3. Micheletti RG, Verth VP. Small vessel vasculitis of the skin. *Rheum Dis Clin North Am*. 2015;41(1):21-32.
4. Fox L, Shinkai K. Cutaneous vasculitis. In: Bolognia J, ed. *Dermatology*. Amsterdam, The Netherlands: Elsevier; 2018: 409-439.

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Patch testing and contact allergen avoidance in patients with lichen planopilaris and/or frontal fibrosing alopecia: A cohort study

The incidence of frontal fibrosing alopecia (FFA) has increased since 1994, suggesting environmental causes in disease etiology.[1,2] The development of FFA has been linked to a xenobiotic-processing enzyme genetic defect, but the exact etiopathogenesis is still unknown.[2] Patch testing in British and Brazilian patients with FFA identified 5 potentially relevant allergens.[1,3] This study sought to identify relevant allergens in patients with FFA and/or lichen planopilaris (LPP) and assess whether avoidance of relevant allergens affected patients' alopecia symptoms and disease activity.

From January 2018 through June 2019, 42 patients with LPP/FFA were referred for patch testing from a specialty alopecia clinic. Patch testing included the North American Baseline Series, Cosmetic and Hairdresser Series, and 8 other potential allergens, identified by 3 experienced contact dermatitis experts (JY, PS, DS), which included *N*-isopropyl-*N*′-phenyl-*p*-phenylenediamine, methylchloroisothiazolinone/methylisothiazolinone (MCI/MI), benzophenone-4, avobenzone, benzalkonium chloride, carvone, polysilicon 15, and aminoazobenzene. Readings were performed at 48 and 96 hours. At least 3 months after patch testing, patients with relevant allergens participated in a brief survey to assess the impact of allergen avoidance. All surveyed patients were following stable LPP/FFA treatment regimens for at least 6 months before patch testing and remained on those treatments during the 3 months before survey administration. Allergens were deemed relevant if they were present in patients' personal care products and had at least a +1 patch test reaction. Because gallates may be present in oils in personal care products in concentrations small enough to be omitted from ingredient lists but still capable of eliciting allergic contact dermatitis, all +1 or higher reactions for these were considered relevant.[4] Local institutional review board approval was granted for this study.

There were 41 women and 1 man, with a mean age of 61 years (range, 25-81 years) who underwent patch testing. Most were white (97.6%) with biopsy-proven LPP (61.9%), FFA (26.2%), or LPP/FFA overlap (11.9%), and 76.2% had clinically relevant allergens found in cosmetic and personal care products applied on the scalp and face. As shown in Table I, the most common relevant allergens included gallates (26.2%), linalool (19.0%), and fragrance mixes (19.0%). Linalool is a ubiquitous fragrance chemical found in many personal care products, including cleansers, cosmetics, creams, lotions, and hair care products (shampoo, conditioner, leave-in products such as hairspray and gel, etc). Gallates are preservatives added to products to prevent the growth of yeast, fungi, and bacteria, and they can be found in cleansers, cosmetics, liquids, and creams.

The distribution of the number or type of relevant allergens in patients with LPP, FFA, or LPP/FAA did not differ widely (Table II). Twenty patients were eligible at the time of survey administration to participate. Of these, 58.3% and 72.7% of surveyed patients who had scalp pruritus or erythema on initial presentation indicated that their scalp pruritus or erythema decreased, respectively, after at least 3 months of allergen avoidance.

Study patients continued clinic visit evaluations by the treating physician (MMS), who was blinded to patient survey responses. Perifollicular scalp erythema was graded from 0 (none) to 3 (confluent) for each scalp section (top, right, left, back). Review of medical records showed that after at least 3 months of allergen avoidance, 70% of patients had decreased scalp erythema on examination. No patient had signs or symptoms of worsening LPP/FFA.

