

Report

Patch test results may vary depending on where testing is performed: a comparison of patch test results from three geographically distinct sites in the USA

Mark D. P. Davis¹, MD, James A. Yiannias², MD, Amy L. Weaver³, MS, Sara A. Farmer³, BS, Leigh Ann Scalf¹, MD, Amy V. Prakash¹, MD, Debra D. Fett¹, MD, Donna M. Richardson¹, RN, Suzanne M. Connolly², MD, James H. Keeling⁴, MD, and Rokea A. el-Azhary¹, MD

¹Department of Dermatology, Mayo Clinic, Rochester, MN, ²Department of Dermatology, Mayo Clinic, Scottsdale, AZ, ³Division of Biomedical Informatics and Statistics, Mayo Clinic, Rochester, MN, and ⁴Department of Dermatology, Mayo Clinic, Jacksonville, FL, USA

Correspondence

Mark D. P. Davis, MD
Department of Dermatology
Mayo Clinic, 200 First Street SW
Rochester
MN 55905
USA
E-mail: davis.mark2@mayo.edu

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Abstract

Background Do patch test results vary from one part of the USA to another? Few reports directly compare the results of patch testing across centers within the USA.

Objectives Our objective was to compare results of patch testing from three geographically disparate Mayo Clinic sites in the USA to ascertain whether there are any differences in allergic patch test rates.

Methods We retrospectively reviewed patch test results for patients tested with a standard allergen series using our enterprise-wide protocol for patch testing. We compared data collected from January 1, 2001, through to December 31, 2007, from our practice sites in the Midwest, Southwest, and Southeast regions of the USA.

Results In total, 5063 patients underwent patch testing. The mean (standard deviation) number of allergens tested per patient was 70.3 (3.8) (range: 10–87; interquartile range: 68–73). Analyses were conducted separately for 72 allergens with positive reactions from at least 20 patients. Risk-adjusted positive reaction rates (RAPRRs) for 44 allergens differed significantly ($P < 0.05$) among the geographic sites; RAPRRs differed significantly across all three sites for 11 allergens and between two of the three sites for 33 allergens.

Conclusions Allergic patch test rates differed among our three practice sites for many allergens. It is likely that many factors contributed to these observed differences, including variations in the population undergoing patch testing, variations in allergen exposure, and variations in climate.

Introduction

How do the results of patch testing compare between different parts of the USA? There is a paucity of data describing if and how reaction rates to individual allergens vary from one part of the USA to another.

Mayo Clinic has three campuses in geographically distinct parts of the country (Fig. 1): the Upper Midwest (Minnesota), the Southwest (Arizona), and the Southeast (Florida). Our aim was to compare rates of allergic patch test reaction across our three patch test sites. To determine whether patch test rates vary from one part of the USA to another, we compared reaction rates for allergens on our standard series. The implications of the results of this study may shed further light on whether we need to customize the standard series on the basis

of geographic area or whether one standard series fits all.

Materials and methods**Study patients**

Having gained study approval from the Mayo Clinic Institutional Review Board, we identified patients who underwent patch testing for suspected allergic contact dermatitis at Mayo Clinic from January 1, 2001, through December 31, 2007, at any of our three practice sites [Mayo Clinic Rochester (MCR), Mayo Clinic Arizona (MCA), and Mayo Clinic Jacksonville (MCJ)]. All sites are considered tertiary referral centers. The patients in the study were identified using the enterprise-wide patch test database (used to collect data for all patients undergoing patch testing at our institution). For this study, we considered only the



Figure 1 Map of the USA showing three Mayo Clinic sites. Mayo Clinic campuses are located in the Upper Midwest (Rochester, MN), the Southwest (Scottsdale and Phoenix, AZ) and the Southeast (Jacksonville, FL)

results of patients tested with the standard allergen series. Data for patients who denied research authorization were excluded from the analysis.

Process of patch testing

Patch testing was conducted in a standardized fashion using methods described by the North American Contact Dermatitis Group^{1–3} and in our previous reports.^{4,5} Patients generally were not patch tested if they applied topical corticosteroids to patch test sites, took immunosuppressive medication (including oral corticosteroids), or had medical conditions that might compromise the evaluation of the skin response.² Sources of allergens, the concentrations and dilutions used for tests, application of the patch test materials, reading of the patch tests, interpretation of patch test results, patient education, and program supervision have been standardized among the practice sites.

