
The value of patch testing patients with a scattered generalized distribution of dermatitis: Retrospective cross-sectional analyses of North American Contact Dermatitis Group data, 2001 to 2004

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Background: A scattered generalized distribution (SGD) of dermatitis is a challenging problem; patch testing is a strategy for evaluating allergic contact dermatitis as a relevant factor.

Objective: We sought to analyze patient characteristics and most frequently relevant positive allergens in patients presenting for patch testing with SGD.

Methods: We conducted retrospective cross-sectional analysis of North American Contact Dermatitis Group 2001 to 2004 data. Patients with SGD were compared with patients without SGD.

Results: Of 10,061 patients, 14.9% (n = 1497) had only a SGD. Men and patients with a history of atopic eczema were more likely to have dermatitis in a SGD ($P < .001$). Preservatives, fragrances, propylene glycol, cocamidopropyl betaine, ethyleneurea melamine formaldehyde, tixocortol pivalate, and budesonide were among the more frequently relevant positive allergens. Top allergen sources included cosmetics/beauty preparations/skin and health care products, clothing, and topical corticoids.

Limitations: This was a retrospective analysis of patch-tested patients with SGD suspected to have allergy.

Conclusions: A total of 49% of patients with SGD had at least one relevant positive allergen, thus demonstrating the benefit of patch testing these patients. (J Am Acad Dermatol 2008;59:426-31.)

Dermatologists are trained to evaluate distribution and rash morphology as clinical clues to possible contact allergy. The hands and eyelids are locations often suggested to be

affected by contact allergy and the North American Contact Dermatitis Group (NACDG) has analyzed and reported the allergens associated with dermatitis in these distributions.^{1,2} Many patients with

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Abbreviations used:

NACDG:	North American Contact Dermatitis Group
RPPT:	relevant positive patch test
SGD:	scattered generalized distribution

eczematous dermatitis referred to dermatologists have a scattered generalized distribution (SGD). Patients with SGD rashes usually present a difficult diagnostic and therapeutic challenge. Depending on the history and the various areas affected, some may be patch tested. The identification of relevant allergens can result in resolution or substantial improvement and enhanced quality of life.³⁻⁶

But how frequently does patch testing patients with SGD uncover potentially relevant results? Little has been published on a nonatopic eczematous SGD dermatitis. The purpose of this study was to examine the yield of patch testing, relevant allergens, and allergen sources in patients with SGD referred for patch testing. We also examined the postpatch testing diagnoses in patients with SGD without relevant positive patch test (RPPT).

METHODS

Patient selection

Deidentified patch testing data from 13 sites are compiled regularly by the NACDG.⁷ Data collection of the NACDG is Health Insurance Portability and Accountability Act compliant and designated as institutional review board exempt (Dartmouth-Hitchcock Medical Center Committee for the Protection of Human Subjects #16236). Although up to 3 anatomic sites affected by a rash can be entered per patient, only patients with the site “scattered generalized” as the sole site entered were included in this study subset. “Scattered generalized” was defined as more than 3 body sites affected by the dermatitis, or 3 sites if the sites were trunk, arms, and legs. The comparison group consisted of all patients without “scattered generalized” listed among any of the 3 sites.

Patch testing and data recording methods

Patch testing was performed in the standard manner of the NACDG.⁷ Six allergens differed from the 2001 to 2002 series to the 2003 to 2004 series, which resulted in a total of 71 allergens in the 4-year period. In few cases, a particular allergen was not tested (eg, a known prior positive). Additional allergens not on the NACDG series but deemed potentially relevant by the clinician were tested at the discretion of the individual clinician based on history

and physical examination. The source (but not name) of a relevant supplementary allergen was noted when applicable. Only one relevant non-NACDG allergen source could be recorded. Allergen relationship to occupation for all positive allergens was also recorded.

