

ORIGINAL ARTICLE

CONTACT
DERMATITIS

WILEY

Occupational and non-occupational allergic contact dermatitis to hair dyes in Greece. A 10-year retrospective study

Stamatis Gregoriou | Styliani Mastrafitsi  | Eleni Hatzidimitriou |
Antonis Tsimpidakis  | Electra Nicolaidou | Alexander Stratigos |
Alexandra Katsarou | Dimitrios Rigopoulos

1st Department of Dermatology and Venereology, Andreas Sygros Hospital for Skin and Venereal Diseases, Faculty of Medicine, National and Kapodistrian University of Athens, Athens, Greece

Correspondence

Styliani Mastrafitsi, 1st Department of Dermatology and Venereology, Andreas Sygros Hospital for Skin and Venereal Diseases, Faculty of Medicine, National and Kapodistrian University of Athens, 5, Ionos Dragoumi str., 16121 Athens, Greece.
Email: stmastrafitsi@yahoo.com

Abstract

Background: Oxidative hair dyes are an important source of chemical exposure and a major risk factor for the development of occupational and non-occupational allergic contact dermatitis (ACD) worldwide.

Objective: To identify the frequency of common allergens associated with occupational and non-occupational ACD to hair dyes during the last 10 years, in Greece.

Methods: We retrospectively reviewed the medical records of patients with suspected ACD to hair dyes from 2010–2019. All patients with patch-test-confirmed ACD to hair dyes were evaluated.

Results: Out of 501 patients with suspected ACD to hair dyes, 362 had at least one positive reaction to hair dye allergens (62.4% were customers and 37.6% were hairdressers). The mean age of customers and hairdressers was 43.8 years and 30.8 years, respectively. Of the customers, 58.9% were exposed to dyes for >10 years and 61% of hairdressers for <5 years. The most common site of ACD among customers was the scalp (85%) and among hairdressers the hands (90%). *p*-Phenylenediamine (PPD) was the most common contact allergen (52.2%), followed by toluene-2,5-diamine, *p*-aminophenol, *m*-aminophenol, and ammonium persulfate.

Conclusions: Sensitization prevalences for PPD and cross-reacting allergens have increased in Greece during the last decade, regardless of occupational or non-occupational exposure to hair dyes.

KEYWORDS

allergic contact dermatitis, customers, hair dyes, hairdressers, patch test, *p*-phenylenediamine, sensitization

1 | INTRODUCTION

Hair dyeing is a well-established part of modern life. Large, population-based studies confirm that more than 50% of the European general population have used hair colourants at least once in their lifetime.¹ About 20% of men and more than 75% of women have at some point in life dyed their hair, starting at a reported median age of 16 years.^{1,2}

Oxidative hair dyes are the most commonly used type of dye, due to their permanent effect on hair colour, and account for 70%–80% of the coloring products on the market in Europe.³ They are chemically produced by an oxidative process involving arylamines. More specifically, a primary intermediate, such as *p*-phenylenediamine (PPD), toluene-2,5-diamine (PTD), *p*-aminophenol, along with a coupler, such as *m*-aminophenol, *m*-phenylenediamine, resorcinol, or *alpha*-naphthol, are mixed under alkaline conditions. In the presence of an

oxidizing agent, the two chemicals oxidatively couple to produce coloured molecules inside the hair shaft.^{4–6} The colour formation depends on the precursors present in the dyeing solution, its pH, and the length of time of contact with the hair.^{5,7}

The use of permanent hair dyes has been recognized as an important source of chemical exposure and a major risk factor for the development of occupational and non-occupational allergic contact dermatitis (ACD) worldwide. Hair dyes include a variety of chemical agents with sensitizing potential for both customers and hairdressers. PPD is the major component of oxidative hair dyes and the contact allergen of prime concern.^{1,8–10} Patch testing is the standard method for investigating sensitization and contact allergy to hair dyes. The aim of our retrospective study was to identify the frequency of common allergens associated with occupational and non-occupational ACD to hair dyes, during the last 10 years, in Greece. The epidemiological and clinical characteristics of patients were also evaluated.

2 | METHODS

In this retrospective study, we reviewed the medical records of patients with suspected ACD to hair dyes, who were referred for patch testing to the Contact Dermatitis Clinic of our tertiary hospital specializing in skin diseases, from 2010–2019. For all patients with patch-test-confirmed ACD to hair dyes, patch test results were evaluated, and epidemiological and clinical information collected. The information investigated included sex, age, occupational and non-occupational exposure to hair dyes (hairdressers vs. customers), personal and family history of atopy, clinical manifestations of contact allergy, localization of ACD, duration of symptoms, duration of hair dye use (years) and frequency of hair dye use (number of applications/year).

All patients with suspected ACD to hair dyes were patch tested with the European baseline series and with an extended hairdressing series including primary intermediates, couplers and oxidizing agents (AllergEAZE, SmartPractice, Calgary, Canada). A 5–7-mm ribbon of the patch test preparation (equivalent to 20 mg) was placed in 8-mm Finn Chambers (Epitest, Helsinki, Finland) on Scanpor tape (Norgesplaster, Oslo, Norway), immediately applied on patients' upper back to prevent evaporation, and left under occlusion for 48 hours.¹¹ Patch test reactions were read on day (D) 2 and D3, according to ESCD criteria.¹²

The study was approved by a local ethics committee. Statistical analyses were performed using STATA software version 11 (Statacorp, College Station, Texas). Comparison of categorical data was performed using Pearson chi-squared or Fisher's exact test if frequencies were less than five. Continuous data were analyzed with the Wilcoxon rank-sum test. A *P*-value < .05 was considered statistically significant.

