

Contact urticaria due to rubber chemicals?

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Contact urticaria due to gloves is mostly related to immediate-type allergy to natural rubber latex (NRL), and rarely due to rubber chemicals. We report the results of prick tests with rubber chemicals carried out on 75 latex-allergic patients. Clinically relevant hypersensitivity was not observed in our patient collection. Thus, we conclude that contact urticaria due to rubber chemicals is a very rare finding in latex-allergic patients, but has to be considered in patients with contact urticaria due to synthetic rubber gloves, as well as in patients with contact urticaria due to NRL gloves but no latex allergy. Therefore prick tests with rubber chemicals are unnecessary in the routine diagnostic assessment of latex-allergic patients.

Key words: contact urticaria; natural rubber latex; rubber chemicals; prick testing; RASTs.
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In 1996, we reported a dental chair assistant who developed contact urticaria due to latex gloves from immediate-type hypersensitivity to natural rubber latex (NRL), and subsequently due to latex-free nitrile gloves from hypersensitivity to morpholinyl-mercaptobenzothiazole contained in the N-DEX nitrile gloves used (1). Stimulated by this observation we carried out skin prick tests with commercially available rubber chemicals, recommended for patch tests, in 75 patients with immediate-type allergy to NRL.

Materials and Methods

Patients

Prick tests were performed on 75 patients (56 female, 19 male) with immediate-type allergy to NRL, aged 16 to 63.1 years (mean age 31.5 years, SD 9.6). 42 probands gave a history of atopic diseases, 18 of atopic eczema and 26 of hand eczema. 59 suffered from localized contact urticaria due to latex gloves, 58 were using gloves professionally.

Skin tests

Prick tests were performed with the following a panel of different *latex extracts*:

(a) self-prepared latex solution from freshly collected latex of Malaysian *Hevea brasiliensis* trees (2); (b) high-ammoniated latex (gift from Regent Hospital Produkte/Mönchengladbach, Germany);

(c) glove extracts produced by shaking glove pieces (Peha taft glove/Hartmann, Germany, Biogel glove / Regent, Germany, N-DEX nitrile gloves/Dr. Best, USA) incubated in a 0.9 % NaCl solution overnight, followed by centrifugation and filtration of the liquid phase through a 0.22 µm membrane. 0.4% phenol was added for preservation.

Carba mix 3% (diethyldithiocarbamate 1%, dibutylthiocarbamate 1%, 1,3-diphenylguanidine 1%) in pet. (HAL Allergie GmbH, Düsseldorf, Germany).

Thiuram mix 2% (dipentamethylthiuram disulfide 0.25%, tetraethylthiuram disulfide 0.25%, tetramethylthiuram disulfid 0.25%, tetramethylthiuram monosulfide 0.25%) in pet. (Hermal, Reinbeck, Germany).

Mercapto mix (N-cyclohexylbenzothiazyl sulfenamide 1%, dibenzothiazyl disulfid 1%, morpholinyl mercaptobenzothiazole 0.5%) in pet. (Hermal, Reinbeck, Germany).

Single components of the mixes in pet. (Hermal, Reinbeck, Germany) in some patients with positive skin prick test reactions to the mixes.

Prick tests were carried out on the volar side of the forearm. Wheal diameters were measured 20 minutes after puncture. Skin tests with 0.1% histamine hydrochloride solution served as positive, and 0.9% NaCl and 0.4% phenol as negative, controls. Wheals measuring more than 2-3 mm in diameter were considered to be +. Wheal diameters of the size of the histamine control were defined as ++, even wider wheals as +++.

IgE and specific IgE

Total IgE concentration and latex-specific IgE antibodies were analyzed in patient sera by the CAP-FEIA method (Pharmacia, Freiburg, Germany), following the manufacturer's instructions. Values of allergen-specific IgE above 0.35 kU/l were considered to be positive.

Results

All patients suffered from immediate-type allergy to latex and had positive prick-test results with different latex preparations. IgE antibodies against latex were detected in 70 sera, range 0.43-99.8 kU/l (median 4.5 kU/l, SD 18.9). None of the 75 patients reported contact urticaria from gloves other than NRL. The prick test results with rubber chemicals and nitrile glove extract are presented in Table 1. In 1 patient, we observed a strong positive prick test reaction to N-DEX nitrile glove extract, similar to that of the patient presented in 1996, but, in contrast, tests with rubber chemicals were not clearly positive (Table 1). Test repetition with rubber chemicals and N-DEX glove extract 6 weeks later gave a completely negative result. Weaker reactions compared with histamine were found in 4 patients with the N-DEX extract, though none of them showed a positive reaction to the chemicals tested. To mercapto mix, 2 patients had weak reactions and 1 had a strong skin reaction. Test repetition gave negative results (Table 1). Due to the patient's history this test reaction was not regarded as clinically significant.

