

ORIGINAL ARTICLE

Positive patch test reactions in older individuals: Retrospective analysis from the North American Contact Dermatitis Group, 1994-2008

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Background: Relatively little is known about the epidemiology of allergic contact dermatitis in older individuals.

Objectives: We sought to determine the frequency of positive and clinically relevant patch test reactions in older individuals (≥ 65 years old) referred for patch testing, and to compare these results with those of adults (≤ 64 -19 years) and children (<18 years).

Design: This was a retrospective cross-sectional analysis of North American Contact Dermatitis Group data from 1994 to 2008.

Results: A total of 31,942 patients (older $n = 5306$; adults $n = 25,028$; children $n = 1608$) were patch tested. The overall frequency of at least one allergic reaction in older individuals was 67.3% as compared with 66.9% for adults ($P = .5938$) and 47% for children ($P = .0011$). Reaction rates that were statistically higher in older individuals as compared with both adults and children included: *Myroxylon pereirae*, fragrance mix I, quaternium-15, formaldehyde, imidazolidinyl urea, diazolidinyl urea, neomycin, bacitracin, methylidibromo glutaronitrile, methylidibromo glutaronitrile/phenoxyethanol, ethyleneurea melamine formaldehyde mix, and carba mix (P values $< .0004$). Patch test reaction rates that were significantly lower in older individuals than both comparison groups included: nickel, thimerosal, and cobalt (P values $< .0001$).

Limitations: Referral population was a limitation.

Conclusions: Older individuals were more likely to have at least one positive patch test reaction as compared with children, but had similar rates to adults. The frequency of positive reactions to specific allergens differed by age group, most likely as a result of exposures. (J Am Acad Dermatol 10.1016/j.jaad.2010.12.022.)

Key words: contact dermatitis; elderly; older individuals; patch testing.

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Relatively little is known about the epidemiology of allergic contact dermatitis in older patients. Of the few studies evaluating this issue (Table 1),¹⁻¹¹ most found that patch test reaction rates are lower in older individuals, possibly because of decreased immune response.^{4-6,9,12-14} In a study of 2776 patch-tested patients, Wohrl et al⁹ found that the positivity rate was highest (62%) in children (<10 years old) and steadily decreased with age to the lowest rate, 35%, in patients older than 70 years. In contrast, the study by Goh¹ of 1873 patch-tested patients found the highest rate (66%) of positive reactions in individuals older than 59 years and the lowest (44%) in patients younger than 20 years; the authors hypothesized that the higher rate in older individuals may be a result of greater exposure to occupational and environmental antigens with time. Similarly Nethercott et al³ found that allergic contact dermatitis in 4955 patch-tested patients was higher in individuals older than 40 years as compared with those younger than 40 years. Another study found that multiple sensitivities may be higher in older patients (aged >75 years).¹¹ The largest study, by Uter et al,⁷ evaluated 6533 patients aged 61 to 75 years and 2500 patients older than 75 years. Although several studies have reported patch test results by age, most were relatively small and only one¹⁰ reported clinical relevance.

The purpose of this study was to: (1) describe the frequency and relevance of positive patch test reactions in older individuals referred for patch testing; and (2) compare these results with results from adults and children who also underwent patch testing during the same time period.

METHODS

This analysis of deidentified data was approved by the Minneapolis Veterans Administration Medical Center's Subcommittee on Human Studies. Between July 1, 1994, and December 31, 2008, 31,942 patients were patch tested to the North American Contact Dermatitis Group (NACDG) standard series of 50 to 65 allergens. Methods for patch testing, coding, and determining final diagnoses and relevance of reactions have been previously described.¹⁵ Briefly, information collected on patients included: demographic information (age, gender, race, and atopy), sites of dermatitis (up to 3 sites), final diagnoses (up

to 3 diagnoses), and occupation. For each positive reaction, clinical relevance, occupational relatedness, and allergen source were identified. All data were manually entered into a computerized database (Access 2003, Microsoft Corp, Redmond, WA) and checked for quality assurance at a central location.

CAPSULE SUMMARY

- Previous data suggest that patch test reactivity differs by age.
- In this analysis of 31,942 patients, older (≥ 65 years) individuals were more likely to have at least one positive patch test reaction as compared with children (<18 years), but had similar rates to adults (19-64 years): rates of at least one clinically relevant positive reaction were significantly higher in older individuals.
- Rates for specific allergens differed by age group.

This analysis focused on older individuals, defined a priori as those 65 years or older. Two comparison groups were also defined: adults (≤ 64 and ≥ 19 years old) and children (≤ 18 years old). "Allergic" patients were defined as individuals who had at least one positive allergic patch test result to a NACDG standard series allergen; this group excluded patients who had doubtful reactions (macular erythema) not thought to be allergic in nature, irritant reactions, or negative reactions. Relevance

coded as "definite" (positive patch or use test to substance containing the allergen), "probable" (allergen verified in patient's skin contactant), or "possible" (allergen in patient's potential exposures) were considered currently clinically relevant. Allergic reactions coded as "past" or "unknown" relevance were not considered currently clinically relevant. In most cases, clinical relevance was assigned at the time of final patch test reading.

Analytical methods

Software (SAS, Version 8.2, SAS Institute Inc, Cary, NC; and Access 2003, Microsoft Corp) were used. Counts and proportions were determined for demographic and allergen-related data. Data from the 3 populations (older, adult, children) were compared using Pearson χ^2 test (Fisher exact test, two tailed, when appropriate). A *P* value of less than or equal to .0013 was considered statistically significant (Bonferroni correction for multiple comparisons = 40/.05). These analyses included data previously published by our group on positive reactions in children,¹⁶ but the current study encompasses a larger population and different study questions.

