

Prevalence of allergen sensitization detected by patch tests

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ABSTRACT

Background: Existing literature on the prevalence of positive reactions to allergens is largely derived from dermatologists who practice at large academic centers. Data from other providers, including allergists who practice in various other settings, is important to assess a more representative and accurate prevalence of contact allergy.

Objective: To determine the prevalence of contact allergy among individuals with at least one positive patch test result by comparing data for positive patch test reaction rates of common contact allergens from 3 groups based in different practice settings, 2 of which are academic.

Methods: We retrospectively analyzed patch test results of an academic center (January 1, 2011, to December 4, 2015) and a national contact allergen database (March 1, 2015, to September 1, 2016). Data from a third, academic-based group was obtained separately from the published literature. Logistic regression analysis was used to compare positive reaction rates of the widely available, patch test allergens among the 3 groups.

Results: The positive reaction rates for 10 of 36 compared allergens (28%) were significantly higher ($p < 0.05$) for the national contact allergen database compared with both the academic groups.

Conclusion: Positive reaction rates to common allergens used in patch testing may be underreported in the literature. Limitations of our study included the retrospective nature of the study, different date ranges among the three groups, and the absence of all allergens tested by the national contact allergen database.

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Allergic contact dermatitis (ACD) is a common condition that affects millions of Americans each year. The symptoms and clinical course of ACD can substantially impact the quality of life of patients who are afflicted.¹ Existing literature about the prevalence of positive reactions to allergens on patch testing is largely derived from dermatologists who practice at academic centers, such as Mayo Clinic,² and the North American Contact Dermatitis Group (NACDG).³ Data from other providers, including allergists who practice in various other settings and geographic regions, could help clarify a more representative prevalence of contact allergy nationwide.

SkinSAFE (EmpowHer, Inc., Scottsdale, AZ) is a data base provided through a Web site and smartphone application that enables consumers to easily find products that are free of potential allergy-causing ingredients. Data from SkinSAFE include results of patch tests

conducted by dermatologists, allergists, pediatricians, family/primary care physicians, and plastic surgeons in both community and academic settings. SkinSAFE users have two options to generate a personal shopping list of products that are free of their specific allergens: (1) to input a unique personal allergy code (PAC) based on patch test results from a health care provider, or (2) opt for virtual patch testing by selecting common allergens to avoid as previously described.⁴ In this study, we attempted to answer the question whether there is a significant difference between the SkinSAFE data base, which represents contact allergy in the general public compared with data from large academic centers with potential referral bias, including NACDG and Mayo Clinic.

METHODS

We conducted a retrospective analysis of positive patch test results for SkinSAFE users who had provider-originated patch test results from March 1, 2015, to September 1, 2016. The Mayo Clinic Institutional Review Board approved the study (15–007853) and waived informed consent for those who gave research authorization. None of the participants were paid. Computer software engineers at EmpowHER (HER, Inc., Scottsdale, AZ), the social health company that hosts SkinSAFE, abstracted data from the Web site and excluded all identifiers of the users. J.E. Ma and J.A. Yiannias had full access to all of the study data and take full responsibility for the integrity of the data and

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Table 1 Top 10 most common Thin-Layer Rapid Use Epicutaneous Patch (T.R.U.E.) Test allergens by group

Allergen (prevalence rate, %)			
	SkinSAFE	Mayo Clinic	NACDG
1.	Nickel sulfate (27.8)	Nickel sulfate (30.7)	Nickel sulfate (30.0)
2.	Balsam of Peru (23.3)	Balsam of Peru (23.1)	Fragrance mix I (17.7); Fragrance mix II (8.5)*
3.	Cobalt dichloride (22.2)	Parthenolide, Compositae mix (21.2)	MCI and MI (9.5); MI only (16.2)
4.	Fragrance I or II (19.8)	Fragrance mix I or II (19.9)	Neomycin sulfate (12.6)
5.	Formaldehyde (17.2)	Cobalt dichloride (16.6)	Cobalt dichloride (11.1)
6.	Gold (17.1)	Neomycin sulfate (15.8)	Bacitracin (11.1)
7.	Potassium dichromate (16.1)	Potassium dichromate (15.2)	Balsam of Peru (10.7)
8.	MCI and MI (14.0); MI only (10.2)	Carba mix (12.8)	p-Phenylenediamine (10.5)
9.	Carba mix (14.0)	Bacitracin (10.3)	Formaldehyde (10.4)
10.	Methylbromoglutaronitrile (13.7)	MCI and MI (9.8); MI only (8.1)	Wool alcohols (8.0)

NACDG = North American Contact Dermatitis Group; MCI = methylchloroisothiazolinone; MI = methylisothiazolinone.

