Patch-Test Results of the North American Contact Dermatitis Group 2005–2006

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<u>Background</u>: The North American Contact Dermatitis Group (NACDG) tests patients who have suspected allergic contact dermatitis with a broad series of screening allergens, and publishes periodic reports of its data.

<u>Objective</u>: To report the NACDG patch-test results from January 1, 2005, to December 31, 2006, and to compare results to pooled test data from the previous 10 years.

<u>Methods</u>: Standardized patch testing with 65 allergens was used at 13 centers in North America. Chi-square statistics were utilized for comparisons with previous NACDG data.

<u>Results:</u> NACDG patch-tested 4,454 patients; 12.3% (557) had an occupation-related skin condition, and 65.3% (2,907) had at least one allergic patch-test reaction. The 15 most frequently positive allergens were nickel sulfate (19.0%), *Myroxilon pereirae* (balsam of Peru, 11.9%), fragrance mix I (11.5%), quaternium-15 (10.3%), neomycin (10.0%), bacitracin (9.2%), formaldehyde (9.0%), cobalt chloride (8.4%), methyldibromoglutaronitrile/phenoxyethanol (5.8%), p-phenylenediamine (5.0%), potassium dichromate (4.8%), carba mix (3.9%), thiuram mix (3.9%), diazolidinylurea (3.7%), and 2-bromo-2-nitropropane-1,3-diol (3.4%). As compared to the 1994–2004 data, there were significant increases in rates of positivity to nickel, quaternium-15, potassium dichromate, lidocaine, and tea tree oil. Of patch-tested patients, 22.9% (1,019) had a relevant positive reaction to a supplementary allergen; 4.9% (219) had an occupationally relevant positive reaction to a supplementary allergen.

<u>Conclusion</u>: Nickel has been the most frequently positive allergen detected by the NACDG; rates significantlyincreased in the current study period and most reactions were clinically relevant. Other common allergens were topical antibiotics, preservatives, fragrance mix I and paraphenylenediamine. Testing with an expanded allergen series and supplementary allergens enhances detection of relevant positive allergens.

P ATCH TESTING is an important tool in the diagnosis of allergic contact dermatitis (ACD). The North American Contact Dermatitis Group (NACDG) is composed of 13 dermatologists in the United States (11 members) and Canada (2 members) who collect deidentified data and periodically report the results of testing with a standardized series of allergens.¹⁻⁹ While many tested allergens remain the same over the years, specific

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test allergens may vary slightly every 2 years, depending on new reports, emerging allergens, prior results, or allergens of particular interest. For the 2005–2006 period, the NACDG screening tray consisted of 65 allergens. As compared to the previous cycle (from 2003 to 2004), two antigens were dropped (sodium gold thiosulfate 0.5% in petrolatum [pet] and tetracaine 1% pet) and two were added (iodopropynyl butyl carbamate 0.5% pet and dithiomorpholine 1% pet).

The purpose of this report is to summarize patch-test data collected by the NACDG during the 2005–2006 period.

Methods and Materials

Sixty-five allergens (Chemotechnique Diagnostics AB, Malmö, Sweden) were tested by the 13 members of the NACDG in 2005 and 2006. Patch testing was performed with a standardized technique using Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster Alpharma A/S, Vennesla, Norway).

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Patches were left in place for 48 hours. First and second patch-test readings were performed at 48 to 72 hours and 72 to 168 hours, respectively, after initial patch-test placement. Allergic patch-test reactions were graded as +, ++, or +++, based on the intensity of positive reactions manifested by erythematous papules, vesicles, or a spreading reaction (sometimes with crusting and ulceration). Doubtful reactions (macular erythema) were generally coded as nonallergic reactions. If the clinical history suggested relevance, or if other positive reactions to the same allergen but in a different vehicle were found, or if a cross-reacting substance was identified, the investigator had the discretion to make the final determination that the macular erythema represented an allergic reaction. Irritant and allergic reactions were differentiated by each investigator, who considered the morphology and timing of the reaction at each reading.

De-identified patient characteristics that were recorded included age, sex, race, and presence or absence of personal atopy (hay fever or allergic rhinitis, asthma, eczema). Up to three sites of dermatitis could be entered; by convention, the first site of involvement was considered the most important (primary) site. The suspected source of exposure for each patch-test-positive allergen was also coded with a three-digit source code. Other collected data included occupation and industry, which were determined by an occupational expert on the basis of answers to five standardized questions.¹⁰ The occupational relationship of allergens and irritants (yes or no), relevant irritants (yes or no), and the source of the irritant (indicated by a threedigit source code) were also recorded.

At the conclusion of patch testing, the investigators determined the clinical relevance of a positive patch-test reaction by considering the patient's history and clinical findings. The relevance of a positive allergen was categorized as present, past, or unknown. Present relevance was further defined as definite (the result of a use test with the suspected item was positive, or a patch-test reaction to the object or product was positive), probable (the allergen could be verified as present in known skin contactants, and clinical presentation was consistent), or possible (the patient was exposed to circumstances in which skin contact with materials known to contain the allergen was likely to occur). On the basis of history, physical examination, and patch-test results, the investigator recorded up to three final diagnoses, which could include ACD, irritant contact dermatitis, atopic dermatitis, stasis dermatitis, nummular eczema, other types of dermatitis, psoriasis, other dermatoses, seborrheic dermatitis, and pompholyx. If a patient had been exposed to irritants

deemed clinically relevant to the presenting dermatitis, the source of the irritant exposure was coded with a three-digit source code.

