

North American Contact Dermatitis Group Patch Test Results for 2007–2008

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Background: The North American Contact Dermatitis Group (NACDG) tests patients with suspected allergic contact dermatitis to a broad series of screening allergens and publishes periodic reports.

Objective: The aims of this study were to report the NACDG patch-testing results from January 1, 2007, to December 31, 2008, and to compare results to pooled test data from the previous 2 and 10 years to analyze trends in allergen sensitivity.

Methods and Materials: Standardized patch testing with 65 allergens was used at 13 centers in North America. χ^2 analysis was used for comparisons.

Results: A total of 5085 patients were tested; 11.8% (598) had an occupationally related skin condition, and 65.3% (3319) had at least 1 allergic patch test reaction, which is identical to the NACDG data from 2005 to 2006. The top 15 most frequently positive allergens were nickel sulfate (19.5%), *Myroxylon pereirae* (11.0%), neomycin (10.1%), fragrance mix I (9.4%), quaternium-15 (8.6%), cobalt chloride (8.4%), bacitracin (7.9%), formaldehyde (7.7%), methyldibromoglutaronitrile/ phenoxyethanol (5.5%), *p*-phenylenediamine (5.3%), propolis (4.9%), carba mix (4.5%), potassium dichromate (4.1%), fragrance mix II (3.6%), and methylchloroisothiazolinone/methylisothiazolinone (3.6%). There were significant increases in positivity rates to nickel, methylchloroisothiazolinone/methylisothiazolinone, and benzophenone-3. During the same period of study, there were significant decreases in positivity rates to neomycin, fragrance mix I, formaldehyde, thiuram mix, cinnamic aldehyde, propylene glycol, epoxy resin, diazolidinyl urea, amidoamine, ethylenediamine, benzocaine, *p*-tert-butylphenol formaldehyde resin, dimethylol dimethyl hydantoin, cocamidopropyl betaine, glutaraldehyde, mercaptobenzothiazole, tosylamide formaldehyde resin, budesonide, disperse blue 106, mercapto mix, and chloroxylonol. Twenty-four percent (1221) had a relevant positive reaction to a non-NACDG supplementary allergen; and 180 of these reactions were occupationally relevant.

Conclusions: Periodic analysis, surveillance, and publication of multicenter study data sets document trends in allergen reactivity incidence assessed in the patch test clinic setting and provide information on new allergens of relevance.

PATCH TESTING is an important tool in the diagnosis and evaluation of allergic contact dermatitis (ACD). The North American Contact Dermatitis Group (NACDG), composed of 14 dermatologists in the United States (12 members) and Canada (2 members), collects deidentified data and periodically reports the results of testing with a standardized series of allergens.^{1–10}

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Although many tested allergens have remained the same over the years, every 2 years, the allergen panel and individual allergens tested may vary, depending on new reports, emerging allergens, prior results, deletion of allergens as study period or performance for screening purposes mandate, or newly identified potential allergens of particular interest. For the 2007–2008 period, the NACDG screening tray consisted of 65 allergens. As compared with the previous cycle (2005–2006), 4 were dropped (ethylenemelamine formaldehyde resin 5% pet, dithiodimorpholine 1% pet, jasmine absolute 2% pet, and iodopropynyl butylcarbamate 0.1% pet), and 5 were added (propolis 10% pet, fragrance mix II 14% pet, hydroxyethyl methacrylate 2% pet, benzyl alcohol 1% pet, and desoximetasone 1% pet). Iodopropynyl butylcarbamate testing was continued at 0.5% in petrolatum.

The report summarizes patch testing data collected by the NACDG during 2007 to 2008 and compares results to pooled

test data from the previous 2 and 10 years to analyze trends in allergen sensitivity.

METHODS AND MATERIALS

Sixty-five allergens (Chemotechnique Diagnostics AB, Malmö, Sweden) were tested. Patch testing was performed with a standardized technique using Finn chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster Alpha AS, Vennesla, Norway).⁴ Patches remained in place for 48 hours. First and second patch test readings were performed at 48 hours and 72 to 168 hours, respectively, after initial test placement. Allergic patch test reactions were graded as +, ++, or +++ based on intensity of positive reactions manifested by erythematous papules, vesicles, and/or a spreading reaction sometimes with crusting and ulceration. A separate, final determination of allergic versus nonallergic reaction was also coded. Doubtful reactions (macular erythema) were generally coded as nonallergic reactions. If the clinical history or other positive reactions to the same allergen in a different vehicle or a cross-reacting substance were identified, however, the investigator had the discretion to make a final determination that the macular erythema represented an allergic reaction.

Deidentified patient characteristics that were recorded included age, sex, race, and presence or absence of personal atopy (hay fever/allergic rhinitis, asthma, atopic eczema). Up to 3 sites of dermatitis location could be entered; by convention, the first site of involvement was considered the most important (primary). The suspected exposure source was also coded using a 3-digit source code from the National Institute for Occupational Safety and Health.¹¹ Other collected data included 3-digit occupation and industry codes, which were determined by an occupational expert based on answers to a series of 7 standardized questions as previously published. Occupational relationship of each allergen reaction (yes/no) and the source of the allergen (3-digit National Institute for Occupational Safety and Health source code) were also recorded.

At the conclusion of testing, the investigators determined clinical relevance of a positive patch-test reaction by consideration of the patient's history and clinical findings.⁴ Relevance of a positive allergen was categorized into present, past, or unknown. Present relevance was further defined as either *definite* (use test with the suspected item resulted positive, or a patch test to the object or product resulted positive), *probable* (the allergen could be verified as present in known skin contactants, and clinical presentation was consistent), and *possible* (the patient was exposed to circumstances in which skin contact with materials known to contain the allergen was likely to occur).

Based on the history, physical examination, and patch testing results, the investigator recorded up to 3 final diagnoses, which included ACD, irritant contact dermatitis, atopic dermatitis, stasis dermatitis, nummular eczema, other dermatitis types, psoriasis, other dermatoses, seborrheic dermatitis, and pompholyx. If a patient had exposure to irritants deemed clinically relevant to the presenting

dermatitis, the relationship to occupation (yes vs no) and the source (3-digit code) of the irritant exposure were coded.¹¹

Relevant positive reactions to supplemental allergens not present on the NACDG standard series (yes/no), whether those allergens were deemed to be occupationally related (yes/no), and the source (3-digit code) of the nonstandard relevant allergen were also recorded. In cases where a positive patch test was seen to 1 or more supplemental allergens, the physician chose the exposure source believed most likely to be related to the presenting dermatitis.

One individual manually checked the data sheets for quality control. At a central location, data were manually entered into a computerized database (Microsoft Excel, 2003; Microsoft Corp, Redmond, WA) and checked for quality assurance. Descriptive statistics were performed using Microsoft Access (Microsoft Corp). Pearson χ^2 test and calculation of relative risk and confidence intervals comparing periods (current vs 2005–2006 and current vs 1996–2006) were performed using Java Stat software system: A Collaborative Statistical Web Application (www.stat.wvu.edu). A significance level of 0.05 was used for all analyses. Because this was an exploratory analysis, no adjustments for multiple comparisons were performed. Relative risk and confidence interval were included, in part because of variable population size in comparing current study period to the preceding 10 years.

