

Prevalence of natural rubber latex allergy (Type I and Type IV) in laboratory workers in The Netherlands

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The objective of the study was to study the prevalence of Type IV and Type I allergy to natural rubber latex (NRL) in a population at risk in the Netherlands. Laboratory workers regularly using gloves were invited to complete a questionnaire and to be tested. We performed patch tests with standard contact allergens, rubber additives, glove powder and pieces of 4 gloves; prick tests with inhalant allergens, glove extracts, glove powder and fruit extracts; and RASTs. Glove-related hand dermatitis was reported in 36.9% of the individuals interviewed. A positive patch test result for rubber additives was seen in only 6.6%. Glove-related urticaria, rhinoconjunctivitis and/or asthma were reported in 24.6% of all cases. Confirmation of an IgE-mediated reaction was achieved in 8.3% by prick test with glove extracts and 5.0% by RAST. No reaction to glove powder was noticed in patch testing or in prick testing. A high prevalence rate of glove-related symptoms and NRL Type I allergy was found in laboratory workers exposed to rubber gloves. Surprisingly, there was no co-existence of Type I and Type IV allergy in this population.

Key words: natural rubber latex; Type I allergy; Type IV allergy; patch testing; prick testing; RASTs; questionnaire; epidemiology; occupational; laboratory workers; rubber gloves. © Munksgaard, 1998.

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Natural rubber latex (NRL) allergy is a growing health care problem. Due to increasing use of rubber gloves, more workers in hospitals and laboratories are exposed to latex allergens. Latex hypersensitivity can induce local symptoms after glove use (usually caused by Type IV allergy to rubber additives), as well as more serious Type I allergic reactions ranging from urticaria and rhinoconjunctivitis to asthma and even anaphylactic shock.

The prevalence of latex sensitization differs considerably in populations with different latex exposure (as reviewed in (1)). In The Netherlands, occupational latex allergy has been described only rarely (2). Therefore, we decided to study the prevalence of Type IV and Type I allergy to natural rubber latex in a population at risk, i.e., laboratory workers with regular contact with latex gloves. After informed consent and ethical approval an extensive questionnaire concerning contact allergy, inhalant atopy and glove-related symptoms was

filled in by the volunteers. To study the prevalence of Type IV allergy, patch tests were performed with standard contact allergens, rubber additives, gloves and glove powder. Prick tests and RASTs were performed in order to study Type I-related sensitization to inhalant allergens, latex and latex-related fruits.

Materials and Methods

Volunteers

All workers ($n=98$) at the Department of Immunology, Erasmus University, Rotterdam, were asked to participate in the study. The volunteers gave informed consent and were asked to fill in an extensive questionnaire concerning age, sex, time in current occupation, smoking habit, use of rubber gloves, symptoms related to glove use, signs of contact allergy and atopic complaints. Subsequently, blood was drawn for RAST and skin tests

(prick and patch) were performed. The answers to the questionnaire were evaluated with each volunteer by the investigator (HdG). The study was conducted according to the World Medical Association Declaration of Helsinki, September 1989, and approved by our Hospital Medical Ethical Committee. Confidentiality was maintained.

Patch tests

The European standard series (including thiuram mix, mercaptobenzothiazole and black rubber mix) was purchased from Van der Bend BV (Brielle, The Netherlands). Patch tests were also performed with an additional rubber additive (carbamix), absorbable dusting powder (10% w/v) and 1 cm² pieces of the 4 gloves. The patch tests were applied to the upper back with Van der Bend square chambers and removed 2 days later. Sites were inspected for erythema and dermatitis 2 and 3 days after application. All patch tests were performed by the same investigator (LG).

Prick tests

Prick tests were performed by application of 1 drop of allergenic extract to the skin of the volar side of the forearm. Subsequently the dermis was punctured with a standardized skin test needle, and results were read after 20 min. Reactions were expressed (mm) of mean wheal diameter (adding the longest diameter to the orthogonal diameter measured at 1/2 of the longest diameter and dividing it by 2). A diameter of 3 mm or more was considered positive (3). Dilution buffer was used as a negative control, histamine chloride 10 mg/ml as the positive control. All skin tests were performed by the same nurse (ED).

