

REPORT

Allergic patch test reactions associated with cosmetics: Retrospective analysis of cross-sectional data from the North American Contact Dermatitis Group, 2001-2004

Erin M. Warshaw, MD, MS,^a Heather J. Buchholz, MD,^a Donald V. Belsito, MD,^b Howard I. Maibach, MD,^c Joseph F. Fowler, Jr, MD,^d Robert L. Rietschel, MD,^e Kathryn A. Zug, MD,^f C. G. Toby Mathias, MD,^g Melanie D. Pratt, MD,ⁱ Denis Sasseville, MD,^j Frances J. Storrs, MD,^k James S. Taylor, MD,^h Vincent A. DeLeo, MD,^l and James G. Marks, Jr, MD^m

Minneapolis, Minnesota; Shawnee, Kansas; San Francisco, California; Louisville, Kentucky; Tucson, Arizona; Lebanon, New Hampshire; Cincinnati and Cleveland, Ohio; Ottawa, Ontario, Canada; Montreal, Quebec, Canada; Portland, Oregon; New York, New York; and Hershey, Pennsylvania

Background: Allergy to cosmetics is common.

Objectives: We sought to characterize patients with positive patch test reactions associated with a cosmetic source, to identify common allergens; and to explore gender and occupational associations.

Methods: We performed a retrospective, cross-sectional analysis.

Results: Of 6621 female and 3440 male patients, 1582 female (23.8%) and 611 of male (17.8%) patients had at least one allergic patch test reaction associated with a cosmetic source. Of "allergic" patients (>1 allergic reaction, $n = 6815$), females were 1.21 times more likely to have an allergic reaction associated with a cosmetic source than were male patients ($p < .0001$, 95% confidence interval [CI] 1.12-1.31). Within the "cosmetic allergic" group ($n = 2243$), head and neck involvement was significantly higher in female than in male patients (49.3% vs 23.7%, $p < .0001$). One hundred twenty-five patients had occupationally related allergic reactions associated with a cosmetic.

From the Department of Dermatology, University of Minnesota, Veterans Affairs Medical Center, Minneapolis^a; American Dermatology Associates, LLC, Shawnee^b; Department of Dermatology, University of California, San Francisco^c; University of Louisville^d; Section of Dermatology, University of Arizona VA Health Care System, Tucson^e; Division of Dermatology, Dartmouth-Hitchcock Medical Center, Lebanon^f; Departments of Dermatology, University of Cincinnati^g and Cleveland Clinic^h; Divisions of Dermatology, University of Ottawa, ONⁱ and Royal Victoria Hospital, McGill University, Montreal, QC^j; Department of Dermatology, Oregon Health Science University, Portland^k; Department of Dermatology, Columbia University, New York City^l; and Department of Dermatology, Pennsylvania State University, Hershey.^m

Supported by a Women's Dermatologic Society Academic Research Grant Program.

Conflicts of interest: Drs Zug, Fowler, Belsito, Maibach, Marks, Mathias, Storrs, and Buchholz declared no conflicts of interest. Dr Rietschel has been a speaker for Coria Labs. Dr Warshaw has been a consultant for Shire and Noven Pharmaceuticals. Drs Sasseville and Pratt have been consultants for Spexell Pharma. Dr. Pratt has also been an investigator for Coria and Dörmer/Chemotechnique. Dr Taylor has been a consultant for the National Institute for Occupational Safety and Health, Betco, Shire, Novartis Pharmaceuticals, Procter & Gamble, BASF, Regent Medical, AMA Press, Consumer Product Safety

Commission, and ConvaTec Inc. Dr Taylor has been a speaker for Medicis, Hermal Labs, Aula Medica, and Watson Laboratories, Inc. Dr Taylor has also been an investigator for Mekos Laboratories and Guidant Corp. The Cleveland Clinic Department of Dermatology has received grants from Amgen, Astellas Pharma, Bristol-Myers Squibb, Genentech, Pfizer, Procter & Gamble, and Centocor. Dr Taylor holds stock in GlaxoSmithKline, Amgen, Johnson & Johnson, Keithley Instruments, Medco Health Solutions, Inc, Merck, Wyeth, and Renovo. Dr Taylor has been on the advisory boards for UnitedHealthcare and Connetics Corporation. Dr DeLeo has been a consultant for La Roche-Posay, Johnson & Johnson, Pfizer, and Orfagen. He has also been on an advisory board for Schering-Plough.

Disclaimer: The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs.

Accepted for publication July 29, 2008.

Reprints not available from the authors.

Correspondence to: Erin M. Warshaw, MD, MS, Dermatology Department 111K, Veterans Affairs Medical Center, One Veterans Drive, Minneapolis, MN 55417. E-mail: erin.warshaw@med.va.gov.

Published online November 5, 2008.

0190-9622/\$34.00

© 2008 by the American Academy of Dermatology, Inc.

doi:10.1016/j.jaad.2008.07.056

Limitations: This study is limited by its cross-sectional, retrospective design.

Conclusion: Of all patients studied, 21.8% had an allergic reaction associated with a cosmetic. Site of dermatitis, cosmetic categories, and specific allergens differed somewhat by gender. (J Am Acad Dermatol 10.1016/j.jaad.2008.07.056.)

BACKGROUND

The US Food and Drug Administration (FDA) defines the term “cosmetic” as “articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and articles intended for use as a component of any such articles; except that such term shall not include [non-skin] soap.”¹ The 13 cosmetic categories defined by the FDA include baby products, bath preparations, eye makeup, fragrances, hair preparations, hair-coloring agents, makeup, manicure products, oral hygiene products, personal cleanliness products, shaving preparations, skin care preparations, and suntan preparations (excluding sunscreens or any combination product listing a sun protection factor; sunscreens are regulated as drugs, not cosmetics).²

Adverse reactions to cosmetics are not uncommon; one estimate indicated that, on average, an adverse reaction to a cosmetic occurs once every 13.3 years per person.³ Irritant reactions to cosmetics are likely more common than allergic reactions.⁴ Despite the widespread use of cosmetic products, the rates of allergic reactions to cosmetic ingredients are relatively low. Studies in Europe and the United States have found a prevalence of cosmetic allergy of less than 1% in the general population.⁵⁻⁹ However, the actual rate of adverse reactions to cosmetics is likely higher because most people do not seek medical care for mild allergic or irritant reactions; they simply discontinue the offending product.¹⁰ Of patients patch tested for suspected allergic contact dermatitis, rates of cosmetic allergy range from 2.4% to 36.3%, with most studies reporting prevalence rates between 4% and 9%.⁶⁻¹³ A recent review of allergic contact dermatitis to cosmetics found a weighted prevalence rate of 0.4% for the general population and 9.8% for patients referred for patch testing.¹⁴ Rates of cosmetic allergy vary with time and geographic location.¹⁵ Nielsen et al¹² patch tested patients in Denmark in 1990 and 1998 and reported that contact sensitization to cosmetic-related allergens had doubled. Not surprisingly, most patients with cosmetic sensitivity are 20 to 55 years of age⁶⁻⁹ and female.^{7,9,13,16}

Abbreviations used:

CAPB:	cocamidopropyl betaine
DMAPA:	dimethylaminopropylamine
FDA:	Food and Drug Administration
MCI:	methylchloroisothiazolinone
MDBGN:	methyldibromoglutaronitrile
MI:	methylisothiazolinone
NACDG:	North American Contact Dermatitis Group
NOS:	not otherwise specified
PE:	phenoxyethanol

The goals of this exploratory analysis were to (1) describe demographic characteristics of patients patch tested by the North American Contact Dermatitis Group (NACDG) with an allergic patch-test reaction associated with a cosmetic source, (2) determine frequencies of specific allergens associated with cosmetic sources, (3) describe occupational associations with cosmetic allergens, (4) estimate the prevalence of cosmetic allergy identified by non-NACDG standard screening allergens, and (5) explore gender associations.

METHODS

The Minneapolis VA Medical Center Human Studies Subcommittee provided institutional review board approval for this cross-sectional analysis of de-identified data from patients patch tested by the NACDG between 2001 and 2004. Methodology of the NACDG has been previously described.^{17,18} Briefly, during this time period, a “standard” screening group of 65 antigens was tested on all patients patch tested by members of the NACDG (including those suspected of contact allergy to products other than cosmetics). Fifty-nine antigens (supplied by Chemotechnique Diagnostics, Vellinge, Sweden) were tested during all 4 years, but 12 antigens were tested only in one of the 2-year cycles; details of specific allergens have been previously described.¹⁷ Collected data included: demographics (age, gender, and race), dermatitis site (up to 3 sites), occupation, and allergens (clinical relevance, source and relationship to occupation for each positive allergen), and final diagnoses (up to 3 diagnoses). Relevance and source codes were linked to specific allergens, while site codes and final diagnoses codes were

linked to patients, but not to specific allergens. Current relevance was defined as “*definite*” (positive use test or positive patch test reaction to the putative item containing the allergen), “*probable*” (the substance identified by patch testing was verified as present in the known skin contactants of the patient), or “*possible*” (patient was exposed to circumstances in which skin contact with materials known to contain the putative allergen were likely). Reactions of past relevance and unknown relevance were also tabulated. Occupationally relevant reactions were determined by clinical history and occupational exposure. Three-digit occupational codes were determined by a coding expert and based on a standardized questionnaire.¹⁹ In addition to information on the 65 standard screening NACDG allergens, currently relevant cosmetic allergen sources from non-NACDG standard screening allergens were also recorded, although the name of the responsible allergen was not. Additional testing (eg, prick testing for contact urticaria²⁰), if performed, was not collected as part of this database, nor were specific subtypes of allergic contact dermatitis (eg, systemic contact dermatitis²¹).