3 | RESULTS

During the last 10 years (2010–2019), a total of 6765 patients were referred for patch testing to our Contact Dermatitis Clinic. Among 501 patients with suspected ACD to hair dyes, based on hair dye exposure history and clinical manifestations, 362 were found to have at least one positive reaction to hair dye allergens, according to the patch testing performed, and were further studied.

Among the 362 patients, the mean age ($\pm$ standard deviation) was 38.9 years ($\pm$ 15.8), ranging from 13–87 years [interquartile range (IQR): 25–49 years]. The majority of patients were female (89.5%) and 226 (62.4%) were customers, while 136 (37.6%) were occupationally exposed to hair dyes. The mean age of customers was 43.8 years ($\pm$ 16.3) [range 13–87 years (IQR: 31–55 years)]; 221 of 226 customers were female. The mean age of hairdressers was 30.8 years ($\pm$ 11.2), [range 19–75 years (IQR: 23–35 years)] and 103 of 136 were female. A personal and family history of atopy was reported by 34.7% and 19.3% of patients, respectively.

Regarding the clinical manifestations of contact allergy, ACD was reported in 96.4% of patients and contact urticaria in 3.6% of patients. Angioedema-like ACD was reported by 10.8% of subjects [mean age 41.7 years ($\pm$ 14), range 16–68 years (IQR: 33–50 years)]. Overall, the most commonly affected body area was the scalp (55.2%), followed by the hands (38.9%), and the face (17.4%). Less frequent body sites affected were the neck (4.7%), the trunk (4.1%) and the legs (2.8%), while generalized ACD was observed in 2.5% of patients. Among customers, the most common site of ACD localization was the scalp, affected in 85% of patients (*P* < .0001), followed by the face (22.6%, *P* = .001), and the hands (8%). Among hairdressers, the most common site of ACD localization were the hands, affected in 90% of subjects (*P* < .0001), followed by the face (8.8%) and the scalp (5.9%). No statistically significant difference was found between customers and

TABLE 1 Body location of allergic contact dermatitis

Body area	Total (n = 362) n (%)	Customers (n = 226) n (%)	Hairdressers (n = 136) n (%)	<i>P</i> -value
Scalp	200 (55.2)	192 (85)	8 (5.9)	<.0001
Hands	141 (38.9)	18 (8)	123 (90)	<.0001
Face	63 (17.4)	51 (22.6)	12 (8.8)	.001
Neck	17 (4.7)	14	3	.065
Trunk	15 (4.1)	10	5	.73
Legs	10 (2.8)	2	8	.007
Generalized	9 (2.5)	6	3	.54

hairdressers regarding localization of ACD on the neck, the trunk or generalized ACD. Although altogether rare, ACD located on the legs was most frequently observed among hairdressers ($P = .007$) (Table 1).

TABLE 2 Duration of exposure to hair dyes

Years of exposure	Customers (n = 226) n (%)	Hairdressers (n = 136) n (%)
<5	54 (23.9)	83 (61)
5–10	39 (17.2)	31 (22.8)
>10	133 (58.9)	22 (16.2)

The mean duration of symptoms at evaluation was 12 months, ranging from 4–36 months. Regarding duration of hair dye use, among customers, 23.9% of patients had been using hair dyes for <5 years, 17.2% for 5–10 years, and 58.9% for >10 years. On the other hand, among hairdressers, 61% of patients had been occupationally exposed to hair dyes for <5 years, 22.8% for 5–10 years and 16.2% for >10 years (Table 2). Regarding frequency of hair dye use among customers, ≤5, 6–12, and >12 hair dye applications per year were reported by 27%, 64.2% and 8.8% of patients respectively.

According to patch testing results, PPD 1% was found to be the most common contact allergen associated with hair dyes (52.2%), with no statistically significant difference between customers and hairdressers (Table 3). PTD 1% was the second most frequent sensitizer

TABLE 3 Patch test results of the European standard series

Baseline series allergen	Concentration %	Total (n = 362) Number of positive (%)	Customers (n = 226) Number of positive	Hairdressers (n = 136) number of positive	P-value
Potassium dichromate	0.5	13 (3.6)			
Neomycin sulfate	20	5 (1.4)			
Thiuram mix	1	14 (3.9)			
PPD	1	189 (52.2)	126	63	.067
Cobalt chloride	1	38 (10.5)	25	13	.64
Caine mix	7	24 (6.6)	21	3	.008 ^a
Formaldehyde	2	9 (2.5)			
Colophonium	20	6 (1.7)			
Quinoline mix	6	3 (0.8)			
<i>Myroxylon pereirae</i> (balsam of Peru)	25	29 (8)	24	5	.017
PPD-black rubber mix	0.1	28 (7.7)	26	2	< .0001
Lanolin alcohols	30	2 (0.6)			
Mercapto mix	2	3 (0.8)			
Epoxy resin	1	3 (0.8)			
Paraben mix	16	0			
BPF-resin	1	2 (0.6)			
Fragrance mix I	8	47 (13)	27	20	.46
Ethylenediamine diHCL	1	11 (3)			
Quaternium 15	1	5 (1.4)			
Nickel sulfate	5	150 (41.4)	104	46	.021
MCI/MI	0.02	11 (3)			
Mercaptobenzothiazole	2	1 (0.3)			
Primin	0.01	0			
Textile dye mix	6.6	4 (1.1)			
Petrolatum control	100	0			
Budesonide	0.01	4 (1.1)			
Thiomersal	0.1	45 (12.4)	20	25	.008
Benzalkonium chloride	0.1	0			
Sesquiterpenelactone mix	0.1	0			
Fragrance mix II	14	1 (0.3)			

Abbreviations: BPF-Resin, *p*-tert-butylphenol formaldehyde resin; MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; PPD, *p*-phenylenediamine. Difference between customers and hairdressers in the most frequent (≥5%) allergens. Comparison with Pearson chi-squared test.

