
The impact of dupilumab on patch testing and the prevalence of comorbid allergic contact dermatitis in recalcitrant atopic dermatitis: A retrospective chart review



Jodie Raffi, BA,^{a,b} Raagini Suresh, BS,^a Nina Botto, MD,^a and Jenny E. Murase, MD^{a,c}
San Francisco, Irvine, and Mountain View, California

Background: It is unclear whether the type 2 T helper cell–specific immunosuppressive action of dupilumab interferes with patch testing.

Objectives: We sought to evaluate the reliability of patch testing on dupilumab and the contribution of allergic contact dermatitis (ACD) to complex dermatitis in patients with residual dermatitis on dupilumab.

Methods: This is a retrospective chart review of 48 patients with atopic dermatitis (AD) who were treated with dupilumab. We compare the results of patch tests performed before and after the initiation of dupilumab and the prevalence of comorbid ACD in patch-tested individuals.

Results: A minority of patch test reactions were “lost” on dupilumab (13/125; 10.4%). Five of 13 lost reactions occurred in individuals with documented immunodeficiency. Thirty-two of 35 patch-tested patients (91.4%) had comorbid ACD; 92.3% of individuals patch tested on dupilumab experienced further clinical improvement with allergen avoidance.

Limitations: This is a nonrandomized study in a small cohort of patients. The clearance of dupilumab was assessed by subjective patient reports.

Conclusions: Dupilumab does not appear to exert a dampening effect on patch test results. AD with comorbid ACD was highly prevalent and allergen avoidance resulted in significant improvement in residual dermatitis that had not resolved without dupilumab therapy. (J Am Acad Dermatol 2020;82:132-8.)

Key words: allergic contact dermatitis; atopic dermatitis; dermatitis; dupilumab; patch testing.

Atopic dermatitis (AD) is a chronic inflammatory skin disorder that demonstrates a strong bias toward type 2 T helper cell (T_H2) inflammation.¹ Dupilumab, a human monoclonal antibody that targets T_H2 inflammation by inhibiting the interleukin-4 receptor alpha subunit, is approved for the treatment of moderate-to-severe AD.²

Allergic contact dermatitis (ACD) is mediated by a predominantly T_H1/T cytotoxic response, with contribution from the T_H2, T_H17, and T_H22 inflammatory pathways.^{3,4} Although an attenuated response to cutaneous allergens⁵⁻⁷ or a reduced rate of contact sensitization^{8,9} has been reported in patients with AD, individuals with AD may in fact

From the Department of Dermatology,^a University of California, San Francisco; Irvine School of Medicine,^b University of California, Irvine; and the Department of Dermatology,^c Palo Alto Foundation Medical Group, Mountain View.

Funding sources: None.

Conflicts of interest: Dr Murase has participated in advisory boards for Genzyme/Sanofi, Dermira, and UCB, participated in disease statement management talks for Regeneron and UCB, and has provided dermatologic consulting services for Ferndale and UpToDate.

Accepted for publication September 14, 2019.

Reprint requests: Jenny E. Murase, MD, Department of Dermatology, Palo Alto Foundation Medical Group, 701 E El Camino Real (31-104), Mountain View, CA 94040. E-mail: jemurase@gmail.com.

Published online September 25, 2019.
0190-9622/\$36.00

© 2019 by the American Academy of Dermatology, Inc.
<https://doi.org/10.1016/j.jaad.2019.09.028>

experience comparable or higher rates of ACD than the general population.¹⁰

Cellular and molecular profiling of ACD lesions suggests that certain contact allergens may elicit immune responses with either a T_H1- or T_H2-biased polarization, including contributions from the T_H22 and T_H17 pathways.¹¹ It is unclear whether the T_H2-specific immunosuppressive action of dupilumab interferes with patch testing. Given the uncertainty surrounding dupilumab and patch testing, we review patch test results in a cohort of AD patients receiving dupilumab, examining the reliability of patch testing on dupilumab.

METHODS

Study population

This study involved retrospective data collection from electronic medical records of patients receiving 300 mg subcutaneous dupilumab for the management of AD between 2017 and 2019. Only patients with a primary dermatologic diagnosis of moderate-to-severe AD were studied. We collected demographics and relevant medical history, including age, sex, history of conjunctivitis or blepharitis, childhood atopy, comorbid dermatologic diagnoses, and treatment history of AD.

