

Positivity Ratio and Reaction Index: Patch-Test Quality-Control Metrics Applied to the North American Contact Dermatitis Group Database

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Background: The positivity ratio (PR) and reaction index (RI) characterize the ability of patch-test preparations to produce strong (++) or (+++) reactions as opposed to weak (+), questionable, or irritant reactions.

Objective: This study evaluates these measures for North American Contact Dermatitis Group (NACDG) patch-test preparations.

Methods: The PR and RI were calculated for 79 NACDG standard allergens tested from 1994 to 2006 ($n = 26,479$ patients). The median values were used as cutoff values for "acceptable" versus "problematic" preparations.

Results: The top 10 "acceptable" patch-test preparations ($PR \leq 55$ and $RI > 0.46$) were mixed dialkyl thioureas 1% in petrolatum (pet), tixocortol-21-pivalate 1% pet, ethylenediamine dihydrochloride 1% pet, sesquiterpene lactone mix 0.1% pet, nickel sulfate 2.5% pet, bacitracin 20% pet, thimerosal 0.1% pet, epoxy resin 1% pet, colophony 20% pet, and mercaptobenzothiazole 1% pet. The most "problematic" patch-test preparations ($PR > 55$ and $RI \leq 0.46$) were cocamidopropyl betaine 1% aqueous (aq), benzalkonium chloride 0.1% aq, jasmine absolute 2% pet, iodopropynyl butyl carbamate 0.1% pet, 2-bromo-2-nitropropane-1,3-diol 0.5% pet, methyldibromoglutaronitrile 0.4% pet, methyldibromoglutaronitrile/phenoxyethanol 2% pet and 2.5% pet, dimethylol dihydroxyethyleneurea 4.5% aq, and clobetasol-17-propionate 1% pet.

Conclusion: Caution should be used when interpreting reactions to "problematic" patch-test preparations with a high proportion of weak, irritant, and questionable reactions.

THE POSITIVITY RATIO (PR) was introduced by Geier and colleagues in 2003 as a measure of the quality of patch-test preparations.¹ The PR is defined as the percentage of + (weak) reactions among the sum of all positive reactions (+, ++, +++) for a given allergen (Table 1). The idea for the PR developed from the observation that some allergen preparations rarely induced strong or extreme reactions and that many of the weak reactions were found to be of questionable clinical relevance. Therefore, many of these weak reactions likely represented false-positive reactions, and this "false positivity" could be quantified mathematically. The PR ranges from 0 to 100%; lower numbers indicate a relatively lower percentage of

mild (+) reactions, representative of patch-test preparations likely to have high diagnostic quality.

The reaction index (RI) is another parameter used to assess the quality of patch-test preparations.² The RI is defined as the number of positive reactions minus questionable and irritant reactions divided by the sum of all three (see Table 1). RI values range from +1 to -1; a value of +1 indicates an ideal patch-test preparation causing no questionable or irritant reactions whereas a value of -1 indicates a preparation that causes no true allergic reactions but only irritant or questionable (doubtful, macular erythema) reactions. An RI of 0 results from an equal number of allergic reactions and questionable or irritant reactions.

Both the PR and RI have been applied to data from the Information Network of Departments of Dermatology (IVDK) in Germany³ and the Odense patch-test group in Denmark.⁴ To date, information on these parameters from patch-test groups outside of Europe have been lacking. The purpose of this study was to determine PR and RI values for patch-test preparations used by the North American Contact Dermatitis Group (NACDG).

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Table 1. Definitions of Positivity Ratio and Reaction Index

Parameter	Mathematical Formula	Range of Values	Value for Perfect Patch-Test Preparation
Positivity ratio	$\frac{\text{weak allergic} \times 100}{\text{allergic}^*}$	0 to 100%	0
Reaction index	$\frac{\text{allergic}^* - (\text{quest} + \text{IR})}{\text{allergic}^* + (\text{quest} + \text{IR})}$	-1 to 1	1

IR = irritant reactions; quest = macular erythema, doubtful, questionable reactions.

*Weak (+), strong (++), or extreme (+++) reaction.

