

Rubber contact urticaria

Allergenic properties of 19 brands of latex gloves

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To compare the immediate skin test reactivity of various latex (natural rubber) surgical and cleaning gloves, prick tests were performed on 40 latex-allergic persons, 26 of whom were sensitized by surgical and 14 by cleaning latex gloves. 6/17 surgical gloves tested and 1/2 cleaning gloves caused positive reactions in almost all (over 87%) of the allergic subjects. In contrast, the frequencies of positive reactions to 4 other surgical latex gloves were as low as 8-21%, suggesting that not all surgical gloves are equally allergenic. Control prick tests with 1 synthetic rubber and 1 polyvinyl chloride (PVC) glove were negative in all subjects. 2 surgical latex gloves causing either a high or low number of positive prick tests in allergic subjects were analyzed with high-pressure liquid chromatography (HPLC). Similar allergenic protein fractions were detected, which showed protein peaks at MW 2000, 5000 and 30000 daltons. Corresponding proteins were detected in 1 latex cleaning glove analyzed and in natural rubber. This result confirms that allergenic proteins persist in various surgical and cleaning latex gloves after manufacture from natural rubber and may cause contact urticaria symptoms in sensitized people.

Key words: contact urticaria; rubber gloves; latex allergen; prick tests; occupational; high-pressure liquid chromatography.

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Contact urticaria from latex (natural rubber) surgical and cleaning gloves seems to be a rather common condition not that easily detected. There is increasing awareness of this allergy in many countries, and in Finland we have found latex allergy in 7.4% of surgeons and 5.6% of operating theatre nurses (1). The diagnosis of latex allergy can be confirmed with prick tests and specific IgE-antibodies can also be demonstrated by latex RAST (2). The sensitizing allergen seems to be a protein derived from natural rubber latex used in the manufacture of these gloves and persisting in the finished gloves. Carillo et al. (3) filtered the latex allergen from natural rubber into 3 fractions and showed that it had a MW over 30,000 daltons.

In order to examine whether there are differ-

ences between the skin reactivity of various latex surgical and cleaning gloves, we eluted the allergens from 21 gloves and performed prick tests in 40 latex-allergic people. We also used high-pressure liquid chromatography (HPLC) to analyze the proteins of 2 surgical and 1 cleaning latex glove to determine the allergenic fractions and to compare these with the proteins found in natural rubber.

Material and Methods

The clinical history of the 40 latex-allergic subjects is shown in Table 1. 26 of them had become sensitized by using latex surgical gloves, and 14 by using cleaning gloves. Their diagnosis was verified by prick and use tests as previously described (2).

Table 1. Clinical history of the 40 subjects with latex contact urticaria examined

Sensitizing glove type	Sex		Mean age (years) (range)	Personal atopy	Symptoms	
	F	M			hand eczema	systemic immediate symptoms
surgical (n = 26)	20	6	36 (27-51)	21 (81%)	22 (85%)	7/26 (27%)
cleaning (n = 14)	14	0	39 (20-69)	13 (93%)	14 (100%)	4/14 (29%)

Prick tests were performed with 17 different latex surgical gloves, 11 of which (nos. 1-7, 14-17) have been in use in our hospital (Table 2). Moreover, 2 latex cleaning gloves were tested and the control non-latex gloves included 1 surgical glove made from synthetic rubber and 1 PVC examination glove. The allergens were eluted from the gloves by incubating glove pieces for 30 min in physiological saline at room temperature as previously described (1). Prick tests were then made on the volar side of the forearm; the controls included histamine (10 mg/ml, Allergologisk Laborato-

rium A/S, Copenhagen, Denmark) and physiological saline. The tests were read after 15 min and the test reaction was regarded as positive if it was bigger than that of histamine (4+), the same size as that of histamine (3+), or half of that of histamine (2+).

