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Supporting Information

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The atopic paradox

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Linked Article: Lagrelius et al. *Br J Dermatol* 2019; **180**:782–789.

Evaluation of underlying allergic contact dermatitis (ACD) in children presenting with chronic inflammatory skin 'eczema' represents a perplexing clinical dilemma and a diagnostic challenge. This issue of the *BJD* includes an article by Lagrelius et al. focusing on the association between atopic dermatitis (AD) in preschool age children and development of contact allergy in adolescence.¹ The team from the Karolinska Institute in Stockholm, Sweden utilized the BAMSE (Swedish acronym for Children, Allergy, Milieu, Stockholm, Epidemiological survey) database to develop a population-based birth cohort of 2215 children. Information on AD was collected at birth, and at age 16 a patch evaluation with a modified 30-allergen TRUE test[®] (Mekos Laboratories AS, Hillerød, Denmark) was performed. Overall, the authors reported that among boys, early childhood AD was associated with contact allergy to at least one of the 30 tested allergens in adolescence. Additionally, AD was found to be associated with adolescent contact allergy to fragrance mix I, but not to nickel.

The authors' conclusions build upon prior work including Czarnobilska et al.'s study of 9320 primary school children

showing that almost half of all children with chronic recurrent eczema (and prick-test confirmed atopy) were found to have a reaction to at least one hapten on the European Baseline Series.² However, the more intriguing finding was the null result for the association of nickel allergy and AD, given the significant incidence of nickel sensitization in children worldwide,³ supporting the report of the U.S. Pediatric Contact Dermatitis collaborative Registry, which also did not find a statistically significant difference in relevant positive patch test rates to nickel among patients with AD as compared with those without.⁴

Thyssen et al. have described at length the paradox of reduced contact sensitization risk in patients with AD.⁵ Thyssen and colleagues summarized experimental and clinical studies reporting that patients with more severe AD had less sensitization to strong allergens such as dinitrochlorobenzene. The pathophysiology of this paradox is debated, but an interplay between T helper (Th)1 and Th2 phenotypes is believed to be at play: Th2 dominant AD phenotype makes it more difficult to mount a Th1 dominant response, which is most commonly responsible for the development of ACD. Thus, patients with AD may have a higher threshold for sensitization to certain allergens (and conversely lower to others) than patients without AD. The importance and complexity of the T-helper cell milieu may extend into treatment modalities as Machler et al. recently reported high effectiveness of a monoclonal interleukin (IL)-4a receptor inhibitor on the downstream effects of Th2-mediated cytokines IL-4 and IL-13 in the treatment of recalcitrant ACD.⁶

That said, it is imperative that children with recalcitrant eczematous dermatitis be evaluated for ACD and considered for patch testing. As Lagrelius et al. report, fragrance mix I and other allergens within emollients, skin care products and antiseptics are frequent causes of ACD in patients with AD, and in cases where patch test placement may be challenging (because of ongoing flares), a pre-emptive avoidance strategy may be implemented proactively to avoid the most common paediatric allergens: nickel, cobalt, neomycin, balsam of Peru, fragrance mix, lanolin, cocamidopropyl betaine, formaldehyde, corticosteroids, methylchloroisothiazolinone/methylisothiazolinone, propylene glycol and benzalkonium chloride.⁷

Overall, Lagrelius et al.'s population-based cohort provides a unique perspective on the nonlinear association between early childhood AD and the development of contact allergy later in adolescence, shedding light on the atopic paradox and paving the way for further research.

Conflicts of interest

None to declare.

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Measuring the quality of life in pemphigus

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Linked Article: Tamási et al. *Br J Dermatol* 2019; **180**:802–809.

This issue of the *BJD* includes a concise, interesting report on health-related quality of life (HRQoL) in patients with pemphigus. Its salient feature is the use of the EuroQoL (EQ-5D) questionnaire in a relatively large group of patients with pemphigus to analyse the convergent and known-groups validity of the EQ-5D in this patient population.¹

HRQoL is a multidimensional concept that describes 'how well a person functions in their life and his or her perceived well-being in physical, mental, and social domains of health'.² Pemphigus diseases, with their main forms vulgaris and foliaceus, are potentially life-threatening chronic autoimmune bullous diseases characterized by intraepithelial cleavage and autoantibodies against desmosomal cadherins.³ As with other (auto)inflammatory and autoimmune diseases, new, increasingly effective but more expensive therapies for pemphigus diseases are currently being translated into use in clinical practice.⁴ Rational decision making on interventional priorities is required, which is also dependent on an accurate assessment of HRQoL. HRQoL data are usually collected using self-report methods of assessment, including questionnaires.

The EQ-5D-5L, developed in 2009 and available in more than 130 languages and in various modes of administration, is a five-dimension, generic, self-reporting instrument validated for a broad range of conditions, including skin diseases.⁵ In the study by Tamási et al., in this issue, the value set for England was used and its validation for other countries or regions

should be a reasonable extension of this study. Both the Autoimmune Bullous Skin Disorder Intensity Score and the Pemphigus Disease Area Index (PDAI) are robust tools to accurately assess pemphigus activity and their subscores correlate with the evolution of the levels of autoantibodies against desmogleins.⁶ To this end, also including PDAI scores and the levels of desmoglein-specific autoantibodies as further outcome measures is worth considering in future studies. Nevertheless, the results of the present study strongly suggest that the EQ-5D is a valid measure of HRQoL in patients with pemphigus and may be used not only in clinical practice and research, but also in economic evaluations to assess the health gains associated with new therapeutic approaches.

Conflicts of interest

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Cellulitis: how can we know what patients don't know?

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Linked Article: Teasdale et al. *Br J Dermatol* 2019; **180**:810–820.

What do patients understand about their cellulitis? In this issue of the *BJD*, Teasdale et al.¹ help answer the question, by