Testing was performed with Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster AS, Vennesla, Norway). Patches were applied to the upper back and removed after 48 hours. Most allergens were purchased from Chemotechnique Diagnostics AB (Vellinge, Sweden). Others were compounded by the Mayo Clinic pharmacy. The allergens used in the standard screening series changed with time; the choice of allergens varied on the basis of clinical experience with previously tested allergens and the introduction of new allergens.

Interpretation of patch test reactions

Reactions were evaluated initially at 48–72 hours and again at 96–168 hours after application of the patch. Patch test readings were performed by the ordering physician or specially trained patch test nurses (or both). The interpretation of results and assessment of relevancy were performed by the ordering physician. A return visit with the ordering physician after patch

testing was completed was conducted to further assess relevancy.

The patch test reactions were interpreted using the following criteria: negative reaction; macular erythema or weak reaction (non-vesicular erythema, infiltration and, possibly, papules); strong reaction (edematous or vesicular), and extreme reaction (spreading, bullous, ulcerative lesions). Reactions (including macular erythema) were further interpreted as relevant or irrelevant on the basis of a history of known contact with substances containing the allergen or a history of circumstances of likely contact with substances containing the allergen. Relevancy for each reaction was recorded as follows: irritant; allergic, not relevant (no exposure to products that contain the allergen); allergic, questionably relevant (current exposure to products likely to contain the allergen); allergic, formerly relevant (past exposure to products likely to contain the allergen), and allergic, relevant (use test or patch test with the product containing the allergen is positive, or ingredient verified in the patient's product and use of that product verified). We defined a positive allergic patch test result as a weak, strong, or extreme reaction at the last reading or as a macular erythema reaction if the result was relevant after irritant reactions had been excluded.

Statistical analysis

Patch test data from all three practice sites were extracted from our patch test database (Sybase, Inc., Dublin, CA, USA). For patients who underwent multiple patch testing episodes during the study period, only the most extreme reaction to each allergen was considered in this analysis. We analyzed patient characteristics, including whether the patient was male, had atopic eczema, hand dermatitis, leg dermatitis, or facial dermatitis, and was aged ≥ 40 years (the MOAHLFA index).⁶ (We note that the MOAHLFA index traditionally includes occupational dermatosis; however, we did not have data

available for that variable.) Prevalences of each characteristic were compared among the three practice sites using the chi-squared test.

Separate analyses were conducted for each allergen, specifically for those allergens with positive reactions in at least 20 patients. For each allergen, a logistic regression model was fit to the combined data from all three practice sites to predict the probability of positive reaction (binary outcome) using the components of the MOAHLFA index as independent variables. Atopy was coded using two indicator variables to accommodate three levels of the condition (present, absent, unknown). Location was also coded using two indicator variables (three possible locations: leg or face; all other locations, including hands; unknown). Age group (<40 vs. ≥40 years) and sex were each treated as dichotomous variables. Some models did not include all the aforementioned variables if the prevalence of a particular characteristic was zero among all patients tested for a given allergen.

Using the results obtained from the logistic model for a particular allergen, the estimated probabilities (of a positive reaction) for all patients were summed across the practice sites to obtain the expected number of positive reactions for a particular allergen. Next, the observed number of positive reactions for a particular allergen was determined separately for each practice site. Finally, for each practice site, the risk-adjusted positive reaction rate (RAPRR) for a particular allergen was determined by dividing the observed number of positive reactions by the expected number of positive reactions (to give the observed : estimate ratio) and multiplying that quantity by the overall observed positive reaction rate for the entire sample; 95% confidence intervals (CIs) for the RAPRR were constructed using a propagation of errors variance estimate for the observed : estimate ratio.⁷

For each allergen, the RAPRRs for any two geographic sites were compared using a standard two-sample *z*-test. All calculated *P*-values were two-sided, and values of <0.05 were considered to indicate statistical significance. If two geographic sites had non-overlapping 95% CIs for an RAPRR estimate, the rates were necessarily significantly different at the 0.05 level; however, if their 95% CIs overlapped, they were not necessarily significantly different.

All statistical analyses were performed using SAS Version 9.1 (SAS Institute, Inc., Cary, NC, USA). The SAS code for calculating the propagation of errors variance estimate was obtained from the APPROACH website.⁸

Results

During the seven-year study period, 5063 patients with suspected allergic contact dermatitis underwent patch testing with the standard allergen series. The mean (standard deviation) number of allergens tested per patient was 70.3 (3.8); the range was 10–87 allergens (interquar-

tile range: 68–73). Patient characteristics comprising the MOAHLFA index are summarized in Table 1.