Three-digit source codes for NACDG standard screening allergens and nonstandard screening allergens have been utilized since 2001. Specific cosmetic codes included in this analysis are listed in Table I. The 3 main differences between the NACDG and FDA categories include (1) baby products (there are no NACDG codes specific to baby products), (2) shaving preparations (there are no NACDG codes specific to shaving products), and (3) suntan preparations (the NACDG codes for sunscreen but not sunless tanners). Because sunscreens can be considered either a “medicine” or a “cosmetic” by the FDA,² the NACDG code for sunscreen was excluded from this analysis.

For this analysis, the main population of interest included patients with at least one allergic reaction to an NACDG standard screening allergen with a cosmetic source (“cosmetic allergic”). For comparison, a second, separate category was defined for patients who had one or more allergic reaction(s) to an NACDG standard screening allergen(s) with a source other than cosmetic (“non-cosmetic allergic”). Patients with allergen sources to both cosmetics and non-cosmetics were included in the “cosmetic allergic” group. Individuals with no allergic reactions (“not allergic”) were excluded from comparison analyses. In addition, because of limited information on non-NACDG antigens, the 438 patients who only reacted to a nonstandard screening allergen associated with a cosmetic source were not included in comparison analyses, but are described separately.

Table I. North American Contact Dermatitis Group codes defined as “cosmetic” in this analysis

810 Hair care products
811 Shampoos
812 Permanent wave solutions
813 Hair dyes
814 Hair sprays and gels
820 Nail care products
821 Nail polish
822 Artificial nails
823 Nail adhesives
824 Nail strengtheners
830 Cosmetics, not otherwise specified
831 Moisturizers, lotions, creams
832 Makeup (including code 836: Lipsticks)
833 Perfumes and fragrances
835 Deodorants and antiperspirants
841 Liquid lotion and bar soaps, cleansers
870 Oral hygiene products

Data analysis

At the time of collection, data were entered at a central location using Access (2003, Microsoft Corporation, Redmond, Wash). Manual verification was performed for quality assurance. Descriptive analyses included frequencies, counts, and proportions. For ease of comparison to previously published studies, we report both frequencies in relationship to number of patients and in relationship to number of reactions. Analyses comparing groups utilized Pearson’s chi-square test and Fisher’s exact test (two tailed, when appropriate) using SAS (Statistical Analysis System, SAS Institute Incorporated, Cary, NC). *t* Tests were utilized for continuous data. A significance level of .05 was utilized for all analyses. Because this was an exploratory analysis, no adjustments for multiple comparisons were performed.

RESULTS

Overall prevalence of positive patch test reactions to cosmetic and non-cosmetic sources

Of the 10,061 patients patch-tested by the NACDG during the period 2001-2004, 6621 patients were female, and 3440 were male. As shown in Fig 1, of the 6621 female patients, 1582 (23.8%) were “cosmetic allergic” and 3065 (46.3%) were “non-cosmetic allergic”; 1974 patients (29.8%) had no allergic reactions and were excluded from the remainder of the analyses. Of the 3440 males, 611 (17.8%) were “cosmetic allergic” and 1557 (45.3%) were “non-cosmetic allergic”; 1222 (35.5%) had no allergic reactions and were excluded from the remainder of the analyses.

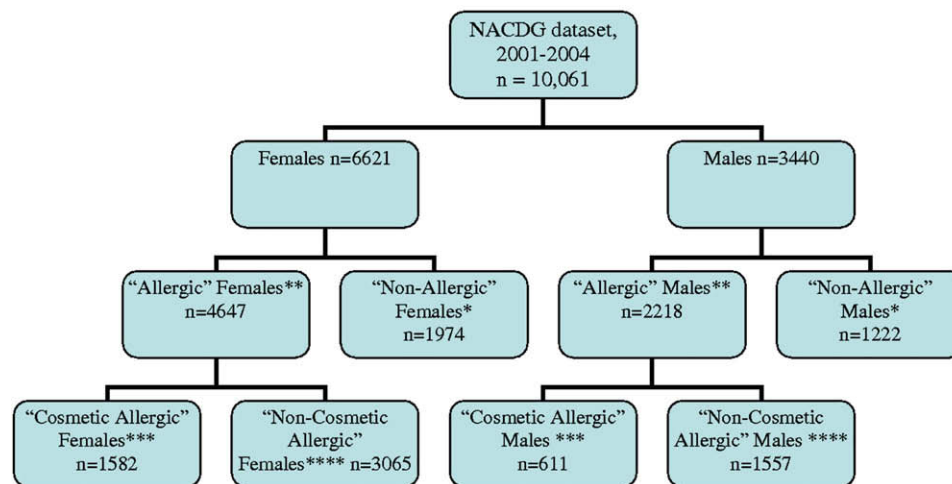


Fig 1. NACDG Study Population and Subgroups. *Patients with no positive allergic patch test reactions to NACDG standard screening allergens. **Patients with at least one positive allergic patch test reaction to a NACDG standard screening allergen. ***Patients with at least one positive allergic patch test reaction to an NACDG standard screening allergen associated with a cosmetic source; excludes 438 patients who only reacted to a non-standard allergen associated with a cosmetic source. ****Patients with one or more positive allergic reaction(s) to an NACDG standard screening allergen(s) with a source other than cosmetic.

“Allergic” patients

Of “allergic” patients (those with at least one positive patch-test reaction, $n = 6815$), females were 1.21 times more likely to have an allergic reaction associated with a cosmetic source than males ($p < .0001$; 95% CI, 1.12-1.31). Within the group of “allergic” females (Table II) and within the group of “allergic” males (Table III), there were no statistical associations of race or atopic status with cosmetic allergy but older age was significantly associated with cosmetic allergy (Tables II and III). Dermatitis on the head and neck was 1.2 times more common than dermatitis elsewhere in female patients with cosmetic allergy ($p < .0001$, Table II) but not in male patients (Table III). Dermatitis on the extremities was 0.74 times less common than dermatitis elsewhere in males with cosmetic allergy ($p < .0001$, Table III) but not in females (Table II). Dermatitis in an “other” pattern (primarily scattered generalized) was 1.3 times more common in males with cosmetic allergy ($p = .0013$, Table III), but not in females (Table II).

“Cosmetic allergic” patients: Females versus males

Table IV summarizes demographics of patients with cosmetic allergy by gender. Within this group, there was no association of gender with race or atopy, but males with cosmetic allergy were significantly older than females with cosmetic allergy (Table IV). Females with cosmetic allergy were two times more likely to have dermatitis on the head and neck and significantly less likely to have dermatitis

on the extremities, trunk, or “other” patterns than males with cosmetic allergy.

Cosmetic sources associated with NACDG standard screening allergens

There were a total of 4206 reactions (1286 in male and 2920 in female patients) to NACDG standard screening allergens associated with a cosmetic source in 2193 patients. The most common product types associated with allergic reactions are listed in Table V. Cosmetics not otherwise specified (NOS), moisturizers, and hair care products were the most common product categories in both males and females. Nail products and make-up were more common in females than in males. In both females and males, the proportion of currently relevant reactions within each category was higher than 79%. The category of deodorants/antiperspirants was the only category for which reactions were more common in males (31 reactions) than in females (8 reactions).

Occupationally related cosmetic sources linked to NACDG screening allergens

Cosmetics NOS, hair care products, and moisturizers were the most common product categories which were occupationally related in both males and females (Table VI). Positive allergic patch test reactions associated with skin cleansers were almost 4 times more frequent in males than in females (19.4% vs 5.3%). In both females and males, the proportions of reactions within each category which were currently relevant were higher than 91%. For both men

Table II. Characteristics of females with allergic patch test reactions: Cosmetic sources versus only noncosmetic sources

	Females with at least one allergic reaction to a cosmetic (AC) N = 1582	Females with allergic reactions to only noncosmetics (ANC) N = 3065	AC versus ANC	
			PR (95% CI)	p Value
Age, mean (STD)	49.3 (16.0)	46.2 (16.2)	3.12 (16-15)*	<.0001
Race, No. (%)				
Caucasian	1416 (89.5)	2685 (87.6)	1.14 (0.99-1.30)	.056
Other	166 (10.5)	380 (12.4)		
Atopic, No. (%)	665 (42.0)	1232 (40.)	1.05 (0.97-1.14)	.2267
Dermatitis site, No. (%)				
Head and neck	780 (49.3)	1309 (42.7)	1.19 (1.10-1.29)	<.0001
Extremities	691 (43.7)	1366 (44.6)	0.98 (0.90-1.06)	.5632
Trunk	184 (11.6)	415 (13.5)	0.89 (0.78-1.01)	.0657
Other location pattern	388 (24.5)	749 (24.4)	1.00 (0.91-1.10)	.9468

CI, Confidence interval; PR, prevalence rate; STD, standard deviation.

*Mean difference (STD), t test.