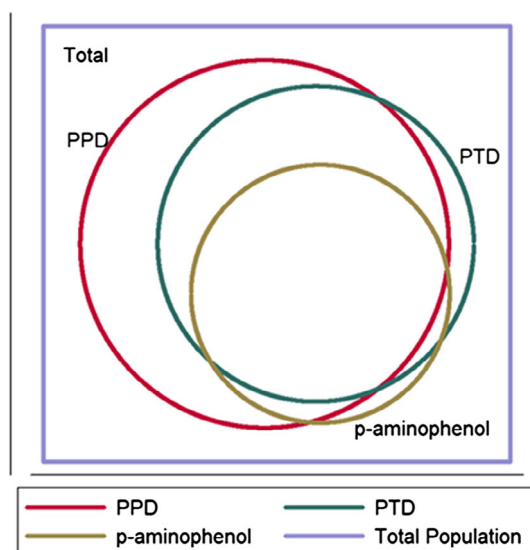
^aFisher's exact test.

TABLE 4 Patch test results of the hairdressing series

Hairdressing series allergen	Concentration %	Total (n = 362) Number of positive (%)	Customers (n = 226) Number of positive tests	Hairdressers (n = 136) number of positive tests	P-value
Toluene-2,5-diamine (PTD)	1	140 (38.67)	92	48	.565
Glyceryl monothioglycolate	1	2 (0.55)			
Ammonium persulfate	2.5	66 (18.2)	11	55	<.0001
<i>p</i> -aminophenol	1	94 (26)	68	26	.02
<i>m</i> -aminophenol	1	70 (19.3)	55	15	.002
Cocamidopropylbetaine	1	31 (8.6)	11	20	.001
Hydroquinone	1	18 (5)	16	2	.022 ^a
Resorcinol	1	1 (0.3)			
Thiourea	0.1	1 (0.3)			
Butylacrylate	0.1	9 (2.5)			
2-Ethylhexyl acrylate	0.1	0			
Benzophenone	10	1 (0.3)			
Pyrogallol	1	7 (1.9)			
Monoethanolamine	2	1 (0.3)			
Cloroacetamide	0.2	1 (0.3)			
Imidazolidinyl urea	2	0			

Difference between customers and hairdressers in the most frequent ($\geq 5\%$) allergens. Comparison with Pearson chi-squared test.

^aFisher's exact test.

**FIGURE 1** Venn diagram of cross-reactions of hair dye allergens. PPD, *p*-phenylenediamine; PTD, toluene-2,5-diamine

associated with hair dyes (38.67%), followed by *p*-aminophenol 1%, *m*-aminophenol 1%, ammonium persulfate 2.5%, cocamidopropyl betaine (CAPB) 1%, and hydroquinone 1%. Statistically significant differences were demonstrated between customers and hairdressers (Table 4).

Regarding other contact allergens included in the baseline series, the most frequent positive patch test reactions were observed to nickel sulfate 5% (41.4%), followed by fragrance mix I 8%, thiomersal

0.1%, cobalt chloride 1%, *Myroxylon pereirae* (balsam of Peru) 25%, PPD-black rubber mix 0.1%, and caine mix 7%. Statistically significant differences were observed between customers and hairdressers (Table 3).

Regarding PPD and the potentially cross-reacting primary intermediates PTD and *p*-aminophenol, 199 (55%) of the 362 patients were positive to a least one of PPD, PTD or, *p*-aminophenol, while 163 (45%) were negative to all the three allergens. Out of the 199 positive patients, 53 (15% of the total population) were positive to PPD only, seven (2%) to PTD only, and one patient to *p*-aminophenol only. Moreover, 45 (12%) patients were positive to both PPD and PTD, five (1%) to both PPD and *p*-aminophenol and one to both PTD and *p*-aminophenol. Positive reactions to all the three allergens were found in 86 (24%) patients (Figure 1).

Regarding PPD and its other potentially cross-reacting allergens studied, all the 24 patients positive to caine mix were also positive to PPD; out of the 11 patients positive to methylchloroisothiazolinone/methylisothiazolinone (MCI/MI), four were also positive to PPD, while out of the 28 patients positive to PPD-black rubber mix, 23 were also positive to PPD.

4 | DISCUSSION

The majority of our 362 patients sensitized to hair dye ingredients were in Greece female (89.5%), in accordance with a reported higher exposure to hair dyes for women in Europe.^{1,2} Hairdressers were younger than hair dye consumers, indicating that occupational exposure to hair dyes started earlier in life than the use of hair dyes for

cosmetic reasons, most frequently for dyeing grey hair. In agreement with our results, hairdressers with ACD have been previously reported to be mainly female, affected at a relatively young age at the beginning of their careers.^{13–16} On the other hand, hair dye consumers are sensitized at a relatively older age, because most customers use hair dyes to conceal their grey hair and hair greying usually starts in the third or fourth decade of life.^{9,10}

In this study, most of the sensitized customers (58.9%) reported prolonged use of hair dyes for >10 years. Most hair dye consumers reported a frequency of 6–12 applications per year (64.2%). This prolonged and regular use of hair dyes could be attributed to the age of customers and their need to conceal grey hair. On the other hand, the majority of hairdressers (61%) developed early contact sensitization to hair dye allergens, after occupational exposure for <5 years. Several studies including hairdressers have also shown a significant and early high risk of developing ACD during the first years of starting their jobs.^{14–17} Moreover, although the association between contact allergy and atopic dermatitis remains controversial in the literature,^{18–21} 34.7% of our patients reported a positive personal history of atopic disease.