Other relevant positive reactions to allergens not on the NACDG standard series (yes or no), whether those allergens were occupation related (yes or no), and the source of the nonstandard relevant allergen were also recorded. In cases in which a positive patch-test reaction to one or more supplemental allergens was seen, the physician chose the allergen thought to be most likely 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 (*Access 2003*, Microsoft Corporation, Redmond, WA) and checked for quality assurance. Descriptive statistics were performed with Microsoft *Access*. The Pearson chi-square test and calculation of relative risk and confidence intervals comparing time periods (current vs 2003–2004 period and current vs 1994–2004 period) were performed with *JavaStat* software (Department of Statistics, West Virginia University; Morgantown, WV). A significance level of 0.05 was used for all analyses. Because this was an exploratory analysis, no adjustments for multiple comparisons were made.

Results

Patient Characteristics

The NACDG patch-tested 4,454 patients between January 1, 2005, and December 31, 2006. Table 1 summarizes patient characteristics according to the MOAHLFA (male, occupation related, atopic dermatitis, hand, leg, face, age > 40 years) index.¹¹ Most patients were Caucasians (n = 3,894 [87.4%]); the remainder were African

Table 1. MOAHLFA Index Data for NACDG Data, 2005 to 2006

Demographic Data (N = 4,454)	n	%
Male	1,667	37.4
Occupation related	557	12.5
Atopic dermatitis	960	21.6
Hand*	1,137	25.5
Leg*	205	4.6
Face ^{*†}	1,083	24.3
Age > 40 yr	3,145	70.6

*Primary site only, n = 4,450.

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

Americans (n = 252 [5.7%]), Asians (n = 170 [3.8%]), Hispanics (n = 97 [2.2%]), and persons of other ethnicities (n = 41 [0.9%]). A history of hay fever and a history of asthma, respectively, were noted in 31% (n =1,379) and 15.3% (n = 683) of patients. Table 2 summarizes data on body sites affected with dermatitis. The most common primary sites were hands, face, and scattered/generalized areas.

Positive Reactions to NACDG Standard Allergens

Overall, 65.3% (2,907) of patch-tested patients had at least one allergic patch-test reaction. Table 3 summarizes the frequency of positive allergic reactions to the NACDG standard allergens. The 10 most common allergens were nickel, *Myroxilon pereirae* (balsam of Peru), fragrance mix I, quaternium-15, neomycin, bacitracin, formaldehyde, cobalt chloride, methyldibromoglutaronitrile, and p-phenylenediamine. Definite relevance (positive patch-test reaction and positive-use or patch-test reaction to the product with the ingredient) was most common for benzophenone-3, paraben mix, mercaptobenzothiazole, mixed dialkyl thioureas, black rubber mix, and tixocortol pivalate.

As compared to the previous test period (2003 to 2004), the frequency of positive patch-test reactions to nine antigens significantly increased in the 2005–2006 period (see Table 3). Allergic reactions to quaternium-15,

Myroxilon pereirae (balsam of Peru), bacitracin, cinnamic aldehyde, fragrance mix I, 2-bromo-2-nitropropane-1,3-diol, glyceryl monothioglycolate, lidocaine, and tea tree oil were at least 1.16 times as common in the 2005–2006 period than in the prior 2-year cycle. Significantly lower frequency rates were noted to the following three allergens: p-tert-butylphenol formaldehyde resin, dl- α -tocopherol, and methyl methacrylate.

As compared to pooled data from the prior 10 years (1994 to 2004), five allergens were statistically more frequently positive in the 2005–2006 period when compared to the prior 10-year cycle: quaternium-15, potassium dichromate, nickel, lidocaine, and tea tree oil (see Table 3). Positive rates for the following 17 allergens were significantly lower from 2005 to 2006 than in the previous 10 years: mercaptobenzothiazole, imidazolidinylurea 2% aqueous (aq), lanolin, carba mix, neomycin, thiuram mix, ethylenediamine, p-tert-butylphenol formaldehyde resin, mercapto mix, chloroxylenol, diazolidinylurea aq, ethyleneurea/melamine formaldehyde resin, dl- α -tocopherol, ethyl acrylate, methyl methacrylate, dimethylol dihydroxy-ethyleneurea, and glutaraldehyde.

Other Relevant Allergens

Of tested patients, 22.9% (1,019) had a relevant positive patch-test reaction to a supplementary allergen not on the

Table 2. Demographics of NACDG Patch-Tested Patients, 2005 to 2006

Dermatitis Site	Site 1 (n = $4,450$)*	Site 2	Site 3
Hand	1,137 (25.5%)	145 (3.3%)	41 (0.9%)
Face	620 (13.9%)	196 (4.4%)	23 (0.5%)
Scattered/generalized	832 (18.7%)	85 (1.9%)	40 (0.9%)
Arm	237 (5.3%)	379 (8.5%)	95 (2.1%)
Trunk	234 (5.3%)	180 (4.0%)	138 (3.1%)
Leg	205 (4.6%)	193 (4.3%)	115 (2.6%)
Eyelids	308 (6.9%)	56 (1.3%)	12 (0.3%)
Foot	176 (4.0%)	179 (4.0%)	23 (0.5%)
Neck	84 (1.9%)	219 (4.9%)	68 (1.5%)
Scalp	136 (3.1%)	67 (1.5%)	19 (0.4%)
Lips	135 (3.0%)	34 (0.8%)	7 (0.2%)
Other	117 (2.6%)	30 (0.7%)	8 (0.2%)
Anal/genital	62 (1.4%)	28 (0.6%)	5 (0.1%)
Only under clothes	52 (1.2%)	9 (0.2%)	0 (0.0%)
Ears	30 (0.7%)	27 (0.6%)	11 (0.3%)
Most-exposed areas	46 (1.0%)	8 (0.2%)	8 (0.2%)
Eyes	48 (1.1%)	14 (0.3%)	2 (0.1%)
Erythroderma	9 (0.2%)	1 (0.1%)	0 (0.0%)
Nose	5 (0.1%)	3 (0.1%)	0 (0.0%)

*No site was identified in 4 patients.