Effectiveness of dupilumab in our study population

The effectiveness of dupilumab was determined by reduction in clinical severity—assessed by posing the question, “What percent better do you feel that your dermatitis is the past 2 months relative to your baseline?”—at the first follow-up office visit. Dupilumab-associated symptoms and sites of residual dermatitis at first follow-up were recorded.

Patch testing on dupilumab

Several participants who had been patch tested before dupilumab but who experienced residual dermatitis were subsequently patch tested on dupilumab with extended series to evaluate for additional undiagnosed ACD. The decision to patch test individuals with AD was made in accordance with criteria set forth by Chen et al.¹⁰ For patients with patch test data available from these 2 time points, we investigated whether dupilumab impacted patch testing by comparing results before and with dupilumab use. In this clinic, patches were only placed

on patients who exhibited eczematous dermatitis on <10% of the surface area of their back. Patch test results were read by the same provider at day 2 and day 5 (D2 and D5) and interpreted in accordance with the International Contact Dermatitis Research Group guidelines.¹²

To determine whether a previously positive patch

test reaction was maintained or lost, each individual patch test result for an individual allergen was first designated as “allergy” (A), “questionable” (Q), or “no allergy” (N) (Table 1). The patch test result (A, Q, or N) for each allergen was compared with the subsequent patch test result on dupilumab. If the patch test result for a particular allergen remained within the same category of reactivity before and on dupilumab (ie, A to A or Q to

Q), the reaction was labeled as “persistent” and “P” was given to denote a maintained allergic reaction. In cases where the reaction changed from “allergy” (A) to “no allergy,” (N) the effect was labelled as “lost” (L). If the reaction was of any other type that we were unable to confidently classify (ie, A to Q, Q to A, or Q to N), the effect was labeled as “unknown” (U).

Patch test series included fragrances, textile colors & finish, sunscreens, and eye medicaments (Chemotechnique Diagnostics, Vellinge, Sweden) and external agents/emulsifiers, corticosteroids, and dietary additives (Allergeaze: SmartPractice, Calgary, Alberta, Canada) as well as the North American Contact Dermatitis Group standard series (SmartPractice and Chemotechnique). Tests were applied with Finn Chambers (SmartPractice, Phoenix, AZ) on Scanpor tape (Norgesplaster Alpha, Vennesla, Norway). The cosmetics cray was custom-designed to include allergens that were not already present in the North American Contact Dermatitis Group, Fragrance, and Emulsifier Series as in Suresh 2018.¹³

This study was approved by the institutional review board of the University of California, San Francisco.

RESULTS

Study population

Forty-eight patients were receiving dupilumab at the time of data collection. The population consisted of adults between 17 and 92 years of age (average

CAPSULE SUMMARY

- This article provides additional evidence that patch testing patients who are receiving dupilumab can yield positive results.
- This article provides evidence that patch testing may continue to be a reliable diagnostic test for allergic contact dermatitis in adults who are receiving dupilumab for the treatment of atopic dermatitis.

Abbreviations used:

A:	allergy
ACD:	allergic contact dermatitis
AD:	atopic dermatitis
L:	lost
LSC/PN:	lichen simplex chronicus or prurigo nodularis
N:	no allergy
ND:	nummular dermatitis
P:	persistent
Q:	questionable
T _H 2:	type 2 T helper cell
U:	unknown

45 years of age; 24 males, 24 females) and a high rate of childhood atopy (68%), defined in this study as the presence of AD, asthma, or hay fever in childhood. Six (12.5%) patients had a comorbid diagnosis of lichen simplex chronicus or prurigo nodularis (LSC/PN), 5 (10.4%) patients had nummular dermatitis (ND), and 4 (8.3%) patients had primary hand dermatitis (Table II). Before receiving dupilumab, 10 (20.8%) had received systemic glucocorticoids on ≥ 5 occasions and 17 (35.4%) had received mycophenolate mofetil, azathioprine, cyclosporine, or methotrexate. At the time of any patch testing, all patients had discontinued prednisone for ≥ 1 month and methotrexate, intramuscular triamcinolone, azathioprine, and mycophenolate mofetil for ≥ 3 months.

