

Consumer Allergy to Oxidative Hair Coloring Products: Epidemiologic Data in the Literature

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Oxidative hair dyes have repeatedly come to the attention of the dermatologic community owing to concerns about contact dermatitis. A review of the scientific literature provides insight into the prevalence of p-phenylenediamine (PPD)-sensitized individuals and on the prevalence of hair dye dermatitis in various types of patient and nonpatient populations mainly from Europe and from the United States and Asia. Most of the results are obtained through patch testing with PPD. PPD is one of the main oxidation colorants; however, patch-test prevalence of PPD is not equivalent to prevalence of hair dye allergy. An analysis shows no clear increase in the frequency of positive patch-test reactions to PPD in eczema patients and in the general population. All the parameters through which the frequency of hair dye dermatitis resulting from exposure to PPD is evaluated have been stable in Europe, with a few exceptions that are discussed in the review. There is a statistically significant decrease ($p < .0001$) in the prevalence of positive patch-test reactions to PPD in North America (1970 to 2002). Data from studies in Asia are difficult to interpret. Pooled prevalence rates of positive patch-test reactions to PPD were calculated for the three continents.

OXIDATIVE HAIR DYES based on intermediates such as p-phenylenediamine (PPD) and p-toluenediamine are among the most studied and regulated consumer products. They have repeatedly come to the attention of the dermatologic community because of concerns about contact sensitivity (type IV allergic reactions). Contact sensitivity to oxidative hair dyes has been known for more than 100 years. Despite intensive research carried out by the industry, no viable alternative technology to oxidation hair coloring has emerged. Consequently, a set of preventive measures have been put in place.¹⁻³

In 2006 and 2007, it was reported that contact allergy to PPD had increased significantly in the general population.^{4,5} In 2006, PPD was named Contact Allergen of the Year by the American Contact Dermatitis Society (ACDS).⁶

The objective of this article is to review published epidemiologic data on consumer allergy to hair coloring products in various types of patient and nonpatient populations during the period of 1967 to 2007. The

purpose of this analysis is to gain insight into the proportion of individuals with hair-dye-related allergic contact dermatitis in the dermatologic and general populations, as well as to determine whether any trend of increase or decrease emerged in the period studied.

Materials and Methods

A literature search was performed on PubMed and Medline. Search terms included "p-phenylenediamine" and related abbreviations, "hair colorant" and synonyms, "patch test," "allergy," "sensitization," "dermatitis," and "prevalence." Referenced articles in available publications were traced and also analyzed.

Studies with unclear methodology and contradicting results were not included in the review. Studies on selected age groups (eg, elderly persons, children) or on particular presentations and pathologies (eg, facial dermatitis, hand eczema, cosmetic dermatitis, hospitalized patients) were not included in the sections on unselected eczema patients and the general population.

Value of Positive Patch-Test Reactions to PPD as Indicators of the Prevalence of Hair Dye Contact Dermatitis

Most of the literature is based on the prevalence of positive patch-test reactions to PPD in the dermatologic population. PPD is included in the standard patch test series,

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which is used to test virtually all dermatologic patients who have clinical manifestations that may correspond to allergic contact dermatitis (eg, patients referred for patch testing, unselected eczema patients). Currently, all standard patch test series include PPD 1% in petrolatum. Patch-test results are evaluated according to the International Contact Dermatitis Research Group (ICDRG) grading scale. A true positive patch-test result (not a false positive) is an indicator that the patient is sensitized to the allergen tested; it does not mean that the patient has already had clinical manifestations of contact dermatitis. In many cases, contact sensitivity is clinically silent,⁷ and exposure under normal product use conditions may not elicit allergic contact dermatitis. When there is a positive patch-test result, the causal relationship with a given type of product containing the allergen to which the patient has reacted should be investigated by looking for a correlation with the clinical symptoms of the patient.^{8,9} Thus, the site and distribution of lesions, the time of onset of the clinical reaction, and the reproducibility of clinical symptoms under product reintroduction and their disappearance under allergen avoidance should be relevant to the possible use of the suspected product.

Strongly positive patch-test reactions (++ and +++) usually have a higher clinical relevance than weakly positive patch-test reactions have.¹⁰ The elicitation and severity of clinical contact dermatitis are dependent on exposure conditions (for example, elicitation with increasing allergen concentration in the product applied),¹¹ and individuals can exhibit a patch-test response to an ingredient but be known to not have any clinical contact dermatitis from exposure to that ingredient. A strong linear relationship was found in a study between the strength of the patch-test reaction to PPD and the possibility of continuing hair dyeing; patients with stronger patch-test reactions (++ and +++) were more likely to have a clear history of reacting to hair dye and were less likely to still be dyeing their hair.¹² However, the rate of strongly positive reactions is reported very infrequently.

For PPD, a true positive patch-test result is not always related to sensitization induced by hair coloring products; it may be secondary to cross-reactions with some other allergens¹³ or be due to black henna tattoos (known to contain high levels of PPD).¹⁴ Therefore, epidemiologic data about the prevalence of positive patch-test reactions to PPD may give some indication of the prevalence of hair dye dermatitis in the respective populations, but the equivalence between these two sets of data is far from automatic.

PPD base was tested at 1% (in petrolatum) under different patch-test chambers (most frequently Finn Chambers [Epitest Ltd Oy, Tuusula, Finland]) throughout the whole period of observation except in the years 1984 to 1988, when it was tested as 0.5% PPD dihydrochloride in Europe. To date, hundreds of thousands of dermatologic patients have been tested with PPD, and the prevalence of positive patch-test reactions throughout the years in different countries may give valuable information as to the rate of contact sensitivity to the chemical. However it should be taken into consideration that the positive patch-test reactions' clinical relevance to hair dye use is rarely reported.

Prevalence of Positive Patch-Test Reactions to PPD in Unselected Eczema Patients

Almost all studies were carried out with standard series, and data on relevance to the different allergens are usually lacking. Most European and North American studies included in this review involved at least 1,000 patients. Studies in Asia are usually done on small panels and with significantly less than 1,000 patients in most instances. To ensure good visibility while representing a maximal number of studies, Figure 1, Figure 2, and Figure 3, respectively, show a minimum of 4,000, 1,000, and 100 patch-tested patients in Europe, North America, and Asia.

Data on the prevalence of positive reactions to PPD were completed with information on the proportion of strong positive reactions (++ and +++) when available (Table 1). In most instances, the prevalence of positive patch-test reactions to PPD in unselected eczema patients in Europe was found to be between 1 and 6%. A decrease in the prevalence of positive patch-test reactions to PPD between 1985 and 1988 was obvious in Europe and is likely owing to a decrease in PPD diagnostic patch-test concentration from 1.0% (PPD base) to 0.5% (PPD dihydrochloride) (Figure 1). This decrease affected studies carried out in periods that included some of these years and for which a mean percentage of positive patch-test reactions to PPD were reported.

Five European multicenter studies have been carried out since 1967. The first European multicenter study (1967 to 1968) found positive reactions to PPD in 4.9% of patients.¹⁵ The last European multicenter study was carried out by the European Surveillance System of Contact Allergies in 2004 in 11 countries (31 dermatology departments) and found a mean prevalence of 4.1%.¹⁶ The mean prevalence in the other three European studies fluctuated between 2.3 and 3.9%. These most representa-

Table 1. Prevalence of Positive Patch-Test Reactions to p-Phenylenediamine in Unselected Eczema Patients in Europe

Country and Study	Dates	PPD Tested (%)*	UE Patients Tested	PPD-Positive Patients	
				No.	%
Austria					
Kränke et al ⁶⁵	1992	1	6,111	110	1.8
	1993		5,433	120	2.2
Belgium					
Oleffe et al ⁶⁶	Before 1972 (no dates)	1	300	37	9.7
Dooms-Goossens ⁶⁷	1978–1985	—	6,818	452	6.6
Bulgaria					
Krasteva ⁶⁸	1978–1990	1	8,051	407	5.1
Czech Republic					
Machovcova et al ⁶⁹	1997–2001	1	12,058	242	2.0
Denmark					
Hammershøj ⁷⁰	1973–1977	1	3,225	42	1.3
Christophersen et al ⁷¹	1985–1986	0.5	2,166	6	0.3
Veien et al ⁷²	1975–1980	1	3,664	46	1.2
	1986–1990		6,759	24	0.4
Thyssen et al ⁶⁰	2001–2005	—	14,284	343	2.4 (0.9 unequivocal, ++/+++)
European Research Group (7 countries)					
Fregert et al ¹⁵	1967–1968	1	4,825	236	4.9
Europe (EECDRG, 6 countries)					
Dooms-Goossens et al ⁷³	Before 1989 (no dates)	1	2,070	47	2.3
Europe (EECDRG, 9 countries)					
Bruynzeel et al ⁷⁴	1996–2000	1	26,210	1,022	3.9
Europe (ESSCA, 9 countries)					
Uter et al ⁷⁵	2002–2003	1	9,140	302	3.3 (1.9 unequivocal, ++/+++)
Europe (ESSCA, 11 countries)					
ESSCA Writing Group ¹⁶	2004	1	9,905	404	4.1
Finland					
Hasan et al ⁷⁶	1995–1997	—	9,373	187	2.0
	2000–2002		11,784	236	2.0
Germany					
Lämmer ⁷⁷	1970–1975	1	4,875	177	3.6
Gollhausen et al ⁷⁸	1977–1983	1	11,962	201	4.1
Enders et al ⁷⁹	1987	—	1,845	90	4.9
Hoeller et al ²³	1980–1986	1	3,606	99	2.5
	1987–1993		3,304	182	5.5
	2004		201	16	8.0
Germany, Austria, Switzerland (IVDK)					
Schnuch et al ¹⁷	1990–1995	1	36,491	1,824	5.0
Uter et al ¹⁸	1992–1996	—	45,250	2,182	4.8 (range, 4.3–5.4)
Brasch et al ⁸⁰	1993–1999	1	32,779	1,367	4.2 (1.7 unequivocal, ++/+++)
Schnuch et al ¹⁹	1992–2000	—	78,067	3,591	4.6 (2.0 unequivocal, ++/+++)
Geier et al ²⁰	1999–2001	1	25,451	1,095	4.3

