

Contact allergy from disperse dyes in textiles—a review

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Summary

Several disperse dyes (DDs) are still considered to be the most important allergens in textile dermatitis, but there are sparse data about their current use in textiles. The aim of this review was to evaluate published studies and reports on contact allergy to DDs published in PubMed during the last 22 years (1990–2012). Prevalence data are provided by study and by dye, as well as by the described clinical peculiarities of DD dermatitis. We reviewed 54 studies. In total, 26 DDs were tested. The average prevalence in screening studies was >1% for Disperse Blue 106, Disperse Blue 124, and Disperse Orange 3. There is a lack of data on patch testing with Disperse Blue 26, Disperse Blue 102, Disperse Orange 37, Disperse Orange 149, Disperse Yellow 23 and Disperse Yellow 49, which are listed as allergens by the EU commission. It is necessary to check the purity and identity of dyes used for patch testing, confirm the clinical relevance of positive reactions by patch testing with suspected textiles, and, if the results are positive, determine the culprit dye.

Key words: allergic contact dermatitis; disperse dyes; textiles.

Disperse dyes (DDs) are the most prevalent causes of textile-related allergic contact dermatitis (1). They are used for dyeing synthetic fabrics made from fibres composed entirely of polyester, acetate, and nylon, or a blend of these with other fibre types; they are not used to dye natural fibres (e.g. wool, cotton, and linen) (2). DDs do not chemically bond to the fibres, and their small, lipophilic molecules can therefore easily migrate onto the skin of the person who is wearing the garment, especially if the textile fastness is poor; they may be removed by rubbing and by exposure to water (3). Approximately 60% of all DDs are azo dyes, and about 25% are anthraquinone

dyes, with the remainder being quinophthalone, methine, naphthalimide, naphthoquinone and nitro dyes (2). Azo dyes are currently employed to create almost the entire range of shades; they are cheap and easy to apply, so this dye class is used most often (2). Within the EU and by the International Oeko-Tex Association (a group of textile research and test institutes), some DDs (mainly azo) are classified as allergenic, and their use is restricted (4, 5) (Table 1). There are sparse data on the presence of the dyes to which individuals are patch test-positive in the garments suspected as the cause of their dermatitis. In 2003, Hatch et al. investigated textiles from textile dye patch test-positive patients, using chemical methods, and concluded that dyes to which patients were patch test-positive were infrequently identified in their clothes (6). However, some DDs are commonly patch tested, and clinical relevance is often reported.

The primary objective of this study was to review articles published in scientific journals concerning contact allergy to DDs, the frequency and prevalence of the contact allergy to the DDs present in the textiles, and the clinical peculiarities of DD dermatitis.

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Table 1. Disperse dyes classified as allergens and listed by the EU Commission and by Oeko-Tex

C.I. Generic name	C.I. number	CAS number
C.I. Disperse Blue 1	C.I. 64 500	2475-45-8
C.I. Disperse Blue 3*†	C.I. 61 505	2475-46-9
C.I. Disperse Blue 7	C.I. 62 500	3179-90-6
C.I. Disperse Blue 26	C.I. 63 305	–
C.I. Disperse Blue 35*	–	12222-75-2
C.I. Disperse Blue 102	–	12222-97-8
C.I. Disperse Blue 106*†	–	12223-01-7
C.I. Disperse Blue 124*†	–	61951-51-7
C.I. Disperse Brown 1*	–	23355-64-8
C.I. Disperse Orange 1*	C.I. 11 080	2581-69-3
C.I. Disperse Orange 3*†	C.I. 11 005	730-40-5
C.I. Disperse Orange 37	C.I. 11 132	–
C.I. Disperse Orange 76	C.I. 11 132	–
C.I. Disperse Red 1*†	C.I. 11 110	2872-52-8
C.I. Disperse Red 11†	C.I. 62 015	2872-48-2
C.I. Disperse Red 17*†	C.I. 11 210	3179-89-3
C.I. Disperse Yellow 1	C.I. 10 345	119-15-3
C.I. Disperse Yellow 3*†	C.I. 11 855	2832-40-8
C.I. Disperse Yellow 9*†	C.I. 10 375	6373-73-5
C.I. Disperse Yellow 39	–	–
C.I. Disperse Yellow 49	–	–
C.I. Disperse Orange 149	–	85136-74-9
C.I. Disperse Yellow 23	C.I. 26 070	6250-23-3

CAS, chemical abstract service; C.I., colour index number.

