for the early persistent subtype.

CONCLUSIONS. The authors identified 4 subtypes of atopic dermatitis by using latent class analysis, and demonstrated associations between early phenotypes of atopic dermatitis and other allergic disease, including food allergy and asthma.

REVIEWER COMMENTS. This is a timely study that reinforces current trends in the literature. Knowing risk association with the early atopic dermatitis phenotypes may help guide future research and clinical care in regard to food allergy and asthma prevention strategies.

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Efficacy and Safety of Crisaborole Ointment, a Novel, Nonsteroidal Phosphodiesterase 4 (PDE4) Inhibitor for the Topical Treatment of Atopic Dermatitis (AD) in Children and Adults

Paller AS, Tom WL, Lebwohl MG, et al. *J Am Acad Dermatol*. 2016;75(3):494–503.e6

PURPOSE OF THE STUDY. To assess the efficacy and safety of crisaborole ointment, which is a phosphodiesterase 4 inhibitor, for the topical treatment of atopic dermatitis.

STUDY POPULATION. This study includes the results from 2 identically designed phase 3 clinical trials conducted in the United States that included a total of 1522 individuals who were 2 years of age or older. About 85% of study participants were less than 18 years of age, and 55% of study participants were female. About 60% of study participants were white and 28% were black.

METHODS. Patients aged 2 years or older were enrolled in 2 identically designed, vehicle-controlled, double-blind studies and were randomly assigned (2:1, crisaborole: vehicle). Study participants had an Investigator's Static Global Assessment (ISGA) score of mild to moderate atopic dermatitis. Exclusion criteria prohibited previous use of biologic therapy or systemic corticosteroids within 28 days or topical corticosteroids or topical calcineurin inhibitors within 14 days. Instructions included the application of a layer of the study drug to cover all atopic dermatitis–affected areas at baseline twice daily for the duration of the 28-day study period. The primary efficacy end point was an ISGA score at day 29 of clear (score 0) or almost clear (score 1) with a 2-grade or more improvement from baseline.

RESULTS. There were no significant differences across treatment groups or across studies in either disease severity or baseline demographics. More patients treated with crisaborole achieved efficacy in an ISGA score at day 29 than vehicle-treated patients (first phase 3 study: 32.8% vs 25.4%, P = .38; second phase 3 study: 31.4% vs 18%, $P < .001$). Furthermore, patients treated with crisaborole achieved efficacy in an ISGA score and improvement in pruritus earlier than those treated with vehicle alone. Crisaborole was well tolerated, with infrequent adverse events of a mild to moderate severity level.

CONCLUSIONS. Crisaborole demonstrated improvement in overall disease severity, pruritus, and other signs of atopic dermatitis with a favorable safety profile.

REVIEWER COMMENTS. This study highlights the results of 2 large phase 3 trials that demonstrated the clinical efficacy and benefit of crisaborole for the treatment of mild to moderate atopic dermatitis. As a phosphodiesterase 4 inhibitor, crisaborole represents a novel, nonsteroidal topical therapy that has been recently FDA approved to improve management for atopic dermatitis.

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Pediatric Patch Testing: A 10-Year Retrospective Study

Ascha M, Irfan M, Bena J, Taylor JS, Sood A. *Ann Allergy Asthma Immunol*. 2016;117(6):661–667

PURPOSE OF THE STUDY. To review the demographics, referral criteria, efficacy of testing, and comorbid conditions among patients who are evaluated by patch testing for concern for allergic contact dermatitis (ACD).

STUDY POPULATION. Data were collected from 157 pediatric patients (3–18 years old, median 13 years old) who were evaluated for patch testing at the Cleveland Clinic Foundation Department of Dermatology from 2005–2015. Of participants, 58.6% were female, and 68.8% were atopic.

METHODS. A retrospective chart review was conducted with institutional review board approval. Outcomes reviewed

included age, sex, history of atopy, comorbidities, referring physician, reason for referral, history of previous patch testing or hospitalization (if any), distribution and appearance of dermatitis, duration of symptoms, skin biopsy results, treatment before patch testing and in follow-up, number of patches placed with result outcomes, and improvement at the follow-up visit. Patch testing was mostly completed based on established criteria outlined by the North American Contact Dermatitis Group (NACDG), and positives were defined as 1+ (weak positive reaction) or greater.

