

Results of patch testing to personal care product allergens in a standard series and a supplemental cosmetic series: An analysis of 945 patients from the Mayo Clinic Contact Dermatitis Group, 2000-2007

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Background: Patch testing to a standard screening series of allergens in combination with supplemental cosmetic allergens is often used to diagnose allergic contact dermatitis due to personal care products.

Objective: To report results of patch testing to skin care product allergens contained in a standard series and a supplemental cosmetic series and to compare efficacy of this combined series in detecting positive reactions to personal care product allergens with the efficacy of various standard screening series.

Methods: Positive reaction rates to skin care product allergens were tabulated for patients who underwent patch testing to both standard and cosmetic series allergens at Mayo Clinic between 2000 and 2007. Data were compared with skin care allergens detected on standard screening series, including the thin-layer rapid use epicutaneous (TRUE) test.

Results: Of 945 patch-tested patients, 68.4% had at least one positive reaction and 47.3% had at least two positive reactions. Also, 49.4% of patients reacted to at least one preservative; 31.2% reacted to at least one fragrance/botanical additive. Compared with use of our standard series and cosmetic series, use of the TRUE test would have missed 22.5% of patients with preservative allergy, 11.3% with fragrance/botanical allergy, and 17.3% with vehicle allergy.

Limitations: Various allergens tested over time, patch test reading by residents, and lack of confirmation of allergen in personal care products.

Conclusion: Standard patch-test screening series miss a substantial number of patients with skin care product ingredient allergy. (J Am Acad Dermatol 10.1016/j.jaad.2009.11.033.)

Key words: allergens; contact dermatitis; cosmetics; patch tests; skin care.

BACKGROUND

Patch testing is the primary diagnostic tool for evaluating patients with suspected allergic contact dermatitis.¹ Previous studies have shown the efficacy of large screening series, such as the series used by

Abbreviations used:

FDA:	Food and Drug Administration
NACDG:	North American Contact Dermatitis Group
TRUE:	thin-layer rapid use epicutaneous (test)

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the North American Contact Dermatitis Group (NACDG), to facilitate more accurate detection of positive reactions and relevant allergens of patients with suspected allergic contact dermatitis than with a limited screening series, such as the thin-layer rapid use epicutaneous (TRUE) test (Allerderm Laboratories, Inc, Phoenix, AZ).²⁻⁵

Although the term “cosmetic” is equated with make-up by the general population, cosmetic was

used broadly in the present study to denote personal care products, including sunscreen and topical medications.

Given the ubiquitous use of and frequent changes in the ingredients of topical skin care products, increasing emphasis has been placed on identification of and patch testing to potential cosmetic and personal care product allergens.⁶ Patch test data obtained from studies in Europe and the United States indicate a 9.8% pooled prevalence of allergic contact dermatitis due to cosmetic allergens.⁶ A study in an adult Danish population showed a doubling of the prevalence of contact sensitivity to cosmetic-related allergens between 1990 and 1998.⁷

The optimal number of allergens in a patch test series for detection of relevant skin care product allergies continues to be unclear. A recent study of 794 patients showed that 34% of patients would have had at least one allergen missed if only the NACDG standard screening series of 65 allergens had been used.³ The aim of the present study is to report the results of patch testing to skin care product allergens contained in the standard series and a supplemental cosmetic series at Mayo Clinic (Rochester, MN; Jacksonville, FL; and Scottsdale, AZ) over 8 years (2000-2007) and to assess the number of allergens that would have been overlooked if testing had been performed to only the Mayo Clinic standard series, the NACDG standard series, or the TRUE test.

METHODS

Patients

Patients who underwent patch testing to the standard screening series and the supplemental cosmetic series for suspected allergic contact dermatitis at Mayo Clinic from Jan. 1, 2000 to Dec. 31, 2007 were identified from an existing clinical database. In general, patients were not patch tested if they had applied topical corticosteroids to patch test sites; had taken immunosuppressive drugs, including oral corticosteroids; or had medical conditions that could compromise the evaluation of skin responsiveness.^{2,8} Information on patient demographics and on results of patch testing to cosmetic allergens was extracted from the clinical database. Patients who

had denied research authorization were excluded from the analysis. This study was approved by the Mayo Clinic Institutional Review Board.

Interpretation of patch-test reactions

The patch-testing method was the same as previously described^{2,9} and was in line with the previously reported method of the NACDG.^{1,8,10} Testing was conducted with Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster Aksjeselskap, Vennesia, Norway), and patches were applied to a patient's upper back and removed after 48 hours. Most allergens were purchased from Chemo-technique Diagnostics AB (Vellinge, Sweden); the other allergens were compounded by the Mayo Clinic Pharmacy.

