

Patch testing with textile dye mix in Italy: A 2-year multicenter SIDAPA study

Luca Stingeni¹  | Leonardo Bianchi¹ | Rossella Marietti¹ | Silvia M. Ferrucci² | Myriam Zucca³ | Caterina Foti⁴ | Paolo Romita⁴  | Monica Corazza⁵  | Donatella Schena⁶ | Paolo Pigatto⁷ | Emanuela Martina⁸  | Cataldo Patruno⁹  | Maddalena Napolitano¹⁰  | Fabrizio Guarneri¹¹  | Vittorio Bini¹² | Marta Tramontana¹ | Katharina Hansel¹ 

¹Section of Dermatology, Department of Medicine, University of Perugia, Perugia, Italy

²UOC Dermatologia, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

³Dermatological Clinic/UC of Dermatology, Department of Medical Science and Public Health, AOU Cagliari, Cagliari, Italy

⁴Section of Dermatology, Department of Biomedical Science and Human Oncology, University of Bari, Bari, Italy

⁵Section of Dermatology, Department of Medical Sciences, University of Ferrara, Ferrara, Italy

⁶Section of Dermatology and Venereology, Department of Medicine, University of Verona, Verona, Italy

⁷Department of Biomedical, Surgical and Dental Sciences, Clinical Dermatology, IRCCS Galeazzi Orthopaedic Institute, University of Milan, Milan, Italy

⁸Dermatological Clinic, Department of Clinical and Molecular Sciences, Polytechnic University of the Marche Region, Ancona, Italy

⁹Section of Dermatology, Health Sciences Department, Magna Graecia University, Catanzaro, Italy

¹⁰Section of Dermatology, Department of Medicine and Health Sciences Vincenzo Tiberio, University of Molise, Campobasso, Italy

¹¹Dermatology, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

¹²Endocrine and Metabolic Sciences Section, Department of Medicine, University of Perugia, Perugia, Italy

Correspondence

Prof. Luca Stingeni, Section of Dermatology, Department of Medicine, University of Perugia, 06129 Perugia, Italy.
Email: luca.stingeni@unipg.it

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Disperse dyes (DDs), mostly represented by azo dyes, are small and lipophilic molecules characterized by low cost and simple application on clothing. If the textile fastness is poor, DDs are easily released onto the skin causing allergic contact dermatitis (ACD). DDs are still common sensitizers despite their reduced use for the coloring of synthetic fibers (polyester, acetate, nylon, or their blend with other fiber types).¹ From the 1990s, several DD mixes of different compositions and concentration were used to save space and time, and in 2015 the ESCD included in the baseline patch test series a textile dye mix (TDM) 6.6% containing eight DDs.² In fact, a large number of dyes are available and patch testing with extracts of the garment per se is not always possible. Moreover, there was a need for a marker because *p*-phenylenediamine (PPD) was not considered sufficient. In Europe the prevalence of TDM 6.6% positivity ranges between 2.1% and 6.9% with a clinical relevance in 31% of cases,³ whereas a representative study on the Italian trend is lacking. In this study, the

prevalence of positivity to TDM 6.6% in a large Italian population sample was analyzed.

METHODS

During a 2-year period between January 2018 and December 2019, data were collected from 10 Italian Dermatology clinics homogeneously distributed in Italy. Consecutive patients (*n* = 11 697, 4198 male; mean age 46.2 years) underwent routine patch testing with the SIDAPA (Società Italiana Dermatologia Allergologica Professionale Ambientale) baseline series containing TDM 6.6% pet. (Disperse Blue 35, Disperse Yellow 3, Disperse Orange 1 and 3, and Disperse Red 1 and 17, all 1.0% pet., and Disperse Blue 106 and 124 0.3% pet. each). Patch testing (40 mg/cm² pet., 30 µL/cm² aq.) was performed with the Haye's Test Chambers (Haye's Service, Alphen aan den Rijn, The Netherlands) on Soffix tape (Artsana, Grandate, Italy), and

allergens from FIRMADiagent (Florence, Italy). Readings were performed on day (D)2, D4, and D7.⁴

The assessment of clinical relevance of positive TDM patch test was based on fulfilling the following three criteria: patient's history of possible exposure to DDs, clinical examination, and remission of dermatitis after the patient stopped wearing colored clothes. TDM-positive patients with clinical relevance were divided into three subgroups based on their geographical distribution throughout North, Center, and South Italy to analyze the differences between the population characteristics according to (Male, Occupational dermatitis, Atopic dermatitis, Hand, Leg, Face, Age) MOAHLFA Index.

The chi-square test with Yates' continuity correction and Fisher's exact test was used to analyze categorical variables. Statistical analysis was performed using IBM-SPSS version 25.0 (IBM, Armonk, New York). In all analyses, a two-sided *P* value $\leq .05$ was considered significant.

RESULTS

Among the 11 697 patch-tested patients, 176 (1.5%) reacted to TDM 6.6% on D4. This prevalence was higher in male (1.6%) than in female (1.4%) patients, but was not significant (*P* = .40). Clinical relevance was documented in 123 subjects (69.9%), with similar prevalence in male and female subjects (71.0% and 69.2%, respectively; *P* = .93) (Table 1). In the same population, 35 patients were sensitized to PPD (28.5%; male 24.5%, female 31.1%) and 5 to *N*-isopropyl-*N*-phenyl-*p*-phenylenediamine (4.1%; male 2.0%, female 5.4%).