			200.	5-2006							16	94-2004			
		ositive		Relevan	ce (%)		2005–2006 vs 2003–2004	2003-	-2004	2001-	-2002	1998–2000	1996–1998	1994–1996	2005–2006 vs 1994–2004 v
	I.	eaction					p Value	Pos		Pos		Pos	Pos	Pos	Value [RR
Patch-Test Allergen	×N	(%)	Definite	Probable	Possible	Past	[RR (95% CI)]	(%)	u	(%)	u	u (%)	u (%)	u (%)	(95% CI)]
Nickel sulfate 2.5% pet	4,428	19.0	1.4	20.3	35.0	28.3	.7129 [1.02 (0.93–1.10)]	18.7	5,129	16.7	4,901	16.2 5,827	14.2 3,429	14.3 3,108	$< 0001 [1.16]{(1.09-1.25)}$
<i>Myroxilon pereirae</i> (balsam of Peru) 25% pet	4,449	11.9	1.3	33.0	53.0	2.7	(1.00-1.26)	10.6	5,140	11.6	4,910	12.3 5,832	11.8 3,439	10.4 3,112	.3651 [1.04 (0.95–1.14)]
Fragrance mix I 8% pet	4,439	11.5	2.0	29.4	54.3	4.3	.0001[1.26 (1.12–1.42)]	9.1	5,140	10.4	4,896	10.9 5,802	11.7 4,095	14.0 3,082	(0.96-1.15)
Quaternium-15 2% pet	4,446	10.3	3.9	34.5	50.7	3.9	(1.02-1.31)	8.9	5,139	9.3	4,910	9.2 5,832	9.0 3,436	9.2 3,110	.0135 [1.13 (1.03-1.24)]
Neomycin 20% pet	4,439	10.0	2.3	10.4	15.3	56.9	(0.84-1.06)	10.6	5,137	11.6	4,904	11.5 5,822	13.1 3,436	11.6 3,104	.0025 [0.86 (0.79-0.95)]
Bacitracin 20% pet	4,437	9.2	5.4	15.2	18.6	42.5	.0228 [1.17 (1.02–1.33)]	7.9	5,143	7.9	4,900	9.2 5,812	8.7 4,103	9.1 3,079	.1484 [1.08 (0.97 - 1.19)]
Formaldehyde 1% aq	4,445	9.0	1.3	34.2	55.3	2.3	(0.91-1.18)	8.7	5,142	8.4	4,909	9.2 5,830	9.3 3,440	9.2 3,111	.8743 [1.01] (0.91-1.12)]
Cobalt chloride 1% pet	4,429	8.4	0.8	8.3	38.8	21.9	$.9946 \ [0.46 (0.43 - 0.50)]$	8.4	5,141	7.4	4,899	7.6 5,811	9.0 4,095	8.0 3,087	$.4231 \ [1.05 (0.94-1.16)]$
Methyldibromo- glutaronitrile 2.5% pet	4,437	5.8	3.9	27.0	44.0	3.9	(0.81-1.11)	6.1	5,140	5.8	4,897	6.0 5,778	7.6 4,054		(0.81-1.05)
para-Phenylenediamine 1% pet	4,428	5.0	4.1	34.2	17.6	22.5	$.4971 \ [1.06 (0.89 - 1.27)]$	4.7	5,136	4.8	4,903	4.9 5,831	6.0 3,441	6.8 3,111	.4575 [0.95 (0.82-1.09)]
Potassium dichromate 0.25% pet	4,449	4.8	4.2	12.7	33.8	9.4	(0.93-1.34)	4.3	5,142	4.3	4,913	5.8 5,833	2.8 3,440	2.0 3,106	.0433 [1.16 (1.00-1.34)]
Carba mix 3% pet	4,443	3.9	9.2	29.3	43.7	4.6	.7781 [0.97 (0.80 - 1.18)]	4.0	5,142	4.9	4,908	4.8 5,829	7.3 3,437	5.7 3,115	.0004 [0.76 (0.65-0.89)]
Thiuram mix 1% pet	4,443	3.9	9.2	34.7	36.4	11.6	$.0924 \ [0.85 \ (0.70 - 1.03)]$	4.6	5,141	4.5	4,907	4.7 5,830	6.9 3,435	6.8 3,115	.0001 [0.74 (0.63 - 0.87)]
Diazolidinylurea 1% pet	4,439	3.7	6.1	37.0	49.7	1.8	.6148 [1.06 (0.86 - 1.30)]	3.5	5,139	3.1	4,897	3.0 5,802	3.7 4,096	3.9 3,085	(0.93-1.29)
2-Bromo-2- nitropropane-1,3-diol 0.5% pet	4,435	3.4	2.0	17.2	47.0	6.0	.0011 [1.48 (1.17-1.88)]	2.3	5,140	3.3	4,897	3.1 5,800	3.2 4,094	2.3 3,074	.0558 [1.19 (1.00-1.41)]

