

Rapid Development of Allergic Contact Dermatitis from Dicyclohexylmethane-4,4'-Diisocyanate

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Isocyanates are widely used in the manufacturing of rigid and flexible foams, fibers, and coatings such as paints, varnishes, and elastomers but are rarely reported as contact sensitizers. The aliphatic diisocyanate dicyclohexylmethane-4,4'-diisocyanate (DMDI) is known to be a strong cutaneous sensitizer. We report a 27-year-old woman who developed a severe eczematous eruption on the arms, trunk, and abdomen within 2 weeks of employment at a company using the product Chem-Dec 808 isocyanate (containing 40–70% weight per weight DMDI). Patch testing was performed with the North American screening series, an isocyanate series, and 1% Chem-Dec 808 isocyanate. At day 7, a +++ reaction to Chem-Dec 808 isocyanate and a ++ reaction to the aromatic isocyanate diphenylmethane-4,4'-diisocyanate were observed. DMDI has strong sensitizing potential and requires rigorous safety monitoring in the workplace.

ISOCYANATES are low-molecular-weight compounds with reactive $-N=C=O$ groups, which make them particularly useful as industrial cross-linking agents. One of the most important applications of isocyanates is in the production of polyurethane. Polyurethanes are resins formed by the reaction of diisocyanates with multifunctional alcohols such as polyesters and polyethers. Polyurethanes are used in a wide range of products, including paints, lacquers, adhesives, coatings, foams, and synthetic rubber.^{1,2} The use of polyurethanes in industry has increased in the last 25 years.³

Isocyanates can be classified as either aromatic or aliphatic. The aromatic isocyanates are less expensive and make up the majority of isocyanates in use today. However, aliphatic isocyanates are often used in the production of polyurethanes for coatings because aromatic isocyanates are subject to oxidative discoloration upon exposure to light and moisture.¹ Common diisocyanates include the aromatic isocyanates toluene diisocyanate (TDI), diphenylmethane-4,4'-diisocyanate (MDI), and isophorone diisocyanate (IPDI), and the aliphatic diiso-

cyanate 1,6-hexamethylene diisocyanate (HDI). We report on a worker who developed allergic contact dermatitis from dicyclohexylmethane-4,4'-diisocyanate (DMDI), an uncommonly used cyclic aliphatic diisocyanate.

Case Report

A 27-year-old woman developed a severe eczematous eruption within 4 days of beginning employment as a nameplate laminator in the company's "doming room." The eruption began on the arms (Fig 1). Prior to assuming the role of nameplate laminator, she had worked for 10 days as a quality control inspector in the same facility. Her work in the doming room required her to use a penlike device to apply a polyurethane resin coating to nameplates placed upon a board at waist level. Chem-Dec 808 isocyanate (Chemque Inc., Rexdale, Ontario, Canada), a urethane prepolymer containing 40 to 70% weight per weight (w/w) DMDI, was mixed with Chem-Dec polyol, and a foot pedal was used to control delivery of the mixture into the penlike device and subsequently onto the nameplates. To apply the coating to distant nameplates, the worker had to reach across several nameplates, which would often result in the resin coming into contact with her arms. Her clothing, especially around the waist, would frequently become coated with the material. Finished products were subsequently taken into a room with a higher temperature to allow them to cure. The worker's sole protective equipment was a pair of gloves that were worn only during the doming process and that extended only to her wrists. She worked in the self-contained doming room without an apron, goggles, or a respirator.