Methods

This analysis of de-identified data was approved by the Minneapolis Veterans Affairs Medical Center's Subcommittee on Human Studies. The data for this analysis came from patients seen by members of the NACDG between July 1, 1994, and December 31, 2006. During that time, the NACDG standard series included a total of 79 different patch-test preparations (supplied by Chemo-technique Diagnostics AB, Malmö, Sweden) although the number of allergens tested for each 2-year cycle ranged from 50 to 65. Details regarding antigens tested during each period and methods used have been reported.⁵⁻¹⁰ Briefly, patch testing was performed with a standard technique with Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster A/S, Vennesla, Norway). The patches remained in place for 48 hours, and tests were evaluated initially at 48 hours (first reading) and again between 72 and 168 hours after placement (second reading). All data were checked for quality assurance and then manually entered into a computerized database (Access 2003, Microsoft Corporation, Redmond, WA).

A positive allergic reaction was interpreted as +, ++, or +++, manifested by erythematous papules, vesicles, a spreading reaction, or all of the signs. Macular erythema reactions were coded as doubtful (questionable). Irritant reactions were determined by morphology (eg, petechial, glazed, epidermal change only). Not all NACDG members routinely recorded irritant reactions. The recorded reaction at the second patch-test reading (72 to 168 hours after patch placement) was used for this analysis.

The PR (with 95% confidence intervals) and the RI for each patch-test preparation were calculated with *Statistical Analysis System* software (SAS Institute Inc., Cary, NC). In some cases, the same allergen was tested in two or more concentrations or in different vehicles; results for each preparation are reported separately. The arbitrary cutoff values for "acceptable" and "problematic" diagnostic-quality preparations were determined by the median values for each

parameter. For the PR, the median value was 55%; for the RI, the median value was 0.46. In accordance with suggested guidelines,^{1,2} we excluded from the main analyses the results for patch-test preparations that yielded fewer than 100 non-negative reactions, but we did report those results separately.

Results

A total of 26,479 patients were tested during the study period. The calculated RI and PR for each patch-test preparation are shown in Table 2, Table 3, Table 4, and Table 5. Excluding patch-test preparations yielding fewer than 100 reactions, 36 preparations had an "acceptable diagnostic-quality" PR that was less than or equal to 55%. Of these, 29 also had an RI of greater than 0.46 (see Table 2). These preparations have a low percentage of weak positive reactions and a low percentage of reactions that were doubtful, irritant or both. Of the 33 preparations with a "problematic diagnostic-quality" PR greater than 55%, 22 had an RI that was less than or equal to 0.46, indicating a high proportion of weak positive reactions, doubtful reactions, or irritant reactions (see Table 3). Eighteen preparations did not meet the defined criteria for "acceptable" or "problematic" and were labeled "indeterminate" (see Table 4). Fewer than 100 patients had positive reactions to the remaining 10 preparations (see Table 5).

Excluding results for patch-test preparations yielding fewer than 100 reactions, PR values ranged from 29 to 79%. Allergens with the lowest (acceptable) PR values included mixed dialkyl thioureas, tixocortol pivalate, ethylenediamine dihydrochloride, sesquiterpene lactone mix, nickel sulfate, bacitracin, thimerosal, budesonide 0.1% in petrolatum (pet), epoxy resin, and colophony. Allergens with the highest (problematic) PR values included cocamidopropyl betaine, cinnamic aldehyde, benzalkonium chloride, jasmine absolute, iodopropynyl butyl carbamate, 2-bromo 2-nitropropane-1,3-diol, dimethylol dihydroxyethyleneurea, methyl dibromoglutar-

