
Patients with negative patch tests: Retrospective analysis of North American Contact Dermatitis Group (NACDG) data 2001-2016



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Background: Little is known regarding the characteristics of patients with negative patch test (NPT) results.

Objective: To characterize patients with NPT results.

Methods: Retrospective cross-sectional analysis of 34,822 patch tested patients. NPT results were defined as negative or irritant final interpretations of all North American Contact Dermatitis Group screening allergens and no relevant allergens on supplemental series.

Results: Almost one-third of patients (n = 10,888 [31.3%]) had NPT results. Patients with NPT results were significantly more likely to be male ($P < .0001$), be age 40 years or younger ($P = .0054$), be nonwhite ($P = .0005$), and have dermatitis primarily having a scattered generalized distribution ($P = .0007$) or primarily located on the lips ($P = .0214$) or eyelids ($P = .0364$). However, the absolute differences in age, race, and site were small and may not be clinically meaningful. Patients with NPT results were significantly less likely to have occupationally related skin disease ($P < .0001$). Overall, 8.3% of patients with NPT results had occupationally related skin disease, with precision production worker/machine operator (28.5%), health care worker (17.0%), and mechanic/repairer (7.5%) being the most commonly related occupations. In all, 22.9% of patients with NPT results had relevant irritants and 41.6% of irritants were occupationally

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related; cosmetics/health care products and soaps were common sources for both occupationally related and non-occupationally related irritants.

Limitations: Retrospective cross-sectional study of tertiary referral population.

Conclusions: Patients with NPT results have distinct characteristics. (J Am Acad Dermatol 2019;80:1618-29.)

Key words: irritants; occupational; patch testing.

The 9-year prevalence of clinical allergic contact dermatitis is estimated to be 7% in the general population.¹ European multicenter studies indicate that the European standard series of 30 allergens yields at least 1 positive reaction in 40% to 50% of individuals referred for patch testing.²⁻⁶ Although the North American Contact Dermatitis Group (NACDG) publishes positivity rates for our screening series every 2 years,⁷⁻¹¹ less is known about the cohort of individuals who test negative. This study characterizes individuals who underwent patch testing by the NACDG and had no positive reactions.

METHODS

Database

This study was approved by the Minneapolis Veterans Affairs Medical Center's Human Studies Subcommittee. The methods for patch testing, evaluation of reactions, and data recording by the NACDG have been published.⁷⁻⁹ Allergens (Chemotechnique Diagnostics AB, Malmö, Sweden, and allergEAZE SmartPractice, Calgary, Canada) were applied with Finn chambers (SmartPractice, Phoenix, AZ) and Scanpor tape (Norgesplaster Alpha AS, Vennessla, Norway). NACDG members collected the following data shortly following each final patch test visit by using a standardized data sheet: sex, age, race, hay fever, eczema (childhood flexural dermatitis), asthma, dermatitis site(s) (a maximum of 3), final diagnosis/diagnoses (a maximum of 3), occupational relatedness, and relevant irritants. An expert in occupational classification determined patient occupation and industry by using the 3-digit codes published in the 1990 US Department of Commerce Census Industrial and Occupational Classification Codes.¹² Detailed 3-digit source codes were entered for relevant irritants. Only

CAPSULE SUMMARY

- We characterized patients with negative patch test results; this population has not been studied previously.
- Patients with negative patch test results have distinct characteristics. They are more likely to be male and have irritant dermatitis and less likely to have occupationally related skin disease when compared with patients with positive patch test results.

1 source was entered per irritant; if multiple sources were present, the most clinically relevant source was recorded.

Study population

From approximately January 2001 through December 2016, a total of 38,542 patients were patch tested to the NACDG screening series (Fig 1). Individuals with at least 1 NACDG allergen not tested (eg, individuals with a strong

previously positive reaction to nickel may not be retested to nickel) or unknown on final interpretation (n = 3720 [9.7%]) were excluded. Thus, the study population comprised 34,822 individuals.

Study design

Data were entered in Access software (Access 2010, Microsoft Corporation, Redmond, WA) and then analyzed in Excel software (Excel 2010, Microsoft Corporation). A negative patch test (NPT) result was defined as having (1) final interpretations of negative or irritant for all NACDG screening allergens and (2) no other relevant allergens from supplemental series. A positive patch test (PPT) result was defined as having (1) a final interpretation of allergic for 1 or more NACDG screening allergens or (2) a positive allergic reaction to a relevant allergen from a supplemental series.

Statistical analysis

Demographics, occupational relatedness, and relevant irritants were presented using counts and proportions. The populations with NPT results and PPT results were compared by using chi-square tests. No correction for multiple tests was used owing to the exploratory nature of this analysis; *P* values less than .05 indicated statistical significance. SAS software (version 9.2; SAS Inc, Cary, NC) was used to

Abbreviations used:

CI:	confidence interval
ESSCA:	European Surveillance System on Contact Allergies
NACDG:	North American Contact Dermatitis Group
NPT:	negative patch test
PPT:	positive patch test
RR:	relative risk
TRUE Test:	Thin-Layer Rapid Use Epicutaneous Test

calculate relative risk (RR) and confidence intervals (CIs).