Among patients with clinical relevance, strong (++) and extreme (+++) positive reactions were observed in 101 of 123 (82.1%), were more frequent in female than in male patients (83.8% and 79.6%, respectively; *P* = .72), and their prevalence in atopic dermatitis

(AD) and non-AD patients (80.0% and 82.5%, respectively; *P* = .79) was similar. Non-occupational exposure was documented in 100 of 123 subjects (81.3%) (Table 1). Occupational exposure was considerably more common in male than in female patients (34.7% vs 8.1%, respectively; *P* = .0005). In particular, occupational exposure was documented in 4 textile workers (21.1%) textile workers (2 males, 2 females), whereas in 19 patients (88.9%) ACD was caused by work clothing. Forty-six of 123 patients (37.4%) were also tested with the eight ingredients of TDM and with the suspected garment with the following results: Disperse Blue 106: 12; Disperse Orange 3: 11; Disperse Blue 124: 10; Disperse Yellow 3: 8; Disperse Orange 1: 8; Disperse Red 17: 8; Disperse Blue 35: 6; Disperse Red 1: 6; and suspected garment: 22 positive reactions. Eight of the 11 Disperse Orange 3-sensitized patients were simultaneously sensitized to PPD.

Among patients without clinical relevance (53/176, 30.1%), ++ and +++ positive reactions were observed in 26 of 53 patients (49.1%) and were more frequent in male than in female patients (55.0% and 45.5%, respectively; *P* = .69) (Table 1). The MOAHLFA index of TDM-positive patients with clinical relevance in North (53/5182, 1.0%), Center (28/2510, 1.1%), and South (42/4005, 1.0%) Italy shows in South Italy a higher proportion of AD (*P* = .027) and lower proportion of hand (*P* = .018) and face (*P* = .014) dermatitis (Figure 1).

DISCUSSION

In this 2-year period study on 11 697 consecutively tested Italian patients the prevalence of sensitization to TDM was 1.5%. This prevalence is considerably lower than that observed among European and American patients in 2011 (108/2907, 3.7%)³ and in 2013 (90/2493, 3.6%),⁵ and recently in Malmö patients (54/2250, 2.4%).⁶ These data, together with ours, support a decreasing trend of contact sensitization to DDs, probably due to the entry of DDs into the REACH restricted substance list (REACH Annex XVII) of EU directives (Regulation No. 1007/2011 and Regulation No. 1907/2006).⁷ After these EU directives, also in Italy DDs use became less common than that documented in Italian garments by Malinauskiene et al in 2012 with regard to Disperse Yellow 3, Disperse Blue 106, and Disperse Blue 124.

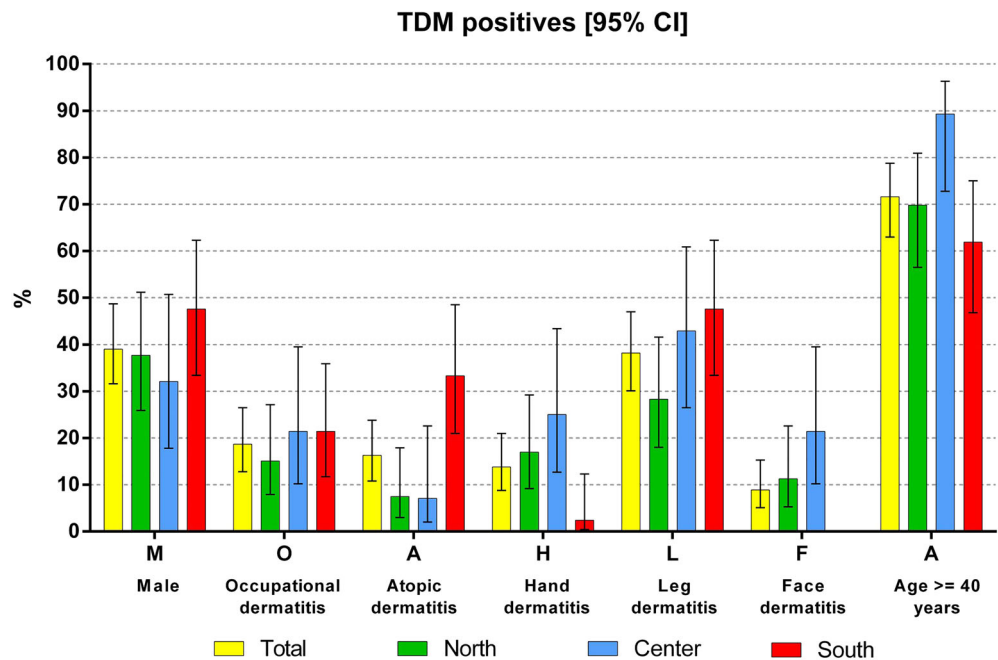
Surprisingly, the prevalence of relevant TDM-positive reactions was lower in female compared to male patients. This is in contrast to the literature,^{3,5,8} and may in part be due to hair coloring and choices of garments worn next to skin in female subjects. Of interest, our study documented clinical relevance of positive TDM reactions, mostly ++ and +++ reactions, in 69.9% of TDM-positive patients. These proportions are far higher than those reported by Ryberg et al in two European³ and Swedish⁸ multicenter studies (31.2% and 37.5%, respectively). This discrepancy could be due to the varying use of the eight DDs present in the mix in different countries⁹ and to the possible cross-reactivity between DDs contained in TDM or not.³