Reactions were evaluated initially at 48 to 72 hours and again at 96 to 168 hours after

patch application. Patch-test reactions were interpreted with the following criteria: negative reaction, macular erythema, weak reaction (nonvesicular erythema, infiltration, and possibly papules), strong reaction (edematous or vesicular lesions), extreme reaction (spreading, bullous, ulcerative lesions), and irritant reaction. Reactions were interpreted by the ordering physician (includes all staff and residents) in all but exceptional circumstances; even when the final patch-test reading was done on the weekend, the ordering physician was the one required to interpret the results. Reactions were further interpreted as relevant or irrelevant on the basis of a history of either known contact with substances containing the allergen or circumstances of likely contact with substances containing the allergen. Each reaction was recorded as follows: I, irritant; N, allergic, not relevant (no exposure to products that contain the allergen); Q, allergic, questionably relevant (current exposure to products likely to contain the allergen); P, allergic, formerly relevant (past exposure to products likely to contain the allergen); and R, allergic, relevant (use test or patch test with the product is positive, or ingredient is verified in patient's product and use of that product is verified). For this study, scores for current, questionable, and past relevance were combined ($R + Q + P = \text{relevance}$). For this study, a positive allergic patch test result was defined as a weak, strong, or extreme

CAPSULE SUMMARY

- Patch testing is the primary diagnostic tool for evaluating patients with suspected allergic contact dermatitis.
- Preservatives are the most commonly identified allergens in skin care products.
- A standard patch test screening series may miss a substantial number of patients with allergy to a skin care product ingredient.
- Patch testing to supplemental allergens enhances the evaluation of patients with suspected allergic contact dermatitis to skin care product allergens.

Table I. MOAHLFA Index of study patients

Index	No. of patients (%)
Male sex	121 (12.8)
Occupational causation of dermatitis	NA
Atopy*	
No	299 (31.6)
Yes	281 (29.7)
Unknown	365 (38.6)
Hand [†]	113 (13.6)
Leg [†]	56 (6.7)
Face [†]	261 (31.4)
Age ≥ 40 years	741 (78.4)

NA, Data not available.

*The MOAHLFA index is an extension of the MOHL and MOAHL indices. Both of these indices included atopy (ie, the presence of atopic eczema, allergic rhinoconjunctivitis, or allergic bronchial asthma). Only atopic eczema is a suggestion for consideration in the MOAHLFA index.

[†]The reported percentages are based on the number of patients with site of affected area recorded (n = 831).

reaction or, when the result was relevant, as a macular erythema reaction.

Allocation of cosmetic allergens

For this study, cosmetic allergens were allocated into one of several subgroups (on the basis of each allergen's inherent properties, function, and use): preservatives, fragrances/botanicals, vehicles, sunscreens, acrylates, medicaments, hairdresser allergens, and miscellaneous (ie, allergens that could not be definitively categorized into one of the other groups). Sunscreens and topical medicaments (which are not considered cosmetic by the US Food and Drug Administration [FDA])¹¹ were included in our analysis.

Statistical analysis

Patient data were entered into a clinical database. The clinical server was written in Uniface (Compuware Corp, Detroit, MI) and the database in Sybase (Sybase, Inc, Dublin, CA). All statistical analyses were performed with the use of SAS software (SAS Institute, Inc, Cary, NC).

Positive reaction rates between selected personal care product groups (preservatives, fragrances/botanicals, vehicles, and sunscreens) were calculated (ie, patients with a result positive to at least one allergen in a particular group who also had a result positive to at least one allergen in another group), and 95% confidence intervals were determined. Comparisons were also made between patients who reacted to any of the Mayo Clinic skin care product allergens and those who reacted to skin care product allergens in (1) the Mayo Clinic standard

series; (2) the NACDG standard series of allergens reported for 2001 and 2002¹²; and (3) the newer, 3-panel TRUE test.

RESULTS

The mean age of the 945 patients who underwent patch testing was 53.4 years (range, 6-91 years; 25th and 75th percentiles, 42.2 and 66.2 years). Most patients were female (87.2%). Other characteristics are listed in Table I. Among all patients, 68.4% had at least one positive reaction and 47.3% had at least two positive reactions. Nearly one third of patients (30.8%) had reactions to 3 or more allergens that could be found in personal care products.

Table II lists the reaction rates for 120 allergens that could be found in personal care products tested in at least 100 patients (range, 107-945 patients) at Mayo Clinic over the 8-year period. The mean number of allergens tested per patient was 102 (range, 59-122 allergens). This large number reflects the constant evolution of the standard series and the supplemental cosmetic series at Mayo Clinic. Reaction rates for 10 individual allergens tested to fewer than 100 patients are listed in Table III.

Preservative allergy was the most common skin care product allergy, with 467 patients (49.4%) reacting to at least one preservative. Fragrances/botanicals were the second most common allergens to cause a reaction; 295 patients (31.2%) had a reaction positive for at least one allergen in this group. Also frequently seen were reactions to at least one vehicle (19.0%) or sunscreen (10.3%).

Table IV lists the percentage of patients who would have had a full category of personal care product allergens missed (ie, preservatives, fragrances/botanicals, vehicles, or sunscreens) if only the skin care product allergens contained in either the Mayo standard series, the NACDG standard series, or the TRUE test had been evaluated. For example, 169 patients (17.9%) had no reaction to all preservatives contained in the NACDG standard series but had a reaction positive for at least one preservative tested at Mayo Clinic that was not present in the NACDG standard series. Similarly, 163 patients (17.3%) had no reaction to all vehicles in the NACDG standard series but reacted to at least one vehicle tested at Mayo Clinic that was not contained in the NACDG series.

