

Several cases of work-related allergic contact dermatitis caused by isocyanates at a company manufacturing heat exchangers

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Summary

Background. A 43-year-old woman was referred by her occupational health service with suspected occupational contact dermatitis. In connection with the investigation, a workplace visit was undertaken at her company, which used an adhesive based on pre-polymeric diphenylmethane diisocyanate in one of its units. During the visit, we became aware of six other employees with skin problems who were then referred to our department for investigation.

Objectives. To investigate the seven employees complaining about skin problems.

Methods. Seven employees were patch tested with a baseline series, an isocyanate series, and a series with work material.

Results. Five of seven patients had occupational contact allergy. Four reacted to isocyanate-related test preparations, and one to a cleanser used at the workplace.

Conclusions. Workplace visits constitute an important part of an occupational investigation, as they might give a broader picture of the problems at a company. In this case, it was found that 5 of 100 employees currently had or had previously had occupation-related skin problems. Owing to 'healthy worker selection', some of these patients might have been missed if we had not performed a full-scale workplace visit.

Key words: 4,4'-diphenylmethane diisocyanate; contact allergy; occupational; pre-polymeric diphenylmethane diisocyanate; workplace visit.

The workplace visit is an important asset in the investigation of occupational contact dermatitis. It provides a better understanding of how the patient works, and an evaluation of exposure to potential allergens and/or irritants. A visit also provides an opportunity to meet the employer, union representative, and occupational health service, in order to discuss the possibility of transferring employees with skin disease to

another post where contact with, for example, irritants or known allergens is minimized. Quite often, a workplace visit, often initiated because of 1 patient, leads to the investigation of other employees. Here, we report such an example at a factory where several employees were found to have occupational contact dermatitis caused by pre-polymeric diphenylmethane diisocyanate (PMDI).

In January 2010, a 43-year-old woman was referred by her occupational health service with suspected occupational contact dermatitis. The referring physician suspected that other employees had similar problems, and a workplace visit was therefore conducted in which two dermatologists and two chemists from the Department of Occupational and Environmental Dermatology, Skåne University Hospital, as well as the physician from the occupational health service, participated. Six other

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employees were identified as having skin problems, and were referred to our department for further investigation.

The company in question produces epoxy-lacquered aluminium heat exchangers. The aluminium sheets used in the production are purchased precoated, so there is no exposure to uncured epoxy at the workplace. In the production of some of the heat exchangers, an assembly step using polyurethane (PUR) adhesive is required. The adhesive used at the time of the investigation was based on PMDI, and was a mixture containing mainly 4,4'-diphenylmethane diisocyanate (4,4'-MDI), and also oligomers with predominantly three to six aromatic rings, but also smaller amounts of oligomers containing a higher number of rings (1). Depending on the characteristics required in the finished product, the isocyanate part was cured with one of two polyols. They differed slightly in composition, containing the same ingredients but in different concentrations; one of them also contained a filler. Cured PUR adhesive was sometimes processed by cutting and drilling, resulting in a lot of dust in the workplace.

Case 1

A 43-year-old woman had worked at the company since 2002, mainly assembling heat exchangers, using silicone adhesive based on vinyltrimethoxysilane. She had had no skin problems until a couple of years prior to our visit, when she was assigned to work at the unit using PUR adhesive. On her first day at work, she developed an itchy rash on the volar forearms and in the face. She was transferred back to her old unit, and after about a week the rash had disappeared. In early January 2010, she again worked in the area using PUR, and there was a recurrence of the rash, which appeared on the same day and lasted for about a week. She also experienced rhinitis, and was referred elsewhere for this.

Case 2

A 32-year-old woman had worked in the area using PUR adhesive since her employment in 2007. Six months after she had started at the company, she developed an itchy dermatitis localized to the hands, backs of the thighs, arms, chest, and face. Strangely, the dermatitis appeared only on the half of her face where she suffered from temporal arteritis. She had had several periods of sick leave because of temporal arteritis and skin problems. On examination, itchy lesions were observed on her hands. She also reported that her skin problems improved during sick leave and when she was off work.

Case 3

A 41-year-old woman had worked at the company since 2006, when she started working with PUR adhesive. After a short period, she developed an itchy rash on the face, neck, and parts of the arms. The rash disappeared after a day. Four months after she started to work at the company she suffered from shortness of breath, and had to seek medical care. She received asthma medication, and was transferred to another unit at the factory, after which her symptoms disappeared. When she came to the Department of Occupational and Environmental Dermatology, she had itchy lesions bilaterally on the dorsal forearms, with a size of approximately $10 \times 15 \text{ cm}^2$. Discrete hyperpigmentation was noted, along with some papules.

Case 4

A 48-year-old woman had worked on and off with PUR adhesive since she started working at the company in 2005. About a month after she started working, she experienced pruritus on the chin and cheeks that, after about a day, developed into erythematous dermatitis. In connection with working with PUR adhesive, she periodically developed dermatitis on the volar aspects of the forearms. The lesions would resolve a couple of days to a week after she stopped working with PUR.

