

# Contact allergy to Disperse Blue 106 and Disperse Blue 124 in German and Austrian patients, 1995 to 1999

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Between 1995 and 1999, 1986 patients were tested in the 31 participating centres of the Information Network of Departments of Dermatology (IVDK), all of them members of the German Contact Dermatitis Research Group, with a textile dyes series containing Disperse Blue (DB) 106 and 124, and since 1997 also with a mix of both. 86 patients (4.3%) reacted positively to DB 106 and/or DB 124; with good concordance between the 2 allergens (Cohen's weighted kappa 0.72), and the single allergens and the mix ( $\kappa=0.75$  in both cases), which had been tested in parallel in 969 and 975 patients, respectively. In contrast, concordance between DB 106/124 and p-phenylenediamine and p-aminoazobenzene, respectively, was poor. Some 70% of positive reactions to DB 106/124 had current clinical relevance. Furthermore, a significant increase in the proportion of DB 106/124-positive patients among those tested was found from 1995 to 1999. Hence, DB 106/124 are important allergens deserving close monitoring. The use of a mix of DB 106 and DB 124 seems justified in view of the close chemical similarity of both compounds. If possible, the presence of the allergen(s) in individual textiles considered causative should be checked by thin layer or column chromatography.

**Key words:** contact allergy; Disperse Blue 106/124; textile dye dermatitis; clinical epidemiology; cross reactivity; p-phenylenediamine; p-aminoazobenzene; clothing; occupational; shoes.  
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Textile dermatitis due to contact allergy to the thiazol-substituted monoazo dyes Disperse Blue (DB) 106 and DB 124 – which are only 2 of an ever-increasing multitude of dyes used in textiles – is a

problem that has been recognized for somewhat less than 2 decades (1–4). Interestingly, the proportions of patch test patients sensitized to DB 106 or DB 124 seem to be particularly high in southern European countries, like Portugal (2) and Italy (5, 6), and also in Israel (7), while in central or northern European countries, like Belgium, DB 106 or DB 124 allergy has so far been diagnosed only occasionally (8). Only recently has awareness concerning these contact allergens increased (9), and, based partly on a current large case series from Canada (10), “disperse blue dyes” were even elected as “contact allergen(s) of the year” for 2000 (11).

Would DB 106 and DB 124 have also qualified for this award from a central European perspective, i.e., is the prevalence of sensitization sufficiently noteworthy, and possibly increasing? To answer this question, the present analysis of multi-

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centre surveillance data of the IVDK was performed, addressing also the issue of cross-reactivity and discussing chemical aspects.

### Materials and Methods

Disperse Blue (DB) 106 and 124 (both 1% pet.) have been tested in a textile dyes series by members of the German Contact Dermatitis Research Group (DKG) between January 1995 and June 1999. These allergens were obtained from Chemotechnique Diagnostics AB, Malmö, Sweden. Their chemical structure is given in Fig. 1. From January 1997 onwards, a mix of DB 106 and 124, 1% pet., obtained from Hermal/Trolab, Reinbek, FRG, has been tested additionally, and has been tested instead of the 2 single allergens since June 1999. During the whole period, p-phenylenediamine (1% pet., Hermal/Trolab, Reinbek, FRG), included in the standard series, and p-aminoazobenzene (1% pet., Hermal/Trolab, Reinbek, FRG), contained in 2 auxiliary series, were also used for patch testing.

In the centres of the Information Network of Departments of Dermatology (IVDK) listed above, as members of the DKG at the same time, both patch test results and a short standardized history are regularly collected and transferred to the Göttingen data centre (<http://www.ivdk.gwdg.de>) for pooled analysis (12). Proportions of sensitizations were calculated based on the day (D) 3 (72 h) readings. Readings followed ICDRG guidelines with slight amendments by the DKG (13).