Table 1. Continued

Country and Study	Dates	PPD Tested (%)*	UE Patients Tested	PPD-Positive Patients	
				No.	%
Worm et al ²¹	2001–2004	1	30,740	1,230	4.0
Hillen et al ⁸¹	2003–2004	1	1,428	46	3.2
Schnuch et al ^{13,22}	1995–2004	1	83,030	3,307	4.0
Italy (GIRDCA)					
Gola et al ⁸²	1984–1988	0.5	42,839	761	2.4–7.6
Sertoli et al ⁸³	1989–1993	1		720	4.1
Lisi et al ⁸⁴	1999	—	8,573	307	3.6
Netherlands					
Young and Houwing ⁸⁵	1974	1	250	5	2.0
	1984		614	21	3.4
De Groot ³⁶	1981–1986	—	1,781	26	1.5
Devos and van der Valk ³⁷	1992–1994	1	678	29	4.3
	1995–1999		2,058	63	3.1
Koopmans and Bruynzeel ³⁸	1996–1999	—	2,375	71	3.0
van der Valk et al ⁸⁶	1995–2000	—	1,701	49	2.9
Poland					
Rudzki and Rebandel ⁸⁷	2000–2006	—	7,125	253	3.6
	2000				3.7
	2006				3.4
Spain					
Romaguera and Grimalt ⁸⁸	1973–1977	1	4,600	278	6.1
Camarasa ⁸⁹	1977	1	2,806	278	9.9
Miranda-Romero et al ⁹⁰	2000	—	4,310	234	5.4
Sweden					
Edman and Möller ³⁰	1969–1980	1	8,933	—	2.2–5.2
Sweden (7 centers)					
Wahlberg et al ³¹	1980–1984	1	—	—	1.7
	1985–1988	0.5	—	—	0.5
	1989–1992	1	—	—	1.5
	1993–2000	1	21,840	358	1.6
Sweden (9 centers)					
Lindberg et al ²⁹	1991–1993	1	3,680	52	1.4
	1999–2001		3,790	76	2.0
Switzerland					
Bruckner-Tuderman et al ⁹¹	1989	—	921	50	5.4
Bangha and Elsner ⁹²	1990–1994	—	5,565	204	3.7
UK					
Vestey et al ⁹³	1982–1985	1	496	24	4.8
Monk ⁹⁴	1993–1996	—	753	18	2.1
UK (St. John's)					
Armstrong et al ²⁴	1982–1998	0.5 and 1	26,706	667	2.5 (range, 0.5–4.2)
Dawe et al ²⁵	1990–2000	—	13,300	—	3.4

Table 1. Continued

Country and Study	Dates	PPD Tested (%)*	UE Patients Tested	PPD-Positive Patients	
				No.	%
Patel et al ²⁶	1999–2004	1	6,177	302	4.9
	1999		1,190		3.6
	2000		1,075		5.4
	2001		1,046		4.7
	2002		941		4.7
	2003		991		4.2
	2004		934		7.1
UK (7 centers)					
Britton et al ²⁷	2000	1	3,062	92	3.0
					(range, 1.0–4.6)
UK (11 centers)					
Statham ²⁸	2004–2007	—	14,064	445	3.8
Total	—	—	685,990	25,154	3.7

EECDRG = European Environmental and Contact Dermatitis Research Group; ESSCA = European Surveillance System of Contact Allergies; GIRDCA = Gruppo Italiano Ricerca Dermatiti da Contatto e Ambientali; IVDK = Information Network of Departments of Dermatology (Germany, Austria, and Switzerland); PPD = p-phenylenediamine; UE = unselected eczema.

*When concentration was specified in the article; when not specified, PPD was usually tested at 1% (PPD base) for the whole period except between 1984 and 1988, when it was tested at 0.5% as PPD dihydrochloride.

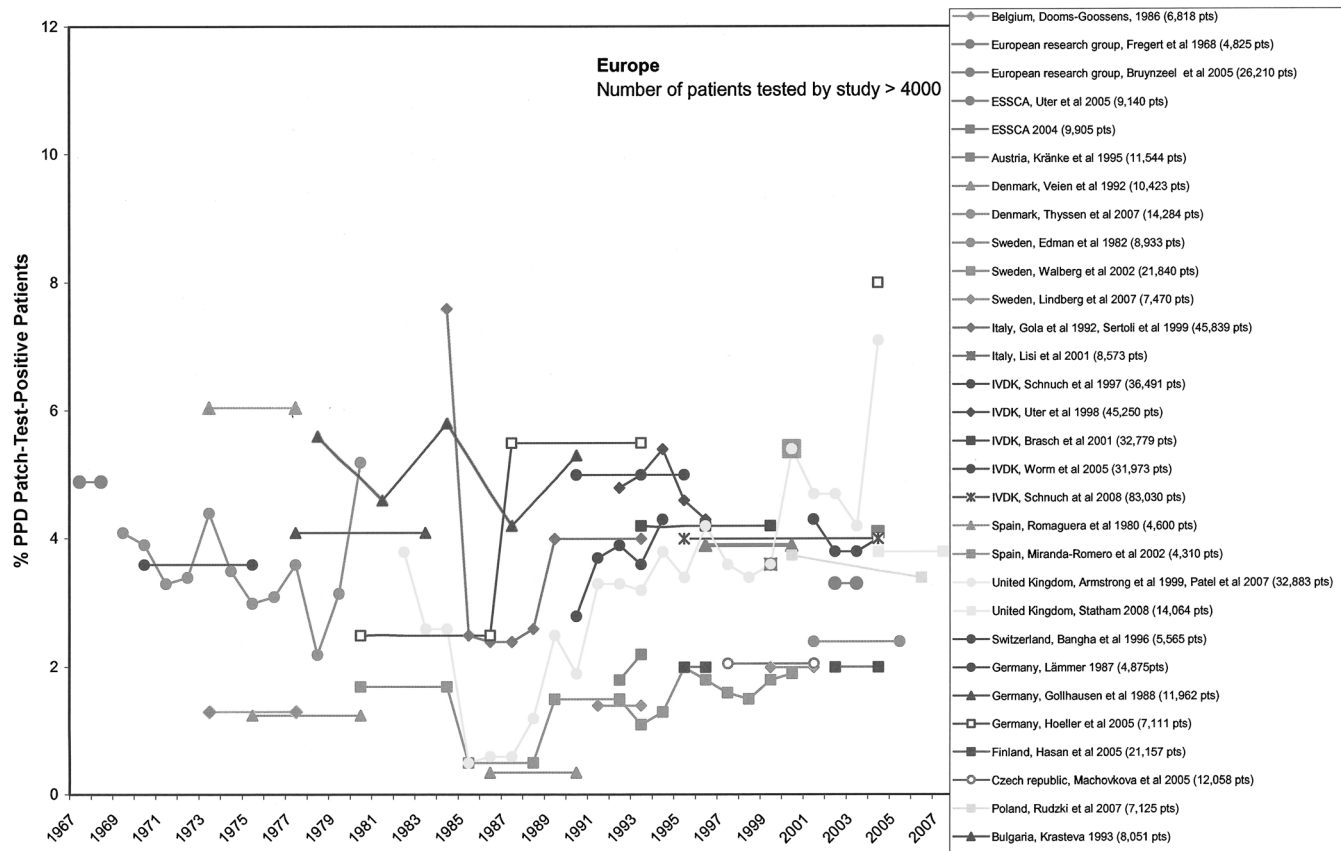


Figure 1. Prevalence of positive patch-test reactions to p-phenylenediamine (PPD) in unselected eczema patients in Europe: 30 studies. (ESSCA = European Surveillance Systems of Contact Allergies; IVDK = Information Networks of Departments of Dermatology; pts = patients.)

tive studies in Europe overall do not show an increase in PPD-positive individuals among patients referred for patch testing.

The following rates of positive response to PPD as reported by the Information Network of Departments of Dermatology (IVDK) in Germany, Austria, and Switzerland show no increase: 5% for the 1990–1995 period,¹⁷ 4.8% for the 1992–1996 period,¹⁸ 4.6% for the 1992–2000 period,¹⁹ 4.3% for the 1999–2001 period,²⁰ and 4% for the 2001–2004 period average²¹ (see Table 1 and Fig 1). These data from overlapping periods of analysis reflect patch testing on thousands of patients. An analysis of 83,030 of the same patients tested during a 10-year period (1995 to 2004) showed an overall prevalence of 4%, with prevalence fluctuating between 4.7% in 1995 and 3.8% in 2004.^{13,22} One of the centers included in the IVDK (Aachen) reported a higher prevalence of positive patch-test reactions to PPD in 2004 as compared to that of previous periods; however, no statistical analysis was performed.²³

St. John's Institute in London, United Kingdom, reported a significant increase of positive patch-test reactions to PPD in the period of 1982 to 2004, from 3.8% in 1982 to 7.1% in 2004 ($p < .001$, Cochran-Armitage trend test).^{24–26} However, two multicenter United Kingdom studies that did not include St. John's Institute found a prevalence of 3% in 2000²⁷ and 3.8% in the 2004–2007 period.²⁸

Generally, the rates of positive patch-test responses to PPD appear lower in northern Europe (Denmark, Finland, and Sweden). A multicenter study demonstrated an increased prevalence of positive patch-test reactions to PPD in Sweden by comparing a 2% prevalence in 2000 with a 1.4% prevalence in 1992 ($p < .05$, chi-square analysis).²⁹ However, previous data from most of the centers included in that study showed prevalence rates similar to those seen in 2000, namely, 2.2 to 5.2% in Malmö between 1969 and 1980³⁰ and 1.7% in seven centers from 1980 to 1984.³¹ Therefore, results seem to be similar during the different periods included in this review.

The prevalence of positive results to PPD testing in a multicenter population in North America has been analyzed for the period 1970 to 2002. A statistically significant decrease ($p < .0001$, Cochran-Armitage trend test) was found despite increasing hair dye use, as shown by the patch-test results of more than 34,000 patients.³² Rates of positive patch-test reactions ranged from 8% in 1971 to 1972 to 4.8% in 2001 to 2002, with some fluctuations (Table 2 and Fig 2). The decrease was

confirmed in a later study (4.7% prevalence in 2003 to 2004).³³

There is no clear indication of an increasing prevalence of positive patch-test reactions to PPD in Asia (Table 3 and Fig 3). Frequencies of positive patch-test reactions to PPD in Asia have varied significantly throughout the years (eg, the same team found 11.5% in 1998 and 6.4% in 2004).^{34,35} The small size of the panels in Asia may contribute to the variability of the results reported.