Table III. Characteristics of males with allergic patch test reactions: Cosmetic sources versus only noncosmetic sources

	Males with at least one allergic reaction to a cosmetic (AC) N = 611	Males with allergic reactions to only noncosmetics (ANC) N = 1557	AC versus ANC	
			PR (95% CI)	p Value
Age, mean (STD)	53.0 (15.3)	47.2 (16.3)	5.8 (16.1)*	<.0001
Race, No. (%)				
Caucasian	539 (88.2)	1367 (87.8)	1.03 (0.83-1.27)	.7877
Other	72 (11.8)	190 (12.2)		
Atopic, No. (%)	214 (35.0)	524 (33.7)	1.04 (0.91-1.20)	.5447
Dermatitis site, No. (%)				
Head and neck	145 (23.7)	312 (20.0)	0.96 (0.82-1.12)	.6138
Extremities	308 (50.4)	947 (60.8)	0.74 (0.65-0.85)	<.0001
Trunk	117 (19.2)	253 (16.3)	1.15 (0.97-1.36)	.1064
Other location pattern	217 (35.5)	443 (28.5)	1.26 (1.09-1.44)	.0013

CI, Confidence interval; PR, prevalence rate; STD, standard deviation.

*Mean difference (STD), t test.

and women, the most common occupation which was related to an allergic reaction to a cosmetic source was hairdressing (including barbers and cosmetologists, [Table VII](#)).

Most common NACDG screening allergens associated with cosmetic sources

The top 20 NACDG standard screening allergens associated with a cosmetic source in females and males are listed in [Tables VIII and IX](#), respectively. Fragrance compounds, preservatives, and emulsifiers were common in both females and males. Several antigens were at least twice as common in females than males: paraphenylenediamine (15.6% of females vs 7.9% of males), tosylamide/formaldehyde resin (6.1% of females vs 0.5% of males), glyceryl thioglycolate (5.3% of females vs 1.5% of males), and methyl methacrylate (4.1% of females vs

0% of males). Antigens which were at least twice as common in males than females included diazolin-dinyl urea (11% of males vs 5% of females) and imidazolidinyl urea (10.5% vs 4.4%).

Common allergens for specific source categories are listed in [Tables X through XIV](#). Three common allergens (>5 reactions) were associated with nail products: tosylamide/formaldehyde resin (n = 98), methylmethacrylate (n = 64), and ethyl acrylate (n = 42). Five common allergens (>5 reactions) were associated with perfumes/fragrances: fragrance mix (n = 118), *Myroxylon pereirae* (n = 101), ylang-ylang oil (n = 26), jasmine absolute (n = 15), and cinnamic aldehyde (n = 9). Two common allergens (>5 reactions) were associated with oral care products and deodorants/antiperspirants, respectively: fragrance mix (n = 10, n = 16), *M pereirae* (n = 5, n = 11).

Table IV. Characteristics of patients with allergic reactions to a cosmetic source: Females versus males

	Females with at least one allergic reaction to a cosmetic N = 1582	Males with at least one allergic reaction to a cosmetic N = 611	Females vs males	
			PR (95% CI)	p Value
Age, mean (STD)	49.3 (16.0)	53.0 (15.3)	3.70 (15.8)*	<.0001
Race, No. (%)				
Caucasian	1416 (89.5)	539 (88.2)	1.01 (0.98-1.05)	.3836
Other	166 (10.5)	72 (11.8)		
Atopic, No. (%)	665 (42.0)	214 (35.0)	1.20 (1.06-1.36)	.0027
Dermatitis site, No. (%)				
Head and neck	780 (49.3)	145 (23.7)	2.08 (1.79-2.42)	<.0001
Extremities	691 (43.7)	308 (50.4)	0.87 (0.79-0.95)	.0046
Trunk	184 (11.6)	117 (19.2)	0.61 (0.49-0.75)	<.0001
Other location pattern	388 (24.5)	217 (35.5)	0.69 (0.60-0.79)	<.0001

CI, Confidence interval; PR, prevalence rate; STD, standard deviation.

*Mean difference (STD), t test.

Table V. Cosmetic product types associated with allergic patch-test reactions

Product category	Females		Males	
	No. of patients with positive allergic reaction to source (% all females allergic to cosmetics, n = 1582)*	No. of currently relevant reactions in category/total category reactions (%)	No. of patients with positive allergic reaction to source (% all males allergic to cosmetics, n = 611)*	No. of currently relevant reactions in category/total category reactions (%)
Cosmetic, NOS	1072 (67.8)	1871/2003 (93.4)	467 (76.4)	973/1025 (94.9)
Moisturizers	529 (33.4)	901/946 (95.2)	306 (50.1)	658/680 (96.8)
Hair care products	475 (30.0)	495/607 (81.2)	134 (21.9)	142/161 (88.2)
Nail products	171 (10.8)	167/211 (79.2)	7 (1.2)	16/17 (94.1)
Perfumes and fragrances	132 (8.3)	156/191 (81.7)	58 (9.5)	73/88 (83.0)
Make-up	88 (5.6)	121/124 (97.6)	0	0
Skin cleansers	64 (4.1)	79/82 (96.3)	59 (9.7)	74/77 (96.1)
Oral care products	12 (0.8)	17/17 (100)	5 (0.8)	6/6 (100)
Deodorants/antiperspirants	7 (0.4)	8/8 (100)	20 (3.3)	27/31 (87.1)

NOS, Not otherwise specified.

*Totals greater than 1582 and 611, respectively, because a single patient could have several reactions, each to a different category of cosmetics.

Cosmetic sources of non-NACDG screening allergens

Seven hundred eighty patients had a currently relevant allergic reaction to a non-NACDG standard allergen which was associated with a cosmetic source. Four hundred thirty-eight patients reacted only to a nonstandard allergen; 342 patients had cosmetic sources for both standard and non-standard allergens.

DISCUSSION

There are several important findings of this study. First, cosmetic allergy is common; 21.8% of patients referred for patch testing (2193/10,061) or 31.9% (2193/6,865) of “allergic” patients in this database had at least one allergic reaction associated with a

cosmetic source. Second, cosmetic allergy was significantly more common in females than in males. Third, within the “cosmetic allergic” group, head and neck involvement was significantly higher in females than in males (49.3% vs 23.7%, $p < .0001$), whereas extremities ($p = .0046$), trunk ($p < .0001$), and “other” patterns ($p < .0001$) were significantly more common in males. Finally, while the prevalence of many common cosmetic allergens differed slightly by gender, fragrance chemicals and preservatives were common in both males and females.

Some of the findings from this study are not surprising. The prevalence of cosmetic allergy in our population (21.8%) was higher than previous studies.^{6-9,11-13,15} This could be due to increased use of cosmetic products, increased rate of contact

Table VI. Common cosmetic product types associated with occupationally related allergic patch-test reactions

Product category*	Females		Males	
	No. of patients with positive allergic reaction to source which was occupationally related/total number with allergy to cosmetics n = 94 (%) [†]	No. of currently relevant reactions/total occupationally related reactions (%)	No. of patients with positive allergic reaction to source which was occupationally related/total number with occupational allergy to cosmetic n = 31 (%) [†]	No. of currently relevant reactions/total occupationally related reactions (%)
Cosmetic, NOS	34 (36.2)	69/69 (100)	18 (58.1)	34/34 (100)
Moisturizers	20 (21.3)	46/46 (100)	8 (25.8)	13/13 (100)
Hair care products	65 (69.2)	116/127 (91.3)	11 (35.5)	16/17 (94.1)
Nail products	8 (8.5)	13/14 (92.9)	0	0
Perfumes and fragrances	3 (3.2)	3/3 (100)	3 (9.7)	5/5 (100)
Make-up	2 (2.1)	2/2 (100)	0	0
Skin cleansers	5 (5.3)	6/6 (100)	6 (19.4)	6/6 (100)
Oral care products	0	0	2 (6.5)	3/3 (100)

NOS, Not otherwise specified.

*No reactions occupationally related to deodorants/antiperspirants.

[†]Totals >94 and 31, respectively, because a single patient could have several reactions, each to a different category of cosmetics.

allergy to cosmetics, differences in study populations, and/or different definitions of the term “cosmetic.” Using the FDA definition of “cosmetic,” our analysis found that females were 1.2 times more likely than males to have an allergic reaction associated with a cosmetic. As expected, there were no males with allergic reactions associated with the more narrowly defined category of “make-up” (which the lay public often equates with the term “cosmetic”). Cosmetics NOS is a large category, likely because this category is often coded when a more specific designation cannot be determined (especially with “possible relevance”). After cosmetics NOS, the most common sources of cosmetic allergies in women were moisturizers, hair products, nail products, and perfumes/fragrances. In males, the top sources after cosmetics NOS included moisturizers, hair care products, skin cleansers, and perfumes/fragrances. These likely reflect gender-specific exposures.

It is not surprising that the most common occupation associated with occupationally relevant reactions to cosmetics was hairdressing (in both males and females) and that the most common occupationally associated source of reactions was hair products (in females). Several studies have documented the higher risk of allergic contact dermatitis in hairdressers. In a multicenter European study, 48% of 2506 individuals suspected of having an allergic reaction to hair products were hairdressers.²² An Italian study of 209 hairdressers found that 43.8% had a positive patch test reaction to one or more antigens in the hairdressing series.²³ Prevalence of allergy in hairdressers may also be

Table VII. Common (>1) occupations associated with specific allergic reactions to cosmetics

Occupation	Women, n = 94 (%)	Men, n = 31 (%)
Hairdresser/barber/cosmetologist	49 (52.1)	9 (29.0)
Healthcare worker	15 (16.5)	3 (9.7)
Food preparation worker	5 (5.5)	1 (3.2)
Student	4 (4.2)	0 (0.0)
Secretarial office clerk	4 (4.2)	1 (3.2)
Manager/administrator	2 (2.2)	2 (6.5)
Automobile/truck/bus mechanic or autobody repair worker	1 (1.1)	2 (6.5)
Machinist/machine operator (molding/casting/printing)	1 (1.1)	3 (9.7)
Engineer (industrial/electrical)	0 (0)	2 (6.5)
Janitor	1 (1.1)	1 (3.2)

increasing. Valks and colleagues²⁴ compared 300 hairdressers patch-tested with a standard screening series and specific hairdressing products between 1994 and 2003 with 300 hairdressers patch tested between 1980 and 1993 and found significant increases in both suspected cases of occupational allergic contact dermatitis (48.8% to 58.0%) and positive patch test rates (58.8% to 78.3%, $p < 0.05$). The second most common industry associated with occupationally relevant reactions to cosmetics was health care, likely due to occupational exposure to soaps and topical products.