Effectiveness of dupilumab

At first follow-up (7.8 weeks on average), the cohort reported a mean of 77.8% improvement; 56.6% in patients with LSC/PN, 65% in those ND, and 84.5% in those with hand dermatitis (Table II). In the 4 of 6 LSC/PN patients with low initial improvement, we observed gradually increasing rates of clearance after longer follow-up. The most common area of residual dermatitis at first follow-up were the face ($n = 21$, 43.8%), eyes ($n = 18$, 37.5%), and trunk ($n = 13$, 27.1%).

Twenty-two (45.8%) patients reported ≥ 1 symptom at first follow-up (Table III). The most common adverse findings were eye-related: eyelid dermatitis (referring to dermatitis of the upper or lower eyelids; $n = 17$, 35.4%), blepharitis (eyelid margin involvement and associated Meibomian gland dysfunction; $n = 11$, 22.9%), and allergic conjunctivitis (ophthalmologist-diagnosed conjunctival inflammation; $n = 9$, 18.8%). Injection site reactions were less frequent than in phase III trials (4.2% vs 8-19%).^{2,14} There was 1 case of dark clothes stained an orange color while on therapy; the effect ceased when dupilumab was discontinued, and after an

Table I. Patch test result designation key

Patch test result designation	Results included (D2/D5)
A	1+/2+, 2+/1+, 1+/3+, -/2+
Q	-/1+, 1+/1+, D/1+, 1+/D, D/D, 1+/-, 2+/D
N	-/-, -/D, D/-
Effect on patch test results*	Patch test result pairs (initial predupilumab patch test - dupilumab patch test result)
P	A-A, Q-Q
U	A-Q, Q-A, Q-N
L	A-N

A, Allergy; D2/D5, day 2/day 5; L, lost; N, no allergy; P, persistent; Q, questionable; U, unknown effect.

*Relative to initial patch test performed while patient *not* receiving dupilumab.

11-month hiatus, the effect was again observed 3 to 4 days after resuming dupilumab. No patients discontinued dupilumab therapy because of adverse symptoms.

Effect of dupilumab on patch test results

Twenty-three of 48 patients were patch tested both before and on dupilumab. One hundred twenty-five before- and on-dupilumab patch test "pairs" were performed in these 23 patients, of which 64 (51.2%) were classified as a "persistent (P)" allergy (Table IV). An unknown effect was observed in 48 (38.4%) of the pairs, where 1 or both of the patch test results were not definitively positive (classified "questionable-Q"), making it difficult to classify whether a change occurred.

An allergic reaction was labelled as "lost" (L) in 13 (10.4%) pairs in 7 patients. The 13 lost allergies included 4 in the emulsifier/surfactant category (propylene glycol 10% and 100%, amerchol, and dimethylaminopropylamine), 2 to fragrances (balsam of peru and fragrance mix 1), 2 to sunscreens (sulisobenzene and phenylbenzimidazole-5-sulfonic acid), 2 to metals (vanadium [III] chloride and phenyl mercuric acetate), and 1 each to a preservative (iodopropynyl butyl carbamate), topical medication (bacitracin), and resin (tosylamide formaldehyde).

Three of 7 patients with lost allergen pairs had a documented immunodeficiency, which accounted for 5 of 13 lost allergies. Three occurred in 1 patient with low immunoglobulin G 1 (IgG1), IgG2, and CD8 counts, 1 in a patient with confirmed B cell and T cell lymphocytopenia, and another in a patient with hypogammaglobulinemia (IgG1 and IgG2 subclass deficiency).

Table II. Patient characteristics and comorbidities and efficacy of dupilumab

Male (n, %)	24 (50)
Mean age, y	45
History of atopy in childhood, n (%)	32 (68)
Mean time to first follow-up, weeks	7.8
Comorbid LSC/PN, n (%)	6 (12.5)
Nummular dermatitis subtype, n (%)	5 (10.4)
Hand dermatitis subtype, n (%)	4 (8.3)
ACD (as diagnosed by patch testing), n (%)	32 (91.4)
Mean clearance at first follow-up, %	77.8

ACD, Allergic contact dermatitis; LSC/PN, lichen simplex chronicus or prurigo nodularis.