The clinical relevance to hair colorant use was investigated in a few studies in Europe and in Asia. In a 4-year period (1997 to 2000), 46 of 181 PPD-positive patients in a Swedish study (25.4%) reported clinical manifestations related to hair dye exposure³¹; 2 (7.7%) of 26 reactions in PPD-positive patients in the Netherlands were related to cosmetic use.³⁶ Devos and van der Valk found that 8 (12.7%) of 63 PPD-positive reactions were probably or definitely related to consumer hair dye use.³⁷ Koopmans and Bruynzeel found that 13% of positive reactions to PPD were related to consumer hair dye use.³⁸ These studies define a range of reactions clinically relevant to hair coloring products in Europe—between 8% and 25% of all positive patch test reactions to PPD in consecutive eczema patients.

In studies from China and India, past and present clinical relevance to hair dye use was found to be between 23 and 73%.^{35,39–41} The PPD-positive patch-test patients who had no manifestations related to hair dye use constituted 2.2 to 6.5% of all consecutive eczema patients in these studies.

The mean prevalence of positive patch-test reactions to PPD was calculated for each of the three continents from studies in which there were sufficient data about the number of unselected eczema patients and the number of PPD-positive patients: 3.7% for Europe, 5.7% for North America, and 4.6% for Asia. Some selected data are suggestive of an increase. Overall, however, the data from patch-testing unselected eczema patients do not indicate clearly that there is an increase in PPD patch-test-positive individuals in the majority of clinics around the world.

Dermatologic Patients with Cosmetic Allergic Contact Dermatitis

Compared to the previous group of unselected patients referred for patch testing, dermatologic patients with cosmetic allergic contact dermatitis constitute a more highly selected population of patients with clinical manifestations suggestive of allergic contact dermatitis

Table 2. Prevalence of Positive Patch-Test Reactions to p-Phenylenediamine in Unselected Eczema Patients in North America

Country and Study	Dates	PPD Tested (%)*	UE Patients Tested	PPD-Positive Patients	
				No.	%
Canada					
Lynde et al ⁹⁵	1972–1981	1	4,190	306	7.3 (range, 5.1–11.4)
Nethercott ⁹⁶	1977–1979	1	200	6	3.0
Hogan et al ⁹⁷	1983–1987	—	542	18	3.3
North America (NACDG)					
Rudner et al ⁹⁸	1971–1972	1	1,200	96	8.0
	1972–1974		3,041	185	6.1
Rudner ⁹⁹	1975–1976	1	900–2,000	—	6.2
Lynde et al ⁹⁵	1979–1980	1	1,753–2,145	—	6.5
Storrs et al ¹⁰⁰	1984–1985	1	1,138	78	6.9
Nethercott et al ¹⁰¹	1985–1989	1	3,980	255	6.4
Marks et al 1995 ¹⁰²	1992–1994	1	3,515	221	6.3
Marks et al 1998 ¹⁰³	1994–1996	1	3,111	211	6.8
Marks et al 2000 ¹⁰⁴	1996–1998	1	3,441	206	6.0
Marks et al 2003 ¹⁰⁵	1998–2000	1	5,831	286	4.9
Pratt et al ¹⁰⁶	2001–2002	1	4,903	235	4.8
Warshaw et al ³³	2003–2004	1	5,136	242	4.7
USA					
Lepine ¹⁰⁷	1973–1975	1	131	11	8.3
Albert et al ¹⁰⁸	1988–1997	1	927	46	5.0
Saripalli et al ¹⁰⁹	1995–2001	1	898	46	5.1
Mohammad et al ¹¹⁰	2000–2003	1	103	3	2.9
Wetter et al ¹¹¹	1998–2000	1	1,320	65	4.9
Davis et al ¹¹²	2001–2005	1	3,832	172	4.5
Total	—	—	47,439	2,688	5.7

NACDG = North American Contact Dermatitis Group; PPD = p-phenylenediamine; UE = unselected eczema.

*When concentration was specified in the article; when not specified, PPD was usually tested at 1% (PPD base) for the whole period except between 1984 and 1988, when it was tested at 0.5% as PPD dihydrochloride.

from hair dyes, hair cosmetics, or any cosmetic ingredient. As a result, the prevalence of positive patch-test reactions to PPD is expected to be greater (Table 4, Figure 4).

A distinction should be made between frequencies of positive patch-test reactions to PPD found among patients with cosmetic dermatitis suspected by clinical examination and among those with cosmetic dermatitis confirmed by patch testing. The percentage of patch-test-positive patients usually increases from the first to the second situation. The prevalence of positive patch-test reactions varies as well according to the selection of patients with cosmetic dermatitis; some studies include patients with manifestations to all kinds of cosmetic products, whereas other studies are aimed particularly at hair cosmetics or scalp dermatitis, resulting in a rise in the prevalence of positive patch-test reactions to PPD.

The prevalence of positive patch-test reactions to PPD among patients with suspected cases of unselected cosmetic

dermatitis (from all types of cosmetics) ranges between 7.3%⁴² and 23%.⁴³ It is higher when only cases related to hair cosmetics are analyzed (15.4–63.5).^{44,45} In a more recent study, however, in which 151 consecutive patients reporting skin reactions to cosmetics were tested during 2 years in three Swedish departments, no causality associated with hair dyes was found for any of the patients.⁴⁶

In European studies, the prevalence of positive patch-test reactions to PPD varies between 4.0% and 10.3%^{36,47–49} in patients with confirmed allergic cosmetic contact dermatitis (from all types of cosmetic products).

The prevalence of positive patch-test reactions is higher when patients are selected on the basis of reactions to hair cosmetics (38–97% in patients with confirmed allergic contact dermatitis from these products).^{42,44,45,47}

No particular trend could be observed in cosmetic dermatitis patients, with one exception: an increased prevalence of positive patch-test reactions to PPD was

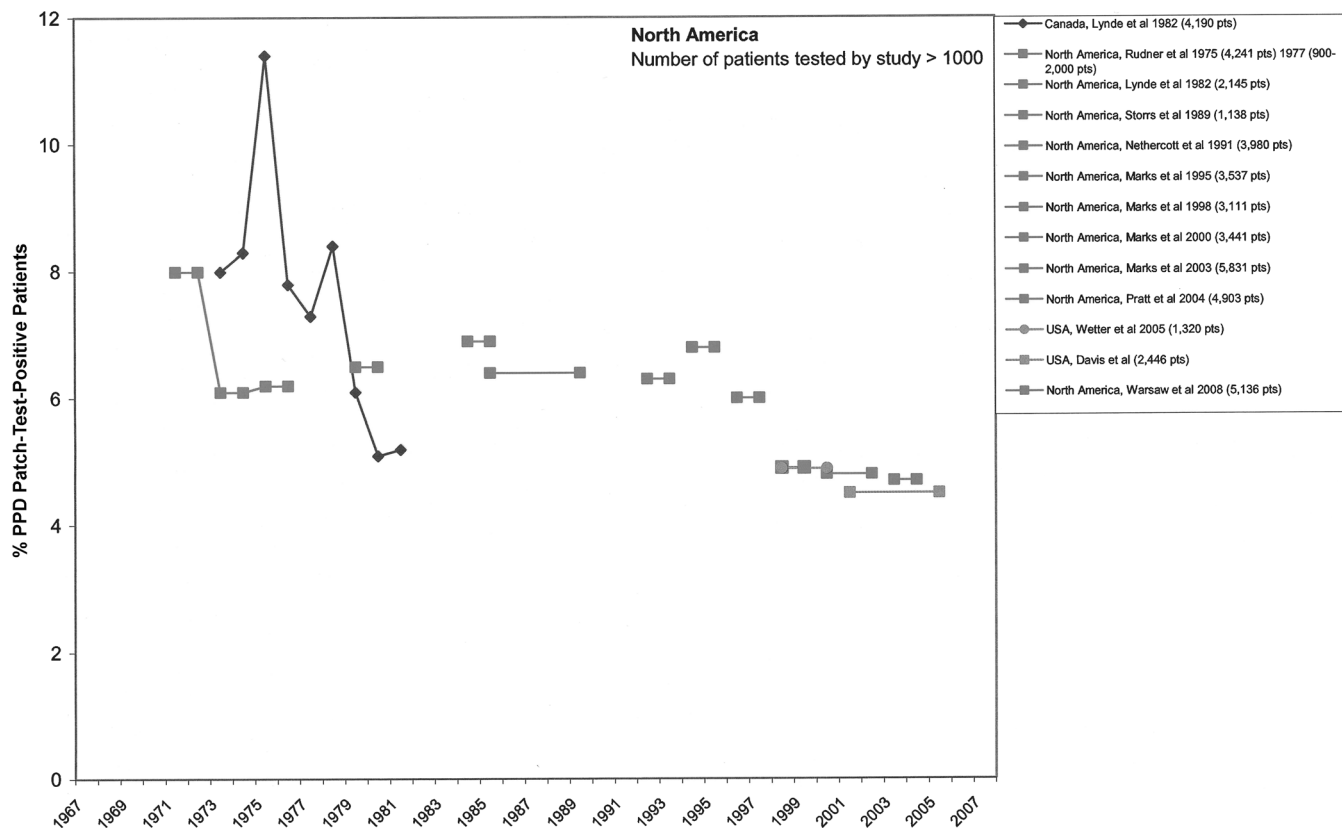


Figure 2. Prevalence of positive patch-test reactions to p-phenylenediamine (PPD) in unselected eczema patients in North America; 13 studies. (pts = patients.)

found by the IVDK from 1995 to 2002 in patients suspected of having contact dermatitis from hair cosmetics ($p < .05$).⁴⁴ The mean prevalence of positive patch-test reactions to PPD in this particular group of patients throughout this period was 15.4%. At the same time, all confirmed cases of contact dermatitis from hair cosmetics (not only hair colorants) represented 0.6% of all unselected eczema patients in this study. The increase seems to be confirmed by a later IVDK study for the 2003–2004 period, in which positive reactions to PPD rose to 20.3% in patients suspected of having contact dermatitis from hair cosmetics. However, the authors suggested that this increase may have been partly related to stricter indications for patch testing.⁵⁰

It is difficult to reach a conclusion about the existence of any trend of increase in hair dye dermatitis by using raw data from individual studies because they vary to a great degree in patient selection. It may be possible to verify any such trend by investigating whether the proportion of confirmed hair dye dermatitis cases (clinical manifestations and positive patch-test reactions to PPD and other

hair colorants) increases in greater and more stable patient populations. Unselected eczema patients and all dermatologic patients are such populations.

