

Occupational allergic contact dermatitis in a company manufacturing boards coated with isocyanate lacquer

MALIN FRICK, MARLÉNE ISAKSSON, BERT BJÖRKNER, MONICA HINDSÉN, ANN PONTÉN AND MAGNUS BRUZE

Department of Occupational and Environmental Dermatology, Malmö University Hospital, Malmö, Sweden

Over a short period of time, there was an outbreak of work-related skin lesions among workers at a company producing flooring laminate boards, after the introduction of a water-repellent lacquer based on diphenylmethane-4,4'-diisocyanate (MDI). In 5 workers, patch testing was performed with a standard series, an isocyanate series and work-environmental products when indicated. 3 of the workers were tested with the lacquer, and contact allergy was found with concurrent reactions to 4,4'-diaminodiphenylmethane (MDA). 1 of the 3 workers also showed a simultaneous reaction to MDI, whereas 1 showed a positive reaction to dicyclohexylmethane-4,4'-diisocyanate (HMDI). Of the 2 individuals not tested with the lacquer, 1 reacted to both MDI and MDA, whereas the other reacted to a soap used at work. In 3 of 4 cases, the isocyanate reactions appeared after D3. Occupational contact with isocyanates should not exclusively be focused upon respiratory hazards, as this report shows that skin contamination probably increases the risk of developing contact allergy to isocyanates and isocyanate-related substances. When aiming at diagnosing contact allergy to isocyanates, it is desirable to perform a late reading, as positive reactions appear late. MDA appears to be a good marker for isocyanate hypersensitivity.

Key words: CAS 101-68-8; CAS 101-77-9; diaminodiphenylmethane; dicyclohexylmethane-4,4'-diisocyanate; diphenylmethane-4,4'-diisocyanate; HMDI; isocyanate-based lacquer; MDA; MDI; occupational allergic contact dermatitis. © Blackwell Munksgaard, 2003.

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In a company producing laminate boards for flooring based upon phenol-formaldehyde resins, measures had been taken to make the joints between the different boards water-repellent. A wax and an oil had been tested without much success before the introduction of a 1-component polyurethane lacquer based on diphenylmethane-diisocyanate (MDI) monomers. The acronym MDI derives from the synonym methylenediphenyldiisocyanate, a name commonly used in industry. According to the material safety data sheet, the lacquer consisted of 80% polymeric MDI with the CAS no. 9016-87-9. This is a mixture of MDI monomers and related higher molecular weight species. Upon personal communication with the manufacturer, it came to hand that the lacquer consisted of approximately 20% each of the monomeric isomers diphenylmethane-2,4-diisocyanate (2,4-MDI) and diphenylmethane-4,4'-diisocyanate (4,4'-MDI). The latter is used in commercial test preparations for diagnosing aller-

gic contact dermatitis and, when previously described, the abbreviation MDI has been used as a synonym for the 4,4'-monomer. This terminology will also be used here from now on.

Inside a hood, the lacquer was sprayed automatically onto the tongue and groove of the boards, which were then picked up by hand and carried by a worker to a nearby bench where different measurements had to be taken manually. There were 20 machine operators working with this procedure in 5 different shifts. The lacquer was used for 2 months. During this time, there was an outbreak of dermatitis among the workers and 5 machine operators were referred to our department, because they developed work-related skin lesions that were suspected to be caused by the lacquer.

Case Reports

In all cases described below, the patients worked as operators by the machine where MDI-based

lacquer was sprayed onto the tongue and groove of the boards.

Case no. 1

A 54-year-old man, who had worked at the company for 15 years with no previous skin disease, had handled the isocyanate-lacquered boards for less than a month when he developed a papular eczema on the flexor forearms.

Case no. 2

A 43-year-old man had worked at the company for 15 years. 5 years ago, he had had a hand eczema with unknown aetiology that disappeared after 1 year. After less than a month of working with the isocyanate lacquer, he developed an eczema on his volar forearms. He had used long-sleeved shirts at work but told us that these became contaminated with the lacquer. He also suspected contamination from the lacquer when donning his protective rubber gloves.