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DECKER



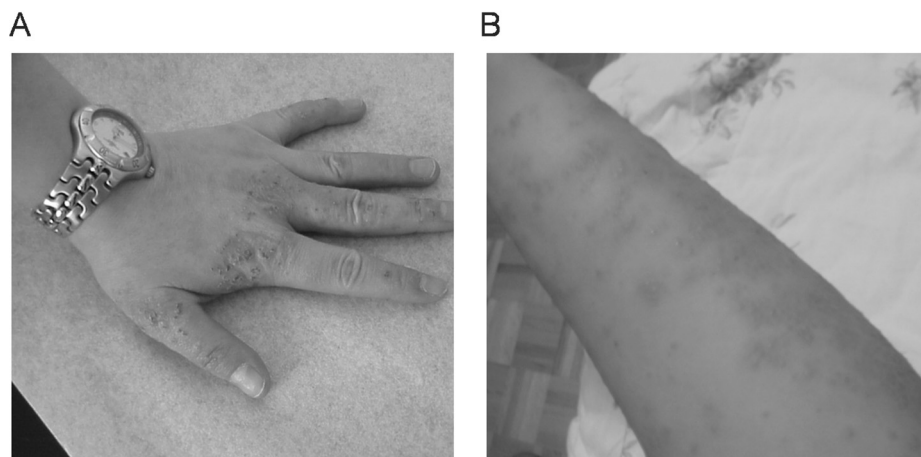


Figure 1. Eczematous eruptions on dorsal hand (A) and forearm (B) after exposure to Chem-Dec 808 containing 40 to 70% dicyclohexylmethane-4,4'-diisocyanate.

She wore a long-sleeved shirt, but it would become covered with the polyurethane coating on the sleeves and abdominal area. The ventilation in the facility was poor, and the isocyanate/polyol mixture could easily be smelled.

The worker saw her family physician 2 days after the eruption began and was treated with the antihistamine desloratadine as well as with amcinonide lotion. She was advised to take a 1-week leave from work. Over the following 2 days, the eruption increased on her face, abdomen, and thighs, and she sought medical advice from another physician, who prescribed a 4-day course of prednisone (50 mg by mouth [PO] once daily), hydroxyzine (50 mg PO every 6 hours as needed [prn]), and betamethasone valerate 0.1% ointment. Two days thereafter and 6 days after the initial eruption began, she presented to the emergency department with erythema and pruritus affecting her face, ears, arms, abdomen, and legs. Vesicles were also present on the arms. The worker was admitted to the hospital for 2 days and treated with intravenous corticosteroids and diphenhydramine. There were no respiratory symptoms at any time, although mild nasal congestion was noted. She was discharged on a tapering course of prednisone (50 mg PO once daily and tapering 5 mg every 2 days).

The worker was patch-tested with the North American Standard Screening Series (Chemotechnique Diagnostics, Malmö, Sweden), an isocyanate series (Chemotechnique), and Chem-Dec 808 isocyanate 1% in petrolatum in IQ-Ultra Chambers (Chemotechnique Laboratories, Inc., Rexdale, Ontario, Canada) affixed with Scanpor tape (Norgesplaster A/S, Vennesla, Norway). A 1% concentration was chosen on the basis of recommendations in the literature.⁴ Reactions were read according to International Contact Dermatitis Research Group (ICDRG) guidelines.⁵ At day 7, a +++ reaction to Chem-Dec 808 isocyanate 1%

in petrolatum and a ++ reaction to the aromatic isocyanate MDI 0.1% in petrolatum were observed (Fig 2, Table 1). A healthy control individual had no reaction at 48 and 96 hours to patch tests with Chem-Dec 808 isocyanate 0.1%, 0.5%, 1%, or 2% in petrolatum and remained negative over a 2-week follow-up period. It was concluded that an allergic contact dermatitis from the workplace isocyanate product had developed. With the exception of some resolving hyperpigmentation on the thighs and abdomen, the worker's skin remained clear following a change in occupation.

Discussion

The worker developed an allergic contact dermatitis from Chem-Dec 808 isocyanate used in her workplace. The reaction was widespread but favored the areas where the isocyanate was in contact, including the forearms (where there was direct contact) and the trunk and waist (where there was transfer via clothing). Although the manufacturer would not release the complete ingredients of Chem-Dec 808 isocyanate, the primary ingredient is known to be DMDI. Additional allergens in Chem-Dec 808 isocyanate besides isocyanates may have contributed to the worker's positive patch-test reaction to Chem-Dec 808 isocyanate. However, her lack of reaction to other allergens when patch-tested with the North American standard tray and her positive patch-test reaction to the isocyanate MDI make this less likely.