RESULTS**Patch test results**

Of 34,822 patients tested by the NACDG, 68.7% (n = 23,934) had 1 or more PPT reactions; this included 22,538 patients who had 1 or more positive reaction(s) to NACDG screening allergen(s) and 1396 with positive reaction(s) to only non-NACDG supplemental allergen(s). These 23,934 patients were excluded from the study. The study cohort comprised 10,888 patients with NPT reactions (31.3%).

Demographics

Table 1 summarizes standardized demographic information (male, occupational dermatitis, atopic

dermatitis, hand, leg, face, age >40, index [MOAHLFA]¹³) of patients with NPT results and patients with PPT results. Patients with NPT results were significantly more likely to be male (RR, 1.22; CI, 1.19-1.26), aged 40 years or younger (RR, 1.05; CI, 1.01-1.09), and nonwhite (RR, 1.08; CI, 1.03-1.12). Patients with NPT results were significantly less likely to have occupationally related skin disease (RR, 0.69; CI, 0.65-0.73). There were no significant differences between the NPT and PPT groups in terms of history of atopic dermatitis, seasonal allergies, asthma, or any of the 3 aforementioned diseases.

Most commonly, the primary dermatitis patterns for patients with NPT results were location on the hands (21.8%), a scattered generalized distribution (19.4%), and location on the face (14.7%), which were the most common primary dermatitis patterns for patients with PPT results as well. However, when sites (≤ 3) were compared between these groups, patients with NPT results were significantly less likely to have dermatitis involving the hands (RR, 0.91; CI, 0.88-0.95), face (RR, 0.88; CI, 0.85-0.92), ears (RR, 0.81; CI, 0.71-0.93), scalp (RR, 0.86; CI, 0.80-0.93), neck (RR, 0.82; CI, 0.77-0.88), arms (RR, 0.86; CI, 0.82-0.90), or anogenital area (RR, 0.87; CI, 0.79-0.96). When only 1 body site (the primary dermatitis site) was analyzed, patients with NPT results were significantly more likely to have dermatitis in a scattered generalized distribution (RR, 1.07; CI, 1.03-1.11), lips (RR, 1.10; CI, 1.02-1.19), eyelids

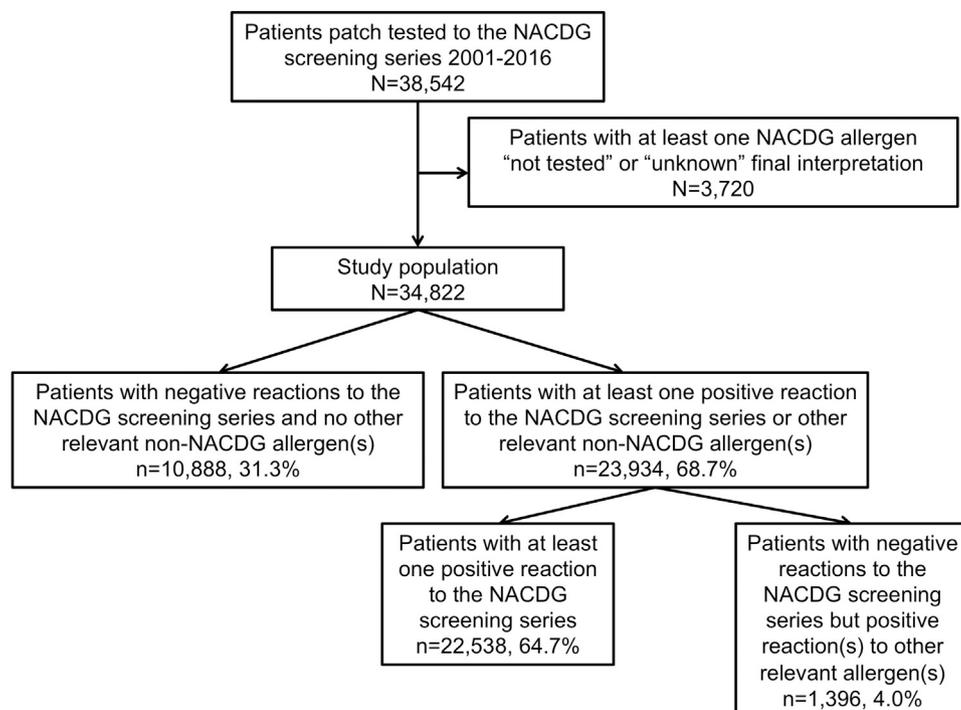


Fig 1. Study population. NACDG, North American Contact Dermatitis Group.