Case no. 3

A 35-year-old man had worked at the company for 4 years. He had no previous skin disease. After a few weeks of working with the lacquer, he developed eczematous lesions on the volar forearms. He had worked in a T-shirt and carried the freshly sprayed boards against his volar forearms.

Case no. 4

A 54-year-old man had worked for 27 years at the company, the first 22 years as a repairman and the following 5 years as a janitor, smith and gardener, assignments thus permitting possible contact with resins based on phenol and formaldehyde as well as isocyanates. He had suffered from a hand eczema while operating a lathe in another company more than 27 years ago, but the exact cause was never elucidated, and afterwards, for several years, he had a hand eczema during the autumn months. Eventually, he developed a chronic, low-grade dermatitis on the hands and arms. 6 months before the introduction of the lacquer, a more active dermatitis appeared on the volar forearms and legs, and as the lesions improved during time off work, a work-relation was suspected.

Case no. 5

A 32-year-old woman had worked at the company for 11 years. 1½ months after the introduc-

tion of the lacquer, a papular eczema developed on her right volar forearm.

Materials and Methods

5 out of a total of 20 machine operators were referred to our department and were patch tested with our standard series and isocyanates series. The standard series used at our department at the time comprised the European standard series excluding clioquinol, N-isopropyl-N-phenyl-4-phenylenediamine, lanolin alcohol and supplemented with diazolidinyl urea, imidazolidinyl urea, thimerosal, methyltribromo glutaronitrile, phenoxyethanol, Euxyl K400, iodopropynyl butylcarbamate, DMDM hydantoin, gold sodium thiosulfate (1), palladium chloride, a resol resin based on phenol and formaldehyde (2), ethylenediamine dihydrochloride, lichen acid mix, tixocortol pivalate, hydrocortisone-17-butyrate, frullanolide, fusidic acid, caine mix II, tosylamide formaldehyde resin, a textile colour mix, Amerchol L-101 and an epoxy resin based on diglycidyl ether of bisphenol F. The isocyanates series used comprised the isocyanate series from Chemotechnique Diagnostics, Malmö, Sweden, supplemented with dicyclohexylmethane-4,4'-diisocyanate (Aldrich Chemical Company Inc, Milwaukee, USA), synonymous with hydrogenated MDI (HMDI) and its corresponding amine, dicyclohexylmethane-4,4'-diamine (Fluka Chemie GmbH, Buchs, Switzerland), synonymous with hydrogenated 4,4'-diaminodiphenylmethane (HMDA). The first 3 patients referred to us were also patch tested with the polyurethane lacquer used at the plant. When patient nos. 4 and 5 came for investigation, the lacquer used at the previous testing had cured and thus could not be tested. Furthermore, it was no longer in use at the company because of insufficient water-repellent properties, and new samples could not be obtained. Consequently, no controls were patch tested with the lacquer. Patient no. 4 was additionally tested to a liquid soap, which he used at work, as well as with its constituents. The Finn Chamber[®] (Epitest Ltd Oy, Tuusula, Finland) on Scanpor (Norgesplaster A/S, Vennesla, Norway) tape technique was used. Patch tests were removed after 2 days and read after 1 additional day, according to ICDRG criteria (3). All patch tests were read a 2nd time 7 days (D7) after the initial application of patches in all cases but for 2 patch test occasions. Patient no. 1 (Table 1) was read only on day 3 (D3) when he was tested with the polyurethane lacquer, as was patient no. 4 when tested with a soap and its constituents. In patient no. 5, an additional reading on day 10 (D10) was performed.