The relevance of positive allergens was recorded as definite, probable, possible, past, unknown, or not relevant.⁷ For the purpose of this study, current relevance was defined as present relevance (definite, probable, or possible), unless otherwise stated. Relevance was considered definite if a use test with the putative item containing the suspected allergen was positive or a positive patch test to the object/product was observed. Relevance was considered probable if the substance identified by patch testing could be verified as present in the known skin contactants of the patient. Relevance was considered possible if the patient was exposed to circumstances in which skin contact with materials known to contain the putative allergen would likely occur. The current relevance estimate was tabulated by adding the number of patients with relevance coded as definite, probable, or possible and converting this to a percentage of patients with a positive test result for the allergen. Source of exposure for each relevant positive allergen was coded (2155 different 3-digit codes used) by the investigator based on discussion with the patient.

An atopic predisposition was defined as having at least one of the atopic markers (a history of atopic eczema, asthma, or hay fever). After patch testing completion, the NACDG investigator determined and recorded up to 3 postpatch testing clinical diagnoses.

Statistical analysis

NACDG patch test data from 2001 to 2002 and 2003 to 2004 were entered into software (Access, Microsoft Corp, Redmond, Wash). Software (SPSS, Version 14, SPSS Inc, Chicago, Ill) was used for the analyses. The study group was defined as patients with the only distribution coded as SGD. This group was compared with those without a site code of SGD. Counts and proportions were determined to examine demographic and patch test data. Proportions of patients for each comparison were compared using χ^2 tests, an alpha level of 0.05 was used, and *P* values less than .05 were considered statistically significant. No adjustments for multiple comparisons were used.

RESULTS

Patient characteristics

Of 10,061 deidentified patients, 1497 (14.9%) met the study criteria of SGD only. In all, 378 patients

Table I. Demographics of patients with and without scattered generalized distribution

	SGD group n = 1497	Non-SGD group n = 8166	P value
Male, n (%)	613 (41)	2666 (33)	<.001
Age, y (%)			
0-18	59 (4)	311 (4)	ns
19-40	354 (24)	2548 (31)	ns
41-65	708 (47)	4233 (52)	ns
>65	376 (25)	1094 (13)	ns
Atopic predisposition			
Any of below	575 (38)	3134 (38)	ns
Hay fever history	362 (24)	2130 (26)	ns
Asthma history	208 (14)	1389 (17)	ns
Eczema history	313 (21)	1078 (14)	.001

ns, Not significant; SGD, scattered generalized distribution.

with site listed as scattered generalized plus another site of involvement were excluded from this analysis. The comparison group consisted of 8186 patients without "scattered generalized" listed as any of the 3 possible site locations. Characteristics of the two study groups are listed in Table I. Men were more likely to have a SGD than were women. In addition, a history of atopic eczema was significantly more frequent in the SGD subset (21% vs 14%, $P < .001$), although atopic disposition overall was not significantly different. Age and race (data not shown) were similar for patients with and without SGD.

Patch testing results

Of the 1497 tested patients with SGD dermatitis, 734 (49%) had at least one positive patch test deemed of definite, probable, or possible current relevance (RPPT). Of these patients, 15% had only one RPPT, 13% had two, 12% had 3 or 4, and 9% had 5 or more. Table II shows the frequency of the most commonly positive allergens in the SGD group and the current relevance estimate of each positive allergen. Men were more frequently positive to diazolidinyl urea (6.70% men positive vs 3.52% women positive, $P < .005$), imidazolidinyl urea (6.05% men positive vs 3.06% women positive, $P < .005$), and mixed dialkyl thioureas (1.31% men positive vs 0.34% women positive, $P < .04$). However when the frequency of these positive allergens with current relevance were compared with the frequency of relevant positives for these allergens in women, the difference was not significant. Women were significantly more frequently positive to neomycin (8.33% men positive vs 11.78% women positive, $P < .04$), nickel (7.83% men positive vs 20.62% women positive, $P < .001$), cobalt (3.27% men positive vs 9.09% women positive, $P < .001$), gold (2.48% men positive vs 11.46

women positive, $P < .001$), di alpha tocopherol (0.66% men positive vs 2.27% women positive, $P < .02$), and methyl methacrylate (0.16% men positive vs 1.93% women positive, $P < .005$), although, except for cobalt, the frequency of clinically relevant positive results to these allergens was not significantly different among men and women.