With respect to clinical manifestations of hair dye contact allergy, ACD was reported by the majority of patients (96.4%), as was expected, and contact urticaria by the rest (3.6%). Angioedema-like ACD occurred in 10.8% of individuals. The most common site of ACD localization among customers was the scalp (85%), followed by the face (22.6%) and the hands (8%). However, among hairdressers, the most common site of ACD localization were the hands (90%), followed by the face (8.8%) and the scalp (5.9%). Hence, hair dye ACD was typically observed on body areas with direct contact exposure. ACD on indirect contact areas or generalized ACD was less frequent.

Contact allergy to oxidative hair dyes and especially PPD has been associated with a variety of clinical manifestations, most commonly ACD, and in some cases contact urticaria, asthma, rhinitis, contact anaphylaxis, and acute renal failure.^{16,22–27} Although often misdiagnosed, angioedema-like ACD related to PPD has also been reported.^{28–30}

Regarding body areas affected, in agreement with our results, a recent analysis of data, from 2009–2014 in eight European countries, reported that contact allergy to PPD was most often associated with ACD of the head (scalp and face).³¹ Furthermore, previous studies have also demonstrated an increased risk for hairdressers of developing occupational hair dye ACD on the hands.^{13–16} A Danish register-based study showed that hairdressers worked an average of 8.4 years before leaving their profession and that occupational hand eczema contributed significantly to this career change.¹⁵

In this study that included 362 patients, among hair dye contact allergens, PPD was found to be the most common allergen, demonstrating a sensitization prevalence of 52.2%, with no statistically significant difference between occupational and non-occupational exposure. In a previous Greek study conducted 25 years ago that included 106 hairdressers, PPD was also identified as the most common contact allergen. However, the proportion of PPD sensitization reported was lower (31%).³² This significant increase in PPD

sensitization in our study indicates that PPD is still extensively utilized in both products used in hairdressing salons and home-applied hair dyes. It also indicates inadequate counselling regarding occupational prevention among hairdressers.

PPD has been recognized as an important contact allergen across different studies worldwide. In agreement with the results of our study, a literature review analyzing data from Europe, the USA, and Asia reported that although in unselected dermatitis patients the PPD sensitization rate ranged from 1%–6%, in selected hair dye dermatitis populations the prevalence of PPD sensitization ranged from 38%–97%.³³ In another epidemiological review, the reported median prevalence of PPD sensitization among dermatitis patients was 4.3% in Asia, 4% in Europe, and 6.2% in North America.³⁴ In a European multi-center study, the weighted average prevalence of PPD sensitization was 4.6% among 21 515 patients. PPD sensitization was more prevalent in Central and Southern Europe compared to Scandinavia.³⁵ In addition, increasing sensitization prevalences for PPD have been observed in Sweden,³⁶ Denmark,³⁷ England,³⁸ India³⁹ and Korea.⁴⁰ On the other hand, several studies performed in the general population have reported lower prevalences of PPD sensitization. The estimated prevalence of PPD allergy in the general population was 1.5% in a data analysis from the USA,⁴¹ 0.8% in a cross-sectional study of five European countries,¹ 1.5% in a recent systematic review and meta-analysis⁴² and a quite high (2.7%) in Thailand.⁴³ The Information Network of Departments of Dermatology demonstrated the use of hair dyes, the application of temporary black henna tattoos, and working as a hairdresser as major risk factors for PPD sensitization.⁴⁴

PPD, belonging to 1,4-substituted benzene derivatives, may cross-react with other chemicals also containing an amine group in their benzene ring at the para position, such as constituents of the black rubber mix, benzocaine group (ester) anesthetics, parabens, *p*-aminobenzoic acid (PABA), sulfonamides, *p*-aminosalicylic acid, thiazides, and azo dyes. Cross-reactions to other chemically related hair dye compounds, such as PTD, *p*-aminophenol, *m*-aminophenol, may also occur.^{45–47} Regarding the contact allergens with potential PPD cross-reactivity investigated in the present study, PTD 1% was the second most frequent, detected in 38.67% of patients, regardless of occupational or non-occupational exposure, followed by *p*-aminophenol 1% (26%), and *m*-aminophenol 1% (19.3%), most frequently found among hair dye consumers. Moreover, positive patch test reactions to PPD-black rubber mix 0.1% and caine mix 7% were identified in 7.7% and 6.6% of patients respectively, and most frequently among hair dye consumers. In the previous Greek study conducted 25 years ago, positive patch test reactions to PTD and *p*-aminophenol were less common, detected respectively in 10.3% and 2.8% of the hairdressers included, while no positive reactions to black rubber mix and benzocaine were reported.³² These data further confirm that sensitization prevalences for PPD and cross-reacting allergens in Greece have increased during the last 10 years, which may be attributed to the increasing use of permanent hair dyes containing major chemical sensitizers.