Analyses were conducted separately for 72 allergens that each had positive reactions from at least 20 patients. Tables 2 and 3 present the number of patients tested per allergen, number of patients with an irritant reaction, and the RAPRRs for each geographic site. The allergens with RAPRRs that differed significantly ($P < 0.05$) between at least two of the three sites ($n = 44$) are summarized in Table 2. Of these 44 allergens, 11 had RAPRRs that differed significantly across all three sites; the RAPRRs for 10 of these 11 allergens were lowest at MCA and highest at MCJ. The 28 allergens with similar RAPRRs ($P > 0.05$) across the three geographic sites are summarized in Table 3.

Discussion

In this report, we compared the results of patch tests for a large number of patients at three geographically disparate sites in the USA. We used a standardized testing protocol that included identical patch test preparations and procedures for reading patch test results. This study showed that many allergens were associated with similar allergic patch test reaction rates. To some extent, these generally consistent findings validate the standardization of our procedures across the three sites, and the large number of patch tests administered strengthens this conclusion.

This information is of importance to the general dermatologist who performs patch testing because it shows that rates of allergic patch test reaction for many allergens may be similar, no matter where in the USA the tests are conducted. Nevertheless, the rates of allergic patch test reactions were significantly different for numerous allergens.

Potential reasons for regional variation

A number of allergens yielded significantly different patch test results across the three sites. We acknowledge that some of the differences may have been caused by random chance. However, we considered several possible explanations for regional variation.

Patient numbers

Considerably fewer patients underwent patch testing at MCJ ($n = 321$), which may well have skewed the results. Smaller patient numbers result in less precision in the estimate of the percentage of patients with positive reactions. We note that the two larger centers (MCR and MCA) showed much less variation in patch testing results.

Patch testing technique

Although we tried to minimize differences in the patch test protocol across the three sites, variation may still

Table 1 Patient characteristics

Characteristic ^a	Practice site								P-value
	Total (n = 5063)		MCR (n = 3277)		MCA (n = 1465)		MCJ (n = 321)		
	n	%	n	%	n	%	n	%	
Male sex	1678	33.1	1039	31.7	537	36.7	102	31.8	0.003
Occupational causation of dermatitis	NA		NA		NA		NA		—
Atopy									0.002
Yes	1413	27.9	935	28.5	386	26.3	92	28.7	
No	1988	39.3	1329	40.6	548	37.4	111	34.6	
Unknown	1662	32.8	1013	30.9	531	36.2	118	36.8	
Location ^b									
Hand	1101	22.7	743	22.9	306	22.4	52	22.4	0.93
Leg	633	13.1	400	12.3	215	15.7	18	7.8	<0.001
Face	680	14.0	422	13.0	229	16.7	29	12.5	0.003
All other locations ^c	3792	78.2	2541	78.2	1082	79.1	169	72.8	0.10
Age ≥40 years	4020	79.4	2475	75.5	1275	87.0	270	84.1	<0.001

^aThe MOAHLFA index comprises the following characteristics: male; atopic eczema; hand dermatitis; leg dermatitis; facial dermatitis; and patient age ≥40 years. Although other indices have included atopic eczema, allergic rhinoconjunctivitis or allergic bronchial asthma in the definition of atopy, only atopic eczema is suggested for consideration in the MOAHLFA index.

^bReported percentages are calculated using the number of patients with a documented location as the denominator. The location was documented in 4851 patients (3251, 1368 and 232 patients at the MCR, MCA and MCJ practice sites, respectively). Patients could have dermatitis in more than one location.

^cAll other locations include ear, eye, eyelid, scalp, lip, mouth, neck, arm, foot, trunk, anal/genital, generalized or scattered generalized. NA, data not available.

have occurred. Different patch test “readers” may account for some of these differences (interobserver variability). However, because much of our data generally showed a high level of consistency across the sites, we think this is unlikely. Additionally, the patch test readings were monitored, and results were discussed frequently by physicians and patch-testing nurse supervisors at our different facilities to minimize discrepancies.

Populations undergoing patch testing

The variation in some of the allergic reaction rates may reflect varying demographic profiles among patients at the different centers. For example, patients seen at MCA and MCJ were older than those at MCR. Sex and age reportedly have an influence on allergic patch test reaction rates, at least for some allergens, such as nickel, fragrances, and balsam of Peru.⁹ A marginal disparity in the reactivity of men compared with women has been noted previously.¹⁰

Variation in exposure to individual allergens

Different reaction rates were apparent mostly for allergens in the following categories: metals, preservatives, fragrances, hair products, and disperse blue dyes. We are dubious about any marked differences in exposure to

fragrances, hair coloring, or permanent wave hair treatments among the patients at our three sites. However, given the climate differences among the three geographic locations, the high reaction rate to disperse blue dyes in the southeast may reflect regional clothing preferences.