As in other studies,^{7,9,16,25,26} fragrances and preservatives were the most frequent causes of cosmetic-related allergic reactions in our study, accounting for more than half of the reactions seen in females (59.4%) and in males (73.5%). Fragrances

Table VIII. Top 20 NACDG standard screening allergens associated with cosmetic source in females

Rank	Allergen	No. of allergic reactions	% Females with allergy to cosmetic source, N = 1582	% Reactions in females associated with cosmetic source, N = 2920
1	Quaternium-15 2%	323	20.4	11.1
2/3	<i>Myroxylon pereirae</i> (balsam of Peru) 25%	302	19.1	10.3
2/3	Fragrance mix 8%	302	19.1	10.3
4	<i>p</i> -Phenylenediamine 1%	247	15.6	8.5
5	Methyldibromoglutaronitrile/phenoxyethanol 2%	131	8.3	4.5
6	Formaldehyde 1%*	108	6.8	3.7
7	Tosylamide formaldehyde resin 10%	97	6.1	3.3
8	Cocamidopropyl betaine 1%*	84	5.3	2.9
9	Glyceryl thioglycolate 1%	83	5.3	2.8
10/11	Diazolidinyl urea 1%	79	5.0	2.7
10/11	Diazolidinyl urea 1%*	79	5.0	2.7
12	DMDM hydantoin 1%	77	4.9	2.6
13	Lanolin alcohol 30%	71	4.5	2.4
14/15	Imidazolidinyl urea 2%	70	4.4	2.4
14/15	Methylchlorisothiazolinone/methylisothiazolinone 100 ppm*	70	4.4	2.4
16	Methyl methacrylate 2%	65	4.1	2.2
17	Amidoamine 0.1%*	63	4.0	2.2
18	Propylene glycol 30%	61	3.9	2.1
19	DMDM hydantoin 1%*	58	3.7	2.0
20	Imidazolidinyl urea 2%*	51	3.2	1.8

*Not in petrolatum; all others are.

provide a pleasant aroma while preservatives are utilized to prevent the overgrowth of microorganisms. While the most frequently used antimicrobial preservatives in cosmetics and toiletries are the paraben esters followed by imidazolidinyl urea, quaternium-15, formaldehyde, and isothiazolinones,^{10,27} allergy to formaldehyde-releasing preservatives was most frequent in our study.

Formaldehyde-releasing preservatives

Formaldehyde-releasing preservatives include quaternium-15, diazolidinyl urea, imidazolidinyl urea, 2-bromo-2-nitropropane-1,3-diol, DMDM hydantoin, and formaldehyde itself. The amount of formaldehyde produced by these chemicals depends on temperature and pH.²⁸ Allergic reactions to formaldehyde-releasers may be due to the preservative, formaldehyde, or both.^{29,30} A recent study from the NACDG found that patch-testing with a petrolatum vehicle for diazolidinyl urea, imidazolidinyl urea, and DMDM hydantoin was more sensitive than an aqueous vehicle.²⁹ In our study, quaternium-15 was the most common cosmetic allergen identified in both males (26.5%) and females (20.4%). Both Eiermann et al⁸ and Adams and Maibach⁹ also found that it was the most common cosmetic preservative allergen.

Diazolidinyl urea was first introduced in 1982 and has a wider antimicrobial spectrum than

imidazolidinyl urea³¹ to which it is structurally related. In a Finnish study of patch-test reactions to cosmetic allergens, diazolidinyl urea was responsible for only 0.9% of allergic reactions in 6539 patients.³² In contrast, we found that diazolidinyl urea represented 2.7% (both aqueous and petrolatum preparations) of reactions in females and 4.9% (aqueous) and 5.6% (petrolatum) of reactions in males to cosmetic products and was commonly implicated in the following sources: cosmetics NOS, moisturizers, and make-up formulations.

DMDM hydantoin is found in many cosmetic products, most frequently in shampoos, followed by skin care preparations, hair conditioners, make-up foundations and bases, and personal cleanliness products.³³ In our study, DMDM hydantoin was in the top 12 allergens for cosmetics overall, as well as for the specific categories of cosmetics NOS, moisturizers, and hair care products.

Imidazolidinyl urea is the second most commonly used preservative in cosmetics, after parabens.^{10,34} Adams and Maibach⁹ found that imidazolidinyl urea was also the second most common preservative responsible for cases of cosmetic allergy in 13,216 patients evaluated from 1977 to 1983. However, the frequency of imidazolidinyl urea allergy (relative to other preservatives) from cosmetics appears to have decreased. More recent studies have shown that imidazolidinyl urea ranks fifth or lower relative

Table IX. Top 20 NACDG standard screening allergens associated with cosmetic source in males

Rank	Allergen	No. of allergic reactions	% Males with allergy to cosmetic source, N = 611	% Reactions in males associated with cosmetic source, N = 1286
1	Quaternium-15 2%	162	26.5	12.6
2	Fragrance mix 8%	138	22.6	10.7
3	<i>Myroxylon pereirae</i> (balsam of Peru) 25%	129	21.1	10.0
4	Methyldibromoglutaronitrile/phenoxyethanol 2%	72	11.8	5.6
5	Diazolidinyl urea 1%	67	11.0	5.2
6	Imidazolidinyl urea 2%	64	10.5	5.0
7/8	Diazolidinyl urea 1%*	63	10.3	4.9
7/8	Cocamidopropyl betaine 1%	63	10.3	4.9
9	Formaldehyde 1%*	59	9.7	4.6
10	DMDM hydantoin 1%	50	8.2	3.9
11	<i>p</i> -Phenylenediamine 1%	48	7.9	3.7
12/13	Lanolin alcohol 30%	41	6.7	3.2
12/13	Amidoamine 1%	41	6.7	3.2
14	Propylene glycol 30%*	40	6.6	3.1
15/16	Imidazolidinyl urea 2%*	34	5.6	2.6
15/16	DMDM hydantoin 1%*	34	5.6	2.6
17	2-Bromo-2-nitropropane diol 0.5%	29	4.8	2.3
18	Methylchloroisothiazolinone/methylisothiazolinone 100 ppm*	27	4.4	2.1
19/20	Cocamide diethanolamine 0.5%	17	2.8	1.3
19/20	Ylang-ylang oil 2%	17	2.8	1.3

*Not in petrolatum; all others are.

to other preservatives as a cause of cosmetic allergy.^{7,13,34} A Belgian study documented only 3 allergic reactions in 279 patients with cosmetic allergy.³⁵ This is consistent with our study which found that other preservatives, including quaternium-15, formaldehyde, methyldibromoglutaronitrile/phenoxyethanol, diazolidinyl urea, and DMDM hydantoin, were more common cosmetic allergens than was imidazolidinyl urea.

2-Bromo-2-nitropropane-1,3-diol is used in a variety of cosmetic and pharmaceutical preparations including shampoos, creams, lotions, cleansers, and eye makeup.³⁶ Since the early 1980s, its use has declined, in part because, at alkaline pH, it breaks down into formaldehyde and bromo compounds which can develop a yellow or brown hue on exposure to light.³⁷ Additionally, it can react with amines or amides to produce potentially carcinogenic nitrosamines or nitrosamides.³⁶ While in the early 1980s, Adams and Maibach⁹ found that 2-bromo-2-nitropropane-1,3-diol was the fourth most common implicated preservative in 713 cases of cosmetic allergy, it was not common in our study, accounting for only 2.3% of cosmetic-associated reactions in males and 1.6% in females.

Fragrances and *M pereirae* (balsam of Peru)

Fragrance mix and *M pereirae* were the second and third most common allergens in both females and males in our study. This is consistent with other

studies which have found that positive reactions to fragrances were found in 42% to 54% of patch-tested patients with suspected cosmetic dermatitis.^{7,13,38} Irritant reactions to fragrance mix may be as high as 50% and definite clinical relevance (confirmation of the specific allergen in a product in addition to a positive use or patch test to the suspected product) is often difficult to establish.³⁹

The fragrance mix tested during this study period was an 8% mixture of eugenol, isoeugenol, cinnamic aldehyde, cinnamic alcohol, oak moss, geraniol, hydroxycitronellal and α -amylcinnamic aldehyde (with 5% sorbitan sesquioleate as an emulsifier). Constituents of commercial fine fragrances and cosmetics has changed over the past several decades.⁴⁰ In a multicenter study, Larsen et al⁴¹ reviewed the patch-test results of 167 fragrance-sensitive patients and found that the 8% fragrance mix identified 86% of fragrance-allergic patients, but sensitivity could be increased to 96% by adding ylang-ylang oil, narcissus oil, sandalwood oil, and *M pereirae*. Subsequently Frosch et al⁴² recommended patch testing with 4-(4-hydroxy-4-methylpentyl)-3-cyclohexane carboxaldehyde (Lylal). A new fragrance mix, fragrance mix II, has been shown to have a lower number of false-positive reactions and to detect additional patients sensitive to fragrances missed by the original 8% fragrance mix.⁴³ While narcissus oil, sandalwood oil, Lylal, and fragrance mix II were not tested during this study period, ylang-ylang oil, jasmine absolute, and