RESULTS

Demographics by age group

As shown in Fig 1, 31,942 patients were patch tested from 1994 to 2008. A total of 5306 patients (16.6%) met our criteria for older individuals (≥ 65

Table I. Studies reporting older patch-tested individuals

Study	Data collection years	Definition of "older," y	No. of older individuals	No. with >1 positive reaction	Clinical relevance	Most common allergens (frequency)
Goh, ¹ 1986	1984-1985	>59	476	59/90 (65.6%)	NR	NR
Rietschel and Rosenthal, ² 1990	1984-1987	>80	55	NR	NR	<i>Myroxylon pereirae</i> (16%) Cinnamic aldehyde (11%) Nickel (11%) Imidazolidinyl urea (11%)* Neomycin (6%) Ethylenediamine (6%)
Nethercott et al, ³ 1991	1985-1989	>40	2557	Allergic: 50.1% Irritant: 17.6%	NR	Nickel sulfate (10.6%) Neomycin sulfate (9.0%) Thimerosal (8.1%) Formaldehyde (8.0%) P-phenylenediamine (7.8%) <i>Myroxylon pereirae</i> (6.7%)
Wantke et al, ⁴ 1996	1991-1994	≥ 70	295	34%	NR	Nickel sulfate (12.2%) <i>Myroxylon pereirae</i> (8.8%) Cobalt chloride (4.4%) Neomycin sulfate (4.1%) Thimerosal (3.4%) Ethyl mercuric chloride (1.4%) Thiosalicylic acid (1.0%)
Gupta et al, ⁵ 1999	1982 and 1997	>65	1982: 39 1997: 41	1982: 25/39 (64%) 1997: 24/41 (59%)	NR	Topical antibacterials (20%, 9%) [†] Rubber accelerators (15%, 10%) [†] Balsams and fragrances (13%, 37%) [†] Nickel (5%, 9%) [†] Colophony (5%, 4%) [†] Lanolin (5%, 2%) [†]
Schafer et al, ⁶ 2001	1997-1998	Age groups 28-39 40-49 50-59 60-78	NR (4 age groups total = 1141)	43.6% 42.0% 36.7% 37.0%	NR	Fragrance mix (15.9%) Nickel sulfate (13.1%) Thimerosal (4.7%) <i>Myroxylon pereirae</i> (3.8%) Turpentine (2.5%) Methyldibromo glutaronitrile (1.7%)
Uter et al, ⁷ 2002	1996-1998	Age groups 61-75 >75	6533 2500	NR	NR	<i>Myroxylon pereirae</i> (15.2%) Fragrance mix (14.4%) Lanolin alcohol (8.4%) Nickel (5.2%) Colophony (5.0%) Neomycin (4.9%)
Önder and Öztas, ⁸ 2003	NR	>56	272	244/272: 90% Allergic: 60% Irritant: 30%	NR	Nickel sulfate (23%) Fragrance mix (10%) Para-phenylenediamine (10%) <i>Myroxylon pereirae</i> (8%) Potassium dichromate (7%) Neomycin sulfate (7%)

Continued

Table I. Cont'd

Study	Data collection years	Definition of "older," y	No. of older individuals	No. with >1 positive reaction	Clinical relevance	Most common allergens (frequency)
Wohrl et al, ⁹ 2003	1997-2000	>70	152	53/152 (34.9%)	NR	Fragrance mix (11.2%) Metallic mercury (8.6%) Nickel sulfate (8.6%) <i>Myroxylon pereirae</i> (3.3%) Ethyl mercury (2.0%) Paraben mix (2.0%)
Tosti et al, ¹⁰ 2004	2002-2003	>65	224	43%	41%	Nickel sulfate (12%) Topical medicaments (13%) Fragrance mix (9%) Potassium dichromate (7%) <i>Myroxylon pereirae</i> (5%) Euxyl K400 (5%)
Green et al, ¹¹ 2007 [‡]	1994-2005	>70	395	31.9%	NR	Fragrance mix I (12.9%) Neomycin sulfate (8.8%) <i>Myroxylon pereirae</i> (8.1%) Lanolin allergens (4.5%) Gentamicin (2.3%) Tixocortol pivalate (1.2%)

NR, Not reported.

*Complete data not available, multiple concentrations used during testing.

†Percentage listed represents data for 1982 and 1997.

‡Only topical medicaments reported.

years old). In all, 78.4% were adults and 5.0% were children. The percentage for Male, Occupational, Atopy, Hand, Leg, Face, and Age >40 (MOAHLFA index)¹⁷ for these 3 study groups are shown in Table II. Not surprisingly, occupationally related dermatitis was highest in the adult population (20.2%) as compared with older individuals (1.9%) or children (3.4%), and atopic dermatitis was highest in the pediatric population (84.4%) as compared with adults (60.2%) and older individuals (36.4%). Hand dermatitis was approximately twice as common in the adult population (34.7%) as compared with the other two groups (13.7% older and 16.0% children).

Frequency of at least one positive reaction by age group

As shown in Table III, the frequencies of at least one positive reaction and at least one positive clinically relevant reaction were highest in older individuals (67.3% and 52.1%, respectively). Older individuals were 1.1 times more likely to have at least one positive patch test reaction than children (95% confidence interval 1.03-1.12, $P = .0011$); although this frequency was slightly higher in older individuals (67.3%) as compared with adults (66.9%), this difference did not reach statistical significance. Older individuals were also 1.1 times more likely to have at least one clinically relevant reaction as compared

with both adults (95% confidence interval 1.04-1.10; $P < .0001$) and children (95% confidence interval 1.05-1.17; $P = .0003$).

