

Emollients for prevention of atopic dermatitis in infancy

Atopic dermatitis (also known as eczema and atopic eczema) is the most common chronic inflammatory disorder of the skin and affects around a quarter of children.¹ Worldwide, its prevalence is increasing² and persistence into adulthood is common.³ The first manifestations usually appear in early life with dry, cracked, scaly, and erythematous skin, and at all ages intractable pruritus. Atopic dermatitis can result in impaired quality of life for individuals and their families, alongside considerable social and financial burden.⁴ Moreover, there is no known cure or established strategies for prevention.

Early onset atopic dermatitis is often the hallmark of an atopic diathesis. Mutations in the filaggrin gene (*FLG*)—which encodes a protein crucial to epidermal function and skin barrier integrity—is associated with atopic dermatitis, food sensitisation, and allergy.⁵ Therefore, the skin barrier might play a key role in the development of atopic dermatitis and subsequently, via epicutaneous sensitisation through damaged skin, in food allergies. However, skin barrier dysfunction can be apparent in the first weeks of life, before the development of atopic dermatitis,⁶ and *FLG* mutations are associated with food allergy even in the absence of atopic dermatitis,⁷ suggesting that interventions to improve skin barrier function from infancy have the potential to prevent the skin condition and development of food allergy independently.

Emollients are the primary management strategy of atopic dermatitis and include leave-on creams or ointments and bath additives. Regular, liberal use of emollients aims to maintain skin moisture, repair or enhance the skin barrier, and reduce the need for anti-inflammatory measures. Small proof of concept pilot studies provided strong efficacy signals for the hypothesis that daily emollient use could prevent atopic dermatitis,^{8–10} and prompted two large pragmatic prevention trials.^{11,12}

The null findings of Håvard Ove Skjerven and colleagues¹¹ and Joanne Chalmers and colleagues¹² in *The Lancet* were unexpected. They found no evidence that daily emollient use in either a population-based¹¹ or high-risk cohort¹² of infants during the first year of life could delay, suppress, or prevent atopic dermatitis.

Skjerven and colleagues report the primary outcome of atopic dermatitis at 12 months of age in the Preventing Atopic Dermatitis and ALLergies in Children

(PreventADALL) study,¹¹ a large pragmatic population-based randomised trial done in Norway and Sweden. 2397 newborn infants (53% boys, 47% girls) were cluster-randomly assigned in a 2×2 factorial design to either: controls with no specific advice on skin care and advice to follow national infant feeding guidelines; regular skin emollients (bath oil and facial cream) from 2 weeks of age; early complementary feeding of common food allergens (peanut, milk, wheat, and egg) introduced between 12 weeks and 16 weeks of age; or both interventions. Atopic dermatitis occurred in 8% of infants in the no intervention group, 11% in the skin intervention group, 9% in the food intervention group, and 5% in the combined intervention group. The primary hypothesis that either skin or food intervention reduced atopic dermatitis was not confirmed, but an unexpected significant interaction was shown between the interventions, which could represent a chance finding or suggests that multiple prevention strategies work synergistically. Notably, the combined intervention was included for the food allergy outcomes and the possible additive effects will be explored further when the infants reach age 36 months. No safety concerns were identified. Compliance to the interventions was suboptimal, with full protocol adherence in only 27% of participants in the skin intervention group and 32% in the food intervention group. As a pragmatic, population-based intervention, these adherence results provide important information on the feasibility of implementing primary prevention strategies at the population level, in which additional bathing regimens and feeding protocols appear challenging to maintain in regular infant care.

Chalmers and colleagues report the primary outcome of eczema at 2 years of age in the Barrier Enhancement for Eczema Prevention (BEEP) study,¹² a multicentre, pragmatic, two-arm, parallel group, randomised controlled trial done in the UK. 1394 newborn infants (53% boys, 47% girls) at high risk of allergy (family history of atopic disease) were randomly assigned to receive daily application of emollient for the first year plus standard skin care advice, or standard skin care advice only. The intervention, commenced at a median age of 11 days, did not prevent the development of eczema at age 2 years, which occurred in 23% of the emollient group and 25% of the control group. Unexpectedly, the secondary outcome of food allergy occurred more frequently in the



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intervention group (7%) than in the control group (5%), (adjusted relative risk 1.47, 95% CI 0.93–2.33), largely attributable to egg allergy; however, less than a third of food allergy diagnoses were based on the gold standard oral food challenge. Contrary to the hypothesis that emollients would enhance the skin barrier, preventing epicutaneous sensitisation and food allergy, emollient use might enhance transfer and uptake of food allergens. Additionally, skin infections occurred more frequently in the emollient group than in the control group (adjusted incidence rate ratio 1.55, 95% CI 1.15–2.09), suggesting that application of emollient can also assist inoculation of pathogens on the infant skin or disturb the natural protective skin microbiome.

The absence of a preventive effect on atopic dermatitis might be associated with the type, frequency of application, and timing of commencement of emollient. Following promising results of a trend to reduced atopic dermatitis and food sensitisation at age 12 months from a pilot study using a ceramide-dominant emollient with a slightly acidic pH, twice daily from birth, a large randomised controlled trial in high-risk infants, Prevention of Eczema by a Barrier Lipid Equilibrium Strategy (PEBBLES), is underway to confirm these findings including food allergy endpoints.¹³ Although, even if the results show a reduction in these atopic outcomes, lessons from PreventADALL suggest this intensive twice daily emollient regimen, not to mention the high cost of this complex formulation, could affect its potential viability as a population-based preventive strategy.

An ongoing prospective individual patient data meta-analysis will provide additional evidence on any association between use of emollients during the first year of life and reduction in atopic dermatitis, food allergy, and associated health outcomes.¹⁴ However, at this stage, emollients should not be recommended for the primary prevention of atopic dermatitis in infants.

We declare no competing interests.

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*Kirsten P Perrett, Rachel L Peters
kirsten.perrett@mcri.edu.au

Population Allergy, Murdoch Children's Research Institute, Parkville, VIC 3052, Australia (KPP, RLP); Department of Allergy and Immunology, Royal Children's Hospital Melbourne, Parkville, VIC, Australia (KPP); and Melbourne School of Population and Global Health (KPP), and Department of Paediatrics (RLP), The University of Melbourne, Parkville, VIC, Australia

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No time to waste: preventing tuberculosis in children

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Tuberculosis takes the life of one in five children developing the disease.¹ Data from the pre-chemotherapy era suggest very young children are at highest risk for tuberculosis after exposure, and highly susceptible to the most severe forms of the disease.^{2,3} As a result, tuberculosis control efforts among children

in high-burden countries are focused on those below 5 years of age.² One of the most important efforts is provision of tuberculosis preventive therapy after tuberculosis exposure, yet only one in four children below 5 years of age who might benefit from life-saving preventive therapy will receive it.¹ In resource-constrained