

Multiple azo disperse dye sensitization mainly due to group sensitizations to azo dyes

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A female patient, with a previous episode of contact dermatitis caused by a blue dress, developed similar dermatitis due to a navy-blue dress. Patch tests revealed multiple allergic positive reactions to paraphenylenediamine (PPD), the navy-blue dress, its extracts, 6 azo disperse dyes in a textile series, as well as 3 dye components, including Disperse (DP) Red 153, which were present in the dress; these were composed of 9 azo disperse dyes, all dyes being of a different chemical structure. On the basis of chemical similarities between these 16 azo dyes including PPD, these are classified into the following 4 groups: thiazol-azo-PPD group (including DP Blue 106, DP Blue 124 and 5 used dyes), aminoazobenzene group (DP Red 1, DP Red 17, DP Brown 1 and 2 used dyes), PPD group (PPD and DP Orange 3) and benzothiazol-azo-PPD group (2 dyes in DP Red 153). With few exceptions, cross-sensitizations between dyes in the same group have been reported by other authors, or are suggested by us, in the former 3 groups. Multiple azo disperse dye sensitization is therefore considered to be attributable mainly to group sensitizations to azo dyes.

Key words: textile contact dermatitis; azo disperse dye; Disperse Red 153; patch testing; multiple azo dye sensitization; group sensitization; cross-sensitivity © Munksgaard, 1996.

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Over a period of 50 years, a great number of different synthetic dyes have been introduced into the textile industry. Despite their large number, only a few have been reported as causing contact sensitization.

Recent studies (1-3) on textile dermatitis demonstrated that the frequency of allergic sensitization to textile dyes is underestimated and more individuals probably acquire contact sensitivity to them than is generally thought. Considered from the viewpoint of these studies and the number of synthetic dyes introduced, it seems likely that many individuals are sensitized to unknown dye allergens, particularly disperse dyes of the azo or anthraquinone type, which are the most frequent dye sensitizers and can cause group sensitizations (4, 5).

However, in tracing such dye allergens, particularly new dyes continuously introduced into the textile industry, there are several difficulties (6-13). Even if a textile dye is found to be positive, precise identification of the responsible sensitizers in the dye is extremely difficult, as dyes frequently have a secret chemical composition, and isolation and

identification of dyes is difficult and time consuming (7).

Recently, we observed a patient, with multiple azo dye sensitization, demonstrating contact allergy to azo disperse dyes in a dress. The present study is aimed to find both the possible cross-sensitivity between disperse dyes, either in responsible dye components in the dress or well-known as textile dye allergens, and the most responsible factor inducing multiple azo dye sensitization.

Case Report

A 62-year-old housewife, with no personal or family atopic history, consulted us in January 1992 because of an itchy erythematous oedematous rash on her neck and both forearms. This had appeared within a day of wearing a new navy-blue 2-piece dress made of 100% polyester for 7 h. The areas protected by underclothing or the lining of the skirt of the dress were not involved. She had a previous similar episode after wearing an unwashed new blue 2-piece dress made of 100% polyester: 3 years before, she had developed a dermatitis local-

Table 1. Patch test results with standard and textile series

Test materials		1st test		2nd test	
		D2	D3	D2	D3
nickel sulphate	2.5% pet.	—	+	+	++
cobalt chloride	1% pet.	—	+	+	++
Disperse Red 1	1% pet.	—	+	++	++
Disperse Red 17	1% pet.	—	+	++	++
Disperse Brown 1	1% pet.	—	+	++	++
Disperse Orange 3	1% pet.	—	+	+	+
Disperse Orange 13	1% pet.	—	+	?+	—
benzotriazole	1% pet.	—	+	—	—
dimethylolpropylene urea	5% pet.	?+	+	—	—
formaldehyde	1% aq.	—	?+	—	—
black rubber mix	0.6% pet.	—	?+	—	—
hydroxycitronellal	1% pet.	NT	NT	?+	?+
fragrance mix	8% pet.	+	+	NT	NT
paraphenylenediamine	1% pet.	++	++	NT	NT
Disperse Blue 106	1% pet.	++	++	NT	NT
Disperse Blue 124	1% pet.	++	++	NT	NT
Disperse Blue 3	1% pet.	—	—	NT	NT
Disperse Blue 85	1% pet.	—	—	NT	NT
Disperse Red 35	1% pet.	—	—	NT	NT
Disperse Yellow 3	1% pet.	—	—	NT	NT
Acid Yellow 36	1% pet.	—	—	NT	NT
Basic red 46	1% pet.	—	—	NT	NT
mercapto mix	2% pet.	—	—	NT	NT
rest of the standard series		—	—	NT	NT
rest of the textile series		—	—	NT	NT
residual fragrance substitutes		NT	NT	—	—

NT: not tested.

ized to areas similar to those of the current presentation after occasional wearing over a period of 5 months. She had also been intolerant both to metal accessories for over 10 years and to oxidation hair dyes for approximately 5 years. As contact dermatitis due to the navy-blue dress was mostly suspected, patch tests were applied for 2 days with Finn Chambers[®] on Scanpor tape[®], readings being made at D2 and D3 following ICDRG guidelines.