Table I. Patient demographics, patients with a negative patch test result versus patients with a positive patch test result

Characteristic	Overall, n (%)	Negative patch test result, [†] n (%)	Positive patch test result, ^{††} n (%)	Negative patch test result vs positive patch test result	
	N = 34,822	n = 10,888	n = 23,934	RR (95% CI)	P value
Sex					
Male [‡]	11,424 (32.8)	4073 (37.4)	7351 (30.7)	1.22 (1.19-1.26)	<.0001 [§]
Age					
Mean (y)	48.0	48.0	48.1		
>40 [‡]	23,270 (66.9)	7160 (65.8)	16,110 (67.3)	0.95 (0.92-0.99)	.0054 [§]
>18	33,127 (95.2)	10,321 (94.9)	22,806 (95.3)	0.94 (0.87-1.01)	.0734
19-29	3819 (11.0)	1247 (11.5)	2572 (10.8)		
30-39	5388 (15.5)	1704 (15.7)	3684 (15.4)		
40-49	6967 (20.0)	2107 (19.4)	4860 (20.3)		
50-59	7755 (22.3)	2333 (21.4)	5422 (22.7)		
≥60	9198 (26.4)	2930 (26.9)	6268 (26.2)		
Race					
White	29,766 (86.1)	9234 (85.1)	20,532 (86.5)	0.93 (0.89-0.97)	.0005 [§]
Nonwhite					
Black	1788 (5.2)	637 (5.9)	1151 (4.9)		
Asian	1732 (5.0)	516 (4.8)	1216 (5.1)		
Hispanic	689 (2.0)	258 (2.4)	431 (1.8)		
Other	597 (1.7)	200 (1.8)	397 (1.7)		
Atopy					
Hay fever	10,161 (29.3)	3216 (29.6)	6945 (29.1)	1.01 (0.98-1.05)	.4026
Eczema	8228 (23.7)	2601 (24.0)	5627 (23.6)	1.01 (0.98-1.05)	.5234
Asthma	5264 (15.2)	1673 (15.4)	3591 (15.1)	1.02 (0.98-1.06)	.4109
Any of the above [‡]	15,314 (44.0)	4829 (44.4)	10,485 (43.9)	1.01 (0.98-1.05)	.3934
Site (≤3 per patient)					
Scattered generalized	7783 (22.4)	2426 (22.3)	5357 (22.4)	1.00 (0.96-1.03)	.8499
Hand [‡]	9223 (26.5)	2692 (24.8)	6531 (27.3)	0.91 (0.88-0.95)	<.0001 [§]
Foot	2362 (6.8)	750 (6.9)	1612 (6.7)	1.02 (0.96-1.08)	.5911
Face [‡]	7537 (21.7)	2128 (19.6)	5409 (22.6)	0.88 (0.85-0.92)	<.0001 [§]
Lips	1582 (4.5)	517 (4.8)	1065 (4.5)	1.05 (0.97-1.13)	.2117
Nose	42 (0.1)	13 (0.1)	29 (0.1)	0.99 (0.63-1.56)	.9659
Eyelids	3760 (10.8)	1193 (11.0)	2567 (10.7)	1.02 (0.97-1.07)	.5098
Eyes	274 (0.8)	89 (0.8)	185 (0.8)	1.04 (0.88-1.23)	.6609
Ears	638 (1.8)	162 (1.5)	476 (2.0)	0.81 (0.71-0.93)	.0013 [§]
Scalp	1895 (5.4)	512 (4.7)	1383 (5.8)	0.86 (0.80-0.93)	<.0001 [§]
Neck	3057 (8.8)	799 (7.3)	2258 (9.4)	0.82 (0.77-0.88)	<.0001 [§]
Arm	5333 (15.3)	1469 (13.5)	3864 (16.2)	0.86 (0.82-0.90)	<.0001 [§]
Leg [‡]	3803 (10.9)	1161 (10.7)	2642 (11.0)	0.97 (0.93-1.02)	.3038
Trunk	4338 (12.5)	1303 (12.0)	3035 (12.7)	0.96 (0.91-1.00)	.0636
Anogenital	992 (2.9)	271 (2.5)	721 (3.0)	0.87 (0.79-0.96)	.0066 [§]
Most exposed areas	531 (1.5)	151 (1.4)	380 (1.6)	0.91 (0.79-1.04)	.1576
Only under clothing	371 (1.1)	106 (1.0)	265 (1.1)	0.91 (0.78-1.07)	.2617
Erythroderma	35 (0.1)	15 (0.1)	20 (0.1)	1.37 (0.94-2.01)	.1386
Other	1006 (2.9)	376 (3.5)	630 (2.6)	1.20 (1.11-1.30)	<.0001 [§]
Primary site					
Scattered generalized	6377 (18.3)	2107 (19.4)	4270 (17.9)	1.07 (1.03-1.11)	.0007 [§]
Hand [‡]	7841 (22.5)	2371 (21.8)	5470 (22.9)	0.96 (0.92-1.00)	.0269 [§]
Foot	1112 (3.2)	337 (3.1)	775 (3.2)	0.97 (0.88-1.06)	.4862
Face [‡]	5398 (15.5)	1596 (14.7)	3802 (15.9)	0.94 (0.90-0.98)	.0035 [§]
Lips	1211 (3.5)	415 (3.8)	796 (3.3)	1.10 (1.02-1.19)	.0214 [§]
Nose	19 (0.1)	7 (0.1)	12 (0.1)	1.18 (0.65-2.12)	.5994
Eyelids	3014 (8.7)	993 (9.1)	2021 (8.5)	1.06 (1.00-1.12)	.0364 [§]
Eyes	171 (0.5)	55 (0.5)	116 (0.5)	1.03 (0.83-1.28)	.7979

