

dominantly used in cosmetics and skin care products, for example diazolidinyl urea, DMDM hydantoin, imidazolidinyl urea, or quaternium 15. Others are more frequently used in technical products such as metalworking fluids, paints etc., for example benzylhemiformal, 1,6-dihydroxy-2,5-dioxahexane, 4,4-dimethyl-1,3-oxazolidine/3,4,4-trimethyl-1,3-oxazolidine (Bioban CS 1135[®]), 7-ethylbicyclooxazolidine (Bioban CS 1246[®]), *N,N'*-methylenebis-5-methyloxazolidine, or 1,3,5-tris(2-hydroxyethyl)-hexahydrotriazine (Grotan BK[®]) (1–4). Allergic reactions to formaldehyde releasers may be caused by sensitization to the whole molecule or to formaldehyde released from the substance (3, 4). Patch testing with formaldehyde is hampered by a relative poor reliability of the test preparation. False-negative as well as false-positive (irritant) reactions to formaldehyde 1% aqu. may occur (5). We report a case of formaldehyde allergy detected by positive patch tests to several formaldehyde releasers.

Case Report

A 39-year-old metalworker presented with a work-related dermatitis localized to the back of the hands and to the lower arms that troubled him for more than 1 year. He worked in a small company producing parts for the automotive industry. When he was drilling, turning, or grinding, he had contact with water-based metalworking fluids (wb MWFs), neat oils and other oils, and greases. At work, he wore protective gloves made of a polyamide liner with a polyurethane coating covering the palms and fingers, but not the backs of the hands (Camapur Comfort[®]; KCL, Eichenzell, Germany). Usually, he wore T-shirts or short-sleeved shirts leaving the lower arms uncovered. Hence, when working with MWF or handling metal parts that were contaminated with MWF, the backs of the hands and the lower arms were exposed, in particular, when piling up rods or arbours. His skin complaints cleared when he was on summer holidays but relapsed within 1 week after restarting work. He had no history of atopy.

The patient was patch tested with the German standard series, preservative series, metalworker series, and ointment base series as recommended

Positive patch test reactions to formaldehyde releasers indicating contact allergy to formaldehyde

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Johannes Geier¹, Holger Lessmann¹,
Simin Hellriegel² and Thomas Fuchs²

¹Information Network of Departments of Dermatology (IVDK), and ²Department of Dermatology, Allergy Unit, Georg August University, 37075 Göttingen, Germany

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Formaldehyde releasers are widely used biocides. Some of them are pre-

Table 1. Non-negative patch test reactions at D3 and D4^a

Number	Patch test substance		D3	D4
1	7-Ethylbicyclooxazolidine (Bioban CS 1246 [®]) (CAS 7747-35-5)	1% pet.	?	?
2	Benzylhemiformal (CAS 2749-70-4; 14548-60-8; 35445-70-6)	1% pet.	+	+
3	4,4-Dimethyl-1,3-oxazolidine/3,4,4-trimethyl-1,3-oxazolidine (Bioban CS 1135 [®]) (CAS 51200-87-4)	1% pet.	+	+
4	<i>N,N'</i> -Methylene-bis-5-methyl-oxazolidine (CAS 66204-44-2)	1% pet.	+	?
5	1,3,5-Tris(2-hydroxyethyl)-hexahydrotriazine (Grotan BK [®]) (CAS 4719-04-4)	1% pet.	?	?
6	Water-based MWF from the patient's workplace used	As is	?	?
7	Fresh MWF concentrate from the patient's workplace	5% aqu.	?	?
8	Neat oil from the patient's workplace	50% oo.	?	?
9	Dodecyl gallate	0.3% pet.	? ^b	? ^b

aqu., water; oo., olive oil; pet., petrolatum; MWF, metalworking fluid.

^aSubstances 1–5 are formaldehyde releasers.