First, patch testing with a standard series and a textile series showed ++ reactions to paraphenylenediamine (PPD), Disperse (DP) Blue 106 and DP Blue 124, + to 9 test materials, and ?+ to 2 (Table 1). In order to minimize the possibility of excited skin syndrome, we retested with the 11 materials giving a + or ?+ reaction, except for fragrance mix (Trolab) which showed a + reaction, 8 months after clearance of the dermatitis. Instead of the fragrance mix, its constituents, each at 1% concentration, were applied. On further testing (Table 1), nickel sulfate, cobalt chloride, DP Red 1, DP Red 17, DP Brown 1 and DP Orange 3 reproduced positive results, but the other 5 materials retested were negative.

The navy-blue dress was cut in 2 cm² pieces, each 2 pieces were soaked in water, ethanol and acetone, each approximately 5 ml, for 30 min before the first patch testing without evaporation of

the vehicles. The acetone extract was rapidly incorporated into water at 25% concentration.

The patient showed positive patch test reactions to a piece of the dress and all 3 of its extracts (Table 2).

A textile mill manufacturer informed us that this dress was dyed with 5 different azo disperse dye components, 2 blue, 1 red, 1 yellow and 1 golden-yellow in colour; these 5 dyes had different brand names and were made by 4 different dye manufacturers; one of the blues, a liquid dye, was made in Germany and the other 4 components, powder dyes, were made in Japan. The manufacturer provided these 5 dyes but did not inform us of the proportion of each component in the dress. Since all 5 components were soluble in water and not dispersible in pet., possibly due to the presence of

Table 2. Patch test results with the navy-blue dress, its extracts and vehicles

Test materials		D2	D3
navy-blue dress	as is	++	++
water extract	as is	++	++
ethanol extract	as is	++	++
acetone extract	25% aq.	+	++
water	as is	—	—
ethanol	as is	—	—
acetone	25% aq.	—	—

Table 3. Patch test results with dye components in the dress.

Test materials		D2	D3
blue component made in Japan	1% aq.	++	++
blue component made in Japan	0.1% aq.	++	++
blue component made in Germany	1% aq.	++	++
blue component made in Germany	0.1% aq.	++	++
red component	1% aq.	++	++
golden-yellow component	1% aq.	+	+
yellow component	1% aq.	?+	?+
water	as is	?+	?+

petrolatum-indispersable agents in these components, they were incorporated in water, each at 1% concentration, for further patch testing. The 2 blue components, suspected most as offending agents, were also applied at 0.1% aq. for this test. Patch test results are shown in Table 3.

She showed ++ reactions to the 2 blue and the red component, and a + reaction to the golden-yellow component.

Patch testing with these 5 components (1% aq.) in 20 controls was negative, except for 2 subjects positive (+) to the golden-yellow.

Based on these patch test results, the 2 blue and the red component were considered to be the offending agents.

The red dye was DP Red 153 but both blue dyes had no Colour Index (CI) number. DP Red 153 and the blue powder component were made by the same dye manufacturer, who provided the following information on the chemical structures of these 2 dye components.

- DP Red 153 (Fig. 1) was based on 2 different benzothiazol-azo-PPD derivatives (Red dye A and B), the proportion of each being unknown.

- The blue dye component (Fig. 2) was based on 2 different thiazol-azo-PPD derivatives (Blue dye A and B), at 60% and 40% concentration, respectively. Both substitutes (X1 and X2) of the amino group were cloaked in secrecy by the manufacturer.

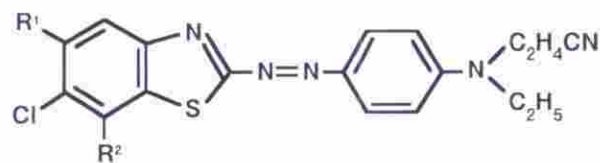
Another blue component was analyzed by the manufacturer using thin-layer chromatography and mass spectrometry. The manufacturer provided the following information on the chemical structures of these 5 dyes.

- Of these 5, one had a CI number, which was unknown because of the manufacturer's secrecy.

- 3 dyes were different thiazol-azo-PPD derivatives (Fig. 2): 2 blues (Blue dye C and D) and 1 violet in colour, with an approximate concentration of 50%, 30% and 10%, respectively.