HPLC was performed on the proteins of 2 brands of latex surgical gloves (no. 1, Ansell Gammex and no. 4, Exona, Table 2), 1 cleaning glove (no. 19, Natura), 1 PVC glove (no. 21, Triflex) and the crushed leaf of the rubber tree. These were incubated in phosphate buffer saline (PBS), pH 8.5, at 37°C overnight. The

Table 2. Trade names and manufacturers of the 21 gloves examined

Latex surgical gloves

1. Ansell Gammex, Ansell Rubber Co. Ltd., Malacca, Malaysia
2. Ansell No Powder, Ansell Rubber Co. Ltd., Malacca, Malaysia
3. Eudermic, Becton Dickinson, New Jersey, USA
4. Exona, Semperit, Vienna, Austria
5. Glads, Ansell Rubber Co. Ltd., Bangkok, Thailand
6. Micro-Touch, Johnson & Johnson, Arlington, Texas, USA
7. Neutalon Brown, Johnson & Johnson, Arlington, Texas, USA
8. Opett, Semperit, Vienna, Austria
9. Opett Comf. Powderfree Brown, Semperit, Vienna, Austria
10. Opett Derma, Semperit, Vienna, Austria
11. Perry microptic, Smith & Nephew, Massilon, Ohio, USA
12. Perry orthopedic, Smith & Nephew, Massilon, Ohio, USA
13. Perry white latex, Smith & Nephew, Massilon, Ohio, USA
14. Puritee, The Puritee Medical Company Ltd., Slough, Berks, UK
15. Sempermed, Semperit, Vienna, Austria
16. Travenol Ultralan, Travenol Laboratories SA, Lessines, Belgium
17. Triflex, Travenol Laboratories SA, Lessines, Belgium

Latex cleaning gloves

18. Marigold, LRC Products Ltd., London, England
19. Natura, Vascongada de Gaucho y Latex, Spain

Non-latex control gloves

20. Elastyren, Danpren Gloves A/S, Albertslund, Denmark
21. Triflex vinyl, Travenol Laboratories SA, Lessines, Belgium

eluate was air dried and then diluted in distilled water according to the protein concentration. Thereafter, the solution was filtered through a 1.2 μ m filter (Millipore®, Molsheim, France), after which the proteins were separated with HPLC using a preparative gel permeation column (LKB, Ultropac TSK-G3000SWG), fractionating proteins with a MW from 1000 to 300,000. The fractions were detected by their UV absorbance at 280 nm. In the first experiment, 7 fractions of one glove (no. 3, Exona) were collected, and all these were prick tested in 3 latex-allergic subjects. The allergenic fractions of all 3 HPLC-examined latex gloves were then tested in 6 latex-allergic subjects sensitized by surgical gloves. Control prick testing was performed with the whole HPLC fraction of the PVC glove. The protein concentrations of the glove eluates and HPLC frac-

tions were measured using Bradford's method, which detects microgram quantities of proteins and uses a bovine albumin as a standard (5).

Results

The prick test results of different gloves are shown in Table 3. A surgical latex glove (no. 4, Table 2) was positive in all, and 5/17 surgical and 1/2 cleaning gloves were positive in over 87% of the tested subjects (Table 3). In contrast, 4 other surgical latex gloves (nos. 1-3, 9, Tables 2, 3) gave a low number of positive prick tests, the frequencies varying from 8-21%. The 2 non-latex gloves were negative in all tested subjects.

The frequencies of positive prick tests in the subjects sensitized either by surgical or cleaning gloves were quite similar. In the surgical

Table 3. Prick test results from different surgical and cleaning latex gloves and non-latex gloves