*Fragrance mix allergens I and/or II were only included once in each of the three groups.

accuracy of the data analysis. The coauthor, N. Zhang, conducted the statistical analyses.

Patients who are patch tested by a health care provider who uses SkinSAFE are given a PAC that contains each patient's unique allergen list. SkinSAFE uses the PAC data to generate a list of safe products for the patient to use by automatically excluding all products that contain ingredients in the patient's allergen list. We identified the most common allergens entered into SkinSAFE by users who were health care providers. We calculated the reaction rate for each allergen, defined as the total number of positive allergic reactions for a given allergen divided by the total number of patients for whom a PAC was created (which thus identified patients who had been patch tested and found to have at least one positive patch test result). We classified SkinSAFE health care providers into two groups: dermatologists and nondermatologists (allergists, pediatricians, primary care/family physicians, and plastic surgeons).

Data from Mayo Clinic were obtained by a retrospective review of reaction rates for Mayo Clinic patch tests from January 1, 2011, to December 4, 2015. NACDG data were obtained from the published literature³ based on patch tests conducted from January 1, 2013, to December 31, 2014. We chose to compare the reaction rates of 36 widely available allergens included in the Thin-Layer Rapid Use Epicutaneous Patch (T.R.U.E.) Test (SmartPractice Denmark, Hillerød, Denmark) among the three groups: the NACDG,³ Mayo Clinic, and SkinSAFE (Table 1). To ensure an appropriate comparison across the three groups, only patients with at least one positive reaction to an allergen were in-

cluded. Because Mayo Clinic used lidocaine instead of dibucaine, the reaction rates for lidocaine were also studied. Thus, instead of the 35 T.R.U.E. test allergens, we studied 36 allergens.

Statistical Analyses

To compare the same set of allergens among the three groups, we conducted a logistic regression analysis by using SkinSAFE as the reference group to assess whether significant differences existed for reaction rates, with $p < 0.05$ considered significant. When there was a 0% reaction rate, the Fisher exact test was used to compare the reaction rates among the groups.

RESULTS

We identified 2119 SkinSAFE users with provider-originated PACs. There were 125 active providers on SkinSAFE: 52% identified as dermatologists, with the remaining 48% identified as nondermatologists. Non-dermatologist specialties who were identified included the following: allergy/immunology (90%), plastic surgery (4%), pediatrics (2%), and family medicine/primary care (4%). The top 10 positive allergens tested by nondermatologists included medication-related allergens (hydrocortisone-17-butyrate and anesthetics [dibucaine, lidocaine, and benzocaine]), preservatives (thimerosal and formaldehyde related allergens [formaldehyde, bronopol, p-tert butylphenol]), disperse blue mix 124/106, and Compositae mix.

The top 10 T.R.U.E. Test allergens with the highest positive reaction rates determined based on patch test data for NACDG, Mayo Clinic, and SkinSAFE are

Table 2 Comparison of reaction rates of Thin-Layer Rapid Use Epicutaneous Patch (T.R.U.E.) Test allergens: SkinSAFE, Mayo Clinic, and NACDG*