Thirty-five patients with AD were patch tested at some point in their electronic medical record history to determine comorbid ACD. Thirty-two of these 35 (91.4%) had ACD evidenced by positive patch test results and subsequent clinical improvement with allergen avoidance. Thirteen patients of the 35 who were patch tested at some point to determine comorbid ACD were also patch tested to extended series while receiving dupilumab specifically to investigate recalcitrant involvement of the head, neck, and hands; 12 of 13 (92.3%) experienced further clinical improvement with allergen avoidance.

DISCUSSION

The effect of dupilumab on patch testing

Dupilumab did not appear to overtly affect patch test results. An allergic reaction was lost—meaning definitively positive before dupilumab and definitively negative while on dupilumab—in only 13 (10.4%) patch tests pairs out of 125 (Table IV). Although a few reactions were not nonreproduced on dupilumab, most reactions were conserved, suggesting that dupilumab does not usually exert a uniformly dampening effect on ACD.

No particular allergen or allergen class appeared to be dependably blocked by dupilumab. The 13 lost allergic reactions spanned a wide range of allergen subtypes, including 4 to emulsifiers/surfactants, 2 each to fragrances, metals, and sunscreen agents, and 1 each to topical medicaments, preservatives, and resins. This wide and nonspecific range of categories does not align with the recently proposed paradigm that certain allergens elicit specific immune polarizations. Specifically, cellular molecular studies by Dhingra et al¹¹ revealed that fragrance and rubber generally exhibited a strong T_H2-specific immune response, whereas nickel strongly induced innate immunity and T_H1/T_H17 inflammation. Given that dupilumab dampens the T_H2 pathway through

Table III. Symptoms and residual dermatitis on dupilumab

Symptoms, n (%)	
Eyelid dermatitis*	17 (35.4)
Blepharitis [†]	11 (22.9)
Conjunctivitis (allergic) [‡]	9 (18.8)
Dry eyes	3 (6.3)
Injection site reaction	2 (4.2)
Dry skin	2 (4.2)
Photosensitivity	1 (2.1)
Dark clothes stained red-orange color	1 (2.1)
Location of residual dermatitis, [§] n (%)	
Face	21 (43.8)
Eyes*	18 (37.5)
Trunk	13 (27.1)
Hands	10 (20.8)
Arms	8 (16.7)
Neck	3 (6.3)
Scalp	1 (2.1)
Axilla	1 (2.1)
Genitals	1 (2.1)
Ankle/foot	1 (2.1)

*Refers to dermatitis of the upper or lower eyelids.

[†]Refers to eyelid margin involvement and associated Meibomian gland dysfunction.

[‡]Denotes ophthalmologist-diagnosed inflammation of the conjunctiva.

[§]Twenty-eight individuals had residual dermatitis at >1 location at the first follow-up.

interleukin-4 receptor alpha subunit inhibition, the logical deduction would be to expect “T_H2-mediated allergens” such as fragrance and rubber to be preferentially dampened by dupilumab while “T_H1-dominant allergens” such as nickel continue unopposed.

Although there were 2 instances of lost allergy to fragrance after starting dupilumab, the overwhelming majority were maintained. The only other case reporting patch test results before and on dupilumab demonstrated loss of reactivity in 1 patient to hydroperoxides of linalool, nickel, and compositae mix¹⁵; the loss of both fragrance and nickel allergy, which supposedly initiate different immune polarizations, further detracts from any conclusion that dupilumab selectively inhibits certain allergens based on immune response. Importantly, variability in patch test reproducibility has been demonstrated even in the absence of immunosuppressive influences.¹⁶⁻¹⁸

Immunodeficiency accounted for 5 of 13 lost allergies in 3 patients. Three lost allergies occurred in a 66-year-old woman who was screened for immunodeficiency due to of a history of multiple squamous and basal cell carcinomas and who was found to have low IgG1, IgG2, and CD8 counts.