^bReaction regarded as irritant.

by the German Contact Dermatitis Research Group (DKG) (6). Additionally, fresh and used wb MWF and 2 neat oils from his workplace were patch tested. Patch tests were performed and read according to DKG guidelines and recommendations for patch testing MWFs from the patients' workplaces (7, 8). Exposure time was 2 days. Finn[™] chambers on Scanpor[™] were used throughout. Non-negative patch test results at D3 and D4 are listed in Table 1. The patch test with formaldehyde 1% aqu. as a part of the standard series remained negative. Negative reactions also were obtained with the following formaldehyde releasers: 4-(2-nitrobutyl)-morpholine/4,4'-(2-ethyl-2-nitro-trimethylene)-dimorpholine (Bioban P 1487[®], CAS 37304-88-4); 2-bromo-2-nitropropane-1,3-diol (Bronopol[®], CAS 52-51-7); diazolidinyl urea (Germall II[®], CAS 78491-02-8); imidazolidinyl urea (Germall 115[®], CAS 39236-46-9); DMDM hydantoin (CAS 6440-58-0); and quaternium 15 (Dowicil 200[®], CAS 4080-31-3, 51229-78-8).

The manufacturer of the wb MWF used at the patient's workplace stated that it contained 2 formaldehyde releasers: 1,6-dihydroxy-1,5-dioxahexane (CAS 3586-55-8) and methylolurea (CAS 1000-82-4). Presently, we had none of these available for patch testing. The constellation of (i) work-related contact dermatitis, (ii) exposure to formaldehyde releasers – and hence to formaldehyde – at work, and (iii) positive patch tests to other formaldehyde releasers made us suspect a formaldehyde allergy in spite of the negative patch test. We repeated the patch test with formaldehyde 1% aqu., this time using a large Finn Chamber (12 mm diameter). The patient reacted with infil-

trated erythema and vesicles, that is a ++ reaction, at D3.

Discussion

In this case, the occupational exposure on the one hand and the location and time course of the dermatitis on the other hand clearly indicated an occupational cause of the skin disease. Irritant contact dermatitis because of contact with wb MWF is more frequently reported than allergic contact dermatitis. However, regarding the multitude of potential MWF allergens and the limited number of patch test substances, it seems likely that cases of contact allergy may be overlooked (9). Formaldehyde and formaldehyde releasers are well-known allergens in wb MWF. In a recent German study, sensitization to formaldehyde was found in 4.8% and to formaldehyde releasers in 0.7–3.8% when patch testing metalworkers with occupational contact dermatitis exposed to wb MWF (10). Formaldehyde releasers, such as Bioban CS 1135[®] or Bioban CS 1246[®] tend to elicit weak and poorly reproducible patch test reactions (11). Formaldehyde itself, is also a problematic patch test substance with poor reproducibility (5). As the reliability of the elicitation of an allergic reaction in sensitized individuals depends on the amount of allergen applied, formaldehyde has been patch tested at 2% aqu. in some countries, for example in North America (12), although there is an increased risk of irritant patch test reactions with this concentration (13). However, in a study conducted by the DKG, it could be shown that patch testing with formaldehyde 1% aqu. in large Finn Chambers does not

elicit significantly more positive test reactions, compared with patch testing with small Finn Chambers (14, 15).

In our case, positive test reactions to several formaldehyde releasers, to which the patient obviously was currently *not* exposed occupationally, lead us to assume a formaldehyde allergy, although the first patch test with formaldehyde was negative. The second test impressively confirmed a contact allergy to formaldehyde in this case, which, in our opinion, was responsible for the weak positive and doubtful reactions to several formaldehyde releasers. The reason for the false-negative reaction to formaldehyde in the first test remains unclear, and any explanation would be purely speculative.

Conclusion

In cases suspected formaldehyde allergy but the patch test with formaldehyde 1% aq. remains negative, repeating the formaldehyde patch test may help to clarify the diagnosis especially when unexplained reactions to formaldehyde releasers are observed.

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Address:

Johannes Geier
 IVDK, University of Göttingen
 von-Siebold-Str. 3
 37075 Göttingen
 Germany
 Tel: ++49 (0) 551 39 89 84
 Fax: ++49 (0) 551 39 60 95
 e-mail: jgeier@ivdk.org