DISCUSSION

We present our data on patch testing of 945 patients to a supplemental cosmetic screening series at Mayo Clinic over an 8-year period. The positive reaction rate of our patients (68.4%) was similar to the rates for the Mayo standard series previously

Table II. Positive reaction rates of testing to skin care product allergens* tested on more than 100 patients

Allergen	No. of patients tested	Positive reaction rate, %	Strength of positive reaction, No. (%) [†]				Relevant, No. (%) [‡]	Group [§]
			M	W	S	E		
Thimerosal 0.1%	942	13.6	23 (2.4)	56 (5.9)	34 (3.6)	16 (1.7)	114 (89.1)	P
Balsam of Peru 25%	936	12.4	58 (6.2)	47 (5.0)	10 (1.1)	1 (0.1)	110 (94.8)	F
Fragrance mix 8%	940	11.3	32 (3.4)	54 (5.7)	19 (2.0)	1 (0.1)	103 (97.2)	F
Benzalkonium chloride 0.1% aq	928	10.7	44 (4.7)	50 (5.4)	5 (0.5)	0 (0.0)	91 (91.9)	P
Dodecyl gallate 0.25%	937	9.2	50 (5.3)	33 (3.5)	4 (0.4)	0 (0.0)	78 (90.7)	P
Oleamidopropyl dimethylamine 0.1% aq	941	7.9	29 (3.1)	40 (4.3)	4 (0.4)	0 (0.0)	73 (98.6)	V
Quaternium 15.1%	942	7.5	10 (1.1)	39 (4.1)	18 (1.9)	4 (0.4)	68 (95.8)	P
<i>p</i> -Phenylenediamine 1%	940	7.3	16 (1.7)	32 (3.4)	14 (1.5)	7 (0.7)	63 (91.3)	H
2-Hydroxy-4-methoxybenzophenone-5-sulfonic acid 10%	864	6.6	32 (3.7)	25 (2.9)	0 (0.0)	0 (0.0)	56 (98.2)	S
Benzoic acid 5%	864	6.1	25 (2.9)	24 (2.8)	1 (0.1)	3 (0.3)	50 (94.3)	P
Methyldibromo glutaronitrile/phenoxylethanol 1.5%	938	5.7	18 (1.9)	34 (3.6)	1 (0.1)	0 (0.0)	52 (98.1)	P
Fragrance mix II	192	5.2	6 (3.1)	5 (2.6)	0 (0.0)	0 (0.0)	10 (100.0)	F
Propolis 10%	500	5.2	17 (3.4)	8 (1.6)	1 (0.2)	0 (0.0)	26 (100.0)	F
Hexahydro-1,3,5-tris(2-hydroxyethyl)triazine 1%	932	4.6	15 (1.6)	24 (2.6)	3 (0.3)	1 (0.1)	43 (100.0)	P
MCI/MI 100 ppm aq	935	4.3	7 (0.7)	23 (2.5)	6 (0.6)	4 (0.4)	38 (95.0)	P
Natural fragrance mix 2%	757	4.2	21 (2.8)	6 (0.8)	5 (0.7)	0 (0.0)	32 (100.0)	F
Ethylenediamine dihydrochloride 1%	944	3.7	7 (0.7)	14 (1.5)	9 (1.0)	5 (0.5)	33 (94.3)	P
Cocamidopropyl betaine 1% aq	935	3.4	15 (1.6)	15 (1.6)	2 (0.2)	0 (0.0)	32 (100.0)	Mi
Phenylmercuric acetate 0.01% aq	870	3.3	14 (1.6)	15 (1.7)	0 (0.0)	0 (0.0)	27 (93.1)	P
