postoperatively, with one of these case reports describing a drop from 70% to 19% after the patient used an e-cigarette in the hospital bathroom.<sup>2,3</sup> Another case report described significant bilateral mastectomy tissue flap necrosis in a patient with substantial e-cigarette use for the 3 months prior.<sup>4</sup> The animal studies with rats found significantly more tissue flap necrosis with e-cigarette exposure compared with controls, with results that were similar to traditional cigarette exposure. Finally, several human studies also found a decrease in transcutaneous oxygen tension and skin microcirculation/blood flow (measured via laser Doppler probes or thermal imaging) in response to acute e-cigarette exposure both with and without nicotine.

These findings suggest that e-cigarettes may negatively impact wound healing similar to traditional cigarettes, likely via a multifactorial mechanism, with nicotine-induced vasoconstriction and subsequent production of a hypoxic tissue environment playing a role. Although the research is limited to a small number of studies including only case reports and animal and human studies using surrogate physiologic markers for cutaneous wound healing, the early evidence supports counseling for e-cigarette cessation in the immediate pre- and postoperative period, especially for graft and flap reconstructions. Impaired wound healing negatively impacts patients and demands significant health resources. Therefore, it is crucial to gather a detailed history that specifically inquires about e-cigarette use to properly counsel patients preoperatively. Patient discussions about the risks of both traditional and ecigarettes on wound healing are important and could also serve as an opportunity to promote long-term smoking cessation and positively impact patient lives.

Taylor Thieman, MD, a Danielle Westmark, MLIS, and Adam Sutton, MD, MBA<sup>c</sup>

From the University of Nebraska Medical Center, College of Medicine, Omaha, Nebraska<sup>a</sup>;Leo S. McGoogan Health Sciences Library, University of Nebraska Medical Center, Omaha, Nebraska<sup>b</sup>; and Department of Dermatology, University of Nebraska Medical Center, Omaha, Nebraska.<sup>c</sup>

Funding sources: None.

IRB approval status: Not applicable.

Key words: cutaneous surgery; dermatologic surgery; electronic cigarettes; e-cigarettes; nicotine; nicotine-free; skin healing; vaping; wound healing.

Correspondence and reprint request to: Adam Sutton, MD, MBA, Department of Dermatology 985645 Nebraska Medical Center, Omaha, NE 68198-5645

E-mail: Adam.sutton@unmc.edu

## **Conflicts of interest**

None disclosed.

#### REFERENCES

- Gill JF, Yu SS, Neuhaus IM. Tobacco smoking and dermatologic surgery. J Am Acad Dermatol. 2013;68(1):167-172. https: //doi.org/10.1016/j.jaad.2012.08.039
- 3. Agochukwu N, Liau JY. Debunking the myth of e-cigarettes: a case of free flap compromise due to e-cigarette use within the first 24 hours. *J Plast Reconstr Aesthet Surg.* 2018;71(3):451-453. https://doi.org/10.1016/j.bips.2017.09.017
- Fracol M, Dorfman R, Janes L, et al. The surgical impact of E-cigarettes: a case report and review of the current literature. Arch Plast Surg. 2017;44(6):477-481. https://doi.org/10.5999/a ps.2017.00087

https://doi.org/10.1016/j.jaad.2022.10.042

# Long-term prognosis of subclinical sensitization with diphenylcyclopropenone in patients with alopecia areata



To the Editor: Contact immunotherapy is widely used in the treatment of severe alopecia areata (AA).<sup>1</sup> However, due to varied treatment response to contact immunotherapy, predicting the prognosis of AA is challenging.<sup>2</sup> A systematic review of contact immunotherapy reported a recurrence rate of 49% in the absence of maintenance treatment.<sup>3</sup> However, there were no results for long-term prognosis. The modified diphenylcyclopropenone (DPCP) treatment protocol, characterized by subclinical sensitization, has a therapeutic efficacy as favorable as that of the standard protocol, with fewer side effects. 4 In a previous study conducted at our institution in 2017, 46 of 159 patients who underwent the modified DPCP treatment protocol showed complete response (CR). After a 2-year follow-up of patients who achieved CR during that time, 20 experienced recurrence.<sup>4</sup> The purpose of this study was to examine the long-term prognosis and related factors by confirming the recurrence of AA in the remaining 26 patients with CR.