Because statistical significance does not correlate with prevalence or impact on the population as a whole, a weighted relevance system put forth by Maouad et al¹² 10 years ago termed the significance-prevalence index number (SPIN) was used in evaluating level of confidence in allergen positivity and performance.^{12,13}

RESULTS

Patient Characteristics

A total of 5085 patients were tested between January 1, 2005, and December 31, 2006. Table 1 summarizes patient characteristics using the MOAHLFA index.^{14,15} The systematic application of these criteria allow optimal comparison of data sets between study years.¹⁰ Most patients were white (n = 4435, 87.2%). A history of hay fever and asthma was noted in 29.9% (n = 1521) and 14.4%

TABLE 1. MOAHLFA Index Data for NACDG 2007–2008 Data

Demographic Data, N = 5085	n	%
Male	1812	35.6
Occupationally related	598	11.8
Atopic dermatitis	1091	21.5
Hand*	1160	22.8
Leg*	199	3.9
Face*†	1317	25.9
Age >40 y	3539	69.6

*Primary site only, n = 4450.

†Site 1 for face is calculated by adding individually coded facial sites—face, lips, nose, eyelids, eyes.

(n = 731) of patients, respectively. Table 2 summarizes data on body site affected with dermatitis. The most common primary sites were hands, scattered/generalized pattern, and face.

Distribution of Dermatitis

Most of our patients exhibited dermatitis over hands, in scattered generalized fashion, and over the face (Table 2). Although the significance of the number is limited, this represents a change from the last 2-year data set reported, when scattered generalized represented the most common first site distribution tested.

Positive Reactions to NACDG Standard Allergens

Overall, 65.3% (2907) of patch-tested patients had at least 1 allergic patch test reaction. Table 3 summarizes the frequency of positive allergic reactions to the specific allergens. The most common allergens were nickel sulfate (19.5%), *Myroxylon pereirae* (11.0%), neomycin (10.1%), fragrance mix I (9.4%), quaternium-15 (8.6%), cobalt chloride (8.4%), bacitracin (7.9%), formaldehyde (7.7%), methylidibromoglutaronitrile/phenoxyethanol (5.5%), and *p*-phenylenediamine (5.3%). Definite relevance rates (positive patch test result and positive use or patch test to product with ingredient) were highest for benzyl alcohol (46.7%), benzophenone-3 (22.7%), propylene glycol (16.2%), tosylamide formaldehyde resin (16.0%), mercapto mix (15.6%), mixed dialkyl thioureas (14.9%), epoxy resin (12.8%), and tixocortol pivalate (12.4%).

TABLE 2. Dermatitis Distribution of NACDG Patch-Tested Patients, 2007 to 2008

Dermatitis Site	Site 1, N = 5085,* n (%)	Site 2, n = 2055, n (%)	Site 3, n = 748, n (%)
Hand	1160 (22.8)	161 (3.2)	40 (0.8)
Scattered generalized	1068 (21.0)	137 (2.7)	80 (1.6)
Face	714 (14.1)	224 (4.4)	57 (1.1)
Eyelids	393 (7.7)	74 (1.5)	22 (0.4)
Trunk	324 (6.4)	182 (3.6)	112 (2.2)
Arm	255 (5.0)	424 (8.3)	115 (2.3)
Leg	199 (3.9)	223 (4.4)	136 (2.7)
Scalp	158 (3.6)	66 (1.3)	27 (0.5)
Foot	171 (3.4)	154 (3.0)	21 (0.4)
Lips	184 (3.1)	36 (0.7)	7 (0.1)
Other	125 (2.5)	20 (0.4)	8 (0.2)
Anal/genital	100 (2.0)	19 (0.4)	12 (0.2)
Neck	79 (1.6)	297 (5.8)	91 (1.8)
Most exposed areas	57 (1.1)	8 (0.2)	8 (0.2)
Ears	34 (0.7)	7 (0.1)	8 (0.2)
Only under clothes	30 (0.6)	3 (0.1)	9 (0.2)
Eyes	4825 (0.5)	15 (0.3)	2 (0.0)
Erythroderma	2 (0.0)	1 (0.0)	0
Nose	1 (0.0)	3 (0.1)	0

No site was identified in 6 patients.

As compared with the previous test period (2005–2006), the frequency of positive patch test reactions to 3 allergens significantly increased in 2007 to 2008 (Table 3). Allergic reactions to methylchloroisothiazolinone/methylisothiazolinone, iodopropynyl butylcarbamate, and bisphenol F were significantly more common than in the prior 2-year cycle. Significantly lower frequency rates were noted to the following 10 allergens: fragrance mix I, quaternium-15, bacitracin, formaldehyde, cinnamic aldehyde, propylene glycol, benzocaine, cocamidopropyl betaine, budesonide, and disperse blue 106.

As compared with pooled data from the prior 10 years (1996–2006), 3 allergens were statistically more frequently positive in 2007 to 2008: nickel, methylchloroisothiazolinone/methylisothiazolinone, and benzophenone-3 (Table 3). Positive rates for 21 allergens were significantly lower in 2005 to 2006 than in the previous 10 years: neomycin, fragrance mix I, formaldehyde, thiuram mix, cinnamic aldehyde, propylene glycol, epoxy resin, diazolidinyl urea, amidoamine, ethylenediamine dihydrochloride, benzocaine, *p*-tert-butylphenol formaldehyde resin, dimethylol dimethyl (DMDM) hydantoin, cocamidopropyl betaine, glutaraldehyde, mercaptobenzothiazole, tosylamide formaldehyde resin, budesonide, disperse blue 106, mercapto mix, and chloroxylenol.

Multiple Contact Allergens

There were 1766 patients with negative patch test results to the standard series and 1088 with only 1 reactive allergen. On the other side of the spectrum, there were 562 (11.4%) patients with 5 or more reactive allergens and 60 (1.2%) with 10 or more positive patch tests.

Other Relevant Allergens

Twenty-four percent (1221) of tested patients had a relevant positive patch test result to a supplementary allergen not on the NACDG standard series; 3.5% (180/5085) had a positive supplementary allergen that was occupationally related. The most frequent sources for these supplementary allergens included cosmetics and beauty aids (n = 260), clothing (n = 84), jewelry (n = 80), and moisturizers and lotions (n = 73).

Relevance of Allergens Tested

Definite relevance was highest for propylene glycol (16.2%) for antigens that tested positive more frequently than 1%. Tixocortol pivalate (12.4%), lanolin alcohol (11.3%), and epoxy resin (11.3%) were also frequently identified as definite positives. Allergens most frequently identified as relevant to past dermatitis include neomycin (54.5%), bacitracin (39.9%), glyceryl thioglycolate (34.1%), ethylenediamine dihydrochloride (32.5%), nickel (25.5%), colophony (25.5%), and benzocaine (23.5%). Significance-prevalence index number calculation, in general, did not result in major rank order differences in the top allergens, although carba mix did increase in rank of significance/prevalence/relevance to number 7, whereas cobalt dropped out of the top 10 (Table 4).

