

Aetiology and prevention of eczema

Eczema is one of the commonest health conditions affecting young children in many regions, although the prevalence varies significantly internationally. In this month's issue, we see a flurry of important papers that move our understanding of eczema forward significantly. First, the current epidemiology in the United Kingdom is described by de Lusignan et al, who as expected show the incidence and prevalence to be highest in infants and young children, but also identify a smaller peak in the elderly. They identify increased eczema in urban settings and important variations according to ethnic and socioeconomic grouping, which may have been influenced by variations in healthcare-seeking behaviour. Eczema is a burdensome condition, both due to the symptoms of the disease and to the associated emotional and behavioural impact.¹ The condition is strongly associated with other atopic disorders, but less well recognized is the association with autoimmune skin diseases such as alopecia areata.² Once eczema manifests, particularly in its more persistent and severe forms, management can be difficult. However, it may be informed by serum biomarkers or machine-learning approaches to predict disease severity.^{3,4} Our current approaches using topical or systemic anti-inflammatory medications and physical measures such as moisturizers only partially suppress symptoms, and curative treatments for eczema are lacking. So the events leading to eczema onset are of great interest, since we may be able to prevent eczema by interrupting these. Epidemiological studies have not yet successfully explained the marked variations seen between and within countries in eczema prevalence. Hygiene hypothesis type exposures such as antibiotics or mode of birth do not always associate with eczema in the same way as for other atopic disorders.⁵ Perhaps the leading area of investigation for eczema prevention at the moment is work on skin barrier integrity, informed by our understanding of the role of defects in epidermal barrier function in disease onset. As reviewed in this issue, there is growing evidence that skin irritants may be important environmental triggers of eczema onset—particularly soaps and detergents such as sodium lauryl sulphate.⁶ So if soaps and detergents can trigger eczema onset, what is the best approach to promoting healthy skin development in early life to prevent the onset of eczema?

In this issue of *Clinical and Experimental Allergy*, the first paper to address this issue is a systematic review by Jabbar-Lopez et al looking at the association between water hardness and eczema. Hard water contains increased minerals, mainly calcium carbonate, and this can potentially damage skin barrier integrity through direct

effects of calcium, through increasing skin surface pH and through increasing deposition of surfactants from wash products on the skin. The authors conducted a systematic review of a wide range of study types, to identify whether these associations were consistent across the literature. They pooled data from 7 studies with almost 386,000 participants and found an association between living in an area with hard water and increased eczema risk (Odds Ratio 1.28, 95% confidence interval 1.09, 1.50); however, the finding was not consistent across studies, perhaps due to variations in cut-offs used, in study design, in bathing frequency and use of wash products in the study populations. Water hardness is, of course, only one aspect of water quality. Previous work in this journal has suggested that the bacterial content of drinking water during the first year of life may also be an important determinant of allergic disease risk, including eczema risk.⁷ The strength of Jabbar-Lopez's work is that it provides a comprehensive overview of the current status of the hard water hypothesis. The findings provide some support for the concept that skin exposure to hard water or other damaging products in early life may promote eczema development.

In a second paper about early skincare, Kelleher et al undertook an independent participant data meta-analysis of randomized controlled trial data evaluating different types of skincare in infancy for preventing eczema or food allergy.⁸ The reason for including food allergy is that eczema and food allergy are closely linked in this age group and share genetic risk factors related to skin barrier function. The authors identified 33 completed clinical trials in this area. However, only about half of these were focussed on eczema as an outcome. Most of the trial authors provided individual participant data, allowing much more precise estimates to be made of treatment effects. There was a notable absence of trials testing interventions such as softened water, reduced bathing frequency or avoidance of soap and detergents. All the trials contributing to analysis tested moisturizers, used from soon after birth for a period of several months. Disappointingly, the team found no effect of moisturizers on eczema development, but they did find evidence that early skin-care matters. Infants randomized to regular moisturizer use had increased food allergy, although the certainty was very low for this estimate. Infants randomized to be bathed daily with a 10% paraffin bath had increased eczema, a very different outcome to direct application of moisturizer, where there was no effect.

