METHODS. The authors isolated coagulase-negative *Staphylococcus* (CoNS) species with identified antimicrobial activity against *S. aureus* from the skin of AD and non-AD subjects. The study identified *Staphylococcus epidermidis* and *Staphylococcus hominis* as sources of these antimicrobial peptides (AMPs). The CoNS strains were applied autologously to the lesional skin of 5 AD patients. *S. aureus* colonization was examined after autologous microbiome transplant.

RESULTS. When the CoNS strains were applied autologously to the lesional skin of AD patients, *S. aureus* colonization decreased.

CONCLUSIONS. Normal skin has CoNS that produce AMPs, which in turn inhibit overgrowth of *S. aureus*. Thus, some skin bacteria produce AMPs that protect against *S. aureus* colonization, and loss of these protective bacteria may contribute to the development of AD.

REVIEWER COMMENTS. This study highlights the importance of the skin microbiome in AD. Peptides made by the skin commensal microbiome may be the first line of defense against pathogens and later AD development. The findings from this study may one day provide the framework for the prevention and treatment of AD by altering the skin bacterial flora or by developing these AMPs as topical medications.

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Association Between Atopic Dermatitis and Attention Deficit Hyperactivity Disorder in U.S. Children and Adults

Strom MA, Fishbein AB, Paller AS, Silverberg JI. *Br J Dermatol*. 2016;175(5):920–929

PURPOSE OF THE STUDY. To determine if an association exists between atopic dermatitis and attention deficit (hyperactivity) disorder (ADD/ADHD) in children and adults and to describe the factors that contribute to such an association.

STUDY POPULATION. This study analyzed pooled data from 19 US population-based surveys that included 354 416 children and adolescents aged 2–17 years.

METHODS. Cross-sectional data were analyzed from 19 US population-based surveys, each assembled by the National Center for Health Statistics, including the 1997–2013 National Health Interview Survey and the 2003–2004 and 2007–2008 National Survey of Children's Health. Associations of both atopic dermatitis and ADD/ADHD were examined in children aged 2–17 years, including sex, age, race, household income, highest level of household/parental education, birthplace in the US or elsewhere, and insurance coverage. Bivariate and multivariate logistic regression models were used in statistical analysis.

RESULTS. The pooled prevalence of atopic dermatitis was 10.1%, and the pooled prevalence of ADD/ADHD was 7.3%. Children with atopic dermatitis demonstrated an association with ADD/ADHD (adjusted odds ratio [95% confidence interval], 1.14 [1.03–1.26]). Children with both severe atopic dermatitis and only 0–3 nights of adequate sleep per week had much higher odds of ADD/ADHD (16.83 [7.02–40.33]) than those with 0–3 nights of adequate sleep per week (1.83 [1.47–2.26]) or mild to moderate atopic dermatitis alone (1.56 [1.22–1.99]). Atopic dermatitis in the absence of other allergic diseases was also associated with increased risk of ADD/ADHD in children. For children with atopic dermatitis, a history of anemia, headaches, and obesity were associated with higher odds of ADD/ADHD.

CONCLUSIONS. Atopic dermatitis in children is associated with increased odds of ADD/ADHD. Headaches, obesity, and anemia occurring in children with atopic dermatitis further increase the risk of ADD/ADHD.

REVIEWER COMMENTS. This study demonstrates that atopic dermatitis in the absence of other allergic diseases in children is associated with increased risk of ADD/ADHD. Furthermore, severe atopic dermatitis and sleep disturbance may act both independently and synergistically to increase the risk of ADD/ADHD. Improved understanding of these risk associations between atopic dermatitis and ADD/ADHD will assist in the clinical care of these children.

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Phenotypes of Atopic Dermatitis Depending on the Timing of Onset and Progression in Childhood

Roduit C, Frei R, Depner M, et al; and the PASTURE study group. *JAMA Pediatr*. 2017;171(7):655–662

PURPOSE OF THE STUDY. To use a symptom-based definition of atopic dermatitis to identify different phenotypes and to determine if certain subtypes are at higher risk to develop comorbid atopic disease.

STUDY POPULATION. A total of 1038 European children from The Protection Against Allergy Study in Rural Environments (PASTURE) birth cohort (designed to assess impact of living on a farm) were recruited between August 2002 and March 2005. This study included participants with data on atopic dermatitis up until age 6 years.

METHODS. Subtypes of atopic dermatitis in children were identified by using latent class analysis. Subtypes were based on the timing of onset and symptom course. The

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

Phenotypes of Atopic Dermatitis Depending on the Timing of Onset and Progression in Childhood

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