Late patch test reaction to Disperse Orange 1 not related to active sensitization

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One of the most important adverse consequences of patch testing is active sensitization, when subjects previously not allergic become sensitized to one or more of the test chemicals by the test procedure. The allergic test reaction then shows up about 10 or more days (late reaction) after the test application. Sometimes, however, late reactions are seen without active sensitization being present, as some allergens are known to give late reactions in the absence of active sensitization.

Here, we describe a female patient shown to be allergic to Disperse Orange 1 from previous patch testing, who was only positive at patch test readings on D7 on the first test occasion and on D14 when patch tested repeatedly.

Case Report
A 34-year-old woman presented with eczematous lesions on the arms and dorsum of the hands, considered to be atopic dermatitis. To rule out contact allergy as a cause or an aggravating factor of the dermatitis in question, she was patch-tested on the upper back with our baseline series containing a textile dye mix 6.6% wt/wt composed of eight disperse dyes, two of which were Disperse Orange 1 (1.0%) and Disperse Yellow 3 (1.0%) (1). In the baseline series, p-phenylenediamine (PPD) 0.94% pet. was present. Because she reacted to the textile dye mix, on D3 she was tested with the textile dyes Disperse Orange 1 and Disperse Yellow 3 (0.5% pet. each). On D7, she was additionally tested with Disperse Orange 1 and Disperse Yellow 3 (1.0% pet. each). The Finn Chambers® technique (diameter 8 mm; Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster A/S, Vennesla, Norway) was used. The patches were applied on the upper back for 48 hr, and readings were made on D3 and D7 for all tested substances and, for some, also on D10 and on D14. There was an allergic patch test reaction to Disperse Orange 1 (1.0% pet.) on D7, to Disperse Yellow 3 (0.5% pet. on D10), and to PPD (0.94% pet.) on D14 (Table 1).

Table 1. Test results from the additional patch testing with components of the textile dye mix 6.6% in 2006 and with p-phenylenediamine in the baseline series (first test occasion) and test results from the scientific study (second test occasion)

<table>
<thead>
<tr>
<th>Test substance</th>
<th>Commercial DO1 1.0% pet a</th>
<th>Commercial DO1 0.5% pet b</th>
<th>Commercial DO1 1.0% acetone</th>
<th>Commercial DY3 1.0% pet a</th>
<th>Commercial DY3 0.5% pet b</th>
<th>Commercial DY3 1.0% acetone</th>
<th>p-Phenylenediamine 0.94% pet c</th>
<th>p-Phenylenediamine 1.0–1 × 10–6% acetone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reading days (first test occasion)</td>
<td>D3</td>
<td>D7</td>
<td>D10</td>
<td>D14</td>
<td>D3</td>
<td>D7</td>
<td>D10</td>
<td>D14</td>
</tr>
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<td>---</td>
</tr>
<tr>
<td>Commercial DO1 1.0% pet a</td>
<td>–</td>
<td>+</td>
<td>NR</td>
<td>NR</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Commercial DO1 0.5% pet b</td>
<td>–</td>
<td>?</td>
<td>+</td>
<td>NR</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Commercial DO1 1.0% acetone</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Commercial DY3 1.0% pet a</td>
<td>–</td>
<td>?</td>
<td>NR</td>
<td>NR</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Commercial DY3 0.5% pet b</td>
<td>–</td>
<td>?</td>
<td>+</td>
<td>NR</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Commercial DY3 1.0% acetone</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>p-Phenylenediamine 0.94% pet. c</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>p-Phenylenediamine 1.0–1 × 10–6% acetone</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>NT</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

DO1, Disperse Orange 1; DY3, Disperse Yellow 3; NT, not tested; NR, not read; –, negative reaction; ?, doubtful reaction; +, positive reaction.
aTested on D7 of the first test occasion.
bTested on D3 of the first test occasion.
cTested on D0 of the first test occasion.

Three years later, the patient was invited to participate in a research project at our department involving patch testing with various disperse dyes. She was again tested with Disperse Orange 1 and Disperse Yellow 3, along with PPD. The same test technique and reading days as mentioned above were used. On D3 and D7, there were no reactions to Disperse Orange 1 or Disperse Yellow 3, so the patient returned for additional readings on D10 and D14. On D14, an allergic reaction was noted for Disperse Orange 1 (1.0% acetone). This time, the patient did not react to PPD or Disperse Yellow 3.

Discussion
Active sensitization by patch testing is characterized by a negative reaction at the conventional time of reading (D4, D4, and D7), followed by a late patch test reaction at least 10 days after the test application. If patch testing is performed with the same test substance but diluted 10–100 times as compared with the original concentration and still gives positive reactions on D2–4, patch test sensitization must be considered to be very likely (2–4). Some allergens are known to give late reactions in the absence of active sensitization, for example, gold, corticosteroids, and acrylates (5–7). On the other hand, a patch test reaction that turns positive on retesting may indicate an increased level of sensitivity in the patient (8). Although
active sensitization is thought to be uncommon (approximately 0.1% of all reactions in a large series), certain allergens may be more likely to cause active sensitization (9). One of them is PPD, for which some authors claim that active sensitization by patch testing may occur in up to 1.5% of tested individuals (10). According to the 4-year review of late reactions by Aalto-Korte et al., some Disperse Orange dyes (among them Disperse Orange 1) induced late reactions in much higher percentages of patients than PPD did, and the authors concluded that these textile colours were primary active sensitizers and that concomitant late reactions to PPD only represented cross-allergy (11). However, other authors point out that a delayed immune response to PPD and some disperse dyes is more prevalent than active sensitization (12, 13).

Our patient initially reacted to commercial Disperse Orange 1 (1.0% in acetone), first noticed on D14. In this case, sensitization by patch testing was impossible, as the patient had previously been shown to be allergic to commercial Disperse Orange 1. Hence, late-appearing reactions are not always associated with patch test sensitization. The patient did not react to PPD or Disperse Yellow 3 on any of the reading days, up to D14, which can be explained by fluctuation in skin reactivity over time.

Interestingly, this patient with known contact allergy to Disperse Orange 1 reacted only to commercial Disperse Orange 1 and not to pure Disperse Orange 1. It has also been shown that commercial disperse dyes used for patch testing are impure (14). These impurities or intentionally added substances (e.g. naphthalene sulfonate, as a dispersing agent) in the raw material, used in the preparation of the commercial patch tests, could facilitate penetration of the actual dyes through the epidermis or act synergistically with them in eliciting an immune response.

Interestingly, the patient reacted to the patch preparation of Disperse Orange 1 (1.0%) on D7 at the first patch test session 3 years prior to our research study, and to the acetone solution of Disperse Orange 1 (1.0%) on D14, although both tests were prepared freshly from the same batch of the raw Disperse Orange 1, bought from Chemotechnique Diagnostics. The vehicles may have had different impacts on the penetration of Disperse Orange 1, or its degradation may have been different in the two vehicles.

To conclude, we consider this case to be an example of a late reaction to Disperse Orange 1 (seen first on D14) and not to represent primary patch test sensitization, as the patient had been shown to be allergic to Disperse Orange 1 on an earlier patch test occasion. The cause may be a delayed immune response, but the physicochemical features of the substance, its metabolism/degradation by skin bacteria (15) and the vehicle may also be factors.

References


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