Positivity rates of specific allergens by age group: top 20 allergens

Specific allergens and the frequency of positive patch test reactions for the 3 age groups are listed in Table IV with comparisons for the 20 most frequent allergens in Table V. Allergen reaction rates that were statistically higher in older individuals as compared with both adults and children included: *Myroxylon pereirae* (balsam of Peru), fragrance mix I, formaldehyde preservatives (quaternium-15, formaldehyde, imidazolidinyl urea in pet, and diazolidinyl urea in both pet and aqueous formulations), antibiotics (neomycin and bacitracin), methyl dibromo glutaronitrile (0.4% and combined with phenoxyethanol 2%), ethyleneurea melamine formaldehyde, and carba mix. Reaction rates that were significantly higher in older individuals as compared with children (but not adults) included p-phenylenediamine and thiuram mix. Allergen reaction rates that were statistically lower in older individuals as compared with both adults and children included nickel, thimerosal, and cobalt. Positive reactions to gold were significantly lower for older patients as compared with adults, but not significantly different from children.

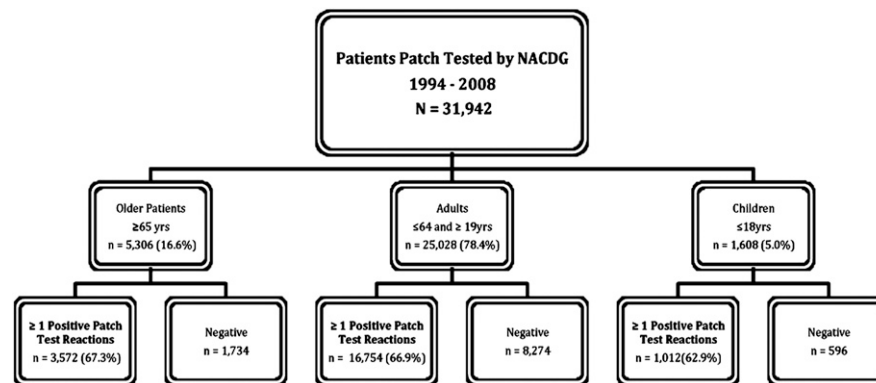


Fig 1. Flow chart of study population. *NACDG*, North American Contact Dermatitis Group.

Table II. MOAHLFA index data

Demographic data (N = 31,942)	Older (≥ 65 y)		Adult (≤ 64 and ≥ 19 y)		Children (≤ 18 y)	
	n	%	n	%	n	%
Male	2107	39.7	8696	34.7	654	40.7
Occupation related	103	1.9	5050	20.2	54	3.4
Atopic dermatitis	1931	36.4	15,074	60.2	1357	84.4
Hand	729	13.7	8680	34.7	264	16.0
Leg	739	13.9	2415	9.7	207	13.0
Face	914	17.2	5431	21.7	290	18.0
Age > 40 y	5306	100	15,658	62.6	0	0

MOAHLFA, Male, Occupational, Atopy, Hand, Leg, Face, and Age >40.

Table III. Frequency of one or more positive or relevant patch test reactions by age group

	Older, n (%)	Comparison, n (%)	χ^2 (P value)	Risk ratio (95% CI)
≥ 1 Positive patch test reactions				
Older vs adult	3572 (67.3)	16,754 (66.9)	.28 (.5938)	1.01 (0.99-1.03)
Older vs children	3572 (67.3)	1012 (62.9)	10.62 (.0011)	1.07 (1.03-1.12)
≥ 1 Relevant positive patch test reactions				
Older vs adult	2762 (52.1)	12,205 (48.8)	18.95 (<.0001)	1.07 (1.04-1.10)
Older vs children	2762 (52.1)	755 (47.0)	12.85 (.0003)	1.11 (1.05-1.17)

CI, Confidence interval.

DISCUSSION

There are several important findings of this study. First, this study describes the frequency of allergic reactions in older individuals referred for patch testing. Second, older individuals had significantly higher reaction rates to specific preservatives, topical antibiotics, and two rubber chemicals as compared with younger groups. Third, reaction rates to metals (cobalt, nickel, and gold) and thimerosal were significantly lower in older individuals than younger patients.

Positive patch test reactivity

Comparison of our results with those from other studies is difficult because of differences in study

designs. Unlike other studies that found lower patch test reactivity rates in older individuals,^{4-6,9,12-14} we found a significantly higher rate in older individuals. The differences in our study, however, were relatively small (0.4% and 4.4% absolute differences in adults and children, respectively) (Table III); statistical significance is likely a result of large sample size.

Fragrances and flavorings

Myroxylon pereirae, a marker for fragrance and flavoring allergy, was the most common allergen in our older population (16.1%). Fragrance mix was the second most common allergen identified (15.1%). Concomitant reactions to fragrances and flavorings are not uncommon and our results are consistent

Table IV. Frequency of positive or clinically relevant patch test reactions to specific allergens by age group