Table 2. “Acceptable” Patch-Test Preparations*

<i>Allergen</i>	<i>No. Tested</i>	<i>No. of Reactions</i>		<i>Positivity Ratio</i>		<i>No. of Reactions</i>		<i>Reaction Index</i>
		<i>+ Only</i>	<i>+, ++, and +++</i>	<i>%</i>	<i>95% CI</i>	<i>Allergic – IR – Quest</i>	<i>Allergic + IR + Quest</i>	
Mixed dialkyl thioureas 1% pet	26,324	77	264	29.2	23.8, 35.0	211	317	0.67
Tixocortol-21-pivalate 1% pet	26,351	221	692	31.9	28.5, 35.6	611	773	0.79
Ethylenediamine dihydrochloride 1% pet	25,793	217	631	34.4	30.7, 38.2	566	696	0.81
Sesquiterpene lactone mix 0.1% pet	26,314	66	192	34.4	27.7, 41.6	161	223	0.72
Nickel sulfate 2.5% pet	25,736	1,617	4,194	38.6	37.1, 40.0	3,774	4,614	0.82
Bacitracin 20% pet	26,350	853	2,190	39.0	36.9, 41.0	1,971	2,409	0.82
Thimerosal 0.1% pet	16,733	699	1,768	39.5	37.3, 41.9	1,547	1,989	0.78
Epoxy resin 1% pet	25,788	206	520	39.6	35.4, 44.0	434	606	0.72
Colophony 20% pet	25,802	248	608	40.8	36.9, 44.8	493	723	0.68
Mercaptobenzothiazole 1% pet	25,795	147	356	41.3	36.1, 46.6	294	418	0.70
Compositae mix 6% pet	17,451	90	213	42.3	35.5, 49.1	167	259	0.64
Quaternium-15 2% pet	25,789	987	2,288	43.1	41.1, 45.2	2,002	2,574	0.78
Sodium gold thiosulfate 0.5% pet	19,863	853	1,975	43.2	41.0, 45.4	1,665	2,285	0.73
p-tert Butylphenol formaldehyde resin 1% pet	25,797	196	454	43.2	38.6, 47.9	382	526	0.73
N-Isopropyl-N-phenyl-p-phenylenediamine 0.1 pet	9,275	49	112	43.8	34.4, 53.4	89	135	0.66
Thiuram mix 1% pet	25,783	539	1,213	44.4	41.6, 47.3	1,005	1,421	0.71
p-Phenylenediamine 1% pet	25,764	573	1,279	44.8	42.1, 47.6	998	1,560	0.64
Benzocaine 5% pet	25,801	210	465	45.2	40.6, 49.8	392	538	0.73
Methylchloroisothiazolinone/methyliso- thiazolinone 100 ppm aq	26,298	304	652	46.6	42.7, 50.5	564	740	0.76
Mercapto mix 1% pet	25,795	135	279	48.4	42.4, 54.4	218	340	0.64
Chloroxylenol (PCMX) 1% pet	26,320	97	197	49.2	42.1, 56.4	151	243	0.62
Neomycin sulfate 20% pet	25,758	1,427	2,814	50.7	48.9, 52.6	2,485	3,143	0.79
Dibucaine 2.5% pet	17,727	94	182	51.6	44.1, 59.1	120	244	0.49
Black rubber mix 0.6% pet	14,490	76	146	52.1	43.6, 60.4	107	185	0.58
Fragrance mix 8% pet	26,329	1,418	2,679	52.9	51.0, 54.8	2,016	3,342	0.60
Methyl methacrylate 2% pet	26,335	185	348	53.2	47.8, 58.5	273	423	0.65
Tosylamide formaldehyde resin 10% pet	26,322	196	365	53.7	48.4, 58.9	293	437	0.67
Tea tree oil (oxidized) 5% pet	9,569	55	101	54.5	44.2, 64.4	85	117	0.73
Ethyl acrylate 0.1% pet	26,315	169	309	54.7	49.0, 60.3	234	384	0.61

aq = aqueous; IR = irritant reactions; pet = petrolatum; + = weak (nonvesicular) reaction—erythema with infiltration and possibly papules; ++ = strong (edematous or vesicular) reaction; +++ = extreme (spreading, bullous, or ulcerative) reaction; ppm = parts per million; Quest = questionable, doubtful, or with macular erythema only.

*Positivity ratio of ≤ 55 and reaction index > 0.46 .

onitrile 0.4%, and methyldibromoglutaronitrile/phenox-yethanol 2% and 2.5%.

Excluding results for patch-test preparations yielding fewer than 100 reactions, RI values ranged from -0.06 to 0.82 . Patch-test preparations with high (acceptable) values included bacitracin, nickel, ethylenediamine dihydrochloride, tixocortol pivalate, neomycin, thimerosal, quaternium-15, methylchloroisothiazolinone/methylisothiazolinone, gold, p-tert butylphenol formaldehyde resin, benzocaine, and tea tree oil. Preparations with the lowest (problematic) RI values included iodopropynyl butyl

carbamate 0.5% pet, benzalkonium chloride, clobetasol-17-propionate, iodopropynyl butyl carbamate 0.1% pet, cocamidopropyl betaine, dithiomorpholine, glutaraldehyde 1% pet, propylene glycol, methyldibromoglutaronitrile 0.4% pet, and potassium dichromate.