DMDI is a very strong sensitizing agent in humans. Cases of confirmed or suspected contact allergy have been reported after intervals of less than 1 week.⁶⁻⁸ Frick and colleagues reported on a group of 16 out of 100 workers referred for patch testing to assess for allergic contact dermatitis from DMDI present in a workplace glue.⁹ In a

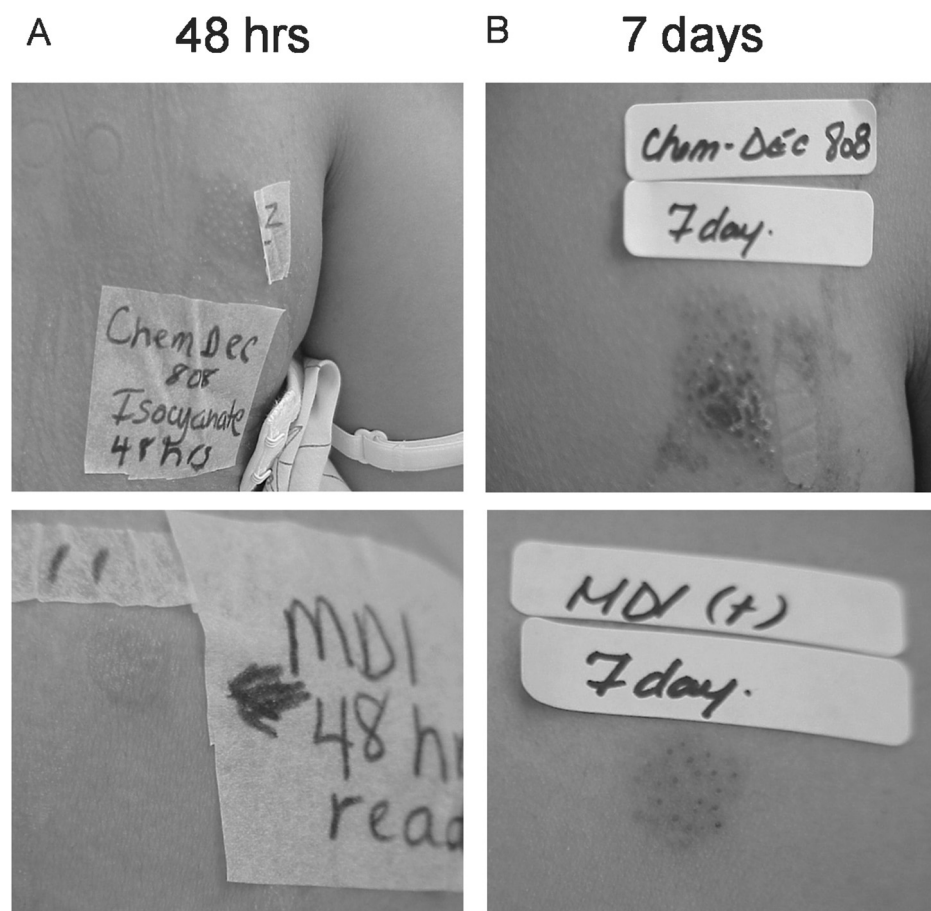


Figure 2. Patch-test reactions to Chem-Dec 808 1% in petrolatum and to diphenylmethane-4,4'-diisocyanate (MDI) 0.1% in petrolatum. A, Results at 48 hours. B, Results at 7 days.

manner similar to the rapid onset of disease in our patient, 8 of these 16 patients developed an eczematous reaction within 6 weeks of starting work at the company. Patch testing was performed with a standard series, an isocyanate series, and the workplace isocyanate glue at 2.0% and 0.2% in petrolatum. There were 13 positive patch-test reactions to DMDI 0.1% and 1.0%, 9 reactions to HDI, and 4 reactions to IPDI. These are all aliphatic isocyanates, and none of the patients had reactions to the aromatic isocyanate MDI. Our patient had a positive reaction to the aliphatic isocyanate DMDI as well as an uncommonly

reported cross-reaction to the aromatic isocyanate MDI (Fig 3). To the best of our knowledge, the worker had had no previous exposure to MDI. Interestingly, Kerre recently reported on a 17-year-old female who developed allergic contact dermatitis from DMDI used in a workplace polyurethane system.⁸ The patient had a positive patch-test reaction to a compound containing DMDI and also had a cross-reaction to MDI 2% in petrolatum.