– indicates that there is no C.I. or CAS number for that dye.

*Present in the Textile Colours & Finish (TF-1000) series by Chemotechnique Diagnostics, Sweden, www.chemotechnique.se.

†Present in the Textile & Leather dyes series by Trolab, Germany, www.hermal.com.

Materials and Methods

Review of the literature

The National Library of Medicine (PubMed, <http://www.ncbi.nlm.nih.gov/ludwig.lub.lu.se/pubmed>, last accessed 5 May 2012) was searched with the MeSH terms 'disperse dyes and contact allergy', 'clothing and contact dermatitis', 'textile and contact dermatitis', and 'disperse dyes and contact dermatitis'. In addition, the journals *Contact Dermatitis* and *Dermatitis* (formerly the *American Journal of Contact Dermatitis*) were searched with the aforementioned terms. References within included articles were followed up when they were not found in the PubMed database. Only literature published in 1991–2012 and in English was included.

Methods

Three tables were created to allow comparison of prevalence data by study and by specific dye. We divided studies reporting patch testing with textile dyes into two

groups, according to the patient population tested. Table 2 contains the records of those studies in which patients appeared for routine patch testing that included textile dyes (screening testing), and Table 3 contains the records of those studies in which patients were suspected to have textile dye allergic contact dermatitis (aimed testing). Additionally, Table 4 was created to record patch test results for each dye used in testing. Each record in these tables consists of dye name, number of patch test-positive patients in the study, number of patients who were patch tested, prevalence, and the reference.

Furthermore, case reports and studies containing clinical descriptions of the dermatitis caused by DDs were evaluated with regard to site and clinical features.

Results

General information

In total, we found 54 studies. Of these, eight studies could not be included because they lacked information about the tested dyes or because the study population was already included in other published study.

Twenty-four studies were conducted by patch testing eczematous patients to determine the cause of allergic contact dermatitis (Table 2). Twenty-two studies were conducted by patch testing eczematous patients who were suspected of being textile dye sensitive (Table 3).

Furthermore, 18 studies were performed in Italian clinics. The remaining studies were performed in Belgium (one study), the United States (two), Portugal (four), Israel (five), Japan (one), Austria (four), France (two), The Netherlands (two), Canada (two), Switzerland (one), China (one), North America (four), Sweden (two), the United Kingdom (three), and Sweden/Belgium (two). Three were reports from the Information Network of Departments of Dermatology, and one was a report from the European surveillance system.

Patients were adults or of mixed ages, except in five studies (15, 21, 29, 50, 51) where patients were children.

Dyes for patch testing were obtained from Fabbrica Italiana Ritrovati Medicinali Affini (FIRMA) (Firenze, Italy), Hermal/Trolab (Hamburg, Germany), or Chemotechnique Diagnostics (Vellinge, Sweden), or directly from dye manufacturers. Usually, the dyes were not checked for identity or purity [exceptions were (10, 25, 27)]. In total, 26 DDs were used for patch testing in 1% pet. Additionally, Disperse Blue 35 was tested in 0.5% pet. and 0.3% pet., and Disperse Blue 106, Disperse Blue 124, Disperse Red 1, Disperse Red 17, Disperse Orange 1, Disperse Orange 3 and Disperse Yellow 3 in 0.5%, 0.3% and 0.1% pet.

Table 2. Review of the literature on the prevalence and clinical relevance of disperse dye (DD) contact allergy in consecutively patch tested dermatitis patients (screening patch testing)