RESULTS. Dermatologists referred the majority of patients (73%), while 20% were referred by primary care providers. Dermatitis was present from <6 months (20%) to 2 years (46.2%). At least 1 positive reaction was seen in 73.25% of cases, and 54.8% had 2 or more positive patch test results. The most frequent positive triggers for ACD were nickel (24.4%) and cobalt (21.7%). Males had more positive results from fragrance mix 1 compared with females ($P = .02$). Patients with atopy were more likely to have a positive reaction to cobalt ($P = .008$) and chromium ($P = .03$). Among the 60 patients who returned for follow-up, 60.7% reported improvement in symptoms after patch testing, and most (88.5%) were being treated with topical corticosteroids.

CONCLUSIONS. Patch testing is useful for guiding treatment options for ACD.

REVIEWER COMMENTS. This study demonstrates the utility of patch testing when a trigger for the diagnosis of dermatitis is not clear from history or if dermatitis is refractory to standard treatment. Targeted patch testing can be cost-effective and may guide management strategies. Given the rising prevalence of allergic disease and its impact on quality of life, it is important for providers to consider referrals for patch testing before starting treatment with systemic immunosuppressants for allergic contact dermatitis.

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Prevention of Hereditary Angioedema Attacks With a Subcutaneous C1 Inhibitor

Longhurst H, Cicardi M, Craig T, et al. *N Engl J Med*. 2017;376(2):1131–1140

PURPOSE OF THE STUDY. To determine if functional levels of C1 inhibitor activity would provide effective prophylaxis against attacks of hereditary angioedema (HAE).

STUDY POPULATION. Patients who were 12 years or older with type 1 or 2 HAE and had 4 or more attacks in a consecutive 2-month period within 3 months before screening.

METHODS. This was an international, prospective, multicenter, randomized, double-blind, placebo-controlled, dose-ranging, phase 3 trial to evaluate the efficacy and safety of self-administered subcutaneous CSL830. Patients were randomly assigned to 1 of 4 treatment sequences in a crossover design consisting of two 16-week treatment periods using either 40 IU or 60 IU of CSL830 per kilogram of body weight twice weekly or a placebo. The primary efficacy end point was the number of attacks of angioedema, and the secondary end point was the portion of patients who had a response of >50% reduction in attacks.

RESULTS. Of the 90 patients who underwent randomization, 78 completed the trial. Both doses compared with the placebo reduced the rate of attacks of HAE: 40 IU, −2.42 attacks per month (95% confidence interval, −3.38 to −1.46); and 60 IU, −3.51 attacks per month (95% confidence interval, −4.12 to −2.81). Response rates were 76% for 40 IU and 90% for 60 IU. The need for rescue medication was reduced from 5.5 uses per month in the placebo group to 1.3 uses per month in the 40 IU group and 0.32 uses per month in the 60 IU group.

CONCLUSIONS. This study highlights that self-administration of subcutaneous CSL830 was safe and showed long-term prevention of HAE. Of patients, >50% had no moderate-to-severe attacks while receiving CSL830.

REVIEWER COMMENTS. This study helps to understand the effectiveness of a self-administered product in decreasing the significant burden of attacks in this rare disease.

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ALLERGIC RHINITIS

Allergic Rhinitis Causes Loss of Smell in Children: The OLFAPEDRIAL Study

Langdon C, Guilemany JM, Valls M, et al. *Pediatr Allergy Immunol*. 2016;27(8):867–870

PURPOSE OF THE STUDY. To evaluate the impact of allergic rhinitis on olfaction in children and characterize it using the ARIA (Allergic Rhinitis and Its Impact on Asthma) criteria for severity and duration.

STUDY POPULATION. This study included 1260 children who were 6–12 years of age with allergic rhinitis diagnosed by an allergist from 271 centers in Spain between May and July 2008.

METHODS. This was an observational, cross-sectional, multicenter study. Inclusion criteria included symptoms of rhinoconjunctivitis for >1 year, sensitization to 1 or more aeroallergens by skin or specific immunoglobulin E testing, and discontinuation of maintenance medications for allergic rhinitis at least 2 weeks prior to inclusion.

Pediatric Patch Testing: A 10-Year Retrospective Study

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Pediatric Patch Testing: A 10-Year Retrospective Study

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