The top 10 “acceptable” patch-test preparations (PR ≤ 55 and RI > 0.46) (see Table 2) included mixed dialkyl thioureas, tixocortol-21-pivalate, ethylenediamine dihydrochloride, sesquiterpene lactone mix, nickel sulfate, bacitracin, thimerosal, epoxy resin, colophony, and mercaptobenzothiazole.

Table 3. “Problematic” Patch-Test Preparations*

Allergen	No. Tested	No. of Reactions		Positivity Ratio		No. of Reactions		Reaction Index
		+ Only	+, ++, and +++	%	95% CI	Allergic – IR – Quest	Allergic + IR + Quest	
dl- α -Tocopherol 100%	14,450	80	137	58.4	49.7, 66.7	72	202	0.36
Paraben mix 12% pet	26,339	188	301	62.5	56.7, 67.9	188	414	0.45
Potassium dichromate 0.25% pet	25,803	691	1,072	64.5	61.5, 67.3	467	1,677	0.28
<i>Myroxilon pereirae</i> (balsam of Peru) resin 25% pet	25,794	1,758	2,724	64.5	62.7, 66.3	1,700	3,748	0.45
Glutaraldehyde 0.2% pet	6,054	51	79	64.6	53.0, 75.0	36	122	0.30
Disperse Blue 106 1% pet	17,721	237	364	65.1	60.0, 70.0	183	545	0.34
Dithiomorpholine 1% pet	4,406	66	100	66.0	55.9, 75.2	31	169	0.18
Benzophenone-3 3% pet	24,318	92	139	66.2	57.7, 74.0	77	201	0.38
Amidoamine 0.1% aq	20,243	309	451	68.5	64.0, 68.5	282	620	0.45
Propylene glycol 30% aq	26,334	590	859	68.7	65.5, 71.2	354	1,364	0.26
Carba mix 3% pet	25,787	811	1,168	69.4	66.7, 72.1	618	1,718	0.36
Iodopropynyl butyl carbamate 0.5% pet	4,433	73	103	70.9	61.1, 79.4	–13	219	–0.06
Clobetasol 17 propionate 1% pet	9,572	41	57	71.9	58.5, 83.0	3	111	0.03
Methyldibromoglutaronitrile/phenoxyethanol 2.5% pet	4,005	211	293	72.0	66.5, 77.1	135	451	0.30
Dimethylol dihydroxyethyleneurea 4.5% aq	17,445	101	139	72.7	64.5, 80.0	76	202	0.38
Methyldibromoglutaronitrile/phenoxyethanol 2.0% pet	20,252	820	1,125	72.9	70.2, 75.5	571	1,679	0.34
Methyldibromoglutaronitrile 0.4% pet	16,702	304	415	73.3	68.7, 77.4	170	660	0.26
2-Bromo 2-nitropropane-1,3-diol 0.5% pet	26,948	547	744	73.5	70.2, 76.7	461	1,027	0.45
Iodopropynyl butyl carbamate 0.1% pet	20,235	56	75	74.7	63.3, 84.0	15	135	0.11
Jasmine absolute 2% pet	14,491	84	112	75.0	65.9, 82.7	71	153	0.46
Benzalkonium chloride 0.1% aq	4,892	173	230	75.2	69.1, 80.6	10	450	0.02
Cocamidopropyl betaine 1% aq	17,454	224	285	78.6	73.4, 83.2	76	494	0.15

aq = aqueous; IR = irritant reactions; pet = petrolatum; + = weak (nonvesicular) reaction—erythema with infiltration and possibly papules; ++ = strong (edematous or vesicular) reaction; +++ = extreme (spreading, bullous, or ulcerative) reaction; Quest = questionable, doubtful, or with macular erythema only.

*Positivity ratio > 55% and reaction index $\leq$ 0.46.

Discussion

This analysis provides useful information to physicians (especially those less experienced in patch testing) about interpreting reactions to specific patch-test preparations. Many of our findings are not surprising. Experienced patch testers often anecdotally state that certain patch-test preparations yield a high proportion of borderline (irritant, doubtful, or weakly positive) patch-test reactions. Many of those patch-test formulations were confirmed in our study as “problematic” by high PR and low RI values (see Table 3), including potassium dichromate, glutaraldehyde, dithiomorpholine, propylene glycol, amidoamine, carba mix, iodopropynyl butyl carbamate, methyldibromoglutaronitrile/phenoxyethanol, benzalkonium chloride, and cocamidopropyl betaine. (The NACDG eliminated dithiomorpholine, benzalkonium chloride, and the 2.5% concentration of methyldibromoglutaronitrile/phenoxyethanol from its standard screening tray for this reason.) Conversely, anecdotally reliable patch-test prepara-