References	Study period (or publication year)	Country	Number of patients tested	Positive reactions, number (%)	Patch testing with the extract/textile	Clinical relevance according to the reference
(7)	1987–1991	Belgium	3336	28 (0.8)	Yes, 3 patients, not positive to dye allergens, were positive to textile	Not stated
(8)	1988–1990	Italy	2752	100 (3.6)	No	Not stated
(9)	1988–1990	Italy	576	19 (3.3)	No	8/19 (42%)
(10)	1990–1995	Italy	6203	236 (3.8)	No	Not stated
(11)	1991	Italy	569	2 (0.4)	No	Not stated
(12)	1992	Portugal	329	2 (0.6)	No	Not stated
(13)	1994	Portugal	78	2 (2.6)	Not stated	100%
(14)	1995–1999	Germany, Austria	1986	86 (4.3)	No	Current clinical relevance 70%
(15)	1996–2000	Italy	1098	51 (4.6)	Not stated	Past/current relevance 70%
(16)	1996–2000	Italy	6478	437 (6.7)	Not stated	371/437 (85%)
(17)	1998	Italy	1012	31 (3.1)	Yes: 10/1012 (1%) 5/10 positive (50%), but 2 were negative to the patch tests with DDs	Not stated
(18)	1999–2003	Sweden	3325	50 (1.5)	No	Not stated
(19)	2001–2002	North America	4888	146 (3.0)	Not stated	45.5% possible relevance, 5.5% past relevance, 10.3% probable relevance
(20)	2001–2002	Germany, Austria, Switzerland	3041	40 (1.3)	Not stated	Not stated
(21)	2001–2004	United States	391	8 (2.1)	Not stated	47.6%
(22)*	2002	Israel	286	15 (5.2)	Not stated	68.7% current relevance, 9.4% past relevance, 21.8% no relevance
(23)	2003–2004	North America	5136	98 (1.9)	Not stated	Not stated
(24)	2003–2005	Germany	24 980	337 (1.35)	Not stated	Not stated
(25)	2004–2005	Sweden, Belgium	1780	35 (2.0)	Not stated	Not stated
(26)	2005–2006	North America	4454	94 (2.1)	Not stated	35.5% possible relevance, 7.5% past relevance, 20.4% probable relevance, 8.6% definite
(27)	2006–2008	Sweden, Belgium	2546	65 (2.6)	Not stated	Not stated
(28)	2007–2008	Finland Italy United Kingdom	760 2938 9201	4 (0.5) 47 (1.6) 37 (0.4)	Not stated	Not stated
(29)	2008	United States	65	7 (4.6)	Not stated	Probable/possible 71.4%
(30)*	2010	China	532	Volunteers 6/205 (2.9%) Eczema patients 13/327 (4.0%)	No	2/6 (33.0%) volunteers—past relevance 6/13 (46.0%) eczema patients – past/present relevance

*Including positive reactions to other class of dyes.

Disperse Blue 1, Disperse Blue 7, Disperse Red 11, Disperse Orange 76, Disperse Yellow 39, Disperse Yellow 54, 27 and 64 Disperse Black 2 were not tested in consecutive dermatitis patients, but were tested only in cases in which textile dye-related dermatitis was suspected.

Sex

Often, the sex distribution of patients positive for DDs was not provided, especially in earlier reports. In the vast majority of studies where the sex distribution of the positive reactions to DDs was reported, an

Table 3. Review of the literature on the prevalence and clinical relevance of disperse dye (DD) contact allergy in patients suspected or thought likely to have contact dermatitis caused by DD allergy (aimed patch testing)

References	Study period (publication date)	Country	Number of patients tested	Positive reactions, no (%)	Patch testing with the extract/textile	Clinical relevance according to the reference
(7)	1987–1991	Belgium	159	28 (17.6)	Yes, 3 patients, not positive to dye allergens, were positive to textile	Not stated
(8)	1988–1990	Italy	198	134 (67.7)	No	Not stated
(9)	1988–1990	Italy	145	23 (15.9)	No	8/19 (42%)
(31)	1988–1992	Portugal	6	6 (100%)	TLC results of the extracts from clothing were compared with those of reference dyes. In all 3 cases, DDs to which patients were patch test-positive were detected	100%
(32)	1989–1994	United States	50	12 (24.0)	Yes, positive 5/12 (41.7%)	Not stated
(33)*	1991–1997	Israel	55	22 (40.0)	Yes	Present relevance 20/22 (90.9%)
(34)	1991	Italy	2	2 (100)	No	100%
(35)	1992	Japan	1	1 (100)	Yes. Dyes were obtained from the manufacturer and analysed by TLC and mass spectrometry	100%
(36)	1993–2006	Australia	2069	114 (5.5)*	Yes (positive 12.8%)	100% in patients positive to extract/textile
(37)	1995	France	1	1 (100)	Yes	100%
(38)	1996–1999	The Netherlands	577	79 (13.7)	No	Relevant (probably) 75%
(39)	1997–1999	Canada	271	40 (14.8)	Yes, 11/271 (41%)	34/40 (85%) relevant 6/40 (15%) unknown relevance
(40)	1996–2000	Italy	130	13 (10.0) only to DDs	No	8/13 (61.5%) in patients sensitized only to DDs
(41)*	1998	Israel	103	30 (29.1)	No	100%
(42)	1998	Italy	1	1 (100)	Yes, positive. Dye detected by HPLC in the suspected garment	100%
(43)*	1999–2002	Israel	644	43 (6.7)	Yes 21/664 (3.2%) Positive 5/21 (23.8%)	Present relevance 81.4% Past relevance 6.8% No relevance 11.7%
(44)	2000	Portugal	5	5 (100)	Yes, 5/5 positive. TLC analysis revealed Disperse Blue 106	100%
(45)	2000	Switzerland	1	1 (100)	Yes: positive. Dyes obtained from manufacturer and analysed by HPLC – not detected	Not stated
(46)	2001	Canada	2	2 (100%)	Yes: negative in 1 patient, positive in another patient	100%
(47)	2004	Australia	1	1 (100)	Yes	100%
(48)	2004	Australia	1	1 (100)	Yes	Yes
(49)	2011	Italy	1	1 (100)	Yes	100%