Table IV. Patch test effect before and on dupilumab by allergen class

Allergen class	Total no. of patch-tested allergens	Patch test effect		
		Persistent	Unknown	Lost
Fragrances	26	19	5	2
Preservatives	23	12	10	1
Emulsifiers and surfactants	32	11	17	4
Hairdressing	5	2	3	0
Sunscreen	3	0	1	2
Topical therapy	10	5	4	1
Metals	19	11	6	2
Adhesives, varnishes	5	2	2	1
Textile dyes	2	2	0	0
Total, n (%)	125 (100)	64 (51.2)	48 (38.4)	13 (10.4)

Another lost allergy occurred in a 74-year-old man who was screened for immunodeficiency because of recurrent molluscum contagiosum infection and who was diagnosed with T cell and B cell lymphocytopenia. One lost allergy occurred in a 55-year-old man who was recurrently hospitalized for bacterial infection of the eyes and skin who was diagnosed with hypogammaglobulinemia due to IgG1 and IgG2 subclass deficiencies and who was treated with immunoglobulin infusions. Notably, his “before” and “on dupilumab” patch tests were separated by 8 years. The possibility of lost patch test reactivity over time has been investigated in multiple longitudinal studies,¹⁹⁻²⁵ and the loss of reactivity has been observed with a number of allergens, particularly metals (nickel, palladium, and aluminum).^{25,26} We postulate that these immune dysregulations may have contributed to the lack of patch test reproducibility in these patients.

An additional 5 lost allergies occurred in a patient with ND who was thought to be in a state of conditioned hyperirritability at the time of his pre-dupilumab patch testing, with 16 of 125 positives. Subsequent patch testing on dupilumab while his dermatitis was quiescent revealed only 11 of the original 16 to be persistently positive. Another lost allergy in another patient was to a 10% aqueous propylene glycol solution. However, because this patient had negative reactions to 3 stronger preparations of propylene glycol (20%, 30%, and 100%), the positive reaction to propylene glycol 10% is considered a likely false positive.

Multiple individual case reports have demonstrated positive patch test reactions on dupilumab^{15,27,28}; however, only 1 other report presents patch test results both before and after dupilumab initiation.¹⁵ Our study substantiates the findings of a 6-patient case series that ACD should be considered

in patients with AD with residual dermatitis on dupilumab,²⁹ although we did not find that dupilumab causes false positives on patch testing but rather that individual immunodeficiency may contribute to false negatives. Our experience does not substantiate claims that dupilumab is effective in the treatment of ACD. A retrospective study in 64 patients focused on the efficacy of dupilumab in patients with comorbid AD and ACD.³⁰ However, this study did not clearly evaluate the effect of dupilumab on ACD specifically, nor did it address the issue of whether dupilumab impacts patch testing. Several other reports attempted to address this question but were limited to individual cases or small series.^{29,31-35} Some of the studies that found dupilumab to be effective for ACD involved significant limitations, including the lack of diagnosis of AD³² or initiation of dupilumab and allergen avoidance simultaneously, making it difficult to interpret which intervention led to improvement.²⁹ In contrast, patients in this cohort had clearly diagnosed AD with recalcitrant dermatitis on dupilumab; they were subsequently patch tested to diagnose comorbid ACD, allowing a clearer understanding of which disease was responsible for which dermatitis and to determine which interventions were effective. Given the substantial additional improvement after initiating allergen avoidance in patients on dupilumab, it appears that dupilumab does not effectively treat ACD compared with allergen avoidance.

Our rates of clearance exceeded those reported in phase III trials,^{2,14,36} which may be related to the diagnosis and treatment of underlying ACD. This may explain the initial perception of these patients as “severe atopics” or treatment failures; 91.4% of patients patch tested in this cohort had comorbid ACD, which was likely contributing to their “recalcitrant AD” profile. Of those patch tested to extended

series on dupilumab, 92.3% had comorbid ACD and demonstrated further clinical improvement beyond the impact of dupilumab alone.

