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## 2,4,6-Tris(dimethylaminomethyl)phenol: the allergen which came in from the cold.

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2,4,6-Tris(dimethylaminomethyl)phenol (tris-DMP; CAS No. 90-72-2) is a hardener / accelerator frequently used in epoxy resin systems (ERS), especially at low ambient temperature [1]. First cases of contact sensitization to tris-DMP have been observed at the Finnish Institute of Occupational Health (FIOH) around 1990 [2]. Since then, contact sensitization to tris-DMP has been described in several case reports from various European countries [1]. In the FIOH, 14 cases of contact sensitization to tris-DMP have been registered from 1991 to 2013, rendering it the second most frequent sensitizer among epoxy resin hardeners [1]. Since 2016, tris-DMP is available as patch test preparation at 0.5% in petrolatum (pet.) from Chemotechnique, Vellinge, Sweden.

## Methods

The German Contact Dermatitis Research Group (DKG) included tris-DMP in the “adhesives and glues” series and the “building trade” series in October 2016. Tris-DMP 0.5% pet. has been patch tested following DKG guidelines [3] in the departments of dermatology joining the Information Network of Departments of Dermatology (IVDK) in 5467 patients in the years 2017 to 2021. Results of these tests were retrospectively analysed.

## Results

Patch test results are shown in table 1. Positive reactions to tris-DMP occurred in 28 patients (0.5%). Seven positive reactions (25%) would have been missed if patch tests would have been read until day 3 (D3) only. In 6 patients, positive reactions occurred at D4, and in one patient at D7. In 2 patients, a weak positive reaction (+) at D3 evolved into a strong positive reaction (++) at D4. Patch tests had been read until D4 or even D7 in 1964 patients (35.9%). Of the 28 tris-DMP-positive patients, 23 were males; the mean age was 47.0 years. Four of the tris-DMP positive patients were floor layers, 4 construction workers or bricklayers, 3 tile setters, and 3 painters. Additional details about those sensitized to tris-DMP, compared to those with a negative tris-DMP patch test, can be found in online supplemental table 1. Of the 28 tris-DMP positive patients, 27 were or had previously been patch tested with epoxy resin based on bisphenol A diglycidyl ether (DGEBA). Of these, 23 (85.2%) reacted to the DGEBA resin. In all, concomitant sensitizations to other ERS components occurred in 26 of the 28 tris-DMP positive patients (online supplemental table 2). For comparison, in the study period, sensitization to m-xylylene diamine (MXDA) was diagnosed in 63 of 5978 tested patients (1.1%), and to isophorone diamine (IPDA) in 32 out of 6097 patients (0.5%).

## Discussion

Consistent with the FIOH data [1], we found sensitizations to tris-DMP less frequently than sensitizations to MXDA, but with a similar frequency as sensitizations to IPDA. Sensitization to tris-DMP without sensitization to other ERS components occurred less, but not significantly, frequently than in the FIOH (IVDK: 2 / 28 pat.; FIOH: 3 / 14 pat). However, 9 out of 14 FIOH patients (64%) sensitized to tris-DMP, but only 3 of the 28 tris-DMP positive IVDK patients (11%), were painters. Among our tris-DMP sensitized patients, there were more floor layers, bricklayers, construction workers, and tile setters.

One quarter of the 28 positive reactions to tris-DMP in our study did not occur before D4. As only about one third of the patch tests have been read after D3, the true frequency of tris-DMP sensitization might have been higher. In the FIOH, late readings at D4, D5 or D6 had been done routinely [1], suggesting that their (higher) reported frequency of sensitization (1.9%) may be more realistic. However, it should be considered that far more occupational dermatitis patients are patch tested in the FIOH than in the IVDK [1], which may explain the higher proportion of positive reactions.

According to information from ERS formulators, tris-DMP is used at higher concentrations in ERS designed for colder ambient temperatures. Thus, it may be that the products used by the Central European patients patch tested in the IVDK contained less tris-DMP than the products used by the Finnish patients tested in the FIOH. Unfortunately, this is not always evident from the safety data sheets, since usually no specific concentration, but rather a concentration range, is declared for tris-DMP.

Summing up, we can confirm that tris-DMP is a relevant sensitizer in ERS. In order not to miss cases of sensitization, late readings at D4 and D7 should be done when patch testing with tris-DMP.

Table 1.

IVDK, 2017-2021, patch test reactions to tris-DMP 0.5% in petrolatum.

Reaction	Day 3		Day 3, 4 or 7	
	Count	Percent	Count	Percent
Negative	5412	99.0	5408	98.9
Doubtful	28	0.5	25	0.5
+	11	0.2	15	0.3
++	7	0.1	10	0.2
+++	3	0.1	3	0.1
Irritant	6	0.1	6	0.1
Total	5467	100.0	5467	100.0

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