Although no recent studies have investigated the prevalence of allergens in the general population in the United States, European studies report the prevalence for Fragrance mix (FM) I (FM I) and FM II to be 1.8% and 1.9%, respectively.[5] Although the prevalence in the North American Contact Dermatitis Group (NACDG) results approach those of our cohort, the NACDG includes +/- or questionable/equivocal reactions in their data, and we did not include these equivocal results in our patient data set. Removing the +/- results from the 2015-2016 NACDG numbers brings the prevalence of FM I, FM II, and MCI/MI allergy to approximately 10%, 4.8%, and 6.8%, respectively.[4] The higher prevalence of allergens in our patient cohort (14.3%, 9.5%, and 11.9% for FMI, FM II, and MCI/MI, respectively) suggests that our results may be important in the treatment and evaluation of patients with LPP and FFA. Although an age- and sex-matched control group for the current study is lacking, the NACDG patients were predominantly female (72%) and

Table I. Prevalence of common allergens, %

Allergen	Our cohort (N = 42)	Aldoori et al[1] (N = 40)	Rocha et al[3] (N = 63)	NACDG[4] (N = 5590+)*
Gallates†	26.2	—	—	—
Dodecyl gallate	16.7	—	—	—
Octyl gallate	4.8	—	—	—
Propyl gallate	4.8	—	—	—
Fragrance mixes†	19.0	—	—	—
Fragrance mix I	14.3	10.0	5.0	11.3
Fragrance mix II	9.5	—	—	—
Linalool‡	19.0	9.0	7.9	2.3
Ammonium persulfate	14.3	22.5	—	—
Benzophenone 4	14.3	—	—	7.0
Propolis	9.5	—	—	1.7
MI/MCI	11.9	17.5	—	13.4
Benzoyl peroxide	9.5	—	—	1.7
Balsam of Peru	7.1	12.5	8.0	—

MI/MCI, Methylchloroisothiazolinone/methylisothiazolinone; *NACDG,* North American Contact Dermatitis Group.
*NACDG data include +/- reactions.
†Indicates that some patients were allergic to more than 1 subtype.
‡Linalool includes hydroperoxides of Linalool.

Table II. Prevalence of allergens by cicatricial alopecia diagnosis, %

Allergen	LPP (n = 26)	FFA (n = 11)	LPP/FFA (n = 5)	Total (n = 42)
Positive reaction	76.9	81.8	60.0	76.2
Gallates	14.2	7.1	4.9	26.2
Fragrance mixes	19.2	27.3	0.0	19.0
Linalool	19.2	18.2	20.0	19.0

FFA, Frontal fibrosing alopecia; *LPP,* lichen planopilaris.

white (82.7%), with an average age of 49 years; therefore, they were slightly younger than but otherwise approximated the current study population.

Whether allergic contact dermatitis directly contributes to the pathogenesis of LPP and/or FFA is unclear. Avoiding relevant allergens on the face and scalp, however, may reduce local inflammation in some patients, consistent with our findings suggesting disease improvement. Further study should be undertaken to determine the role of these allergens in cicatricial alopecia development, especially because previous studies have suggested a correlation between lichenoid reactions and pigmented cosmetic allergic contact dermatitis.[6] In the FFA population, lichen planus pigmentosus has been increasingly reported to occur on the face and neck.[7-9]Acquired dermal macular hyperpigmentation is a term that includes lichen planus pigmentosus and pigmented contact/cosmetic dermatitis; in 1 study, hair dye was shown to be the cause of these eruptions in up to 33% of patients.[10] Future studies could help to determine if LPP and FFA represent a lichenoid type of contact allergy of the scalp.

This study is limited by the small sample size and inclusion of a nonvalidated, noncontrolled survey. Strengths of this study include the reporting of patch testing results in US patients with LPP/FFA and assessment of outcome measures after allergen avoidance. Given the high prevalence of relevant contact allergens in patients with LPP/FFA, clinicians may consider recommending routine patch testing for this patient population.