Exposure sources of NACDG allergens

The major source categories of allergen exposure in patients with RPPT are listed in Table III. Cosmetics/beauty preparations/skin and health care products were responsible for more than half of the RPPT in the SGD group, followed by drugs and medications (13%).

Positive relevant supplemental allergens

In all, 16% (n = 240) of patients in the SGD group had at least one other relevant allergen not on the NACDG screening series. In all, 38 patients had their only RPPT to a non-NACDG screening allergen, but this number was not significantly different from that of the non-SGD group ($P > .3$). Cosmetics/beauty preparations/skin and health care products were responsible for 40% of the RPPT to non-NACDG supplemental allergens in the SGD group, followed by clothing (20%) (Table III).

Occupationally related skin condition and allergen sources

A total of 5% of patients in the SGD group and 16% in the non-SGD group were deemed to have an occupationally related problem. Of the total number of 2155 RPPT recorded from the 1497 SGD subset, only 120 RPPT (5.6%) were coded as occupationally related. The most common occupationally related allergens were formaldehyde (n = 10), thiuram mix (n = 10), carba mix (n = 9), epoxy resin (n = 5), formaldehyde, mercaptobenzothiazole (n = 4), and mercapto mix (n = 3). Of the 10 positive reactions to sources included metalworking fluids (n = 4), coatings (n = 1), cream (n = 1), phenolic resins (n = 1), furniture fixtures structures and surfaces (n = 1), and unknown (n = 1).

Postpatch testing diagnoses

After patch testing, investigators could enter up to 3 final diagnoses corresponding to final diagnoses for a patient's skin problem. Approximately a third of patients in the SGD study group (31%, n = 458) were given a single diagnosis of allergic contact dermatitis. Of patients, 51% had allergic contact dermatitis listed as one of the 3 possible final diagnosis codes. Postpatch testing diagnoses in patients without RPPT are tabulated in Table IV.

Table II. Fifty most frequently positive allergens in patients with scattered generalized distribution