The occupational exposure to DDs (18.7%) results were quite comparable to that observed in a previous Italian study (12.5%),¹⁰

TABLE 1 Positive patch test reactions to TDM 6.6% in 11 697 consecutive patch-tested patients (4198 men, 7499 women)

	Total (%)	M (%)	F (%)
Positive reactions	176 (1.5)	69 (1.6)	107 (1.4)
Relevant reactions	123 (69.9)	49 (71.0)	74 (69.2)
Scoring			
+	22 (17.9)	10 (20.4)	12 (16.2)
++	60 (48.8)	27 (55.1)	33 (44.6)
+++	41 (33.3)	12 (24.5)	29 (39.2)
Exposure			
Occupational	23 (18.7)	17 (34.7)	6 (8.1)
Nonoccupational	100 (81.3)	32 (65.3)	68 (91.9)
Nonrelevant reactions	53 (30.1)	20 (29.0)	33 (30.8)
Scoring			
+	27 (50.9)	9 (45.0)	18 (54.5)
++	18 (34.0)	7 (35.0)	11 (33.3)
+++	8 (15.1)	4 (20.0)	4 (12.2)

FIGURE 1 The MOAHLFA index in TDM mix positives in 10 dermatologic units distributed in North (5182), Center (2510), and South (4005) Italy, accompanied by the respective 95% confidence interval (CI)



with a significant male predominance. In the occupational setting only four patients (21.1%) were textile workers, while in the remaining patients ACD was caused by work clothing in other working environments.

Patient characteristics according to the MOAHLFA index revealed that hand and face involvement was significantly lower in South Italy, probably due to clothing habits related to the large climatic differences in Italy. In central Italy, hand dermatitis was more frequent (7/28, 25.0%): Because the involvement of hands in this geographical area was correlated mainly with clothing gloves in non-occupational setting (5/7, 71.4%), we could exclude other occupational settings in this part of Italy.

In conclusion, our data support the importance of still testing TDM 6.6% in the baseline series, although the decreasing trend documented in Italy. Considering the ongoing proposal at the European level concerning the REACH-restricted substance list in textiles, studies at the international level are needed to monitor the trend of contact sensitivity to TDM.

CONFLICTS OF INTEREST

All authors have no conflicts of interest to report.

AUTHOR CONTRIBUTIONS

Luca Stingeni: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; software; supervision; validation; visualization; writing-original draft; writing-review and editing. **Leonardo Bianchi:** Data curation; formal analysis; investigation; methodology; project administration; software; supervision; writing-review and editing. **Rossella Marietti:** Data curation; investigation; methodology; project administration; software; supervision; writing-review and editing. **Silvia Ferrucci:** Data curation;

investigation; methodology; visualization; writing-review and editing.

Myriam Zucca: Data curation; investigation; methodology; visualization; writing-review and editing. **Foti Caterina:** Data curation; investigation; methodology; visualization; writing-review and editing. **Paolo Romita:** Data curation; investigation; methodology; visualization; writing-review and editing. **Monica Corazza:** Data curation; investigation; visualization; writing-review and editing. **Donatella Schena:** Data curation; investigation; methodology; visualization; writing-review and editing. **Paolo Pigatto:** Data curation; investigation; methodology; supervision; visualization; writing-review and editing. **Emanuela Martina:** Data curation; investigation; methodology; visualization; writing-review and editing. **Cataldo Patruno:** Data curation; investigation; methodology; supervision; visualization; writing-review and editing. **Maddalena Napolitano:** Data curation; investigation; methodology; visualization; writing-review and editing. **Fabrizio Guarneri:** Data curation; investigation; methodology; visualization; writing-review and editing. **Vittorio Bini:** Data curation; formal analysis; software; validation. **Marta Tramontana:** Data curation; formal analysis; investigation; methodology; project administration; software; supervision; writing-review and editing. **Katharina Hansel:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; software; supervision; validation; visualization; writing-original draft.

ORCID

Luca Stingeni <https://orcid.org/0000-0001-7919-8141>

Paolo Romita <https://orcid.org/0000-0002-5559-9722>

Monica Corazza <https://orcid.org/0000-0003-2105-6217>

Emanuela Martina <https://orcid.org/0000-0003-0815-172X>

Cataldo Patruno <https://orcid.org/0000-0001-8661-2822>

Maddalena Napolitano <https://orcid.org/0000-0003-3309-8190>

Fabrizio Guarneri  <https://orcid.org/0000-0003-0805-8496>

Katharina Hansel  <https://orcid.org/0000-0002-6674-4278>

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