Table 3. Frequencies of Positive Reactions to NACDG Standard Allergens

Continued
3.
Table

			2005	2006							19	94–2004				
	Ц	ositive		Relevana	ce (%)		2005–2006 vs 2003–2004	2003-	-2004	2001-	2002	1998–2000	1-9661	98 199.	4–1996	2005-2006 vs 1994-2004 n
	R	eaction					p Value	Pos		Pos		Pos	Pos	Pos		Value [RR
Patch-Test Allergen	N*	(%)	Definite	Probable	Possible	Past	[RR (95% CI)]	(%)	u	(%)	u	n (%)	(%) r	(%)	u	(95% CI)]
Cinnamic aldehyde	4,435	3.1	1.5	33.8	50.0	2.9	.0369 [1.29	2.4	5,138			3.7 4,735	2.8 3,4	43 2.4	3,112	.4226 [1.08
1% pet							(1.02 - 1.64)									(0.90 - 1.30)
Imidazolidinylurea	4,438	2.9	4.7	45.3	43.0	2.3	.983 [1.00	2.9	5,139	3.0	4,897	2.5 5,784	3.2 4,0	94 3.1	3,080	.9827 [1.00
2% pet							(0.80 - 1.26)									(0.83 - 1.21)
Propylene glycol	4,439	2.9	7.9	37.0	42.5	1.6	.2622 [0.88	3.3	5,143	4.2	4,899	3.7 5,804	3.8 4,0	95 1.1	3,077	98.0] 6660.
30% aq							(0.70 - 1.10)]									(0.71 - 1.03)
MCI/MI 100 ppm aq	4,437	2.8	6.5	37.4	40.7	4.9	.0617 [1.27	2.2	5,137	2.3	4,895	2.7 5,792	2.9 4,0	83 3.0	3,075	.4126 [1.08
							(0.99 - 1.63)									(0.90 - 1.31)
Tixocortol-21-pivalate	4,437	2.7	12.5	39.2	24.2	15.8	.9969 [1.00]	2.7	5,142	3.0	4,901	2.7 5,807	2.3 4,1	00 2.3	3,091	.8028 [1.25
1% pet							(0.79 - 1.27)]									(0.85 - 1.24)]
DMDM hydantoin	4,439	2.6	4.3	41.0	51.3	1.7	.3501 [1.13	2.3	5,140	2.8	4,897	2.0 5,801	2.6 4,0	93 2.3	3,082	.4155 [1.09
1% pet							(0.88 - 1.45)									(0.89 - 1.32)
Iodopropynyl butyl carbamate 0.5 pet	4,435	2.4	0.9	22.4	51.4	0.0	ΓN		I							LN
Colophony 20% pet	4,447	2.2	4.1	15.5	30.9	22.7	.0634 [0.79	2.8	5,143	2.6	4,908	2.5 5,833	2.0 3,4	43 2.6	3,113	.2051 [0.87
•							(0.61 - 1.01)]									(0.71 - 1.08)]
Diazolidinylurea 1% aq	4,433	2.2	4.1	46.9	42.9	1.0	.3384 [0.88	2.5	5,141	3.2	4,897	2.6 5,778	2.9 4,0	94 3.7	3,060	.0103 [0.76
•							(0.68 - 1.14)									(0.62 - 0.94)
Ethyleneurea/melamine-	4,426	2.1	1.1	25.3	45.1	4.4	.7376 [1.05	2.0	5,140	2.3	4,897	5.0 5,799	7.2 4,0	95 5.0	3,071	<.0001 [0.51
formaldehyde 5% pet							(0.80 - 1.38)]									(0.41 - 0.63)
Disperse Blue 106	4,426	2.1	8.6	20.4	35.5	7.5	.501 [1.10	1.9	5,136	3.0	4,888					.2216 [0.86
1% pet							(0.83 - 1.46)]									(0.68 - 1.09)
Amidoamine 0.1% aq	4,434	2.0	2.3	31.0	55.2	2.3	.2537 [1.19	1.7	5,139	2.3	4,897	3.4 5,773				.0555 $[0.80$
							(0.89 - 1.59)]									(0.64 - 1.01)
Benzocaine 5% pet	4,446	1.9	7.2	10.8	10.8	33.7	.4641 [1.12	1.7	5,145	1.7	4,908	1.7 5,833	2.0 3,4	44 2.6	3,112	.9361 [1.01
							(0.83 - 1.50)]									(0.80 - 1.27)]
Ethylenediamine	4,444	1.9	1.2	9.4	16.5	23.5	.0921 [0.79	2.4	5,143	2.8	4,909	2.5 5,831	2.6 3,4	39 2.9	3,113	.0048 [0.72
1% pet							(0.60 - 1.04)									(0.58 - 0.91)
Lanolin alcohol	4,451	1.8	3.7	42.7	46.3	2.4	.165 [0.82	2.2	5,145	2.2	4,908	2.4 5,834	3.3 3,4	42 3.3	3,114	.0021 [0.70
30% pet							(0.62 - 1.09)]									(0.55-0.88)
Epoxy resin 1% pet	4,439	1.8	6.4	24.4	24.4	15.4	.9822 [1.00	1.8	5,143	2.3	4,909	2.7 5,832	1.9 3,4	39 2.2	3,114	.0829 [0.81
							(0.74 - 1.34)]									(0.64 - 1.03)