Diazolidinyl urea 1%	942	3.1	11 (1.2)	12 (1.3)	6 (0.6)	0 (0.0)	26 (89.7)	P
Sodium benzoate 5%	868	3.1	16 (1.8)	11 (1.3)	0 (0.0)	0 (0.0)	25 (92.6)	P
Hexylresorcinol (0.25%)	935	3.0	10 (1.1)	18 (1.9)	0 (0.0)	0 (0.0)	23 (82.1)	P
4-Aminobenzoic acid 5%	107	2.8	2 (1.9)	1 (0.9)	0 (0.0)	0 (0.0)	3 (100.0)	S
Glyceryl thioglycolate 1%	942	2.8	8 (0.8)	14 (1.5)	3 (0.3)	1 (0.1)	23 (88.5)	H
Lanolin alcohol (Amerchol L101) 50%	935	2.8	17 (1.8)	6 (0.6)	3 (0.3)	0 (0.0)	25 (96.2)	V
Amidoamine 0.1% aq	412	2.7	8 (1.9)	1 (0.2)	2 (0.5)	0 (0.0)	11 (100.0)	Mi
Benzocaine 5%	694	2.6	4 (0.6)	11 (1.6)	2 (0.3)	1 (0.1)	15 (83.3)	M
Colophony 20%	942	2.5	7 (0.7)	9 (1.0)	7 (0.7)	1 (0.1)	22 (91.7)	F
<i>tert</i> -Butylhydroquinone 1%	937	2.3	12 (1.3)	9 (1.0)	0 (0.0)	1 (0.1)	21 (95.5)	V
Imidazolidinyl urea 2%	941	2.3	6 (0.6)	12 (1.3)	4 (0.4)	1 (0.1)	22 (100.0)	P
Lyril 5%	354	2.3	2 (0.6)	4 (1.1)	2 (0.6)	0 (0.0)	8 (100.0)	F
Abitol (hydroabietyl alcohol) 10%	943	2.2	9 (1.0)	8 (0.8)	4 (0.4)	0 (0.0)	18 (85.7)	F
Clove oil 2%	326	2.1	4 (1.2)	3 (0.9)	0 (0.0)	0 (0.0)	7 (100.0)	F
Coconut diethanolamide (cocamide DEA) 0.5%	939	2.1	11 (1.2)	7 (0.7)	2 (0.2)	0 (0.0)	16 (80.0)	V
Hexamethylenetetramine (methenamine) 2%	870	2.1	5 (0.6)	11 (1.3)	0 (0.0)	2 (0.2)	18 (100.0)	P
Tea tree oil 5%	869	2.1	3 (0.3)	9 (1.0)	5 (0.6)	1 (0.1)	18 (100.0)	F
Diazolidinyl urea 1% aq	940	2.0	5 (0.5)	8 (0.9)	6 (0.6)	0 (0.0)	19 (100.0)	P
Sandalwood oil 2%	870	2.0	8 (0.9)	7 (0.8)	2 (0.2)	0 (0.0)	14 (82.4)	F
Cinnamic aldehyde 1%	943	1.8	6 (0.6)	9 (1.0)	2 (0.2)	0 (0.0)	17 (100.0)	F
DMDM hydantoin 2% in aq	327	1.8	3 (0.9)	3 (0.9)	0 (0.0)	0 (0.0)	6 (100.0)	P
Imidazolidinyl urea 2% aq	943	1.8	4 (0.4)	11 (1.2)	2 (0.2)	0 (0.0)	17 (100.0)	P
Wool alcohols (lanolin alcohol) 30%	942	1.8	8 (0.8)	7 (0.7)	1 (0.1)	1 (0.1)	16 (94.1)	V
2-Hydroxy-4-methoxybenzophenone 10%	867	1.7	6 (0.7)	8 (0.9)	1 (0.1)	0 (0.0)	15 (100.0)	S
Methyl methacrylate 2%	943	1.7	2 (0.2)	10 (1.1)	4 (0.4)	0 (0.0)	16 (100.0)	A
Ascorbic acid (vitamin C) 5%	869	1.6	7 (0.8)	7 (0.8)	0 (0.0)	0 (0.0)	12 (85.7)	P
Lavender absolute 2%	870	1.6	5 (0.6)	8 (0.9)	1 (0.1)	0 (0.0)	14 (100.0)	F