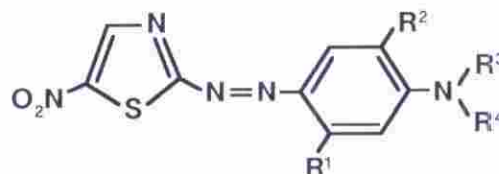
- Residual 2 dyes (Fig. 3) were different aminoazobenzene derivatives used as shading components: an orange and a blue (Blue dye E), both with an approximate 5% concentration.

The substitutions (X3-8 and Y1-4) of amino groups in these 5 dyes were also concealed by the manufacturer.



Disperse dyes	R ¹	R ²
Red dye A	Cl	H
Red dye B	H	Cl

Fig. 1. Chemical structures of azo disperse dyes in Disperse Red 153.



Disperse dyes	R ¹	R ²	R ³	R ⁴
Disperse Blue 106	CH ₃	H	C ₂ H ₅	C ₂ H ₄ OH
Disperse Blue 124	CH ₃	H	C ₂ H ₅	C ₂ H ₄ OC(OCH ₃)
Blue dye A*	NHCOCH ₃	OCH ₃	X1***	X1***
Blue dye B*	Cl	H	X2***	X2***
Blue dye C**	CH ₃	H	X3***	X4***
Blue dye D**	NHCOCH ₃	OCH ₃	X5***	X6***
Violet dye**	CH ₃	H	X7***	X8***

* present in blue powder dye component made in Japan.

** present in blue liquid dye component made in Germany.

*** unknown.

Fig. 2. Chemical structures of disperse dyes in thiazol-azo-PPD derivatives.



Disperse dyes	R ¹	R ²	R ³	R ⁴	R ⁵
Disperse Red 1	H	H	H	C ₂ H ₅	C ₂ H ₄ OH
Disperse Red 17	H	H	H	C ₂ H ₄ OH	C ₂ H ₄ OH
Disperse Orange 3	H	H	H	H	H
Orange dye*	H	H	H	Y1**	Y2**
Disperse Brown 1	Cl	Cl	Cl	C ₂ H ₄ OH	C ₂ H ₄ OH
Blue dye E*	CN	Br	NHCOCH ₃	Y3**	Y4**

* present in blue liquid dye component made in Germany.

** unknown.

Fig. 3. Chemical structures of disperse dyes in aminoazobenzene group.

There has been no further relapse after both discontinuing to wear the navy-blue dress and avoidance of direct contact with synthetic fabrics, particularly polyester and nylon, which are frequently dyed with disperse dyes (4, 5).

Discussion

It is difficult to be certain of cause and effect in patients with multiple reactions to several allergens, because several factors responsible for such reactions have to be considered (14–17): excited skin syndrome, concomitant allergy, and cross-reaction between allergens of similar chemical structure. As our patient showed multiple positive reactions to several substances tested at the first patch testing, to minimize the possibility of excited skin syndrome, we retested with 9 substances showing a + reaction, and 6 of them reproduced positive reactions, thus minimizing the possibility.

The 9 positive responses, including 3 showing a ++ reaction at the first patch testing, are considered to be exhibited either due to concomitant allergy or cross-sensitivity. In relation to her previous history, the positive reactions to nickel sulfate and cobalt chloride could be attributed to her intolerance to metal accessories, and PPD to oxidation hair dyes.

Although a few substituents of 2 dye components (Fig. 2, 3) were concealed by the manufacturer, this seems to have little influence on considering cross-sensitivity, because of the chemical similarity between these dyes and dye allergens to which the patient reacted. On the basis of chemical similarity between 16 azo dyes, either in the responsible compounds in the dress or well-known as textile dye allergens, to which the patient was sensitive, these dyes can be classified into the following 4 groups: thiazol-azo-PPD, aminoazobenzene, PPD and benzothiazol-azo-PPD. Although we could not carry out patch testing with each of the dyes in the dress, considering the close chemical relation between the azo dyes in the same group, the following group sensitizations are suggested.

Cross-sensitivity between disperse dyes belonging to thiazol-azo-PPD (TAP) group (Fig. 2)

DP Blue 106 and DP Blue 124 are classified in this group, the former being a strong sensitizer (18, 19), the latter being one of the most frequent textile sensitizers (2, 8, 11, 20). Both dyes are chemically closely related, the only differences being the presence or absence of an acetate group (19). Constant cross-reactivity between both dyes has been reported (13, 21). As the 5 dyes (Blue dyes A–D and

Violet) in the navy blue dress are chemically closely related to both dyes, with differences in substituents in the benzene ring, or in the amino group, all or most of them seem to be able to cross-react with both dyes. Thus, the patch test response to both dyes could be attributable to group sensitization to disperse dyes belonging to this group.