Medical records of patients with AA who maintained CR for more than 2 years after modified DPCP

**Table I.** Patient demographics and disease- and treatment-associated factors (N = 25)

Characteristic	Relapse $(n = 5)$	Nonrelapse (n = 20)	P value	
Sex				
Male	3 (60.0)	16 (80.0)	.562	
Female	2 (40.0)	4 (20.0)		
Age at visit, y	$37.8 \pm 15.5$ $40.6 \pm 12.6$		.818	
Alopecia type			>.99	
Patchy	3 (60.0)	14 (70.0)		
Alopecia totalis	0 (0.0)	0 (0.0)	-	
Alopecia universalis	2 (40.0)	6 (30.0)		
Age at onset, y	$37.4 \pm 15.4$	$38.5 \pm 11.9$	.622	
Disease duration before DPCP treatment, mo	6.0 (1.0-13.0)	5.0 (1.0-125.0)	.921	
Disease-free duration after CR, y	$5.4 \pm 4.9$	$10.4 \pm 5.9$		
ANA abnormality	1 (20.0)	3 (15.0)	>.99	
Autoimmune disease history	0 (0.0)	0 (0.0)	-	
Atopic dermatitis history	0 (0.0)	2 (10.0)	>.99	
Family history of AA	0 (0.0)	1 (5.0)	>.99	
Severity at initial visit				
Mild (0%-24%)	2 (40.0)	7 (35.0)	>.99	
Moderate (25%-49%)	0 (0.0)	4 (20.0)	.549	
Severe (50%-74%)	1 (20.0)	4 (20.0)	>.99	
Total (75%-100%)	2 (40.0)	5 (25.0)	.597	
Treatment duration, mo	11.0 ± 12.9	$22.1 \pm 23.9$	.272	
Highest DPCP treatment concentration				
0.01%	1 (20.0)	7 (35.0)	>.99	
0.025%	3 (60.0)	7 (35.0)	.358	
0.05%	0 (0.0)	3 (15.0)	>.99	
0.1%	1 (20.0)	3 (15.0)	>.99	
AEs after treatment				
Pruritus	3 (60.0)	15 (75.0)	.597	
Eczematous reaction	0 (0.0)	2 (10.0)	>.99	
Hyperpigmentation	0 (0.0)	2 (10.0)	>.99	
Hypo/depigmentation	0 (0.0)	0 (0.0)	-	
DPCP-MT				
Number of patients	5 (100.0)	15 (75.0)	.544	
Interval, wk	2.0 (1.0-4.0)	3.0 (1.0-6.0)	.197	
Treatment duration, mo	11.0 (1.0-29.0)	8.0 (2.0-82.0)	.866	
DPCP-MT concentration	,	,	.800	
0.01%	2 (40.0)	5 (25.0)		
0.025%	2 (40.0)	4 (20.0)		
0.05%	0 (0.0)	2 (10.0)		
0.1%	1 (20.0)	4 (20.0)		

Values are presented as mean  $\pm$  SD or n (%) or median (range). Significant values are in bold text.

AA, Alopecia areata; AE, adverse event; ANA, antinuclear antibody; CR, complete response; DPCP, diphenylcyclopropenone; DPCP-MT, diphenylcyclopropenone maintenance treatment.

treatment were retrospectively reviewed. The patients were subdivided into relapse and nonrelapse groups, and disease-/treatment-associated variables were compared between the 2 groups. Relapse was evaluated in the same way as in the prior study.<sup>4</sup>

The presence or absence of recurrence could be confirmed in 25 patients; of these, nonrecurrence was confirmed in 20 (80%) patients. Among the disease-/treatment-associated factors between the relapse and nonrelapse groups, there were no

significant differences except for the disease-free duration after CR (Table I). The period from CR to recurrence in 5 patients varied between 23 and 216 months. Regarding recurrence, patchy type was observed in 4 patients and alopecia universalis in 1. The disease-free duration after CR was shortest in the patient with alopecia universalis, at 23 months. Of the 5 patients, only 1 improved after relapse (Table II). Twenty out of 25 patients received maintenance treatment (DPCP-MT). Regarding all

**Table II.** Characteristics of the relapse group (N = 5)

	Case number					
Variables	1	2	3	4	5	
Disease-free duration after CR, mo	23	39	79	125	216	
Type of recurrent AA	AU	Patchy	Patchy	Patchy	Patchy	
Treatment after relapse	No	No	No	No	Yes	
Treatment modality	-	-	-	-	TCS	
CR after relapse	No	No	Yes	No	No	
Duration of DPCP-MT, mo	11	21	1	6	29	
Disease-free duration since last DPCP-MT, mo	12	18	78	82	161	

Statistical analysis could not be performed due to the small number of patients in the relapse group.

