

Patch Testing Custom Isocyanate Materials From the Workplace

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Background: Patch testing with standard trays of commercially available allergens is the current practice for investigating suspected cases of isocyanate-induced allergic contact dermatitis (ACD). In some facilities, these standard trays are further supplemented with custom preparations of isocyanate-containing materials.

Objective: The aim was to determine whether added value exists in patch testing patients to custom isocyanate preparations in suspected cases of ACD.

Methods: We performed a retrospective analysis of 11 patients referred to our specialty clinic between January 2003 and March 2011 for suspected patients of ACD who had custom testing with isocyanate materials from their workplace. In addition to standard trays of allergens, all patients were patch tested with custom isocyanate materials from their workplaces.

Results: Three (27%) of 11 patients showed an added value in testing to custom isocyanate allergens. Of these 3 patients, one had a reaction that reinforced positive reactions to the standard isocyanate tray, but the other 2 (18%) had no reactions to any of the commercially available allergens.

Conclusions: Because of the high proportion of reactions (27%), we recommend the use of custom testing to workplace isocyanate products as a supplement to current standard patch testing procedures.

BACKGROUND

Isocyanates are organic compounds containing one or more reactive $-N = C = O$ groups. They are mostly used in the production of polyurethanes when combined with other compounds such as polyacrylates, polyethers, and polyesters. Polyurethanes are found in adhesives, coatings, foams, and synthetic rubber. Two classes of isocyanates are used in polyurethane products. Aliphatic isocyanates such as isophorone diisocyanate and hexamethylene diisocyanate are used in the manufacture of light-stable coatings. Aromatic isocyanates such as 2,4-toluene diisocyanate and 4,4'-diphenylmethane diisocyanate (MDI) are used where oxidative discoloration (yellowing) due to ultraviolet radiation is not an issue.¹

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Historically, isocyanates have been well described in the literature as an important workplace chemical with the potential to cause occupational asthma and other respiratory problems. There has been a gradual switch worldwide to use the less volatile MDI instead of the more volatile 2,4-toluene diisocyanate when possible. This transition, as well as stricter respiratory protection measures, has contributed to a decreased number of isocyanate-induced respiratory problems. However, the importance of sensitization through skin with possible airway reactivation later on has been recently described.²

A number of reported cases of allergic contact dermatitis (ACD) caused by isocyanates have been described in the last 10 years, emphasizing their importance as potential contact allergens.³ This is consistent with animal experiments showing isocyanates, especially MDI, as strong contact sensitizers.⁴ Two volunteers were also actively sensitized to MDI in a dermal uptake study.⁵ Still, workers and employers may not be aware of the possibility of contact dermatitis from isocyanates.

A variety of different individuals are exposed to isocyanates in their work environments, including but not limited to the following: casters, painters,⁶ artists,⁷ textile workers,⁸ assembly line workers, laboratory technicians,⁹ machine operators,¹⁰ and jewelry makers.¹¹ One author even reports an office worker who developed a contact allergy to the isocyanates in a 2-part adhesive.¹²

TABLE 1. Cases Information

	Occupation	Standardized Allergens Tested	Custom Materials Tested	Positive Test Results	Diagnosis/Additive
1	Assembly line worker, auto	NAS, IS, OCS, TS	Rear snap as is Front snap as is Seat cushion as is R side trim as is Beige leather as is Black leather as is Beige vinyl as is Black vinyl as is Tensor bandage as is Foam as is	1+ carba mix 2+ dialkyl thioureas 1+ bronopol 1+ chloroxylenol 1+ Tensor bandage	ACD/no added value
2	Production worker, manufacturing	NAS, IS	Isocyanate resin A 1% Pet	2+ MDI 0.1% 3+ isocyanate resin A 1% 2+ nickel sulphate	ACD/reinforced
3	Assembly line worker, auto	NAS, IS	Molded wood mat as is Trim as is Fabric as is Foam 1 as is Foam 2 as is Foam 3 as is Filler (insulator pad) as is	2+ epoxy resin 1+ isophorone diisocyanate	ACD/no added value
4	Assembly line worker, auto	NAS, IS, PGS	Isocyanate resin B 0.1% Pet Isocyanate resin C 0.1% Acet Isocyanate resin D 0.1% Pet Isocyanate resin E 0.1% Pet	IR isocyanate resin B IR isocyanate resin C	ICD/no added value
5	Assembly line worker, auto	NAS, IS, ES	Isocyanate resin F 1%, 2% Pet Isocyanate resin G 1%, 2% Pet	1+ epoxy resin 1+ balsam of Peru	ACD + ICD/no added value
6	Machine operator, auto	NAS, IS	Foam dust 10% Pet	1+ neomycin sulfate 2+ ethylene diamine 1+ propylene glycol	ICD/no added value
7	Machine operator, auto	NAS, IS, ES	Isocyanate resin H as is Isocyanate resin I as is Isocyanate resin J as is Isocyanate resin K as is Isocyanate resin L as is Isocyanate resin M as is	1+ isocyanate resin H 1+ isocyanate resin I 1-2+ isocyanate resin K	ACD/definite
8	Production worker, auto	NAS, IS, ES, HS, PGS	Gray foam as is Blue foam as is Purple foam as is Plastic foam as is	2+ glyceryl monothiolglycolate	ACD/no added value
9	Assembly line worker, auto	NAS, IS, OCS	Isocyanate resin N 1%, 10% OO Black foam as is White foam as is Leather as is	1+ budesonide 1+ triclosan 1+ black foam 1+ white foam	ACD/definite
10	Production worker, forestry	NAS, IS	Clean dust 5% Pet Treated dust 5%, 10% Pet	1 fragrance mix (+/-) balsam of Peru	ICD/no added value