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REFERENCES

1. Aldoori N, Dobson K, Holden CR, McDonagh AJ, Harries M, Messenger AG. Frontal fibrosing alopecia: possible association with leave-on facial skin care products and sunscreens; a questionnaire study. *Br J Dermatol*. 2016;175(4):762-767.
2. Tziotzios C, Petridis C, Dand N, et al. Genome-wide association study in frontal fibrosing alopecia identifies four susceptibility loci including HLA-B*07:02. *Nat Commun*. 2019;10(1):1150.
3. Rocha VB, Donati A, Contin LA, et al. Photopatch and patch testing in 63 frontal fibrosing alopecia patients: a case series. *Br J Dermatol*. 2018;179:1402-1403.
4. DeKoven JG, Warshaw EM, Zug KA, et al. North American Contact Dermatitis Group patch test results: 2015—2016. *Dermatitis*. 2018;29(6):297-309.
5. Diepgen TL, Ofenloch RF, Bruze M, et al. Prevalence of contact allergy in the general population in different European regions. *Br J Dermatol*. 2016;174(2):319-329.
6. Nakayama H, Matsuo S, Hayakawa K, Shigematsu T, Ota S. Pigmented cosmetic dermatitis. *Int J Dermatol*. 1984;23(5):299-305.
7. Romiti R, Biancardi Gavioli CF, Anzai A, Munck A, Costa Fechine CO, Valente NYS. Clinical and histopathological findings of frontal fibrosing alopecia-associated lichen planus pigmentosus. *Skin Appendage Disord*. 2017;3(2):59-63.
8. Moreno-Arrones OM, Saceda-Corralo D, Rodrigues-Barata AR, et al. Risk factors associated with frontal fibrosing alopecia: a multicentre case-control study. *Clin Exp Dermatol*. 2019;44(4):404-410.
9. Uwakwe LN, Cardwell LA, Dothard EH, Baroudi BI, McMichael AJ. Frontal fibrosing alopecia and concomitant lichen planus pigmentosus: a case series of seven African American WOMEN. *J Drugs Dermatol*. 2018;17(4):397-400.
10. Bishnoi A, Vinay K, Arshdeep, et al. Contact sensitization to hair colours in acquired dermal macular hyperpigmentation: results from a patch and photo-patch test study of 108 patients. *J Eur Acad Dermatol Venereol*. 2019;33(7):1349-1357.

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Risk of malignancy in histiocytoid Sweet syndrome: A systematic review and reappraisal

To the Editor: Histiocytoid Sweet syndrome (HSS) is a distinct variant of Sweet syndrome (SS) where a predominance of histiocytoid mononuclear immature myeloid cells in the infiltrate is seen on histology, as opposed to the classical neutrophilic infiltrate of SS (NSS).[1,2] Compared with NSS, distinctive demographic, clinical and prognostic features have been suggested in HSS, and a higher risk of association with hematologic malignancies have been proposed by some authors[3] and refuted by others.[4] Our goal is to determine whether HSS is more frequently associated with malignancies than NSS.

Table I. Associated diseases and medications in patients with histiocytoid Sweet syndrome

Disease/medication	No. (%) (N = 218)
Idiopathic	108 (49.5)
Inflammatory disorders	9 (4.1)
Crohn's disease	3 (1.3)
Relapsing polychondritis	1 (0.4)
Uveitis	1 (0.4)
Rheumatoid arthritis	2 (0.9)
Familial Mediterranean fever	1 (0.4)
Polyarteritis nodosa	1 (0.4)
Upper respiratory tract infections	6 (2.7)
Drugs	7 (3.2)
Bortezomib	3 (1.3)
Trimethoprim/sulfamethoxazole	1 (0.4)
Azacitidine	1 (0.4)
Piperacillin tazobactam	2 (0.9)
Postvaccination	1 (0.4)
Malignancies	87 (40)
Myelodysplastic syndrome	40 (18)
Hematologic malignancies	37 (17)
Lymphoma	4 (1.8)
Lung cancer	1 (0.4)
Renal cancer	1 (0.4)
Bladder cancer	1 (0.4)
Endometrial cancer	1 (0.4)
Breast cancer	2 (0.9)

A systematic literature review was performed in PubMed/MEDLINE, Embase, and Cochrane Collaboration databases, searching for all articles on HSS with no limits on publication date, participant age, sex, or nationality. Papers published in English or French were included in this study. Supplemental Table I (available via Mendeley at https://doi.org/10.17632/tcmmmpwv6m.1) shows the stepwise approach for study selection.

Included were 43 articles: 31 case reports, 8 case series, and 4 retrospective studies (Supplemental Material 2). There were 218 patients total, with a mean age at presentation of 52 years (range, 0.4-93 years). The female predominance seen in NSS (female-to-male ratio, 4:1)[2] does not appear to apply to HSS (1.11:1). Extracutaneous involvement in HSS is extremely rare. All cases of HSS were confirmed by histology. Compared with NSS,[2,4] 11 patients (5%) had only subcutis involvement, which emphasizes the importance of a specimen from a deep skin biopsy for the diagnosis of HSS. Table I summarizes all reported associated conditions with HSS.

Approximately 40% of patients newly diagnosed with HSS were subsequently diagnosed or already diagnosed with a hematologic or solid cancer vs 21% in NSS.[2,5] HSS was more commonly associated with