Final Diagnoses

Table 5 summarizes the final diagnoses of patch-tested patients; 2534 patients (49.9%) had a final diagnosis that included ACD. The second and third most common diagnoses were “other eczematous dermatitis” (15.8%) and atopic dermatitis (9.7%), and irritant contact dermatitis (8.0%) and “other dermatosis” were both cited as primary diagnoses in 8% to 10% of cases.

DISCUSSION

The top 10 most frequently positive allergens during 2007 to 2008 were metals (nickel and cobalt), topical antibiotics (neomycin and bacitracin), fragrances (*Myroxylon pereirae* and fragrance mix I), and preservatives (quaternium-15, formaldehyde, and methyl dibromoglutaronitrile/phenoxyethanol, and paraphenylenediamine); although there were minor changes in the order of these top performers, the inhabitants of this list of frequent allergen were unchanged from the 2005–2006 study period. The frequency of positivity for formaldehyde and the formaldehyde-releasing biocide quaternium-15 were significantly lower compared with the previous 2 years and at their lowest positivity rate in the past decade.

Of the top 10 most frequently positive allergens, nickel was the only allergen with a consistent trend (increasing positivity over the last 10 years).¹⁶ The frequency of positive patch tests to nickel in the populations tested by the NACDG continued to rise over time and was the most frequently positive allergen at 19.5%; the combined definite and probable relevance rate for nickel was 28%, whereas past relevance was nearly as common (25.2%). A call for US regulation comparable with that already in place in the European Union has been forwarded and is supported by the current data.^{17,18}

Fragrances (fragrance mix I, followed closely by *Myroxylon pereirae*) still represented, along with preservatives, the most common causes of ACD reported in patients with cosmetic allergy. A new fragrance-screening mix, the fragrance mix II, was added to the NACDG standard screening tray in the 2007–2008 study period and has immediately entered the list of top 20 allergens at number 14 (3.6% positivity rate). Although definite relevance ascribed to these 3 fragrance allergens was very low (1.1%–1.5%), combined probable and possible relevance was very high at 90.1% for fragrance mix II, 87% for fragrance mix I, and 85.6% for *Myroxylon pereirae*. With fragrances being such an important causative agent for cosmetic allergy, the addition of a new screening tool is welcome.¹⁹ Coreactivity between these fragrance-screening materials, as well as the frequency and probability of missing dermatitis causation with failure to test to all 3 moieties, needs further clarification and study.

In addition to the fragrance mix II, newcomers to the top 20 allergens for 2007 to 2008 compared with the previous 2-year cycle include propolis at number 11 (4.9% positivity) and iodopropyl butylcarbamate and long-time standard tray resident colophony at rank order 19th and 20th, respectively.²⁰ Iodopropyl butylcarbamate is increasingly used in the United States as a cosmetic preservative and therefore was added to the NACDG standard tray

in the 2005–2006 study period. The increasing frequency of positivity from 2.4% to 3.1% over the 2 study periods achieved statistical significance. The role of concentration of allergen used in a proportion of these positive reactions and the relevance of positive patch test results need further study for clarification. Propolis registered a stellar debut at 4.9% positivity rate.²¹ Dropping out of the top 20 list of positive allergens were the fragrance screen cinnamic aldehyde (matching the decrease of fragrance mix I and *Myroxylon pereirae*), propylene glycol, and imidazolidinyl urea, which all showed statistically significant decreases compared with the past study period. The relevance of positive reactions to the fragrance mixes in light of the complex nature of scent and perfume formulation is another area where further study is necessary. Tixocortol pivalate has also decreased in frequency, although this difference was not statistically significant.

No universal agreement exists regarding the definition of polysensitization. Using the suggested guidelines forwarded by Carlsen et al²² (contact allergy to ≥ 3 allergens), 26.3% of our population qualified as polysensitized, which places the frequency in the range reported by other investigators in hospital patch test populations.

On the other end of the positivity spectrum, 18 of the 65 allergens tested exhibited a positivity rate of 1% or less; ongoing experience has been deemed appropriate and necessary for most of these less frequent performers. Three allergens were removed from the NACDG screening tray this period, including ethyleneurea-melamine formaldehyde resin, jasmine absolute, and dithiodimorpholine. The latter allergen was added to the standard tray during the 2005–2006 study period for screening and monitoring for shoe dermatitis causation; positivity rate of 1.8% was not felt to require ongoing inclusion because most people with foot dermatitis are additionally screened to a battery of allergens found in shoes, which includes dithiodimorpholine. Iodopropynyl butylcarbamate 0.1% was also dropped from the tray, but it was still included at the higher 0.5% concentration.

Early in 2012, the TRUE TEST screening series panel 3 has received Food and Drug Administration approval for the addition of 7 new allergens. This includes 2 of the NACDG current series top 10 performers (bacitracin and methyl dibromoglutaronitrile/phenoxyethanol), as well as Bronopol, disperse blue 106, hydrocortisone-17-butyrate, parthenolide, and gold sodium thiosulfate. These additions bring the total number of allergens that are tested with this medium to 36 and are expected to increase the sensitivity of this battery for screening ACD.²³ Bacitracin is particularly important in light of the high patch test positivity rates, the widespread use of bacitracin-containing antibacterial ointments, and the direct-to-consumer marketing blitz by antibiotic ointment and bandage manufacturers with the goal of increased public use to facilitate healing; this is particularly important in light of clinical studies showing no benefits with respect to infection rates or healing outcomes over simple petrolatum.²⁴ MDBGN/PE has been widely used both domestically and abroad for preservation of cosmetics, pharmaceutical preparations, toiletries, household and car cleaning products, adhesives, paints, and metal working fluids with an aqueous