Continued

Table I. Cont'd

Characteristic	Overall, n (%)	Negative patch test result, [†] n (%)	Positive patch test result, ^{†‡} n (%)	Negative patch test result vs positive patch test result	
	N = 34,822	n = 10,888	n = 23,934	RR (95% CI)	P value
Ears	338 (1.0)	97 (0.9)	241 (1.0)	0.92 (0.77-1.09)	.3076
Scalp	1188 (3.4)	316 (2.9)	872 (3.6)	0.85 (0.77-0.93)	.0004 [§]
Neck	622 (1.8)	196 (1.8)	426 (1.8)	1.01 (0.90-1.13)	.8907
Arm	1719 (4.9)	531 (4.9)	1188 (5.0)	0.99 (0.92-1.06)	.7356
Leg [‡]	1464 (4.2)	464 (4.3)	1000 (4.2)	1.01 (0.94-1.10)	.7132
Trunk	1989 (5.7)	637 (5.9)	1352 (5.7)	1.03 (0.96-1.10)	.4466
Anogenital	736 (2.1)	199 (1.8)	537 (2.2)	0.86 (0.77-0.97)	.0125 [§]
Most exposed areas	443 (1.3)	129 (1.2)	314 (1.3)	0.93 (0.80-1.08)	.3285
Only under clothing	329 (0.9)	97 (0.9)	232 (1.0)	0.94 (0.80-1.12)	.4853
Erythroderma	26 (0.1)	12 (0.1)	14 (0.1)	1.48 (0.97-2.24)	.1012
Other	794 (2.3)	316 (2.9)	478 (2.0)	1.28 (1.17-1.40)	<.0001 [§]
Final diagnosis (≤3 per patient)					
Allergic contact dermatitis	19,510 (56.2)	392 (3.6)	19,118 (80.1)	0.03 (0.03-0.03)	<.0001 [§]
Irritant contact dermatitis	5687 (16.4)	2491 (23.0)	3196 (13.4)	1.52 (1.47-1.58)	<.0001 [§]
Atopic dermatitis	5549 (16.0)	2292 (21.1)	3257 (13.6)	1.41 (1.36-1.46)	<.0001 [§]
Psoriasis	1695 (4.9)	796 (7.3)	899 (3.8)	1.54 (1.46-1.63)	<.0001 [§]
Stasis dermatitis	280 (0.8)	104 (1.0)	176 (0.7)	1.19 (1.02-1.39)	.0319 [§]
Nummular eczema	725 (2.1)	356 (3.3)	369 (1.5)	1.59 (1.48-1.72)	<.0001 [§]
Photo dermatitis	480 (1.4)	167 (1.5)	313 (1.3)	1.12 (0.99-1.26)	.0893
Other dermatitis	5810 (16.7)	3291 (30.4)	2519 (10.5)	2.17 (2.11-2.23)	<.0001 [§]
Other dermatoses	3821 (11.0)	2051 (18.9)	1770 (7.4)	1.89 (1.82-1.95)	<.0001 [§]
Seborrheic dermatitis	771 (2.2)	420 (3.9)	351 (1.5)	1.77 (1.66-1.90)	<.0001 [§]
Pompholyx	278 (0.8)	152 (1.4)	126 (0.5)	1.76 (1.58-1.96)	<.0001 [§]
Contact urticaria	287 (0.8)	125 (1.2)	162 (0.7)	1.40 (1.23-1.60)	<.0001 [§]
Primary final diagnosis					
Allergic contact dermatitis	16,283 (46.9)	290 (2.7)	15,993 (67.0)	0.03 (0.03-0.03)	<.0001 [§]
Irritant contact dermatitis	3345 (9.6)	1949 (18.0)	1396 (5.8)	2.06 (1.99-2.13)	<.0001 [§]
Atopic dermatitis	4059 (11.7)	2013 (18.6)	2046 (8.6)	1.72 (1.66-1.79)	<.0001 [§]
Psoriasis	1179 (3.4)	655 (6.0)	524 (2.2)	1.83 (1.73-1.93)	<.0001 [§]
Stasis dermatitis	185 (0.5)	93 (0.9)	92 (0.4)	1.62 (1.40-1.87)	<.0001 [§]
Nummular eczema	583 (1.7)	321 (3.0)	262 (1.1)	1.79 (1.66-1.93)	<.0001 [§]
Photo dermatitis	328 (0.9)	133 (1.2)	195 (0.8)	1.30 (1.14-1.49)	.0003 [§]
Other dermatitis	4882 (14.1)	3051 (28.1)	1831 (7.7)	2.39 (2.33-2.46)	<.0001 [§]
Other dermatoses	2924 (8.4)	1754 (16.2)	1170 (4.9)	2.10 (2.03-2.17)	<.0001 [§]
Seborrheic dermatitis	547 (1.6)	347 (3.2)	200 (0.8)	2.07 (1.93-2.21)	<.0001 [§]
Pompholyx	222 (0.6)	135 (1.2)	87 (0.4)	1.96 (1.76-2.18)	<.0001 [§]
Contact urticaria	184 (0.5)	100 (0.9)	84 (0.4)	1.75 (1.53-2.00)	<.0001 [§]
Occupationally related [¶]	4026 (11.6)	902 (8.3)	3124 (13.1)	0.69 (0.65-0.73)	<.0001 [§]

CI, Confidence interval; RR, relative risk.