Allergen	Older (≥ 65 y), n = 5306		Adult (≤ 64 and ≥ 19 y), n = 25,028		Children (≤ 18 y), n = 1608	
	Positive %	Relevant %	Positive %	Relevant %	Positive %	Relevant %
1. <i>Myroxylon pereirae</i> 25% pet	(853/5306) 16.1	(719/5306) 13.6	(2626/25,028) 10.5	(2136/25,028) 8.5	(79/1608) 4.9	(63/1608) 3.9
2. Fragrance mix 8% pet	(799/5306) 15.1	(701/5306) 13.2	(2439/25,028) 9.8	(2071/25,028) 8.3	(94/1608) 5.9	(84/1608) 5.2
3. Neomycin sulfate 20% pet	(692/5306) 13.0	(270/5306) 5.1	(2585/25,028) 10.3	(900/25,028) 3.6	(122/1608) 7.6	(37/1608) 2.3
4. Quaternium-15 2% pet	(629/5306) 11.9	(533/5306) 10.0	(2111/25,028) 8.4	(1836/25,028) 7.3	(51/1608) 3.2	(48/1608) 3.0
5. Formaldehyde 1% aq	(629/5306) 11.9	(464/5306) 8.7	(2020/25,028) 8.1	(1460/25,028) 5.8	(47/1608) 2.9	(32/1608) 2.0
6. Bacitracin 20% pet	(587/5306) 11.1	(276/5306) 5.2	(1949/25,028) 7.8	(812/25,028) 3.2	(72/1608) 4.5	(32/1608) 2.0
7. Nickel sulfate 2.5% pet	(532/5306) 10.0	(241/5306) 4.5	(4312/25,028) 17.2	(2242/25,028) 9.0	(416/1608) 25.9	(286/1608) 17.8
8. Methyl dibromo glutaronitrile/phenoxyethanol 2.5% pet (1996) (n = 4094)	(65/723) 9.0	(41/723) 5.7	(232/3246) 7.2	(132/3246) 4.1	(3/125) 2.4	(1/125) 0.8
9. Methyl dibromo glutaronitrile/phenoxyethanol 2.0% pet (1998-2007) (n = 25,813)	(344/4215) 8.2	(223/4215) 5.3	(1126/20,162) 5.6	(734/20,162) 3.6	(19/1436) 1.3	(10/1436) 0.7
10. Sodium gold thiosulfate 0.5% pet (1996-2003) (n = 20,368)	(244/3346) 7.3	(90/3346) 2.7	(1586/15,897) 10.0	(644/15,897) 4.1	(69/1125) 6.1	(37/1125) 3.3
11. Thimerosal 0.1% pet (1994-2000) (n = 16,877)	(204/2897) 7.0	(22/2897) 0.8	(1447/13,379) 10.8	(123/13,379) 0.9	(80/601) 13.3	(10/601) 1.7
12. Diazolidinyl urea 1% pet	(337/5306) 6.4	(292/5306) 5.5	(667/25,028) 2.7	(607/25,028) 2.4	(17/1608) 1.1	(17/1608) 1.1
13. Ethyleneurea melamine formaldehyde 5% (1994-2005) (n = 26,857)	(276/4462) 6.2	(200/4462) 4.5	(680/21,043) 3.2	(412/21,043) 2.0	(13/1352) 1.0	(10/1352) 0.7
14. Carba mix 3% pet	(308/5306) 5.8	(203/5306) 3.8	(1143/25,028) 4.6	(946/25,028) 3.8	(37/1608) 2.3	(35/1608) 2.2
15. Imidazolidinyl urea 2% pet	(286/5306) 5.4	(258/5306) 4.9	(587/25,028) 2.4	(529/25,028) 2.1	(13/1608) 0.8	(13/1608) 0.8
16. P-phenylenediamine 1% pet	(275/5306) 5.2	(129/5306) 2.4	(1252/25,028) 5.0	(696/25,028) 2.8	(44/1608) 2.7	(32/1608) 2.0
17. Diazolidinyl urea 1% aq	(262/5306) 4.9	(222/5306) 4.2	(575/25,028) 2.3	(509/25,028) 2.0	(16/1608) 1.0	(16/1608) 1.0
18. Cobalt chloride 1% pet	(248/5306) 4.7	(87/5306) 1.6	(2031/25,028) 8.1	(984/25,028) 3.9	(205/1608) 12.8	(109/1608) 6.8
19. Methyl dibromo glutaronitrile 0.4% pet (1998-2000) (n = 10,748)	(82/1806) 4.5	(56/1806) 3.1	(248/8513) 2.9	(156/8513) 1.8	(4/429) 0.9	(1/429) 0.2
20. Thiuram mix 1% pet	(238/5306) 4.5	(173/5306) 3.3	(1149/25,028) 4.6	(975/25,028) 3.8	(29/1608) 1.8	(16/1608) 1.6
21. Benzalkonium chloride 0.1% aq (2000) (n = 4913)	(36/824) 4.4	(8/824) 1.0	(168/3891) 4.3	(47/3891) 1.2	(6/198) 3.0	(0/198) 0.0
22. Cinnamic aldehyde 1% pet (1994-1998 and 2003-2007) (n = 27,029)	(194/4482) 4.3	(162/4482) 3.6	(520/21,137) 2.5	(433/21,137) 2.1	(15/1410) 1.1	(14/1410) 1.0
23. Tixocortol-21-pivalate 1% pet	(227/5306) 4.3	(188/5306) 3.5	(583/25,028) 2.3	(498/25,028) 2.0	(15/1608) 0.9	(13/1608) 0.8
24. 2-Bromo-2-nitropropane-1,3-diol 0.5% pet	(206/5306) 3.9	(139/5306) 2.6	(727/25,028) 2.9	(489/25,028) 2.0	(37/1608) 2.3	(22/1608) 1.4
25. DMDM* hydantoin 1% pet	(204/5306) 3.9	(188/5306) 3.5	(556/25,028) 2.2	(512/25,028) 2.1	(14/1608) 0.9	(12/1608) 0.8
26. Potassium dichromate 0.25% pet	(190/5306) 3.6	(80/5306) 1.5	(1063/25,028) 4.3	(604/25,028) 2.4	(58/1608) 3.6	(42/1608) 2.6