Gloves	Subjects sensitized by surgical gloves				Subjects sensitized by cleaning gloves				All subjects positive
	positive	4+	3+	2+	positive	4+	3+	2+	
<i>Surgical</i>									
1.	3/25 ^a	1	0	2	5/14 ^a	1	2	2	8/39 ^a
2.	4/25	1	0	3	3/11	0	0	3	7/36
3.	0/25	0	0	0	3/11	0	0	3	3/36
4.	26/26	12	6	8	14/14	6	4	4	40/40
5.	7/25	1	0	6	6/13	1	0	5	13/38
6.	19/26	8	5	6	8/11	2	0	6	27/37
7.	17/26	5	2	10	7/11	2	1	4	24/37
8.	11/13	7	4	0	5/5	3	1	1	16/18
9.	3/13	1	0	2	1/6	1	0	0	4/19
10.	11/13	6	4	1	6/6	4	0	2	17/19
11.	11/13	6	1	4	2/3	0	1	1	13/16
12.	12/13	9	1	2	2/3	2	0	0	14/16
13.	11/13	6	2	3	3/4	2	0	1	14/17
14.	11/26	1	2	8	6/11	0	0	6	17/37
15.	22/24	14	1	7	10/11	6	2	2	32/35
16.	9/25	1	2	6	6/11	1	0	5	15/36
17.	22/22	9	6	7	11/12	4	1	6	33/34
<i>Cleaning</i>									
18.	18/25	4	3	11	7/11	2	1	4	25/36
19.	22/24	13	3	6	11/11	6	2	3	33/35
<i>Non-latex</i>									
20.	0/25	0	0	0	0/12	0	0	0	0/36
21.	0/25	0	0	0	0/14	0	0	0	0/39

^a No. positive/no. tested.

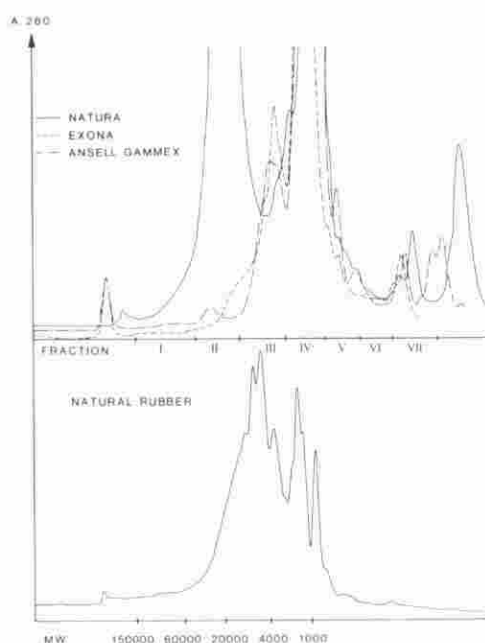


Fig. 1. High-pressure liquid chromatography (HPLC) analysis of 3 latex gloves and natural rubber derived from the leaf of the rubber tree. The different fractions were collected for prick testing.

glove group 21 subjects, and in the cleaning glove group, 9 subjects, were prick tested with the same set of surgical and cleaning gloves. 11 different surgical gloves (nos. 1-7, 14-15, Tables 2, 3) caused 115/231 (50%) positive prick tests in the surgical-glove-sensitized and 54/99 (55%) in the cleaning-glove-sensitized subjects. The corresponding figures for the 2 cleaning gloves (nos. 18-19, Tables 2, 3) were

34/42 (81%) and 14/18 (78%), respectively. The amounts of protein eluting from the 2 surgical gloves examined (nos. 1, 4) were 0.025 mg and 0.046 mg per 1 g of glove, and that of 1 cleaning glove (no. 19) was 0.28 mg/1g glove.

The HPLC curves of the proteins of the 3 latex gloves and that of natural rubber are shown in Fig. 1. These were quite similar, except that the cleaning glove showed a high peak at MW 30,000. The prick-test-positive fractions showed protein peaks at MW 2000, 5000 and 30,000. The fractions with a MW below about 1000 (fractions V-VII, Fig. 1) or over 150,000 were clearly negative in the prick tests. The allergenic fractions of 1 surgical and 1 cleaning glove caused positive prick tests in 3/6-6/6 subjects, whereas the corresponding fractions of a second surgical glove (no. 1) were positive in only 1/6 subjects tested (Table 4). The HPLC analysis of the PVC glove (no. 21) revealed only minimal amounts of proteins, and prick tests with the whole fraction were negative.