Considered under structure-activity aspects in TAP derivatives, it seems that on cleavage at the azo bridge, these can be degraded into nitro-thiazol derivatives and PPD derivatives (19). It has been reported that none of patients allergic to DP Blue 124 react to PPD (21). In addition to this, in our previous patch tests in another 12 patients with primary sensitization to PPD and no history of textile dermatitis, all were negative to DP Blue 106 and DP Blue 124, with the exception of a female patient who had multiple patch test reactions with no relation to her previous history. In these patients, there was no apparent cross-sensitization from PPD to both blue dyes.

These TAP derivatives have 1 or 2 substituents in the 3 or 6 positions of a benzene ring, and 2 substituents of the amino groups, and the latter seem not to be further easily reduced to NH_2 . Moreover, it can be considered that the introduction of these substituents is responsible for further decrease in sensitizing potency, and gradual loss of cross-sensitizing potential between PPD derivatives.

From these findings, it is suggested that the thiazol group contributes greatly to the allergenicity of dyes belonging to the TAP group, in accordance with the findings of Hausen & Menezes (19).

Cross-sensitivity between disperse dyes belonging to aminoazobenzene group, and between PPD and DP Orange 3

DP Red 1 and DP Red 17, DP Orange 3 and the 2 dyes in the navy blue dress belong to this group (Fig. 3). Cross-sensitivity between DP Red 1 and DP Red 17, and between DP Red 1 and DP Orange 3, has been reported (17), and the former 2 are chemically closely related to the orange dye present in the dress and probably differ from this only in the substituents of the amino groups. Therefore, the orange dye seems most likely to cross-react with both dyes. The positive reaction to DP Brown 1 may be due to group allergy to disperse dyes in this group. Moreover, the residual blue dye (Blue dye E) may cross-react with these dyes, unless the substituents (CN, Br, NHCOCH_3 , Y3 and Y4) of both dyes on both benzene rings or of amino groups lose or extremely decrease their cross-sensitizing potential. However, we have no evidence to suggest these cross-sensitizations.

Because DP Orange 3 is degraded into PPD and nitroaniline derivatives in the skin (5), it can cross-react with both derivatives. In our previous study, positive reactions to DP Orange 3 were observed only in 14 out of 17 patients primarily sensitized by PPD and with no history of textile dermatitis; these 14 patients and patients with suspected textile dermatitis did not show any obvious allergic response to any other disperse dyes, including DP Red 1 and DP Red 17, except for a female subject with PPD allergy who reacted to DP Yellow 3, with suspected relation to her previous history of textile dermatitis. In our patients patch tested, there were cross-sensitizations only from PPD to DP Orange 3, in agreement with Shehade & Beck (22). The positive reaction to DP Orange 3 in this case is therefore attributable to cross-sensitivity with PPD, rather than with DP Red 1 and/or DP Red 17. PPD is quite unreliable as a screening agent for textile dye dermatitis in Japan, similar to several investigators experiences in other countries (8–11, 13).

2 benzothiazol-azo-PPD (BTAP) derivatives in DP Red 153 (Fig. 1) differ only in position of chloride on the benzothiazol ring, so would cross-react with each other. There has been no case report of textile dye dermatitis due to BTAP derivatives, as far as we know. Although mercapto mix in the standard series contains 4 benzothiazyl compounds possessing a more-or-less distinct sensitizing potency, each at 0.5% concentration, it failed to demonstrate cross-sensitivity with DP Red 153 (Table 1). Although the possibility of cross-sensitivity between TAP derivatives and BTAP derivatives is also considered, there is, in our study on textile dermatitis, no evidence to support this.

Apart from cross-sensitivity between the BTAP derivatives, with few exceptions, cross-sensitizations between the dyes in the same group have been reported by other authors or are suggested in this study. The multiple azo disperse dye sensitization is thus considered to be mainly multiple azo disperse dye sensitization, and hence mainly due to group sensitizations to azo dyes.

Since the onset of the recent dermatitis caused by the new navy blue dress appeared within a day of wearing, the patient might have previously been sensitized to the same or other dyes in the blue dress, and could cross-react with dyes in the navy-blue dress.

Despite a number of disperse azo dyes to which this patient was sensitive, the patient did not react to the dyes of non-azo type or non-disperse type. Furthermore, it is noted that the 9 disperse dyes of the 3 dye components with a positive result were not included in the group of well-known dye allergens tested, but were similar to the dye allergens

with + or ++ positive results, with the exceptions of the 2 dyes in DP Red 153.

By cooperation with the textile manufacturers, the offending dyes in the dress were identified. This might enable the manufacturers to improve their knowledge of which dyes are related to consumer problems, which might then lead to improvement in industrial procedures.

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