Continued

Table II. Cont'd

Allergen	No. of patients tested	Positive reaction rate, %	Strength of positive reaction, No. (%) [†]				Relevant, No. (%) [‡]	Group [§]
			M	W	S	E		
Rose oil, Bulgarian 2%	679	1.6	6 (0.9)	5 (0.7)	0 (0.0)	0 (0.0)	11 (100.0)	F
Dimethylol dihydroxyethylene urea 4.5% aq	327	1.5	2 (0.6)	3 (0.9)	0 (0.0)	0 (0.0)	5 (100.0)	P
DMDM hydantoin 1%	937	1.5	2 (0.2)	11 (1.2)	1 (0.1)	0 (0.0)	14 (100.0)	P
Jasmine absolute, Egyptian 2%	869	1.4	6 (0.7)	6 (0.7)	0 (0.0)	0 (0.0)	11 (91.7)	F
Menthol 2%	870	1.4	6 (0.7)	6 (0.7)	0 (0.0)	0 (0.0)	12 (100.0)	F
Lemon grass oil 2%	868	1.3	5 (0.6)	3 (0.3)	2 (0.2)	1 (0.1)	11 (100.0)	F
(±)- α -Tocopherol 100% (vitamin E)	318	1.3	2 (0.6)	3 (0.9)	0 (0.0)	0 (0.0)	3 (75.0)	M
Bergamot—natural 2%	500	1.2	2 (0.4)	4 (0.8)	0 (0.0)	0 (0.0)	6 (100.0)	F
Ethyl acylate 0.1%	941	1.2	3 (0.3)	2 (0.2)	5 (0.5)	1 (0.1)	10 (90.9)	A
Geranium oil, bourbon 2%	486	1.2	1 (0.2)	4 (0.8)	1 (0.2)	0 (0.0)	6 (100.0)	F
2-Hydroxy-4-methoxybenzophenone 3%	944	1.2	8 (0.8)	3 (0.3)	0 (0.0)	0 (0.0)	11 (100.0)	S
Lichen mix 0.3%	500	1.2	1 (0.2)	2 (0.4)	2 (0.4)	1 (0.2)	6 (100.0)	F
Sesquiterpene lactone mix 0.1%	943	1.2	3 (0.3)	4 (0.4)	3 (0.3)	1 (0.1)	10 (90.9)	F
Spearmint oil 2%	500	1.2	3 (0.6)	3 (0.6)	0 (0.0)	0 (0.0)	6 (100.0)	F
Ethyl cyanoacrylate 10%	871	1.1	3 (0.3)	6 (0.7)	2 (0.2)	0 (0.0)	8 (80.0)	A
Lyril 2%	444	1.1	1 (0.2)	4 (0.9)	0 (0.0)	0 (0.0)	5 (100.0)	F
Cananga oil 2%	486	1.0	2 (0.4)	2 (0.4)	1 (0.2)	0 (0.0)	5 (100.0)	F
4-Chloro-3-cresol (PCMC) 1%	943	1.0	6 (0.6)	2 (0.2)	1 (0.1)	0 (0.0)	9 (100.0)	P
Chlorhexidine digluconate 0.5% aq	944	1.0	5 (0.5)	4 (0.4)	0 (0.0)	0 (0.0)	9 (100.0)	P
Paraben mix 16%	941	1.0	5 (0.5)	4 (0.4)	0 (0.0)	0 (0.0)	9 (100.0)	P
Peppermint oil 2%	500	1.0	4 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	5 (100.0)	F
Phenyl salicylate 1%	866	1.0	7 (0.8)	1 (0.1)	1 (0.1)	0 (0.0)	9 (100.0)	S
Propylene glycol 10%	944	1.0	4 (0.4)	4 (0.4)	1 (0.1)	0 (0.0)	8 (88.9)	V
Lemon oil 2%	345	0.9	2 (0.6)	1 (0.3)	0 (0.0)	0 (0.0)	3 (100.0)	F
Narcissus absolute 2%	863	0.9	6 (0.7)	1 (0.1)	1 (0.1)	0 (0.0)	8 (100.0)	F
Sodium-2-pyridinethiol-1-oxide 0.1 aq	939	0.9	4 (0.4)	3 (0.3)	1 (0.1)	0 (0.0)	8 (100.0)	P
Sorbic acid 2%	871	0.9	2 (0.2)	5 (0.6)	1 (0.1)	0 (0.0)	8 (100.0)	P
Sorbitan sesquileate 20%	870	0.9	6 (0.7)	2 (0.2)	1 (0.1)	0 (0.0)	6 (75.0)	V
Titanium dioxide 1%	921	0.9	2 (0.2)	4 (0.4)	2 (0.2)	0 (0.0)	7 (87.5)	S
Ylang-ylang oil 2%	870	0.9	3 (0.3)	3 (0.3)	2 (0.2)	0 (0.0)	8 (100.0)	F
Bergamot—synthetic 2%	500	0.8	1 (0.2)	3 (0.6)	0 (0.0)	0 (0.0)	4 (100.0)	F
2-Ethylhexyl-4-methoxycinnamate 10%	870	0.8	4 (0.5)	3 (0.3)	0 (0.0)	0 (0.0)	7 (100.0)	S
Vanillin 10%	871	0.8	3 (0.3)	4 (0.5)	0 (0.0)	0 (0.0)	7 (100.0)	F
Almond oil 2%	864	0.7	5 (0.6)	1 (0.1)	0 (0.0)	0 (0.0)	6 (100.0)	F
Benzyl salicylate 2%	870	0.7	2 (0.2)	4 (0.5)	0 (0.0)	0 (0.0)	6 (100.0)	V
Chloroxylenol (PCMX) 1%	944	0.7	1 (0.1)	3 (0.3)	2 (0.2)	1 (0.1)	7 (100.0)	P
Compositae mix 5%	303	0.7	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)	2 (100.0)	F
Iodopropynyl butylcarbamate 0.1%	871	0.7	2 (0.2)	4 (0.5)	0 (0.0)	0 (0.0)	6 (100.0)	P
Lidocaine 5%	555	0.7	0 (0.0)	3 (0.5)	1 (0.2)	0 (0.0)	4 (100.0)	M
3-(4-Methylbenzyliden)-camphor 10%	922	0.7	3 (0.3)	3 (0.3)	0 (0.0)	0 (0.0)	6 (100.0)	S
Polyethylene glycol (PEG 400) 100%	870	0.7	1 (0.1)	5 (0.6)	0 (0.0)	0 (0.0)	6 (100.0)	V
Propyl gallate 1%	943	0.7	1 (0.1)	4 (0.4)	1 (0.1)	1 (0.1)	7 (100.0)	P
Sorbitan monooleate (Span 80) 5%	945	0.7	3 (0.3)	3 (0.3)	1 (0.1)	0 (0.0)	6 (85.7)	V
<i>Achillea millefolium</i> (yarrow) 1%	174	0.6	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (100.0)	F
Anethole 5%	322	0.6	0 (0.0)	2 (0.6)	0 (0.0)	0 (0.0)	2 (100.0)	F
2- <i>tert</i> -Butyl-4-methoxyphenol (BHA) 2%	944	0.6	2 (0.2)	5 (0.5)	0 (0.0)	0 (0.0)	5 (83.3)	P
Clioquinol 5%	945	0.6	1 (0.1)	4 (0.4)	1 (0.1)	0 (0.0)	6 (100.0)	P
Eucalyptus oil 2%	679	0.6	2 (0.3)	2 (0.3)	0 (0.0)	0 (0.0)	4 (100.0)	F
Jasmine synthetic 2%	871	0.6	2 (0.2)	4 (0.5)	0 (0.0)	0 (0.0)	5 (100.0)	F
Orange oil 2%	678	0.6	1 (0.1)	3 (0.4)	0 (0.0)	0 (0.0)	4 (100.0)	F