Reaction Rate Comparison	Allergen
SkinSAFE reaction rates significantly higher ($p < 0.05$) than both Mayo Clinic and NACDG rates	Black rubber mix
	Cobalt dichloride
	Disperse blue mix 124/106
	Formaldehyde
	Imidazolidinyl urea
	MCI and MI
	Mercaptobenzothiazole
	Methylbromoglutaronitrile
	<i>p</i> -tert Butylphenol formaldehyde resin
	Quaternium-15
SkinSAFE reaction rates significantly higher ($p < 0.05$) than Mayo Clinic only rates (not NACDG)	Gold (I) sodium thiosulfate dihydrate 0.5% pet (NACDG data not available)
	Mercapto mix (NACDG data not available)
	MI (NACDG reaction rate for this allergen is significantly higher than that of SkinSAFE)
	<i>p</i> -Phenylenediamine
	Thimerosal (NACDG data not available)
	Wool alcohols
	2-Bromo-2-nitropropane-1,3-diol
SkinSAFE reaction rates significantly lower ($p < 0.05$) than Mayo Clinic rates (Mayo Clinic rates significantly higher)	Neomycin sulfate
	Nickel sulfate
SkinSAFE reaction rates significantly higher ($p < 0.05$) than NACDG only rates (but not Mayo Clinic)	Parthenolide (Compositae mix)
	Balsam of Peru
	Carba mix
	Colophony
	Diazolidinyl urea
	Ethylenediamine dihydrochloride
	Hydrocortisone-17-butyrate
	Paraben mix
	Potassium dichromate
	Tixocortol 21 pivalate
	Bacitracin
	Budesonide
	Caine mix (benzocaine)
No significant ($p > 0.05$) reaction rates between SkinSAFE and the other two groups	Epoxy resin
	Fragrance mix I or II (NACDG data not available)
	Lidocaine
	Parthenolide (sesquiterpene lactone mix)
	Thiuram mix

NACDG, North American Contact Dermatitis Group; MCI = methylchloroisothiazolinone; MI = methylisothiazolinone.

*We were unable to analyze quinolone mix reaction rates because Mayo Clinic and NACDG data were unavailable for this allergen.

shown in Table 1. Five allergens were represented in the top 10 lists of all three groups (balsam of Peru, cobalt dichloride, fragrance mix, methylchloroisothiazolinone and methylisothiazolinone, and nickel sulfate). Of note, NACDG did not have patch test data available in their 2013–2014 data set for gold, mercapto mix, thimerosal, and quinolone mix. The difference in

reaction rates of the 36 T.R.U.E. test equivalent allergens among the NACDG, Mayo Clinic, and SkinSAFE groups are shown in Table 2. Of the three groups, SkinSAFE reaction rates were significantly higher ($p < 0.05$) than those of Mayo Clinic and NACDG for 10 of the 36 allergens (28%). Mayo Clinic reaction rates had significantly higher ($p < 0.05$) positive reaction rates

than those of the SkinSAFE group for 4 of 36 (11%) of the allergens. None of the NACDG reaction rates were significantly higher than that of SkinSAFE and Mayo Clinic.

DISCUSSION

Most currently published literature regarding contact dermatitis in North America comes from academic dermatology practices. Our goal was to include results of patch test data from various other sources, including allergy practices, which have been underrepresented.⁵ A recent study included the top 35 allergens based on the frequency of searches conducted with the American Contact Dermatitis Society's Contact Allergy Management Program; however, the rates of provider type (dermatologist versus allergist) were not available.⁶ The investigators of this study indicated that more data are needed from other centers across North America, including smaller practices, to provide a broader view of the prevalence of contact allergens. Our study results showed that more than one-fourth (28%) of SkinSAFE allergens were significantly higher positive reaction rates for comparable allergens in the SkinSAFE data base than in the Mayo Clinic and NACDG data bases. The variability in patch test results data between the SkinSAFE data base compared with Mayo Clinic and NACDG was significant in that it highlighted a difference between community practices and academic centers. Based on our findings, we indicated that the reaction rates for some allergens may be underreported in the current literature.

Underreporting may occur for several reasons. Patch test results data for the NACDG is derived from 13 dermatologists who practice at centers in North America. The Mayo Clinic data set includes results of patch tests performed by >35 dermatologists from all three major sites of this large academic institution (Arizona, Florida, Minnesota). Potential referral bias is likely to occur in both academic centers, where one would expect higher numbers of patch test reactions. In contrast, the data for SkinSAFE includes results of patch tests conducted by various providers (dermatologists, allergists, pediatricians, family/primary care physicians, and plastic surgeons), and their patient base may represent contact allergy in the general public. Many of the SkinSAFE providers practice in community settings, which contrasts with data from large, academic centers in NACDG and Mayo Clinic.

There is inherent variability in patients who are patch tested in these different geographic and practice settings as well as in the types and formulations of allergens tested, which may impact reporting of patch test results data. It is also possible that positive patch test results are being overread, which highlights the subjectivity of interpreting patch test results. The dif-

ferences in the purposes of the data bases may also account for some variability in positive patch test results data. In this study, we presented the positive patch test reaction rates rather than the clinical relevance of the respective positive allergens. Because SkinSAFE guides its users to avoid allergy-causing consumer products, this data base may more heavily reflect data on clinically relevant allergens; in contrast, data from NACDG and Mayo Clinic represent all positive reactions that do not necessarily correspond to clinical relevance of allergens. Interestingly, the most common positive allergens tested by nondermatologists (primarily allergists) in the SkinSAFE group included medication-related allergens, a plant-derived allergen, and preservatives. This potentially indicates that differences in positive patch test results may be linked to the use of different allergen panels or series used by dermatologists and allergists.