tions were confirmed to be of “acceptable” diagnostic quality by low PR and high RI values (see Table 2); these include mixed dialkyl thioureas, tixocortol pivalate, epoxy resin, bacitracin, and quaternium-15. The major exception to the anecdotally “problematic” allergen preparations is fragrance mix, which is commonly cited as a borderline irritant; a substantial number of patients who have positive reactions to the fragrance mix do not react to the individual components of the mix.^{11–14} In our study, fragrance mix had a PR of 53% and an RI of 0.60, placing it in our defined “acceptable” category for diagnostic quality, albeit at the bottom of the category and borderline for “indeterminate.” This most likely reflects the arbitrary nature of the median cutoff values for each category rather than reality. Geier and colleagues used a PR value of 80% as the cutoff value between “good” and “not-so-good” patch-test preparations;¹ we chose the median PR value of our data, 55%, which is more conservative.

Table 6 summarizes data from the IVDK, the Odense group and our study. Comparing PR and RI values across

Table 4. “Indeterminate” Patch-Test Preparations*

<i>Allergen</i>	<i>No. Tested</i>	<i>No. of Reactions</i>		<i>Positivity Ratio</i>		<i>No. of Reactions</i>		<i>Reaction Index</i>
		<i>+ Only</i>	<i>+, ++, and +++</i>	<i>%</i>	<i>95% CI</i>	<i>Allergic – IR – Quest</i>	<i>Allergic + IR + Quest</i>	
Budesonide 0.1% pet	26,156	128	324	39.5	34.2, 45.1	185	463	0.40
Cobalt chloride 1% pet	26,332	893	2,072	43.1	41.0, 45.3	1,252	2,892	0.43
Lidocaine 15% pet	17,700	68	155	43.9	35.9, 52.1	98	212	0.46
Glutaraldehyde 1% pet	23,465	173	389	44.5	39.5, 49.6	131	647	0.20
Budesonide 0.01% pet	9,575	59	130	45.4	36.6, 54.3	59	201	0.29
Hydrocortisone-17-butyrate 1% pet	17,736	117	232	50.4	43.8, 57.0	138	326	0.42
Cocamide diethanolamine 0.5% pet	17,454	98	183	53.6	46.1, 60.9	109	257	0.42
Ethyleneurea/melamine formaldehyde 5% pet	26,309	512	927	55.2	52.0, 58.5	753	1,101	0.68
Ylang ylang oil 2% pet	17,456	117	210	55.7	48.7, 62.5	168	252	0.67
Glyceryl thioglycolate 1% pet	26,298	252	452	55.8	51.0, 60.4	312	592	0.53
Formaldehyde 1% aq	25,794	1,335	2,225	60.0	57.9, 62.0	1,827	2,623	0.70
Imidazolidinylurea 2% pet	26,311	395	652	60.6	56.7, 64.3	484	820	0.59
Diazolidinylurea 1% pet	26,333	467	766	61.0	57.4, 64.4	583	949	0.61
Diazolidinylurea 1% aq	26,286	424	635	66.8	63.0, 70.4	469	801	0.59
Lanolin alcohol 30% pet	25,807	396	590	67.1	63.2, 70.9	410	770	0.53
DMDM hydantoin 1% pet	26,327	354	515	68.7	64.5, 72.7	336	694	0.48
DMDM hydantoin 1% aq	26,280	267	386	69.2	64.3, 73.7	250	522	0.48
Cinnamic aldehyde 1% pet	20,871	430	568	75.7	72.0, 79.1	405	731	0.55

aq = aqueous; DMDM = dimethylol dimethyl; IR = irritant reactions; pet = petrolatum; + = weak (nonvesicular) reaction—erythema with infiltration and possibly papules; ++ = strong (edematous or vesicular) reaction; +++ = extreme (spreading, bullous, or ulcerative) reaction; Quest = questionable, doubtful, or with macular erythema only.