In 13 studies (eight in Europe, four in Asia, and one in the United States), enough data are available to calculate confirmed hair dye dermatitis rates in which the denominator used is the number of unselected eczema patients (see Table 4). These prevalence rates were sometimes those of confirmed scalp dermatitis from hair cosmetics in general because it was impossible to determine the number of cases of contact dermatitis clearly caused by hair dye.^{44,47,49} These rates ranged from 0.11 to 5.9% (0.11–1.6% in Europe).^{36,39,47} The mean prevalence of confirmed hair dye dermatitis in unselected eczema patients thus appears to be less than 1%. Prevalence tends to be higher in Asia (mean, 2.4%) than in Europe (mean, < 0.6%).

We have compared the prevalence of confirmed hair dye dermatitis in unselected eczema patients in Europe during the period before 1995 and the period after 1995. Data from three European studies were available for the

Table 3. Prevalence of Positive Patch-Test Reactions to p-Phenylenediamine in Unselected Eczema Patients in Asia

Country and Study	Dates	PPD Tested (%)*	UE Patients Tested	PPD-Positive Patients	
				No.	%
Bangladesh					
Akhtar et al ¹¹³	2000–2003	—	250	14	5.6
China					
Zhang et al ¹¹⁴	1989	0.5	124	10	8.0
Wang et al ¹¹⁵	1992–1993	—	88	0	0.0
Fan and Zhao ¹¹⁸	1988–1989	—	204	18	8.8
Liu et al ¹¹⁹	1988–1996	0.5	1,135	91	8.0
Li et al ¹²¹	2001–2002	—	217	23	10.6
Wang et al ¹⁴⁰	2001–2003	1	378	38	10.1
Li et al ⁴¹	2003–2005	—	599	46	7.7
China-Hong Kong					
Lee and Lam 1989 ¹¹⁶	1986	—	231	0	0.0
Lee and Lam 1996 ¹¹⁷	1987–1988	0.5	437	1	0.2
Lam et al ¹²⁰	1995–1999	1	2,585	154	6.0
India					
Sharma and Chakrabarti ³⁴	Before 1998 (no dates)	1	200	23	11.5
Sharma et al ¹³⁵	Before 2004 (no dates)	—	220	9	6.4
Bajaj et al ¹²²	1997–2006	1	1,000	53	5.3
Iran					
Kashani et al ¹²³	2002–2004	—	250	5	2.0
Israel					
Freireich-Astman et al ¹²⁴	1999–2000	1	943	—	2.5
Lazarov ¹²⁵	1998–2004	1	2,156	38	1.8
Japan					
Fujiwara et al ¹²⁶	Before 1976 (no dates)	1	155	25	16.1
Hirano and Kunihiro ¹²⁷	1976–1980	1	434	31	7.1
Adachi ¹²⁸	1994	1	1,507	92	6.1
Natsuaki ¹²⁹	1998	1	1,573	75	4.8
Korea					
Eun ¹³⁰	1983–1985	1	937	68	7.3
Moon ¹³¹	1986–1993	—	2,326	79	3.4
Pakistan					
Hussain et al ¹³²	Before 2002 (no dates)	—	350	20	5.7
Saudi Arabia					
El-Rab and Al-Sheikh ¹³³	Before 1995 (no dates)	1	240	9	3.8
Singapore					
Goh ¹³⁴	1984–1985	1	2,471	83	3.4
Lim et al ¹³⁵	1986–1990	1	5,557	255	4.5
Chan et al ³⁹	1998–1999	1	406	33	8.1
Thailand					
Wongpiyabovorn and Puvabanditsin ⁶³	2003–2004	—	129	2	1.55

Table 3. Continued

Country and Study	Dates	PPD Tested (%)*	UE Patients Tested	PPD-Positive Patients	
				No.	%
Turkey					
Akasya-Hillenbrand and Ozkaya-Bayazit ¹³⁶	1996–1999	1	542	20	3.7
Akyol et al ¹³⁷	1992–2004	1	1,038	19	1.8
Total	—	—	29,095	1,346	4.6

NACDG = North American Contact Dermatitis Group; PPD = p-phenylenediamine; UE = unselected eczema.

*When concentration was specified in the article; when not specified, PPD was usually tested at 1% (PPD base) for the whole period except between 1984 and 1988, when it was tested at 0.5% as PPD dihydrochloride.

first period, and data from four studies were available for the second period (Table 5). According to available data, the mean prevalence of allergic contact dermatitis from hair coloring products was less than 0.6% for both periods. This is in line with a 10-year analysis on 83,030 unselected eczema patients (IVDK data).^{13,22} Using patch-test outcomes, clinical manifestations, and occupation (but no

definite data on consumer hair dye exposure in each case), the authors found that consumer allergy to hair dyes is responsible for positive patch-test reactions in 0.9% of unselected eczema patients.

The prevalence of confirmed allergic hair dye dermatitis in the studies reviewed is between 0.01% and 0.14% of all patients, with and without eczema^{36,51,52} (see Table 4).

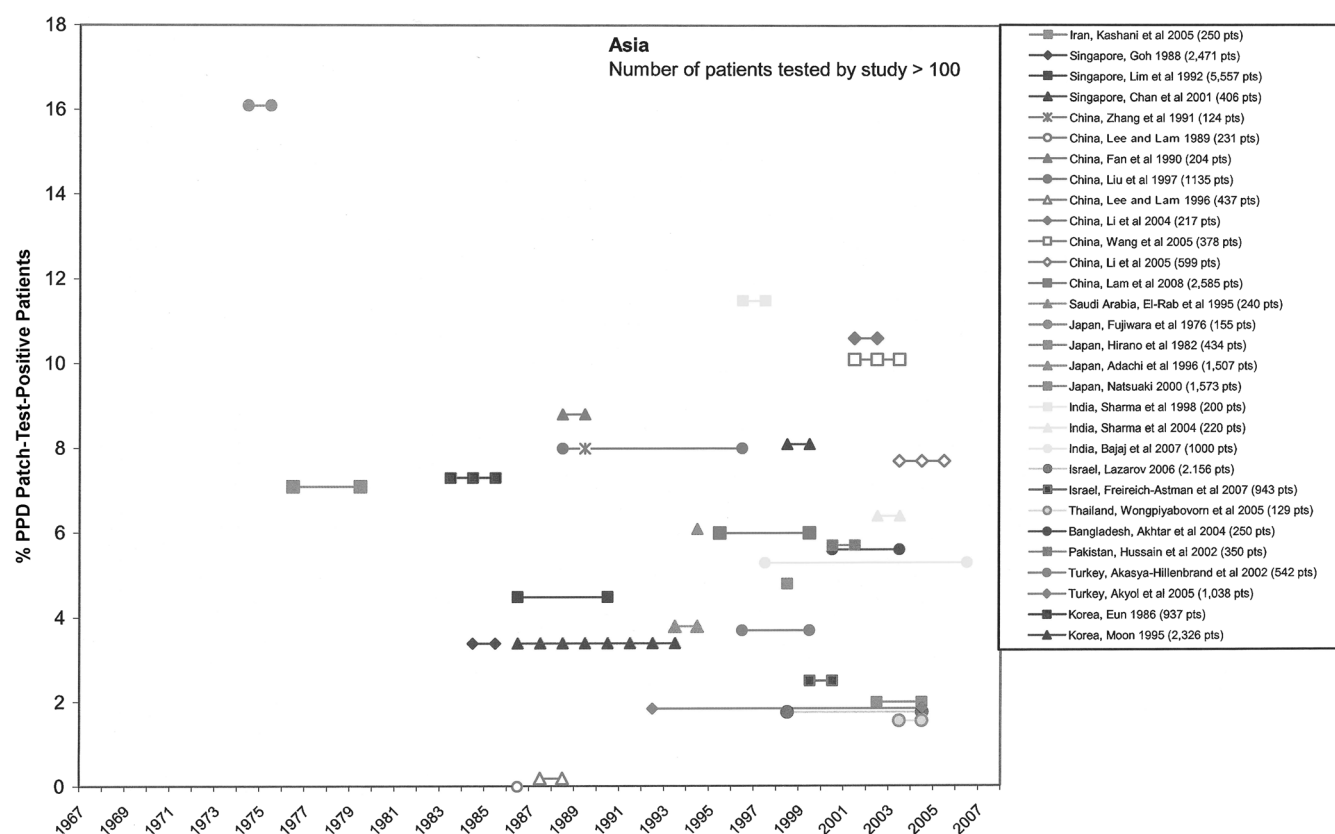


Figure 3. Prevalence of positive patch-test reactions to p-phenylenediamine (PPD) in unselected eczema patients in Asia: 30 studies. (pts = patients.)

Table 4. Prevalence of Positive Patch-Test Reactions to p-Phenylenediamine in Patients with Allergic Cosmetic Contact Dermatitis and Prevalence of Patients with Allergic Hair Dye Contact Dermatitis among Unselected Eczema Patients and All Dermatologic Patients