Table 1. Patch test reactions to substances in Chemotecnique Diagnostics' (Malmö, Sweden) isocyanate series supplemented with dicyclohexyl-4,4'-diisocyanate and 4,4'-diaminodicyclohexylmethane as well as work material

Isocyanate series and work material	Case no. 1		Case no. 2		Case no. 3		Case no. 4		Case no. 5		
	D3	D7	D3	D7	D3	D7	D3	D7	D3	D7	D10
Test occasion 1											
Toluene diisocyanate 2% pet.	-	-	-	-	-	-	-	-	-	-	-
Diphenylmethane-4,4'-diisocyanate 2% pet.	-	-	-	-	+	+	-	-	-	-	++
4,4'-Diaminodiphenylmethane 0.5% pet.	-	+++	-	++	+	++	-	-	-	-	+
Isophoronediiisocyanate 1% pet.	-	-	-	-	-	-	-	-	-	-	-
Isophorone diamine 0.1% pet.	-	-	-	-	-	-	-	-	-	-	-
1,6-Hexamethylenediiisocyanate 0.1% pet.	-	-	-	-	-	-	-	-	-	-	-
Dicyclohexyl-4,4'-diisocyanate 1% pet.	-	++	-	-	-	-	-	-	-	-	-
4,4'-Diaminodicyclohexylmethane 0.1% pet.	-	-	-	-	-	-	-	-	-	-	-
Polyurethane lacquer 2% pet.	NT	NT	-	++	++	++	NT	NT	NT	NT	NT
Polyurethane lacquer 0.2% pet.	NT	NT	-	-	-	-	NT	NT	NT	NT	NT
Test occasion 2*											
Polyurethane lacquer 2% pet.	++		NT		NT		NT		NT		
Polyurethane lacquer 0.2% pet.	-		NT		NT		NT		NT		
Soap 5% aq.	NT		NT		NT		++		NT		
Test occasion 3†											
Cocamide DEA 0.5% aq.	NT		NT		NT		+		NT		

NT = not tested.

*The application was performed at the 2nd reading of the 1st test occasion.

†Supplemented testing with only 1 reading on D3.

Results

4 of the 5 patients investigated reacted to 4,4'-diaminodiphenylmethane, synonymous with methylene dianiline (MDA). 1 of these 4 reacted to MDI and 1 to HMDI as well. In addition, the suspected lacquer elicited ++ reactions in all 3 patients who were tested with it. The 5th patient reacted to a hand cleanser used at the workplace and, when tested with its ingredients, contact allergy to cocamide DEA was found. In all cases except 1, the positive reactions to isocyanates and/or corresponding amines appeared late, i.e. negative on D3 but positive on D7. In 1 case, the positive reactions to MDI and MDA were not seen on D7 but were noted on D10.

Patch test reactions are shown in Table 1.

Discussion

Isocyanates, chemicals with the general formula $R-(N=C=O)_n$, are used in the manufacture of polyurethanes. There are both 1-component and 2-component isocyanate systems available on the market. In the latter case, polyurethane is formed when isocyanates react with the hydroxyl groups of multifunctional alcohols (polyols). Generally, the polyols are polyesters or polyethers with terminal OH-groups, or castor oil or tall oil with secondary OH-groups (4). In 1-component systems, environmental water serves as chain extender instead of polyols (5). By altering the kind of isocyanate or polyol used and by adding various additives such as blowing agents, bactericides,

catalysts and/or crosslinkers, one can get a wide range of products stretching from flexible and rigid foams to lacquers and adhesives.

Depending on the molecular structure, isocyanates can be divided into aromatic and aliphatic isocyanates. They can also be termed after the number of reactive groups, e.g. monoisocyanates, diisocyanates and multifunctional isocyanates. There are also prepolymerized isocyanates, which are produced by partial polymerization of mainly diisocyanates.

