

in HS-affected skin. Further, results from IL-37 and IL-38 analysis were not included.^{9,10} The discrepancy of the findings in, to our knowledge, the first three studies of the IL-36 cytokine family in patients with HS, may be due to several factors, most importantly the selection of the skin samples, the skin region and the variation of disease severity.

There are no published clinical trials addressing the IL-36 cytokine complex in HS. Interestingly, according to a small randomized clinical trial, anakinra, an IL-1 receptor antagonist, has the potential to be an effective and safe treatment for severe HS.¹¹ Also, the beneficial effect of anakinra was prolonged.¹¹ Both comparable and conflicting results have been published for anakinra treatment in HS in one small open study and in several case reports.

The gold standard for treatment of HS is surgery,¹² but this is not always clinically feasible or available. Most patients with HS will need long-term anti-inflammatory treatment.¹² As shown by Hessam et al.⁸ and by two other studies,^{9,10} the agonistic IL-36 isoforms, IL-36- α , - β , and - γ , have been shown to be upregulated in HS lesions. We look forward to future studies that will determine the role of IL-36 in the pathogenesis of HS, and could hopefully be a new basis for treatment development.

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Conflicts of interest

None to declare.

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Extended patch-test screening for fragrance contact allergy: findings and challenges

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Contact allergy to fragrances is a well-recognized clinical problem.¹ In view of more than 2000 fragrances, manmade or as extracts, currently being used in many products, routine patch testing² is thus necessarily restricted to the ‘most important’ fragrance allergens. These are compounded into two mixes, namely, fragrance mix (FM) I and FM II. *Myroxylon pereirae* (balsam of Peru) is another, natural mixture of fragrance allergens. The only single compound tested in the baseline series is hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC) at 5% pet., due to its outstanding importance.³

From this background, some departments routinely test with all 26 substances which currently need to be labelled according to the EU Cosmetics Regulation to (i) avoid uncertainty following skipped breakdown testing of the mixes, and (ii) achieve a broader diagnostic coverage with (iii) exactly those substances to which previous exposure can be identified, and which can be avoided in the future, if contact allergy is diagnosed, thanks to labelling requirements [Regulation EC 1223/2009, Article 19(1)(g)].

In the present issue, Ung et al.⁴ follow up on an earlier study,⁵ presenting patch-test results obtained in 2015/16 at St John's in 2084 consecutively tested patients, now using oxidized linalool and limonene. This had an enormous impact on results, with 7.4% (4.3%) positive reactions to oxidized linalool (limonene), even higher than the 3.9% and 2.5%, respectively, recently reported from Copenhagen.⁶ As

elsewhere, fairly limited 'overlap' between positive reactions to the oxidized terpenes and the remaining fragrances, including baseline series markers, was observed. Therefore, their addition to the baseline series could probably be suggested, as favoured e.g. for the U.K.⁷ Ideally, the discussion on inclusion should consider clinical relevance of positive reactions, in particular, as at least some of the weak-positive reactions (erythema and infiltration) may be irritant. Reassuringly, the above-mentioned Copenhagen study based on 6004 consecutive patients has found clinical relevance in about 75% of patients,⁶ which is similar to other fragrance allergens.

An important challenge still remains: hitherto, clinical relevance of contact allergy to linalool and limonene, as to all other cosmetic ingredients, relies on scrutinizing the ingredient labelling of products. However, the concentration of (hydro)peroxides of these prehapten⁸ to which patients are tested nowadays, in the products they have actually used, and presumably became sensitized by, is mostly unknown. Chemical analysis is very difficult, especially in more complex matrices beyond hydroalcoholic solutions. Therefore, careful diagnostic work-up² combined with advanced analytical methods is needed to provide more insights into those concentrations of hydroperoxides that are able to sensitize and elicit allergic contact dermatitis.⁹

Conflicts of interest

None to declare.

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Spectrum of cutaneous manifestations among patients with GATA2 deficiency

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The guanine-adenine-thymine-adenine (GATA)-binding protein family of transcription factors comprises six proteins (GATA 1–6), which are involved in a variety of physiological and pathological factors.¹ GATA binding proteins 1–3 are required for differentiation of mesoderm- and ectoderm-derived tissues, including haematopoietic stem cells and the central nervous system.¹ GATA binding proteins 4–6 are implicated in development and differentiation of endoderm- and mesoderm-derived tissues, such as induction and differentiation of embryonic stem cells, cardiovascular embryogenesis and guidance of epithelial cell differentiation in the adult.¹

GATA2, a zinc finger transcription factor, is a key regulator of haematopoiesis, required for development and maintenance of a healthy stem-cell pool.² Haploinsufficiency of GATA2 underlies monocytopenia and mycobacterium avium complex (MonoMAC syndrome); dendritic cell, monocyte and lymphoid cell (DCML) deficiency; familial myelodysplastic syndrome (MDS)/acute myeloid leukemia (AML); and primary lymphoedema with MDS (Emberger syndrome).

The underlying cause of the above syndromes as familial or *de novo* heterozygous mutations of the GATA2 gene was uncovered by four different groups in 2011, each working with a different focus.^{2,3} Because there is considerable overlap of clinical characteristics among all cohorts studied, these syndromes are now recognized to represent different manifestations of a single genetic disorder.³

GATA2 deficiency is thus a multifaceted disorder that encompasses susceptibility to various infections, pulmonary dysfunction, autoimmunity, lymphoedema and malignancy. The protean manifestations related to GATA2 mutations and clinical progression of patients were elucidated in two large cohort studies from North America and Europe.^{3,4} The various skin manifestations reported in patients include viral warts (both genital and extragenital), other skin infections, panniculitis/erythema nodosum, lymphoedema, skin tumours and Sweet syndrome (related to MDS/AML).