The results of our study demonstrate the potential cross-reaction of PPD to PTD, and its increased likelihood of cross-reaction to PTD

and *p*-aminophenol simultaneously. Potential cross-reactivity of PPD with caine mix, PPD-black rubber mix, and MCI/MI was also observed. Similarly, several studies have also reported cross-reactivity of chemically related allergens in PPD-allergic individuals.^{46–51} A retrospective study including 221 PPD-sensitized patients demonstrated the association of a stronger patch test reaction to PPD with an increasing likelihood of cross-reactions to PPD-black rubber, caine mix, and Disperse yellow 3.⁴⁷ Furthermore, high sensitization prevalences to PTD of 43%⁴⁶ and 51%⁴⁸ in PPD-allergic patients have been reported, although PTD was developed as an alternative to PPD for use in permanent hair dyes. A retrospective analysis of 175 individuals showed that PTD-positive patients also had a concomitant positive reaction to PPD in five of every six cases, while patch test reactions to other hair dye allergens, including *p*-aminophenol and *m*-aminophenol, were normally positive only when a PPD-positive reaction was also present.⁴⁹ In concordance with the results of our study, a previous study that included 2939 eczema patients from different countries in Europe, reported positive reactions to PPD in 4.5% of patients, while PTD was the second after PPD most frequent hair dye allergen (2.8%), followed by *p*-aminophenol (1.8%) and *m*-aminophenol (1%). PPD identified the majority (80.7%–86.8%) of positive reactions to PTD, *p*-aminophenol, and *m*-aminophenol.⁵⁰

Among the other most common hair cosmetic contact allergens found in the present study, ammonium persulfate 2.5% and CAPB 1% were identified in 18.2% and 8.6% of our patients respectively and were mostly associated with occupational exposure of hairdressers. Hydroquinone 1% followed, with positive patch test reactions in 5% of patients, most frequently among hair dye consumers.

In the previous Greek study, ammonium persulfate exhibited an equal share of sensitization of 18% among hairdressers. However, it was the second most common hair dye allergen after PPD, since PTD and *p*-aminophenol were less frequent³² than we found. In addition, that study reported contact sensitization to glyceryl monothioglycolate (GMTG) and resorcinol in 6% and 5% of the hairdressers respectively.³² In the present study, positive patch test reactions to GMTG and resorcinol were very rare, found respectively in 0.55% and 0.3% of our patients. Our results demonstrate a changing trend of hair dye contact allergens in Greece, probably reflecting changes in the composition of current permanent hair dyes.

Hairdressers have an increased risk of developing hair dye ACD because of their intense occupational contact with hair dye chemicals. Similarly to our results, the Danish contact dermatitis group identified PPD, ammonium persulfate, PTD, *m*-aminophenol, and *p*-aminophenol as frequent sensitizers in hairdressers with ACD during 2002–2011.¹³ Another study based on data collected by the Information Network of Departments of Dermatology, between 2007 and 2012 demonstrated that some allergens mainly affected hairdressers, such as ammonium persulfate (18.7% positive) and GMTG (4.7% positive), while some increase in sensitization to oxidative hair dye components in clients was observed.⁵² Comparable to the results of our study, a sensitization prevalence of 9.8% to CAPB was reported in China.⁵³ However, another retrospective analysis of data collected by the Information Network of Departments of Dermatology from 1996–2009, reported that although being a hairdresser was one of the risk factors

associated with positive patch test reactions to CAPB, allergic reactions to CAPB were very rare, and supported the notion of CAPB “not being a significant skin sensitizer.”⁵⁴

Regarding the remainder of contact allergens included in the baseline series, nickel sulfate, demonstrating a high contact sensitization prevalence of 41.4%, was the second most common allergen after PPD, followed by fragrance mix I, thiomersal, cobalt chloride, and *Myroxylon pereirae* (balsam of Peru). The more frequent positive patch test reactions observed among hair dye consumers might be associated with their age, since customers were older than hairdressers. A similar burden of nickel allergy (42%) was reported 25 years ago in Greece among hairdressers.³² Positive patch test reactions to thiomersal were observed in 12.4% of our patients and most frequently among hairdressers. The corresponding contact sensitization prevalence among hairdressers in the previous Greek study was lower (2.8%).³² Furthermore, compared to the results of our study, the sensitization prevalence to cobalt chloride reported 25 years ago in Greece was similar (8.5%), while positive reactions to fragrance mix and *Myroxylon pereirae* were very rare.³²

Nickel is the most frequent cause of contact allergy worldwide.^{42,55–58} Regarding occupational exposure, a retrospective analysis of the North American Contact Dermatitis Group data, during 1998–2016, reported that the most frequent occupations associated with nickel allergy were hairdressers/cosmetologists/barbers (14.3%).⁵⁹ Moreover, nickel in metal tools used in hairdressing is considered a major source of exposure for hairdressers.⁶⁰

Limitations in this study include the retrospective design, the lack of data on verified contact urticaria, since patients were referred to allergists in other hospitals for in vivo tests, and the evaluation of consecutive hair dye dermatitis patients of a tertiary hospital. Sensitization prevalences among hair dye consumers and hairdressers in the Greek general population might be different.