Discussion

Contact urticaria from latex gloves due to immediate-type allergy to NRL proteins is an increasing occupational problem of general interest (3). Patients with a diagnosis of latex allergy are recommended to use latex-free gloves, preventing increasing sensitization and subsequent severe allergic reactions.

From use of rubber chemicals in NRL gloves, as well as in most of the available synthetic rubber gloves, skin problems may persist in patients with hypersensitivity to rubber chemicals. Subsequent to our observation of a dental chair assistant who developed contact urticaria due to latex and 1 year later due to morpholinyl mercaptobenzothiazole (1), we carried out prick tests with rubber chemicals in NRL-allergic patients routinely. Except in 2 patients, only weak test reactions were observed. Even on test repetition a few weeks later, and provocation test with N-DEX nitrile gloves in some patients, we failed to demonstrate significant hypersensitivity to rubber chemicals or N-DEX nitrile gloves in any of the latex-allergic patients. Furthermore, there was no sign of clinically relevant sensitization to these chemicals by patient history.

Test procedures for evaluation of contact urticaria are prick, scratch or intradermal tests, with vehicle-dependent results. Reactions to chemicals in pet. appear somewhat later compared to ethanol as vehicle (4). As in the present study scratch and prick tests with rubber chemicals both produced similar test results, as also with nitrile glove extract (1), we regard the chemicals as suitable for both test modalities. Therefore, we chose prick tests with the chemicals for routine testing and scratch tests for additional testing in case of ambiguous prick test results. Helander et al. (5) also reported scratch chamber tests, and Wrangsjö et al. (6) scratch tests, with rubber chemicals in pet. as suitable for the diagnosis of contact urticaria.

Positive prick test results using rubber chemicals in pet. have to be discussed critically. We found no significance for the mostly weak positive test reactions in our patients suspected of having irritant reactions. So far, it is not known whether contact urticaria from rubber chemicals is of pseudo-allergic origin or IgE antibody mediated. Until now, allergen-specific IgE antibodies to these chemicals have not been determined; thus, diagnosis is solely based on skin tests.

As a result of the present study, we find routine

Table 1. Positive test results using rubber chemicals and N-DEX nitrile glove extract (n.d./not done)

Patient no.	Prick test with					Repetition of positive prick tests	Provocation test with N-DEX glove
	N-DEX extract	carba mix	thiuram mix	mercapto mix	components of mixes		
1	++	(+)	(+)	(+)	n.d.	-	n.d.
2	+	(+)	-	-	n.d.	n.d.	-
3	+	-	-	-	n.d.	n.d.	n.d.
4	+	-	-	-	-	n.d.	n.d.
5	+	-	-	-	n.d.	n.d.	n.d.
6	-	-	-	++	-	-	-
7	-	-	-	+	n.d.	n.d.	n.d.
8	-	-	-	+	-	-	-

prick tests with rubber chemicals in latex-allergic patients unnecessary. Besides, the literature gives very rare information about immediate-type reactions to rubber chemicals. Contact urticaria from benzothiazoles (1, 7–9), thiurams (8) and carbamates (5, 6, 10), and rhinitis due to diphenylguanidine (11) have been observed only in isolated cases. The diagnosis is worth considering in patients with immediate-type reactions to synthetic rubber gloves, as well as in patients with contact urticaria from NRL gloves but no latex allergy. Attention has to be paid to the large amounts of benzothiazoles contained in N-DEX nitrile gloves, as well as in most other synthetic rubber gloves (12).

Data about amounts of soluble rubber chemicals in latex as well as in synthetic rubber gloves is not yet available. As repetitive leaching procedures in manufacturing NRL gloves reduce protein concentrations, we predict only small amounts of rubber chemicals in NRL gloves. Information about manufacturing procedures of synthetic rubber gloves is rare. As there are no washing procedures in their production, amounts of soluble rubber chemicals may be higher. Increasing use of synthetic rubber gloves may even result in increasing allergy problems in the future.

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