Table X. Top 20 allergens for cosmetics, NOS

Rank	Allergen	Females			Males		
		No. of reactions	% Patients N = 1072	% Reactions N = 2003	No. of reactions	% Patients N = 1072	% Reactions N = 1025
1	Quaternium-15 2%	292	27.2	14.6	148	31.7	14.4
2	<i>Myroxylon pereirae</i> (balsam of Peru) 25%	274	25.6	13.7	117	25.1	11.4
3	Fragrance mix 8% pet	273	25.5	13.6	118	25.3	11.5
4	Methyldibromoglutaronitrile/phenoxyethanol 2%	122	11.4	6.1	69	14.8	6.7
5	Formaldehyde 1%*	95	8.9	4.7	57	12.2	5.5
6/7	Diazolidinyl urea 1%	77	7.2	3.8	65	13.9	6.3
6/7	Diazolidinyl urea 1%*	77	7.2	3.8	60	12.9	5.9
8/9	Imidazolidinyl urea 2%	68	6.3	3.4	62	13.3	6.1
8/9	Lanolin alcohol 30%	68	6.3	3.4	40	8.6	3.9
10	DMDM hydantoin 1%	65	6.1	3.3	46	9.9	4.5
11	Propylene glycol 30%*	57	5.3	2.9	36	7.7	3.5
12	Imidazolidinyl urea 1%*	50	4.7	2.5	32	6.9	3.1
13	Methylchloroisothiazolinone/methylisothiazolinone 100 ppm*	49	4.6	2.5	22	4.7	2.2
14	DMDM hydantoin 1%*	47	4.4	2.4	32	6.9	3.1
15	Methyldibromoglutaronitrile 0.4%	42	3.9	2.1	13	2.8	1.3
16	2-Bromo-2-nitropropane-1, 3-diol 0.5%	41	3.8	2.1	28	6.0	2.7
17	Ylang-ylang oil 2%	33	3.1	1.7	14	3.0	1.4
18/19	Thiuram mix 1%	32	3.0	1.6	0	0	0
18/19	DL-alpha tocopherol 100%	32	3.0	1.6	3	0.6	0.3
20	Cinnamic aldehyde 1%	28	2.6	1.4	10	2.2	1.0

*Not in petrolatum; all others are.

cinnamic aldehyde, which were tested, were common allergens in the specific category of fragrances/perfumes in our study.

Other preservatives

The methyldibromoglutaronitrile/phenoxyethanol (MDBGN/PE) preservative system is a combination of two active ingredients, 2-phenoxyethanol and methyldibromoglutaronitrile, in ratio of 4:1. Contrary to initial animal studies, MDBGN/PE has been increasingly recognized as a sensitizing agent in humans, predominantly in Europe where it was first introduced in 1985 and then later in the United States.⁴⁴ In June 2008, the European Commission Scientific Committee on Consumer Products banned the use of MDBGN in all cosmetics, including soaps and shampoos (see ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_060.pdf, accessed 7-24-08). Most reported cases of MDBGN allergy are from exposure to cosmetics.^{45,46} In our study, MDBGN/PE accounted for 5.6% of reactions in females and, in males, 4.5% of reactions.

Methylchloroisothiazolinone (MCI) and methylisothiazolinone (MI) are the active ingredients of a commonly used preservative system consisting of a mixture of these two isothiazolinones: 1.15% MCI and 0.35% MI. After its introduction in Europe in the mid-1970s and in the United States in the early 1980s,

MCI/MI rapidly became a common preservative and a frequent sensitizer.⁴⁷ MCI/MI was the most important cosmetic allergen in a 1986-1987 study from the Netherlands, causing reactions in 27.7% of 119 patients with cosmetic allergy.²⁷ Subsequently, the allowed concentration in Europe was limited to 7.5 parts per million (ppm) in leave-on products and 15 ppm in rinse-off products.³⁴ Throughout the 1990s, the level of MCI/MI sensitivity in the European Union remained high, but stable, between 2% and 2.5%⁴⁸ and appears to now be decreasing.³⁴ The decrease is likely due to the restriction of MCI/MI use and the replacement with newer, more popular preservatives, such as MDBGN.³⁴ Our study found that MCI/MI is still an important cosmetic allergen in North America, eliciting reactions in 8.3% of cosmetic allergic females and 11.8% of cosmetic allergic males overall. It was also the second most common allergen associated with moisturizers in our study.

Parabens are esters of 4-hydroxy benzoic acid. The 5 most commonly used parabens include methyl-, ethyl-, propyl-, butyl-, and benzyl-paraben.⁴⁹ It has been estimated that 87% to 93% of investigated cosmetic products contain one or more of the parabens,⁵⁰ especially mascara, eye shadow, skin care products, and moisturizers. Despite the widespread use of parabens in cosmetics, they are rare causes of allergic contact

Table XI. Top 20 allergens associated with a moisturizer source

Rank	Allergen	Females			Males		
		No. of reactions	% Patients N = 529	% Reactions N = 946	No. of reactions	% Patients N = 529	% Reactions N = 946
1	Quaternium-15 2%	182	34.4	19.2	123	40.2	18.1
2	Methyldibromoglutaronitrile/phenoxyethanol 2%	92	17.4	9.7	57	18.6	8.4
3	Fragrance mix 8%	71	13.4	7.5	36	11.8	5.3
4	<i>Myroxylon pereirae</i> (balsam of Peru) 25%	62	11.7	6.6	37	12.1	5.4
5	Lanolin alcohol 30%	54	10.2	5.7	35	11.4	5.2
6	Formaldehyde 1%*	53	10.0	5.6	46	15.0	6.8
7	Diazolidinyl urea 1%	51	9.6	5.4	48	15.7	7.1
8	Diazolidinyl urea 1%*	45	8.5	4.8	46	15.0	6.8
9	DMDM hydantoin 1%	41	7.8	4.3	40	13.1	5.9
10/11	Methyldibromoglutaronitrile 0.4%	37	7.0	3.9	9	2.9	1.3
10/11	Propylene glycol 30%*	37	7.0	3.9	24	7.8	3.5
12	Imidazolidinyl urea 2%	35	6.6	3.7	48	15.7	7.1
13	Methylchloroisothiazolinone/methylisothiazolinone 100 ppm*	32	6.1	3.4	16	5.2	2.4
14	Imidazolidinyl urea 2%*	30	5.7	3.2	26	8.5	3.8
15	DMDM hydantoin 1%*	26	4.9	2.8	27	8.8	4.0
16	DL-alpha tocopherol 100%	25	4.7	2.6	2	0.7	0.3
17	2-Bromo-2-nitropropane-1, 3-diol 0.5%	18	3.4	1.9	20	6.5	2.9
18	Tea tree oil, oxidized 5%	8	1.5	0.9	2	0.7	0.3
19	Paraben mix 12%	7	1.3	0.7	8	2.6	1.2
20	DL-alpha tocopherol acetate 100%	6	1.1	0.6	3	1.0	0.4

*Not in petrolatum; all others are.

Table XII. Common (≥ 5 reactions) allergens associated with hair care products

Allergen	Females			Males		
	No. of reactions	% Patients N = 475	% Reactions N = 607	No. of reactions	% Patients N = 134	% Reactions N = 161
<i>p</i> -Phenylenediamine 1%	242	51.0	39.9	46	34.3	28.6
Glyceryl thioglycolate 1%	83	17.5	13.7	9	6.7	5.6
Cocamidopropyl betaine 1%*	74	15.6	12.2	42	31.3	26.1
Amidoamine 0.1%*	54	11.4	8.9	24	17.9	14.9
Quaternium-15 2%	20	4.2	3.3	3	2.2	1.9
Cocamide diethanolamine 0.5%	20	4.2	3.3	8	6.0	5.0
Methylchloroisothiazolinone/methylisothiazolinone 100 ppm*	19	4.0	3.1	4	3.0	2.5
<i>Myroxylon pereirae</i> (balsam of Peru) 25%	13	2.7	2.1	3	2.2	1.9
DMDM hydantoin 1%	10	2.1	1.7	2	1.5	1.2
Fragrance mix 8%	10	2.1	1.7	7	5.2	4.4
Formaldehyde 1%*	8	1.7	1.3	1	0.8	0.6
DMDM hydantoin 1%*	8	1.7	1.3	1	0.8	0.6
Methyldibromoglutaronitrile/phenoxyethanol 2%	6	1.3	1.0	2	1.5	1.2

*Not in petrolatum; all others are.

dermatitis.⁵¹ Our data is consistent with this finding; only 0.8% (13/1582) of cosmetic allergic females and 1.6% (10/611) of cosmetic allergic males had reactions to paraben mix.

Other common cosmetic allergens

p-Phenylenediamine and its derivatives are common hair dye ingredients used in both permanent

and semipermanent preparations. In a European study including 2506 patients with suspected hair product allergy, *p*-phenylenediamine was the most common sensitizer, causing allergic reactions in 15.4% of individuals suspected to have allergy to hair cosmetics.⁵² We found that *p*-phenylenediamine was the most common contact allergen in hair cosmetics, causing reactions in approximately half

Table XIII. Common allergens (≥ 5 reactions) associated with make-up in females*

	No. of reactions	Females	
		% Patients N = 88	% Reactions N = 124
Thiuram mix 1%	23	26.1	18.6
Carba mix 3%	13	14.8	10.5
Fragrance mix 8%	11	12.5	8.9
Potassium dichromate 0.25%	10	11.4	8.1
<i>Myroxylon pereirae</i> (balsam of Peru) 25%	9	10.2	7.3
Quaternium-15 2%	8	9.1	6.5
Colophony 20%	5	5.7	4.0

*There were no reactions associated with make-up in males.

of females (50.1%) and one third of males (34.3%) with documented sources of hair products.