Limitations

This is a retrospective chart review, and therefore the data reflect findings from real-world nonrandomized clinical situations. Furthermore, we assessed the effectiveness of dupilumab by reporting patient-estimated “% improvement from baseline,” which is a subjective measure subject to recall bias compared with Global Assessment and Eczema Area and Severity Index scoring. Regarding the patch tests with an “unknown effect,” this is an unavoidable result of the overlap in the appearance of irritant/doubtful reactions and doubtful/1+ reactions; as such, obtaining clearly delineated groups of persistent versus lost allergies with every patch test pair is not feasible. Finally, because repeat patch testing was only performed in individuals receiving dupilumab, with no nondupilumab control subjects, this study does not account for the possibility that some of the lost patch test reactions may have been related to natural variations in patch test reproducibility.

In conclusion, dupilumab does not appear to exert a reliable or uniform dampening effect on patch test results, as evidenced by the small proportion of nonreproduced patch test results after initiation of dupilumab. In addition, dupilumab does not appear to suppress patch test reactivity to any particular allergen subclass. We observed higher rates of clearance on dupilumab than reported in clinical trials, which may be because of the diagnosis and management of underlying ACD in many of these patients. This work underscores the importance of considering patch testing in patients with residual dermatitis on dupilumab therapy. Although AD can occur as a result of immunodeficiency, it can also occur alongside immunodeficiency. For dermatologists considering patch testing in patients with AD, recurrent infection may be a sign of underlying immunodeficiency and laboratory testing may be appropriate along with patch testing.

The authors thank Lindsay Beck and April Martinez for their assistance with data collection.

REFERENCES

1. Gittler JK, Shemer A, Suarez-Farinas M, et al. Progressive activation of T(H)2/T(H)22 cytokines and selective epidermal proteins characterizes acute and chronic atopic dermatitis. *J Allergy Clin Immunol*. 2012;130:1344-1354.
2. Blauvelt A, de Bruin-Weller M, Gooderham M, et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. *Lancet*. 2017;389:2287-2303.
3. Thyssen JP, McFadden JP, Kimber I. The multiple factors affecting the association between atopic dermatitis and contact sensitization. *Allergy*. 2014;69:28-36.
4. Gittler JK, Krueger JG, Guttman-Yassky E. Atopic dermatitis results in intrinsic barrier and immune abnormalities: implications for contact dermatitis. *J Allergy Clin Immunol*. 2012;131:300-313.
5. Newell L, Polak ME, Perera J, et al. Sensitization via healthy skin programs Th2 responses in individuals with atopic dermatitis. *J Invest Dermatol*. 2013;133:2372-2380.
6. Correa da Rosa J, Malajian D, Shemer A, et al. Patients with atopic dermatitis have attenuated and distinct contact hypersensitivity responses to common allergens in skin. *J Allergy Clin Immunol*. 2015;135:712-720.
7. Uehara M, Sawai T. A longitudinal study of contact sensitivity in patients with atopic dermatitis. *Arch Dermatol*. 1989;125:366-368.
8. Jones HE, Lewis CW, McMarlin SL. Allergic contact sensitivity in atopic dermatitis. *Arch Dermatol*. 1973;107:217-222.
9. Thyssen JP, Johansen JD, Linneberg A, Menne T, Nakilde K. The association between contact sensitization and atopic disease by linkage of a clinical database and a nationwide patient registry. *Allergy*. 2012;67:1157-1164.
10. Chen JK, Jacob SE, Nedorost ST. A pragmatic approach to patch testing atopic dermatitis patients: clinical recommendations based on expert consensus opinion. *Allergy*. 2016;27:186-192.
11. Dhingra N, Shemer A, Correa da Rosa J, et al. Molecular profiling of contact dermatitis skin identifies allergen-dependent differences in immune response. *J Allergy Clin Immunol*. 2014;134:362-372.
12. Wilkinson DS, Fregert S, Magnusson B, et al. Terminology of contact dermatitis. *Acta Derm Venereol*. 1970;50:287-292.
13. Suresh R, Murase JE. The role of expanded series patch testing in identifying causality of residual facial dermatitis following initiation of dupilumab therapy. *JAAD Case Rep*. 2018;4:899-904.
14. Simpson EL, Bieber T, Guttman-Yassky E. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med*. 2016;375:2335-2348.
15. Raffi J, Botto N. Patch testing and allergen-specific inhibition in a patient taking dupilumab. *JAMA Dermatol*. 2019;155:120-121.
16. Ale IS, Maibach HI. Reproducibility of patch test results: a concurrent right-versus-left study using TRUE Test. *Contact Dermatitis*. 2004;50:304-312.
17. Belsito DV, Storrs FJ, Taylor JS, et al. Reproducibility of patch tests: a United States multicenter study. *Am J Contact Dermat*. 1992;3:193-200.
18. Gollhausen R, Przybilla B, Ring J. Reproducibility of patch tests. *J Am Acad Dermatol*. 1989;21:1196-1202.
19. Siemund I, Mowitz M, Zimerson E, Bruze M, Hindsén M. Variation in aluminium patch test reactivity over time. *Contact Dermatitis*. 2017;77:288-296.
20. Hindsén M, Bruze M, Christensen OB. Individual variation in nickel patch test reactivity. *Am J Contact Dermat*. 1999;10:62-67.
21. Keczek K, Basheer AM, Wyatt EH. The persistence of allergic contact sensitivity: a 10-year follow-up in 100 patients. *Br J Dermatol*. 1982;107:461-465.
22. Schubert H, Kohánka V, Korossy S, et al. Epidemiology of nickel allergy: results of a follow-up analysis of patients with positive patch tests to nickel. *Contact Dermatitis*. 1988;18:237-239.
23. Rystedt I. Evaluation and relevance of isolated test reactions to cobalt. *Contact Dermatitis*. 1979;5:233-238.