Allergens

The latex allergens for prick testing were prepared by extracting pieces, cut from a pair of gloves, in phosphate-buffered saline (PBS), pH 7.4, containing 0.03% human serum albumin and 0.5% phenol, for 72 h at 4°C. After centrifugation at 3000 g, 15 min, supernatants were collected and dialysed with a 3500 D molecular weight cutoff membrane (Molecularpouros Dialyses Membrane, Spectrum, California) against deionized water for 72 h. The dialysate was centrifuged at 13,000 g for 15 min, and the supernatants were sterilized with a 0.22 µm Millex GS filter (Millipore, the Netherlands) and freeze-dried. A 1% solution in PBS was made of the freeze-dried material (4).

4 types of gloves were used for skin testing: (a) sterile latex surgeon's gloves (powdered), Baxter

Healthcare Corporation, Valencia, USA; (b) latex examination gloves (powdered), Romed, Omnilabo, the Netherlands; (c) hypoallergenic latex examination gloves (unpowdered), Savacare, Van der Bend BV, Brielle, the Netherlands; (d) non-sterile synthetic medical gloves (powdered), Elastyren, ECI Medical Technologies Inc. Nova Scotia, Canada.

The protein content was determined by the method of Watanabe using pyrogallol red molybdate complex (5). The protein concentrations of the 4 glove extracts (1% w/v), used for prick testing, were in the range of 5.5–7.4 g/l.

From the glove powder (absorbable dusting powder, Keoflo 7136P-USP, van der Bend BV, Brielle, the Netherlands), a 10% extract (w/v) was made in PBS. After 1 h the extract was centrifuged for 10 min at 2000 g and supernatant was passed through a 0.22 µm filter.

Avocado, kiwi, and banana extracts were prepared from small ripe pieces of the fruits without peel or core. The pulps were homogenized in a food processor and the slurries were passed through a 0.22 µm filter.

All extracts were stored in appropriate aliquots at –20°C until use in prick tests. Before use, extracts were defrosted for 1 h before the skin test and centrifuged for 45 s at 3200 g.

Table 1. Results from the questionnaire concerning natural latex allergy in laboratory workers

	<i>n</i>	(%)
number of participants	66	
age: range (years)	19–56	
avg (years)	33.1	
sex F/M	42/24	
smoking/non-smoking	10/55	
duration of exposure		
0–5 years	37	56.1
5–10 years	24	36.4
>10 years	5	7.6
glove use: h/day		
range	0–6.5	
average	1.2	
glove use: h/week		
range	0–30	
average	5.0	
glove use: h/month		
range	0–100	
average	21.0	
glove-related complaints		
itching	22	33.8
redness	19	29.2
eczema	6	9.2
urticaria	9	13.8
angioedema	4	6.2
rhinoconjunctivitis	10	15.4
asthma	2	3.1
inhalant atopy	25	41.7

Table 2. Positive patch test results (61 individuals tested)

Allergen	n	(%)
nickel	14	23.0
colophony	4	6.6
fragrance mix	4	6.6
thiuram mix	3	4.9
balsam of Peru	3	4.9
Romed glove	3	4.9
cobalt chloride	2	3.3
formaldehyde	1	1.6
Kathon CG	1	1.6
carba mix	1	1.6
Baxter glove	1	1.6

Finally, prick tests were performed with common inhalant allergens from ALK Benelux (Groningen, the Netherlands): grass mix (SQ 293), tree mix (SQ 108), *Dermatophagoides pteronyssinus* (SQ 503), cat dander (SQ 555) and dog dander (SQ 553).

RASTs

For the RASTs, the Pharmacia Cap RIA (with allergen k82 *Hevea braziliensis*) and total IgE were measured according to the manufacturer's instructions.

Results

Clinical history

Of the 98 individuals invited, 66 participated in the study (67.3%). Reasons for failure to attend were irregular (part-time) working schedules, lack of interest because of absence of work-related symptoms, and other individual causes. Demographic characteristics of the volunteers and data from the questionnaire are shown in Table 1.

Glove-related symptoms were reported by 28 individuals (43.1%); complaints consisted of local dermatitis in 36.9% and of urticaria, rhinoconjunctivitis and/or asthma in 24.6%.

Patch tests

Patch tests with standard contact allergens were positive in 42.6% of the 61 individuals tested (Table 2). Positive test results for nickel were found frequently, viz., in 14 women with complaints about jewellery. The rubber additives were positive in only 4 individuals, 3 of them with complaints of glove-related itching and redness. A positive patch test with the Romed glove was seen in 3 individuals with a very strong prick test result for the latex gloves. Patch tests with the rubber additives, however, were negative in these patients. Glove powder extract gave no positive reaction in any of the individuals tested.