*For patients with a negative patch test result: sex missing for 1 patient, age missing for 10 patients, race missing for 33 patients, hay fever status missing for 13 patients, eczema status missing for 28 patients, asthma status missing for 22 patients, site missing for 13 patients, final diagnosis missing for 47 patients, and occupational relatedness missing for 19 patients. Denominators have been adjusted accordingly.

[†]For patients with a positive patch test result: sex missing for 4 patients, age missing for 9 patients, race missing for 207 patients, hay fever status missing for 94 patients, eczema status missing for 127 patients, asthma status missing for 82 patients, site missing for 18 patients, final diagnosis missing for 54 patients, and occupational relatedness missing for 51 patients. Denominators have been adjusted accordingly.

[‡]Male, occupational, atopic, hand, leg, face, age older than 40 years, positive patch test (MOAHLFAP) index.¹³

[§]Indicates statistical significance, P value less than .05.

^{||}Likely comprising patients with poison ivy, poison oak, and/or poison sumac allergic contact dermatitis; we do not patch test urushiol.

[¶]Refers to overall skin disease being occupationally related.

(RR, 1.06; CI, 1.00-1.12), or other (RR, 1.28; CI, 1.17-1.40) sites (with the term *other* meaning not falling into the 18 named categories as shown in Table D). The primary site for patients with NPT results was

significantly less likely to be the hand (RR, 0.96; CI, 0.92-1.00), face (RR, 0.94; CI, 0.90-0.98), scalp (RR, 0.85; CI, 0.77-0.93), or anogenital area (RR, 0.86; CI, 0.77-0.97).

Table II. Occupations and industries of patients with negative patch test results with occupationally related skin disease

Occupation	%	n
Precision production workers and machine operators	28.5	257
Health care workers	17.0	153
Mechanics and repairers	7.5	68
Transportation and material moving occupations	6.3	57
Construction occupations	5.4	49
Food preparation and service occupations	4.8	43
Personal service occupations	4.3	39
Not otherwise specified (n = 9)		
Hairdressers and cosmetologists (n = 30)		
Management occupations	3.5	32
Administrative occupations	2.8	25
Technicians	2.5	23
Cleaning and building service occupations	2.1	19
Engineers and scientists	1.8	16
Protective service and military occupations	1.4	13
Sales occupations	1.3	12
Agricultural occupations	1.3	12
Writers, artists, entertainers, and athletes	0.7	6
Teachers	0.7	6
Unknown or other	8.0	72
Total		902
Industry	%	n
Manufacturing	36.3	327
Metal, machinery, and equipment (n = 204)		
Chemicals and allied products (n = 30)		
Food and kindred products (n = 24)		
Lumber, wood, stone, clay, glass, and concrete products (n = 23)		
Printing, publishing, and allied industries (n = 17)		
Textile and paper products (n = 16)		
Petroleum, coal, rubber, and plastics products (n = 13)		
Professional and related services	22.2	200
Not elsewhere classified (n = 194)		
Physician clinics (n = 6)		
Retail trade	7.5	68
Personal services	5.0	45
Construction	4.9	44
Finance, insurance, real estate, business, and repair services	4.7	42
Transportation, communications, utilities, and sanitary services	4.5	41
Public administration	2.1	19
Agriculture, forestry, fisheries, and mining	1.8	16
Wholesale trade	1.4	13
Entertainment and recreation services	1.0	9
Unknown or other	8.6	78
Total		902

The most common primary final diagnoses for patients with NPT results were other dermatitis (28.1%), atopic dermatitis (18.6%), and irritant contact dermatitis (18.0%). For all final diagnoses (≤ 3 per patient), patients with NPT results were significantly less likely to have their disease diagnosed as allergic contact dermatitis (RR, 0.03; CI, 0.03-0.03)

and significantly more likely to have all other diagnoses (irritant contact dermatitis, atopic dermatitis, psoriasis, stasis dermatitis, nummular eczema, other dermatitis, other dermatoses, seborrheic dermatitis, pompholyx, and contact urticaria [P values of ≤ 0.0319 for ≤ 3 , except for photo dermatitis ($P = .0893$), and P values of $\leq .0003$ for primary]).