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TABLE 1. (Continued)

Occupation	Standardized Allergens Tested	Custom Materials Tested	Positive Test Results	Diagnosis/Additive
11 Production worker, manufacturing	NAS, IS, ES	Sawdust A 10% Pet Sawdust B 10% Pet Sawdust C 10% Pet Sawdust D 10% Pet	1+ cinnamic aldehyde 1+ carba mix 3% 1+ formaldehyde 1% 2+ Kathon CG 2+ Euxyl K400 1+ dermatophagoides mix 1+ Grotan BK 1+ hexamethylenetetramine 1+ urea formaldehyde resin	ACD/no added value

IS, isocyanate series; ES, epoxy series; HS, health care series; PGS, plastic and glues series; OCS, oils and coolants series; Pet, petrolatum; Acet, acetone; OO, olive oil; TS, textile series.

For cases of suspected allergic ACD from isocyanates, the testing protocol includes patch testing to a standard tray of allergens, supplemented with a commercially available isocyanate series.¹² Although experts agree on the use of patch testing, all may not agree on the combination of chemicals that should be applied. Many recommend that additional preparations of isocyanate-based products from the work environment should also be included in the testing.^{4,10,13}

The objective of this study was to review our experience with testing custom isocyanate materials from the workplace in our patients and to try to determine if this practice has an additive value in diagnosing ACD to isocyanates.

METHODS

This study was approved by the research ethics board of St Michael's Hospital in Toronto, Ontario, Canada.

We performed a retrospective review of 11 patients seen in our clinic between January 2003 and March 2011 who were tested with workplace-related isocyanate materials, in addition to the North American Standard (NAS) series and the isocyanate series (Chemotechnique Diagnostics, Malmö, Sweden).

All patients were assessed by a dermatologist (S.S. or J.D.) who reviewed their material safety data sheets and information provided by the clinic industrial hygienist. The dermatologist then recommended testing with the NAS series, the isocyanate series, and workplace materials. Depending on the suspected exposures, some patients were also tested with other commercial series (Table 1).

The isocyanate-related workplace materials were made up using the recommendations from De Groot patch testing.¹⁴ We have previously described our method when testing custom materials as well as our detailed patch test procedure and data interpretation.¹⁵

The added value of testing custom isocyanate allergens for each patient was rated as follows:

- No additive value—the custom materials had no positive reaction.

- Reinforced additive value—the custom materials had positive reaction(s) and listed an allergen from the commercial series that also had a positive reaction.
- Definite additive value—the custom materials had positive reaction(s), but the allergens from the commercial series had no positive reaction.

RESULTS

Our patient population ranged from 26 to 63 years (mean, 43 years), and 73% were male. Seventy-three percent of the patients worked in the automotive sector, and more than half of these were assembly line workers.

Dermatitis was most commonly reported on the arms (91%) and hands (55%) despite the use of personal protective equipment. All patients had both direct and airborne exposure to their respective chemicals except for one, who had only airborne exposure (Table 2).

For 3 (27%) of 11 patients, there was an additive value of testing custom isocyanate allergens. Of these, 1 patient had a positive reaction to custom material that reinforced the test results found with the standardized allergens, and 2 had positive reactions only to custom isocyanate materials. Therefore, for those 2 patients (18%), there was a definite additive value of testing custom isocyanate materials. No adverse reactions were observed in any of the patients.

Of the 11 patients who received custom material testing, 6 were tested with solid foams or foam dusts, 4 were tested with only the resin form of the suspected isocyanate-containing products, and one was tested with both resin and foam products. There was 1 positive reaction (definite additive value) in the patients tested to solid foams (patient 9). Of note, 1 patient (patient 3) who did not react to the solid foam did have a positive reaction to one of the standardized allergens from the isocyanate tray.