Country	Dates	Tested Patients with ACCD	PPD-Positive ACCD Patients	Positive Patch-Test Reactions to PPD among ACCD Patients	Allergic Hair Dye Dermatitis among Dermatologic Patients
Belgium					
Broeckx et al ⁴⁷	Before 1987 (no dates)	5,202 UE pts, 156 with confirmed ACCD, 42 with confirmed ACCD from hairdressing products	16	10.3% of confirmed ACCD; 38.1% of confirmed ACCD from hairdressing products	< 0.8% of UE pts (<i>n</i> = 42 allergic to hair cosmetics)
Kohl et al ⁴⁹	1998–1999	819 UE pts, 297 with confirmed ACCD	17	2.1% of confirmed ACCD	< 1.6% of UE pts (<i>n</i> = 13 with scalp dermatitis)
China					
Wang et al ⁴⁰	2001–2003	378 UE pts, 138 with suspected ACCD, 37 with confirmed ACCD	22	17.4% of suspected ACCD, 59.5% of confirmed ACCD	5.8% of UE pts (<i>n</i> = 23)
Li et al ⁴¹	2003–2005	599 UE pts, 93 with suspected ACCD, 48 with confirmed ACCD	20	21.5% of suspected ACCD, 41.7% of confirmed ACCD	3.3% of UE pts (<i>n</i> = 20)
European survey					
Frosch et al ¹³⁸	1988–1991	104 with suspected ACCD from hair cosmetics	20	19.2% of suspected ACCD	—
Europe (6 centers)					
Goossens et al ⁴⁸	1996	475 pts with confirmed ACCD	33	6.9% of confirmed ACCD	—
Germany, Austria, Switzerland (IVDK)					
Uter et al ⁴⁴	1995–2002	77,901 UE pts, 1,217 with suspected dermatitis from hair cosmetics	—	15.4% of suspected dermatitis from hair cosmetics	< 0.6% of UE pts (<i>n</i> < 473 allergic to hair dyes and hair cosmetics)
	1995–1996	266	33	12.6%	
	1997–1998	391	47	12.0%	
	1999–2000	257	49	19.0%	
	2001–2002	303	50	16.6%	
	1995–2002 (confirmed dermatitis from hair cosmetics)	473	179	37.8% of confirmed dermatitis from hair cosmetics	
Uter et al ⁵⁰	2003–2004	394 with suspected dermatitis from hair cosmetics	80	20.3% of suspected dermatitis from hair cosmetics	—
Hillen et al ¹³⁹	1993–2003	1,222 with suspected allergic contact dermatitis of scalp	144	11.8% of allergic contact dermatitis of scalp	—
India					
Penchalaiah et al ¹⁴⁰	Before 2000 (no dates)	50 with suspected ACCD, 31 with suspected ACCD from hair dyes	8	16% of suspected ACCD, 25.8% of suspected ACCD from hair dyes	—

Table 4. Continued

Country	Dates	Tested Patients with ACCD	PPD-Positive ACCD Patients	Positive Patch-Test Reactions to PPD among ACCD Patients	Allergic Hair Dye Dermatitis among Dermatologic Patients
Mehta and Reddy ¹⁴¹	Before 2001 (no dates)	50 with suspected ACCD	9	18% of suspected ACCD	—
Tomar et al ¹⁴²	Before 2005 (no dates)	50 with suspected ACCD, 33 with confirmed ACCD	7	14% of suspected ACCD, 21.2% of confirmed ACCD	—
Kumar and Paulose ¹⁴³	Before 2006 (no dates)	50 with suspected ACCD	7	14% of suspected ACCD	—
Italy					
Angelini et al ⁴⁵	1968–1983	8,230 UE pts, 52 with suspected ACCD from hair cosmetics, 34 with confirmed ACCD from hair cosmetics	33	63.5% of suspected ACCD from hair cosmetics, 97% of confirmed ACCD from hair cosmetics	0.4% of UE pts (<i>n</i> = 34)
Guerra et al ⁴²	1985–1990	261 with suspected ACCD from hairdressing products, 49 with confirmed ACCD from hairdressing products	19	7.3% of suspected ACCD from hairdressing products, 38.8% of confirmed ACCD from hairdressing products	—
Japan					
Ishihara et al ⁵²	1970	24,564 (all pts)	—	—	0.14% of all pts (<i>n</i> = 34)
	1978–1980	13,787 (all pts)	—	—	0.12% of all pts (<i>n</i> = 17)
Netherlands					
De Groot ³⁶	1981–1986	18,747 (all pts), 1,781 UE pts, 75 with confirmed ACCD	3	4% of confirmed ACCD	0.01% of all pts, 0.1% of UE pts, (<i>n</i> = 2)
Devos and van der Valk ³⁷	1995–1999	2,058 UE pts	—	—	0.4% of UE pts (<i>n</i> = 8)
Portugal					
Antunes ¹⁴⁴	1993–1998	1,934 UE pts	—	—	0.6% of UE pts (<i>n</i> = 12)
Singapore					
Goh ¹⁴⁵	1984–1985	70,289 (all pts); 2,471 UE pts, 115 with confirmed ACCD	24	20.9% of confirmed ACCD	0.03% of all pts, 1% of UE pts (<i>n</i> = 24)
Chan et al ³⁹	1998–1999	406 UE pts	—	—	5.9% of UE pts (<i>n</i> = 24, present and past relevance)
Spain					
Gomez-Vazquez et al ⁴³	2000	53 with suspected ACCD, 34 with confirmed ACCD	8	23% of confirmed ACCD	—
Sweden					
Wahlberg et al ³¹	1997–2000	≈10,920 UE pts (mean, 2,730 per year)	—	—	0.4% of UE pts (<i>n</i> = 46)
USA					
Adams and Maibach ⁵¹	1977–1983	281,100 (all pts); 13,216 UE pts, 713 with confirmed ACCD	41	5.7%	0.02% of all pts, 0.3% of UE pts (<i>n</i> = 45)

ACCD = allergic cosmetic contact dermatitis; IVDK = Information Network of Departments of Dermatology; PPD = p-phenylenediamine; pts = patients; UE pts = unselected eczema patients.

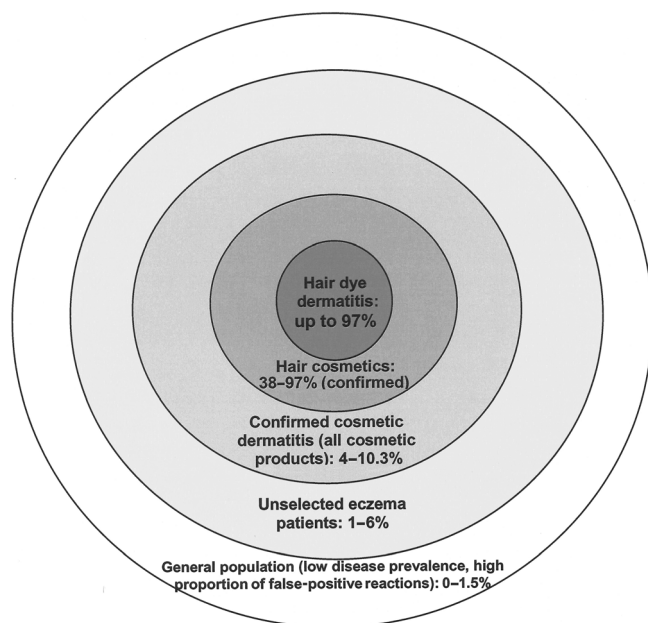


Figure 4. The prevalence of positive patch-test reactions to p-phenylenediamine (PPD) differs whether assessed in patient or nonpatient populations.

Prevalence of Positive Patch-Test Reactions to PPD in the General Population

There have been a few patch-test studies in the general population. It has been acknowledged that patch testing has a limited diagnostic performance (in terms of a low positive predictive value and a high proportion of false-positive reactions) in a population with low disease prevalence.^{53,54} The prevalence of positive patch-test reactions to PPD in the European general population ranges from 0 to 1.5% (Table 6).^{55,56} However, the highest prevalence (1.5%) was found in a population that was not totally unselected but had a significant proportion of patients with a history of adverse skin reactions (32.3%) and previous patch testing (27.2%). A causal relationship of PPD-positive patch-test reactions with hair dye use was not documented in any of these studies. A review of the available studies found no indication of an increase of PPD-sensitized individuals in the general population. The three studies carried out in the last decade (later than 1997) found the prevalence of positive patch-test reactions to PPD to be less than 0.3%.^{57–59}

Table 5. Prevalence of Patients with Confirmed Hair Dye Allergic Contact Dermatitis among Unselected Eczema Patients

Country and Study	Dates	Consecutive Eczema Patients	Patients with Confirmed Allergic Hair Dye Contact Dermatitis	Prevalence of Patients with Allergic Hair Dye Dermatitis among UE Patients (%)
Belgium				
Broeckx et al ⁴⁷	Before 1987 (no dates)	5,202	< 42*	< 0.8*
Kohl et al ⁴⁹	1998–1999	819	< 13*	< 1.6*
Italy				
Angelini et al ⁴⁵	1968–1983	8,230	34	0.41
Netherlands				
De Groot ³⁶	1981–1986	1,781	2	0.11
Devos and van der Valk ³⁷	Before 1995	15,213	< 52	< 0.52
	1995–1999	2,058	8	0.39
Sweden				
Wahlberg et al ³¹	1997–2000	10,920	46	0.42
Germany, Austria, Switzerland (IVDK)				
Uter et al ⁴⁴	1995–2002	77,901	< 473*	< 0.6*
	After 1995	91,698	< 540	< 0.59

IVDK = Information Network of Departments of Dermatology; UE = unselected eczema.

*Confirmed cases of allergic contact dermatitis from hair cosmetics and not only to hair coloring products.

Table 6. Prevalence of Positive Patch-Test Reactions to p-Phenylenediamine in the General Population (population-based epidemiological studies and estimations)

<i>Country and Study</i>	<i>Dates</i>	<i>Individuals Tested</i>	<i>Positive Patch-Test Reactions to PPD* (%)</i>
Australia			
Greig et al ⁶¹	Before 2000 (no dates)	219	0.0
Denmark			
Nielsen Menné ⁵⁵	1990	290	0.0
Mortz et al ¹⁴⁶	1995–1996	1,146	0.2
Nielsen et al ¹⁴⁷	1998	469	0.2
Denmark (extrapolation from DCDG data)			
Thyssen et al ⁶⁰	1996–2005 (based on 2001–2006 patch-test data)	14,248	Worst-case scenario: 0.53 (all); 0.2 (unequivocal) Medium-case scenario: 0.39 (all); 0.15 (unequivocal)
Italy			
Seidenari et al ¹⁴⁸	Before 1990 (no dates)	593	0.5
Germany			
Schäfer et al ¹⁵⁶	1994–1995	1,141	1.5
Germany (extrapolation from IVDK data)			
Schnuch et al ¹⁹	Based on 1992–2000 patch-test data	9,266	Worst-case scenario: 1.6 (all); 0.7 (unequivocal) Medium-case scenario: 0.7 (all); 0.3 (unequivocal)
Schnuch et al ^{13,22}	Based on 1995–2004 patch-test data	83,030	0.49 overall; 0.11 consecutive to consumer hair dye use
Norway			
Dotterud and Smith-Sivertsen ⁵⁹	2007 (no dates)	1,236	0.3
Poland			
Spiewak ⁵⁸	2002	135	0.0
Portugal			
Oliveira ⁵⁷	1997–1998	205	0.0
Thailand			
White et al ⁶²	Before 2007 (no dates)	2,545	2.7

DCDG = Danish Contact Dermatitis Group; IVDK = Information Network of Departments of Dermatology; PPD = p-phenylenediamine.