The adverse health effects from isocyanates on the respiratory tract are well known and a health hazard can arise even at low air concentrations of isocyanates. However, none of our patients had any respiratory problems. Delayed hypersensitivity and allergic contact dermatitis from isocyanates are less frequently reported. It has been suggested that the strict rules applied to isocyanate-associated work to avoid respiratory problems have contributed to minimizing contamination of the skin and thus also contact allergy to isocyanates (6). However, it was evident that the workers described here were contaminated with the MDI-based polyurethane lacquer used at the plant. According to the manufacturer, the lacquer cured just minutes after the spraying but, according to the operators, the lacquer took up to 14 h to dry. The company had equipped the operators with long-sleeved shirts and rubber gloves, and they were told to wash contaminated skin with soap and water or to use a prepacked wet tissue for cleaning the skin. Nevertheless, we found that 20% of the

workforce exposed to the isocyanate lacquer was struck with contact allergy to MDI or MDI-related compounds. The real figure might be even higher because not all operators were referred to us for investigation.

Malten wrote in 1984 (5) that 1-component systems, such as the lacquer in question, have such an avid reaction with water that they should polymerize within minutes to form long chains with urea links, which then are able to react with free isocyanates for cross-linking. In contact with moist skin, such a system ought to harden within a few minutes. During this time, it will also be able to react with other substances on or in the skin, such as alcohols, urea, lactic acid, amino acids and proteins. The latter reaction might generate complete antigens. However, Malten continues by stating that it is believed that the reactivity of 1-component lacquers is generally so high that macromolecular structures of film-like nature will be formed on top of the stratum corneum and that these films slow down the penetration (5). However, this is partly contradicted by the reports from the operators that the curing process seemed to be slow. This might also explain the high figure of contact allergy to the lacquer.

We have not found an explanation to the absence of the expected positive reactions to MDI in case nos. 1 and 2, which ought to be present concurrent with positive reactions to the MDI-based lacquer. Instead, these patients were positive to MDA, which can be formed from MDI by hydrolysis (Fig. 1). It is unlikely that the sole reactivity to MDA is due to MDA contamination of the MDI-based lacquer as, when MDI is in excess, it reacts immediately with any MDA formed, resulting in the formation of urea compounds (4). According to the manufacturer, the lacquer consisted mainly of prepolymerized MDI but also 2 monomeric isomers. These were 4,4'-MDI and 2,4'-MDI, and the lacquer was said to contain approximately 20% of each monomer. The patch test substance used was a commercial product (Chemotechnique Diagnostics) which, according to the labelling, consists of pure 4,4'-MDI. Therefore, it might be possible that the positive reactions to the lacquer are

because of the 2,4'-isomer, at least in case nos. 1 and 2 (Table 1). There is also a possibility that the discrepancy between positive reactions to the lacquer and the absence of positive reactions to MDI is explained by contact allergy to an unknown sensitizer. Another explanation might be that the composition of the lacquer enhances the penetration, and thus the bioavailability of MDI in the skin, making the MDI-containing lacquer more reactive than the petrolatum preparation with MDI. We did not analyse the commercial test preparation or the lacquer with regard to stability and/or impurities. Therefore, it is possible that the composition of the commercial patch test preparation as well as the lacquer might be different from that expected. However, it seems that testing only with commercial test preparations of MDI is inadequate when aiming at diagnosing occupational allergic contact dermatitis from MDI-containing products and that it is advisable to test also with the products themselves.

Simultaneous patch test reactions to MDI and MDA, as observed in case nos. 3 and 5, have been reported before. The suggested explanation is either cross-reactivity or an exclusive sensitization to MDA; in the latter case, the patch test reaction to MDI is not directed to MDI itself but to MDA formed when MDI reacts with water, e.g. on or in moist skin (4, 7–10). Theoretically, a 3rd explanation exists wherein both MDI and MDA being primary sensitizers. Recently, Goossens et al. (11) reported on 22 cases diagnosed with occupation-related contact dermatitis from isocyanates and/or polyurethane products and, of these, there were 10 patients with allergic contact dermatitis from isocyanates showing concurrent reactions to MDA. In 5 of these patients, the positive isocyanate was MDI, whereas in the other 5 cases the exact character of the positive isocyanate product was not established. There were also 9 patients who only reacted to MDA and not to the isocyanates to which they had been exposed. Goossens et al. as well as Estlander et al. suggest that MDA might be an important marker for isocyanate hypersensitivity (4, 11). This is in accordance with our own findings.

