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***p*-phenylenediamine patch test reactions associated with hair dye and nonscalp anatomic areas: Retrospective cross-sectional analysis of North American Contact Dermatitis Group data, 2001 to 2016**



To the Editor: Contact allergy to *p*-phenylenediamine (PPD) in hair dye commonly affects adjacent anatomic sites. A previous retrospective cohort analysis by our group addressed allergens in patients with scalp involvement, but questions remained regarding contact allergy to PPD associated with hair dye excluding the scalp.

Methods for our follow-up study were identical to the previous analysis,¹ with exception of the following criteria for study cohort: individuals without scalp involvement (within up to 3 anatomic sites) who had a patch test interpretation of “allergic” to PPD (1.0% in petrolatum) with current (definite/probable/possible) clinical relevance and associated with hair dye source. Individuals with occupationally related dermatitis were considered separately from those not associated. Occupational relationship was to overall skin disease at time of patch testing.

Of 38,775 individuals patch tested, 1.8% (n = 692) met inclusion criteria (Table I). Most were women (84.2%), >40 years old (75.6%), and were less likely to report occupationally related dermatitis (79.8%). PPD allergy in occupationally related skin disease was statistically associated with male sex, White race, and coexistent irritant contact dermatitis.

For all, the top 3 primary anatomic sites included the face (36.6%), hands (24.9%), and scattered-generalized (18.9%; Table II). Compared with nonoccupational cases, occupational cases had significantly more hand/arm involvement and significantly less face, neck, trunk, or scattered-generalized involvement.

Most reactions were +++/+++ (n = 380 [54.9%]). Current clinical relevance was categorized as “definite” (positive use test/patch test to hair dye containing PPD) in 51 (7.4%), “probable” (PPD identified in patient’s hair dye) in 422 (61.0%), or “possible” (PPD likely present in patient’s hair dye) in 219 (31.6%).

We previously found that isolated scalp involvement in patch-tested patients was rare (1.0% [505 of 48,753]), ACD was significantly lower in that group than when other anatomic sites were involved (38.6% vs >52.0%), and PPD accounted for 29.3% (68 of 232) of cases.¹ Here we focused on a different cohort—individuals with currently relevant PPD reactions associated with hair dye without scalp involvement.

Not surprisingly, occupational cases were associated with concurrent irritant contact dermatitis, a common comorbidity in hairdressers.² Occupational cases were also associated with hand and arm involvement, whereas nonoccupational cases were associated with face, neck, trunk, and a scattered-generalized pattern. This is consistent with a study of 271 patients which found that while 80% of PPD-sensitized patients dyed their hair, only 57% reported scalp involvement.³ Unique properties of the scalp, including increased skin thickness, protective

Table I. Demographics of nonscalp patients with clinically relevant *p*-phenylenediamine allergy

Variable	All patients (N = 692)	Occupationally related skin disease (n = 140)	Not occupationally related skin disease (n = 552)	Occupationally related vs not occupationally related skin disease	
	No. (%)	No. (%)	No. (%)	RR (95% CI)	P value
Male	109 (15.8)	30 (21.4)	79 (14.3)	1.50 (1.03-2.18)	.0390
Related to occupation	140 (20.2)	140 (100)	0 (0)	n/a	n/a
History of atopic dermatitis	176 (25.4)	34 (24.3)	142 (25.7)	0.94 (0.68-1.31)	.7270
Hand*	201 (29.0)	120 (85.7)	81 (14.7)	5.84 (4.72-7.22)	<.0001
Leg*	45 (6.5)	5 (3.6)	40 (7.2)	0.49 (0.20-1.23)	.1153
Face*†	353 (51.0)	35 (25.0)	318 (57.6)	0.43 (0.32-0.58)	<.0001
Age >40 y	523 (75.6)	68 (48.6)	455 (82.4)	0.59 (0.49-0.70)	<.0001
White	539 (77.9)	122 (87.1)	417 (75.5)	1.15 (1.07-1.25)	.0031
Current atopic dermatitis*	75 (10.8)	14 (10.0)	61 (11.1)	0.90 (0.52-1.57)	.7209
Current irritant contact dermatitis*	66 (9.5)	37 (26.4)	29 (5.3)	5.03 (3.21-7.88)	<.0001

CI, Confidence interval; n/a, not applicable; RR, relative risk.

*Any of up to 3 sites/final diagnoses.

†Includes all facial sites.

Table II. Other anatomic sites involved in nonscalp patients with clinically relevant *p*-phenylenediamine allergy