Since permanent hair dyes remain an important cause of ACD worldwide, the attempt to develop hair dyes with lower allergenic potential should be reinforced. Recently, 2-methoxymethyl-*p*-phenylenediamine (ME-PPD), with lower sensitization potency, has been introduced as a safer alternative for PPD/PTD-allergic individuals.^{61–63} In an attempt to prevent allergic reactions to hair dyes, a preceding open skin allergy test, has been recommended to hair dye consumers.^{64–66} Furthermore, the use of semi-permanent tattoos should be discouraged, since black henna tattoos appear to be a significant risk factor for PPD contact allergy. Customers previously sensitized to PPD by black henna tattoos may be at higher risk of developing severe reactions after hair dye use.¹ On the other hand, the use of protective gloves by hairdressers should be encouraged. The effort to increase the awareness of users concerning the potential adverse effects of hair dyes and the systematic evaluation of changes in the prevalence of contact allergens could also contribute to hair dye ACD control.

ACKNOWLEDGEMENTS

This work would not have been possible without the help and support of Maria Pesli and Polyxeni Lagiokappa, who have applied the patch tests on the patients for the last 25 years.

AUTHOR CONTRIBUTIONS

Stamatis Gregoriou: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing-original draft; writing-review and editing. **Styliani Mastrafsi:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; validation; visualization; writing-original draft; writing-review and editing. **Eleni Hatzidimitriou:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; validation; visualization; writing-original draft; writing-review and editing. **Antonis Tsimpidakis:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; validation; visualization; writing-original draft; writing-review and editing. **Electra Nicolaidou:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; validation; visualization; writing-original draft; writing-review and editing. **Alexander Stratigos:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; validation; visualization; writing-original draft; writing-review and editing. **Alexandra Katsarou:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; validation; visualization; writing-original draft; writing-review and editing. **Dimitrios Rigopoulos:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing-original draft; writing-review and editing.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ORCID

Styliani Mastrafsi  <https://orcid.org/0000-0003-3617-5497>

Antonis Tsimpidakis  <https://orcid.org/0000-0003-0220-0762>

REFERENCES

- Diepgen TL, Naldi L, Bruze M, et al. Prevalence of contact allergy to p-Phenylenediamine in the European general population. *J Invest Dermatol*. 2016;136(2):409-415.
- Søsted H, Hesse U, Menné T, et al. Contact dermatitis to hair dyes in an adult Danish population: an interview-based study. *Br J Dermatol*. 2005;153(1):132-135.
- European Commission Scientific Committee on Consumer Products (SCCP). Opinion on Exposure to Reactants and Reaction Products of Oxidative Hair Dye Formulations. 2016. https://ec.europa.eu/health/sites/health/files/scientific_committees/docs/citizenshairdyes_en.pdf. Accessed January 10, 2020.
- Lewis D, Mama J, Hawkes J. A review of aspects of oxidative hair dye chemistry with special reference to N-nitrosamine formation. *Materials*. 2013;6(2):517-534.
- European Commission Scientific Committee on Consumer Products (SCCP). Updated Recommended Strategy for Testing Oxidative Hair Dye Substances for Their Potential Mutagenicity/Genotoxicity. 2006. https://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_s_02.pdf. Accessed January 10, 2020.
- Handa S, Mahajan R, De D. Contact dermatitis to hair dye: an update. *Indian J Dermatol Venereol Leprol*. 2012;78(5):583-590.
- Corbett JF. An historical review of the use of dye precursors in the formulation of commercial oxidation hair dyes. *Dyes Pigm*. 1999;41(1):127-136.
- Hamann D, Yazar K, Hamann CR, Thyssen JP, Lidén C. P-Phenylenediamine and other allergens in hair dye products in the United States: a consumer exposure study. *Contact Dermatitis*. 2014;70(4):213-218.
- Han JH, Lee HJ, Bang CH, Lee JH, Park YM, Lee JY. P-Phenylenediamine hair dye allergy and its clinical characteristics. *Ann Dermatol*. 2018;30(3):316-321.
- Boonchai W, Winayanuwattikun W, Limphoka P, Sukakul T. Contact allergy to hair cosmetic allergens in Thailand. *Contact Dermatitis*. 2019;81(6):426-431.
- Bruze M, Isaksson M, Gruvberger B, Frick-Engfeldt M. Recommendation of appropriate amounts of petrolatum preparation to be applied at patch testing. *Contact Dermatitis*. 2007;56(5):281-285.
- Johansen JD, Aalto-Korte K, Agner T, et al. European Society of Contact Dermatitis guideline for diagnostic patch testing - recommendations on best practice. *Contact Dermatitis*. 2015;73(4):195-221.
- Schwensen JF, Johansen JD, Veien NK, et al. Occupational contact dermatitis in hairdressers: an analysis of patch test data from the Danish contact dermatitis group, 2002-2011. *Contact Dermatitis*. 2014;70(4):233-237.
- Warshaw EM, Wang MZ, Mathias CG, et al. Occupational contact dermatitis in hairdressers/cosmetologists: retrospective analysis of north American contact dermatitis group data, 1994 to 2010. *Dermatitis*. 2012;23(6):258-268.
- Lysdal SH, Andersen KE, Johansen JD. Hand eczema in hairdressers: a Danish register-based study of the prevalence of hand eczema and its career consequences. *Contact Dermatitis*. 2011;65(3):151-158.
- Carøe TK, Ebbelhøj NE, Agner T. Occupational dermatitis in hairdressers-influence of individual and environmental factors. *Contact Dermatitis*. 2017;76(3):146-150.
- Valks R, Conde-Salazar L, Malfeito J, Ledo S. Contact dermatitis in hairdressers, 10years later: patch-test results in 300 hairdressers (1994 to 2003) and comparison with previous study. *Dermatitis*. 2005;16(1):28-31.
- Thyssen JP, Linneberg A, Engkilde K, Menné T, Johansen JD. Contact sensitization to common haptens is associated with atopic dermatitis: new insight. *Br J Dermatol*. 2012;166(6):1255-1261.
- Halling-Overgaard AS, Kezic S, Jakasa I, Engebretsen KA, Maibach H, Thyssen JP. Skin absorption through atopic dermatitis skin: a systematic review. *Br J Dermatol*. 2017;177(1):84-106.
- Hamann CR, Hamann D, Egeberg A, Johansen JD, Silverberg J, Thyssen JP. Association between atopic dermatitis and contact sensitization: a systematic review and meta-analysis. *J Am Acad Dermatol*. 2017;77(1):70-78.
- Teo Y, McFadden JP, White IR, Lynch M, Banerjee P. Allergic contact dermatitis in atopic individuals: results of a 30-year retrospective study. *Contact Dermatitis*. 2019;81(6):409-416.
- Helaskoski E, Suojalehto H, Virtanen H, et al. Occupational asthma, rhinitis, and contact urticaria caused by oxidative hair dyes in hairdressers. *Ann Allergy Asthma Immunol*. 2014;112(1):46-52.
- Davari P, Maibach HI. Contact urticaria to cosmetic and industrial dyes. *Clin Exp Dermatol*. 2011;36(1):1-5.
- Iwata JI, Inomata N, Sato M, Miyakawa M, Kawaguchi T, Aihara M. Contact dermatitis with concomitant contact urticaria syndrome due to multiple ingredients of oxidative hair dye. *Allergol Int*. 2019;68(1):114-116.