Data from population-based studies are completed by prevalence estimates.^{19,56,60} One IVDK study and one Danish study are based on extrapolations from patch-test data on dermatologic patients, using correction factors such as sales data on patch-test allergens, country population size, and patch testing practices.^{19,60} These two studies provide data on worst-case and medium-case scenarios, which are further subdivided into (1) the total number of positive patch-test reactions expected (+, ++, and +++) and (2) unequivocal reactions (++ and +++). Thus, as determined from the two studies, the percentages of unequivocal reactions to PPD expected in the general

population are between 0.15% and 0.30% for the medium-case scenario and between 0.2% and 0.7% for the worst-case scenario.

A second IVDK study based on the 10-year prevalence of positive patch-test reactions to PPD (1995 to 2004) estimated the prevalence of such reactions to PPD in the general population at 0.49%.^{13,22} The study also estimated that 0.11% of the general population had positive patch-test reactions causally related to consumer hair dye use.

The only studies on the prevalence of positive patch-test reactions to PPD in the general population outside

Table 7. Consumer Complaint-Based Studies

<i>Country and Study</i>	<i>Dates</i>	<i>No. of Individuals Surveyed</i>	<i>Individuals Reporting Reactions $\pm$ Confirmation by Patch Test</i>
Denmark (interview)			
Søsted et al 2002 ¹⁴⁹	2000–2002 (called specifically for individuals with reactions)	55 (published ad, 89,200 copies); 88 responded, but 33 did not fit inclusion criteria	16 patch-tested and positive; impossible to determine %
Søsted et al 2005 ¹⁵⁰	2003	1,254 who had ever dyed their hair; 2,593 total surveyed	5.3% (67) 2.6%
Italy Di Giovanni et al ¹⁵¹	2004	3,528	< 1.4% (all hair cosmetics)
Sweden Berne et al ⁶⁴	1991	1,077	0.0%

Europe have been carried out in Australia (0% prevalence)⁶¹ and Thailand.⁶² A prevalence higher than that found in Europe was found in the Thailand study (2.7%). As in Europe, the relevance of positive patch-test reactions has been unreported. The use of darker dyes in Thailand was suggested as an explanation for the higher prevalence of positive patch-test reactions to PPD. The high prevalence in the Thai general population found in this study is, however, in contradiction with a study of Thai unselected eczema patients.⁶³ Paradoxically, a lower prevalence (1.55%) was found in unselected eczema patients in the same area (Greater Bangkok) in the same period.

Consumer Complaint-Based Studies

In consumer complaint-based studies, consumers are actively invited to report data about clinical manifestations occurring after cosmetic (hair colorant) use (Table 7). Consumer complaint-based studies may be organized easily, can be performed quickly, and are cost effective. They are very sensitive tools for detecting complaints that may be connected with the use of a consumer product in the general population. However, they involve the analysis of clinical manifestations that are difficult to ascribe specifically to allergy or to irritation, and they therefore tend to overestimate the rate of allergic manifestations when they are not medically validated and confirmed by patch testing. Indeed, when consumers are further examined and patch-tested, the prevalence of confirmed hair dye dermatitis may be reduced to 0%.⁶⁴ Interview-based studies report levels of 0 to 2.6% for the general population, but the numbers of subjects are small, thus

making extrapolation to a larger population difficult. Series of clinical cases cannot be used to calculate frequencies; it is believed that such series serve more usefully as an alert, signaling that a more in-depth investigation is required.

Conclusion

Based on our review of the literature, a robust large-scale epidemiology study examining the incidence of hair dye allergy based on consumers' reactions to product use has not been conducted. If such a study is conducted, it should be based on consumer data collected via questionnaire, and diagnoses of hair dye dermatitis should be confirmed by patch testing and be medically validated.

An overall analysis of the literature with several parameters does not indicate an increase in PPD patch-test-positive individuals in the majority of clinics around the world despite increasing hair dye use (in terms of consumers and products sold). However, the increasing prevalence reported by some selected centers should be followed carefully, and population-based studies should be carried out to determine the risk factors for hair dye allergy and the effect of risk management measures.

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References

1. 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;12:322–6.

2. 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;15:18–25.
3. Schlatter H, Long T, Gray J. An overview of hair dye safety. *J Cosmet Dermatol* 2007;6:32–6.
4. Memorandum on hair dye substances and their skin sensitizing properties. Proceedings of the 10th plenary meeting of the Scientific Committee for Consumer Products (SCCP), Brussels; 2006 Dec 19 Belgium;2007:1–11.
5. McFadden JP, White IR, Frosch PJ, et al. Allergy to hair dye. *Br Med J* 2007;334:220.
6. DeLeo V. p-Phenylenediamine. *Dermatitis* 2006;17:53–5.
7. Hostinek JJ, Maibach HI. Thresholds of elicitation depend on induction conditions. Could low level exposure induce sub-clinical allergic states that are only elicited under the severe conditions of clinical diagnosis? *Food Chem Toxicol* 2004;42:1859–65.
8. Ale SI, Maibach HI. Clinical relevance in allergic contact dermatitis. An algorithmic approach. *Dermatosen* 1995;43:119–21.
9. Lachapelle JM. A proposed relevance scoring system for positive allergic patch test reactions: practical implications and limitations. *Contact Dermatitis* 1997;36:39–43.
10. Frosch PJ, Pilz B, Burrows D, et al. Testing with fragrance mix. Is the addition of sorbitan sesquioleate to the constituents useful? *Contact Dermatitis* 1995;32:266–72.
11. Robinson MK, Gerberick GF, Ryan CA, et al. The importance of exposure estimation in the assessment of skin sensitization risk. *Contact Dermatitis* 2000;42:251–9.
12. Ho SG, Basketter DA, Jefferies D, et al. Analysis of para-phenylenediamine allergic patients in relation to strength of patch test reaction. *Br J Dermatol* 2005;153:364–7.
13. Schnuch A, Lessmann H, Frosch PJ, Uter W. para-Phenylenediamine: the profile of an important allergen. Results of the IVDK. *Br J Dermatol* 2008;159:379–86.
14. Brancaccio RR, Brown LH, Chnag YT, et al. Identification and quantification of para-phenylenediamine in a temporary black henna tattoo. *Am J Contact Dermat* 2002;13:15–8.
15. Fregert S, Hjorth N, Magnusson B, et al. Epidemiology of contact dermatitis. *Trans St Johns Hosp Dermatol Soc* 1968;55:17–35.
16. ESSCA Writing Group. The European Surveillance System of Contact Allergies (ESSCA): results of patch testing the standard series, 2004. *J Eur Acad Dermatol Venereol* 2008;22:174–81.
17. Schnuch A, Geier J, Uter W, et al. National rates and regional differences in sensitization to allergens of the standard series. Population-adjusted frequencies of sensitization (PAFS) in 40,000 patients from a multicenter study (IVDK). *Contact Dermatitis* 1997;37:200–9.
18. Uter W, Schnuch A, Geier J, Frosch PJ. Epidemiology of contact dermatitis. The Information Network of Departments of Dermatology (IVDK) in Germany. *Eur J Dermatol* 1998;1:36–40.
19. Schnuch A, Uter W, Geier J, Gefeller O. Epidemiology of contact allergy: an estimation of morbidity employing the clinical epidemiology and drug-utilization research (CE-DUR) approach. *Contact Dermatitis* 2002;47:32–9.
20. Geier J, Uter W, Lessmann H, Schnuch A. The positivity ratio—another parameter to assess the diagnostic quality of a patch test preparation. *Contact Dermatitis* 2003;48:280–2.
21. Worm M, Brasch J, Geier J, et al. Epikutantestung mit der DKG—Standardreihe 2001–2004. *Hautarzt* 2005;56:1114–24.
22. Schnuch A, Lessmann H, Frosch PJ, Uter W. para-Phenylenediamine: the profile of an important allergen. Results of the IVDK [erratum]. *Br J Dermatol* 2008;159:772.
23. Hoeller OD, Vens N, Merk HF, Schroeder CM. Kontaktallergene der Standardreihe von 1980–2004 an der Universitäts-hautklinik Aachen. *Hautarzt* 2005;56:1125–32.
24. Armstrong DKB, Jones AB, Smith HR, et al. Occupational sensitisation to p-phenylenediamine: a 17-year review. *Contact Dermatitis* 1999;41:348–9.
25. Dawe SA, White IR, Rycroft RJG, et al. Active sensitization to para-phenylenediamine and its relevance: a 10-year review. *Contact Dermatitis* 2004;51:96–7.
26. Patel S, Basketter DA, Jefferies D, et al. Patch test frequency to p-phenylenediamine: follow up over the last 6 years. *Contact Dermatitis* 2007;56:35–7.
27. Britton JER, Wilkinson SM, English JSC, et al. The British standard series of contact dermatitis allergens: validation in clinical practice and value for clinical governance. *Br J Dermatol* 2003;148:259–64.
28. Statham B. Quality assurance of contact dermatitis services. *Contact Dermatitis* 2008;58(Suppl 1):54.
29. Lindberg M, Edman B, Fischer T, Stenberg B. Time trend in Swedish patch test data from 1992 to 2000. A multi-center study based on age- and sex-adjusted results of the Swedish standard series. *Contact Dermatitis* 2007;56:205–10.
30. Edman B, Möller H. Trends and forecasts for standard allergens in a 12-year patch test material. *Contact Dermatitis* 1982;8:95–104.
31. Wahlberg JE, Tammela M, Anderson C, et al. Contact allergy to p-phenylenediamine in Sweden. *Occup Environ Dermatol* 2002;50: 51–4.
32. Nguyen SH, Dang TP, MacPherson C, et al. Prevalence of patch test results from 1970 to 2002 in a multi-center population in North America (NACDG). *Contact Dermatitis* 2008;58:101–6.
33. Warshaw EM, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group patch test results, 2003–2004 study period. *Dermatitis* 2008;19:129–36.
34. Sharma VK, Chakrabarti A. Common contact sensitizers in Chandigarh, India. A study of 200 patients with the European standard series. *Contact Dermatitis* 1998;38:127–31.
35. Sharma VK, Sethuraman G, Garg T, et al. Patch testing with the Indian standard series in New Delhi. *Contact Dermatitis* 2004;51: 319–21.
36. De Groot AC. Contact allergy to cosmetics: causative ingredients. *Contact Dermatitis* 1987;17:26–34.
37. Devos SA, van der Valk PGM. The risk of active sensitisation to PPD. *Contact Dermatitis* 2001;44:273–5.
38. Koopmans AK, Bruynzeel DP. Is PPD a useful screening agent? *Contact Dermatitis* 2003;48:89–92.
39. Chan YC, Ng AK, Goh CL. Positive patch-test reactions to para-phenylenediamine, their clinical relevance and the concept of clinical tolerance. *Contact Dermatitis* 2001;45:217–20.
40. Wang WH, Li L-F, Lu XY, Wang J. Cosmetic dermatitis in Chinese eczema patients patch tested with a modified European standard series of allergens. *Contact Dermatitis* 2005;53:314–9.
41. Li L-F, Liu G, Wang J. Patch test in Chinese patients with cosmetic allergic contact dermatitis to common cosmetic allergens from a European cosmetic series. *Contact Dermatitis* 2007;57:50–4.
42. Guerra L, Bardazzi F, Tosti A. Contact dermatitis in hairdressers' clients. *Contact Dermatitis* 1992;26:108–11.