In addition to descriptive statistical analyses, agreement beyond chance was quantified with Cohen's weighted kappa coefficient for the original 5×5 tables, accompanied by the respective 95% confidence interval (CI). The five categories of this

ordinal scale comprised – in ascending order – “neg.”, “?” (erythematous), “+”, “++” and “+++” reactions, see (Table 2). For data management and analysis, the statistical software package SAS 6.12 (SAS Institute, Cary, NC) was employed.

### Results

Between January 1995 and December 1999, 49493 patients altogether were patch tested in the participating centres of the IVDK. Of these, 1986 were tested with the textile dyes series. Due to the changes mentioned above, and temporary unavailability of the allergens, 1847 and 1829 patients were tested with DB 106 and 124, respectively, and 1108 with the mix. As a consequence of approximately 2.5 years overlap, 975 and 969 patients, respectively, had been tested both with the single dyes and the mix.

Test reactions to the 3 test preparations analysed here are shown in Table 1. The proportion of positive reactions always exceeds the percentage of questionable reactions, resulting in a positive “reaction index” (14). Frank irritant reactions were not observed. Current clinical relevance of positive reactions was found in around 70% of cases for all 3 test preparations, while past or occupational relevance was documented much less often. As far as this was detailed, clothing objects were identified as culprits most often, namely blue to black T-shirts, blouses, costumes, trousers, socks and underwear. In 1 case, a pair of dark blue shoes had apparently caused acute allergic contact dermatitis of the feet.

The joint distribution of reactions to DB 106 and DB 124 is shown in Table 2. Agreement as quantified with the weighted kappa coefficient was high ( $\kappa$ -value: 0.72, 95% CI: 0.64–0.79). The parallel testing of DB 106 and DB 124 with the mix containing both compounds enabled a comparison of reactivity; the results are shown in Table 3 as collapsed 2×2 tables, aggregating positive (+, ++ and +++) and non-positive (neg., ?) results. For the original 5×5 quadratic contingency table, agreement between the mix and DB 106 and DB 124, respectively, was measured with Cohen's  $\kappa$ ; the  $\kappa$ -value was 0.75, 95% CI 0.67–0.84 in both cases, indicating good agreement. The diagnostic performance of the mix, referring to the 2 single substances as the “gold standard”, is shown in Table 3.

Altogether, 1832 patients were patch tested with any one of the DB preparations and p-phenylenediamine (PPD), and 647 with p-aminoazobenzene. Concordance was weak in both cases (Table 4).

To assess a possible time trend in DB reactivity, the proportions of patients found to be sensitized

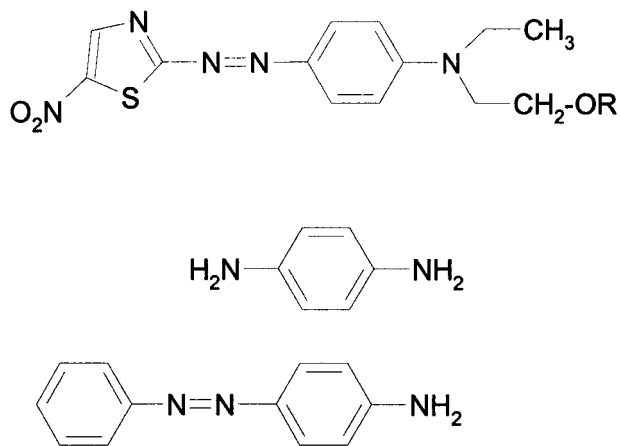


Fig. 1. Chemical structures of Disperse Blue 106 (R=H) and 124 (R=-COCH<sub>3</sub>) (top), p-phenylenediamine (centre) and p-aminoazobenzene (bottom).