Table III. Sources of occupationally related irritants

Source	%	n
Chemicals and chemical products	32.8	340
NOS (n = 35)		
Coatings, adhesives, dyes, inks, photographic and copying chemicals (n = 72)		
NOS (n = 4)		
Coatings (paint, lacquer, shellac, varnish, stains) (n = 19)		
Adhesives, glues, bonding agents (n = 41)		
Dyes, coloring agents, inks, photographic chemicals (n = 8)		
Solvents, oils, lubricants, fuels (n = 205)		
NOS (n = 32)		
Coal, coal products, gasoline, diesel, jet fuel, kerosene, heating oil (n = 7)		
Solvents, degreasers, petroleum distillates (n = 66)		
Lubricating oils and greases (n = 23)		
Automotive oils and fluids (n = 23)		
Metalworking fluid, cutting oils (n = 54)		
Miscellaneous (acrylic, epoxy, urethane, and formaldehyde resins) (n = 28)		
Soaps, detergents, cleansers, disinfectants, laundry aids (nonskin)	17.3	179
NOS (n = 23)		
Soaps and detergents, miscellaneous (n = 119)		
Laundry detergents and aids (n = 2)		
Disinfectants (n = 35)		
Cosmetics, beauty preparations, skin and health care products	15.5	161
NOS (n = 6)		
Hair care products (n = 34)		
Nail care products (n = 3)		
Cosmetics (n = 5)		
NOS (n = 3)		
Moisturizers, lotions, creams (n = 2)		
Soaps and cleansers (personal hygiene) (n = 109)		
NOS (n = 58)		
Disinfectants (eg, alcohol, povidone-iodine) (n = 41)		
Hand sanitizers (n = 10)		
Dentistry materials and products (n = 4)		
Building and construction materials, tools, equipment, supplies	8.8	91
NOS (n = 10)		
Building materials (n = 33)		
Bricks, blocks, stone (n = 2)		
Cement, concrete, mortar (n = 15)		
Wood, lumber (n = 16)		
Sealants, caulking, and insulating materials (n = 17)		
Tools, equipment, instruments, miscellaneous supplies (n = 9)		
Paper products and supplies (n = 22)		
Clothing, wearing apparel, protective equipment, textiles	7.9	82
Clothing (n = 68)		
NOS (n = 11)		
Gloves (n = 40)		
Shoes, boots, sandals, slippers (n = 6)		
Shirts, pants, blouses, dresses, skirts (n = 8)		
Suits, coats, jackets (n = 3)		
Glasses and contact lenses (n = 1)		
Safety equipment, miscellaneous (eg, masks, respirators) (n = 6)		
Animals, plants, minerals, persons	4.1	42
Animals and plants (n = 13)		
Food products (n = 15)		
Minerals and persons (n = 14)		
Sewage, waste, debris, scrap	2.1	22

Continued

Table III. Cont'd

Source	%	n
Machinery and vehicles	1.2	12
Environmental, water	1.0	10
Furniture, fixtures, structures, and surfaces	0.4	4
Medications	0.2	2
Unknown or other	8.8	91
Total		1036

NOS, Not otherwise specified.

Dermatitis related to occupation

Overall 11.6% of patients tested (4026 of 34,822) had dermatitis deemed to be related to their occupation. Patients with PPT results were significantly more likely to have occupationally related dermatitis than were patients with NPT results (13.1% vs 8.3%, respectively [$P < .0001$]). Among the 902 patients with NPT results with occupationally related skin disease, the top 7 primary final diagnoses were irritant contact dermatitis (71.1%), atopic dermatitis (7.1%), other dermatitis (4.9%), allergic contact dermatitis (4.3%), psoriasis (3.7%), other dermatoses (3.5%), and contact urticaria (3.5%). The occupations and industries of patients with NPT results with occupationally related skin disease are listed in Table II. The most common occupations were precision production worker/machine operator (28.5%), health care worker (17.0%), and mechanic/repairer (7.5%). The most common industries were manufacturing (36.3%), professional and related services (22.2%), and retail trade (7.5%).

Relevant irritants

Of the 10,888 patients with NPT results, 22.9% ($n = 2489$) had relevant irritants. In this subgroup ($n = 2489$), 41.6% ($n = 1036$) had irritants that were occupationally related. Sources of irritants, both occupationally related and non-occupationally related, are summarized in Tables III and IV, respectively. The most common occupationally related sources of irritants were industrial chemicals/chemical products (32.8%); soaps/detergents/cleansers/disinfectants/laundry aids (nonskin) (17.3%); and cosmetics/beauty preparations/skin and health care products (15.5%). The most common non-occupationally related sources of irritants were cosmetics/beauty preparations/skin and health care products (47.9%); animals/plants/minerals/persons (11.9%); and soaps/detergents/cleansers/disinfectants/laundry aids (nonskin) (11.3%).

DISCUSSION

This study yielded several key findings. First, approximately one-third of patients referred for patch testing had NPT results (31.3%). Second, patients with NPT results were significantly more likely to be male ($P < .0001$); be age 40 years or younger ($P = .0054$); be nonwhite ($P = .0005$); and have dermatitis primarily with a scattered generalized distribution ($P = .0007$) or located primarily on the lips ($P = .0214$), eyelids ($P = .0364$), or other sites ($P < .0001$). Third, although patients with NPT results were less likely to have occupationally related skin disease than were patients with PPT results, 8.3% had occupationally related skin disease. The most commonly affected occupations were precision production worker/machine operator (28.5%), health care worker (17.0%), and mechanic/repairer (7.5%). Lastly, almost one-quarter of patients with NPT results had relevant irritants (22.9%) and 41.6% of these were related to occupation. Cosmetics/health care products and soaps were common sources for both occupationally related and non-occupationally related irritants.