TABLE 3. Frequencies of Positive Reactions to NACDG Standard Allergens

Patch Test Allergen	2007–2008						2007–2008 vs 2005–2006 <i>P</i> [IRR (95% CI)]
	n*	Positive Reaction, %	Relevance, %				
			Definite	Probable	Possible	Past	
Nickel sulfate 2.5% pet.	5045	19.5	2.4	24.6	33.4	25.2	0.5287 [1.0269 (0.9454–1.1155)]
<i>Myroxylon pereirae</i> 25% pet.	5083	11.0	1.3	32.9	52.7	3.4	0.1714 [0.9249 (0.8270–1.0344)]
Neomycin 20% pet.	5072	10.1	3.7	16.0	12.1	54.5	0.9753 [0.9981 (0.8848–1.1259)]
Fragrance mix I 8% pet.	5079	9.4	1.5	33.5	53.5	2.3	0.0062 [0.8466 (0.7514–0.9539)]
Quaternium-15 2% pet.	5081	8.6	3.2	32.6	52.5	3.2	0.0046 [0.8349 (0.7370–0.9458)]
Cobalt chloride 1% pet.	5080	8.2	0.7	12.9	33.2	18.6	0.7369 [0.9773 (0.8549–1.1173)]
Bacitracin 20% pet.	5077	7.9	6.0	23.9	13.7	39.9	0.0238 [0.8589 (0.7529–0.9800)]
Formaldehyde 1% aq.	5081	7.7	2.3	35.5	52.7	1.3	0.0215 [0.8551 (0.7483–0.9772)]
Methyldibromoglutaronitrile 2.5% pet	5083	5.5	2.9	25.1	47.3	4.3	0.5496 [0.951 (0.8068–1.1210)]
<i>p</i> -Phenylenediamine 1% pet.	5074	5.3	6.4	35.6	16.1	17.6	0.4948 [1.0622 (0.8932–1.2632)]
Propolis 10% pet.	5067	4.9	2.8	16.5	40.3	6.5	NC
Carba mix 3% pet.	5080	4.5	7.4	39.4	36.4	4.3	0.1375 [1.1577 (0.9542–1.4046)]
Potassium dichromate 0.25% pet.	5081	4.1	2.9	23.6	26.8	8.7	0.0902 [0.8511 (0.7062–1.0256)]
Fragrance mix II 14% pet.	5071	3.6	1.1	38.5	51.6	2.7	NC
Methylchlorisothiazolinone/ methylisothiazolinone 100 ppm. aq.	5075	3.6	5.5	44.8	40.4	2.7	0.026 [1.2903 (1.0309–1.6149)]
Thiuram mix 1% pet.	5079	3.4	8.1	35.8	35.8	6.4	0.1904 [0.8708 (0.7078–1.0712)]
Diazolidinyl urea 1% pet.	5082	3.1	3.8	28.8	58.3	1.9	0.1153 [0.8415 (0.6789–1.0431)]
2-Bromo-2-nitropropane-1,3-diol 0.5% pet.	5081	3.1	0.6	12.5	53.8	1.9	0.4179 [0.9133 (0.7334–1.1374)]
Iodopropynyl butylcarbamate 0.5% pet.	5082	3.1	3.2	31.0	48.7	1.3	0.0337 [1.3008 (1.0204–1.65820)]
Colophony 20% pet.	5083	2.8	5.7	18.4	33.3	25.5	0.0675 [1.2677 (0.9831–1.6346)]
DMDM hydantoin 1% pet.	5082	2.7	7.4	31.1	53.3	1.5	0.7499 [1.0406 (0.8148–1.3289)]
Tixocortol-21-pivalate 1% pet.	5083	2.5	12.4	51.9	17.4	15.5	0.5283 [0.9238 (0.7222–1.1818)]
Imidazolidinyl urea 2% pet.	5082	2.4	2.5	29.8	58.7	4.1	0.1247 [0.8259 (0.6469–1.0544)]
Cinnamic aldehyde 1% pet.	5079	2.4	1.7	36.4	50.4	0.8	0.0405 [0.7776 (0.6113–0.9892)]
Hydroxyethyl methacrylate 2% pet.	5065	2.4	5.6	37.9	19.4	21.8	NC
Lanolin alcohol 30% pet.	5079	2.1	11.3	40.6	38.7	2.8	0.2779 [1.1721 (0.8798–1.5616)]
Propylene glycol 30% aq.	5083	2.1	16.2	43.8	28.6	1.9	0.0125 [0.7244 (0.8798–1.5616)]
Glyceryl thioglycolate 1% pet.	5073	1.8	1.1	9.9	9.9	34.1	0.4802 [1.1172 (0.6953–1.2715)]
Epoxy resin 1% pet.	5075	1.7	12.8	29.1	10.5	14.0	0.6892 [0.9403 (0.6953–1.2715)]
Diazolidinyl urea 1% aq.	5081	1.7	2.3	43.0	47.7	1.2	0.0797 [0.7734 (0.5801–1.0309)]
Amidoamine 0.1% aq.	5081	1.6	2.4	24.1	62.7	2.4	0.13 [0.7942 (0.5894–1.0702)]
Imidazolidinyl urea 2% aq.	5082	1.5	2.7	32.4	54.1	2.7	0.4294 [1.1466 (0.8169–1.6099)]
Ethylenediamine 1% pet.	5078	1.5	3.9	9.1	14.3	32.5	0.137 [0.7918 (0.5821–1.0770)]
Bisphenol F 1% pet.	5042	1.4	11.1	25.0	11.1	15.3	<0.0001 [6.9047 (3.4552–13.7982)]
Compositae mix 6% pet.	5080	1.4	5.7	22.9	35.7	1.4	0.3859 [1.1693 (0.8211–1.6651)]
Tea tree oil 5% pet.	5078	1.4	5.7	31.4	40.0	5.7	0.9993 [1.0002 (0.7131–1.4028)]
Ylang ylang 2% pet.	5080	1.4	1.4	15.3	55.6	5.6	0.6445 [0.9249 (0.6640–1.2884)]
Benzocaine 5% pet.	5082	1.3	11.8	5.9	26.5	23.5	0.0216 [0.6874 (0.4992–0.9465)]
<i>p</i> -tert-Butylphenol formaldehyde resin 1% pet.	5080	1.2	1.6	16.1	37.1	17.7	0.6475 [0.9201 (0.6437–1.3150)]
Ethyl acrylate 0.1% pet.	5076	1.2	11.3	40.3	19.4	14.5	0.1585 [1.3303 (0.8947–1.9781)]
Methyl methacrylate 2% pet.	5077	1.2	8.3	45.0	10.0	18.3	0.3349 [1.2089 (0.8221–1.7776)]
Cocamide DEA 0.5% pet.	5082	1.2	6.5	38.7	50.0	1.6	0.3317 [1.2104 (0.8232–1.7798)]
Paraben mix 12% pet.	5082	1.1	10.3	46.6	31.0	6.9	0.6737 [0.9229 (0.6353–1.3408)]
DMDM hydantoin 1% aq.	5082	1.1	11.1	44.4	37.0	1.9	0.1931 [0.7879 (0.5502–1.1283)]
Dibucaine 2.5% pet.	5074	1.1	7.3	9.1	21.8	27.3	0.9873 [0.9969 (0.6809–1.4596)]
Cocamidopropylbetaine 1% aq.	5082	1.1	10.3	41.4	43.1	0.0	0.0044 [0.611 (0.4353–0.8577)]
Glutaraldehyde 1% pet.	5072	1.1	0.0	9.3	29.6	14.8	0.4016 [0.8548 (0.5925–1.2333)]
Mercaptobenzothiazole 1% pet.	5083	1.0	7.8	45.1	35.3	3.9	0.6069 [1.1142 (0.7380–1.6823)]
Black rubber mix 0.6% pet.	5082	1.0	2.0	26.0	22.0	12.0	0.9492 [1.0131 (0.6783–1.5133)]