Emmet reported an outbreak of dermatitis among 8 of 65 employees exposed to both DMDI and diaminodiphenylmethane (MDA) at a polyurethane molding plant.¹⁰

Table 1. Patch-Test Results

Patch-Test Allergen*	Reading at 48 h	Reading at Day 7
Diphenylmethane-4,4'-diisocyanate (MDI) 0.1%	+	++
1,6-Hexamethylene diisocyanate (HDI) 0.1%	—	—
Toluene diisocyanate (TDI) 0.5%	—	—
Isophoronediamine (IPD) 0.5%	—	—
Chem-Dec 808 (40–70% w/w DMDI) 1%	++	+++

DMDI = dicyclohexylmethane-4,4'-diisocyanate; w/w = weight per weight.

*In petrolatum.

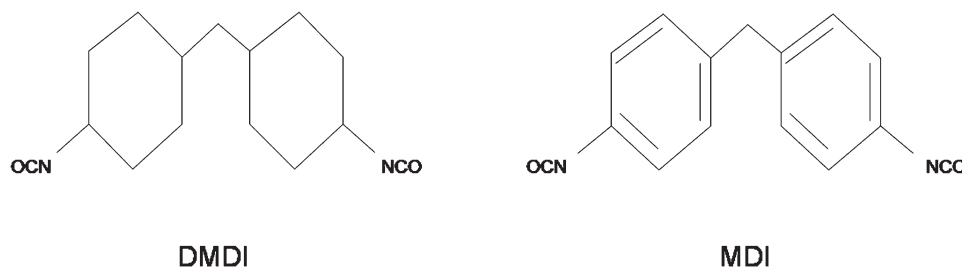


Figure 3. Chemical structures of the aliphatic diisocyanate dicyclohexylmethane-4,4'-diisocyanate (DMDI) (*left*) and the aromatic diisocyanate diphenylmethane-4,4'-diisocyanate (MDI) (*right*). The worker had a positive patch-test reaction to DMDI and a positive reaction to MDI.

Only two workers were patch-tested, but both showed positive reactions to DMDI 1% in petrolatum and to MDA. Malten reported on a patient exposed to DMDI who had a positive patch-test reaction to DMDI 1% in petrolatum and cross-reacted to MDA.¹¹

The adverse respiratory health effects of isocyanates are well recognized. It has been suggested that, in contrast to the strong skin-sensitizing potential of DMDI, aliphatic diisocyanates such as DMDI are weak respiratory sensitizers.¹⁰ DMDI has a low vapor pressure, and airborne exposure is unlikely to occur unless the product is heated.¹² In our case, airborne exposure may have occurred, given that the product was cured at an elevated temperature. In addition, the worker had evidence of mild nasal turbinate congestion, suggesting DMDI-related irritation of airway mucous membranes. The worker clearly had numerous sources of skin contamination, but isolated airway exposure to isocyanates may lead to skin sensitization.¹² We cannot conclude whether the worker in our case was initially sensitized via a respiratory route or a dermal route. Animal models have shown that the ability to induce contact hypersensitivity after inhalation exposure depends on the concentration of DMDI in the inhaled air; below a certain threshold, contact sensitization did not occur.¹³ The poor ventilation in the workplace may have added to the potential for sensitization via a respiratory route as well as via a cutaneous route. Of note, the company employed 15 other workers. Three of our patient's co-workers were similarly affected with skin disease, and three others quit their jobs on account of skin problems. As a consequence of our patient's case, the employer was subsequently ordered by a government labor board to improve the ventilation system in the doming room.

Conclusion

Isocyanates are an important cause of occupational contact dermatitis. Although isocyanate contact hypersensitivity to dicyclohexylmethane-4,4'-diisocyanate (DMDI) is not commonly reported, the increasing industrial use of isocyanates

may increase the incidence.¹² Some isocyanates, including DMDI, are not routinely available on isocyanate patch test series and may need to be added in the future. This case report highlights the importance of patch-testing with actual isocyanates used in the workplace.

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