Frequency of NPT results

The frequency of NPT results in our North American multicenter study was 31.3%. The European Surveillance System on Contact Allergy (ESSCA) is a large multicenter surveillance program that encompasses 12 European countries. The reported frequency of NPT results has varied widely; NPT rates for the European standard series tested by the ESSCA by year were as follows: in 2002-2003, from 36% in Italy to 74% in Denmark (10,511 patients)²; in 2004, 56% overall (11,643 patients)³; in 2005-2006, from 56.0% in northeastern Europe to 58.5% in southern Europe (19,793 patients)⁴; in 2007-2008, from 46% in Austria to 60% in Denmark (25,181 patients)⁵; and in 2009-2012, from 46.4% in Poland to 63.4% (59,728 patients).⁶ The frequency of NPT results was higher in the ESSCA data (typically 50%-60%) than in our data (31.3%). This difference is likely a reflection of the number of allergens tested

Table IV. Sources of non—occupationally related irritants

Source	%	n
Cosmetics, beauty preparations, skin and health care products	47.9	696
NOS (n = 186)		
Hair care products (n = 82)		
Nail care products (n = 5)		
Cosmetics (n = 171)		
NOS (n = 41)		
Moisturizers, lotions, creams (n = 49)		
Make-up (n = 47)		
Perfumes and fragrances (n = 5)		
Tattoos (n = 1)		
Deodorants and antiperspirants (n = 17)		
Lipsticks (n = 11)		
Soaps and cleansers (personal hygiene) (n = 86)		
NOS (n = 72)		
Disinfectants (eg, alcohol, povidone-iodine) (n = 12)		
Wipes (baby wipes, toilettes, etc) (n = 2)		
Sunscreens (n = 37)		
Eye care products (n = 20)		
Oral hygiene products (n = 12)		
Dentistry materials and products (n = 25)		
Miscellaneous health aids (n = 72)		
NOS (n = 10)		
Tapes, adhesive strips, other adhesives aids (n = 22)		
Essential oils, massage oils, aromatherapy (n = 25)		
Orthopedic implants, prostheses, medical and miscellaneous health devices (n = 15)		
Animals, plants, minerals, persons	11.9	173
Animals and plants (n = 10)		
Food products (n = 6)		
Minerals and persons (n = 157)		
Soaps, detergents, cleansers, disinfectants, laundry aids (nonskin)	11.3	164
NOS (n = 11)		
Soaps and detergents, miscellaneous (n = 138)		
Laundry detergents and aids (n = 5)		
Disinfectants (n = 9)		
Air fresheners, deodorizers (n = 1)		
Clothing, wearing apparel, protective equipment, textiles	6.4	93
Clothing (n = 79)		
NOS (n = 34)		
Gloves (n = 5)		
Shoes, boots, sandals, slippers (n = 34)		
Shirts, pants, blouses, dresses, skirts (n = 6)		
Jewelry, watches (n = 7)		
Safety equipment, miscellaneous (eg, masks, respirators) (n = 7)		
Building and construction materials, tools, equipment, supplies	5.2	75
NOS (n = 8)		
Tools, equipment, instruments, miscellaneous supplies (n = 60)		
Paper products and supplies (n = 7)		
Medications	3.8	55
Chemicals and chemical products	2.1	30
NOS (n = 7)		
Coatings, adhesives, dyes, inks, photographic and copying chemicals (n = 12)		
Coatings (paint, lacquer, shellac, varnish, stains) (n = 4)		
Adhesives, glues, bonding agents (n = 8)		
Solvents, oils, lubricants, fuels (n = 11)		
Environmental, water	1.8	26

Continued

Table IV. Cont'd

Source	%	n
Sewage, waste, debris, scrap	0.6	8
Miscellaneous consumer items	0.2	3
Coins, currency (n = 1)		
Personal grooming devices, applicators (n = 2)		
Furniture, fixtures, structures, and surfaces	0.1	1
Unknown or other	8.9	129
Total		1453

NOS, Not otherwise specified.

(the European standard series has 30 allergens, whereas the NACDG screening series has 70 allergens). Previous calculations of a hypothetical yield of the NACDG screening series as compared with that of the Thin-Layer Rapid Use Epicutaneous (TRUE) test (35 allergens) found that one-quarter to one-third of allergens identified by the NACDG series would have been missed by testing to the TRUE test.⁷ Additionally, our data accounted for additional relevant allergens; the frequency of negative patch tests for the NACDG screening series alone was 35.3%. Referral patterns and patch test population variations also likely play a significant role.

Demographics

Patients with NPT results were significantly more likely to be male ($P < .0001$), age 40 years or younger ($P = .0054$), and nonwhite ($P = .0005$). These results are not surprising, as women have increased skin exposure to allergens compared with men.¹⁴ For example, women have greater exposure to nickel through jewelry.¹⁵ Likewise, older individuals have accumulated more exposures to allergens than have younger individuals.^{16,17} Our group previously reported significant differences in PPT frequencies to specific allergens for white versus black patients; these differences are likely due to cultural practices and exposures.¹⁸ Importantly, although *statistically* significant, the differences in terms of age older than 40 years (65.8% in patients with NPT results vs 67.3% in patients with PPT results) and white race (85.1% vs 86.5%, respectively) are small and may not be *clinically* meaningful.