Climate

Regional climate variations (arid vs. humid, cold vs. warm) may affect sensitivity to allergens in our series. Because local humidity and temperature varied considerably among test sites, these factors may have influenced patch test results. Climate may also account for the difference in allergenicity rates to sesquiterpene lactones, a marker of the *Compositae* family of plants, which includes daisies. This may also explain the higher reactivity in Florida.

Does climate truly affect patch test reactions? Studies of this issue have reported conflicting results.^{11,12} Some report that ultraviolet (UV) light during the summer months decreases allergic patch test rates, at least for some allergens, whereas others report that summertime UV exposure does not affect allergic patch test rates, and others state that meteorological conditions do not compromise patch testing.

The proportion of irritant reaction rates (e.g., to formaldehyde) is reportedly higher in winter because of the

Table 2 Patch test allergens for which reaction rates differed significantly among geographic sites

Allergen ^a	Patients tested, <i>n</i>				Patients with irritant reactions, <i>n</i>				RAPRR (95% CI)				<i>P</i> -values			
	MCR	MCA	MCJ	MCR	MCA	MCJ	MCR	MCA	MCR	MCA	MCJ	MCR	MCA	MCR	MCA	MCJ
	MCR	MCA	MCJ	MCR	MCA	MCJ	MCR	MCA	MCR	MCA	MCJ	MCR	MCA	MCR	MCA	MCJ
MCR vs. MCA vs. MCJ																
Balsam of Peru 25%	3277	1448	313	87	1	26	14.4	(13.7–15.1)	9.4	(8.0–10.8)	20.0	(16.2–23.9)	<0.001	0.004	<0.001	<0.001
Benzalkonium chloride 0.1% Aq	3243	1452	316	51	8	7	9.0	(4.1–6.5)	5.3	(4.1–6.5)	19.1	(16.0–22.2)	<0.001	<0.001	<0.001	<0.001
Benzoic acid 5%	2025	956	204	31	0	11	5.1	(4.5–5.7)	3.9	(2.8–5.0)	9.9	(7.0–12.8)	0.049	0.002	<0.001	<0.001
Cobalt chloride 1%	3260	1454	309	115	15	39	10.1	(9.5–10.6)	8.3	(7.0–9.7)	21.0	(17.6–24.4)	0.02	<0.001	<0.001	<0.001
Disperse blue #124 1%	2117	998	212	31	1	23	5.3	(4.7–5.8)	2.8	(1.6–4.0)	16.9	(13.5–20.4)	<0.001	<0.001	<0.001	<0.001
Ethyleneurea-melamine formaldehyde mix 5%	3277	1458	319	11	0	7	2.3	(2.0–2.6)	1.5	(0.9–2.1)	5.7	(3.9–7.5)	0.03	<0.001	<0.001	<0.001
Nickel sulfate hexahydrate 2.5%	3264	1453	319	46	7	10	18.4	(17.7–19.1)	12.4	(10.7–14.1)	22.7	(18.7–26.7)	<0.001	0.04	<0.001	<0.001
Potassium dichromate 0.25%	3277	1452	314	74	16	21	6.8	(6.3–7.3)	5.6	(4.5–6.6)	10.9	(8.2–13.5)	0.04	0.003	<0.001	<0.001