Continued

Table IV. Cont'd

Allergen	Older (≥ 65 y), n = 5306		Adult (≤ 64 and ≥ 19 y), n = 25,028		Children (≤ 18 y), n = 1608	
	Positive %	Relevant %	Positive %	Relevant %	Positive %	Relevant %
27. Imidazolidinyl urea 2% aq	(186/5306) 3.5	(162/5306) 3.1	(366/25,028) 1.5	(328/25,028) 1.3	(6/1608) 0.4	(6/1608) 0.4
28. Fragrance mix II, 14.0% pet (2007) (n = 5085)	(29/844) 3.4	(26/844) 3.1	(146/3985) 3.7	(134/3985) 3.4	(5/256) 2.0	(4/256) 1.6
29. Methyl dibromo glutaronitrile/phenoxyethanol 1.0% pet (1994-1996) (n = 6129)	(36/1091) 3.3	(27/1091) 2.47	(119/4866) 2.45	(74/4866) 1.5	(1/172) 0.6	(0/172) 0.0
30. Methylchloroisothiazolinone/ methylisothiazolinone 100 ppm aq	(168/5306) 3.2	(141/5306) 2.7	(635/25,028) 2.5	(548/25,028) 2.2	(23/1608) 1.4	(19/1608) 1.2
31. Propylene glycol 30% aq	(163/5306) 3.0	(148/5306) 2.8	(869/25,028) 3.5	(746/25,028) 3.0	(52/1608) 3.2	(46/1608) 2.9
32. Methylchloroisothiazolinone/ methylisothiazolinone 100 ppm pet (1994) (n = 2035)	(11/368) 3.0	(8/368) 2.2	(52/1620) 3.2	(47/1620) 2.9	(1/47) 2.1	(1/47) 0.1
33. Benzocaine 5% pet	(150/5306) 2.8	(66/5306) 1.2	(382/25,028) 1.5	(310/5306) 0.6	(10/1608) 0.6	(1/1608) 0.1
34. DMDM hydantoin 1% aq	(141/5306) 2.7	(122/5306) 2.30	(391/25,028) 1.6	(335/25,028) 1.3	(10/1608) 0.6	(10/1608) 0.6
35. Lanolin alcohol 30% pet	(136/5306) 2.6	(123/5306) 2.3	(563/25,028) 2.3	(476/5306) 1.9	(45/1608) 2.8	(36/1608) 2.2
36. Ethylenediamine dihydrochloride 1% pet	(133/5306) 2.5	(28/5306) 0.5	(543/25,028) 2.2	(165/25,028) 0.7	(23/1608) 1.4	(6/1608) 0.4
37. Black rubber mix 0.6%/IPPD [†] 0.1% pet (1994) (n = 2035)	(9/368) 2.4	(2/368) 0.5	(31/1620) 1.9	(17/1620) 1.1	(0/47) 0.0	(0/47) 0.0
38. Budesonide 0.01% (2003-2005) (n = 9980)	(32/1565) 2.0	(27/1565) 1.7	(447/7664) 5.8	(67/7664) 0.9	(37/751) 4.9	(9/751) 1.2
39. 2-Hydroxyethyl methacrylate, 2.0% pet (2007) (n = 5085)	(17/844) 2.0	(11/844) 1.3	(99/3985) 2.5	(62/3985) 1.6	(0/256) 0.0	(0/256) 0.0
40. Propolis 10.0% pet (2007) (n = 5085)	(17/844) 2.0	(4/844) 0.5	(216/3985) 5.4	(137/3985) 3.4	(12/256) 4.7	(6/256) 2.3
41. Colophony 20% pet	(106/5306) 2.0	(47/5306) 0.9	(630/25,028) 2.5	(324/25,028) 1.3	(30/1608) 1.9	(24/1608) 1.5
42. Tosylamide formaldehyde resin 10% pet	(101/5306) 2.0	(68/5306) 1.1	(347/25,028) 1.4	(236/25,028) 0.9	(4/1608) 0.3	(3/1608) 0.2
43. Glyceryl thioglycolate 1% pet	(99/5306) 1.9	(25/5306) 0.5	(461/25,028) 1.8	(183/25,028) 0.7	(2/1608) 0.1	(0/1608) 0.0
44. Budesonide 0.1% pet	(94/5306) 1.8	(73/5306) 1.4	(275/25,028) 1.1	(226/25,028) 0.9	(16/1608) 1.0	(14/1608) 0.9
45. Iodopropynyl butylcarbamate 0.5% pet (2005-2007) (n = 9539)	(27/1592) 1.7	(20/1592) 1.3	(405/7511) 5.4	(145/7511) 1.9	(3/436) 0.7	(3/436) 0.7
46. Epoxy resin 1% pet	(90/5306) 1.7	(21/5306) 0.4	(518/25,028) 2.1	(366/25,028) 1.5	(10/1608) 0.6	(5/1608) 0.3
47. Cocamidopropyl betaine 1% aq	(86/5306) 1.6	(78/5306) 1.5	(332/25,028) 1.3	(296/25,028) 1.2	(17/1608) 1.1	(11/1608) 0.7
48. Paraben mix 12% pet	(78/5306) 1.5	(66/5306) 1.2	(254/25,028) 1.0	(221/25,028) 0.9	(8/1608) 0.5	(7/1608) 0.4
49. Dithiomorpholine 1% pet (2005) (n = 4454)	(11/748) 1.5	(4/748) 0.5	(21/3526) 0.6	(4/3526) 0.1	(0/180) 0.0	(0/180) 0.0
50. Glutaral 1% pet (1994-2007) (n = 31,942)	(78/5306) 1.5	(16/5306) 0.3	(406/25,028) 1.6	(198/25,028) 0.8	(5/1608) 0.3	(2/1608) 0.1
51. Bisphenol F epoxy resin 0.25% pet (2007) (n = 5085)	(12/844) 1.4	(2/844) 0.2	(57/3985) 1.4	(31/3985) 0.8	(2/256) 0.8	(1/256) 0.4