Case 5

A 52-year-old woman worked daily with PUR adhesive during her first 6 months at the company in 2005, but now only worked occasionally in the area using PUR. She did not have any skin problems when she was examined, but reported that, when working with PUR, she used to develop itchy skin lesions on her chest, stomach, arms, and face.

Case 6

A 43-year-old woman started at the company in 2004. For a couple of months in 2006/2007, she worked at the PUR unit. She developed itching skin lesions on the hands, arms and face that remained for a couple of days. She also experienced shortness of breath. She was transferred to another unit, after which her symptoms disappeared.

Case 7

A 48-year-old woman started working at the company in 2004, and in 2006 was found to have contact allergy to 4,4'-MDI and its corresponding amine 4,4'-diaminodiphenylmethane (4,4'-MDA) when investigated

at the Department of Occupational and Environmental Dermatology. After being diagnosed with occupational contact dermatitis, she was transferred to another department. However, at the previously mentioned workplace visit, she reported that she still experienced problems when she was in the vicinity of the PUR area. In addition to skin problems, she described symptoms of rhino-conjunctivitis. She also reported that she experienced skin problems when in contact with rubber materials, as well as when working with a lubricant used in the assembly of some of the heat exchangers. As she was exposed to work materials that had not been tested in the previous investigation, she was included in the study and retested.

Materials and Methods

Patch testing was performed with a supplemented baseline series, an isocyanate series (Chemotechnique Diagnostics, Vellinge, Sweden) supplemented with PMDI and the cycloaliphatic isocyanate 4,4'-dicyclohexylmethane diisocyanate (DMDI), and a series composed of samples from the work environment (Table 1). Twenty milligrams of each patch test preparation was applied on 8 mm Finn Chambers® (Allerderm, Phoenix, AZ, USA) on Scanpor® tape (Norgesplaster A/S, Vennesla, Norway) and placed on the upper back for 2 days. Readings were performed on day 3 or day 4, as well as on day 7 (2, 3).

Results

Positive reactions in the patch tests are shown in Table 2. Five of the seven patients had occupationally related

contact allergy. Three patients reacted to the adhesive and/or 4,4'-MDI and/or PMDI (cases 1, 5, and 7), one reacted to 4,4'-MDA (case 4), and one reacted to a liquid soap (case 6) used at the company.

Discussion

Four of the investigated patients had isocyanate-related contact allergy. Three reacted to the adhesive used at the workplace (cases 1, 5, and 7). One of the four patients (case 4) reacted only to 4,4'-MDA, which is considered to be an important marker for isocyanate contact allergy (4). Therefore, the allergy was considered to be occupationally related. However, it should be noted that this patient also had a simultaneous reaction to *p*-phenylenediamine, and it is possible that the positive reaction to 4,4'-MDA was the result of cross-reactivity with *p*-phenylenediamine (5, 6). She reported that she coloured her hair on a regular basis, but had never experienced any discomfort in this connection. Two patients (cases 5 and 7) also reacted to DMDI. According to the company, this isocyanate had never been used. Concurrent reactions to DMDI and 4,4'-MDI and/or PMDI and/or 4,4'-MDA have been reported previously (7–10). Often, there has been no explanation for these concurrent reactions. The differences in chemical structure between 4,4'-MDI and DMDI do not suggest cross-reactivity, but cross-reaction between the substances cannot be excluded.

This investigation shows that aimed testing with patients' own work material is preferable. One of the patients investigated (case 1; Table 2) would not have been detected if testing had been performed with the isocyanate series only. She reacted to PMDI and the PUR adhesive, but not to 4,4'-MDI and 4,4'-MDA. In our experience, patch testing with 4,4'-MDI can be difficult, as there can be significant individual variation in test response from one test occasion to another, and we have seen a case where the same patient showed both an early reaction, a late reaction and no reaction at all to 4,4'-MDI when tested on different occasions (11). Patch testing with 4,4'-MDI might also give false-negative reactions, as these preparations are unstable (12). No retesting with 4,4'-MDI and 4,4'-MDA or analysis of the preparations was performed, and therefore no conclusions can be drawn on whether the patch test result reflects a variation in test response, false-negative reactions because of the content being too low, or specific contact allergy to oligomers of PMDI. Furthermore, aimed testing with work material also detected what was suspected to be occupationally related contact allergy to a soap used at the workplace (case 6). Such exposure might be a neglected cause of occupationally related contact

Table 1. Work material series

Work material	Concentration and vehicle (wt/wt)
1. Isocyanate part of PUR adhesive	1% pet.
2. Isocyanate part of PUR adhesive	0.1% pet.
3. Polyol 1 part of PUR adhesive	3% pet.
4. Polyol 1 part of PUR adhesive	0.3% pet.
5. Polyol 2 part of PUR adhesive	3% pet.
6. Polyol 2 part of PUR adhesive	0.3% pet.
7. Silicone-based adhesive	10% pet.
8. Silicone-based adhesive	1% pet.
9. Lubricant	10% pet.
10. Lubricant	1% pet.
11. Dust	40% pet.
12. Cleanser 1	5% aqua
13. Cleanser 1	0.5% aqua
14. Cleanser 2	5% aqua
15. Cleanser 2	0.5% aqua

PUR, polyurethane.