1996–2006										
2005–2006		2003–2004		2001–2002		1998–2000		1996–1998		2007–2008 vs 1996–2006
Positive, %	n	Positive, %	n	Positive, %	n	Positive, %	n	Positive, %	n	P [IRR (95% CI)]
19.0	4428	18.7	5129	16.7	4901	16.2	5827	14.2	3429	<0.0001 [1.1423 (1.0729–1.2162)]
11.9	4449	10.6	5140	11.6	4910	12.3	5832	11.8	3439	0.1935 [0.9947 (0.8182–0.9786)]
10.0	4439	10.6	5137	11.6	4904	11.5	5822	13.1	3436	0.015 [0.8948 (0.8182–0.9786)]
11.5	4439	9.1	5140	10.4	4896	10.9	5802	11.7	4095	0.0121 [0.8879 (0.8091–0.9743)]
10.3	4446	8.9	5139	9.3	4910	9.2	5832	9.0	3436	0.1018 [0.9215 (0.8354–1.0163)]
8.4	4429	8.4	5141	7.4	4899	7.6	5811	9.0	4095	0.8239 [1.0116 (0.9142–1.1193)]
9.2	4437	7.9	5143	7.9	4900	9.2	5812	8.7	4103	0.1136 [0.9206 (0.8309–1.0199)]
9.0	4445	8.7	5142	8.4	4909	9.2	5830	9.3	3440	0.0059 [0.8647 (0.7797–0.9591)]
5.8	4437	6.1	5140	5.8	4897	6.0	5778	7.6	4054	0.0546 [0.8856 (0.7824–1.0024)]
5.0	4428	4.7	5136	4.8	4903	4.9	5831	6.0	3441	0.3872 [1.0585 (0.9305–1.2040)]
NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NC
3.9	4443	4.0	5142	4.9	4908	4.8	5829	7.3	3437	0.3142 [0.9313 (0.8108–1.0697)]
4.8	4449	4.3	5142	4.3	4913	5.8	5833	2.8	3440	0.1607 [0.9013 (0.7794–1.0422)]
NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NC
2.8	4437	2.2	5137	2.3	4895	2.7	5792	2.9	4083	<0.0001 [1.4068 (1.1964–1.6541)]
3.9	4443	4.6	5141	4.5	4907	4.7	5830	6.9	3435	<0.0001 [0.7059 (0.6031–0.8263)]
3.7	4439	3.5	5139	3.1	4897	3.0	5802	3.7	4096	0.3411 [0.9218 (0.7796–1.0900)]
3.4	4435	2.3	5140	3.3	4897	3.1	5800	3.2	4094	0.8083 [1.0211 (0.8623–1.2092)]
2.4	4435	NT	NT	NT	NT	NT	NT	NT	NT	NC
2.2	4447	2.8	5143	2.6	4908	2.5	5833	2.0	3443	0.169 [1.1353 (0.9475–1.3604)]
2.6	4439	2.3	5140	2.8	4897	2.0	5801	2.6	4093	0.2657 [1.1097 (0.9238–1.3331)]
2.7	4437	2.7	5142	3.0	4901	2.7	5807	2.3	4100	0.4311 [0.9274 (0.7688–1.1188)]
2.9	4438	2.9	5139	3.0	4897	2.5	5784	3.2	4094	0.0609 [0.834 (0.6897–1.0083)]
3.1	4435	2.4	5138	NT	NT	3.7	4735	2.8	3443	0.0269 [0.0803 (0.6612–0.9752)]
NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NC
1.8	4451	2.2	5145	2.2	4908	2.4	5834	3.3	3442	0.3268 [0.9027 (0.7356–1.1077)]
2.9	4439	3.3	5143	4.2	4899	3.7	5804	3.8	4095	<0.0001 [0.5859 (0.4804–0.7144)]
1.6	4422	1.1	5134	1.9	4897	2.0	5800	1.9	4094	0.6412 [1.0549 (0.8425–1.3210)]
1.8	4439	1.8	5143	2.3	4909	2.7	5832	1.9	3439	0.0444 [0.7927 (0.6320–0.9942)]
2.2	4433	2.5	5141	3.2	4897	2.6	5778	2.9	4094	0.0001 [0.6319 (0.5057–0.7896)]
2.0	4434	1.7	5139	2.3	4897	3.4	5773	—	—	0.0006 [0.6654 (0.5270–0.8402)]
1.3	4447	1.6	5143	1.8	4909	2.0	5821	2.5	4101	0.1007 [0.817 (0.6419–1.0400)]
1.9	4444	2.4	5143	2.8	4909	2.5	5831	2.6	3439	0.0001 [0.6143 (0.4846–0.7788)]
0.2	4413	0.1	5128	NT	NT	NT	NT	NT	NT	NC
1.2	4434	1.3	5138	1.0	4887	NT	NT	NT	NT	0.2031 [1.1958 (0.9080–1.5748)]
1.4	4435	0.9	5137	NT	NT	NT	NT	NT	NT	NC
1.5	4434	1.2	5137	1.1	4893	NT	NT	NT	NT	0.2031 [1.1958 (0.9080–1.5748)]
1.9	4446	1.7	5145	1.7	4908	1.7	5833	2.0	3444	0.0175 [0.7317 (0.5655–0.9468)]
1.3	4444	1.8	5142	1.9	4911	1.6	5832	1.8	3442	0.0142 [0.7154 (0.5473–0.9350)]
0.9	4428	1.1	5141	1.3	4899	1.3	5802	1.3	4095	0.9256 [1.0132 (0.7699–1.3332)]
1.0	4427	1.6	5143	1.4	4900	1.4	5812	1.6	4099	0.2623 [0.8565 (0.6534–1.1229)]
1.0	4437	1.1	5137	1.3	4888	NT	NT	NT	NT	0.7333 [1.0521 (0.7857–1.4088)]
1.2	4439	1.1	5142	0.6	4898	1.0	5803	1.7	4096	0.9668 [1.0061 (0.7555–1.3399)]
1.4	4433	1.4	5141	2.2	4897	1.6	5767	1.9	4093	0.0024 [0.6508 (0.4931–0.8589)]
1.1	4426	1.0	5137	0.9	4891	NT	NT	NT	NT	0.5134 [1.1078 (0.8149–1.5059)]
1.8	4436	1.8	5137	2.8	4887	NT	NT	NT	NT	<0.0001 [0.5157 (0.3886–0.6842)]
1.3	4413	1.2	5135	1.4	4878	1.9	5802	2.6	4094	0.0042 [0.6664 (0.5047–0.8798)]
0.9	4442	1.3	5143	0.9	4907	2.0	5834	1.8	3440	0.0284 [0.7204 (0.5373–0.9659)]
1.0	4442	1.0	5141	1.0	4908	NT	NT	NT	NT	0.9516 [1.0099 (0.7350–1.3877)]

TABLE 3. (Continued)