Order of positive allergen frequency	Allergen	No. tested	Percent positive (n)	Relevance			
				Current $\pm$ percent (n)	Definite percent (n)	Probable percent (n)	Possible percent (n)
1	Nickel sulfate, 2.5% pet	1491	15.4 (229)	46 (106)	1.3 (3)	14.8 (34)	30.1 (69)
2	Myroxylon pereirae, 25% pet ($P = .001$)	1495	13.4 (200)	82 (164)	0.5 (1)	17.5 (35)	64 (128)
3	Quaternium 15, 2% pet ($P = .001$)	1495	11.9 (178)	89 (158)	4.5 (8)	29.8 (53)	54.5 (97)
4	Formaldehyde, 1% aq ($P = .001$)	1496	11.4 (170)	75 (128)	0 (0)	24.7 (42)	50.6 (86)
5	Fragrance mix, 8% pet ($P = .05$)	1495	11.1 (166)	83 (137)	1.8 (3)	20.5 (34)	60.2 (100)
6	Thimerosal, 0.1% pet*	743	10.8 (80)	2.5 (2)	0 (0)	0 (0)	2.5 (2)
7	Neomycin, 20% pet	1495	10.4 (155)	28 (44)	4.5 (7)	13.5 (21)	10.3 (16)
8	Methyldibromoglutaronitrile/phenoxylethanol, 2% pet ($P = .001$)	1494	9.0 (134)	69 (92)	2.2 (3)	26.1 (35)	40.3 (54)
9	Bacitracin, 20% pet	1495	8.2 (123)	32 (39)	5.7 (7)	12.2 (15)	13.8 (17)
10	Sodium gold thiosulfate, 0.5% pet	1487	7.8 (116)	39 (45)	0 (0)	4.3 (5)	34.5 (40)
11	Cobalt chloride, 1% pet	1492	6.7 (100)	44 (44)	0 (0)	11 (11)	33 (33)
12	Propylene glycol, 30% aq ($P = .001$)	1494	6.0 (89)	94 (83)	30.3 (27)	20.2 (18)	42.7 (38)
13	Benzalkonium chloride, 0.1% aq*		5.7 (42)	17 (7)	2.4 (1)	2.4 (1)	11.9 (5)
14	Diazolidinyl urea, 1% pet ($P = .001$)	1493	4.8 (72)	92 (66)	30.6 (22)	30.6 (22)	54.2 (39)
15	2-Bromo-2-nitropropane-1,3-diol, 0.5% pet ($P = .02$)	1493	4.8 (72)	55 (40)	0 (0)	8.3 (6)	47.2 (34)
16	Potassium dichromate, 0.25% pet	1496	4.7 (70)	41 (29)	2.9 (2)	11.4 (8)	27.1 (19)
17	Diazolidinyl urea, 1% aq ($P = .001$)	1493	4.5% (67)	91 (61)	7.5 (5)	31.3 (21)	52.2 (35)
18	Carba mix, 3% pet	1496	4.4% (66)	65 (43)	1.5 (1)	12.1 (8)	51.5 (34)
19	Imidazolidinyl urea, 2% pet ($P = .001$)	1493	4.3 (64)	94 (60)	3.1 (2)	29.7 (19)	60.9 (39)
20	Tixocortol pivalate, 1% pet ($P = .001$)	1493	4.2 (62)	84 (52)	9.7 (6)	35.5 (22)	38.7 (24)
21	p-Phenylenediamine, 1% pet	1490	3.9 (58)	50 (29)	1.7 (1)	25.9 (15)	22.4 (13)
22	DMDM hydantoin, 1% pet ($P = .001$)	1494	3.7 (55)	96 (53)	0 (0)	25.5 (14)	70.9 (39)
23	Cocamidopropyl betaine, 1% aq ($P = .001$)	1493	3.6 (54)	89 (48)	14.8 (8)	25.9 (14)	53.7 (26)
24	Methyldibromoglutaronitrile, 0.4% pet*	741	3.4 (25)	72 (18)	12 (3)	24 (6)	36 (9)
25	Ethyleneurea melamine formaldehyde, 5 pet ($P = .001$)	1493	3.2 (47)	85 (40)	0 (0)	23.4 (11)	61.7 (29)
26	Ethylenediamine dihydrochloride, 1% pet	1496	3.1 (47)	36 (17)	14.9 (7)	8.5 (4)	12.8 (6)
27	DMDM hydantoin, 1% aq ($P = .001$)	1493	3.0 (44)	95 (42)	2.3 (1)	27.3 (12)	66.0 (29)
28	Amidoamine, 0.1% aq ($P = .01$)	1493	2.8 (42)	88 (37)	4.8 (2)	23.9 (10)	59.5 (25)
29	Thiuram mix, 1% pet	1496	2.7 (41)	68 (28)	0 (0)	26.8 (11)	41.5 (17)
30	Budesonide, 0.01% pet [†] ($P = .005$)	752	2.7 (20)	90 (18)	15.0 (3)	35.0 (7)	40.0 (8)
31	Lanolin alcohol, 30% pet	1497	2.5 (38)	82 (31)	7.9 (3)	18.4 (7)	55.2 (21)
32	Budesonide, 0.1% pet	1492	2.4 (36)	86 (31)	11.1 (4)	30.6 (11)	44.4 (16)
33	Methylchloroisothiazolinone/methylisothiazolinone, 100 ppm aq	1493	2.4 (36)	88 (32)	5.6 (2)	41.7 (15)	38.9 (14)
34	Imidazolidinyl urea, 2% aq	1496	2.4 (36)	97 (35)	2.8 (1)	36.1 (13)	58.3 (21)
35	Disperse blue 106, 1% pet	1493	2.2 (33)	82 (27)	0 (0)	24.2 (8)	57.8 (19)
36	Colophony, 20% pet	1496	2.1 (32)	41 (13)	3.1 (1)	0 (0)	37.5 (12)
37	Cinnamic aldehyde, 1% pet [†]	752	2.0 (15)	73 (11)	0 (0)	26.7 (4)	46.7 (7)
38	Benzocaine, 5% pet	1496	1.9 (28)	46 (13)	10.7 (3)	14.3 (4)	21.4 (6)
39	Ylang-ylang oil, 2% pet	1490	1.7 (26)	81 (21)	3.8 (1)	11.5 (3)	65.4 (17)
40	Glyceryl thioglycolate, 1% pet	1491	1.7 (26)	15 (4)	0 (0)	11.5 (3)	3.8 (1)
41	Cocamide DEA, 0.5% pet	1491	1.7 (25)	64 (16)	4.0 (1)	28.0 (7)	32.0 (8)
42	Epoxy resin, 1% pet	1496	1.7 (25)	28 (7)	4.0 (1)	16.0 (4)	8.0 (2)
43	DI alpha tocopherol, 100%	1490	1.6 (24)	83 (20)	12.5 (3)	25.0 (6)	45.8 (11)
44	Tosylamide formaldehyde resin, 10% pet	1493	1.3 (19)	68 (13)	0 (0)	31.6 (6)	36.8 (7)
45	Paraben mix, 12% pet	1494	1.3 (19)	90 (17)	10.5 (2)	31.6 (6)	47.4 (9)
46	Dibucaine, 2.5% pet	1493	1.2 (18)	17 (3)	0 (0)	11.1 (2)	5.6 (1)
47	Methyl methacrylate, 2% pet	1494	1.2 (18)	22 (4)	0 (0)	11.1 (2)	11.1 (2)
48	p-tert-Butylphenol formaldehyde resin, 1% pet	1496	1.1 (16)	19 (3)	12.5 (2)	0 (0)	6.3 (1)
49	Glutaral, 1% pet	1484	1.0 (15)	13 (2)	0 (0)	6.7 (1)	13.3 (2)
50	Ethyl acrylate, 0.1% pet	1492	1.0 (15)	40 (6)	6.7 (1)	13.3 (2)	20.0 (3)