			2005								19	94–2004				I	
	4	ositive		Relevan	ce (%)		2005–2006 vs 2003–2004	2003-	-2004	2001-	2002	1998–20	00 13	3661–966	1994–1	966	2005-2006 vs 1994-2004 n
	R	eaction					p Value	Pos		Pos		Pos	P_{-}	SC	Pos		Value [RR
Patch-Test Allergen	N*	(%)	Definite	Probable	Possible	Past	[RR (95% CI)]	(%)	u	(%)	u	(%) n	6)	6) n	(%)	n	(95% CI)]
Dithiomorpholine 1% pet	4,408	1.8	1.2	13.6	37.0	7.4	NT		I	I	I	I	1		I	I	NT
Cocamidopropyl betaine	4,436	1.8	1.3	30.4	59.5	2.5	.9634 [1.01	1.8	5,137	2.8	4,887		I				.0651 [0.79
1% aq							(0.75 - 1.35)]										[0.61 - 1.02)]
Glyceryl thioglycolate 1% pet	4,422	1.6	1.4	16.9	9.6	33.8	.0284 [1.47 (1.04 - 2.08)]	1.1	5,134	1.9	4,897	2.0 5,8	00	.9 4,094	2.0 3,	,075	.4691 [0.91
Budesonide 0.01% pet	4,435	1.5	9.2	13.8	44.6	21.5	.7405 [0.95	1.6	5,142				1				.7405 [0.95
							(0.69 - 1.30)										[0.69 - 1.30]
Budesonide 0.1% pet	4,439	1.5	7.7	18.5	44.6	20.0	.2538 [0.83	1.8	5,141	1.1	4,901	1.4 5,8	06 1	.2 4,098	1.1 1,	,678	.4517 [1.11
Ylang ylang 2% pet	4,434	1.5	4.6	10.8	73.8	1.5	(0.61 - 1.14)] .1982 $[1.25$	1.2	5,137	1.1	4,893		1				[0.85 - 1.44)] .0698 $[1.32]$
- 							(0.89 - 1.76)										[0.98-1.78]]
DMDM hydantoin	4,433	1.4	3.1	39.1	50.0	3.1	.9937 [1.00	1.4	5,141	2.2	4,897	1.6 5,7	67 1	.9 4,093	2.1 3,	,064	.0592 [0.78
1% aq							(0.71 - 1.40)										[0.60 - 1.01)]
Tea tree oil 5% pet	4,435	1.4	8.2	27.9	36.1	9.8	.0203 [1.56	0.9	5,137								.0203 [1.56
							(1.07 - 2.28)]										(1.07 - 2.28)
Imidazolidinylurea	4,447	1.3	3.3	41.7	43.3	0.0	.2374 [0.82	1.6	5,143	1.8	4,909	2.0 5,8	21	.5 4,101	2.6 3,	,101	.0011 [0.64
2% aq							(0.59 - 1.14)										[0.49-0.84)]
p-tert-Butylphenol	4,444	1.3	1.7	13.8	48.3	6.9	.0483 [0.72	1.8	5,142	1.9	4,911	1.6 5,8	32 1	.8 3,442	2.7 3,	,114	.0069 [0.69
formaldehyde resin 1% pet							(0.52 - 1.00)										0.53-0.90)]
Tosylamide	4,434	1.3	5.3	33.3	43.9	10.5	.1242 [0.77	1.7	5,139	1.6	4,897	1.3 5,8	00	.5 4,097	1.6 3,	,077	.2652 [0.86
formaldehyde resin 10% pet							(0.56 - 1.07)]										(0.65–1.13)]
Glutaraldehyde 1% pet	4,413	1.3	3.4	18.6	20.3	8.5	.7114 [1.07 (0.75–1.53)]	1.2	5,135	1.4	4,878	1.9 5,8	02 2	.6 4,094	2.2 3,	,076	.0171 [0.72 (0.55–0.94)]
Paraben mix 12% pet	4,439	1.2	17.0	50.9	24.5	0.0	(0.74-1.56)	1.1	5,142	0.6	4,898	1.0 5,8	03 1	.7 4,096	1.7 3,	,086	.8256 [1.03 0 77–1 38)]
Compositae mix	4,434	1.2	9.8	21.6	47.1	3.9	.6336 [0.92	1.3	5,138	1.0	4,887		I				.8438 [1.03
6% pet	1		0			- \	(0.64-1.31)		1.1.2 1.1.2		000						0.75-1.43)]
Jasmine absolute 2% pet	4,44/	1.1	0.0	C. 1 2	c. /0	1.0	(0.83–1.83)	6.0	c41,c	0.7	4,900		1				.001.1.04) [(0.96–1.94)]