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Table IV. Cont'd

Allergen	Older (≥ 65 y), n = 5306		Adult (≤ 64 and ≥ 19 y), n = 25,028		Children (≤ 18 y), n = 1608	
	Positive %	Relevant %	Positive %	Relevant %	Positive %	Relevant %
52. Methyl methacrylate 2% pet	(71/5306) 1.3	(37/5306) 0.7	(348/25,028) 1.4	(230/25,028) 0.9	(2/1608) 0.1	(1/1608) 0.1
53. Disperse blue 106 1% pet	(65/5306) 1.2	(42/5306) 0.8	(352/25,028) 1.4	(202/25,028) 0.8	(22/1608) 1.4	(8/1608) 0.5
54. N-isopropyl-N-phenyl-p-phenylenediamine 0.1% pet (1996-1998) (n = 9929)	(21/1705) 1.2	(10/1705) 0.6	(85/7868) 1.1	(44/7868) 0.6	(2/356) 0.6	(2/356) 0.6
55. Dibucaine 2.5% pet	(59/5306) 1.1	(19/5306) 0.4	(166/25,028) 0.7	(43/25,028) 0.2	(5/1608) 0.3	(3/1608) 0.2
56. Glutaraldehyde 0.5% (1996) (n = 4094)	(8/723) 1.1	(2/723) 0.3	(60/3246) 1.9	(38/3246) 1.2	(0/125) 0.0	(0/125) 0.0
57. Jasmine absolute 2% pet (2000-2005) (n = 14,893)	(24/2389) 1.0	(19/2389) 0.8	(94/11,555) 0.8	(73/11,555) 0.6	(8/949) 0.8	(7/949) 0.7
58. Lidocaine 15% pet	(50/5306) 0.9	(27/5306) 0.5	(137/25,028) 0.6	(47/25,028) 0.2	(5/1608) 0.3	(5/1608) 0.3
59. Mercaptobenzothiazole 1% pet	(47/5306) 0.9	(25/5306) 0.5	(350/25,028) 1.4	(310/25,028) 1.2	(24/1608) 1.5	(23/1608) 1.4
60. Sesquiterpene lactone mix .1% pet	(46/5306) 0.9	(32/5306) 0.6	(163/25,028) 0.7	(108/25,028) 0.4	(13/1608) 0.8	(8/1608) 0.5
61. Dimethylol dihydroxyethyleneurea 4.5% aq	(45/5306) 0.9	(38/5306) 0.7	(154/25,028) 0.6	(100/25,028) 0.4	(2/1608) 0.1	(1/1608) 0.1
62. Hydrocortisone-17-butyrate 1% pet	(45/5306) 0.9	(31/5306) 0.6	(220/25,028) 0.9	(167/25,028) 0.7	(16/1608) 1.0	(10/1608) 0.6
63. Ethyl acrylate 0.1% pet	(45/5306) 0.9	(21/5306) 0.4	(336/25,028) 1.3	(228/25,028) 0.9	(5/1608) 0.3	(2/1608) 0.1
64. Compositae mix 6% pet	(41/5306) 0.8	(29/5306) 0.6	(223/25,028) 0.9	(141/25,028) 0.6	(22/1608) 1.4	(12/1608) 0.8
65. p-tert-Butylphenol formaldehyde resin 1% pet	(40/5306) 0.8	(19/5306) 0.4	(481/25,028) 1.9	(239/25,028) 1.0	(29/1608) 1.8	(17/1608) 1.1
66. Ylang-ylang oil 2% pet	(39/5306) 0.7	(33/5306) 0.6	(236/25,028) 0.9	(184/25,028) 0.7	(16/1608) 1.0	(12/1608) 0.8
67. Benzophenone-3 3% pet (1996-2007) (n = 29,907)	(36/4938) 0.7	(28/4938) 0.6	(156/23,408) 0.7	(115/23,408) 0.5	(3/1561) 0.2	(3/1561) 0.2
68. Mercapto mix 1% pet	(37/5306) 0.7	(26/5306) 0.4	(270/25,028) 1.1	(225/25,028) 0.9	(19/1608) 1.2	(19/1608) 1.2
69. Mixed dialkyl thioureas 1% pet	(37/5306) 0.7	(21/5306) 0.4	(249/25,028) 1.0	(193/25,028) 0.8	(16/1608) 1.0	(12/1608) 0.8
70. Cocamide diethanolamide 0.5% pet	(33/5306) 0.6	(20/5306) 0.4	(233/25,028) 0.9	(187/25,028) 0.8	(7/1608) 0.4	(2/1608) 0.1
71. Amidoamine 0.1% aq (1998-2007) (n = 25,813)	(25/4215) 0.6	(20/4215) 0.5	(156/20,162) 0.8	(136/20,162) 0.7	(14/1436) 1.0	(10/1436) 0.7
72. Iodopropynyl butylcarbamate 0.1% pet (1998-2005) (n = 20,728)	(19/3371) 0.6	(16/3371) 0.5	(52/16,177) 0.3	(37/16,177) 0.2	(7/1180) 0.6	(5/1180) 0.4
73. Clobetasol 17 propionate 1% pet	(29/5306) 0.6	(23/5306) 0.4	(119/25,028) 0.5	(98/25,028) 0.4	(12/1608) 0.8	(10/1608) 0.6
74. dl alpha tocopherol acetate 100% (2000) (n = 4913)	(4/824) 0.5	(4/824) 0.5	(20/3891) 0.5	(13/3891) 0.3	(1/198) 0.5	(1/198) 0.5
75. Chloroxylonol (PCMX) 1% pet	(25/5306) 0.5	(10/5306) 0.2	(195/25,028) 0.8	(137/25,028) 0.6	(2/1608) 0.1	(2/1608) 0.1
76. Butylated hydroxyanisole 2% pet (1994-1996) (n = 6129)	(5/1091) 0.5	(5/1091) 0.5	(15/4866) 0.3	(10/4866) 0.2	(0/172) 0.0	(0/172) 0.0
77. dl alpha tocopherol 100% (2000-2007) (n = 19,978)	(13/3323) 0.4	(10/3323) 0.3	(39/15,540) 0.3	(30/15,540) 0.2	(4/1205) 0.3	(2/1205) 0.2