Table 1. Reactions to Disperse Blue 106, 124 and a mix of the 2 substances, tested in 32 German and Austrian patch test clinics between 1995 and 1999

| Allergen                          | N (test) | n (%)    |          |          |         | RI  |
|-----------------------------------|----------|----------|----------|----------|---------|-----|
|                                   |          | ?        | +        | ++       | +++     |     |
| Disperse Blue 106 1.0% pet.       | 1847     | 34 (1.8) | 44 (2.4) | 12 (0.6) | 8 (0.4) | 0.3 |
| Disperse Blue 124 1.0% pet.       | 1829     | 39 (2.1) | 33 (1.8) | 14 (0.8) | 8 (0.4) | 0.2 |
| Disperse Blue 106 & 124 1.0% pet. | 1108     | 29 (2.6) | 32 (2.9) | 11 (1.0) | 9 (0.8) | 0.3 |

?: erythematous reaction. +: erythema, infiltration, possibly papules. ++: erythema, infiltration, papulovesicles “+++” erythema, infiltration, confluent papulovesicles (13). RI=reaction index (14).

Table 2. Pattern of concomitant reactivity to Disperse Blue 106 and 124 in patients tested with the textile dyes series

| DB 106          | DB 124 |    |    |    |     | sums for DB 106 |
|-----------------|--------|----|----|----|-----|-----------------|
|                 | neg.   | ?  | +  | ++ | +++ |                 |
| neg.            | 1689   | 24 | 6  | 2  | 0   | 1721            |
| ?               | 20     | 15 | 0  | 0  | 0   | 35              |
| +               | 17     | 1  | 25 | 1  | 0   | 44              |
| ++              | 0      | 0  | 1  | 10 | 1   | 12              |
| +++             | 0      | 0  | 0  | 1  | 7   | 8               |
| Sums for DB 124 | 1726   | 40 | 32 | 14 | 8   | 1820            |

For explanation of symbols see Table 1.

Table 3. Concomitant reactivity between Disperse Blue 106 and 124 single and the DB 106 & 124 mix; measures of diagnostic performance refer to the ability of the mix to “diagnose” contact allergy to DB 106 and 124, respectively, and are accompanied by exact 95% confidence intervals

|                           |      | DB 106           |      | DB 124           |      |
|---------------------------|------|------------------|------|------------------|------|
|                           |      | pos.             | neg. | pos.             | neg. |
| DB 106 & 124 mix          | pos. | 37               | 8    | 32               | 13   |
|                           | neg. | 9                | 921  | 5                | 919  |
| sensitivity               |      | 80.4 (66.1–90.6) |      | 86.5 (71.2–95.5) |      |
| specificity               |      | 99.1 (98.3–99.6) |      | 98.6 (97.6–99.3) |      |
| positive predictive value |      | 82.2 (67.9–92.0) |      | 71.1 (55.7–83.6) |      |
| negative predictive value |      | 99.0 (98.2–99.6) |      | 99.5 (98.7–99.8) |      |

Table 4. Cross-reactivity between Disperse Blue 106 or 124 and p-aminoazobenzene (PAAB) and p-phenylenediamine (PPD), respectively

|                          |      | PAAB                   |      | PPD                    |      |
|--------------------------|------|------------------------|------|------------------------|------|
|                          |      | pos.                   | neg. | pos.                   | neg. |
| DB 106 or 124            | pos. | 11                     | 15   | 12                     | 69   |
|                          | neg. | 62                     | 559  | 98                     | 1653 |
| $\kappa$ value (95 % CI) |      | 0.173<br>(0.056–0.283) |      | 0.079<br>(0.012–0.145) |      |

Table 5. Time course of reactivity to either DB 106 or DB 124 or the mix (“DB pos.”)

| Year   | N       |           |              | (%)                     |                           |                     |
|--------|---------|-----------|--------------|-------------------------|---------------------------|---------------------|
|        | DB pos. | DB tested | total tested | DB pos. of total tested | DB tested of total tested | DB pos of DB tested |
| 1995   | 4       | 359       | 10,153       | 0.04                    | 3.54                      | 1.11                |
| 1996   | 12      | 378       | 10,023       | 0.12                    | 3.77                      | 3.17                |
| 1997   | 17      | 449       | 10,008       | 0.17                    | 4.49                      | 3.79                |
| 1998   | 25      | 381       | 9877         | 0.25                    | 3.86                      | 6.56                |
| 1999   | 28      | 419       | 9432         | 0.30                    | 4.44                      | 6.68                |
| total: | 86      | 1986      | 49493        | 0.17                    | 4.01                      | 4.33                |

were calculated for each year of the period considered (Table 5). Using the Cochran-Armitage Trend Test (2-sided), a significant increase in the proportion of patients sensitized to DB was found ( $p < 0.001$ ).