Bold indicates statistically significant more commonly positive relevant allergens in patients with scattered generalized distribution than those without.

$\pm$ Current relevance = definite, probable, or probable relevance.

*This allergen was tested only during data cycle 2001-2002.

[†]This allergen was tested only during data cycle 2003-2004.

Table III. Summary of the most common sources coded for positive relevant antigens in the scattered generalized distribution group

	NACDG antigens (%) [*]	Non-NACDG antigens (n = 240) [†]
Cosmetics, beauty preparations, skin and health care products	1207 (56)	68 (40%)
Clothing	182 (8)	49 (20)
Drugs and medications	280 (13)	31 (13)
Steroids		
Pain relief, antipruritics, analgesics		
Medications, topical-other		
Sunscreens	0	6 (3)
Jewelry	129 (6)	0
Poison ivy, oak	n/a	5 (2)
Adhesives, glues, bonding agents	n/a	5 (2)

n/a, Not applicable; NACDG, North American Contact Dermatitis Group.

^{*}Expressed as a percent of the relevant positive NACDG allergens in the scattered generalized distribution group.

[†]Expressed as a percent of the relevant positive supplemental allergens tested in the scattered generalized distribution group.

DISCUSSION

Approximately 15% of the patients patch tested by the NACDG had an SGD only. This is similar to a study from Thailand that found that 9.3% of 129 patients referred for patch testing had SGD.⁸ Approximately half of our patients with SGD had a final diagnosis that included allergic contact dermatitis.

Interestingly, men presenting for patch testing were statistically more likely than women to have SGD. The reasons for this finding are unknown and require further study. The higher prevalence of a history of atopic dermatitis in the SGD group is not surprising, given the known widespread distribution of atopic dermatitis in some patients. Atopic dermatitis was considered to be a contributing factor in 16% (121 of 763 of patients) (Table IV) of patients with SGD without RPPTs.

The two most common allergens we identified in patients with SGD were nickel and *Myroxylon pereirae* (balsam of Peru). Although *Myroxylon pereirae* was significantly more common in patients with SGD as compared with the non-SGD group, nickel was not more common in the SGD group. A widespread dermatitis raises the possibility of a systemic exposure. Oral challenge with both of these allergens is primarily associated with hand eczema.⁹ However, Hjorth¹⁰ reported two children who were patch test positive to *Myroxylon pereirae* whose eczema flared after oral intake of naturally occurring balsams.