Variable	All patients (N = 692)			Occupationally related skin disease* (n = 140)			Not occupationally related skin disease† (n = 552)			Occupationally related vs not occupationally related for any site	
	Any site, No. (%)	Primary site, No. (%)	Nonprimary sites‡ No. (%)	Any site, No. (%)	Primary site, No. (%)	Nonprimary sites,‡ No. (%)	Any site, No. (%)	Primary site, No. (%)	Nonprimary sites,‡ No. (%)	RR (95% CI)§	P value
Total face	353 (51.0)	253 (36.6)	100 (14.5)	35 (25.0)	15 (10.7)	20 (14.3)	318 (57.6)	238 (43.1)	80 (14.5)	0.43 (0.32- 0.58)	<.0001
Face, NOS	239 (34.5)	174 (25.1)	65 (9.4)	34 (24.3)	15 (10.7)	19 (13.6)	205 (37.1)	159 (28.8)	46 (8.3)	n/a	n/a
Eyelids	86 (12.4)	64 (9.2)	22 (3.2)	0 (0)	0 (0)	0 (0)	86 (15.6)	64 (11.6)	22 (4.0)	n/a	n/a
Lips	23 (3.3)	13 (1.9)	10 (1.4)	1 (0.7)	0 (0)	1 (0.7)	22 (4.0)	13 (2.4)	9 (1.6)	n/a	n/a
Eyes	4 (0.6)	2 (0.3)	2 (0.3)	0 (0)	0 (0)	0 (0)	4 (0.7)	2 (0.4)	2 (0.4)	n/a	n/a
Nose	1 (0.1)	0 (0)	1 (0.1)	0 (0)	0 (0)	0 (0)	1 (0.2)	0 (0)	1 (0.2)	n/a	n/a
Hand	201 (29.0)	172 (24.9)	29 (4.2)	120 (85.7)	117 (83.6)	3 (2.1)	81 (14.7)	55 (10.0)	26 (4.7)	5.84 (4.72-7.22)	<.0001
Scattered-generalized	160 (23.1)	131 (18.9)	29 (4.2)	9 (6.4)	5 (3.6)	4 (22.9)	151 (27.4)	126 (22.8)	25 (4.5)	0.24 (0.12-0.45)	<.0001
Neck	134 (19.4)	34 (4.9)	100 (14.5)	13 (9.3)	0 (0)	13 (9.3)	121 (21.9)	34 (6.2)	87 (15.8)	0.42 (0.25-0.73)	.0007
Arm	123 (17.8)	31 (4.5)	92 (13.3)	43 (30.7)	2 (1.4)	41 (29.3)	80 (14.5)	29 (5.3)	51 (9.2)	2.12 (1.54-2.92)	<.0001
Trunk	109 (15.8)	27 (3.9)	82 (11.8)	6 (4.3)	1 (0.7)	5 (3.6)	102 (18.5)	26 (4.7)	76 (13.8)	0.23 (0.10-0.52)	<.0001
Leg	45 (6.5)	11 (1.6)	34 (4.9)	5 (3.6)	0 (0)	5 (3.6)	40 (7.2)	11 (2.0)	29 (5.3)	0.49 (0.20-1.23)	.1153
Most exposed areas	13 (1.9)	11 (1.6)	2 (0.3)	0 (0)	0 (0)	0 (0)	13 (2.4)	11 (2.0)	2 (0.4)	n/a	n/a
Anal/genital	13 (1.9)	8 (1.2)	5 (0.7)	0 (0)	0 (0)	0 (0)	13 (2.4)	8 (1.4)	5 (0.9)	n/a	n/a
Ears	17 (2.5)	7 (1.0)	10 (1.4)	1 (0.7)	0 (0)	1 (0.7)	16 (2.9)	7 (1.3)	9 (1.6)	0.25 (0.03-1.84)	.2186
Other	6 (0.9)	4 (0.6)	2 (0.3)	1 (0.7)	0 (0)	1 (0.7)	5 (0.9)	4 (0.7)	1 (0.2)	0.79 (0.09-6.70)	>.99
Foot	21 (3.0)	2 (0.3)	19 (2.7)	4 (2.9)	0 (0)	4 (2.9)	17 (3.1)	2 (0.4)	15 (2.7)	0.93 (0.32-2.71)	>.99
Only under clothing	2 (0.3)	1 (0.1)	1 (0.1)	0 (0)	0 (0)	0 (0)	2 (0.4)	1 (0.2)	1 (0.2)	n/a	n/a
Erythroderma	1 (0.1)	0 (0)	1 (0.1)	0 (0)	0 (0)	0 (0)	1 (0.2)	1 (0.2)	1 (0.2)	n/a	n/a

CI, Confidence interval; n/a, not applicable; No., number; NOS, not otherwise specified; RR, relative risk.

*For patients with occupational relevance, the nose, eyelids, eyes, anal/genital, most exposed areas, only under clothing, and erythroderma were not sites listed (primary and nonprimary).

†Nonoccupational includes uncertain/unknown occupational relevance.

‡Percentages do not total 100% because patients could have up to 2 nonprimary sites coded.

§If comparisons included <5 patients in either group, a 2-sided Fisher exact test was used instead of a Pearson χ^2 test.

sebum, and moderation by hair follicle regulatory T cells, likely promote tolerance.¹ “Rinse-off” areas (eg, face, neck, and arms), may therefore be presenting sites. Some cases could also be explained by dying of facial/body hair.

PPD is banned in leave-on personal care products but is permitted in concentrations up to 6% in hair dyes marketed in the United States. One study investigated 159 hair dye kits purchased at major United States supermarket chains and found 21% contained PPD.⁴ Common potential dye cross-reactors include 2,5-toluenediamine sulfate, *p*-aminophenol, and *m*-aminophenol.⁵

In summary, common sites of consumer PPD hair dye allergy include face, neck, trunk, and scattered-generalized. In contrast, PPD allergy from hair dye in patients with occupationally related skin disease occurred more frequently in men and on hands/arms.

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