25. Sahoo B, Handa S, Penchallaiah K, Kumar B. Contact anaphylaxis due to hair dye. *Contact Dermatitis*. 2000;43(4):244.
26. Wilkinson M, Solman L, Coenraads PJ, Goebel C. Immediate hypersensitivity to p-phenylenediamine. *Contact Dermatitis*. 2019;80(3):177-178.
27. Anuradha S, Arora S, Mehrotra S, Arora A, Kar P. Acute renal failure following Para-phenylenediamine (PPD) poisoning: a case report and review. *Ren Fail*. 2004;26(3):329-332.
28. Gokalp H, Kaya K. Angioedema-like allergic contact dermatitis related to black henna. *Dermatol Online J*. 2014;20(2):doi_21549.
29. Ngwanya RM, Spengane Z, Khumalo N. Angioedema, an unusual reaction to hair dye. *Pan Afr Med J*. 2018;30:103.
30. Søsted H, Agner T, Andersen KE, Menné T. 55 cases of allergic reactions to hair dye: a descriptive, consumer complaint-based study. *Contact Dermatitis*. 2002;47(5):299-303.
31. Oosterhaven JAF, Uter W, Aberer W, et al. European surveillance system on contact allergies (ESSCA): contact allergies in relation to body sites in patients with allergic contact dermatitis. *Contact Dermatitis*. 2019;80(5):263-272.
32. Katsarou A, Koufou B, Takou K, Kalogeromitros D, Papanayiotou G, Vareltzidis A. Patch test results in hairdressers with contact dermatitis in Greece (1985-1994). *Contact Dermatitis*. 1995;33(5):347-348.
33. Krasteva M, Bons B, Ryan C, Gerberick GF. Consumer allergy to oxidative hair coloring products: epidemiologic data in the literature. *Dermatitis*. 2009;20(3):123-141.
34. Thyssen JP, White JM. European Society of Contact Dermatitis Epidemiological data on consumer allergy to p-phenylenediamine. *Contact Dermatitis*. 2008;59(6):327-343.
35. Thyssen JP, Andersen KE, Bruze M, et al. P-Phenylenediamine sensitization is more prevalent in central and southern European patch test centres than in Scandinavian: results from a multicentre study. *Contact Dermatitis*. 2009;60(6):314-319.
36. Lindberg M, Edman B, Fischer T, Stenberg B. Time trends in Swedish patch test data from 1992 to 2000. A multi-Centre study based on age- and sex-adjusted results of the Swedish standard series. *Contact Dermatitis*. 2007;56(4):205-210.
37. Thyssen JP, Carlsen BC, Sosted H, Menné T, Johansen JD. Frequency of p-phenylenediamine sensitization among Danish eczema patients tested between 1985 and 2007. *Contact Dermatitis*. 2008;59(3):184-185.
38. Patel S, Basketter DA, Jefferies D, et al. Patch test frequency to p-phenylenediamine: follow up over the last 6 years. *Contact Dermatitis*. 2007;56(1):35-37.
39. Handa S, De D, Mahajan R. Epidemiological trends in contact dermatitis to hair dye: comparing Para-phenylenediamine positivity after a decade long interval. *Indian J Dermatol Venereol Leprol*. 2011;77(4):511-512.
40. Hong YJ, Choi HY, Kim KJ, et al. TRUE test in patients with contact dermatitis: a multicenter study. *Korean J Dermatol*. 2011;49(8):661-669.
41. Mirshahpanah P, Maibach HI. Relationship of patch test positivity in a general versus an eczema population. *Contact Dermatitis*. 2007;56(3):125-130.
42. Alinaghi F, Bennike NH, Egeberg A, Thyssen JP, Johansen JD. Prevalence of contact allergy in the general population: a systematic review and meta-analysis. *Contact Dermatitis*. 2019;80(2):77-85.
43. White JM, Gilmour NJ, Jeffries D, et al. A general population from Thailand: incidence of common allergens with emphasis on Para-phenylenediamine. *Clin Exp Allergy*. 2007;37(12):1848-1853.
44. Schubert S, Lessmann H, Schnuch A, Uter W, Geier J, IVDK. Factors associated with p-phenylenediamine sensitization: data from the information network of departments of dermatology, 2008-2013. *Contact Dermatitis*. 2018;78(3):199-207.
45. Xie Z, Hayakawa R, Sugiura M, et al. Experimental study on skin sensitization potencies and cross-reactivities of hair-dye-related chemicals in Guinea pigs. *Contact Dermatitis*. 2000;42(5):270-275.
46. Scheman A, Cha C, Bhinder M. Alternative hair dye products for persons allergic to Para-phenylenediamine. *Dermatitis*. 2011;22(4):189-192.
