

Comparison of diagnostic methods in latex surgical glove contact urticaria

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Surgical rubber gloves contain allergens derived from natural rubber latex which may sensitize, causing contact urticaria and even systemic reactions. We examined 15 hospital employees allergic to latex surgical gloves, using various skin tests and RAST, to determine the most reliable diagnostic method and to investigate coexistent allergy to glove powder and rubber chemicals. Prick testing using a stock solution made from one brand of latex glove yielded positive (2+ to 4+) reactions in all 15 employees: 8 retained positive reactions at a 1/10 dilution, 1 at 1/100 and 4 at 1/1000. A prick test using rubber-tree sap (*Hevea brasiliensis*) was positive in 12/15 employees and a scratch-chamber test using crushed rubber-tree leaf was positive in 13/15. A latex glove use test was positive in 12/13 employees and a latex RAST detected measurable amounts of specific IgE in 8/15. No positive prick test reactions were obtained using glove powder. On patch testing, 2/15 employees showed delayed allergy to rubber chemicals but no immediate reactions were detected. The present results indicate that in addition to the use test, prick testing with a stock solution prepared from latex surgical gloves is an adequate test method for routine practice when diagnosing latex glove contact urticaria. The correlation between prick tests and whole glove use tests was good, but latex RASTs yielded some negative results.

Key words: surgical rubber gloves; rubber latex allergy; type I allergy; contact urticaria; prick test; use test; RAST.

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The first case of contact urticaria from rubber cleaning gloves was described by Nutter in 1979 (1) and soon after Förström (2) detected that surgical latex gloves can also cause this allergy. The symptoms can vary from local itching and redness to systemic reactions such as generalized urticaria, asthma and even anaphylactic reactions (3, 4). Some cases of doctors and nurses suffering from this allergy have been described (5-9), and we found that the frequency was as high as 3% in our hospital (10). Previously, prick, scratch or use tests with glove pieces or natural rubber latex have been used, but the test method best suited to routine diagnosis remained unidentified. We used the scratch-chamber (S-C) test as a screening test, but it seemed to give some false positive reac-

tions (10). This led us to examine other tests, and in the present study, we report the results of prick tests, use tests and RASTs with latex in 15 allergic patients and 20 controls.

Patients and Methods

Patients

15 hospital employees allergic to latex surgical gloves, 12 of whom were detected in a previous screening study (10), were examined. 7 were doctors, 5 were operating room or laboratory nurses, and 3 were assistant staff. Their mean age was 36 years and they had been in the profession for an average of 12 years (Table 1). 12 were atopic, 13 had a previous history of hand eczema and 6 still had hand eczema.

Table 1. Clinical history of 15 latex glove allergic and 20 control employees

Hospital employees	Mean age (range) (years)	Profession			Mean years in profession (range)	Personal atopy**	Hand eczema	
		D*	N*	A*			past	present
with latex glove allergy (n=15)	36 (26-50)	7	5	3	12 (3-24)	12	13	6
with glove irritation (n=10)	43 (29-62)	2	8	0	17 (7-33)	10	7	4
with no glove irritation (n=10)	39 (24-59)	2	8	0	15 (2-35)	10	1	2

*D=doctor, N=nurse, A=assistant staff.

**Past or present allergic rhinitis and/or asthma and/or atopic eczema.

20 glove-using employees with a negative latex scratch-chamber test from the same screening study volunteered as controls (Table 1). All 20 were atopic, and 10 had experienced hand irritation when using either rubber or vinyl gloves.

Prick tests

Latex glove allergen for use in prick testing was obtained from sterile latex gloves containing glove powder (Exona[®], Semperit, Vienna, Austria). Twenty 1 cm² freshly-cut glove pieces (400 mg total weight) were incubated for 30 min in 5 ml of sterile physiological saline. This was taken from a plastic bag in order to avoid contamination from rubber bungs. The incubation fluid was used as a stock solution for prick testing. Its different dilutions (1/10, 1/100, 1/1000) in sterile physiological saline were used to grade the allergy. Physiological saline and histamine (10 mg/ml, Allergologisk Laboratorium A/S, Copenhagen, Denmark) served as controls. A prick test reaction was regarded as weak positive (2+) when it was equal to halve the reaction to histamine, clear positive (3+) when the reaction was the same as that resulting from histamine, and strong positive (4+) when the reaction was greater than the histamine test reaction (11). Latex-allergic employees were also prick tested using rubber-tree sap. Crushed rubber-tree leaf,