Table 3. Continued

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Table	

			2005	-2006							19	94-200	4				
	F	ositive		Relevanco	e (%)		2005–2006 vs 2003–2004	2003-	2004	2001–	2002	1998–2	1 000	6 I–966	61 86	1996	2005–2006 vs 1994–2004 р
	R	eaction					p Value	Pos		Pos		Pos	P	05	Po:		Value [RR
Patch-Test Allergen	N*	(%)	Definite	Probable	Possible	Past	[RR (95% CI)]	(0)	u	(%)	u	(%)) u	%) n	(%)	u ((95% CI)]
Lidocaine 15% pet	4,429	1.1	8.3	10.4	27.1	27.1	.0071 [1.83	0.6	5,137	0.7	4,892			1		I	.0041 [1.71
		-					(1.18-2.86)										(1.18-2.46)
Dibucaine 2.5% pet	4,426	1.1	4.2	6.3	18.8	35.4	.5838 [1.12	1.0	5,137	0.9	4,891		1	1			.3728 [1.17
							(0.76 - 1.64)]										(0.83 - 1.64)
Black rubber mix	4,442	1.0	13.0	23.9	23.9	13.0	.9942 [1.00]	1.0	5,141	1.0	4,908		1	1			.9796 [1.00
0.6% pet							(0.67 - 1.49)										(0.70 - 1.41)]
Mixed dialkyl thioureas	4,430	1.0	14.0	25.6	23.3	14.0	.996[1.00]	1.0	5,140	0.8	4,897	1.1 5,	307	.3 4,0	98 0.	7 3,075	.9917 [1.00
1% pet							(0.67 - 1.49)										(0.73 - 1.37)]
Methyl methacrylate	4,427	1.0	4.7	39.5	20.9	25.6	.0102 [0.62	1.6	5,143	1.4	4,900	1.4 5,	812	.6 4,0	99 1.	2 3,080	.0162 [0.68
2% pet							(0.43 - 0.90)]										(0.50 - 0.93)]
Cocamide DEA	4,437	1.0	4.5	45.5	36.4	4.5	.5733 [0.89	1.1	5,137	1.3	4,888			1			.2821 [0.83
0.5% pet							(0.61 - 1.32)										(0.59 - 1.17)]
Mercaptobenzothiazole	4,442	0.9	15.8	42.1	26.3	13.2	.0616 [0.69	1.3	5,143	0.9	4,907	2.0 5,	334	.8 3,4	40 2.	3,115	.0006 [0.57]
1% pet							(0.47 - 1.02)										(0.41 - 0.79)]
Ethyl acrylate 0.1% pet	4,428	0.9	2.6	36.8	26.3	18.4	.3173 [0.82	1.1	5,141	1.3	4,899	1.3 5,	302	.3 4,0	95 1.3	3 3,074	.0221 [0.68
							(0.55 - 1.22)										(0.49-0.95)
Mercapto mix 1% pet	4,444	0.8	11.8	35.3	32.4	11.8	.6547 [0.91	0.9	5,143	0.7	4,908	1.3 5,	334	.8 3,4	39 2.	2 3,115	.0088 [0.63
							(0.59 - 1.39)]										(0.45-0.89)
Clobetasol-17-	4,435	0.8	5.6	38.9	41.7	5.6	.6136 [1.13	0.7	5,140				1	1			.6136 [1.13
propionate 1% pet							(0.71 - 1.78)										(0.71 - 1.78)
Sesquiterpene lactone	4,432	0.7	3.4	24.1	44.8	3.4	.5579 [1.16	0.6	5,140	0.6	4,896	0.9 5,	300 (.7 4,0	95 0.9	3,073	.8009 [0.95
mix 0.1% pet							(0.71 - 1.90)										(0.65 - 1.39)
Benzophenone-3	4,436	0.7	17.2	34.5	34.5	0.0	.9952 [1.00	0.7	5,144	0.6	4,899	0.6 5,	300 -	1			.6192 [1.11
3% pet							(0.62 - 1.60)]										(0.74 - 1.65)]
dl-α-Tocopherol 100%	4,435	0.7	6.7	26.7	60.0	0.0	.036 [0.63	1.1	5,139	0.5	4,874	1	1	1			.0245 [0.64
							(0.41 - 0.97)										(0.43 - 0.94)
Hydrocortisone-17-	4,438	0.6	7.7	19.2	57.7	11.5	.4999 [1.20	0.5	5,140	0.5	4,874			1			.4027 [1.22
butyrate 1% pet							(0.71 - 2.05)										(0.77 - 1.94)
Dimethylol	4,424	0.6	0.0	48.0	28.0	0.0	.2762 [0.77	0.8	5,138	1.1	4,889			1			.0412 [0.64
dihydroxyethyleneurea							(0.47 - 1.24)]										(0.42 - 0.98)
4.5% aq																	

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		Docitive		Relevan	ce (%)		2005-2006 vs	2003-,	2004	2001-,	2002	1998–20	1 000	8661-966	1994–1996	2005-2006 V
	R -	leaction					p Value	Pos		Pos		Pos	F	05	Pos	Value [RR
Patch-Test Allergen	N*	(%)	Definite	Probable	Possible	Past	[RR (95% CI)]	(%)	u	(%)	u	(%)) u	u (%	u (%)	(95% CI)]
Chloroxylenol 1% pet	4,436	0.5	4.2	33.3	29.2	4.2	.1988 [0.71	0.7	5,141	0.6	4,898	0.8 5,	300	.0 4,093	1.2 3,074	.0216 [0.60
							(0.42 - 1.20)									(0.39 - 0.93)
lodopropynyl butyl	4,433	0.5	4.3	30.4	47.8	0.0	.9458 [0.98	0.5	5,137	0.3	4,897	0.4 5,	- 0/2			.3744 [1.25
carbamate 0.1% pet							(0.56 - 1.72)]									(0.77 - 2.01)]
Triamcinolone	4,438	0.3	0.0	26.7	60.0	13.3	.9917 [1.00	0.3	5,141				' 			.9917 [1.00
acetonide 1% pet							(0.49-2.07)]									(0.49 - 2.07)]
Bisphenol F 1% pet	4,413	0.2	0.0	11.1	11.1	11.1	.1757 [2.09	0.1	5,128				' 			.1757 [2.09
							(0.74-5.95)]									(0.74 - 5.95)]

NACDG standard series; 4.9% (219) had positive reactions to supplementary allergens that were occupation related. The most frequent sources of these supplementary allergens were cosmetics and beauty aids, moisturizers and lotions, jewelry, adhesives and glues, and clothing.