43. Gomez-Vasquez M, Fernandez-Redondo V, Toribo J. Allergic contact eczema/dermatitis from cosmetics. *Allergy* 2002;57:268–9.
44. Uter W, Lessmann H, Geier J, Schnuch A. Contact allergy to ingredients of hair cosmetics in female hairdressers and clients—an 8-year analysis of IVDK data. *Contact Dermatitis* 2003;49:236–40.
45. Angelini G, Vena GA, Giglio G, et al. Contact dermatitis due to cosmetics. *J Appl Cosmetol* 1985;3:223–36.
46. Berne B, Tammela M, Farm G, et al. Can the reporting of adverse skin reactions to cosmetics be improved? A prospective clinical study using a structured protocol. *Contact Dermatitis* 2008;58:223–7.
47. Broeckx W, Blondeel A, Dooms-Goossens A, Achten G. Cosmetic intolerance. *Contact Dermatitis* 1987;16:189–94.
48. Goossens A, Beck MH, Haneke E, et al. Adverse cutaneous reactions to cosmetic allergens. *Contact Dermatitis* 1999;40:112–3.
49. Kohl L, Blondeel A, Song M. Allergic contact dermatitis from cosmetics. *Dermatology* 2002;204:334–7.
50. Uter W, Lessmann H, Geier J, Schnuch A. Contact allergy to hairdressing allergens in female hairdressers and clients—current data from IVDK, 2003–2006. *J Dtsch Dermatol Ges* 2007;5:993–1001.
51. Adams RM, Maibach HI. A five-year study of cosmetic reactions. *J Am Acad Dermatol* 1985;13:1062–9.
52. Ishihara M, Nogami T, Itoh M, et al. Basic studies on contact dermatitis due to hair colourings and cold permanent wave solutions. *Nippon Kosho Kaishi* 1983;7:272–82.
53. Uter W, Ludwig A, Balda BR, et al. The prevalence of contact allergy differed between population-based and clinic-based data. *J Clin Epidemiol* 2004;57:627–32.
54. Thyssen JP, Linneberg A, Menné T, Johansen JD. The epidemiology of contact allergy in the general population—prevalence and main findings. *Contact Dermatitis* 2007;57:287–99.
55. Nielsen NH, Menné T. Allergic contact sensitisation in an adult population: two cross-sectional surveys eight years apart (The Copenhagen Allergy Study). *Acta Derm Venereol* 1992;72:456–60.
56. Schäfer T, Böhler E, Ruhdorfer S, et al. Epidemiology of contact allergy in adults. *Allergy* 2001;56:1192–6.
57. Oliveira H. Reactivity to 35 standard allergens in a normal population. *Proceedings of the 4th Congress of the European Society of Contact Dermatitis*; 1998 July; Helsinki, Finland. p. 105.
58. Spiewak R. Atopy and contact hypersensitivity: a reassessment of the relationship using objective measures. *Ann Allergy Asthma Immunol* 2005;95:61–5.
59. Dotterud LK, Smith-Sivertsen T. Allergic contact sensitization in the general adult population: a population-based study from Northern Norway. *Contact Dermatitis* 2007;56:10–5.
60. Thyssen JP, Uter W, Schnuch A, et al. 10-year prevalence of contact allergy in the general population in Denmark estimated through the CE-DUR method. *Contact Dermatitis* 2007;57:265–72.
61. Greig JE, Carson CF, Stuckey MS, Riley TV. Prevalence of delayed hypersensitivity to the European standard series in a self-selected population. *Australas J Dermatol* 2000;41:86–9.
62. 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;37:1848–53.
63. Wongpiyabovorn J, Puvabanditsin P. Results of standard patch test in patients suspected of having allergic contact dermatitis. *J Med Assoc Thai* 2005;88 Suppl 4:S177–83.
64. Berne B, Lundin A, Malmros PE. Side effects of cosmetics and toiletries in relation to use. A retrospective study in Swedish population. *Eur J Dermatol* 1994;4:189–93.
65. Kränke B, Binder M, Derhaschnig J, et al. Epikutantestung mit der “Standardreihe Österreich”—Testepidemiologische Kenngrößen und Ergebnisse. *Wien Klin Wochenschr* 1995;107:323–30.
66. Oleffe J, Nopp-Oger MJ, Achten G. Batterie européenne de tests épicutanées—Bilan de 300 observations. *Berufsdermatosen* 1972;20:209–17.
67. Dooms-Goossens A. A computerized retrieval system of contact allergenic substances. *Semin Dermatol* 1986;5:249–54.
68. Krasteva M. Immuno-allergological study on contact sensitivity to p-phenylenediamine [thesis]. Sofia, Bulgaria: Medical Academy of Sofia, Bulgaria; 1993.
69. Machovcova A, Dastychova E, Kostalova D, et al. Common contact sensitizers in the Czech Republic. Patch test results in 12,058 patients with suspected contact dermatitis. *Contact Dermatitis* 2005;53:162–6.
70. Hammershoy O. Standard patch test results in 3,225 consecutive Danish patients from 1973 to 1977. *Contact Dermatitis* 1980;6:263–8.
71. Christophersen J, Menne T, Tanghoj P, et al. Clinical patch test data evaluated by multivariate analysis. Danish Contact Dermatitis Group. *Contact Dermatitis* 1989;21:291–9.
72. Veien K, Hattel T, Laurberg G. Patch test results from a private dermatologic practice for two periods of 5 years with a 10-year interval. *Am J Contact Dermat* 1992;3:189–92.
73. Dooms-Goossens A, Scheper RJ, Andersen KE, et al. Comparative patch testing with PPD-base and PPD-dihydrochloride: human and animal data compiled by the European Environmental Contact Dermatitis Research Group. In: Frosch PJ, Dooms-Goossens A, Lachapelle JM, et al, editors. *Current topics in contact dermatitis*. Berlin: Springer-Verlag; 1989. p. 281–5.
74. Bruynzeel DP, Diepgen TL, Andersen KE, et al. Monitoring the European standard series in 10 centers 1996–2000. *Contact Dermatitis* 2005;53:146–9.
75. Uter W, Hegewald J, Aberer W, et al. The European standard series in 9 European countries, 2002/2003—first results of the European Surveillance System on Contact Allergies. *Contact Dermatitis* 2005;53:136–45.
76. Hasan T, Rantanen T, Alanko K, et al. Patch test reactions to cosmetic allergens in 1995–1997 and 2000–2002 in Finland—a multicenter study. *Contact Dermatitis* 2005;53:40–5.
77. Lämmer D. Testergebnisse von 1008 Patienten mit Kontaktallergie. *Z Hautkr* 1979;54:571–9.
78. Gollhausen R, Enders F, Przybilla B, et al. Trends in allergic contact sensitization. *Contact Dermatitis* 1988;18:147–54.
79. Enders F, Przybilla B, Ring J, Gollhausen R. Patch test results in 1987 compared to trends from the period 1977–1983. *Contact Dermatitis* 1989;20:230–2.
80. Brasch J, Uter W, Geier J, Schnuch A. German Contact Dermatitis Research Group, IVDK. Associated positive patch test reactions to standard contact allergens. *Am J Contact Dermat* 2001;12:197–202.
81. Hillen U, Jappe U, Frosch PJ, et al. Late reactions to the patch-test preparations para-phenylenediamine and epoxy resin: a prospective multicenter investigation of the German Contact Dermatitis Research Group. *Br J Dermatol* 2006;154:665–70.
82. Gola M, Sertoli A, Angelini G, et al. GIRDCA data bank for occupational and environmental contact dermatitis (1984 to 1988). *Am J Contact Dermat* 1992;3:179–88.

