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Article Type: Research Letter**Title: Dupilumab use in allergic contact dermatitis**

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Dupilumab is an interleukin-4 receptor (IL-4R α) inhibitor indicated in recalcitrant moderate-to-severe atopic dermatitis (AD).¹ While contact dermatitis is considered a Th₁ cell-mediated process, certain allergens sensitize by induction of Th₂-pathways.² Our retrospective case-study suggests that dupilumab may be effective in the inhibition of "weaker" allergens that elicit a Th₂-mediated IL-4 dependent ACD.

A retrospective chart review was performed to identify all patients treated with dupilumab for recalcitrant dermatitis by two dermatologists at their respective clinical sites (Center for Dermatology, P.A., Florham Park, NJ and Loma Linda Veterans Hospital, CA). Clinical evaluations had been performed by the respective dermatologist as part of the clinical management, using a modified physician global assessment. All patients had been assessed at baseline and 10-12 weeks after starting dupilumab for body surface area (BSA) of involvement, severity index, and itch. The patients continued to receive clinical care on an as needed basis thereafter. No side effects were associated with dupilumab. Table 1 depicts pertinent information including areas involved, patch test proven allergen sensitivities, previous failed systemic therapies, and treatment outcomes of all (fifteen) patients. (Table 1.)

The majority of these adult patients had a history of childhood AD and current hand dermatitis (73%). Recalcitrant facial dermatitis was prevalent during the dupilumab treatment in a significant number of the cases. The percent BSA affected by dermatitis ranged from 10%-80% (m=48%), and the percent improvement after dupilumab ranged from 70%-100% (m=85%). A weak-negative ($R=-0.1181$, $R^2=0.0139$) correlation to patient age and weak-positive correlation to BSA ($R=0.06$, $R^2=.0038$) were associated with improvement on dupilumab. Collectively, the fifteen patients had sensitivities to 46 distinct allergens. The most frequent clinically relevant allergens were cocamidopropyl betaine [CAPB] (40%), nickel (33%), oleamidopropyl dimethylamine [OPD] (27%), *myroxylon perei* (20%), and fragrance mix 1 (20%).

The majority of these adult patients had been diagnosed with AD, a predominant Th₂-axis immune disorder. It has been reported that inflamed atopic skin is predisposed to the development of Th₂-mediated contact sensitization to “weaker” potency allergens, such as fragrances, emulsifiers and surfactants (e.g.: CAPB).^{2,3} Of note, a recent report by Puza and Atwater described a patient who elicited a 1+ patch reaction to the potent sensitizer methylisothiazolinone in contrast to an indeterminant (+/-) reaction to the “weaker” allergen, dimethylaminopropylamine, (a precursor of CAPB), while on dupilumab for severe AD.⁴ The role of IL-4 in ACD has been demonstrated by IL-4 knockout mice, which preserved the ability to elicit contact sensitivities to oxazolone but not 2,4,6-trinitrochlorobenzene, a contact allergen with Th₂-mediated sensitization.⁵

The high prevalence of nickel sensitization was expected given the ubiquitous exposures and association with AD hand dermatitis.² That said, the remarkable clinical and quality of life improvements achieved by this group of prior “frequent flyer” patients, was serendipitous and mirrors the dramatic impact seen in the early years of the biologic era for psoriasis patients. This study highlights the untapped potential of IL-4 inhibitors in the treatment of adult patients with a history of AD and recalcitrant and systematized ACD to certain allergens.²

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Table 1: Demographics of systematized patch test confirmed ACD patients

Patient	Age of subject when dupilumab was initiated	Gender (M/F)	History of childhood atopic dermatitis	Hand involvement (Yes/No)	Percent BSA at onset of dupilumab	Estimated % improvement within 10-12 weeks on dupilumab	Recalcitrant dermatitis sites while on dupilumab (e.g. Face, Arm, Legs, Trunk)	Previously failed systemic therapies
1.	28	F	Yes	Yes	55%	95%	• Hands • Feet	• CysA • Pred
2.	29	M	Yes	Yes	65%	80%	• Face	• MM • CysA • MTX • Pred
3.	35	M	Yes	Yes	50%	80%	• Face • Arms • Hands	• CysA • Apremilast • AZA • Pred
4.	44	F	Yes	Yes	15%	80%	• Face	• MM • Pred
5.	53	M	No	No	65%	100%	• Legs	• CysA • Pred
6.	54	F	Yes	Yes	45%	80%	• Face	• CysA • MM • MTX • Pred
7.	54	M	Yes	No	30%	90%	• Face • Scalp	• CysA • MM • Pred
8.	55	F	Yes	Yes	55%	90%	• Face • Eyelids • Chest • Hands	• MM • Pred
9.	56	F	Yes	Yes	50%	80%	• Neck • Face	• CysA • Pred
10.	58	F	No	Yes	50%	95%	• Face • Eyelids • Legs	• CysA • Ustekinumab • Pred
11.	58	F	No	Yes	25%	85%	• Scalp • Face • Chest • Arms • Legs	• CysA • Ustekinumab • Pred
12.	60	M	Yes	Yes	60%	90%	• Face • Trunk • Legs • Hands	• CysA • MM • Pred
13.	64	M	Yes	Yes	80%	70%	• Arms • Legs	• CysA • MM • AZA • Etanercept • Pred
14.	69	F	Yes	No	65%	85%	• Face • Eyelids • Breast	• CysA • MM • Pred
15.	72	F	No	No	10%	80%	• Trunk	• CysA • Pred

MTX = methotrexate; Pred = 'rescue' prednisone > 3 times per year.