Patch Test Allergen	n*	2007–2008					2007–2008 vs 2005–2006 <i>P</i> [RR (95% CI)]
		Positive Reaction, %	Relevance, %			Past	
			Definite	Probable	Possible		
DI alpha-tocopherol 100%	5082	1.0	6.1	53.1	34.7	2.0	0.1108 [1.4357 (0.9205–2.2394)]
Tosylamide formaldehyde resin 10% pet.	5078	1.0	16.0	32.0	22.0	14.0	0.1662 [0.7678 (0.5282–1.1161)]
Mixed dialkyl thioureas 1% pet.	5081	0.9	14.9	29.8	23.4	12.8	0.6588 [0.9115 (0.6041–1.3753)]
Benzophenone-3 3% pet.	5083	0.9	22.7	36.4	22.7	6.8	0.2641 [1.295 (0.8227–2.0384)]
Budesonide .01% pet.	5083	0.9	4.4	35.6	37.8	11.1	0.0072 [0.5996 (0.4129–0.8708)]
Disperse blue 106 1% pet.	5080	0.9	0.0	29.2	37.5	4.2	<0.0001 [0.4309 (0.3034–0.6121)]
Lidocaine 15% pet.	5077	0.9	11.4	6.8	20.5	22.7	0.3282 [0.819 (0.5488–1.2222)]
Mercapto mix 1% pet.	5082	0.6	15.6	37.5	37.5	3.1	0.1989 [0.7287 (0.4496–1.1810)]
Sesquiterpene lactone mix 0.1% pet.	5078	0.6	3.1	37.5	43.8	0.0	0.5083 [0.8446 (0.5121–1.3931)]
Clobetasol-17-propionate 1% pet.	5082	0.6	7.1	28.6	17.9	14.3	0.2416 [0.748 (0.4601–1.2161)]
Dimethyldihydroxyethyleneurea 4.5% aq.	5078	0.6	3.4	27.6	44.8	3.4	0.9022 [0.968 (0.5764–1.6256)]
Hydrocortisone-17-butyrate 1% pet.	4937	0.5	0.0	38.5	30.8	15.4	0.5073 [0.8323 (0.4838–1.4319)]
Chloroxylenol 1% pet.	5083	0.4	0.0	28.6	42.9	4.8	0.4528 [0.7934 (0.4336–1.4517)]
Benzyl alcohol 1% pet.	5083	0.4	46.7	27.8	27.8	0.0	NC
Triamcinolone acetonide 1% pet.	5081	0.3	0.0	42.9	28.6	14.3	0.8936 [1.0078 (0.4801–2.1158)]
Desoximetasone 1% pet.	5070	0.2	0.0	0.0	70.0	10.0	NC

component. The positivity rate in our data series over the past 12 years has been a robust 7.6% to 5.5%; the latter rate over the past 2 years represents a slight diminution, which did not achieve statistical significance. This trend may represent variation in exposure because the cosmetics industry recognizes the potential problem and reactively uses a lower concentration of MDBGN/PE in the final product and also uses alternative preservation systems, notably combinations of biocides and the new preservative iodopropynyl butylcarbamate.²⁵ In Europe, MDBGN/PE has been banned in both leave-on and rinse-off products.²⁶ The positivity rates for this allergen, along with methylchloroisothiazolinone/methylisothiazolinone and formaldehyde, have stabilized after achieving “epidemic” status, largely based on the reaction of industry to identified allergens occupationally and nonoccupationally identified by contact dermatitis investigators.²⁷

Of the other 5 new allergens in the TRUE TEST Panel III, NACDG positivity rate span from a low 0.9% for disperse blue 106 and an even lower 0.5% for hydrocortisone 17-butyrate to Bronopol (2-bromo-2-nitropropane-1,3-diol, BNPD) positivity at 3.1% in the current reported series. The NACDG does not currently test to parthenolide separately, although it is present in the composita mix at 0.1% (positivity rate for this mix is currently relatively low at 1.4%); parthenolide is tentatively slated for addition to the 2013–2014 NACDG series. Thimerosal was removed from the NACDG standard series years ago because of the remarkably low relevance ascribed to positive reactions; many group members

continue to test to thimerosal as a screen for mercury salt sensitization in their supplemental trays. Gold, the final new allergen in the third T.R.U.E Test Panel, was eliminated from routine testing by the NACDG after completion of the 2003–2004 study period. All members continue to test for gold allergy in selected situations, especially when jewelry allergy is suspected or when dermatitis is present on the eyelids or face; many again test this routinely as part of their supplemental tray. Gold patch test reactions may be strong and may persist for long periods (occasionally weeks to months), creating a difficult situation for patient and investigator alike, particularly in light of this allergen’s controversial and generally low relevance, casting doubt in the patient’s mind about the value of other positive reactions. Aimed testing with gold, rather than routine screening, has been deemed the optimal approach.²⁸

Of the top 30 most frequently positive NACDG allergens for 2007 to 2008, the following 10 allergens are not currently available for testing and identification using the TRUE TEST panels: propolis (4.9% positive), fragrance mix II (3.6% positive), iodopropynyl butylcarbamate (3.1% positive), DMDM hydantoin (2.7% positive), cinnamic aldehyde (2.4% positive), hydroxyethyl methacrylate (2.4% positive), and propylene glycol (2.1% positive). Several deserve specific mention. Propolis, a botanical used in a variety of cosmetic/cosmeceutical/naturopathic/homeopathic products, was a new addition to the NACDG standard series with numerous case reports and series of contact sensitivity recently published. In the current series, only 19.3% of those with positive patch test reactions were

1996–2006										
2005–2006		2003–2004		2001–2002		1998–2000		1996–1998		2007–2008 vs 1996–2006
Positive, %	n	Positive, %	n	Positive, %	n	Positive, %	n	Positive, %	n	<i>P</i> [RR (95% CI)]
0.7	4435	1.1	5139	0.5	4874	NT	NT	NT	NT	0.1247 [1.2946 (0.9311–1.7999)]
1.3	4434	1.7	5139	1.6	4897	1.3	5800	1.5	4097	0.01 [0.6817 (0.5092–0.9126)]
1.0	4430	1.0	5140	0.8	4897	1.1	5807	1.3	4098	0.4195 [0.8791 (0.6429–1.2020)]
0.7	4436	0.7	5144	0.6	4899	0.6	5800	NT	NT	0.0482 [1.4009 (1.0026–1.9574)]
1.5	4439	1.8	5141	1.1	4515	1.4	5806	1.2	4098	0.0041 [0.6388 (0.4702–0.8678)]
2.1	4426	1.9	5136	3.0	4888	NT	NT	NT	NT	<0.0001 [0.1439 (0.1060–0.1954)]
1.1	4429	0.6	5137	0.7	4892	NT	NT	NT	NT	0.4242 [1.1491 (0.8172–1.6158)]
0.8	4444	0.9	5143	0.7	4908	1.3	5834	1.8	3439	0.002 [0.5524 (0.3788–0.8055)]
0.7	4432	0.6	5140	0.6	4896	0.9	5800	0.7	4095	0.3664 [0.8368 (0.5685–1.2318)]
0.8	4435	0.7	5140	NT	NT	NT	NT	NT	NT	NC
0.6	4424	0.8	5138	1.1	4889	NT	NT	NT	NT	0.0789 [0.6998 (0.4700–1.0420)]
0.6	4438	0.5	5140	0.5	4874	NT	NT	NT	NT	0.8247 [0.9504 (0.6060–1.4906)]
0.5	4436	0.7	5141	0.6	4898	0.8	5800	1.0	4093	0.0144 [0.551 (0.3472–0.8744)]
										NC
0.3	4438	0.3	5141	—	—	—	—	—	—	NC
										NC