Environmental Irritants

Of the tested patients, 15.2% (678) had exposure to relevant environmental irritants as identified by history; 8.9% had exposure to occupation-related irritants. The most frequent sources of irritants were detergents, cosmetics and beauty aids, cleansers, solvents, degreasers, oils, lubricating oils, metalworking fluids, lotions, automotive oils, and shoes.

Final Diagnoses

Table 4 summarizes the final diagnoses of patch-tested patients; 2,612 patients (58.6%) had a final diagnosis that included ACD. The second and third most common diagnoses were "other eczematous dermatitis" (18.9%) and irritant contact dermatitis (16.8%).

Discussion

Some of the changes in the NACDG allergen series for this time period deserve further comment. Sodium gold thiosulfate was eliminated from routine testing, although the members all 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. Patch-test reactions to gold may be strong and may persist for long periods, leading to patient concerns. Therefore, it was felt that aimed testing with gold, rather than routine screening, was more reasonable. Reactions to tetracaine were rarely seen, and other "caines" are on the test panel. Iodopropynyl butyl carbamate (IPBC) is a preservative that is coming into more use and was therefore deemed worthy of surveillance. A number of cases of shoe dermatitis are unexplained with current allergens, so dithiomorpholine (a rubber allergen) was added in an attempt to identify potential rubber allergy.

The 10 most frequently positive allergens during the 2005–2006 period included metals (nickel [19.0%] and cobalt [8.4%]), topical antibiotics (neomycin [10.0%] and bacitracin [9.2%]), fragrances (fragrance mix I [11.5%] and *Myroxilon pereirae* [11.9%]), preservatives (quaternium-15 [10.3%], formaldehyde [9.0%], and methyldibromoglutaronitrile [5.8%]), and p-phenylenediamine

North American Contact Dermatitis Group 2005–2006 Patch-Test Results

	Primary Diagnosis		
Diagnosis	(n = 4,454)	Second Diagnosis	Third Diagnosis
Allergic contact dermatitis	2,129 (47.8%)	437 (9.8%)	46 (1.0%)
Other dermatitis	658 (14.8%)	161 (3.6%)	23 (0.5%)
Irritant contact dermatitis	411 (9.2%)	311 (7.0%)	28 (0.6%)
Atopic dermatitis	429 (9.6%)	152 (3.4%)	25 (0.6%)
Other dermatoses	415 (9.3%)	94 (2.1%)	21 (0.5%)
Psoriasis	155 (3.5%)	64 (1.4%)	10 (0.2%)
Seborrheic dermatosis	69 (1.5%)	38 (0.9%)	5 (0.1%)
Nummular dermatitis	73 (1.6%)	17 (0.4%)	3 (0.1%)
Photodermatitis	34 (0.8%)	21 (0.5%)	2 (0.0%)
Pompholyx	34 (0.8%)	8 (0.2%)	2 (0.0%)
Stasis dermatitis	23 (0.5%)	20 (0.4%)	2 (0.0%)
Contact urticaria	16 (0.4%)	1 (0.0%)	2 (0.0%)

Table 4. Final Diagnoses after Patch Testing, 2005–2006 Data

(5.0%). Of these 10 most frequently positive allergens, nickel¹² and bacitracin demonstrate a consistent upward trend.

The frequency of positive patch-test reactions to nickel in the populations tested by the NACDG continues to rise over time, and nickel continues to be the most frequently positive allergen. The frequency of positive patch-test reactions to bacitracin is up to 9.2%; bacitracin is now the sixth most frequently positive allergen, just behind neomycin. Nickel frequency increased to 19.0% of patients tested. The combined present relevance for a positive patch-test reaction to nickel was 56.7%; the relevance of this allergen was deemed of past importance in 28.3%. Bacitracin, on the other hand, had a combined present relevance of 39.2% and a past relevance of 42.5%.

Newcomers to the top 20 allergens for the 2005–2006 period as compared to the previous 2-year cycle included 2-bromo-2-nitropropane-1,3,-diol 0.5% pet, cinnamic aldehyde 1% pet, and methylchloroisothiazolinone/meth-ylisothiazolinone 100 parts per million (ppm) aq.

Of the top 30 most frequently positive NACDG allergens for the 2005–2006 period, the following 10 allergens are not currently available for testing and identification with Thin-Layer Rapid Use Epicutaneous (T.R.U.E.) Test panels (Mekos Laboratories A/S, Hillerød, Denmark): bacitracin (9.2% positive), methyldibromoglutaronitrile (5.8%), 2-bromo-2-nitropropane-1,3-diol (3.4%), cinnamic aldehyde (3.1%), propylene glycol (2.9%), dimethylol dimethyl (DMDM) hydantoin (2.6%), IPBC (2.4%), ethyleneurea/melamine formalde-hyde (2.1%), Disperse Blue 106 (2.1%), and amidoamine (2.0%). Of these, bacitracin is likely the most important. Named Allergen of the Year in 2003 by the American