Continued

Table II. Cont'd

Allergen	No. of patients tested	Positive reaction rate, %	Strength of positive reaction, No. (%) [†]				Relevant, No. (%) [‡]	Group [§]
			M	W	S	E		
Stearyl alcohol 30%	944	0.6	2 (0.2)	4 (0.4)	0 (0.0)	0 (0.0)	6 (100.0)	V
<i>Taraxacum officinale</i> (dandelion) 2.5%	326	0.6	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)	1 (50.0)	F
Triclosan 2%	938	0.6	4 (0.4)	1 (0.1)	1 (0.1)	0 (0.0)	6 (100.0)	P
Tricresyl phosphate 5%	944	0.6	1 (0.1)	3 (0.3)	2 (0.2)	0 (0.0)	5 (83.3)	V
Triethanolamine 2%	944	0.6	2 (0.2)	4 (0.4)	0 (0.0)	0 (0.0)	6 (100.0)	V
Dibutyl phthalate 5%	944	0.5	2 (0.2)	3 (0.3)	0 (0.0)	0 (0.0)	4 (80.0)	V
Hydrogenated castor oil 5%	870	0.5	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)	4 (100.0)	V
Polyoxyethylene sorbitan monooleate 5%	870	0.5	3 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	4 (100.0)	V
4-Aminobenzoic acid 10%	835	0.4	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	3 (100.0)	S
Amylcinnamaldehyde 2%	254	0.4	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	F
<i>Arnica montana</i> (mountain tobacco) 0.5%	544	0.4	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (100.0)	F
Chlorquinaldol 5%	940	0.4	0 (0.0)	4 (0.4)	0 (0.0)	0 (0.0)	4 (100.0)	P
2,6-Di- <i>tert</i> -butyl-4-cresol (BHT) 2%	934	0.4	3 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	4 (100.0)	P
Diocetyl phthalate 2%	942	0.4	3 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	4 (100.0)	V
Isopropyl myristate 20%	944	0.4	2 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)	4 (100.0)	V
Benzyl alcohol 1%	869	0.3	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	2 (66.7)	F
4- <i>tert</i> -Butyl-4-methoxydibenzoylmethane 10%	869	0.3	2 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	3 (100.0)	S
2-Ethylhexyl-4-dimethylaminobenzoate 5%	870	0.3	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	3 (100.0)	S
Musk mix 3%	870	0.3	1 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	3 (100.0)	F
Neroli oil 2%	324	0.3	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)	1 (100.0)	F
<i>Chamomilla romana</i> (<i>Anthemis nobilis</i>) 1%	545	0.2	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (100.0)	F
2-Chloroacetamide 0.2%	871	0.2	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	2 (100.0)	P
2-Phenylphenol 1%	871	0.2	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	2 (100.0)	P
Cetyl alcohol 5%	945	0.1	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	V

alc, Alcohol; aq, aqueous; DMDM hydantoin, 1,3 dimethylol-5,5'-dimethylhydantoin; MCI/MI, methylchloroisothiazolinone/methylisothiazolinone.

*Includes allergens from both the standard and the supplement cosmetic series.

[†]Based on positive reactions only (E, extreme; M, macular erythema; S, strong; W, weak).

[‡]Based on positive reactions only.

[§]For "Group," A, acrylate; F, fragrance/botanical; H, hairdresser; P, preservative; M, medicament; Mi, miscellaneous; S, sunscreen; V, vehicle.

reported (69.3% and 69.1%, respectively)^{2,9} and to those of the NACDG for 2003 and 2004 (66.7%).¹³ The results of our study are difficult to compare with those of other studies because of the varying use of the term "cosmetic". Some studies use the FDA definition (excluding sunscreens).¹¹ Also, many studies do not define the term and it could simply mean make-up.¹⁴ We also did not collect data verifying that a cosmetic and personal care product was the source of the allergen. Many allergens in a supplemental cosmetic series can also be found in sources other than personal care products, such as metalworking fluids.

Previous studies have consistently shown fragrances and preservatives to be the two most common causes of cosmetic allergic contact dermatitis,⁶ with most of the studies citing fragrances as the most

common cosmetic culprit.^{6,14-17} Specifically, studies have found positive reactions to fragrances in 42% to 54% of patch-tested patients with suspected cosmetic allergic contact dermatitis,⁶ with preservative allergy occurring in 31.6%¹⁴ to 39.3%¹⁶ of patients. Our study showed similar findings, although more patients had a reaction to at least one preservative (49.4%) than had a reaction to fragrances/botanicals (31.2%).

The higher reaction rate to preservatives observed in the present study than in others may reflect at least partially the broad panel of preservatives to which patients at Mayo Clinic are tested: 169 patients (17.9%) had no reaction to all preservatives contained in the NACDG standard series but had a reaction positive to at least one preservative tested at Mayo Clinic and not present in the NACDG standard

Table III. Positive reaction rates of testing to skin care product allergens (<100 tested)*

Allergen	No. of patients tested	Positive reaction rate, %	Strength of positive reaction, No. (%) [†]				Relevant, No. (%) [‡]	Group [§]
			M	W	S	E		
Octyl gallate 0.25%	75	16.0	11 (14.7)	1 (1.3)	0 (0.0)	0 (0.0)	11 (91.7)	P
Dimethylaminopropylamine 1% aq	68	7.4	1 (1.5)	4 (5.9)	0 (0.0)	0 (0.0)	5 (100.0)	V
Musk ambrette 1% alc	76	3.9	3 (3.9)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)	F
2-Bromo-2-nitropropane-1,3-diol 0.5%	72	2.8	0 (0.0)	2 (2.8)	0 (0.0)	0 (0.0)	2 (100.0)	P
4- <i>tert</i> -Butyl-4-methoxydibenzoylmethane 5%	67	1.5	1 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	S
2-Ethylhexyl-4-dimethylaminobenzoate 2%	76	1.3	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	S
Aloe vera 10%	72	0.0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	F
4- <i>tert</i> -Butyl-4-methoxydibenzoylmethane 2%	9	0.0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	S
2-Ethylhexyl-4-methoxycinnamate 7.5%	52	0.0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	S
3-(4-Methylbenzyliden)-camphor 2%	10	0.0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	S

alc, Alcohol; aq, aqueous.