stored at -20°C, was used as an allergen in the S-C test. All allergic and control employees were also prick tested using a vinyl glove (Triflex[®], Travenol Laboratories S.A., Lessines, Belgium) stock solution and corn-starch glove powder (0.5 g in 1 ml sterile physiological saline) obtained directly from the glove manufacturer (Biosorb[®], Johnson & Johnson, Arlington, Texas, USA). A routine prick test series with 20 common inhalant allergens (Allergologisk Laboratorium A/S, Copenhagen, Denmark) was also performed on all employees.

Use test

A 15-min use test was carried out simultaneously with whole sterile latex glove (Exona[®]) and vinyl glove (Triflex[®]) on the dampened hands of 13 allergic employees, excluding 2 highly allergic employees. The test was graded as susceptible (1+) if some redness occurred in the contact area, positive (2+) if some wheals were seen there, or as strong positive (3+) if 10 or more wheals appeared. Latex glove use tests were also performed on 10 control employees with a history of glove irritation.

RAST

Commercial allergen discs made from rubber-tree sap (Latex, k82, Pharmacia Diagnostics,

Uppsala, Sweden) were used (7). All serum samples were examined simultaneously and the results are given both in PRU/ml and RAST scores.

Patch and scratch-chamber tests

A 2-day patch test using a 1 cm² piece of sterile latex glove covered with Scanpor[®] tape was performed on all 15 allergic employees and the results were read on days 2 and 4. Standard patch tests with the ICDRG series and with 10 rubber chemicals (Epicon Ltd., Helsinki, Finland), using Finn Chambers[®] on Scanpor[®] tape, were also performed, and the results were read on days 1 and 4. Certain rubber chemicals, mercapto mix, PPD mix, thiuram mix and zinc dibutyldithiocarbamate (ZBC), all in pet. were also tested in a 15-min S-C test to reveal immediate allergy.

Results

Prick and use tests

Latex prick test stock solution provoked a 4+ reaction in 4, a 3+ reaction in 7 and a 2+ reaction in 4 employees. The dilution series showed that 2/15 employees reacted only to the stock solution, 8 were still positive at 1/10, 1 at 1/100, and 4 at 1/1000 (Table 2). The prick test using rubber-tree sap was positive in 12/15, and the S-C test using rubber-tree leaf was positive in 13/15 employees. No positive glove powder or vinyl prick tests were found (Table 3). 1 control employee showed a 2+ prick test reaction to latex glove stock solution but was negative to the dilution series. In the routine prick test series, 9/15 latex-allergic employees had at least 1 positive test result; 5 were allergic to birch, 6 to grass, 7 to mugwort pollen, 9 to animal epithelia and 3 to house-dust mite. In the control employees, 12/20 were positive; 7 to birch, 5 to grass, 7 to mugwort pollen, 7 to animal epithelia and 1 to house-dust mite (Table 3).

Use tests with latex glove gave positive results in 12/13 employees (Table 2). The only allergic employee with a negative 15 min use

test had not used latex gloves for the last 4 years, but after a 4-h use test, he suffered from severe itching and wheals on the hands. In the control group, the only person with a positive latex-glove prick test also had a negative 15-min use test, but was found to have contact urticaria after using latex gloves for 2 days. The vinyl glove use test remained negative in all employees tested.

Latex RAST and total IgE

The latex RAST was positive in 8 allergic employees, but all controls were negative (Tables 2, 3). The mean serum total IgE was 3516 kU/l in the 15 latex allergic employees and 81 in the 20 control employees, which is a significant difference ($p=0.0044$, Mann-Whitney *U*-test). The 8 latex RAST-positive employees had significantly higher ($p=0.0001$, Mann-Whitney *U*-test) total IgE levels than the 7 latex RAST-negative allergic employees. The figures were 6549 ± 12685 kU/l and 50 ± 65 kU/l, respectively. The latex RAST of the only prick test positive control-employee was negative (<0.1 PRU/ml) and her total IgE was 674 kU/l.