Table IV. Final postpatch testing diagnoses in patients with scattered generalized distribution without clinically relevant positive patch tests

Diagnosis	No. of patients with this diagnosis as one of 3 possible diagnosis entries
Other dermatitis [*]	156
Other dermatosis [†]	116
Atopic	121
Nummular	26
Psoriasis	25
Irritant	24
Contact urticaria	8
Stasis dermatitis	2
Photodermatitis	1
Seborrheic	1
Pompholyx	1

These are the patients with no clinically relevant allergens, no final interpretation of allergic, and no other relevant allergens.

^{*}Lichen simplex chronicus, spongiotic dermatitis not otherwise specified.

[†]Any other nonspongiotic dermatitis diagnosis not listed in the above choices, ie, connective tissue diseases, lichen planus.

An important finding in this study is that almost half (49%) of the patients with SGD had positive patch test results that were deemed at least possibly relevant to their dermatitis. Allergens that were most commonly relevant were those that are often found in multiple different topical products such as preservatives (formaldehyde, quaternium 15, methylidibromoglutaronitrile/phenoxyethanol, diazolidinyl urea, 2-bromo-2-nitropropane-1,3-diol, imidazolidinyl urea, and DMDM hydantoin). These allergens are often found in cosmetics/skin beauty products/health care products and, thus, consistent with these as major sources of allergens in patients with SGD. Although these allergens were also common in the non-SGD population, they were statistically significantly more common in patients with SGD. The frequency of positive reactions to propylene glycol was 6% in the SGD group. Propylene glycol as a relevant allergen in this group makes sense, as many over-the-counter and prescription products (eg, topical corticosteroids) with this ingredient would be likely to be used by a patient with an SGD rash. A similar explanation could be surmised about allergy to tixocortol pivalate, a marker for hydrocortisone allergy.

It is also significant that 51% of patients with SGD did not have RPPTs. Of this group of patients with SGD without RPPT, one-third (10% of the total SGD group) were not otherwise classifiable and were given a final diagnosis of "other dermatitis". Patients who have intractable dermatitis without a history of atopic eczema who are patch test negative are

considered to have unclassified endogenous eczema by some authorities.¹¹ Data from the Skin and Cancer Foundation of Australia found the frequency of unclassified dermatitis was 8% in their patients. This is similar to our findings.

The need for continued care of a persistent and troublesome skin condition in patients with SGD often entails expensive medications and potential adverse effects. Causes and treatment in this significantly large patch test–negative group of patients with scattered generalized dermatitis that is spongiotic but not otherwise specific should be further studied.

Study limitations

There are several limitations to this study. First, only those patients suspected of having allergic contact dermatitis are included in the NACDG database, thus these results may not be reflective of patients with SGD in the general dermatology population. Second, relevance was determined by the physician based on patient history and potential exposure, and nearly always is recorded soon after patch testing. Definite and probable categories of relevance represent the most robust elements of the relevance data. However, relevance for many allergens is coded as “possible,” which means the allergen identified can be found in products of the type used by the patient, but confirmation of the actual presence of the allergen in said product is not required. Relevance data should be considered a relevance estimate, with the “possible” category of relevance being the least certain. Improved relevance data would ideally allow for long-term follow-up and clinical outcome of the patient given avoidance of an allergen. This is not practical given that many NACDG patients are referred and travel long distances for testing.

Conclusion

Our data show that half of the patients with SGD suspected of contact allergy and patch tested had a contact allergen of current relevance. Advising patients with a persistent SGD dermatitis to only use

skin care products without the most frequent, relevant allergens identified in this study (formaldehyde-releasing preservatives, fragrances, and propylene glycol) is one treatment strategy that may be very helpful while awaiting patch testing. This study supports the role of patch testing in the evaluation of patients with SGD. More research is needed to understand the origin of SGD not caused by contact allergy, especially the 8% to 10% in the unclassified eczema category.

Melody S. Berens, PhD, was paid to complete the data analysis.

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