<i>Dermatophagoides</i> mix 20%	545	233	61	70	19	2	27.8	(25.8–29.9)	18.5	(13.7–23.3)	48.0	(40.9–55.1)	<0.001	<0.001	<0.001	<0.001
<i>Dermatophagoides</i> mix 0.1%	1248	516	96	41	2	0	5.5	(4.8–6.2)	1.0	(0.0–2.8)	15.7	(11.1–20.3)	<0.001	<0.001	<0.001	<0.001
Ethyl acrylate 0.1%	3265	1461	320	14	1	9	0.8	(0.6–1.1)	1.4	(0.9–1.9)	2.8	(1.6–4.1)	0.03	0.002	0.04	0.04
MCR vs. MCA																
Cinnamic aldehyde 1%	2792	1249	287	15	1	5	2.3	(2.0–2.6)	1.4	(0.7–2.0)	1.6	(0.0–3.2)	0.01	0.40	0.82	0.82
Cocamidopropyl betaine 1% Aq	1449	682	160	13	0	9	4.8	(4.2–5.4)	2.3	(1.1–3.6)	4.6	(1.6–7.7)	<0.001	0.90	0.17	0.17
Coconut diethanolamide [cocamide diethanolamine (DEA)] 0.5%	1018	496	129	7	0	3	1.8	(1.4–2.2)	0.5	(0.0–1.5)	0.9	(0.0–3.0)	0.02	0.41	0.72	0.72
Hexachlorophene 1%	2275	965	191	38	0	10	1.7	(1.4–2.0)	0.2	(0.0–0.9)	1.3	(0.0–2.7)	<0.001	0.64	0.13	0.13
Hydrocortisone 17-butyrate 1% Alc	2573	1173	250	4	0	6	1.2	(0.9–1.4)	0.6	(0.1–1.1)	0.8	(0.0–2.0)	0.03	0.59	0.71	0.71
Quaternium 15 1%	3277	1452	320	21	1	5	8.7	(8.2–9.2)	7.1	(6.0–8.3)	7.9	(5.0–10.8)	0.01	0.60	0.61	0.61
Triamcinolone acetonide 1%	3276	1461	321	16	0	4	0.7	(0.5–0.9)	0.0	(0.0–0.3)	0.4	(0.0–1.2)	<0.001	0.50	0.38	0.38
MCR vs. MCJ																
Methyl methacrylate 2%	3277	1462	320	19	1	5	1.3	(1.0–1.5)	1.6	(1.1–2.2)	2.6	(1.3–3.9)	0.19	0.049	0.19	0.19
Neomycin sulfate 20%	3276	1451	315	22	6	6	11.8	(11.1–12.4)	12.3	(10.9–13.6)	15.3	(11.9–18.6)	0.50	0.04	0.10	0.10
Sesquiterpene lactone mix 0.1%	3276	1459	321	12	1	6	0.7	(0.5–0.9)	1.1	(0.7–1.5)	2.6	(1.1–3.4)	0.14	0.01	0.07	0.07
MCA vs. MCJ																
DMDM hydantoin 1% Aq	2276	962	190	8	0	5	1.3	(1.0–1.5)	1.0	(0.4–1.5)	2.8	(1.2–4.4)	0.34	0.06	0.03	0.03
Glutaraldehyde 0.2%	3264	1458	320	15	1	8	0.8	(0.6–0.9)	0.5	(0.1–0.9)	1.4	(0.4–2.3)	0.08	0.15	0.04	0.04
Caine mix III	1086	507	82	7	1	2	4.9	(4.1–5.6)	3.6	(2.1–5.0)	8.7	(4.5–13.0)	0.13	0.08	0.02	0.02
MCJ vs. MCR and MCJ vs. MCA																
Hexahydro-1,3,5-tris(2-hydroxyethyl) triazine 1%	3148	1455	320	25	0	10	4.1	(3.7–4.6)	3.6	(2.8–4.4)	9.3	(6.9–11.8)	0.25	<0.001	<0.001	<0.001
Benzocaine 5%	2180	958	235	12	0	4	1.8	(1.5–2.2)	1.2	(0.5–1.9)	5.7	(3.5–7.9)	0.12	<0.001	<0.001	<0.001
Carba mix 3%	3277	1448	320	69	4	28	4.3	(3.8–4.7)	3.7	(2.9–4.6)	9.9	(7.6–12.1)	0.28	<0.001	<0.001	<0.001