*Number tested to specific allergen.

aq, aqueous; CI, confidence interval; DEA, diethanolamine; MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; NC, not calculated; NT, not tested; pet, petrolatum; RR, risk ratio.

deemed by the investigator to be of definite or probable relevance; however, in absolute numbers, this translates to 50 patients, which represents 1 of the largest series reported to date.²⁴ The other missing allergens of importance include propylene glycol, an humectant and stabilizer in numerous products including topical medicaments; DMDM hydantoin, a formaldehyde-releasing biocide that may not be detected by formaldehyde screening; and iodopropynyl butylcarbamate, a new preservative and allergen with increasing use that, despite the name, goes undetected by screening with the carba mix.²⁹ A new to the NACDG series, hydroxyethyl methacrylate is a chemical used in UV inks, adhesives, lacquers, dental materials, and increasingly in artificial nails; a brisk 43.5% definite or probable relevance was seen in the current 2-year study.³⁰ The sensitivity and cross-reactivity of this allergen with the other acrylates on the standard tray has been investigated extensively in the past and will be further clarified with ongoing NACDG experience.³¹

In all, the NACDG recorded a total of 9,424 positive patch test reactions using its standard tray of 65 screening allergens. Removing positive reactions to the 30 allergens shared in common between our series and the T.R.U.E test battery of 3 panels (35 allergens and 1 petrolatum control), it is calculated that screening with the TRUE TEST allergen series of 3 complete panels alone would have missed 2563 (27.2%) of the relevant positive reactions identified in the current series. TRUE TEST allergens caine mix, quinoline mix, gold, parthenolide, and thimerosal were not screened by the NACDG

in the current study period, whereas parthenolide is present at 0.1% in compositae mix.

An ongoing strength of these data is the estimate of relevance assessed to a given allergen (Table 3). Patients are more likely to benefit from avoidance of identified allergens that are deemed relevant to their actual problem and may be demonstrated in the products they use at home or in the workplace. Although definite relevance is uncommon because it requires testing to an actual product or item containing the allergen, probable relevance requires that the allergen is identified as an ingredient or component of a contactant used by the patient; possible relevance is ascribed when the patient is exposed to circumstances in which skin contact with the type of materials known to contain the allergen occur. Just as confidence in allergen positivity is proportional to strength of reaction, confidence in relevance would of necessity be highest with definite relevance, high with probable relevance, and much less certain with possible relevance.

The finding of definite relevance being highest for propylene glycol is a figure somewhat higher than that reported in a retrospective analysis of NACDG data by Warshaw et al,³² where 12.8% of patients were deemed to have definite relevance; this allergen is frequently seen in cosmetics and rarely appears to be relevant occupationally.

Another method of data assessment obtained by selective weighting of definite/probable/possible relevance (the SPIN calculation)

TABLE 4. Significance-Prevalence Index Number

Allergen	SPIN	Allergen	SPIN
Nickel sulfate 2.5% pet.	577	Paraben mix 12% pet.	56
<i>Myroxylon perei</i> 25% pet.	444	Tea tree oil 5% pet.	55
Fragrance mix I 8% pet.	388	DL alpha-tocopherol 100%	53
Quaternium-15 2% pet.	361	Amidoamine 0.1% aq.	52
Formaldehyde 1% aq.	332	Methyl methacrylate 2% pet.	50
Bacitracin 20% pet.	208	Mercaptobenzothiazole 1% pet.	49
Carba mix 3% pet.	205	Benzophenone-3 3% pet.	49
Methyldibromoglutaronitrile 2.5% pet	193	Lidocaine 15% pet.	48
<i>p</i> -Phenylenediamine 1% pet.	187	Compositae mix 6% pet.	46
Neomycin 20% pet.	185	Bisphenol F 1% pet.	44
Methylchlorisothiazolinone/methylisothiazolinone	174	Tosylamide formaldehyde resin 10% pet.	44
Cobalt chloride 1% pet.	166	Ylang ylang 2% pet.	42
Fragrance mix II 14% pet.	157	Mixed dialkyl thioureas 1% pet.	38
Thiuram mix 1% pet.	148	Budesonide .01% pet.	36
Propolis 10% pet.	132	Mercapto mix 1% pet.	32
Diazolidinyl urea 1% pet.	131	Benzocaine 5% pet.	31
Tixocortol-21-pivalate 1% pet.	131	Benzyl alcohol 1% pet.	30
Iodopropynyl butylcarbamate 0.5% pet.	125	<i>p</i> - <i>tert</i> -butylphenol formaldehyde resin 1% pet.	29
DMDM hydantoin 1% pet.	123	Ethyl acrylate 0.1% pet.	29
Propylene glycol 30% aq.	114	Disperse blue 106 1% pet.	29
Potassium dichromate 0.25% pet.	112	Black rubber mix 0.6% pet.	27
Lanolin alcohol 30% pet.	107	Sesquiterpene lactone mix 0.1% pet.	25
Cinnamic aldehyde 1% pet.	102	Dibucaine 2.5% pet.	23
Imidazolidinyl urea 2% pet.	100	Ethylenediamine 1% pet.	22
Hydroxyethyl methacrylate 2% pet.	89	Dimethyldihydroxyethyleneurea 4.5% aq.	22
2-Bromo-2-nitropropane-1,3-diol 0.5% pet.	83	Glyceryl thioglycolate 1% pet.	20
Colophony 20% pet.	81	Clobetasol-17- propionate 1% pet.	19
Diazolidinyl urea 1% aq.	79	Hydrocortisone-17-butyrate 1% pet.	18
Imidazolidinyl urea 2% aq.	63	Glutaraldehyde 1% pet.	17
Epoxy resin 1% pet.	60	Chloroxylenol 1% pet.	13
Cocamide DEA 0.5% pet.	58	Triamcinolone acetonide 1% pet.	11
DMDM hydantoin 1% aq.	58	Desoximetasone 1% pet.	5
Cocamidopropylbetaine 1% aq.	57		

SPIN is a weighted calculation depending upon degree of certainty ascribed to relevance. Calculation: $(\text{Proportion of Population Allergic}) \times (1 \times R_{\text{definite}} + 0.66 \times R_{\text{possible}} + 0.33 \times R_{\text{probable}}) \times 100$.

was undertaken to obtain a firmer understanding and perspective of allergen importance.^{11,12} The calculation of SPIN index for the current data set is presented in Table 5.

Surprisingly little variation was seen in the most frequent responders between their overall positivity and their sensitivity-prevalence index number. Longitudinal study after elimination of exposure to a positive allergen followed by improvement or resolution of a dermatitis would more firmly confirm definite or probable relevance and raise a hapten's SPIN index. Specificity confirmation and statistical analysis of such data would be complicated because of the number of variables, particularly when multiple reactive allergens are identified (≥ 2 positive reactions were seen in 55.7% of our population). However, confirmation of clinical relevance over time is often not possible because of limited follow-up in this largely referral population.