83. Sertoli A, Francalanci S, Acciai MC, Gola M. Epidemiological survey of contact dermatitis in Italy (1984-1993) by GIRDCA (Gruppo Italiano Ricerca Dermatiti da Contatto e Ambientali). *Am J Contact Dermat* 1999;10:18-30.
84. Lisi P, Hansel K, Cristaudo A, et al. Prevalenza della sensibilizzazione da contatto ad alcuni coloranti permanenti per capelli. *Ann Ital Dermatol Allergol* 2001;55:29-32.
85. Young E, Houwing RH. Patch test results with standard allergens over a decade. *Contact Dermatitis* 1987;17:104-7.
86. van der Valk PGM, Devos SA, Coenrads PJ. Evidence-based diagnosis in patch testing. *Contact Dermatitis* 2003;48:121-5.
87. Rudzki E, Rebandel P. Sensitivity to paraphenylenediamine in Warsaw (Poland). *Contact Dermatitis* 2007;57:347-8.
88. Romaguera C, Grimalt F. Statistical and comparative study of 4600 patients tested in Barcelona (1973-1977). *Contact Dermatitis* 1980;6:309-15.
89. Camarasa JM. First epidemiological study of contact dermatitis in Spain - 1977. Spanish Contact Dermatitis Research Group. *Acta Derm Venereol Suppl (Stockh)* 1979;59:33-7.
90. Miranda-Romero A, Aguirre A, Alomar A, et al. Serie estandar de alergenos del GEIDC: resultados de su aplicacion en 4.310 pacientes en el ano 2000. *Dermatitis de Contacto* 2002;29:6-10.
91. Bruckner-Tuderman L, Konig A, Schnyder UW. Patch test results of the dermatology clinic Zurich in 1989: personal computer-aided statistical evaluation. *Dermatology* 1992;184:29-33.
92. Bangha E, Elsner P. Sensitizations to allergens of the European standard series at the department of dermatology in Zurich 1990-1994. *Dermatology* 1996;193:17-21.
93. Vestey JP, Gawkrödger DJ, Wong WK, Buxton PK. An analysis of 501 consecutive contact clinic consultations. *Contact Dermatitis* 1986;15:119-25.
94. Monk BE. Patch testing in a British district general hospital. *Clin Exp Dermatol* 1999;24:484-6.
95. Lynde CW, Warshawski L, Mitchell JC. Screening patch tests in 4190 eczema patients 1972-81. *Contact Dermatitis* 1982;8:417-21.
96. Nethercott JR. Results of routine patch testing of 200 patients in Toronto, Canada. *Contact Dermatitis* 1982;8:389-95.
97. Hogan DJ, Hill M, Lane PR. Results of routine patch testing of 542 patients in Saskatoon, Canada. *Contact Dermatitis* 1988;19:120-4.
98. Rudner EJ, Clendenning WE, Epstein E, et al. The frequency of contact sensitivity in North America 1972-74. *Contact Dermatitis* 1975;1:277-80.
99. Rudner EJ. North American Group results. *Contact Dermatitis* 1977;3:208-9.
100. Storrs FJ, Rosenthal LR, Adams RA, et al. Prevalence and relevance of allergic reactions in patients patch tested in North America - 1984 to 1985. *J Am Acad Dermatol* 1989;20:1038-45.
101. Nethercott JR, Holness DL, Adams RM, et al. Patch testing with routine screening tray in North America, 1985 through 1989: I. Frequency of response. *Am J Contact Dermat* 1991;2:122-9.
102. Marks JG, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group standard tray patch test results (1992-1994). *Am J Contact Dermat* 1995;6:160-5.
103. Marks JG, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group patch test results for the detection of delayed-type hypersensitivity to topical allergens. *J Am Acad Dermatol* 1998;38:911-8.
104. Marks JG, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group patch test results, 1996-1998. *Arch Dermatol* 2000;136:272-3.
105. Marks JG, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group patch test results, 1998 to 2000. *Am J Contact Dermat* 2003;14:59-62.
106. Pratt MD, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group patch-test results, 2001-2002 study period. *Dermatitis* 2004;15:176-83.
107. Lepine EM. Results of routine office patch testing. *Contact Dermatitis* 1976;2:89-91.
108. Albert MR, Chang YC, Gonzalez E. Concomitant positive reactions to allergens in a patch test standard series from 1988-1997. *Am J Contact Dermat* 1999;10:219-23.
109. Saripalli YV, Achen F, Belsito D. The detection of clinically relevant contact allergens using a screening tray of 23 allergens. *J Am Acad Dermatol* 2003;49:65-9.
110. Mohammad AH, Cohen S, Hadi S. Patch testing: a retrospective analysis of 103 patients with emphasis on practical aspects for the clinician. *Skinmed* 2005;4:340-4.
111. Wetter DA, Davis MDP, Yiannias JA, et al. Patch test results from the Mayo Clinic contact dermatitis group. *Am J Contact Dermat* 2005;53:416-21.
112. Davis MD, Scalf LA, Yiannias JA, et al. Changing trends and allergens in the patch test standard series: a Mayo Clinic 5-year retrospective review, January 1, 2001, through December 31, 2005. *Arch Dermatol* 2008;144:67-72.
113. Akhtar N, Rashid MM, Chowdhury AQ, et al. Patch test for the detection of contact allergens. *Mymensingh Med J* 2004;13:181-4.
114. Zhang XM, Niklasson B, Li SY. Patch testing in cases of eczema and dermatitis in Beijing. *Contact Dermatitis* 1991;53:224-5.
115. Wang XM, Lin YF, Cheng XF, et al. Patch testing with the European standard series in Shanghai. *Contact Dermatitis* 1994;30:173-4.
116. Lee TY, Lam TH. Patch testing in Hong Kong. *Contact Dermatitis* 1989;21:148-53.
117. Lee TY, Lam TH. Patch testing of 490 patients in Hong Kong. *Contact Dermatitis* 1996;35:23-6.
118. Fan WX, Zhao B. Study on Chinese common allergens of contact dermatitis. *Derm Beruf Umwelt* 1990;38:158-61.
119. Liu YQ, Zhao B, Zhuang LH, Fan WX. Patch test reactions to the Chinese standard screening allergens in 1,135 patients investigated for allergic contact dermatitis. *Am J Contact Dermat* 1997;8:141-3.
120. Lam WS, Chan LY, Ho SC, et al. A retrospective study of 2585 patients patch tested with the European standard series in Hong Kong (1995-99). *Int J Dermatol* 2008;47:128-33.
121. Li L-F, Guo J, Wang J. Environmental contact factors in eczema and the results of patch testing Chinese patients with a modified European standard series of allergens. *Contact Dermatitis* 2004;51:22-5.
122. Bajaj AK, Saraswat A, Mukhija G, et al. Patch testing experience with 1000 patients. *Indian J Dermatol Venereol Leprol* 2007;73:313-8.
123. Kashani MN, Gorouhi F, Behnia F, et al. Allergic contact dermatitis in Iran. *Contact Dermatitis* 2005;52:154-8.
124. Freireich-Astman M, David M, Trattner A. Standard patch test results in patients with contact dermatitis in Israel: age and sex differences. *Contact Dermatitis* 2007;56:103-7.

125. Lazarov A. European standard series patch test results from a contact dermatitis clinic in Israel during the 7-year period from 1998 to 2004. *Contact Dermatitis* 2006;55:73–6.
126. Fujiwara N, Sasaki M, Higashi N, et al. Standardization of patch tests in Japan. *Contact Dermatitis* 1976;2:205–11.
127. Hirano S, Kunihiro Y. Patch testing with European and American standard allergens in Japanese patients. *Contact Dermatitis* 1982;8: 48–50.
128. Adachi A. JSCD Research Group study. Results of patch tests with standard allergen series of the Research Group of the Japanese Society for Contact Dermatitis in 1994 and annual variations of patients with pigmented contact dermatitis of lichenoid type in 1993. *Environ Dermatol* 1996;3:140–50.
129. Natsuaki M. Results of patch testing with standard allergens of the Japanese Society for Contact Dermatitis and topical nonsteroidal anti-inflammatory preparations in 1998. *Environ Dermatol* 2000;7: 1–5.
130. Eun HC. [An epidemiological study of contact dermatitis (I).] *Kor J Dermatol* 1986;24:335–9.
131. Moon KC. [An epidemiological study of contact dermatitis in Korea (1986-1993).] *Kor J Dermatol* 1995;33:445–52.
132. Hussain I, Rani Z, Rashid T, Haroon TS. Suitability of the European standard series of patch test allergens in Pakistani patients. *Contact Dermatitis* 2002;46:50–1.
133. El-Rab MOG, Al-Sheikh OA. Is the European standard series suitable for patch testing in Riyadh, Saudi Arabia? *Contact Dermatitis* 1995;33:310–4.
134. Goh CL. Epidemiology of contact allergy in Singapore. *Int J Dermatol* 1988;27:308–11.
135. Lim JTE, Goh CL, Ng SK, Wong WK. Changing trends in the epidemiology of contact dermatitis in Singapore. *Contact Dermatitis* 1992;26:321–6.
136. Akasya-Hillenbrand E, Ozkaya-Bayazit E. Patch test results in 542 patients with suspected contact dermatitis in Turkey. *Contact Dermatitis* 2002;46:17–23.
137. Akyol A, Boyvat A, Peksari Y, Gurgey E. Contact sensitivity to standard series allergens in 1038 patients with contact dermatitis in Turkey. *Contact Dermatitis* 2005;52:333–7.
138. Frosch PJ, Burrows D, Camarasa JG, et al. Allergic reactions to hairdressers' series: results from 9 European centers. *Contact Dermatitis* 1993;28:180–3.
139. Hillen U, Grabbe S, Uter W. Patch test results in patients with scalp dermatitis: analysis of data of the Information Network of Departments of Dermatology. *Contact Dermatitis* 2007;56: 87–93.
140. Penchalaiah K, Handa S, Lakshmi SB, et al. Sensitizers commonly causing allergic contact dermatitis from cosmetics. *Contact Dermatitis* 2000;43:311–3.
141. Mehta SS, Reddy BSN. Pattern of cosmetic sensitivity in Indian patients. *Contact Dermatitis* 2001;45:292–3.
142. Tomar J, Jain VK, Aggarwal K, Gupta S. Contact allergies to cosmetics: testing with 52 cosmetic ingredients and personal products. *J Dermatol* 2005;32:951–5.
143. Kumar P, Paulose R. Cosmetic dermatitis in an Indian city. *Contact Dermatitis* 2006;55:114–5.
144. Antunes MA. Acute dermatitis after application of hair dyes. *Proceedings of the 4th Congress of the European Society of Contact Dermatitis*; 1998 July; Helsinki, Finland. p. 9.
145. Goh CL. Allergic contact dermatitis from cosmetics. *J Dermatol* 1987;14:248–52.
146. Mortz CG, Lauritsen JM, Bindslev-Jensen C, Andersen KE. Prevalence of atopic dermatitis, asthma, allergic rhinitis, and hand and contact dermatitis in adolescents. The Odense Adolescence Cohort Study on Atopic Diseases and Dermatitis. *Br J Dermatol* 2001;144:523–32.
147. Nielsen NH, Linneberg A, Menné T, et al. Allergic contact sensitisation in an adult population: two cross-sectional surveys eight years apart (the Copenhagen Allergy Study). *Acta Derm Venereol* 2001;81:31–4.
148. Seidenari S, Manzini BM, Danese P, Motolese A. Patch and prick test study of 593 healthy subjects. *Contact Dermatitis* 1990;23: 162–7.
149. Søstved H, Agner T, Andersen KE, Menné T. 55 cases of allergic reactions to hair dye: a descriptive, consumer complaint-based study. *Contact Dermatitis* 2002;47:299–303.
150. Søstved H, Hesse U, Menné T, et al. Contact dermatitis to hair dyes in a Danish adult population: an interview-based study. *Br J Dermatol* 2005;153:132–5.
151. Di Giovanni C, Arcoraci V, Gambardella L, Sautebin L. Cosmetovigilance survey: are cosmetics considered safe by consumers? *Pharmacol Res* 2006;53:16–21.