HPLC, high-performance liquid chromatography; TLC, thin-layer chromatography.

*Including positive reactions to other classes of dyes.

overrepresentation of women was seen: from 56% to 100% (8, 9, 16, 17, 19, 33, 35, 39, 40, 43, 44, 47, 49, 52, 53). Only in one study did males slightly predominate (51%) (54).

Atopy

Among 16 studies in which atopic status (allergic rhinitis/conjunctivitis, asthma with/without atopic dermatitis) was described in patients positive for DDs, its

Table 4. Prevalence of each disperse dye by study

Disperse dye	Concentration (wt/wt)	Aimed testing		Studies (no.)	Screening		Studies (no.)
		Number of patients positive/total tested	%		Number of patients positive/total tested	%	
Disperse Blue 1	1.0% pet.	1/19	5.3	2		NR	
Disperse Blue 3	1.0% pet.	14/1441	1.0	13	3/2682	0.2	3
Disperse Blue 7	1.0% pet.	2/12	16.7	3	NR		
Disperse Blue 35	1.0% pet.	30/1779	1.7	13	11/4135	0.3	3
	0.5% pet.		NR		3/3325	0.1	1
	0.3% pet.		NR		4/2376	0.2	2
Disperse Blue 85	1.0% pet.	31/1599	2.0	9	15/2682	0.6	3
Disperse Blue 106	1.0% pet.	342/2051	16.7	16	639/35334	1.9	13
	0.3% pet.		NR		3/2049	0.2	1
	0.1% pet.		NR		5/3325	0.2	1
Disperse Blue 124	1.0% pet.	376/2363	15.5	15	517/19964	1.7	14
	0.3% pet.		NR		4/2049	0.2	1
	0.1% pet.		NR		6/3325	0.2	1
Disperse Blue 153	1.0% pet.	7/1453	0.7	5	3/2682	0.2	3
Disperse Red 1	1.0% pet.	171/2266	7.5%	17	236/30120	0.8	13
	0.5% pet.		NR		6/3325	0.2	1
Disperse Red 11	1.0% pet.	0/24	0	2	NR		
Disperse Red 17	1.0% pet.	64/1883	3.4	16	17/6511	0.3	5
	0.5% pet.		NR		5/3325	0.2	
Disperse Red 35	1.0% pet.	0/1	0	1		NR	
Disperse Orange 1	1.0% pet.	34/1498	2.3	9	52/6184	0.9	4
	0.5% pet.		NR		17/3325	0.5	1
Disperse Orange 3	1.0% pet.	244/2256	10.6	17	334/27899	1.2	12
	0.5% pet.		NR		1/3325	0.03	1
Disperse Orange 13	1.0% pet.	11/810	1.4	5	1/2355	0.04	2
Disperse Orange 76	1.0% pet.	26/282	9.2	4		NR	
Disperse Yellow 1	1.0% pet.	2/40	5.0	1		NR	
Disperse Yellow 3	1.0% pet.	157/2265	6.95	18	218/28053	0.8	12
	0.5% pet.		NR		8/3325	0.2	1
Disperse Yellow 9	1.0% pet.	26/1607	1.6	13	2/2355	0.06	2
Disperse Yellow 39	1.0% pet.	0/6	0	1		NR	
Disperse Yellow 54	1.0% pet.	6/131	4.6	2		NR	
Disperse Yellow 27	1.0% pet.	1/104	1.0	2		NR	
Disperse Yellow 64	1.0% pet.	1/5	20.0	1		NR	
Disperse Brown 1	1.0% pet.	22/1498	1.5	10	2/2355	0.1	2
Disperse Black 1	1.0% pet.	18/137	13.1	3	1/569	0.2	1
Disperse Black 2	1.0% pet.	4/6	66.7	1		NR	

NR, no reports found.

prevalence ranged from 0% to 72% among an adult or mixed population (15, 32, 33, 40, 41, 43, 46, 53, 54) (excluding case reports of 1 patient).