47. Thomas BR, White IR, McFadden JP, Banerjee P. Positive relationship-intensity of response to p-phenylenediamine on patch testing and cross-reactions with related allergens. *Contact Dermatitis*. 2014;71(2):98-101.
48. Winhoven SM, Rutter KJ, Beck MH. Toluene-2,5-diamine may be an isolated allergy in individuals sensitized by permanent hair dye. *Contact Dermatitis*. 2007;57(3):193.
49. Basketter DA, English J. Cross-reactions among hair dye allergens. *Cutan Ocul Toxicol*. 2009;28(3):104-106.
50. Søsted H, Rustemeyer T, Gonçalves M, et al. Contact allergy to common ingredients in hair dyes. *Contact Dermatitis*. 2013;69(1):32-39.
51. Hasan T, Rantanen T, Alanko K, et al. Patch test reactions to cosmetic allergens in 1995-1997 and 2000-2002 in Finland-a multicentre study. *Contact Dermatitis*. 2005;53(1):40-45.
52. Uter W, Gefeller O, John SM, Schnuch A, Geier J. Contact allergy to ingredients of hair cosmetics-a comparison of female hairdressers and clients based on IVDK 2007-2012 data. *Contact Dermatitis*. 2014;71(1):13-20.
53. Li LF. A study of the sensitization rate to cocamidopropyl betaine in patients patch tested in a university hospital of Beijing. *Contact Dermatitis*. 2008;58(1):24-27.
54. Schnuch A, Lessmann H, Geier J, Uter W. Is cocamidopropyl betaine a contact allergen? Analysis of network data and short review of the literature. *Contact Dermatitis*. 2011;64(4):203-211.
55. Ahlström MG, Thyssen JP, Wennervaldt M, Menné T, Johansen JD. Nickel allergy and allergic contact dermatitis: a clinical review of immunology, epidemiology, exposure, and treatment. *Contact Dermatitis*. 2019;81(4):227-241.
56. Diepgen TL, Ofenloch RF, Bruze M, et al. Prevalence of contact allergy in the general population in different European regions. *Br J Dermatol*. 2016;174(2):319-329.
57. Veverka KK, Hall MR, Yiannias JA, et al. Trends in patch testing with the Mayo Clinic standard series, 2011-2015. *Dermatitis*. 2018;29(6):310-315.
58. DeKoven JG, Warshaw EM, Zug KA, et al. North American contact dermatitis group patch test results: 2015-2016. *Dermatitis*. 2018;29(6):297-309.
59. Warshaw EM, Schlarbaum JP, DeKoven JG, et al. Occupationally related nickel reactions: a retrospective analysis of the north American contact dermatitis group data 1998-2016. *Dermatitis*. 2019;30(5):306-313.
60. Symanzik C, John SM, Strunk M. Nickel release from metal tools in the German hairdressing trade - a current analysis. *Contact Dermatitis*. 2019;80(6):382-385.
61. Tammaro A, Muscianese M, Chello C, et al. Cross-elicitation responses to 2-methoxymethyl-p-phenylenediamine in p-phenylenediamine highly allergic volunteers using allergy alert test: the Italian experience. *Eur Ann Allergy Clin Immunol*. 2019;51(2):62-67.
62. Schuttelaar ML, Dittmar D, Burgerhof JGM, Blömeke B, Goebel C. Cross-elicitation responses to 2-methoxymethyl-p-phenylenediamine in p-phenylenediamine-allergic individuals: results from open use testing and diagnostic patch testing. *Contact Dermatitis*. 2018;79(5):288-294.
63. Kock M, Coenraads PJ, Blömeke B, Goebel C. Continuous usage of a hair dye product containing 2-methoxymethyl-Para-phenylenediamine by hair-dye-allergic individuals. *Br J Dermatol*. 2016;174(5):1042-1050.

64. Krasteva M, Cristaudo A, Hall B, et al. Contact sensitivity to hair dyes can be detected by the consumer open test. *Eur J Dermatol*. 2002;12(4):322-326.
65. Krasteva M, Cottin M, Cristaudo A, et al. Sensitivity and specificity of the consumer open skin allergy test as a method of prediction of contact dermatitis to hair dyes. *Eur J Dermatol*. 2005;15(1):18-25.
66. Coenraads PJ, Aberer W, Cristaudo A, et al. Allergy alert test for p-Phenylenediamine-allergic hair dye users. *Dermatitis*. 2018;29(5):250-257.

How to cite this article: Gregoriou S, Mastrafitsi S, Hatzidimitriou E, et al. Occupational and non-occupational allergic contact dermatitis to hair dyes in Greece. A 10-year retrospective study. *Contact Dermatitis*. 2020;1-9. <https://doi.org/10.1111/cod.13598>