Table 2. Positive patch test reactions seen in the 7 investigated patients

Case	Positive reactions to substances in the isocyanate and/or work material series																
	TDI							Isocyanate part of adhesive 1% pet. (wt/wt)							Isocyanate part of adhesive 0.1% pet. (wt/wt)		
	D3	D7	D3	D7	D3	D7	D3	D7	D3	D7	D3	D7	D3	D7	D3	D7	Liquid cleanser
1	-	-	-	?	?	?	-	-	+	+	?	-	-	-	?	-	-
2	-	-	-	?	-	-	-	-	-	?	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4	-	-	-	-	?	+	-	-	-	-	-	-	-	-	-	-	-
5	?	+	+	?	?	+	+	?	?	+	?	-	-	?	-	-	-
6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-
7	-	-	+++	++	+++	++	?	++	++	++	++	-	-	++	-	-	-

DMDI, 4,4'-dicyclohexylmethane diisocyanate 0.5% pet.; 4,4'-MDA, 4,4'-diaminodiphenylmethane 0.5% pet. (wt/wt); 4,4'-MDI, 4,4'-diphenylmethane diisocyanate 2% pet. (wt/wt); PMDI, polymeric MDI 1% pet.; TDI, toluene diisocyanate 2% pet. (wt/wt).

*Rhinitis.

†Shortness of breath.

‡Rhino-conjunctivitis.

Positive patch test reactions to other tested substances.

Nickel sulfate; diazolidinyl urea; gold sodium thiosulfate; sodium tetrachloropalladate; palladium chloride; formaldehyde

Cobalt chloride; sodium tetrachloropalladate; *Myroxy/on pereirae*; sorbitan sesquileate

—

p-Phenylenediamine; lichen acid mix; methylolbromo glutaronitrile

—

Gold sodium thiosulfate

Nickel sulfate; sodium tetrachloropalladate; palladium chloride; formaldehyde

Yes*

No

Yes†

No

No

Yes†

Yes‡

dermatitis. When 5 patients at a company manufacturing flooring boards coated with an isocyanate lacquer were investigated, another patient was detected who, just like the one reported here, was allergic only to the soap used at the workplace (9). In the present case, no control testing was performed, and therefore it was never fully established whether it was an allergic or an irritant reaction. However, the morphology of the reaction agreed with that of an allergic one.

According to the company, the PUR adhesive was not regularly used in the production process, but only on about 1 day every fifth week. However, at the workplace visit, employees claimed that they had been assembling heat exchangers using PUR adhesive every day for over a week, and that they did so more often than 1 day every fifth week. Among the ~100 employees at the factory, there were three working regularly with PUR and another four who occasionally worked with it. Communication with the employees gave the impression that there was a 'healthy worker selection' in the area handling PUR, as several persons claimed that they had worked in that area earlier but had been transferred because of skin problems. At the workplace visit, it was noted that the handling of the PUR adhesive was performed in a very manual manner. One drum containing isocyanate and one drum containing polyol were connected through hoses to a dispenser. The dispenser automatically mixed the two components, and the PUR mixture was poured out of the mixing tap onto the heat exchangers for gluing. However, there was a need to check that the dispenser had correctly mixed the two components; this was performed by pouring the mixture into a plastic cup, which was then weighed. Also, the mixing tap needed cleaning during the work day, and the PUR mixture was removed regularly with paper towels. The workers used thin vinyl gloves when conducting these operations. When the work operations were observed, it was evident that there was

a risk of skin exposure, and also that the work area was contaminated with PUR adhesive.

After an inspection by the Swedish work environment authority, the company implemented thorough measures to minimize the amount of isocyanate in the air by performing all isocyanate work in a closed compartment and by installing fume extraction equipment in this compartment. However, less care had been taken to minimize skin exposure. When representatives from the Department of Occupational and Environmental Dermatology visit companies handling isocyanates, there is generally an awareness of air levels of isocyanates, but the possibility of skin exposure is neglected (10). Recently, however, concerns have arisen that skin exposure might be of importance for the induction of respiratory diseases (13), and it is therefore of even more importance to alert companies working with isocyanates about the skin aspects of isocyanate exposure.

Conclusion

The workplace visit remains an important part of an occupational investigation, as it might give a broader picture of the problems at a company. In this case, it was found that 5 of 100 employees currently had or had previously had occupation-related skin problems. Owing to 'healthy worker selection', some of these patients might have been missed if inspection had not involved those areas at the company that did not handle isocyanates. There seems to be a need to alert companies handling isocyanates that monitoring of isocyanates in the air is not sufficient, and that skin exposure also needs to be taken into account.

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