Taken together, the studies of Jabbar-Lopez and Kelleher suggest that the next step in a long journey towards effective eczema

prevention will be to test interventions which reduce exposure to damaging products such as soap, detergent or even water, during the first months of life. Of course, skin barrier function and allergic inflammation are not necessarily separate processes and work in this journal has identified a lectin galectin-7, highly expressed in active eczema lesions, as a possible mediator for Th2-mediated impairment of skin barrier function in the stratum corneum.⁹ So other approaches may still be necessary, including interventions aimed at promoting healthy immune development.

COVID-19 has presented unique challenges to human skin—not only in the cutaneous manifestations of the disease but in the cutaneous insults engendered by repeated hand hygiene to control the spread of the virus. This presents a challenge to dermatologists, allergists and their patients. A more acute challenge presented by COVID-19 is the occurrence of anaphylactic reactions to the first COVID-19 vaccines, largely thought to be triggered by polyethylene glycol in these mRNA-based vaccines. Therefore, it is timely that in this issue of *Clinical and Experimental Allergy*, Bruusgaard-Mouritsen et al present what is probably the largest case series of polyethylene glycol allergy reported in the literature. They emphasize the variety of products and severity of reactions for this uncommon form of allergy. Their series covers the pre-COVID era, where antibiotic and analgesic tablets, depot steroids, antacids and laxatives were the commonest triggers of polyethylene glycol allergy. Most patients reported multiple triggers among health care, cosmetic and personal hygiene products and most patients suffered at least one episode of anaphylaxis.¹⁰ Given the number of mRNA COVID-19 vaccines now being administered worldwide, vaccines are likely to become the commonest trigger of polyethylene glycol allergy.

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REFERENCES

1. Ballardini N, Kramer MS, Oken E, et al. Associations of atopic dermatitis and asthma with child behaviour: results from the PROBIT cohort. *Clin Exp Allergy*. 2019;49(9):1235-1244.
2. Wei YH, Tai YH, Dai YX, Chang YT, Chen TJ, Chen MH. Bidirectional association between alopecia areata and atopic dermatitis: a population-based cohort study in Taiwan. *Clin Exp Allergy*. 2020;50(12):1406-1414.
3. Bakker DS, Drylewicz J, Nierkens S, et al. Early identification of atopic dermatitis patients in need of systemic immunosuppressive treatment. *Clin Exp Allergy*. 2019;49(12):1641-1644.
4. Hurault G, Dominguez-Huttinger E, Langan SM, Williams HC, Tanaka RJ. Personalized prediction of daily eczema severity scores using a mechanistic machine learning model. *Clin Exp Allergy*. 2020;50(11):1258-1266.
5. Richards M, Ferber J, Chen H, et al. Caesarean delivery and the risk of atopic dermatitis in children. *Clin Exp Allergy*. 2020;50(7):805-814.
6. Yue H, Umehara Y, Trujillo-Paez JV, et al. Exogenous factors in the pathogenesis of atopic dermatitis: Irritants and cutaneous infections. *Clin Exp Allergy*. 2021. <https://doi.org/10.1111/cea.13820>
7. Turkalj M, Drkulec V, Haider S, et al. Association of bacterial load in drinking water and allergic diseases in childhood. *Clin Exp Allergy*. 2020;50(6):733-740.
8. Kelleher MM, Cro S, Van Vogt E, et al. Skin care interventions in infants for preventing eczema and food allergy: a Cochrane systematic review and individual participant data meta-analysis. *Clin Exp Allergy*. 2021. <https://doi.org/10.1111/cea.13847>
9. Umayahara T, Shimauchi T, Iwasaki M, et al. Protective role of Galectin-7 for skin barrier impairment in atopic dermatitis. *Clin Exp Allergy*. 2020;50(8):922-931.
10. Bruusgaard-Mouritsen MA, Johansen JD, Garvey LH. Clinical manifestations and impact on daily life of allergy to polyethylene glycol (PEG) in ten patients. *Clin Exp Allergy*. 2021. <https://doi.org/10.1111/cea.13822>