

Is PPD a useful screening agent?

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In this study, the usefulness was assessed of *para*-phenylenediamine (PPD) base as a marker for contact allergy to *para*-compounds and disperse dyes. 59 patients with a positive reaction to PPD were patch tested with a series of *para* compounds and disperse dyes. This dyes series was also tested in patients with a suspect medical history of contact allergy to hair, fabric or leather dyes. In total 610 patients were tested. As 24 patients became positive over the weekend, late readings, day 6 or 7, are important. These reactions were most probably relevant in 17/24 patients. Positive reactions to PPD correlated well with reactions to *para* compounds like *p*-aminoazobenzene and *p*-toluenediamine sulphate but not with disperse dyes. Reactions to Disperse Blue (106, 124) and Orange (1 and 3) were seen most frequently. PPD is a good screening agent for hair dye, but not for disperse dye, sensitivity.

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Azo dyes are a broad group of chemicals used in a variety of applications, for instance in hair dyes, foods, and the paper and textile industries (1, 2). Contact allergy to azo dyes is rather frequent (0.05–15.9%) and some authors state that the incidence is rising (3, 4). According to their broad spectrum of application, azo dye contact sensitization can show various clinical manifestations. Most frequently contact allergy to azo dyes is attributed to hair- and textile dyes. *para*-Phenylenediamine (PPD) base, being part of the European standard series, is regarded as screening agent for contact allergy to *para* and azo compounds. It is doubtful whether it is the best screening agent (1, 2, 5, 6). The first aim of this study was to assess the usefulness of PPD as a marker of contact allergy to *para* and azo compounds. We analysed the frequency of positive reactions to these compounds and to PPD. The second aim was to study the frequency of cross-reactivity between PPD and a series of azo and *para* compounds.

Materials and Methods

In this retrospective study, covering the period from January 1996 to December 1999, data of all patients patch tested in our clinic with the European standard series (Trolab Hermal, Reinbek, Germany) and showing a positive reaction to PPD were included. They were further tested if possible

with a series of *para* and azo dyes ($n = 59$; Table 1) (Chemotechnique, Malmö, Sweden). If the medical history indicated the possibility for contact allergy to *para* or azo dyes, e.g. in clothing and shoe dermatitis or dermatitis occurring after using a hair dye, patients were tested directly with the dyes series in addition to the standard series. Data of these patients ($n = 551$) are included as well.

Patch tests were performed according to internationally accepted guidelines, readings were done at day (D) 2, 3 and 6 or 7, and graded according to the ICDRG classification. All positive reactions were interpreted for relevance. Data of patients showing at least a + reaction to PPD and/or one of the compounds from the dyes series were included in this study.

The dyes series used in our clinic can be divided into 2 parts (Table 1), one part consisting of *para* compounds frequently used in hair dyes, the other part consisting of azo dyes, used mainly in the textile industry. Depending on the history and localization of the dermatitis, patients were tested with either part or with the whole series.

Results

During the years 1996–99, 2375 patients were tested with the European standard series, and in 71 (3%) a positive reaction to PPD was seen. 59

Table 1. Dyes (para and azo compounds) series used in our clinic. Positive reactions found in 1996–1999. A positive reaction to PPD as well as one of the para or azo compounds was seen in 31 patients, these data being shown for each compound

Compound	Number of positive reactions	PPD +
<i>Para</i> compounds (tested in 154 patients and were positive in 41 patients, with a total of 53 positive reactions)		
<i>p</i> -Aminoazobenzene	23	20
<i>p</i> -Toluenediamine sulphate	15	14
<i>p</i> -Aminophenol	5	4
<i>o</i> -Nitro- <i>p</i> -phenylenediamine	5	4
<i>p</i> -Aminodiphenylamine	4	3
Resorcinol	1	0
Disperse (azo)dyes (tested in 577 patients and positive in 79 patients, with a total of 156 positive reactions)		
Disperse Blue 106	34	1
Disperse Blue 124	29	1
Disperse Orange 3	29	21
Disperse Orange 1	19	5
Disperse Brown 1	8	3
Disperse Yellow 3	8	2
Disperse Blue 35	7	1
Disperse Red 1	7	2
Disperse Blue 153	3	1
Disperse Orange 13	3	0
Disperse Red 17	3	0
Disperse Yellow 9	3	1
Disperse Blue 85	2	0
Disperse Blue 3	1	0

of these patients were further tested with the *para* compounds, 31 (53%) showing a positive reaction to 1 or more of these compounds. In total, 610 patients were tested with the *para* and azo dyes series: 121 patients were tested with the whole series, whereas 33 patients were only tested with the *para* dyes and 456 with the azo dyes of this series. The number of positive reactions to this dyes series is listed in Table 1. Table 1 also shows the concurrence of a positive reaction to PPD and 1 of the compounds of the *para* series. There is a relation between a positive reaction of PPD and *para* dyes but not with azo dyes.