Cocamidopropyl betaine (CAPB) is a widely used surfactant in shampoo, liquid soap, and skin cleansers⁵¹ and commonly causes irritant patch-test reactions.⁵³ Responsible allergens (which also cross-react with CAPB) include dimethylamino-propylamine (DMAPA)^{22,54} and cocamidopropyl dimethylamine (also known as amidoamine or cocamidoamine).^{55,56} In our study, CAPB was the eighth most common allergen overall, causing reactions in 6.1% and 10.3% of females and males, respectively, with cosmetic allergy. Within specific allergen categories, CAPB was a common allergen in hair products and skin cleansers, as expected. CAPB, DMAPA, and amidoamine are not thought to cross-react with cocamide diethanolamide.⁵⁷

Glyceryl monothioglycolate is a common component of acid permanent wave solutions. As an allergen, it is especially problematic since it may remain on hair for up to 3 months⁵⁸ and can penetrate rubber gloves.⁵⁹ In fact, allergic reactions to glyceryl monothioglycolate are more common in hairdressers than in clients.⁶⁰ In a European study including 2506 patients with suspected hair product allergy, glyceryl monothioglycolate was responsible for 1.9% of reactions due to hair products.²² In our study, it was the second most common allergen in hair products, responsible for causing reactions in 17.5% and 6.7% of females and males, respectively.

Colophony, or rosin, is obtained from the tree species *Pinaciae* and is used primarily in mascara, eye shadow, eyeliner, and lipstick. Abietic acid is a major component of colophony and is considered to be the main allergen.⁶¹ Sensitization from cosmetic sources are relatively rare.⁶²⁻⁶⁴ Our findings are consistent with this; there were only 5 reactions to colophony due to a makeup source.

Propylene glycol is used in cosmetics as a solvent and humectant; it also has antimicrobial properties.³⁶ It is a known irritant⁶⁵⁻⁷³ and has occasionally been reported as a cosmetic allergen.^{74,75} In our study, it was a relatively uncommon cosmetic allergen, affecting 3.9% of females and 3.1% of males, overall with cosmetic allergy.

Lanolin is a variable mixture of fatty acids esterified with monohydric alcohols derived from sheep's wool and is used in cosmetic products as an emollient and emulsifier.^{15,76} From 1977 to 1983, Adams and Maibach⁹ reported that lanolin was the fourth most common allergen causing cosmetic reactions (after fragrances, preservatives, and *p*-phenylenediamine). DeGroot⁷ reported that lanolin derivatives were responsible for 6.1% of 82 reactions to cosmetic allergens. In our study, overall, lanolin was the 13th most common cosmetic allergen representing 2.4% and 3.7% of reactions in females and males, respectively. Within specific cosmetic categories, lanolin was the fifth most common cosmetic allergen in moisturizers. Amerchol 101, a related lanolin allergen, was not tested as an NACDG standard screening allergen during this study period.

Tosylamide formaldehyde is a common component of nail polish; it interacts with nitrocellulose to form a glossy, durable enamel finish.⁷⁷ In Europe, tosylamide formaldehyde is present in more than 90% of nail polishes⁷⁸; an informal Internet search of major US brands found that it was in almost all polishes, although a few polyester resin nail polishes do not contain this ingredient (Web search, May 2008). The eyelids, lateral part of the neck, and face are common sites of allergic contact dermatitis to tosylamide formaldehyde.⁷⁹ In a study of 215 patients with eyelid contact dermatitis, 7 (3.2%) had positive patch test reactions to tosylamide formaldehyde resin.⁸⁰ Less common sites of involvement include the chest, groin, and even gingival mucosa (in a habitual nail biter⁸¹). The NACDG reported that 16 of 389 cases (4.1%) of cosmetic contact allergy from 1977 to 1980 were due to tosylamide formaldehyde resin.⁸ Our study found a higher prevalence of 6.1%, but this was specifically in females. Of the 171 females with allergy specifically to nail products, 55.6% had reactions to tosylamide formaldehyde.

Acrylics are synthetic resins commonly used in artificial nails and other nail cosmetics, including nail primers, lacquers, wraps, and hardeners, as well as in non-cosmetic sources such as dentures, insulin pumps, and artificial joints.⁸²⁻⁸⁴ In the 1970s, hundreds of products containing 100% methyl methacrylate monomer were removed from the market because of reports of injury associated with the use of artificial nails.⁸⁵ Currently the ethyl methacrylate

Table XIV. Common allergens (≥ 5 reactions) associated with skin cleansers

Allergen	Females			Males		
	No. of reactions	% Patients N = 64	% Reactions N = 82	No. of reactions	% Patients N = 59	% Reactions N = 77
Cocamide diethanolamine 0.5%	13	20.3	15.9	18	30.5	23.3
Quaternium-15 2%	11	17.2	13.4	10	17.0	13.0
Fragrance mix 8%	9	14.1	11.0	11	18.6	14.3
<i>Myroxylon pereirae</i> (balsam of Peru) 25%	8	12.5	9.8	7	11.9	9.1
Amidoamine 0.1%*	7	10.9	8.5	13	22.0	16.9
Cocamidopropyl betaine 1%*	7	10.9	8.5	4	6.8	5.2

*Not in petrolatum; all others are.

monomer is the most commonly used methacrylate in nail products. Although the use of methyl methacrylate in cosmetics, including nail products, has been banned by the FDA, methyl methacrylate continues to be used illegally in some nail salons. Cyanoacrylate glues, used to attach preformed plastic nails and in nail wraps, is a rare sensitizer and usually does not cross-react with ethyl or methyl methacrylate.⁸⁶ Screening allergens for nail acrylic sensitivity may also include ethyl acrylate, hydroxyethyl acrylate, hydroxyethyl methacrylate, ethylene glycol dimethacrylate, triethylene glycol diacrylate, hydroxypropyl methacrylate, and hydroxyethyl methacrylate.⁸⁷⁻⁹⁰

Alpha tocopherol, or vitamin E, has rarely been reported to cause allergic contact dermatitis in cosmetics.^{91,92} In our study, 4 and 8 males reacted to dl-alpha tocopherol acetate 100% and dl-alpha tocopherol 100%, respectively. Thirty-four and 9 females reacted to dl-alpha tocopherol acetate 100% and dl-alpha tocopherol 100%, respectively.

Iodopropynyl butylcarbamate was originally used as a fungicide in paint and wood but has been identified as a relatively new allergen in cosmetics⁹³⁻⁹⁵; it was a rare cosmetic sensitizer in our study, responsible for only 6 reactions in females and one reaction in males.

Thiuram mix and carba mix were responsible for 23 and 13 reactions, respectively, in females with makeup allergy (Table XIII). It is likely that these represent allergy to rubber sponges, not the active ingredients of cosmetics, as has been previously reported.⁹⁶

Non-NACDG standard allergens associated with cosmetics

In our study, 438 of 2681 cosmetic-allergic patients (16.3%) only reacted to a non-NACDG standard allergen. Nonstandard allergens could include personal products or commercially-prepared allergens. A European study found that of 5911 patients who were patch tested with their own cosmetics and toiletries, one third reacted only to a personal

product, and no other allergen.⁹⁷ Potential cosmetic allergens which are not on the NACDG standard screening tray include butylhydroxyanisole, butylated hydroxytoluene,^{98,99} gallate esters,¹⁰⁰⁻¹⁰³ and propolis.¹⁰⁴ Therefore, it is important to test for antigens beyond standard screening tray allergens as well as for personal products. Comprehensive lists of suggested cosmetic patch test allergens are available in several references.^{14,63}

Limitations

This study has several limitations. First, the data were cross sectional; therefore only association, not causation, can be determined. Second, the study sample was drawn from patients who were referred for patch-testing; as such, they are representative of neither the general population nor the general dermatology population. Third, our strict definition of "cosmetic" excluded reactions to sunscreens, which are considered cosmetics in Europe; this should be considered in comparing data from our study with those from European studies. Fourth, attribution of source and clinical relevance are limited by investigator knowledge. Fifth, specific names of non-NACDG standard allergens are not collected as part of the NACDG database. Finally, associations with body site locations should be interpreted with caution as this analysis included patients who could also have had reactions to other antigens associated with noncosmetic sources.

In summary, cosmetic sources of allergens were common, representing 21.8% of patients referred for patch-testing by the NACDG, 2001-2004. Cosmetics NOS, moisturizers, and hair care products were the most common product categories in both males and females and common cosmetic-associated allergens included fragrance compounds, preservatives, and emulsifiers, all of which were common in both females and males. Four hundred thirty-eight of 2681 cosmetic-allergic patients (16.3%) only reacted to a non-NACDG standard allergen, underscoring

the need to test with additional antigens beyond standard screening series.

The authors are grateful to An Liu, MS, for his assistance with data analysis.