Although most tested patients had at least 1 positive patch test reaction, approximately one third (34.7%) had no positive reactions.

Some of these patients with no standard series allergens reaction are still classified as ACD; this may occur on the basis of positivity of nonstandard allergen in other series or individually tested, due to positivity to patient supplied products, or compound allergy. Much more frequently, more specific diagnosis not related to contact allergy is ascribed, such as irritant contact or atopic dermatitis or a combination of alternative diagnoses, which best explain or categorize a particular patient's dermatitis. In some cases, however, a specific diagnostic "label" for the clinical presentation that resulted in patch testing, even if afforded follow-up, is impossible. Of the patients, 18.9% were given a dermatitis type code of "other dermatitis"; prognosis in this group is typically poor, and treatment options are limited with variable outcomes and higher risk profile therapeutically.^{33,34} Although the use of an expanded screening series of allergens for patch testing to identify positive relevant allergens is useful for many patients with dermatitis, this other group of patients with negative patch test results and categorized as having

TABLE 5. Final Diagnoses After Patch Testing, 2007–2008 Data (N = 5085)

Diagnosis	Primary Diagnosis, n = 5085,* n (%)	Second Diagnosis, n = 1420, n (%)	Third Diagnosis, n = 136, n (%)
ACD	2534 (49.9)	444 (8.7)	41 (0.8)
Other dermatitis	802 (15.8)	194 (3.8)	16 (0.3)
Atopic dermatitis	495 (9.7)	189 (3.7)	18 (0.4)
Irritant contact dermatitis	407 (8.0)	295 (5.8)	19 (0.4)
Other dermatoses	371 (7.3)	112 (2.2)	14 (0.3)
Psoriasis	183 (3.6)	69 (1.4)	14 (0.3)
Nummular dermatitis	92 (1.8)	22 (0.4)	3 (0.1)
Seborrheic dermatosis	65 (1.3)	34 (0.7)	3 (0.1)
Photo dermatitis	48 (0.9)	20 (0.4)	3 (0.1)
Stasis dermatitis	29 (0.6)	18 (0.4)	1 (0.0)
Pompholyx	24 (0.5)	5 (0.1)	1 (0.0)
Contact urticaria	24 (0.5)	13 (0.3)	2 (0.0)

*Five cases have no primary diagnosis assigned.

“other dermatitis,” or nonspecific endogenous eczema, would be appropriate for further study. Casting the net further with additional appropriate series, photopatch testing, biopsy and laboratory studies, and therapeutic trial can further clarify a subset population of these patients.

This study has several limitations, many of which stem from the highly selected patient population tested by the NACDG. Some of these patients have already been tested by their primary or regional dermatologist, and thus, there would be of necessity a degree of selection bias at play. The lack of follow-up ability over time inherent in a heavily represented tertiary referral population is a limitation in the designation of positive allergen relevance. Several of our members perform patch testing at a much higher frequency than others in the group; the European experience with respect to variability of positivity based on geographic, population, and exposure differences as well as testing variation would suggest that this may skew data to a minor degree. More uniform standards used across geographic barriers would likely remove multiple confounding factors in drawing definitive conclusions.³⁴ Although exposure variation may be higher in Europe than in North America, 2 of our busier members are Canadian, and a degree of exposure differences is inevitable. Another limitation is that only 1 positive supplemental allergen can be recorded on the data collection form. If a patient is positive to more than 1 supplemental allergen, neither the number of reactions nor the allergen source is captured. This likely underestimates the potential value of patch testing with supplemental allergens or the patient's own products. The source (ie, toiletry, shoe, cooling fluid) of this supplemental allergen is identified but not the allergen itself; thus, the ability to summarize data on supplemental allergens, or use of additional screening series, is curtailed. There is variability in reading/scoring traditions between different contact dermatitis groups and between contact dermatitis specialists within a group. The application of reaction indices and positivity ratios to sweeping statements regarding allergen trends may be of limited value without universal standardization of both allergen sources and reading parameters.³⁵ Similarly, the data

presented represent a highly selected group of dermatitis patients, and findings in this subset of individuals should not be extrapolated to the general population as a whole. Population-based epidemiologic studies have been appropriately suggested to be a prerequisite in the surveillance of national and international contact allergy “epidemics.”^{36,37} All of these factors have the potential to impact our data and thus both results and conclusions but do not affect the use of this information to both practitioners and investigators if these factors are kept in mind; control of these variables is both problematic and ongoing.

As a final disclaimer, a word of caution is given regarding the application of statistical significance to disease prevalence and to confirmation or lack thereof of the null hypothesis being true. The current statistically laden data analysis is provided in hopes of further confirmation of trends already reported, the announcement of possible new trends to be further studied, and the comparison of current screening patch test results to those of previous study results; further conclusions boldly drawn from the information provided may not be supported over the course of ongoing study.³⁸

CONCLUSIONS

The reporting of patch test results to screening series is useful in individual patient management, is vital in allergen monitoring, and allows the study of epidemiologic variation stemming from geographic and cultural diversity. Comparison of published series originating in North America, Europe, and Asia gives us a better understanding of emerging allergens in different locales and patient population differences, albeit an imperfect correlation due to the differences in the allergens composing these series. These reports, in conjunction with reports on emerging allergens through limited series and case reports, help optimize our efficacy in the diagnosis of ACD and in helping our patients. This important diagnostic tool remains the only viable way to confirm ACD. A screening standard series and the patient's own products should be

tested in all patients in whom contact allergy is suspected, with the addition of extended allergen series based on historical, occupational, and presentation characteristics.

Increasing and decreasing prevalence of positive patch tests over time are common. Changes in usage and exposure patterns may in part account for variation in allergen positivity. Large data sets such as this are useful to assess changing trends in positive allergen frequency, which may reflect formulation changes or new patterns of use or exposure for a given allergen.

Subset analysis of the NACDG data set has been useful in determining the most frequent allergens in patients with specific dermatitis distribution,^{39–43} occupation,⁴⁴ exposure source,^{45–48} and differences in demographic subpopulations.^{49,50} Patch test frequency data from large database sources are discussed and analyzed by groups interested in contact allergy, industry, and government regulators. Such discussions may contribute to enhanced product safety, as apparent in the MDBGN/PE experience.²⁵ The NACDG database summary information provided over the years has been a useful reference to dermatologists and others involved in patch testing. By providing guidance regarding the most frequent and relevant allergens in North America, these data continue to have an important role in patient diagnosis and management. Application of a universal standard for patch testing would not only facilitate more definitive statements regarding allergy prevalence and trends in sensitization but also provide both interesting and enlightening data regarding differences in geographic allergen exposure and population immunoreactivity.³⁵ Until that time, the reporting and comparison of data in North America, Europe, and worldwide of necessity must serve as an imperfect but useful assay of such differences.^{51–60}

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