EDITORIAL

Emollients to Prevent Atopic Dermatitis—Is New Evidence a Game Changer?

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Pediatric atopic dermatitis (AD) is common, with a median prevalence rate in children aged 6 to 7 years of 6% but ranging from 1.6% to 15.7% across different regions globally.[1] It represents a substantial financial and emotional burden for affected families.[2] A low-cost, practical intervention that prevents AD in infancy and early childhood could have a substantial effect on individual and public health.

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Several studies have evaluated the potential benefits of different emollient regimens in infants without eczema with mixed results. A 2022 Cochrane review included 7 studies in which 3052 term infants without eczema were randomized to emollient regimens compared with standard of care.[3] Pooling of these studies did not detect a protective benefit of interventions on the development of eczema by age 1 to 2 years (risk ratio, 1.03; 95% CI, 0.81-1.31). A few additional studies have been published since then, with most also finding no benefit of emollient use.[4]

In this issue of *JAMA Dermatology,* the results of the Community-based Assessment of Skin Care, Eczema, and Allergies (CASCADE) trial are presented, contradicting previous studies and suggesting some benefit of preventive emollient use.[5] CASCADE randomized 1247 term infants without a history of eczema to either once-daily full-body emollient use starting within the first 9 weeks of life or standard of care.[5] The primary outcome was a diagnosis of AD at age 2 years as determined by a clinician, which was significantly lower in the infants randomized to the intervention (36.1% vs 43.0%), with a relative risk of 0.84 (95% CI, 0.73-0.97). There was no significant difference between groups in risk of skin infections or adverse reactions to skin products. Secondary analyses suggested a possible trend toward a greater protective benefit in children without a family history of atopy and for those without a dog in the home. AD rates were high in both groups, even considering the known higher prevalence of eczema during the first 2 years of life.[6]

CASCADE did have multiple strengths, including a large primary care population from different locations in the US and a pragmatic study design. There was representation from rural and urban settings and across different racial and ethnic backgrounds.

This study differentiated itself from previous studies on emollients for AD prevention in several ways, specifically the timing and duration of the intervention. In CASCADE, the mean age of enrollment was 24 days, with more than 60% having already initiated use of moisturizers before enrollment. This differed from most other studies, in which randomization occurred at or shortly after birth. There is evidence to support that neonatal skin has increased permeability and an underdeveloped stratum corneum and that this changes substantially during the first few weeks of life.[7] The use of moisturizers by many of the participants in this period may have provided a baseline protection (or harm) that needs to be considered. This does not necessarily diminish the study findings, but rather clarifies the study question being asked and may explain why the results differed compared with other emollient studies. Another unique feature of the intervention in CASCADE was that it included full-body application recommendations for almost 2 years, which was longer than previous studies included in the Cochrane review in which no intervention period was greater than 12 months.

An interesting point of discussion is the larger protective effect of the intervention in participants deemed to be at low risk of AD. Most, but not all, prior studies focused on infants at high risk of AD, usually defined as having a first degree relative with atopy. There were 2 previous studies not restricted to high-risk infants.[8,9] These included the largest trial in this area, PreventADALL, in which daily bathing with a paraffin-based moisturizer and face cream did not reduce eczema by age 1 to 2 years.[9] In CASCADE, participants included high-risk and low-risk infants, with high risk being defined as those with a history of atopy in a parent or sibling. Subgroups were equally distributed at randomization, and in the secondary analysis stratified by AD risk, the protective effect of the intervention was accentuated in the lower-risk group (relative risk [RR], 0.75; 95% CI, 0.6-.9) and not in the high-risk group (RR, 0.93; RR, 0.8-1.1).

The authors proposed that the protection demonstrated in low-risk infants may have resulted from blunting of external irritants, which could represent a key mechanism triggering the development of AD in this group specifically. Unfortunately, exposure to these factors was not captured and would be very challenging to dissect, as they would be expected to include a wide range of culprits. Growing research has identified potential roles for environmental substances (eg, tobacco smoke, metals, detergents), diet and lifestyle factors, and airborne allergens in the pathogenesis of AD. Given that participants were randomly distributed among urban and rural sites across different states, a differential contribution of environmental irritants from pollution or climate factors is unlikely in the low-risk group. However, many individual-level irritants could have played a role.

Conversely, the high-risk group did clearly benefit from the intervention, aligning with findings from many prior skin intervention studies. Perhaps in this population, the genetically predisposed barrier dysfunction cannot be overcome by emollients, and the effect of external irritants is lower. Moreover, in the Cochrane review, individual participant data meta-analysis allowed

exploration of atopy risk based on family history or genotype as an effect modifier and found no significant interaction.

The protective effect of dog ownership was also highlighted in the results of the CASCADE study. Although dog ownership was associated with decreased incidence of AD, this was only significant in the intervention group and warrants further exploration in future studies. Dog ownership may be a marker of other lifestyle choices and practices in the family that may themselves be more correlated with the development of eczema.

The lack of an increase in skin infection is reassuring. In the Cochrane review, emollient interventions were associated with a probable increase in skin infections based on data from 2728 infants in 6 studies. As already highlighted, these studies mostly included infants at high risk of developing AD, with a possible predisposed defect in skin barrier that would facilitate transcutaneous organism introduction.