Discussion

All 17 latex surgical and 2 latex cleaning gloves examined produced positive prick tests, confirming that they contain the allergen. However, the frequencies of positive test reactions varied from 100% to 8%, suggesting differences either in the composition or in the amount of latex allergen eluting from these gloves. We performed protein measurements on the eluates of 3 different latex gloves, and

Table 4. Prick test results with different HPLC fractions from 2 surgical and 1 cleaning latex glove in 6 latex-allergic subjects

Fraction no. (MW)	Glove no. 1		Glove no. 4		Glove no. 19	
	protein concentration (mg/ml)	no. positive prick tests	protein concentration (mg/ml)	no. positive prick tests	protein concentration (mg/ml)	no. positive prick tests
I (>45,000)	0.04	1	0.09	4	ND	ND
II (45,000-10,000)	0.01	1	0.18	6	0.38	5
III (10,000-3,000)	0.04	0	0.11	6	0.04	6
IV (3,000-1,000)	0.01	1	0.07	3	0.05	5

ND = not done.

found the lowest total protein concentration (0.025 mg/lg glove) in the glove causing only a few positive prick tests. This is in agreement with our previous clinical observation that almost half of the hospital employees allergic to latex surgical gloves can continue with their work by using this special glove (1). It was, however, surprising to detect a 6-fold higher protein concentration (0.28 mg/lg) in the cleaning glove than in the surgical glove (0.046 mg/lg), because both gloves caused positive prick tests at the same high frequency. Therefore, the amount of total protein eluting from gloves does not seem to predict the allergenicity of a particular glove.

The protein amounts from all 3 gloves examined were low, and could be measured only after the eluate was concentrated. It is interesting that such small amounts of proteins persisting after the manufacture of gloves can sensitize, and can cause contact urticaria and even systemic immediate reactions (2, 6). Although the protein content of latex gloves seems to be very low, their continuous use, the close contact with the skin, and the effect of sweat may all be important in releasing amounts of latex allergen sufficient to sensitize.

We analyzed the proteins eluting from different gloves by HPLC. 1 surgical glove and 1 cleaning glove causing a high number of positive prick tests and 1 surgical glove causing a low number of positive prick tests were examined. The HPLC curves were quite similar except for 1 prominent protein peak at MW 30,000 in the cleaning glove. These results suggest that there are no major qualitative differences between the proteins of these gloves. Interestingly, the natural rubber in the rubber tree leaf had a similar HPLC protein profile, confirming that some proteins derived from natural rubber still persist in latex gloves after their manufacture.

The allergenic fractions from the gloves had distinct peaks at MW 2000, 5000 and 30,000. In accordance with this, previous studies have shown that the MWs of major pollen and other

protein allergens cover a range from 2000 to 70,000, with a majority between 10,000 and 40,000 (7). Although the protein profiles of the 3 latex gloves were similar, their allergenic fractions caused different results when prick tested (Table 4). Fractions from 1 surgical and 1 cleaning glove were positive in most subjects tested, whereas only 1/6 subjects reacted to the fractions deriving from a 2nd surgical glove. The lower incidence of positive prick test reactions from this surgical glove may be due to the lower amount of allergen persisting or eluting. However, examination methods more refined than HPLC are needed to confirm whether the amount or composition of latex allergen in this special glove really differs from other gloves.

The 1st group of our subjects allergic to latex had become sensitized by surgical gloves, and the 2nd group by cleaning gloves. However, we could not detect any major differences between these 2 groups of allergic subjects in the frequency of positive prick tests, either for surgical or cleaning gloves. Together with the HPLC results, this indicates that the allergens in the latex surgical and cleaning gloves are cross-reacting or are the same. In accordance with this, we have seen a kitchen worker allergic to latex, who became sensitized by using cleaning gloves and who experienced an anaphylactic reaction when a use test was performed with surgical gloves (2). For practical purposes, it is therefore important that people sensitized to latex surgical gloves avoid latex cleaning gloves, and vice versa. Sensitized subjects can easily replace cleaning gloves by PVC gloves and in surgical work, one can use elastic synthetic rubber gloves. These are rather expensive and, therefore, it is necessary to develop glove manufacturing processes in which the latex allergen is totally eliminated.

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