It is not surprising that patients with NPT results were significantly less likely to have a final diagnosis of allergic contact dermatitis ($P < .0001$) than were patients with PPT results, as patch testing is an important diagnostic tool in the diagnosis of allergic contact dermatitis. These patients may have had their disease diagnosed as allergic contact dermatitis from Repeat Open Application Tests, which is not captured in the NACDG database. We also do not

patch test for poison ivy, poison oak, or poison sumac, which likely accounted for the small number of individuals with an NPT result and a clinical diagnosis of allergic contact dermatitis.

There were no significant differences in atopic markers between patients with PPT results and patients with NPT results. The relationship between atopy and allergic contact dermatitis is unclear. Our results are similar to those of other large multicenter studies. The Information Network of Departments of Dermatology and the German Contact Dermatitis Research Group showed that frequency of PPT results to most allergens differed little between patients with and without eczema¹⁹; a study from Denmark had similar findings.²⁰

Body site location of dermatitis

We found that patients with NPT results were more likely to have dermatitis primarily with a scattered generalized distribution ($P = .0007$) or located primarily on the lips ($P = .0214$) or eyelids ($P = .0364$). Although there are numerous studies of allergens responsible for allergic contact dermatitis in specific body locations, there are few published data for patients with NPT results. Clinically, it is conceivable that dermatitis in these locations may have other underlying causes. Scattered generalized dermatitis is a common pattern for atopic dermatitis, dermatitis of senescence, or bullous pemphigoid, all of which may have histopathology findings of spongiotic dermatitis with eosinophils. Lip and eyelid dermatitis are often irritant or multifactorial. Sites categorized as other likely represent patients with conditions with body sites not listed (eg, burning mouth syndrome, systemic symptoms). Lastly, although the absolute differences in site may be statistically significant, clinical relevance may be lacking.

Occupational considerations

In all, 8.3% of patients with NPT results had occupationally related skin disease, and 71.1% of

them were given a final diagnosis of irritant contact dermatitis. Patients with NPT results were significantly less likely to have occupationally related skin disease ($P < .0001$) than were patients with PPT results. Although irritant contact dermatitis is more common than allergic contact dermatitis in population-based studies of occupationally related skin disease,²¹⁻²³ typically the only individuals who are referred for patch testing are those in whom allergic contact dermatitis is suspected. Therefore, this referral bias may result in an increased number of PPT results compared with NPT results in individuals with occupationally related skin disease.

In our study, the most common occupations for patients with NPT results and occupationally related skin disease were precision production worker/machine operator (28.5%), health care worker (17.0%), and mechanic/repairer (7.5%). Previous studies have found health care worker,²¹⁻²³ cleaning occupation,²¹⁻²³ kitchen worker,^{22,23} hairdresser,^{21,22} mechanic,²² metal surface processor,²¹ and craftsman²³ to be common occupations in populations with occupationally related skin disease that is predominantly irritant in nature. We found manufacturing (36.3%), professional and related services (22.2%), and retail trade (7.5%) to be the most common industries associated with skin disease in patients with NPT results. In a study analyzing 18,066 cases of irritant-predominant occupational contact dermatitis in the United Kingdom, the most common industries involved were manufacturing, health care, and personal services.²² In a study of 965 patients with irritant-predominant occupational skin disease in Singapore, the most common industries involved were metal/engineering, building/construction, and electrical/electronics.²⁴

Relevant irritants

In all, 22.9% of patients with NPT results had relevant irritants and 41.6% of irritants were occupationally related. The most common sources of occupationally related irritants were chemicals (including solvents, oils, lubricants, and fuels), soaps, and cosmetics/health care products. Previous studies have found soaps/wet work,²²⁻²⁴ solvents,^{22,24} oils/coolants,²²⁻²⁴ petroleum products,²² foods,¹⁹ and gloves¹⁹ to be the most common sources of occupationally related irritants. We found the most common sources of non-occupationally related irritants to be beauty/health care products, animals/plants/minerals/persons, and soaps.

Limitations

Limitations of this study include its retrospective, cross-sectional nature and lack of follow-up.

Additionally, the patients represent a tertiary referral population. No test is 100% sensitive; it is possible that contact allergy may have been missed if the allergen was not known, suspected, or available for testing. An informal survey of our group indicated that approximately 95% of individuals in this cohort were tested to supplemental allergens in addition to the NACDG screening series. Thus, the number with allergic contact dermatitis to an unidentified allergen is likely low (<5% of patients).

SUMMARY

This study provides a unique insight into an uncharacterized population. We found that almost one-third of patch tested patients had negative results (31.3%). Patients with NPT results were statistically more likely to be male, aged 40 years or younger, and nonwhite. Occupationally related skin disease was less common than in patients with PPT results, but among the patients with NPT results with occupationally related skin disease, the most common occupations were precision production worker/machine operator, health care worker, and mechanic/repairers. Relevant irritants were found in almost one-quarter of patients with NPT results; cosmetics/health care products and soaps were common sources for both occupationally related and non-occupationally related irritants.

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