Textile identification

Of 18 studies in which testing with the suspected textile or with an extract made from the textile was carried out, textile composition was reported in five (17, 35, 37, 39, 46). The reports concerned 100% navy blue or black 100% polyester (35, 37), dark wool synthetic mix (17), 100% wool dyed a dark blue–green colour (46), black/blue/dark green 100% acetate or 100% polyester,

52% acetate/42% cotton, and blue cotton/polyester (39). In other articles, 'textile' was mainly referred to as 'synthetic material' or 'stockings', or not described at all.

Prevalence of contact allergy to DDs

In a few studies, testing of patients was performed with a textile series, and thus the prevalence data obtained concerned positive reactions to allergens included in the series. A majority of the positive reactions were to DDs. Nevertheless, when possible, we calculated the prevalence rate only for DDs, and if this was not possible, the prevalence of positive reactions to textile series was recorded.

In those studies in which patients appeared for routine patch testing and DDs were included (Table 2), prevalence values ranged from 0.4% (11, 27) to 6.7% (16). Prevalence values in patient populations known to be or very probably sensitized to DDs ranged from 5.5% to 100% (Table 3).

The amount of prevalence data collected for various DDs varies considerably (Table 4). Disperse Blue 124 was evaluated in 34 studies, with the highest number of tested patients, followed by Disperse Red 1 (32 studies), and Disperse Blue 106, and Disperse Yellow 3, which were evaluated in 31 studies.

There was considerable variation in the prevalence data for the aimed testing studies, but the lowest value was usually higher than the lowest prevalence value for the dye in screening studies. Average prevalence values were highest for Disperse Blue 106 (1.9%), Disperse Blue 124 (1.7%) and Disperse Orange 3 (1.2%) in screening testing, but in aimed testing Disperse Black 2 was positive in 66.7% of cases (although this is based on the data from only one study), Disperse Yellow 64 in 20%, and Disperse Blue 7 in 16.7%.

Clinical relevance and patch testing with patients' textile

Of 46 reviewed studies (Tables 2 and 3), patch testing with the suspected textile or its extract was reported in 18 (7, 17, 31–33, 35–37, 39, 42–49). In two studies, identification of the culprit dye in the patient's textile was based on the similarity with the reference dye in a thin-layer chromatography (TLC) system (31, 44). In one case, dyes obtained from the manufacturer were investigated with mass spectrometry, and the DDs to which the patient was positive were detected (35). One study confirmed the presence of the dye by high-performance liquid chromatography (HPLC) (42). Of 28 studies in which the clinical relevance was stated, testing with the suspected garment or extract was carried out in 13. The clinical relevance of positive reactions as assessed by the authors was >70% in the majority of studies: in the aimed testing, 75–100%; and in the screening testing, 42–78%. In almost all studies, the most common DDs found to be positive on patch testing and thus clinically relevant were Disperse Blue 106 and Disperse Blue 124. Clinical relevance was mostly judged by the disappearance of dermatitis after the patient had ceased wearing dark synthetic clothing.

Monosensitization

Six studies reported rates of monosensitization to DDs (7, 8, 10, 15, 42, 48). The prevalence rate varied from 2.3%

to 17%. The monosensitized patients most frequently had positive patch test reactions to Disperse Blue 124, Disperse Blue 106, Disperse Red 1, Disperse Orange 3, Disperse Yellow 3, and Disperse Red 17, but no associations with positive reactions to *p*-phenylenediamine (PPD) or clinical relevance were reported. Only one case report, by Foti et al., showed the monosensitization to Disperse Yellow 27 to be of clinical importance, by detecting the dye in the extract of the patient's clothes with HPLC (42).

Children

A recently published systematic review and meta-analysis of allergens responsible for allergic contact dermatitis among children by Bonitsis et al. (55) also covers children's sensitivity to several DDs: Disperse Blue 124, Disperse Blue 106, Disperse Orange 3, Disperse Red 1, and Disperse Yellow 3. According to this review, the prevalence of positive reactions in at least 1% of tested children was found to be statistically significant only when they were positive to Disperse Blue 124 but not to other DDs.