Table 2 (Continued)

Allergen ^a	Patients tested, <i>n</i>				Patients with irritant reactions, <i>n</i>				RAPRR (95% CI)			<i>P</i> -values		
	MCR	MCA	MCJ		MCR	MCA	MCJ		MCR	MCA	MCJ	MCR vs. MCA	MCR vs. MCJ	MCA vs. MCJ
Disperse blue #106 1%	2118	996	211		20	0	32		3.7 (3.2–4.3)	4.1 (3.1–5.2)	13.6 (10.5–16.7)	0.51	<0.001	<0.001
Glyceryl thioglycolate 1%	3277	1456	319		10	2	12		1.5 (1.2–1.7)	1.1 (0.6–1.7)	3.3 (2.1–4.4)	0.23	0.003	<0.001
MCI/MI 100 ppm	1758	755	159		8	0	2		1.2 (0.9–1.5)	1.0 (0.3–1.7)	4.0 (1.7–6.3)	0.62	0.02	0.02
MCI/MI 100 ppm Aq	3175	1456	320		10	1	8		2.4 (2.0–2.7)	2.7 (2.0–3.5)	7.9 (5.9–10.0)	0.35	<0.001	<0.001
Methyldibromo glutaronitrile/phenoxyethanol 1.5%	3277	1448	316		58	1	24		5.8 (5.4–6.3)	5.2 (4.2–6.1)	11.1 (8.6–13.7)	0.22	<0.001	<0.001
<i>p</i> -Phenylenediamine 1%	3270	1454	317		20	1	22		3.9 (3.5–4.3)	4.5 (3.6–5.3)	9.3 (7.0–11.6)	0.24	<0.001	<0.001
Thimerosal 0.1%	1174	464	108		17	1	4		10.6 (9.7–11.5)	8.1 (5.7–10.6)	19.2 (14.6–23.7)	0.06	<0.001	<0.001
Diazolidinyl urea 1%	3277	1457	319		15	0	5		3.0 (2.6–3.4)	3.2 (2.5–3.9)	6.0 (4.1–7.9)	0.68	0.003	0.007
Propylene glycol 10%	3277	1457	321		7	0	4		0.4 (0.3–0.6)	0.2 (0.0–0.5)	1.5 (0.6–2.4)	0.17	0.02	0.007
Natural fragrance mix 2%	2896	1287	274		30	0	9		3.6 (3.2–4.0)	3.0 (2.1–3.8)	6.3 (4.0–8.5)	0.14	0.02	0.006
MCA vs. MCR and MCA vs. MCJ														
2-Bromo-2-nitropropane-1,3-diol 0.25%	3137	1368	287		36	0	14		2.2 (1.9–2.5)	0.8 (0.2–1.4)	3.3 (1.8–4.9)	<0.001	0.16	0.003
Black rubber mix 0.6%	3277	1455	319		16	0	3		1.1 (0.9–1.3)	0.5 (0.0–0.9)	2.1 (1.0–3.3)	0.012	0.08	0.009
Formaldehyde 1% Aq	3277	1452	317		17	0	11		9.2 (8.6–9.7)	7.0 (5.8–8.1)	11.2 (8.3–14.2)	0.001	0.18	0.009
Fragrance mix 8%	3277	1460	317		46	2	11		11.5 (10.9–12.2)	9.1 (7.7–10.4)	14.0 (10.7–17.3)	<0.001	0.15	0.006
Gold sodium thiosulfate 0.5%	3155	1394	305		74	10	20		14.6 (14.0–15.3)	6.3 (4.7–7.8)	17.1 (13.6–20.7)	<0.001	0.17	<0.001
Hexylresorcinol 0.25%	3277	1453	313		55	0	24		3.7 (3.3–4.1)	1.6 (0.8–2.4)	5.5 (3.6–7.4)	<0.001	0.07	<0.001
Chloroxylenol (PCMX) 1%	3277	1457	321		12	0	3		1.0 (0.8–1.2)	0.1 (0.0–0.6)	1.5 (0.6–2.3)	<0.001	0.31	0.005

RAPRR, risk-adjusted positive reaction rate; 95% CI, 95% confidence interval; MCA, Mayo Clinic Arizona; MCJ, Mayo Clinic Jacksonville; MCR, Mayo Clinic Rochester; Alc, alcohol; Aq, aqueous; DMDM, 1-3-dimethyl-5,5-dimethyl; MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; PCMX, parachlorometaxylenol.

^aAllergens are categorized by statistically significant differences in RAPRR among practice sites ($P < 0.05$).

Table 3 Patch test allergens for which reaction rates were similar among geographic sites