In 2 of 5 patients tested with isocyanate resins, the custom preparation either confirmed (patient 2) or definitively made the diagnosis of ACD (patient 7). Patient 2 showed an additional

TABLE 2. Clinical Exposure Information

	n (%)
Skin areas affected	
Hands	6 (55)
Arms	10 (91)
Face and neck	5 (45)
Torso	4 (36)
Legs	5 (45)
Feet	2 (18)
Time of exposure before eruption	
Mean	8 months
Range	3 d to 6 y
Type of exposure	
Direct	11 (100)
Airborne	9 (82)
Both	9 (82)
Personal protective equipment	
Gloves	
Cloth	6 (55)
Rubber/plastic	6 (55)
Cloth/synthetic rubber combination	4 (36)
Coveralls (long-sleeved)	3 (27)
Coveralls (short-sleeved)	1 (9)
Apron	1 (9)
Cloth sleeves	3 (27)
Mask	2 (18)
Safety glasses	5 (45)
Safety boots	1 (9)

positive reaction to a standard isocyanate, whereas patient 7 did not react to the standard isocyanates. One patient (patient 4) was judged to have an irritant reaction (IR) to the custom isocyanate material based on the timing and appearance of the reaction. The 3 patients (patients 4, 5, and 9) who did not react to the custom materials were also negative to all allergens of the isocyanate tray (see Table 1 for full results).

DISCUSSION

Isocyanate compounds are common in assembly line, production, manufacturing, and machine operating jobs in a variety of different forms. Plastics, foams, paints, adhesives, textile finishes, lacquers, and other coatings used by workers commonly contain isocyanates and thus are potential sources of contact sensitization that can lead to ACD or irritant contact dermatitis (ICD).¹³ Isocyanates should be considered and tested when suspecting a possible occupational contact dermatitis in the context of the above exposures.

Commercial patch test preparations of MDI have been proven to be unstable, leading to a much lower concentration than expected and adding the possibility of false-negative patch tests.¹⁶ It has also been described that isocyanate-induced ACD tends to

present with mild symptoms.⁴ It is therefore not surprising that ACD to isocyanates is seldom diagnosed and reported.

In our experience, we have found that testing patients to preparations of their workplace products can be important when investigating a potential isocyanate-induced ACD. As shown, had we not tested our patients to custom material preparations, we would have missed the diagnosis in 18% of individuals presenting with a suspected isocyanate ACD. This could have important implications, especially with regard to the present and future health of sensitized workers and their financial well-being.

One interesting issue brought forward with our cases is that the usefulness of this additional testing may vary depending on the type of isocyanate exposure (solid/foam versus resin). Based on our experience, we believe that it is useful to perform custom testing for patients exposed to isocyanate liquid resins. Of the 5 patients tested to custom isocyanate resins, 2 (40%) had their diagnoses made or confirmed by the custom preparation.

In light of this, we would recommend adding the parent compounds to the custom testing materials if they are available, particularly liquid resins to which patients may have had exposure.

A note of caution would be to appreciate the irritant nature of isocyanates. Indeed, one of our patients (patient 4) had an irritant type of reaction on patch testing. In this case, a diagnosis of ACD would have been erroneous. Although cases of active sensitization while testing isocyanates have been described,⁵ none of the 11 patients reviewed in our study experienced active sensitization to isocyanates.

Given the small number of patients included in our review, it is possible that the number of patients with a definite additive value (18%) might not reflect the actual proportion of patients exposed to isocyanates that would only react to their own materials from the workplace and not to standardized allergens. There might also be a bias of selection for those patients because complicated cases are referred to our tertiary occupational clinic.

4,4'-Diphenylmethane diisocyanate has been described as being a late reactant with patch test reactions appearing after 7 days.¹⁷ To our knowledge, none of our studied patients experienced a late reaction.

It is interesting to note that of those 11 patients tested to standardized isocyanate allergens, only 2 reacted to them. One patient reacted to MDI, and the other reacted to isophorone diisocyanate. Consistent with other reports, we have found no cross-reactivity between isocyanates.¹⁸

In our review, no patient reacted to diaminodiphenylmethane or to other members of the para group of allergens. Therefore, we cannot confirm that diaminodiphenylmethane is a good marker for isocyanate allergy, in contrast to previous reports.^{4,19}

Finally, this article emphasizes the usefulness of testing custom materials from the workplace in selected patients. Although this practice might not be advisable in a community patch testing clinic, it should be considered when resources allow it in a tertiary care setting supervised by experienced patch test physicians. We have previously described the added value of this practice with epoxy resin materials. Based on our cases, we believe it could also be of use for patients exposed to isocyanate materials.

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