AA, Alopecia areata; AU, alopecia universalis; CR, complete response; DPCP-MT, diphenylcyclopropenone maintenance treatment; TCS, topical corticosteroid.

5 patients who relapsed, no recurrences occurred during DPCP-MT, and all relapsed at least 1 year after DPCP-MT was ended. To date, 5 patients have received DPCP-MT, and none have relapsed. The nonrelapse group maintained CR for up to 18 years.

In this follow-up study, up to 80% of patients did not experience recurrence when CR was maintained for more than 2 years with the modified DPCP treatment. It was found that the long-term prognosis was quite good, and the period without recurrence was maintained for nearly 18 years. Alternately, no significant differences between the relapse and non-relapse groups were confirmed, indicating that the prognosis of AA was not easy to predict.

This study had its limitations as a single-institutional retrospective study with a small sample size. However, despite the small sample size, long-term prognosis was confirmed by ensuring a long observation period ranging between 4 and 18 years.

In conclusion, the modified DPCP treatment protocol may be considered a good treatment option for AA. In particular, maintaining a response beyond 2 years was a good long-term prognostic indicator.

Sang-Hoon Lee, MD, Yeon Woo Heo, MD, and Won-Soo Lee, MD, PhD

From the Department of Dermatology and Institute of Hair and Cosmetic Medicine, Yonsei University Wonju College of Medicine, Wonju, Republic of Korea.

Funding sources: None.

IRB approval status: Reviewed and approved by the Yonsei University Wonju Severance Christian Hospital IRB (Approval No. #CR322024).

Patient consent: Not applicable.

Key words: alopecia areata; contact immunotherapy; diphenylcyclopropenone; prognosis; recurrence; subclinical sensitization. Correspondence to: Won-Soo Lee, MD, PhD, Department of Dermatology, Yonsei University Wonju College of Medicine, Ilsan-ro 20, Wonju, Gangwon 26426, Republic of Korea

E-mail: leewonsoo@yonsei.ac.kr

## **Conflicts of interest**

None disclosed.

#### REFERENCES

- Meah N, Wall D, York K, et al. The alopecia areata consensus of experts (ACE) study: results of an international expert opinion on treatments for alopecia areata. J Am Acad Dermatol. 2020; 83(1):123-130.
- Lamb RC, Young D, Holmes S. Retrospective review of diphencyprone in the treatment of alopecia areata. Clin Exp Dermatol. 2016;41(4):352-358.
- Lee S, Kim BJ, Lee YB, et al. Hair regrowth outcomes of contact immunotherapy for patients with alopecia areata: a systematic review and meta-analysis. *JAMA Dermatol*. 2018;154(10): 1145-1151.
- **4.** Choe SJ, Lee S, Pi LQ, et al. Subclinical sensitization with diphenylcyclopropenone is sufficient for the treatment of alopecia areata: retrospective analysis of 159 cases. *J Am Acad Dermatol.* 2018;78(3):515-521.e4.
- Choe SJ, Lee S, Lee H, et al. Efficacy of topical diphenylcyclopropenone maintenance treatment for patients with alopecia areata: a retrospective study. J Am Acad Dermatol. 2018;78(1): 205-207.e1.

https://doi.org/10.1016/j.jaad.2022.10.044

# A perfect match: A cross-sectional analysis of couples matching in dermatology



To the Editor: The number of residency candidates applying via the National Residency Matching Program's couples match has more than doubled from 1125 couples in 2017 to 2444 couples in 2022. Factors associated with successful couple matching with dermatology are unknown and may inform decision-making for applicants considering couples matching. We examined predictors of successful couple matching with dermatology using a cross-