Allergen	Patients tested, <i>n</i>			Patients with irritant reactions, <i>n</i>			RAPRR (95% CI)		
	MCR	MCA	MCJ	MCR	MCA	MCJ	MCR	MCA	MCJ
Bacitracin 20%	3277	1455	320	26	2	6	8.3 (7.8–8.9)	8.4 (7.3–9.6)	7.6 (4.7–10.5)
Budesonide 0.1%	3156	1377	292	39	0	12	1.8 (1.5–2.1)	1.0 (0.5–1.5)	0.0 (0.0–1.5)
Colophony 20%	3277	1458	318	33	0	10	2.9 (2.6–3.2)	2.2 (1.5–2.9)	2.5 (0.7–4.3)
DMDM hydantoin 1%	3202	1447	319	14	0	8	2.1 (1.8–2.4)	1.9 (1.3–2.5)	2.3 (0.8–3.8)
Diazolidinyl urea 1% Aq	3277	1456	318	11	1	4	2.1 (1.8–2.4)	2.0 (1.5–2.6)	3.6 (1.9–5.2)
Dimethylol dihydroxyethylene urea 4.5% Aq	1019	498	129	1	0	1	1.1 (0.7–1.5)	1.3 (0.4–2.1)	2.7 (0.6–4.8)
Disperse orange #3 1%	2115	1000	212	13	2	10	1.4 (1.1–1.6)	0.9 (0.4–1.5)	0.0 (0.0–1.5)
Epoxy resin 1%	3277	1457	321	10	2	7	1.7 (1.5–2.0)	1.2 (0.7–1.7)	2.2 (0.8–3.7)
Ethylenediamine dihydrochloride 1%	3276	1456	321	15	1	8	2.4 (2.1–2.7)	2.4 (1.7–3.0)	2.2 (0.5–4.0)
Glutaraldehyde 1%	477	213	53	18	4	4	5.2 (4.2–6.3)	2.8 (0.3–5.3)	9.4 (3.8–15.1)
Imidazolidinyl urea 2%	3256	1454	320	17	0	7	2.6 (2.2–2.9)	2.6 (1.9–3.2)	4.3 (2.5–6.0)
Imidazolidinyl urea 2% Aq	3277	1457	320	19	0	7	1.8 (1.5–2.0)	2.0 (1.5–2.6)	2.8 (1.5–4.1)
Mercapto mix 1%	3277	1455	321	9	0	6	0.5 (0.3–0.6)	0.8 (0.5–1.2)	1.3 (0.4–2.1)
Mixed dialkyl thioureas 1%	3277	1456	320	9	0	5	0.7 (0.5–0.8)	0.5 (0.1–0.8)	0.9 (0.0–1.9)
4- <i>tert</i> -butylphenol formaldehyde resin 1%	3277	1454	321	11	0	6	1.9 (1.6–2.1)	1.9 (1.3–2.5)	2.3 (0.9–3.7)
Paraben mix 16%	3277	1455	318	15	1	15	1.7 (1.4–2.0)	1.6 (1.0–2.1)	2.4 (1.0–3.8)
Thiuram mix 1%	3276	1454	318	23	0	11	3.3 (3.0–3.7)	3.4 (2.6–4.2)	4.2 (2.5–5.9)
Tixocortol-21-pivalate 1%	3276	1459	320	12	2	4	2.8 (2.4–3.1)	3.0 (2.3–3.7)	2.0 (0.3–3.7)
Toluenesulphonamide formaldehyde resin 10%	3277	1458	320	8	1	8	1.2 (1.0–1.4)	1.3 (0.8–1.8)	2.3 (1.0–3.5)
Triethanolamine 2%	3277	1458	321	31	1	7	0.9 (0.7–1.1)	0.6 (0.2–1.0)	1.7 (0.5–2.8)
Mercaptobenzothiazole 1%	3277	1456	320	13	0	5	0.9 (0.7–1.1)	0.8 (0.4–1.1)	0.7 (0.0–1.6)
Wool alcohols (lanolin alcohol) 30%	3277	1454	320	22	1	14	2.3 (2.0–2.5)	1.6 (1.0–2.2)	1.1 (0.0–2.7)
Phenol formaldehyde resin 1%	3257	1457	321	18	1	9	1.5 (1.3–1.8)	1.3 (0.8–1.8)	2.1 (0.8–3.5)
2-Hydroxy-4-methoxybenzophenone 3%	3276	1458	320	16	1	4	0.6 (0.5–0.8)	0.5 (0.2–0.8)	0.9 (0.0–1.4)
Gold sodium thiosulfate 0.25% in petrolatum	1018	496	129	7	0	2	5.2 (4.4–5.9)	3.7 (2.1–5.3)	7.1 (3.5–10.7)
<i>Compositae</i> mix 5%	886	498	128	9	0	1	2.2 (1.6–2.8)	2.3 (1.2–3.3)	0.9 (0.0–3.4)
Fragrance mix II	460	308	76	7	0	1	7.0 (5.6–8.5)	4.5 (2.5–6.6)	3.0 (0.0–8.3)
Amidoamine 0.1% Aq	1420	706	162	2	0	4	1.6 (1.1–2.0)	1.6 (0.9–2.4)	3.4 (1.3–5.5)

RAPRR, risk-adjusted positive reaction rate; 95% CI, 95% confidence interval; MCA, Mayo Clinic Arizona; MCJ, Mayo Clinic Jacksonville; MCR, Mayo Clinic Rochester; Aq, aqueous; DMDM, 1,3-dimethylol-5,5-dimethyl.

cold, dry weather.¹³ Recently, Uter *et al.*¹⁴ further investigated fluctuating skin irritability induced by low ambient temperatures and low humidity. They collected patch test results for 73,691 patients tested with 12 standard allergen series (including fragrances, biocides, and topical compounds) and combined them with meteorological data obtained by government agencies. A rise in irritant and allergic reactions and positive reactions was noted, and the authors hypothesized that this was caused by impairment of the epidermal barrier function. Nevertheless, the impact of dry or cold weather on potentially false positive reactions was restricted to only a few allergens. Notably, at MCA, irritant reactions were less common, despite the low local humidity.