Patch and scratch-chamber tests

2 of the latex allergic employees showed a positive patch test result to rubber chemicals (Table 3). Both reacted to thiuram mix, and the rubber series showed that the first employee was allergic to TMTM (tetramethylthiuram monosulphide) and PTD (dipentamethylenethiuram disulphide) and the other to TETD (tetramethylthiuram disulphide) and also to MBTS (dibenzothiazyl disulphide), although mercapto mix gave a negative reaction. S-C testing with rubber chemicals showed no immediate reactions. Patch testing with latex glove pieces showed no delayed reactions (Table 3).

Discussion

In the present study, we compared various test methods in order to evaluate their diagnostic

Table 2. Skin tests, use tests and RASTs, with serum total IgE values, in 15 latex-allergic hospital employees

Case no.	Present atopy or hand eczema	Prick tests			Scratch-chamber test (crushed leaf)	Use test (one hand 15 min)	Latex-RAST		Total IgE (kU/l)
		stock solution	latex glove dilution series	sap of rubber tree			(PRU/ml)	(score)	
1.	AE*, AR, A	4+	1/1000**	4+	4+	3+	5.7	3	542
2.	AE, HE	4+	1/1000	4+	4+	ND	>17.5	4	9790
3.	-	4+	1/1000	4+	4+	ND	6.7	3	530
4.	-	4+	1/1000	4+	3+	3+	4.9	3	1008
5.	-	3+	1/100	3+	3+	2+	2.6	2	1400
6.	-	3+	1/10	4+	3+	2+	0.23	0	6
7.	HE	3+	1/10	4+	3+	2+	<0.1	0	7
8.	-	3+	1/10	3+	3+	2+	1.45	2	1957
9.	-	3+	1/10	-	-	2+	<0.1	0	190
10.	-	3+	1/10	4+	3+	3+	0.19	0	33
11.	AR	3+	-	-	-	3+	<0.1	0	69
12.	-	2+	1/10	3+	3+	3+	0.49	1	205
13.	AE, HE	2+	1/10	3+	2+	3+	2.75	2	36962
14.	AE, HE	2+	1/10	2+	2+	3+	<0.1	0	23
15.	HE	2+	-	-	2+	3+	0.13	0	24

AE = atopic eczema. A = asthma.

AR = allergic rhinitis. HE = hand eczema.

** Lowest positive dilution.

*** Positive after 4 h exposure.

Table 3. Skin and serum test results in 15 latex glove allergic and 20 control employees

	latex glove	Prick test vinyl glove glove powder	standard series	Use test latex glove	Patch tests rubber chemicals	S-C test rubber chemicals	Latex RAST (PRU/ml)	Total IgE (kU/l)
Employees with latex allergy	15/15*	0/15	0/15	9/15	12/13	2/15	0/15	2.9** ±4.6
Controls with glove irritation	1/10	0/10	0/10	7/10	0/10	0/10	0/10	110 ±204
Controls without glove irritation	0/10	0/10	0/10	5/10	0/10	0/10	0/10	51 ±57

* No. positive/number tested.

** Mean ± s.d.

value for latex glove contact urticaria. Previously, we had found that a scratch-chamber test using latex glove pieces seems to give false positive reactions when evaluated by prick and use test methods (10). In this study, our examination of 15 latex glove allergic hospital employees was more thorough.

Latex glove prick tests with the same glove brand stock solution showed that 4 of the 15 employees had a strong (4+), 7 a moderate (3+) and 4 a weak (2+) test reaction. The dilution series showed that all 4 employees with 4+ prick test results were positive at 1/1000 dilution and also had clearly positive test reactions to rubber-tree sap and leaf. 2 of these 4 employees had consistently experienced systemic reactions when using latex gloves.

However, some discrepancy existed between the weaker latex glove prick test reactions and the skin tests using rubber sap and leaf. For example, 1 employee had negative reactions when tested with rubber sap and leaf, although she had positive reactions to a 1/10 dilution of latex glove stock solution. In agreement with this, Wrangsjö et al. (7) reported 6 latex glove scratch test positive patients of whom 3 were negative when tested with dried suspension of natural rubber.