The North American Contact Dermatitis group compared sensitivity to Disperse Blue 106 in children and adults, and did not find a significant difference (21): the prevalence rate was 2.1% in children and 2.4% in adults (Table 5). The Portuguese Contact Dermatitis group, in a study performed in 1992, found a low prevalence of positive reactions to DDs – in 0.3% of 327 tested children (12). Studies performed in Italy (15, 50, 51) found that the most prevalent DD contact allergens in children are Disperse Blue 106 and Disperse Red 1, followed by Disperse Blue 124, Disperse Orange 3, and Disperse Yellow 3. Seidenari et al. described the sensitivities of 23 DD-positive children. In their study, the most prevalent sensitizers were Disperse Red 1 and Disperse Orange 3 (10).

Clinical picture

In 22 studies in which the clinical picture was described, DD-related dermatitis most commonly developed on the extremities (upper more frequently than lower), and especially on the hands, followed by the trunk, face, genitalia, buttocks, and the folds, including the neck, axillae, and groin (8, 14–18, 31–34, 36, 42–44, 51, 54). In children with positive patch test reactions to DDs, especially those suffering from atopic dermatitis, the flexural areas of the limbs were involved more often (52.9%) in those with atopic dermatitis than in those without it (15).

Table 5. Contact sensitization to disperse dyes in children

Dye tested	Reference						
	(15), n = 1098	(50), n = 1094	(29), n = 65	(12), n = 329	(21), n = 391	(51), n = 670	(10)*, n = 23
Disperse Yellow 3	17 (1.5%)	15 (1.4%)	ND	1 (0.3%)	ND	4 (0.6%)	4 (17.6%)
Disperse Blue 106	4 (0.4%)	44 (4.0%)	7 (8.8%)	ND	8 (2.1%)	ND	ND
Disperse Blue 124	14 (1.3%)	20 (1.8%)	ND	ND	ND	5 (0.7%)	4 (17.6%)
Disperse Orange 3	15 (1.4%)	20 (1.8%)	ND	1 (0.3%)	ND	6 (0.9%)	12 (52.2%)
Disperse Red 1	8 (0.7%)	25 (2.3%)	ND	1 (0.3%)	ND	8 (1.2%)	14 (60.1%)

ND, not done.

*Aimed testing.

Frequently, the clinical features of dermatitis related to DDs had uncommon features, an atypical localization, and unusual clinical patterns. It could present not only like typical chronic dermatitis, but also as persistent erythematous wheal-type or transient urticarial dermatitis (8), prurigo-like eczema (49), diffuse itching (8), erythema multiforme-like eruptions (8, 56), purpuric dermatitis (33, 42, 57), nummular dermatitis, erythroderma (43), or pseudolymphoma (52). Before the diagnosis of DD-related dermatitis was established, patients were diagnosed with lichen simplex chronicus, parapsoriasis, mycosis fungoides, drug eruption, post-inflammatory hyperpigmentation, pigmented purpura, or scabies (33).

According to Lazarov, chronic dermatitis was diagnosed in 35.4% of cases, and acute dermatitis in 6.8%; the remainder consisted of atypical forms of allergic contact dermatitis in patients with textile dye allergy (43). Seidenari described 50 of 437 patients positive to DDs and presenting with atypical allergic contact dermatitis features – erythema and oedema with or without marginal desquamation (16). It has been reported that dermatitis can be so monomorphic and infiltrated that, at first, the diagnosis of allergic contact dermatitis may not be obvious (7). It is also not uncommon to see sterile pustular lesions or purpura on sites of DD-induced dermatitis (43). There are reports of peculiar presentations of DD-related dermatitis, such as airborne contact dermatitis (58), as well as dermatitis on the incision scar of hip replacement caused by the black trousers of the patient (59).

Patch test reactions to DDs

Patch testing with DDs usually results in strong (+++/+++) reactions. Sometimes, they can be purpuric (60). Massone et al. described persistent patch test reactions to Disperse Blue 124 and Disperse Red 1, which were already strongly positive on the D2 reading, and remained active and itching on D14 and D22 (34).

Dawes Higgs described a patient who developed a flare-up of the dermatitis in skin folds when patch tested with

DDs and an extract from her textile, to which she was positive, as well as to Disperse Blue 106 at D3 (48). We also described a patient with systemic contact dermatitis that developed during patch testing with Disperse Orange 1 (61). The patient was tested with the dilution series of Disperse Orange 1, and was positive to the 0.000001% concentration.