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Table IV. Cont'd

Allergen	Older (≥ 65 y), n = 5306		Adult (≤ 64 and ≥ 19 y), n = 25,028		Children (≤ 18 y), n = 1608	
	Positive %	Relevant %	Positive %	Relevant %	Positive %	Relevant %
78. Phenoxyethanol 1% pet (2000 and 1994) (n = 6948)	(4/1192) 0.3	(3/1192) 0.3	(7/5511) 0.1	(3/5511) 0.1	(0/245) 0.0	(0/245) 0.0
79. Triamcinolone acetonide 1% pet (2003-2007) (n = 15,065)	(3/2409) 0.3	(2/2409) 0.3	(14/11,649) 0.3	(11/11,649) 0.2	(7/1007) 0.4	(1/1007) 0.4
80. Tea tree oil, oxidized, 5% pet (2003-2007) (n = 15,065)	(8/2409) 0.3	(6/2409) 0.3	(35/11,649) 0.3	(22/11,649) 0.2	(4/1007) 0.4	(4/1007) 0.4
81. Black rubber mix 0.6% pet (2000-2007) (n = 19,978)	(9/3233) 0.3	(1/3233) 0.0	(38/15,540) 0.2	(19/15,540) 0.1	(1/1205) 0.1	(0/1205) 0.0
82. Butylated hydroxytoluene 2% pet (1994) (n = 2035)	(1/368) 0.3	(1/368) 0.3	(5/1620) 0.3	(1/1620) 0.1	(0/47) 0.0	(0/47) 0.0
83. Glutaraldehyde 0.2% pet (1994) (n = 2035)	(1/368) 0.3	(0/368) 0.0	(17/1620) 1.1	(11/1620) 0.7	(0/47) 0.0	(0/47) 0.0
84. Tetracaine 1% pet (2000-2003) (n = 10,439)	(4/1641) 0.2	(1/1641) 0.1	(30/8029) 0.4	(7/8029) 0.1	(6/769) 0.8	(2/769) 0.3
85. Desoximetasone 1.0% pet (2007) (n = 5085)	(1/844) 0.1	(0/844) 0.0	(9/3985) 0.2	(7/3985) 0.2	(0/256) 0.0	(0/256) 0.0
86. Bisphenol F 1% pet (2003-2005) (n = 9980)	(1/1565) 0.1	(0/1565) 0.0	(12/7664) 0.2	(6/7664) 0.1	(0/751) 0.0	(0/751) 0.0

*1,3-Dimethylol-5,5-Dimethyl.

†N-isopropyl-N-phenyl-p-phenylenediamine.

Table V. Comparison of positive patch test reactions to 20 most common allergens in older individuals versus adults or children

Allergen	Older vs adults		Older vs children	
	χ^2 Statistic P value	Risk ratio (95% CI)	χ^2 Statistic P value	Risk ratio (95% CI)
<i>Myroxylon pereirae</i> 25% pet	134.43 <.0001*	1.53 (1.42-1.64)	131.85 <.0001*	3.27 (2.62-4.09)
Fragrance mix 8% pet	129.62 <.0001*	1.55 (1.44-1.66)	93.12 <.0001*	2.58 (2.1-3.17)
Neomycin sulfate 20% pet	33.45 <.0001*	1.26 (1.17-1.37)	35.35 <.0001*	1.72 (1.43-2.07)
Quaternium-15 2% pet	62.32 <.0001*	1.41 (1.29-1.53)	104.91 <.0001*	3.74 (2.83-4.95)
Formaldehyde 1% aq	78.63 <.0001*	1.47 (1.35-1.60)	111.60 <.0001*	4.06 (3.03-5.43)
Bacitracin 20% pet	61.31 <.0001*	1.42 (1.30-1.55)	62.06 <.0001*	2.47 (1.95-3.14)
Nickel sulfate 2.5% pet	169.24 <.0001*	0.58 (0.53-0.63)	261.84 <.0001*	0.39 (0.35-0.44)
Methyldibromo glutaronitrile/ phenoxyethanol 2.5% pet	2.90 .0885	1.26 (0.97-1.64)	6.28 .0122	3.75 (1.19-11.73)
Methyldibromo glutaronitrile/ phenoxyethanol 2.0% pet	40.84 <.0001*	1.46 (1.30-1.64)	83.32 <.0001*	6.17 (3.90-9.75)
Sodium gold thiosulfate 0.5% pet	23.15 <.0001*	0.73 (0.64-0.83)	1.74 .1875	1.19 (0.92-1.54)
Thimerosal 0.1% pet	37.21 <.0001*	0.65 (0.57-0.75)	26.23 <.0001*	0.53 (0.41-0.67)
Diazolidinyl urea 1% pet	185.89 <.0001*	2.38 (2.10-2.71)	71.20 <.0001*	6.01 (3.70-9.75)
Ethyleneurea melamine formaldehyde 5%	89.05 <.0001*	1.91 (1.67-2.19)	59.95 <.0001*	6.43 (3.70-11.18)
Carba mix 3% pet	14.73 .0001*	1.27 (1.12-1.44)	31.95 <.0001*	2.52 (1.80-3.53)
Imidazolidinyl urea 2% pet	145.20 <.0001*	2.30 (2.00-2.64)	62.61 <.0001*	6.67 (3.84-11.59)
P-phenylenediamine 1% pet	0.30 .5851	1.04 (0.91-1.18)	16.78 <.0001*	1.89 (1.38-2.59)
Diazolidinyl urea 1% aq	113.75 <.0001*	2.15 (1.86-2.48)	49.71 <.0001*	4.96 (3.00-8.20)
Cobalt chloride 1% pet	74.60 <.0001*	0.58 (0.51-0.65)	131.42 <.0001*	0.37 (0.31-0.44)
Methyldibromo glutaronitrile 0.4% pet	12.74 .0004*	1.56 (1.22-1.99)	12.20 .0005*	4.87 (1.79-13.21)
Thiuram mix 1% pet	0.11 .7386	0.98 (0.85-1.12)	23.91 <.0001*	2.49 (1.70-3.64)

CI, Confidence interval.