The MOAHLFA index (15) in the subgroups of patients either reacting to DB 106 or DB 124 or the mix ( $N=86$ ) was as follows (with the proportions found in the whole group given in parentheses): 18.5% (35.4%) males, 14.8% (14.6%) with occupational dermatitis, 18.5% (17.9%) with atopic dermatitis, 25.0% (28.1%) with hand, 12.0% (8.5%) with leg and 4.6% (14.8%) with face dermatitis, and 60.2% (57.9%) age 40 and above. Thus, female patients and patients with leg dermatitis were slightly over-represented. Conversely, patients with face dermatitis were markedly under-represented ( $p=0.007$ ,  $\chi^2$  test). Interestingly, dermatitis in 43 of the 86 patients involved the trunk and/or proximal extremities. The final diagnosis was allergic contact dermatitis in 70% – in accordance with current clinical relevance of DB reactions found in the majority of cases, see above – while for the whole test population this percentage was 30%.

### Discussion

National surveillance data analysed here emphasise that DB 106 and 124 are indeed important allergens, because they caused clinically relevant positive test reactions in a considerable number of patients and a definite time trend, i.e., an increase in the proportion of sensitized patients among those tested, can be observed. Thus, to answer the introductory question, these textile dyes surely call for close monitoring. While only 4% of our patients have been tested with DB 106/124 (with 4.3% positive reactions among these, corresponding to 0.2% of all 49493 patients tested), a much larger proportion of all consecutively tested patients (34.4%) were exposed to these dyes by Pratt and Taraska, who found 11.8% positive reactions to either DB 106 or 124 in this subgroup, corresponding to 4.1% of all patients tested (10). After adding DB 124 to the standard series, Seidenari et al. detected 104 sensitized patients, i.e., 1.7% (6). It is therefore not unreasonable to assume that our figures would have even been higher, and probably several more patients could have been diagnosed as textile dermatitis, if the dyes had been tested in more patients with chronic eczema of the trunk, extremities, etc.

According to our data, both the two single compounds and the mix perform well as patch test substances. As found previously, p-phenylenediamine would be a poor screening agent for this type of

dye (1, 6, 8), and p-aminoazobenzene performed only slightly better. Therefore, the actual dyes have to be used for patch testing to detect sensitization reliably. Due to the very close structural similarity between DB 106 and DB 124 (Fig. 1) a high degree of cross-reactivity was to be expected; it had been described earlier (4) and was confirmed in our analysis. Despite this close similarity, however, cross-reactivity is not perfect, as was also shown in previous case series (4, 7, 8, 10). At least partly, this may be attributed to some degree of unexplained discordance, which is even seen with exactly the same allergen applied synchronously in duplicate (16).

Although the dyes are not necessarily used in combination in textiles (17, 18), their combined use for patch testing is acceptable. Furthermore, while complete chemical isolation of the respective 2 dyes from the rather impure raw materials available on the market is possible with preparative thin layer chromatography (TLC) or column chromatography (19), this process is quite costly and would probably be prohibitive on a production scale. Unrestricted availability, however, seems an important goal to enable broad scale surveillance of textile dye contact allergy.

The analytical procedure (TLC) mentioned above can be used to detect the presence of one (or both) of these 2 compounds in clothing items that are considered causative in case of sensitization to DB 106/124 (mix) (18), if sufficient laboratory facilities are available. However, as in most reports on contact allergy to DB 106 or DB 124 (including the present paper) such an analysis of clothing items was not performed, it often remains unclear whether DB 124 contained in textiles actually caused sensitization, or DB 106 – however, this may be an academic question anyway, in view of their close similarity.

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