MDA has several other fields of application and is used as hardener in epoxy systems, as an antioxidant in rubber, a catalyst in polyurethane systems as well as in the manufacturing of synthetic fibers within the textile industry (12). However, it seems highly unlikely that the concurrent reactions to MDI and MDA in our case are because of a separate sensitization.

Patient no. 1 reacted to HMDI, although he, to our knowledge, had not been in contact with

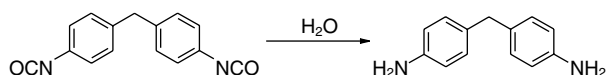


Fig. 1. Hydrolysis of diphenylmethane-4,4'-diisocyanate (MDI) into diaminodiphenylmethane (MDA) on reaction with water.

HMDI before. Concurrent positive reactions to HMDI and MDA, as shown in case no. 1, have been described earlier. In 1976, Emmet (12) reported on an outbreak of dermatitis among at least 8 out of 65 employees who were exposed to both HMDI and MDA at a polyurethane moulding plant. 2 workers were patch tested, and they both showed positive reactions to HMDI as well as to MDA, which was used as a catalyst in the process. In 1977, Malten (13) reported on a chemical engineer working with HMDI. On patch testing, he showed simultaneous reactions to HMDI and MDA, although he had had no known prior contact with MDA. Malten suggested this pattern to be due to cross-reactivity. Furthermore, in a very recent report (14) on an outbreak of dermatitis amongst workers at a company manufacturing medical equipment, 13 cases of contact allergy to HMDI present in a glue were described. 5 of these reacted to the corresponding amine, HMDA, and 5 also to MDA. In 2 of these cases, the reactions to HMDI, HMDA and MDA were simultaneous.

Patient no. 5 showed no positive reactions at the readings on D3 and D7. However, 10 days after the application of the patches, she returned because of an itchy sensation on her back. Contact allergy to MDI and MDA was confirmed, implying that she was also sensitized to the lacquer. As shown in Table 1, there is a late appearance of patch test reactions to MDI, MDA and/or HMDI in all cases except no. 3. Usually, such late-appearing reactions as shown in patient no. 5 are considered to be caused by active sensitization, i.e. induction of sensitization because of patch testing. However, it has been shown earlier that several substances, such as gold and corticosteroids, have a pattern of late-appearing reactions beyond D7 without this being a sign of sensitization (15, 16). This could also be true for the case presented here, and it is supported by the fact that most of the positive reactions to MDI, MDA and/or HMDI were seen for the first time on D7. It seems that the ordinary reading on D3/D4 is insufficient when diagnosing contact allergy to substances such as those described above. We would have missed 75% of the contact allergies to MDI and MDA, if a late reading had not been performed. Therefore, it is advisable that isocyanate patch tests are also read on D7 and patients should be advised to make contact with the clinic, if any reactions appear after they have left the clinic.

Patient no. 4 did not react to any isocyanate. However, his dermatitis was aggravated while he was working, and he was shown to be contact allergic to a soap that he used at work.

Additional testing with the constituents of the soap disclosed a contact allergy to an emulsifier, cocamide DEA.

When working with isocyanates, attention should be focused not only on the respiratory hazards but also on the risk of allergic contact dermatitis. Poor hygienic conditions as being responsible for contact allergies amongst workers using isocyanates have been pointed out before (12) as well as the importance of good hand protection (4). Including patient no. 4, 25% of the work force at the company in question had occupational contact dermatitis. Therefore, it is of importance to avoid skin contamination from isocyanates in order to minimize the risk of sensitization and the development of allergic contact dermatitis.

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Address:

Malin Frick

*Department of Occupational and Environmental Dermatology
Malmö University Hospital*

S-205 02 Malmö

Sweden

Tel: +46 40 33 78 24

Fax: +46 40 33 62 13

e-mail: malin.frick@skane.se