Late readings

Times given for the interval between the removal of patch tests and the reading of the skin response were 2 days and 3–4 days. Not all authors reported the reading procedure.

Of the identified studies, 11 also performed late (D7) readings (23–26, 39, 41–43, 48, 49), whereas in four only some patients were read on D7 (18, 19, 27, 39). Several studies reported late positive reaction rates. Koopmans and Bruynzeel pointed out that 10% of the total reactions to the *para*-dyes were late reactions, 17% of them being for azo dyes, of which 84% were relevant (38). Ryberg et al. showed that 13 patients of 62 (21%) positive to DDs were positive only on D7 (27) in one study, and 3 of 35 (8.6%) patients positive to textile dye mixture (TDM) and 4 of 34 patients (11.2%) positive to ingredients of TDM were positive only on D7 in another study (25). Pratt and Taraska noted delayed positive patch test reactions to Disperse Blue 124 on D7/10 in 2 of 32 tested patients (6.3%), and all of them were clinically relevant (39).

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 at 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. According to the 4-year review of late reactions by Aalto-Korte et al., some Disperse Orange dyes induced late reactions in a much higher percentage of patients than PPD did, and

the authors concluded that these textile colours were primary active sensitizers (62). However, other authors have pointed out that a delayed immune response to some DDs is more prevalent than active sensitization (63, 64).

Discussion

More work has been done since the last review was published by Hatch and Maibach on the prevalence of textile dye allergic contact dermatitis: more countries are represented and more patients are tested (65). The prevalence of DD contact allergy varies with the population and the dyes tested. The available data indicate that positive patch test reaction prevalence rates for at least three dyes (Disperse Blue 106, Disperse Blue 124, and Disperse Orange 3) were >1% in screening of dermatitis patients. Therefore, according to Bruze et al., they should be included in the baseline series (66).

On the other hand, there are some DDs for which the prevalence rate in aimed testing is >10% (Disperse Blue 7, Disperse Yellow 64, Disperse Black 1, and Disperse Black 2), but they are not included in the series of the commercial patch test manufacturers (e.g. Trolab or Chemotechnique), so relevant allergies to these dyes could be missed if testing is performed only with commercial series.

There is a lack of data on patch testing with Disperse Blue 26, Disperse Blue 102, Disperse Orange 37, Disperse Orange 149, Disperse Yellow 23 and Disperse Yellow 49, which are listed by the EU Commission and by Oeko-Tex as allergens. It is also obvious that there are many more allergenic DDs than those that are classified as such by these institutions, so Oeko-Tex labelling or a label 'Made in the EU' does not mean that no allergenic dyes are used, as was also pointed out by Carozza and Nestle in their case report, where they described allergic contact dermatitis caused by 'ecological' (i.e. not listed in Oeko-Tex standard) disperse textile dyes (45).

The purity of the patch test preparations is also an important issue. In 1986, Foussereau et al. (67) reported on problems with the purity of several dyes in a commercially available patch test series. A study by Ryberg et al. found that some commercial patch test preparations labelled as containing Disperse Orange 3 did not contain that dye, but did contain another orange DD (68). Differences may also occur from batch to batch, as well as among different manufacturers. A study in Malmö showed that the raw material of DDs used for preparing patch tests contained 39–76% contaminants or other substances (68). These can be relevant, as almost 25% of patients allergic to commercial Disperse Blue 106, Disperse Blue 124, Disperse Yellow 3 or Disperse

Orange 1 did not react to (or not only to) the main spot, but to other spots on the TLC plates made from the commercial dyes (61, 69). When patch test preparations of dyes contain more than one compound, it may not be the dye molecule that causes the skin reaction, and it is also difficult to compare the results of patch testing with different batches and in different clinics.

The high frequency of sensitization to DDs in women constantly reported in the studies may reflect the proportions in the study population, but it could also be caused by women's tendency to wear tighter-fitting clothes, lace underwear, or tights, which are always synthetic. Therefore, whether women are more susceptible to sensitization to DDs is not yet known.