REFERENCES

1. Is it a cosmetic, a drug, or both? (Or is it soap?) Available at: <http://www.cfsan.fda.gov/~dms/cos-218.html>. Accessed April 20, 2008.
2. Meadows M. A century of ensuring safe foods and cosmetics. Available at: http://www.fda.gov/fdac/features/2006/106_cfsan.html. Accessed April 20, 2008.
3. Menkart J. An analysis of adverse reactions to cosmetics. *Cutis* 1979;24:599, 662.
4. Emmons WW, Marks JG Jr. Immediate and delayed reactions to cosmetic ingredients. *Contact Dermatitis* 1985;13:258-65.
5. Skog E. Incidence of cosmetic dermatitis. *Contact Dermatitis* 1980;6:449-51.
6. Romaguera C, Camarasa JMG, Alomar A, Grimalt F. Patch tests with allergens related to cosmetics. *Contact Dermatitis* 1983;6:167-8.
7. DeGroot AC. Contact allergy to cosmetics: causative ingredients. *Contact Dermatitis* 1987;17:26-34.
8. Eiermann HJ, Larsen W, Maibach HI, Taylor JS. Prospective study of cosmetic reactions: 1977-1980. *J Am Acad Dermatol* 1982;6:909-17.
9. Adams RM, Maibach HI. A five-year study of cosmetic reactions. *J Am Acad Dermatol* 1985;13:1062-9.
10. Wolf R, Wolf D, Tüzün B, Tüzün Y. Contact dermatitis to cosmetics. *Clin Dermatol* 2001;19:502-15.
11. Nielsen NH, Menné T. Allergic contact sensitization in an unselected Danish population. The Glostrup Allergy Study, Denmark. *Acta Derm Venereol* 1992;72:456-60.
12. Nielsen NH, Linneberg A, Menné T, Madsen F, Frølund L, Dirksen A, et al. Allergic contact sensitization in an adult Danish population: two cross-sectional surveys eight years apart (The Copenhagen Allergy Study). *Acta Derm Venereol* 2001;81:31-4.
13. Kohl L, Blondeel A, Song M. Allergic contact dermatitis from cosmetics: retrospective analysis of 819 patch-tested patients. *Dermatology* 2002;204:334-7.
14. Biehl K, Warsaw EM. Allergic contact dermatitis to cosmetics. *Dermatol Clin* 2006;24:215-32.
15. Orton DI, Wilkinson JD. Cosmetic allergy: incidence, diagnosis and management. *Am J Clin Dermatol* 2004;5:327-37.
16. Penchalaiah K, Handa S, Lakshmi SB, Sharma VK, Kumar B. Sensitizers commonly causing allergic contact dermatitis from cosmetics. *Contact Dermatitis* 2000;43:311-3.
17. Pratt MD, Belsito DV, DeLeo VA, Fowler JF Jr, Fransway AF, Maibach HI, et al. North American Contact Dermatitis Group patch-test results, 2001-2002 study period. *Dermatitis* 2004; 15:176-83. Erratum in: *Dermatitis* 2005;16:106.
18. Marks JG, Belsito DV, DeLeo VA, Fowler JF Jr, Fransway AF, Maibach HI, et al. North American Contact Dermatitis Group patch test results for the detection of delayed hypersensitivity to topical allergens. *J Am Acad Dermatol* 1998;38:911-8.
19. U.S. Census Bureau. Industry and Occupation 2000. http://www.census.gov/hhes/www/oiindex/cens_300_354.html. Accessed September 25, 2007.
20. Bourrain JL. Occupational contact urticaria. *Clin Rev Allergy Immunol* 2006;30:39-46.
21. Jacob SE, Zapolanski T. Systemic contact dermatitis. *Dermatitis* 2008;19:9-15.
22. Angelini G, Foti C, Rigano L, Vena GA. 3-Dimethylaminopropylamine: a key substance in contact allergy to cocamidopropylbetaine? *Contact Dermatitis* 1995;32:96-9.
23. Iorizzo M, Parente G, Vincenzi C, Pazzaglia M, Tosti A. Allergic contact dermatitis in hairdressers: frequency and source of sensitisation. *Eur J Dermatol* 2002;12:179-82.
24. Valks R, Conde-Salazar L, Malfeito J, Ledo S. Contact dermatitis in hairdressers, 10 years later: patch-test results in 300 hairdressers (1994 to 2003) and comparison with previous study. *Dermatitis* 2005;16:28-31.
25. DeGroot AC, Bruynzeel DP, Bos JD, van der Meeren HLM, van Joost T, Jagtman BA, et al. The allergens in cosmetics. *Arch Dermatol* 1988;124:1525-9.
26. Goossens A, Beck MH, Haneke E, McFadden JP, Nolting S, Durupt G, et al. Adverse cutaneous reactions to cosmetic allergens. *Contact Dermatitis* 1999;40:112-3.
27. Rastogi SC. Analytical control of preservative labeling on skin creams. *Contact Dermatitis* 2000;43:339-43.
28. Fisher AA. Dermatitis due to formaldehyde-releasing agents in cosmetics and medicaments. *Cutis* 1978;22:655, 658, 662, 664, 708.
29. Rietschel RL, Warsaw EM, Sasseville D, Fowler JF Jr, DeLeo VA, Belsito DV, et al. Sensitivity of petrolatum and aqueous vehicles for detecting allergy to imidazolidinylurea, diazolidinylurea, and DMDM hydantoin: a retrospective analysis from the North American Contact Dermatitis Group. *Dermatitis* 2007;18:155-62.
30. Brancaccio RR. What's new in contact dermatitis. *Am J Contact Dermatitis* 1993;4:55-7.
31. Kantor GR, Taylor JS, Ratz RL, Evey PL. Acute allergic contact dermatitis from diazolidinyl urea (Germall II) in a hair gel. *J Am Acad Dermatol* 1985;13:116-9.
32. Hasan T, Rantanen T, Alanko K, Harvima RJ, Jolanki R, Kalimo K, et al. Patch test reactions to cosmetic allergens in 1995-1997 and 2000-2002 in Finland—a multicentre study. *Contact Dermatitis* 2005;53:40-5.
33. DeGroot AC, van Joost T, Bos JD, van der Meeren HLM, Weyland JW. Patch test reactivity to DMDM hydantoin. *Contact Dermatitis* 1988;18:197-201.
34. Larsen WG, Jackson EM, Barker MD, Bednarz RM, Engasser PG, O'Donoghue MN, et al. A primer on cosmetics. *J Am Acad Dermatol* 1992;27:469-84.
35. Dooms-Goossens A, de Boule K, Dooms M, Degreef H. Imidazolidinyl urea dermatitis. *Contact Dermatitis* 1986;14: 322-4.
36. Storrs FJ, Bell DE. Allergic contact dermatitis to 2-bromo-2-nitropropane-1,3-diol in a hydrophilic ointment. *J Am Acad Dermatol* 1983;8:157-70.
37. Fisher AA. Cosmetic dermatitis part II. Reactions to some commonly used preservatives. *Cutis* 1980;26:136-7, 141-2, 147-8.
38. Malten KE, van Ketel WG, Nater JP, Liem DH. Reactions in selected patients to 22 fragrance materials. *Contact Dermatitis* 1984;11:1-10.
39. Devos SA, Constandt L, Tupker RA, Noz KC, Luckner GP, Bruynzeel DP, et al. Relevance of positive patch-test reactions to fragrance mix. *Dermatitis* 2008;19:43-7.
40. Rastogi SC, Menné T, Johansen JD. The composition of fine fragrances is changing. *Contact Dermatitis* 2003;48:130-2.
41. Larsen W, Nakayama H, Lindberg M, Fischer T, Elsner P, Burrows D, et al. Fragrance contact dermatitis: a worldwide multicenter investigation (part I). *Am J Contact Dermatitis* 1996;7:77-83.
42. Frosch PJ, Johansen JD, Menné T, Rastogi SC, Bruze M, Andersen KE, et al. Lyril is an important sensitizer in patients sensitive to fragrances. *Br J Dermatol* 1999;141:1076-83.