Contact Dermatitis Society, bacitracin is now the sixth most frequently positive allergen. The increase in allergic reactions to bacitracin likely parallels an increase in exposure through use for routine wound care both by the lay public (who purchase it over the counter) and by medical professionals.¹³ In one randomized double-blind prospective trial comparing infection and allergy incidence with petrolatum versus bacitracin in ambulatory surgery patients, 922 patients with a total of 1,249 wounds were compared. No clinically significant difference in postprocedural infection was demonstrated between treatment groups. Additionally, in contrast to four patients in the group treated with bacitracin, no patient in the group treated with petrolatum developed contact dermatitis.¹⁴ Bacitracin contact allergy may be misdiagnosed as infection, leading to increased costly and unnecessary interventions.¹⁵ Itch (rather than pain) is a tip-off favoring ACD over infection. Methyldibromoglutaronitrile/ phenoxyethanol (MDBGN/PE) has been widely used for toiletries, household cleaning products and dishwashing liquids, veterinary shampoos, car care products, adhesives, paints, and metalworking fluids. It has been used in the United States in both leave-on and rinse-off products. In Europe, this biocide has been banned in leave-on products and was determined by the Scientific Committee for Consumer Products to have no safe concentration in rinseoff products.¹⁶ As of July 2008, MDBGN/PE was also banned from rinse-off products in the European Economic Community. Bronopol (2-bromo-2-nitropropane-1,3diol) is another important preservative and can be found in cosmetics, baby wipes, cleansers, bubble baths, shampoos, conditioners, sunscreens, and disinfectants, as well as in paper mills and water treatment plants. Bronopol can

release low levels of formaldehyde on decomposition in aqueous solution. Since the late 1980s, the use of bronopol in personal care products has declined. IPBC is a preservative found in similar personal care products. The identification of these relevant allergens demonstrates that it is important to use a patch-test allergen series that is flexible, responsive, and able to detect allergens that are newly recognized and rising in exposure.

Although T.R.U.E. Test panels include fragrance mix I, which contains cinnamic aldehyde, it can be important for patients (especially those with cheilitis) to be aware of this specific allergen, given its use as a flavoring agent. Other allergens of importance include propylene glycol, an emulsifier in numerous products, including topical medicaments; DMDM hydantoin, a formaldehyde-releasing preservative that may not be detected by testing with formaldehyde; IPBC, a new preservative with increasing use that (despite its name) goes undetected by tests with carba mix; ethyleneurea/melamine formaldehyde and Disperse Blue 106, important allergens in textiles and clothing; and amidoamine, a cocamidopropyl betaine contaminant causing reactions to soaps, detergents, and shampoos.

One strength of these data is the estimate of relevance assessed for a given allergen (see Table 3). Patients are more likely to benefit from avoiding identified allergens that are deemed relevant to their actual problem. Definite relevance is uncommon because its determination requires testing with an actual product or item containing the allergen, but probable relevance requires only that the allergen be identified as an ingredient or component of a contactant used by the patient. Another way to convey the strength of a relevance determination could be to combine relevance into two categories: (1) definite and probable and (2) possible. The "definite and probable" category might convey a more robust estimate of the relevance of an allergen. Elimination of exposure to a positive allergen followed by improvement or resolution of dermatitis would constitute the most robust confirmation of relevance. However, confirmation of clinical relevance over time is often impossible because of limited follow-up in this referral population.

While the majority of tested patients had at least one positive patch-test reaction, approximately one-third (34.7%) had no positive reactions. In some cases, a diagnosis of ICD, atopic dermatitis, or a combination of the two can explain or categorize a particular patient's dermatitis; in other cases, a more specific diagnostic "label" for the problem that resulted in patch testing remains elusive. A dermatitis type code of "other dermatitis" was given to 18.9% of the patients. The etiology of eczematous dermatitis for this group of patients is elusive; prognosis is typically poor, and treatment options are limited and often undesirable.^{17,18} Although 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 "other dermatitis" or nonspecific endogenous eczema) would be appropriate for further study.

This study has several limitations, including the highly selected patient population tested by the NACDG. The lack of follow-up ability over time limits the designation of positive allergen relevance. Another limitation is that only one positive supplemental allergen can be recorded on the data collection form. If a patient is positive to more than one supplemental allergen, the number of reactions or allergen sources is not documented. This likely leads to underestimation of the potential value of patch-testing with supplemental allergens or the patient's own products. The source (eg, 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 the use of additional screening series, is curtailed.

Conclusions

Patch testing with a screening series is useful in individual patient management; the determination of whether allergens are causing or contributing to a dermatitis can result in improvement or cure of the problem. The definitive diagnosis of allergic contact dermatitis requires patch testing, typically with an extended allergen series and, in some cases, a specialized allergen series (eg, the oil and cooling fluid series for machinists).^{19,20}

Increases and decreases in the prevalence of positive patch-test results over time are common. Changes in use and exposure patterns may account for these changes in prevalence. Large data sets such as this are useful in assessing changing trends in positive allergen frequency, which may reflect formulation changes or new patterns of use or exposure for a given allergen. Such data are also useful in determining the most relevant allergens for testing in a given population. Particular subset analysis of the North American Contact Dermatitis Group (NACDG) data set has been useful in determining the most frequent allergens in patients with a specific dermatitis distribution,^{21–25} occupation,²⁶ or exposure source.^{27–30} Patch-test frequency data from large database sources are discussed and analyzed by groups

interested in contact allergy, such as industry and government regulators. Such discussion may contribute to enhanced product safety.³¹ The NACDG database summary information provided over the years has been a useful reference for dermatologists and others involved in patch testing. By providing guidance regarding the most frequent and relevant allergens in North America, these data continue to play an important role in patient diagnosis and management.

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