*Positivity ratio ≤ 55% and reaction index ≤ 0.46, or positivity ratio > 55% and reaction index > 0.46.

different patch-test groups is difficult for several reasons. First, specific manufacturers of patch-test materials may differ. The Odense group evaluated 24 Thin-Layer Rapid Use Epicutaneous (T.R.U.E.) Test allergens (Mekos

Laboratories A/S, Hillerød, Denmark), the IVDK evaluated 15 allergen preparations from Hermal (Reinbek, Germany), and our data included patch-test preparations produced by Chemotechnique Diagnostics (Malmö, Sweden). In addi-

Table 5. Patch-Test Preparations Yielding 100 or Fewer Allergic, Irritant, or Questionable Reactions

<i>Allergen</i>	<i>No. Tested</i>	<i>No. of Reactions</i>		<i>Positivity Ratio</i>		<i>No. of Reactions</i>		<i>Reaction Index</i>
		<i>+ Only</i>	<i>+, ++, and +++</i>	<i>%</i>	<i>95% CI</i>	<i>Allergic – IR – Quest</i>	<i>Allergic + IR + Quest</i>	
dl- α -Tocopherol acetate 100%	4,874	12	25	48.0	27.8, 68.7	13	37	0.35
Black rubber mix 0.6%/IPPD 0.1% pet	2,027	20	42	47.6	32.0, 63.6	25	59	0.42
Prilocaine 2.5% pet	4,890	3	6	50.0	11.8, 88.1	1	11	0.09
Triamcinolone acetonide 1% pet	9,576	16	29	55.2	35.7, 73.5	13	45	0.29
Methylchloroisothiazolinone/ methylisothiazolinone 100 ppm pet	2,009	37	62	59.7	46.5, 71.9	49	75	0.65
Phenoxyethanol 1% pet	6,897	9	13	69.2	38.6, 90.9	–1	27	–0.03
Tetracaine 1% pet	10,027	31	41	75.6	59.7, 87.6	23	59	0.39
Bisphenol F 1% pet	9,539	13	16	81.3	54.4, 96.0	11	21	0.52
BHT 2% pet	2,008	5	6	83.3	35.9, 99.6	3	9	0.33
BHA 2% pet	6,054	19	20	95.0	75.1, 99.9	11	29	0.38

BHA = butylated hydroxyanisole; BHT = butylated hydroxytoluene; IPPD = N-isopropyl-N-phenyl paraphenylenediamine; IR = irritant reactions; pet = petrolatum; + = weak (nonvesicular) reaction—erythema with infiltration and possibly papules; ++ = strong (edematous or vesicular) reaction; +++ = extreme (spreading, bullous, or ulcerative) reaction; ppm = parts per million; Quest = questionable, doubtful, or with macular erythema only.

Table 6. Positivity Ratio and Reaction Index Values from the NACDG, Odense Patch-Test Group, and IVDK

Patch-Test Preparation	Positivity Ratio			Reaction Index		
	NACDG (%; 95% CI)	Odense* (%)	IVDK† (%; 95% CI)	NACDG	Odense	IVDK (95% CI)
Ethylenediamine dihydrochloride 1% pet	34; 31, 38	36	NA	0.81	−0.65	NA
Nickel sulfate 5% pet	39; 37, 40	24	48; 47, 50	0.82	0.32	0.8
Epoxy resin 1% pet	40; 35, 44	40	NA	0.72	−0.20	NA
Colophony 20% pet	41; 37, 45	46	NA	0.68	0.33	NA
Mercaptobenzothiazole 1% pet	41; 36, 47	40	NA	0.70	−0.43	NA
Cobalt 1% pet	43; 41, 45	51	NA	0.43	−0.32	NA
p-tert Butylphenol formaldehyde resin 1% pet	43; 39, 48	48	NA	0.73	−0.56	NA
Quaternium-15 2% pet	43; 41, 45	51	NA	0.78	0.08	NA
Thiuram mix 1% pet	44; 42, 47	55	57; 54, 61	0.71	0.10	0.6
p-Phenylenediamine 1% pet	45; 42, 48	38	57; 53, 59	0.64	0.07	0.5
Methylchloroisothiazolinone 100 ppm	47; 43, 51	39	NA	0.76	0.19	NA
Mercapto mix 1% pet	48; 42, 54	42	NA	0.64	−0.43	NA
Neomycin 20% pet	51; 49, 53	53	NA	0.79	0.06	NA
Black rubber mix 0.6% pet	52; 44, 60	44	NA	0.58	−0.52	NA
Fragrance mix 8% pet	53; 51, 55	56	67; 65, 69	0.60	−0.18	0.5
Formaldehyde 1% aq	60; 58, 62	49	81; 77, 84	0.70	0.22	0.3
Paraben mix 12% pet	63; 57, 68	67	NA	0.45	−0.65	NA
Potassium dichromate (NACDG 0.25% pet; IVDK 0.5% pet)	65; 62, 67	55	68; 65, 71	0.28	−0.42	0.5
Balsam of Peru (<i>Myroxilon pereirae</i>) 25% pet	65; 63, 66	54	72; 71, 74	0.45	−0.18	0.5
Wool alcohol 30% pet	67; 63, 71	75	NA	0.53	−0.35	NA
Propylene glycol (NACDG 30% aq; IVDK 20% aq)	69; 66, 71	NA	86; 82, 89	0.26	NA	0.0
Carba mix 3% pet	69; 67, 72	63	NA	0.36	−0.27	NA
Cocamidopropyl betaine 1% aq	79; 73, 83	NA	94; 92, 96	0.15	NA	−0.2