43. Frosch PJ, Pirker C, Rastogi SC, Andersen KE, Bruze M, Svedman C, et al. Patch testing with a new fragrance mix detects additional patients sensitive to perfumes and missed by the current fragrance mix. *Contact Dermatitis* 2005;52:207-15.
44. DeGroot AC, van Ginkel CJW, Weijland JW. Methylidibromoglutaronitrile (Euxyl K 400): an important "new" allergen in cosmetics. *J Am Acad Dermatol* 1996;35:743-7.
45. McFadden JP, Ross JS, Jones AB, Rycroft RJG, Smith HR, White IR. Increased rate of patch test reactivity to methylidibromoglutaronitrile. *Contact Dermatitis* 2000;42:54-5.
46. de Groot AC, de Cock PA, Coenraads PJ, van Ginkel CJW, Jagtman BA, van Joost T, et al. Methylidibromoglutaronitrile is an important contact allergen in The Netherlands. *Contact Dermatitis* 1996;34:118-20.
47. Marks JG Jr, Moss JN, Parno JR, Adams RM, Belsito DV, DeLeo VA, et al. Methylchloroisothiazolinone/methylisothiazolinone (Kathon CG) biocide: second United States multicenter study of human skin sensitization. *Am J Contact Dermatitis* 1993;4:87-9.
48. Wilkinson JD, Shaw S, Andersen KE, Brandao FM, Bruynzeel DP, Bruze M, et al. Monitoring levels of preservative sensitivity in Europe. A 10-year overview (1991-2000). *Contact Dermatitis* 2002;46:207-10.
49. Cashman AL, Warshaw EM. Parabens: a review of epidemiology, structure, allergenicity, and hormonal properties. *Dermatitis* 2005;16:57-66.
50. Rastogi SC, Schouten A, De Kruijf N, Weijland J. Contents of methyl-, ethyl-, propyl-, butyl- and benzylparaben in cosmetic products. *Contact Dermatitis* 1995;32:28-30.
51. Menne T, Hjorth N. Routine patch testing with paraben esters. *Contact Dermatitis* 1988;19:189-91.
52. Uter W, Lessmann H, Geier J, Schnuch A. Contact allergy to ingredients of hair cosmetics in female hairdressers and clients—an 8-year analysis of IVDK data. *Contact Dermatitis* 2003;49:236-40.
53. Moreau L, Sasseville D. Allergic contact dermatitis from cocamidopropyl betaine, cocamidoamine, 3-(dimethylamino)-propylamine, and oleamidopropyl dimethylamine: co-reactions or cross-reactions? *Dermatitis* 2004;15:146-9.
54. Pigatto PD, Bigardi AS, Cusano F. Contact dermatitis to cocamidopropylbetaine is caused by residual amines: relevance, clinical characteristics, and review of the literature. *Am J Contact Dermatitis* 1995;6:13-6.
55. McFadden JP, Ross JS, White IR, Basketter DA. Clinical allergy to cocamidopropyl betaine: reactivity to cocamidopropylamine and lack of reactivity to 3-dimethylaminopropylamine. *Contact Dermatitis* 2001;45:72-4.
56. Fowler JF, Fowler LM, Hunter JE. Allergy to cocamidopropyl betaine may be due to amidoamine: a patch test and product use test. *Contact Dermatitis* 1997;37:276-81.
57. Shaffer KK, Jaimes JP, Hordinsky MK, Zielke GR, Warshaw EM. Allergenicity and cross-reactivity of coconut oil derivatives: a double-blind randomized controlled pilot study. *Dermatitis* 2006;17:71-6.
58. Morrison LH, Storrs FJ. Persistence of an allergen in hair after glyceryl monothioglycolate-containing permanent wave solutions. *J Am Acad Dermatol* 1988;19:52-9.
59. Rietschel RL, Fowler JF, Fisher AA. *Fisher's contact dermatitis*. 5th ed. Philadelphia: PA: Lippincott Williams & Wilkins; 2001.
60. Tosti A, Melino M, Bardazzi F. Contact dermatitis due to glyceryl monothioglycolate. *Contact Dermatitis* 1988;19:71-2.
61. Engasser PG. Cosmetics and contact dermatitis. *Dermatol Clin* 1991;9:69-80.
62. Doooms-Gooens A, Degreef H, Luytens E. Dihydroabietyl alcohol (Abitol®). A sensitizer in mascara. *Contact Dermatitis* 1979;5:350-3.
63. Fisher AA. Allergic contact dermatitis to rosin (colophony) in eyeshadow and mascara. *Cutis* 1988;42:507-8.
64. Batta K, Bourke JK, Foulds IS. Allergic contact dermatitis from colophony in lipsticks. *Contact Dermatitis* 1997;36:171-2.
65. Fan W, Kinnunen T, Niinimäki A, Hannuksela M. Skin reactions to glycols used in dermatologic and cosmetic vehicles. *Am J Contact Dermatitis* 1991;2:181-3.
66. Wahlberg JE, Nilsson G. Skin irritancy from propylene glycol. *Acta Derm Venereol (Stockh)* 1984;64:286-90.
67. Willis CM, Stephens JM, Wilkinson JD. Experimentally induced irritant contact dermatitis: determination of optimum irritant concentrations. *Contact Dermatitis* 1988;18:20-4.
68. Zesch A. Skin irritation by topical drugs. *Derm Beruf Umwelt* 1983;31:74-8.
69. Andersen KE, Storrs FJ. Skin irritation caused by propylene glycols. *Hautarzt* 1982;33:12-4.
70. Frosch PJ, Pekar U, Enzmann H. Contact allergy to propylene glycol. Do we use the appropriate test concentration? *Dermatol Clin* 1990;8:111-3.
71. Lahti A, Poutianen A-M, Hannuksela M. Alcohol vehicles in tests for non-immunological immediate contact reactions. *Contact Dermatitis* 1993;29:22-5.
72. Hannuksela M, Salo H. The repeated open application test (ROAT). *Contact Dermatitis* 1986;14:221-7.
73. Funk JO, Maibach HI. Propylene glycol dermatitis: re-evaluation of an old problem. *Contact Dermatitis* 1994;31:236-41.
74. Kerre S. Allergic contact dermatitis to pentylene glycol in a cosmetic cream. *Contact Dermatitis* 2008;58:122-3.
75. Kuznetsov AV, Erlenkeuser-Uebelhoeer I, Thomas P. Contact allergy to propylene glycol and dodecyl gallate mimicking seborrheic dermatitis. *Contact Dermatitis* 2006;55:307-8.
76. Lee B, Warshaw EM. Lanolin allergy: a review of history, epidemiology, responsible allergens, and management. *Dermatitis* 2008;19:63-72.
77. Yokota M, Thong H-Y, Hoffman CA, Maibach HI. Allergic contact dermatitis caused by tosylamide formaldehyde resin in nail varnish: an old allergen that has not disappeared. *Contact Dermatitis* 2007;57:277.
78. Lidén C, Berg M, Färm G, Wrangsjö K. Nail varnish allergy with far-reaching consequences. *Br J Dermatol* 1993;128:57-62.
79. Thorne N. Nail varnish. *Br J Clin Pract* 1963;17:479-82.
80. Guin JD. Eyelid dermatitis: a report of 215 patients. *Contact Dermatitis* 2004;50:87-90.
81. Staines KS, Felix DH, Forsyth A. Desquamative gingivitis, sole manifestation of tosylamide/formaldehyde resin allergy. *Contact Dermatitis* 1998;39:90.
82. Fisher AA. Allergic sensitization of the skin and oral mucosa to acrylic denture materials. *JAMA* 1954;156:238.
83. Romaguera C, Vilaplana J, Grimalt F, Ferrando J. Contact sensitivity to meth(acrylates) in a limb prosthesis. *Am J Contact Dermatitis* 1990;1:183-5.
84. Draelos ZD. Nail cosmetic issues. *Dermatol Clin* 2000;18:675-83.
85. CFSAN/Office of Cosmetics and Colors. Methacrylate monomers in artificial nails. Available at: <http://www.cfsan.fda.gov/~dms/cos-nail.html#mono>. Accessed May 10, 2008.
86. Mowad C, Ferringer T. Allergic contact dermatitis from acrylates in artificial nails. *Dermatitis* 2004;15:51-3.
87. Teik-Jin Goon A, Bruze M, Zimerson E, Goh CL, Isaksson M. Contact allergy to acrylates/methacrylates in the acrylate and nail acrylics series in southern Sweden: simultaneous positive patch test reaction patterns and possible screening allergens. *Contact Dermatitis* 2007;57:21-7.

88. Lazarov A. Sensitization to acrylates is a common adverse reaction to artificial fingernails. *J Eur Acad Dermatol Venereol* 2007;21:169-74.
89. Rietschel RL. Experience with supplemental allergens in the diagnosis of contact dermatitis. *Cutis* 2000;65:27-30.
90. Koppula SV, Fellman JH, Storrs FJ. Screening allergens for acrylate dermatitis associated with artificial nails. *Am J Contact Dermatitis* 1995;6:78-85.
91. Perrenoud D, Homberger HP, Auderset PC, Emmenegger R, Frenk E, Saurat JH, et al. An epidemic outbreak of papular and follicular contact dermatitis to tocopheryl linoleate in cosmetics. Swiss Contact Dermatitis Research Group. *Dermatology* 1994;189:225-33.
92. Goldman MP, Rapaport M. Contact dermatitis to vitamin E oil. *J Am Acad Dermatol* 1986;14:133-4.
93. Bryld LE, Agner T, Menné T. Allergic contact dermatitis from 3-iodo-2-propynyl-butylcarbamate (IPBC)—an update. *Contact Dermatitis* 2001;44:276-8.
94. Pazzaglia M, Tosti A. Allergic contact dermatitis from 3-iodo-2-propynyl-butylcarbamate in a cosmetic cream. *Contact Dermatitis* 1999;41:290-304.
95. Badreshia S, Marks JG Jr. Iodopropynyl butylcarbamate. *Am J Contact Dermatitis* 2002;13:77-9.
96. Fisher AA. Allergic contact dermatitis (caused by rubber cosmetic sponges) simulating cosmetic dermatitis. *Cutis* 1993;51:320-1.
97. Uter W, Balzer C, Geier J, Frosch PJ, Schnuch A. Patch testing with patients' own cosmetics and toiletries—results of the IVDK, 1998-2002. *Contact Dermatitis* 2005;53:226-33.
98. Roed-Petersen J, Hjorth N. Contact dermatitis from antioxidants. *Br J Dermatol* 1976;94:233-41.
99. White IR, Lovell CR, Cronin E. Antioxidants in cosmetics. *Contact Dermatitis* 1984;11:265-7.
100. Giordano-Labadie F, Schwarze HP, Bazex J. Allergic contact dermatitis from octyl gallate in a lipstick. *Contact Dermatitis* 2000;42:51.
101. Wilson AG, White IR, Kirby JD. Allergic contact dermatitis from propyl gallate in lip balm. *Contact Dermatitis* 1989;20:145-6.
102. Cronin E. Lipstick dermatitis due to propyl gallate. *Contact Dermatitis* 1980;6:213.
103. Serra-Baldrich E, Puig LL, Gimenez Arnau A, Camarasa JG. Lipstick allergic contact dermatitis from gallates. *Contact Dermatitis* 1995;32:359-72.
104. Walgrave SE, Warsaw EM, Glesne LA. Allergic contact dermatitis to propolis. *Dermatitis* 2005;16:209-15.