*Statistically significant P value $\leq .0013$ (Bonferroni correction for multiple comparisons 40/.05).

with previous studies,^{2-6,8-11} which also found that reactions to fragrance allergens were common in older individuals.¹⁸ Uter et al⁷ found a significantly higher rate in older patients (61-75 years and >75 years) as compared with younger patients (<60 years) for fragrance chemicals including *Myroxylon pereirae*, fragrance mix, oil of turpentine, colophony, and propolis. The significantly higher reaction rate in older individuals (as compared with

adults and children) in our study could be explained either by cumulative exposure to these allergens over time or by exposure to fragrance mix allergens in previous decades that are no longer commonly used.^{19,20} A recent study found that only one (geraniol) of the top 6 fragrance allergens in British products is present in fragrance mix I.²¹ In our study, the frequency of reactions to fragrance mix II, which contains many of the “newer” fragrance allergens

used in products today, were similar in all 3 age groups (3.4%, 3.7%, and 2.0%; differences not statistically significant, data not shown) (Table IV), supporting the latter hypothesis.

Preservatives

Older individuals were at least 1.3 times more likely than adults and 3.7 times more likely than children to have positive reactions to several common preservatives including methyl-dibromoglutaronitrile (alone or with phenoxyethanol), quaternium-15, formaldehyde, diazolidinyl urea, and imidazolidinyl urea. This higher rate of reactions to preservatives most likely represents increased exposure to these preservatives in personal care products or topical medications over time. Similarly, Uter et al⁷ found significant increase in sensitivity with age to several preservatives including methyl-dibromoglutaronitrile and diazolidinyl urea but no significant trend for formaldehyde (quaternium-15 and imidazolidinyl urea not reported in Uter's study). In our study the high positivity rate to ethyleneurea melamine formaldehyde mix in older individuals as compared with children (6.4 times greater risk) may be a result of historical exposure to this fabric finisher in the second half of the 20th century^{22,23} or simply cumulative exposure over time.

Topical antibiotics

The higher positivity rate to bacitracin and neomycin in older individuals in our study is consistent with Green et al,¹¹ who evaluated the frequency of positive patch test reactions to topical medications by age in 4384 patients (including 395 older individuals) and found that reaction rates were almost two times greater in individuals older than 70 years as compared with younger individuals. Uter et al⁷ also found a significant trend with age for neomycin. These findings are likely a result of the known risk factor for topical antibiotic allergy of stasis dermatitis and stasis ulcerations, which usually occur in older individuals.^{7,24}

Rubber chemicals

Reactions to two common rubber accelerators, carba mix and thiuram mix, were the 14th and 20th most common allergens in our older population. Reactions to carba mix were significantly more common in older individuals as compared with the two younger groups and reactions to thiuram mix were significantly more common in older individuals as compared with children, but not adults. Gupta et al,⁵ also found that reactions to rubber accelerators were common (second highest group after topical antibiotics) in older individuals. Similarly, Uter et al⁷

found a significant trend for higher reactivity rates to thiuram mix and zinc diethyldithiocarbamate, but not mercapto mix, with increasing age. The higher rates to rubber accelerators may be a result of longer duration of exposure to sources in shoes²⁵ and gloves²⁶ or relatively greater exposure to rubber in medical devices (eg, support stockings).

Metals

Although reactions to nickel and cobalt were relatively common in older patients in our study (7th and 18th, respectively), rates were significantly lower than younger groups, which is consistent with previous data from our group that showed that sensitivity to nickel increased overall from 15% in 1992 to 19% in 2004, and that most of this increase was a result of girls younger than 18 years (25% in 1992 to 36% in 2004),²⁷ possibly because of body piercing.^{28,29} Although nickel regulation does not exist in the United States, the frequency of allergy to these metals has decreased in younger individuals in Europe, where nickel release from objects has been regulated since the 1990s.³⁰ Uter et al⁷ also reported a significant decrease in positivity rate with increasing age for both nickel and cobalt. Gold thiosulfate was the 10th most common allergen in older individuals. Frequency was significantly lower, however, than adults. The higher rates in adults could be a result of use of titanium dioxide in cosmetics, which has been hypothesized to adsorb gold released from jewelry or eyeglass frames.³¹

Thimerosal

Thimerosal was the 11th most common allergen in our older population but was significantly less common in this group than in adults or children. These findings are consistent with data from Europe.⁷ Although thimerosal has been removed from many ophthalmic preparations,³² it is possible that younger individuals are still exposed through these products or vaccines.³³

Limitations

Our study has several limitations. First the data were cross-sectional; therefore only association, not causation, can be assessed. Second, only those patients suspected of having allergic contact dermatitis are included in the NACDG database. Therefore, the characteristics of the NACDG referral population are not representative of the general population or the general dermatologic patient population. Third, in most cases, clinical relevance was determined at the time of patch test completion without the benefit of long-term follow-up.³⁴ Fourth, explanations of the differences in reactivity between older and younger

individuals are only speculative. Finally, analyses are limited to variables collected.

CONCLUSIONS

Older individuals had significant reactivity to contact allergens; 67% of those tested had at least one positive reaction and 52% had at least one clinically relevant positive reaction. The latter rate was slightly, but significantly, greater than that of adults and children. Positive rates to specific preservatives, fragrance and flavoring markers, and topical antimicrobials were also significantly higher in older individuals, whereas reactions to metals and thimerosal were less common. More research is needed to elucidate the pathophysiologic mechanisms and exposure patterns to further explain these findings.

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