It is very important to know whether dyes to which a patient has a contact allergy are used in textiles. Indeed, in the majority of studies reporting positive reactions to DDs, clinical relevance was not stated, although it was shown that dyes to which patients are patch test-positive are infrequently found in the suspected garment (6). As some of the DDs (e.g. Disperse Blue 106) are potent sensitizers (70), it seems that the clinical relevance of the positive patch test reactions could sometimes be overestimated. Unfortunately, not all studies provide the fibre composition of the 'culprit' textile; this could indirectly indicate the possibility of the DDs being present in the garment. DDs are not used to dye all types of synthetic fibre, and are not used for wool or cotton, where other types of dye are employed. Thus, positive patch test reactions to a disperse azo dye and to such types of textile could not be related aetiologically. On the other hand, other substances causing positive patch test reactions could be present in the textile, and positive patch test reactions to disperse azo dyes could be a marker of sensitization to other *para*-compounds (such as PPD or black rubber substances).

When establishing the clinical relevance of the positive patch test reaction to the DDs, patch testing either with the suspected fabric or with an extract from it should be performed, and the relevant DDs in the textile must be detected; that is, exposure to that DD should be confirmed. However, the extraction procedure is not standardized. Sensitivity to a dye placed directly on the skin would be expected to be higher than that seen in testing with the dyed textile, because a lower concentration of the dye would migrate onto the skin. Therefore, ideally, identification of the dye content in the suspected fabric should also be carried out, although this is not always possible. Indeed, the latest reports that we found when reviewing the literature on chemical analysis of the suspected textile were published in 2000 (44, 45).

For patients allergic to DDs, the common advice is to avoid dark, synthetic clothes. This is partially correct, as Disperse Yellow 3 and Disperse Orange 3 are found in ladies' tights and 'stockings' (not specified in the description), which are not necessarily dark, but are rather brown, or even beige (71). Also, one colour may be obtained by mixing several dyes, so even light colours may contain several allergenic DDs. It seems that the most appropriate advice would be to wear garments made from non-synthetic fibres.

A few studies reported figures for monosensitization to a particular dye, but only one of them reported the clinical relevance of this finding or an association with positive reactions to other *para*-compounds (42). In almost all of the case reports that we reviewed, sensitization to at least two DDs was reported. It seems that co-sensitization to several dyes, usually of similar structure or having the same impurities, exists, but it could be that a particular sensitization to one dye can be important. These DDs, for which monosensitization is reported, are some of the most prevalent dye allergens. Some of them have been shown to be strong allergens. This could mean that a positive reaction to one DD is related to the strength of the allergen, and shows a general predisposition of the immune system to recognize a particular pattern of the structure, rather than that this is the culprit allergen for the patient's dermatitis. The DD can be a marker for group sensitization, as is seen, for example, with the corticosteroid budesonide (72).

It is difficult to prove that the dyed textile contains the primary sensitizer. The primary sensitizer may be another substance or be a cross-sensitizer (10). It was reported that 18% of the surveyed dermatitis patients suspected textiles (especially synthetic) as a cause of their skin problems, but there was no statistical correlation with the positive patch test reactions to DDs (73). Interestingly, self-reported textile-related skin problems were statistically significantly associated with contact allergy to PPD,

which is frequently found in cases with contact allergy to the azo dyes (73).

In order to diagnose allergic contact dermatitis caused by textile dyes, a high index of suspicion is required, as its clinical presentation does not always indicate the cause, because the clinical presentation is usually atypical, and its appearance is not always confined to sites of direct contact. On the other hand, a diagnosis of textile dye dermatitis could be missed even if patch testing with the commercial DD preparations is performed, because it could be that these DDs are currently uncommon in textiles. Hatch and Maibach identified the prevalence rates for 18 DDs described as allergens (65). We identified 26 allergenic DDs, but this still represents a very small fraction of the total of ~8000 commercially used dyes, in which DDs are one of the largest classes used. A study in Malmö showed that, in the 121 textile items analysed with different chemical methods, the most commonly named allergenic DDs were detected in three garments only (74). Therefore, it could be that other DDs are used in the textiles that we are wearing today.

Conclusions

Allergic contact dermatitis caused by DDs shows a polymorphic clinical picture, which is often atypical. Specific textile dye series contain substances that are currently employed in a limited group of garments or not used anymore, because new dyes are continuously being introduced. It is necessary to check the purity and identity of dyes used for patch testing, confirm the clinical relevance of positive reactions by patch testing suspected textiles, and, if the results are positive, determine the culprit dye. Late readings (D7) of the patch test reactions should be encouraged, as they give important and clinically relevant information.

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