Both atopic and contact dermatitis substantially impair the quality of life of persons with these conditions, yet little literature exists about patient-centered research efforts that incorporate patients' unique perspectives or about specific tools to evaluate disease-related quality of life.⁷⁻⁹ The SkinSAFE program, which, to our knowledge, is the first allergen data base available to both physicians and consumers, is a new patient-centered tool that can help determine the evolving prevalence of allergens and help patients avoid contact with allergens. SkinSAFE provides two options for its users: (1) bypassing traditional patch testing and allowing users to avoid any combination of the most common allergens, and (2) guiding patients away from patch test-identified allergens under the direction of their health care provider. SkinSAFE empowers patients to become educated about allergy avoidance through a personalized experience, with the goal of reducing the number of dermatitic skin reactions by guiding patients away from allergy-causing consumer products and, thus, improving their quality of life.

CONCLUSION

In this study, we analyzed the positive patch test results data of SkinSAFE, a data base that includes providers from specialties other than dermatology and from a variety of geographic and practice settings and compared that data with data from NACDG and Mayo Clinic, two large academic-based groups. By comparing data among these groups, we found that positive reaction rates for some allergens seemed to be underreported in the current literature. Continued prospective studies on patch testing of patients from a breadth of practice and geographic settings are warranted to estimate an accurate prevalence of contact allergens.

Limitations

We acknowledge the limitations of our study, including the retrospective nature of the study. In addition, the positive patch test results data may be affected by our comparison of different date ranges among the three groups. There was inherent subjectivity of interpreting patch test positivity among different providers, and the methodology of patch testing done outside of NACDG and Mayo Clinic settings was unknown. Also, in this study, we presented the positive patch test reaction rates rather than the clinical relevance of the respective positive allergens. We also did not have complete patch test data on all the allergens tested in SkinSAFE. For instance, NACDG did not have patch test results data available for four allergens that were tested by SkinSAFE providers (gold, mercapto mix, thimerosal, and quinolone mix). Also, SkinSAFE does not collect data for all allergens tested, unlike traditional reports of contact allergy incidence.

REFERENCES

1. Benyamini Y, Goner-Shilo D, Lazarov A. Illness perception and quality of life in patients with contact dermatitis. *Contact Dermatitis*. 2012; 67:193–199.
2. Wentworth AB, Yiannias JA, Keeling JH, et al. Trends in patch-test results and allergen changes in the standard series: a Mayo Clinic 5-year retrospective review (January 1, 2006, to December 31, 2010). *J Am Acad Dermatol*. 2014; 70:269–275.e4.
3. DeKoven JG, Warshaw EM, Belsito DV, et al. North American Contact Dermatitis Group patch test results 2013–2014. *Dermatitis*. 2017; 28:33–46.
4. Yiannias JA, El-Azhary R. Virtual patch testing: data driven empiric contact allergen avoidance. *Ann Allergy Asthma Immunol*. 2013; 111(suppl): A18.
5. Camacho-Halili M, Axelrod S, Michelis MA, et al. A multi-center, retrospective review of patch testing for contact dermatitis in allergy practices. *Ann Allergy Asthma Immunol*. 2011; 107:487–492.
6. Scheman A, Severson D. American Contact Dermatitis Society Contact Allergy Management Program: an epidemiologic tool to determine relative prevalence of contact allergens. *Dermatitis*. 2016; 27:9–10.
7. Drucker AM, Wang AR, Qureshi AA. Research gaps in quality of life and economic burden of atopic dermatitis: the national eczema association burden of disease audit. *JAMA Dermatol*. 2016; 152:873–874.
8. Capozza K, Shao Y, Zeng Q. “Crowdsourcing” a patient-centered research agenda for pediatric atopic dermatitis. *Int J Dermatol*. 2016; 55:1414–1416.
9. Swietlik J, Reeder M. Current quality-of-life tools available for use in contact dermatitis. *Dermatitis*. 2016; 27:176–185. □

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