*Includes allergens from both the standard and the supplemental cosmetic series.

[†]Based on positive reactions only (E, extreme; M, macular erythema; S, strong; W, weak).

[‡]Based on positive reactions only.

[§]For "Group," F, fragrance/botanical; P, preservative; S, sunscreen; V, vehicle.

Table IV. Comparison of reaction rates to selected Mayo Clinic skin care product allergens* with various standard screening series[†]

Skin care product allergen group	Patients, No. (%) (N = 45)		
	With reactions negative to Mayo Clinic standard series but positive to at least one supplemental cosmetic series allergen [‡]	With reactions negative to NACDG standard series but positive to at least one supplemental cosmetic series allergen [§]	With reactions negative to TRUE test but positive to at least one supplemental cosmetic series allergen
Preservatives	69 (7.3)	169 (17.9)	212 (22.5)
Fragrances/botanicals	79 (8.4)	95 (10.1)	107 (11.3)
Vehicles	120 (12.7)	163 (17.3)	163 (17.3)
Sunscreens	86 (9.1)	86 (9.1)	NA [¶]

NA, Not applicable; NACDG, North American Contact Dermatitis Group; TRUE, thin-layer rapid use epicutaneous.

*Cosmetic allergens in the standard series and supplemental cosmetic series at Mayo Clinic. These allergens can be found in sources other than personal care products.

[†]Standard screening series of Mayo Clinic, NACDG, and TRUE test.

[‡]Skin care product allergens not found in the Mayo Clinic standard series.

[§]Skin care product allergens tested at Mayo Clinic (in either the standard series or supplemental cosmetic series) that were not present in the NACDG standard series.

^{||}Skin care product allergens tested at Mayo Clinic (in either the standard series or the supplemental cosmetic series) that were not present in the TRUE test.

[¶]TRUE test contained no allergen present in the sunscreens cosmetic subgroup; thus no comparison could be made.

series. Regional differences in demographic characteristics, occupations, and variations in referral patterns to Mayo Clinic compared with other tertiary care centers may, in part, also be responsible.^{2,9,18}

It is well documented that larger screening series more accurately identify allergens that caused a positive reaction and were relevant in patients who have suspected allergic contact dermatitis.²⁻⁵ Recent medical literature suggests that the addition of

supplemental allergens to large standard series (such as those used by the NACDG) may enhance the diagnostic accuracy of patch testing in 34% of patients.³ In a series of 794 patients who received patch testing to the NACDG standard series with or without additional supplemental allergens, 25% of patients reacted to at least one NACDG standard allergen and one supplemental allergen, whereas 9% of patients reacted to supplemental allergens

exclusively.³ Rietschel¹⁹ reviewed patient experiences with 12 supplemental series of allergens used from 1990 to 1998 and found that although 129 tests showed positive reactions in 177 patients tested to the supplemental cosmetic series, more than half of these reactions were thought to be either “worthless or redundant.” Thus, the overall utility of the cosmetic series was believed to be questionable. However, Rietschel noted that the addition of selected cosmetic allergens, including imidazolidinyl urea, diazolidinyl urea, DMDM hydantoin, and cocamidopropyl betaine, increased the diagnostic yield for cosmetic allergic contact dermatitis over the yield of a screening series such as the TRUE test.

In contrast, a Swedish study of 1075 patch-tested patients identified 25 persons who did not react to the standard series with the addition of 12 supplemental allergens related to cosmetic and skin care products.²⁰ Similarly, a study of 244 patch-tested patients in Israel found that nearly one third of patients (32.8%) reacted to at least one allergen in the cosmetic series and thus recommended supplemental testing to a cosmetic series (in addition to the standard series) in all patients with suspected cosmetic contact dermatitis.²¹

In keeping with recent findings by Cohen, Rao, and Brancaccio,³ our data illustrate the value of patch testing to a supplemental cosmetic series. Table IV enumerates the striking percentage of patients who would have had a full category of personal care product allergens missed (ie, preservatives, fragrances/botanicals, vehicles, or sunscreens) if only a standard series of allergens (Mayo Clinic, NACDG, or TRUE test) had been used. Use of solely the TRUE test in our series of 945 patients would have overlooked 22.5% of patients with preservative allergy, 11.3% with fragrance/botanical allergy, and 17.3% with vehicle allergy.

Newly reported retrospective, cross-sectional data of the NACDG from 2001 to 2004 provide additional support for patch testing to a supplemental cosmetic series.¹¹ Although 21.8% of patients referred to the NACDG for patch testing had at least one allergic reaction associated with a cosmetic source, 16.3% of patients with cosmetic allergy reacted only to a non-NACDG standard allergen (defined as personal products or commercially prepared allergens), “underscoring the need to test with additional antigens beyond standard screening series,” reported Warshaw et al.¹¹ It should be emphasized that the new NACDG data focus on cosmetic allergen sources present in its standard screening series and do not provide information on the specific non-NACDG standard allergens to which cosmetic-allergic patients reacted. In contrast, our study analyzed rates of

positive reaction to cosmetic allergens present in the Mayo Clinic standard screening series and the supplemental cosmetic series, providing a quantitative assessment of how many patients with skin care product allergy would have been missed with use of only a standard screening series of allergens.