There were several additional important limitations to consider. The allowance of different emollients to be used limited the ability to analyze differences in efficacy between these, and reliance on patient-reported adherence introduced the potential for recall bias. Additionally, information on bathing practices was not collected, including frequency and additives used. Although all participants were given the same twice weekly bathing recommendation, it is possible that any deviations in this practice were not equally distributed among the groups. Another factor suggesting caution when interpreting the results of CASCADE is the pattern of results in sensitivity analyses that used different definitions of AD. The protective effect of emollients was substantially attenuated when using validated AD assessment tools, such as the UK Working Party criteria and the Children's Eczema Questionnaire, to define the outcome. AD identified by health record review, parental report, or prescription that does not meet validated case definitions may represent milder disease or different forms of eczema.

Still, CASCADE does provide some evidence and a framework for a low-risk, skin-directed intervention that primary care clinicians could recommend in their routine well-child visits, with safety data up to 2 years. However, more data are needed before this can be recommended to the general population, given the discrepancy between these study findings and previous work. This is especially so in areas where the prevalence of AD may be lower and the cost of emollients more substantial and not reimbursed by health systems.[10] An analysis of costs from the BEEP trial suggested that the use of emollient in high-risk infants is not cost-effective.[11] A similar analysis would be beneficial in a cohort of low-risk infants, especially with the possibility of a larger benefit in this subgroup in preventing AD.

Inclusion of CASCADE trial data in an update of the Cochrane individual participant data meta-analysis is under way, and this will allow for further exploration of the effect of atopy risk based on family history or genotype on outcomes. It would be helpful to have more data that builds on the framework of this pragmatic study, focusing on participants who are defined as low risk for AD, with fewer emollient options, and more comprehensive monitoring of all products and potential environmental allergens for the duration of the intervention. More work is also needed to understand the mechanism and effect of different emollient ingredients, allowing a standardized classification of emollient interventions according to these ingredients. Until then, clinicians and families should consider shared decision-making when considering emollients as a preventive strategy for AD, weighing the potential benefits and financial implications on an individual basis.

ARTICLE INFORMATION

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REFERENCES

1. Langan SM, Mulick AR, Rutter CE, et al. Trends in eczema prevalence in children and adolescents: a Global Asthma Network phase I study. *Clin Exp Allergy*. 2023;53(3):337-352. doi:10.1111/cea.14276

2. Filanovsky MG, Pootongkam S, Tamburro JE, Smith MC, Ganocy SJ, Nedorost ST. The financial and emotional impact of atopic dermatitis on children and their families. *J Pediatr*. 2016;169:284-90.e5. doi:10.1016/j.jpeds.2015.10.077

3. Kelleher MM, Phillips R, Brown SJ, et al. Skin care interventions in infants for preventing eczema and food allergy. *Cochrane Database Syst Rev*. 2022;11(11):CD013534. doi:10.1002/14651858.CD013534.pub3

4. Grześk-Kaczyńska M, Petrus-Halicka J, Kaczyński S, Bartuzi Z, Ukleja-Sokołowska N. Should emollients be recommended for the prevention of atopic dermatitis? new evidence and current state of knowledge. *J Clin Med*. 2024;13(3):863. doi:10.3390/jcm13030863

5. Simpson EL, Michaels LC, Ramsey K, et al; CASCADE Consortium. Emollients to prevent pediatric eczema: a randomized clinical trial. *JAMA Dermatol*. Published online July 23, 2025. doi:10.1001/jamadermatol.2025.2357

6. Al-Naqeeb J, Danner S, Fagnan LJ, et al. The burden of childhood atopic dermatitis in the primary care setting: a report from the Meta-LARC Consortium. *J Am Board Fam Med*. 2019;32(2):191-200. doi:10.3122/jabfm.2019.02.180225

7. Choi EH. Skin barrier function in neonates and infants. *Allergy Asthma Immunol Res*. 2025;17(1):32-46. doi:10.4168/aair.2025.17.1.32

8. Yonezawa K, Haruna M. Short-term skin problems in infants aged 0-3 months affect food allergies or atopic dermatitis until 2 years of age, among infants of the general population. *Allergy Asthma Clin Immunol*. 2019;15:74. doi:10.1186/s13223-019-0385-7

9. Lødrup Carlsen KC, Rehbinder EM, Skjerven HO, et al. Preventing atopic dermatitis and allergies in children—the PreventADALL study. *Allergy*. 2018;73(10):2063-2070. doi:10.1111/all.13468

10. Bylund S, Kobyletzki LB, Svalstedt M, Svensson Å. Prevalence and incidence of atopic dermatitis: a systematic review. *Acta Derm Venereol*. 2020;100(12):adv00160. doi:10.2340/00015555-3510

11. Sach TH, Lartey ST, Davies C, et al; BEEP Study Team. Emollients for preventing atopic eczema: cost-effectiveness analysis of the BEEP trial. *Clin Exp Allergy*. 2023;53(10):1011-1019. doi:10.1111/cea.14381