Adapted from Geier J et al¹ (Odense group positivity ratios); Andersen KE, Andersen F⁴ (IVDK positivity ratios).

aq = aqueous; IVDK = Information Network of Departments of Dermatology; NA = not applicable because not reported in the study; NACDG = North American Contact Dermatitis Group; pet = petrolatum; ppm = parts per million.

*Odense study population: $n = 7,635$; Thin-Layer Rapid Use Epicutaneous (T.R.U.E.) Test patch-test preparation, concentration mg/cm².

†IVDK study population: $n \approx 25,000$, except for propylene glycol ($n = 16,832$) and cocamidopropyl betaine ($n = 17,323$); allergen preparations by Hermal, Reinbek, Germany.

tion, several preparations from the IVDK group were tested in different concentrations. Patch-test concordance is problematic even with the same allergens; up to one-third of patients with initial negative results will have positive reactions on retesting.^{15–17} A study comparing the results of 318 patients who were simultaneously patch-tested with antigens in petrolatum and with the T.R.U.E. Test found that patch-testing with the T.R.U.E. Test missed many relevant positive reactions to four allergens (fragrance mix, balsam of Peru, thiuram mix, and carba mix).¹⁸ The second reason comparing PR and RI values across different patch-test groups is difficult in that there is evidence that the duration of patch-test occlusion and the timing of the final reading (which differs by patch-test group) may affect RI values. Third, different groups use different scoring definitions; the Odense group used International Contact Dermatitis Research Group scoring (similar to NACDG

scoring) whereas the IVDK used the German Contact Dermatitis Research Group scoring system. Finally, there is evidence that testing patients who have a low irritancy threshold may result in lower RI values, higher PR values, or both.¹⁹ For these reasons, RI and PR should primarily be used as internal measures of patch-test quality.²⁰

Despite the difficulties in comparing PR and RI values from different patch-test groups, some similarities are evident (see Table 6). The order of allergens by PR as determined from our data and from the IVDK data is similar, except for formaldehyde, which had a higher IVDK PR value. The order of allergens by PR for the Odense group resembles that from our data. Odense values were lower (better) for nickel, methylchloroisothiazolinone/methylisothiazolinone, p-phenylenediamine, and black rubber mix.

There are several limitations to this study. First, we chose to focus primarily on PR values rather than RI values

because not all NACDG members routinely coded irritant reactions during the study period. Underestimating irritant reactions would result in higher values for the RI. Therefore, our RI values should be interpreted with caution. Second, although previous studies evaluated the RI by duration of antigen occlusion and time of last patch-test reading, we did not perform analyses by these factors; all of the NACDG patients' patches were occluded for 48 hours, but the specific timing of the last patch-test reading is not recorded in the NACDG database. Third, the RI and PR do not include information regarding clinical relevance (which has been incorporated into other parameters, such as the significance-prevalence index number).²¹ Determining the reliability of patch-test preparations is only one step in evaluating potential allergic contact dermatitis; the interpretation of the clinical relevance of a positive reaction to a given allergen is equally important.²² For example, the relevance of positive reactions to thimerosal and gold is notoriously low even though both had PR and RI values that put them in the "acceptable" diagnostic-quality group in our study.

Conclusion

Because the reaction index (RI) and the positivity ratio (PR) do not address the clinical relevance of positive reactions, they are primarily useful for assessing the quality of patch-test preparations. The standardization of patch-test preparations and the interpretation of their results continue to be among the most important issues in contact allergy. The RI and PR are best used for internal quality assurance although certain trends are apparent across patch-test groups.

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