Previous reports have compared the Mayo Clinic standard series to the NACDG standard series.^{2,9} The Mayo Clinic standard series contains 75 allergens; the NACDG standard series is composed of 65 allergens.¹³ The two series are similar, with some variance in a few of the allergens included, although the Mayo Clinic standard series has a few additional personal care product allergens, a fact that possibly explains why more patients who have skin care product ingredient allergy would have been missed with the NACDG standard series than with the Mayo Clinic standard series. In addition, Mayo Clinic includes relevant macular erythema reactions in the calculation of allergic patch-test reaction rates, given that they commonly occur and may be of clinical relevance, as previously reported.²² Of note, a number of reactions to skin care product allergens also would have been missed with the use of the Mayo Clinic standard series alone: compared with the Mayo Clinic standard series and supplemental cosmetic series, use of the Mayo Clinic standard series alone would have missed 7.3% of patients with preservative allergy, 8.4% with fragrance/botanical allergy, 12.7% with vehicle allergy, and 9.1% with sunscreen allergy.

On the basis of this study, which additional allergens beyond those in the TRUE test should be considered for patch testing of a patient with suspected allergic contact dermatitis to personal care products? In general, allergens that commonly cause reactions should be included, as well as allergens that are commonly encountered. It is also important to include allergens that are used with increasing frequency in personal care products. We found several allergens with a positive reaction rate above 5.0% that are not included in the 3-panel TRUE test. On the basis of the present analysis, as well as newly reported NACDG data regarding the 20 most common screening allergens associated with a cosmetic source,¹¹ we have enumerated 16 additional allergens beyond those in the TRUE test that may increase diagnostic yield in the evaluation of a patient with suspected allergic contact dermatitis to personal care products (Table V).

In the present study, the supplemental cosmetic series was chosen whenever the physician deciding on patch testing suspected that a “cosmetic” product was a potential factor in a patient’s dermatitis. There were no set criteria for testing with the supplemental

Table V. Additional allergens beyond those in the TRUE test that could be considered for patch testing of a patient with suspected allergic contact dermatitis

Amidoamine
Benzalkonium chloride
Benzoic acid
Cinnamic aldehyde
Cocamidopropyl betaine
DMDM hydantoin
Dodecyl gallate
2-Hydroxy-4-methoxybenzophenone-5-sulfonic acid
Jasmine absolute
Methyldibromo glutaronitrile/phenoxyethanol
Oleamidopropyl dimethylamine
Propolis
Propylene glycol
α -Tocopherol (vitamin E)
Triclosan
Ylang-ylang oil

DMDM hydantoin, 1,3-Dimethylol-5,5'-dimethylhydantoin; *TRUE*, thin-layer rapid use epicutaneous.

series; the decision depended on the ordering physician and was based in part on a thorough history, occupational factors, and the distribution of dermatitis on cutaneous examination.

Limitations of our study include the varying number of personal care product allergens to which patients were tested during the study's 8 years. However, this variation reflects the dynamic nature of patch testing because new allergens were added and other allergens were deleted as experience with the cosmetic series evolved.² Furthermore, the patients tested at Mayo Clinic (Rochester, MN; Jacksonville, FL; and Scottsdale, AZ) may have differing characteristics than those seen at other patch-test centers and thus perhaps precluded our findings from generalizability to other centers in the United States and abroad.

Information on the source of allergens for patients with relevant reactions, as well as data on how many patients were tested to and reacted to their own personal products, was not available in our study, and its unavailability is an additional limitation. Given that some of the personal care product allergens analyzed in our study can also be found in non-skin care products (such as cutting oils and industrial sources), the source of potentially relevant allergens could not always be confirmed to be a personal care product, which is a study limitation. At Mayo Clinic, interpretation of patch-test results is performed by the ordering physician (regardless of whether he or she has a special interest in patch testing), and this source of interpretation is a possible limitation. The

specific types of relevance denoted in the present study differ from those used by the NACDG (which categorizes relevance as definite, probable, possible, past, and unknown).¹¹ The high relevancy rates of individual allergens in our study reflect that scores for current, questionable, and past relevance were combined, another limitation of the study.

Thus our study should be interpreted with caution, given the high rate of macular erythema and weak reactions, the combined relevancy rates reported, and the inability to always confirm that the source of potentially relevant allergens was a personal care product. The results presented herein are challenging to compare with those of other studies because of the wide variation among published studies as to what constitutes a "cosmetic" product. The high rate of macular erythema and weak reactions suggests that these results could be nonreproducible, especially for such well-known irritants as benzalkonium chloride, gallates, and oleamidopropyl dimethylamine. (A reaction that increases, rather than decreases, in intensity between the initial and the final patch test readings is more likely to be allergic and can be a helpful sign in excluding an irritant patch-test reaction.) Despite these shortcomings, our study offers striking quantitative data showing the importance and utility of a supplemental cosmetic patch-test series and provides additional allergens beyond those in standard screening series, such as the TRUE test, that may greatly benefit general dermatologists in their evaluation of patients with suspected allergic contact dermatitis to personal care products.

In summary, our results on patch testing to personal care product allergens in 945 patients at Mayo Clinic during these recent 8 years corroborate previous reports highlighting the increased prevalence of allergy to preservatives and fragrances/botanicals among patients with cosmetic-induced allergic contact dermatitis. More importantly, our findings illuminate both the substantial number of patients with skin care product allergy who would be overlooked with use of a standard screening series and the ability of supplemental cosmetic series to augment the evaluation of patients with suspected allergic contact dermatitis due to cosmetics.

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