Comparison with previous studies

Differences in the degree of exposure to allergens around the world may account for some of the varying rates of positive patch test reactions to similar allergens. For

example, reports from Saudi Arabia^{3,15} deemed the European Standard Series to be suitable but recommended the exclusion of benzocaine and primin from the series because they were of low yield. The addition of three allergens of local relevance was suggested, including black seed oil, local perfume mix, and henna.

The regional variation in our patch test results supports similar findings in other studies. Thompson and Belsito¹⁶ noted differences in patch test reaction rates when comparing data from the Midwestern city of Kansas City with data from other North American Contact Dermatitis Group centers. Patients in Kansas City were significantly more likely to react to potassium dichromate, formaldehyde and its releasers, methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) and glutaraldehyde. Although hypotheses about regional, demographic, and occupational differences were proposed to explain these differences, none were fully adequate. The authors concluded that although awareness of national trends is important,

dermatologists must be cognizant of variations in allergen sources within their communities and referral networks. In a different study, paraphenylenediamine sensitization caused by exposure to hair dyes was recently noted to be more prevalent in patch test centers located in central and southern Europe compared with those in Scandinavia.¹⁷

Thomson *et al.*¹ compared rates of corticosteroid allergy and corticosteroid-prescribing habits in two different areas in the UK. Their results suggested that the predominant use of non-fluorinated corticosteroids (hydrocortisone, hydrocortisone-17-butyrate, and budesonide) resulted in a higher prevalence of corticosteroid contact allergy than those in areas in which greater proportions of fluorinated corticosteroids were used.

Comparison of individual allergens

We were interested to observe that the greatest differences in positive patch test reaction rates occurred for the most common allergens (e.g., metals, fragrances, preservatives). Indeed, the greatest differences were observed for the eight allergens in the standard series that induced the most positive reactions. Although different regions of the USA may have true differences in allergen exposure levels and allergenicity, examination of our results did not reveal any consistent pattern. No simple explanation for the variation in rates of positive patch test reactions could be advocated or verified with our data. Nevertheless, exposure to nickel sulfate hexahydrate, gold sodium thiosulfate, and cobalt chloride may vary across the three US sites studied, and exposure to fragrances (balsam of Peru, fragrance mix) and topical antibiotics (neomycin) certainly may vary.

Many preservatives yielded different positive patch test rates at our three sites. This is an intriguing finding because about an equal number of other preservatives yielded no difference in positive patch test rates (Table 2).

A difference in allergenicity rates to common disperse dyes and several rubber allergens was observed. This variation is difficult to explain.

Statistical significance vs. clinical significance

Many allergens for which regional differences in reaction rates were observed (e.g., preservatives and emollients) generated very low rates of positive patch test reaction. For example, isopropyl myristate had RAPRRs of 0.1, 0.5, and 0.9% at the MCR, MCA, and MCJ sites, respectively ($P = 0.006$; data are not shown in the tables because the reaction rates were very low). Other allergens, including propylene glycol and chloroxylenol, had similarly low positive rates that showed significant differences among sites (data not shown; reaction rates were very low). Given its large sample size, this study was

sufficiently statistically powered to detect differences. Therefore, it is important to examine the actual positive patch test reaction rates and not only statistical significance when deciding whether results are clinically meaningful.

Limitations of the study

We acknowledge the limitations of this study. The number of patients patch tested at the three different clinics varied widely (3277 at MCR, 1465 at MCA, 321 at MCJ). We did not have information about residency (including duration of residency) for patients in the study. For example, patients may have recently arrived in an area or may have been visiting temporarily.

Conclusions

The three geographically disparate Mayo Clinic sites used a standardized approach to patch testing. When the results of patch tests using the standard allergen series over a seven-year period were examined, we observed significantly different allergic patch test reaction rates for many allergens. However, when we excluded the findings from the site with the fewest patients, regional variations were observed for far fewer allergens. Our results indicate that even when patch testing is standardized, regional variations in positive patch test reaction rates exist for many allergens in the standard series. No single explanation accounts for this variability in allergic patch test reaction rates. Importantly, however, many patch test allergens were associated with similar rates of positive patch test reactions.

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