The relevance of positive reactions was interpreted based on the medical history (Table 2). Also listed are the products involved. A rather high percentage (75%) of these patch test reactions were (probably) relevant. Compounds that showed a positive reaction on D6 or D7, while being negative at D2 and D3, are listed in Table 3, as well as

the relevance of these reactions. 10% of the total reactions to the *para* dyes were late reactions; this was 17% for azo dyes.

Discussion

The study population was selected in 2 ways: patients giving a positive patch test reaction to PPD or a positive reaction to 1 of the compounds of our dyes series. The majority of all reactions found (75%) were thought to be relevant, based on exposure, localization of the dermatitis and the medical history (Table 2). In contrast to Devos & van der Valk, we found no higher rate of irrelevant reactions on D7 (2). On the contrary, in more than 10% of the cases we found reactions on D7 only and nearly all (20/24) of these were relevant. No reactions were reported to us occurring after D7, from which is tempting to conclude that there was no active sensitization (7, 8).

As all patients were tested with PPD, it is possible to look for a possible correlation between a positive reaction to PPD and a reaction to 1 of the compounds of the dyes series. Table 1 shows that there is a good correlation between PPD and *para* compounds, especially *p*-aminobenzene and *p*-toluenediamine sulphate, but not with disperse dyes. These data are consistent with publications by Cronin and Seidenari et al. (1, 5). This makes PPD a good screening agent for contact allergy to hair dyes. A striking point in Table 2 is the almost 2× higher frequency of contact allergy to *para* compounds used in hair dyes in clients compared to

Table 2. Interpretation of the relevance of positive reactions to PPD and/or compounds of the dyes series in 130 patients. About 75% of the reactions were (probably) relevant

Causative agent	<i>n</i> = 130
Relevant (probably)	98 (75%)
Hair dye (in consumers)	17
Hair dye (in hair dressers)	9
Textile	31
Shoes	34
Cosmetics	1
Various	6
Not/doubtful relevant	32 (25%)

Table 3. Positive reactions on D6 or D7 while negative at D2 and D3 (total positive reactions between brackets) and the interpretation of these reactions

Compound	Number of positive reactions on D 6/7	Relevant	Probably relevant	Doubtful/not relevant
<i>p</i> -Toluenediamine sulphate	2 (15)	2		
<i>p</i> -Aminoazobenzene	1 (23)			1
<i>p</i> -Aminodiphenylamine	1 (4)	1		
<i>p</i> -Aminophenol	1 (5)	1		
Total	5 (47) = 10%	4		1
Disperse Blue 124	7 (29)	6	1	
Disperse Blue 106	6 (34)	5	1	
Disperse Orange 3	3 (29)	2	1	
Disperse Blue 35	1 (7)	1		
Disperse Blue 85	1 (2)	1		
Disperse Red 1	1 (7)	1		
Total	19 (108) = 17%	16	3	

hairdressers. This fact, which is inconsistent with data found by Frosch et al. might be due to better awareness in hairdressers, leading to precautions taken when handling hair dyes (9–11). We can not prove this as we see relatively few hairdressers in our clinic. In the Netherlands, many hairdressers with skin complaints visit a special hairdressers' clinic. Worth mentioning was a patient (Table 2, various) who developed dermatitis following a temporary tattoo, caused by PPD. Various authors have previously described this phenomenon, and with the popularity of these tattoos still rising, one should be aware of this source of contact dermatitis (12).

The disperse dyes show less structural similarity to PPD than *para* compounds do, their structures being more complex. However, metabolic activation taking place in the skin may lead to the formation of unstable and reactive intermediates, oxidation products or radicals, similar to what happens with PPD (1). This could be the reason that the azo compound with the formula closest to PPD, Disperse Orange 3, shows the best correlation to PPD. The correlation between positive reactions to PPD and the other azo dyes is weak. So PPD is not a good screening agent for contact allergy to disperse dyes (1, 3, 5, 13, 14).

Table 1 shows that contact allergies to most of the disperse dyes were relatively seldom seen apart from Disperse Blue 106 and 124, and Disperse Orange 1 and 3; these findings are in line with the literature. Several authors have proposed for the use of Disperse Blue 106 and 124 as screening agents, either as a mix or separately (1, 3, 4, 6). In Italy, Disperse Blue 124, Orange 3, Red 1 and Yellow 3 have been part of the standard series (1). In Portugal testing has been carried out – with satisfactory results – with a stable mix composed of Disperse Blue 35, 106 and 124, and a mix composed of Disperse Orange 1 and 3, Disperse Yellow

3 and Disperse Red 1 and 7 (6, 14). The incidence of contact allergies to Disperse Blue 35, Disperse Yellow 3 and 9 and Red 1 and 17 is, at least in our series, much lower than to Disperse Blue 106 and 124, and Disperse Orange 1 and 3.

From this study, we conclude that testing with the European standard series is usually sufficient for detecting contact allergy to hair dyes, but not for textile and leather dye allergy. Therefore, we suggest adding the most frequently positive disperse dyes to an additional series. Which dyes would best be used is not yet fully clear. Tests with a series of *para* and azo dyes is a useful instrument in preselected populations. Late readings are recommended.

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