We also compared the prick test results and whole-glove use test results for the present employees. The correlation was good, and only 1

negative use test result was found. The use-test-negative employee had clearly positive prick tests and immediately after prolonged glove use, he suffered several wheals on his hands. This indicates that a 15-min use test can sometimes give false negative results, possibly because 15 min is too short a period for the allergen to penetrate through the intact skin.

Even so, the use test always seems to be positive when the patient has eczematous skin or is highly allergic. However, the use test using the whole glove may be dangerous for such people and we have observed one anaphylactic reaction in a patient who had a 3+ latex glove prick test reaction (12). We agree with the opinion of Axelsson et al. (8) that when the use test is performed, it should be started with one finger exposure and only when this is negative should a whole-glove use test be conducted.

Specific IgE antibodies can be detected by using the RAST method in latex glove allergic persons. Previous studies have shown positive results in 3/5, 3/3, 3/6 and 5/5 patients, respectively (3, 6, 7, 8). A commercial RAST is now available, and using it we found that 8 of the present 15 employees were positive. The highest specific IgE levels were found in those 4 employees who had the strongest prick test reactions, showing that a latex RAST is a good indicator of highly allergic persons. A negative

RAST was observed in 7 employees and therefore the RAST seems not to be as good an indicator of latex glove allergy as skin and use tests for those people with milder allergy.

Interestingly, the 8 employees with a positive latex RAST had significantly higher total serum IgE levels than the 7 employees with negative RAST results, although no clear difference was found between the latex prick test results for these 2 groups. The latex allergen is derived from a plant, the rubber tree (*Hevea brasiliensis*) and as in other type I allergies of plant origin, the amount of circulating specific IgE seems to correlate with the total IgE levels in the serum (13). In latex allergy, sensitization occurs through the skin and not through the mucous membranes, and this may have some consequences when homing specific IgE into the skin and other tissues. This may be one reason for the high incidence of positive latex skin tests observed, in contrast to a rather low frequency of positive RASTs in the present employees.

Concomitant occurrence of immediate and delayed allergy to rubber gloves has been reported (14), the immediate allergen being latex protein and the delayed allergen one of various rubber chemicals. Interestingly, in the present study we found that 2 employees with latex contact urticaria also had a delayed allergy to rubber chemicals on patch testing. A coexistence of IgE- and cell-mediated glove allergy in 2/15 of the present latex-allergic employees is also interesting and previously Kleinhans (14) reported 1 latex allergic male nurse who was patch test positive to various rubber chemicals.

There is little information available on the identity and amount of rubber chemicals contained in latex surgical gloves, although some of these gloves are regarded as "hypoallergenic", which means avoidance of sensitizing rubber accelerators and use of only 1 antioxidant (15, 16). Our 2 thiuram mix positive employees did not react in any way when patch tested with the piece of one latex surgical glove, suggesting that at least this glove brand did not

contain thiuram chemicals. Moreover, cases of allergic dermatitis from thiuram chemical in surgical gloves have been reported in operating theatre staff (17), indicating that in addition to causing contact urticaria, latex surgical gloves are also potential initiators of delayed allergy to rubber chemicals.

In the present study, we found 1 positive latex glove prick test among the 20 control employees, although this person's previous S-C latex glove test was negative. This employee also had a negative latex RAST and a negative 15-min use test, but she developed contact urticaria symptoms after prolonged glove exposure, confirming the validity of the prick test. This also shows that a mild latex glove allergy may remain undetected if only 1 test is used for screening.

Our latex allergic employees were from a selected hospital personnel group screened for this allergy, and so the present skin test results should also be confirmed in another population, such as patients referred for routine allergy testing. However, the present results strongly indicate that prick testing with a latex stock solution made from an allergenic glove brand is a convenient, safe and sensitive method of diagnosing latex glove contact urticaria, although the need for a standardized prick test allergen clearly remains. The positive prick test results can be verified with the use test. Moreover, highly allergic individuals can easily be detected by means of a latex RAST, but milder cases seem quite often to be RAST-negative.

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