24. Bruze M, Hedman H, Björkner B, Möller H. The development and course of test reactions to gold sodium thiosulfate. *Contact Dermatitis*. 1995;33:386-391.
25. Gente Lidholm A, Bergfors E, Inerot A, et al. Unexpected loss of contact allergy to aluminium induced by vaccine. *Contact Dermatitis*. 2013;68:286-292.
26. Bergfors E, Trollfors B, Inerot A. Unexpectedly high incidence of persistent itching nodules and delayed hypersensitivity to aluminium in children after the use of adsorbed vaccines from a single manufacturer. *Vaccine*. 2003;22:64-69.
27. Hoot JW, Douglas JD, Falo LD Jr. Patch testing in a patient on dupilumab. *Dermatitis*. 2018;29:164.
28. Puza C, Atwater A. Positive patch test reaction in a patient taking dupilumab. *Dermatitis*. 2018;29:89.
29. Stout M, Silverberg JI. Variable impact of dupilumab on patch testing results and allergic contact dermatitis in adults with atopic dermatitis. *J Am Acad Dermatol*. 2019;51:157-162.
30. Chipalkatti N, Lee N, Zancanaro P, Dumont N, Kachuk C, Rosmarin D. A retrospective review of dupilumab for atopic dermatitis patients with allergic contact dermatitis. *J Am Acad Dermatol*. 2019;80:1166-1167.
31. Crepy MN, Nosbaum A, Bensefa-Colas L. Blocking type 2 inflammation by dupilumab does not control classic (Type 1-driven) allergic contact dermatitis in chronic hand eczema. *Contact Dermatitis*. 2019;81:145-147.
32. Chipalkatti N, Lee N, Zancanaro P, Dumont N, Donovan C, Rosmarin D. Dupilumab as a treatment for allergic contact dermatitis. *Dermatitis*. 2018;29:347-348.
33. Goldminz AM, Scheinman PL. A case series of dupilumab-treated allergic contact dermatitis patients. *Dermatol Ther*. 2018;31:e12701.
34. Joshi SR, Khan DA. Effective use of dupilumab in managing systemic allergic contact dermatitis. *Dermatitis*. 2018;29:282-284.
35. Machler BC, Sung CT, Darwin E, Jacob SE. Dupilumab use in allergic contact dermatitis. *J Am Acad Dermatol*. 2019;80:280-281.e1.
36. de Bruin-Weller M, Thaçi D, Smith CH, et al. Dupilumab with concomitant topical corticosteroid treatment in adults with atopic dermatitis with an inadequate response or intolerance to ciclosporin A or when this treatment is medically inadvisable: a placebo-controlled, randomized phase III clinical trial. *Br J Dermatol*. 2018;178:1083-1101.