Prick tests

Atopy for inhalant allergens was demonstrated in 25 out of 60 individuals tested (41.7%). Prick tests were positive for *Dermatophagoides pteronyssinus* in 26.7%, for grass pollen in 25.0%, for tree pollen in 15.0%, for cat dander in 20.0% and for dog dander in 11.7% of the volunteers. In 5 individuals, there was a positive prick test with the glove extracts. These cases are shown in Table 3. All were atopic and used rubber gloves very often. Complaints consisted of glove-related dermatitis in 5, urticaria in 4, and rhinoconjunctivitis in 3 individuals. Latex-associated food sensitization was demonstrated in 4 out of 5 latex-positive individuals and in 5 out of 55 latex-negative individuals. There was no positive reaction to glove powder extract or to the non-latex glove extract (Elastyren).

RASTs

NRL-specific IgE was demonstrated in 3 cases (Table 3), with strongly positive prick test results for glove extracts. The other 2 cases with moderately positive prick tests were RAST negative, as were all other individuals with negative skin test results for glove extracts.

Table 3. Positive prick test results (Ro=Romed glove; Ni=Nickel)

Case no.	L05	L15	L21	L31	L43
age (years)	26	29	29	30	23
sex	F	M	F	F	F
years of occupation	0-5	6-10	0-5	0-5	0-5
glove use					
h/day	2	2	4	1	2
h/month	35	40	80	20	30
atopy	+	+	+	+	+
glove-related complaints					
itching	+	+	+	+	+
redness	+	-	+	+	+
urticaria	+	+	+	+	-
angioedema	-	-	+	-	-
rhinoconjunctivitis	+	+	+	-	-
asthma	-	-	-	-	-
prick test (mm)					
glove powder	0	0	0	0	0
Baxter	9	10	9	0	6
Romed	17	21	14	4	9
Savacare	8	13	8	0	4
Elastyren	0	0	0	0	0
avocado	4	5	0	4	8
banana	4	6	0	0	5
kiwi	0	8	0	5	0
RAST latex (kU _A /l)	2.79	9.29	8.62	<0.35	<0.35
total IgE (kU/l)	208	60	534	368	128
patch test positive	Ro	Ro	Ro	-	-
			Ni		

Table 4. Correlation between inhalant allergy (positive case history and positive SPT to common inhalant allergens) and the diagnosis of Type I NRL allergy

	Total number	With NRL allergy	(%)
atopic	25	5	20
non-atopic	35	0	0

Discussion

Latex sensitization is seen frequently as an “allergic disease” in our daily practice. Health care workers in particular are at risk due to their frequent contact with rubber gloves. Prevalence rates of latex atopy (i.e., positive prick test) range from 2.8 to 16.9% for hospital personnel in general (6–9); from 5.0 to 17.6 for ward nurses (8–10); from 5.4 to 14.4 for O.R. personnel (7, 11–15); and, finally, from 7.4 to 9.9 for physicians (7, 9, 16). Regarding laboratory workers, 2 studies provide information about the existence of Type I NRL allergy. In a children’s hospital in the USA, positive prick tests were found in 17.1% of 41 laboratory workers (9). In a small primary care hospital in Belgium, the prevalence was 5.0% in 36 laboratory workers (8). In The Netherlands, only 1 report regarding latex allergy in health care workers was found (2). All surgeons, gynaecologists and urologists practising in the Netherlands were sent a questionnaire on the incidence of glove-related symptoms. The response rate was 64.0%. Glove-related dermatoses were reported in 9.5%, of which 1.1% consisted of contact urticaria. None mentioned rhinoconjunctivitis or asthma-like symptoms. No confirmatory tests, such as patch tests or prick tests were performed.

We investigated the prevalence of allergy to NRL in a population at risk in The Netherlands. For this purpose, we studied laboratory workers of the Department of Immunology, Erasmus University, Rotterdam. Approximately 40,000 pairs of powdered NRL gloves were used in 1996 at this department and workers were exposed frequently. Glove-related dermatitis was reported by 37% ($n=25$) of the individuals, the main symptoms being itching and redness of the skin. In only 4 of these 25 individuals did a positive patch test with rubber additives confirm the diagnosis of allergic contact dermatitis. Overall a high prevalence of positive patch tests with standard contact allergens was seen. The allergens most frequently found were nickel, colophony and fragrance mix.

Regarding immediate-type allergy, a high % of atopic individuals was seen; inhalant allergens most frequently found were *Dermatophagoides pteronyssinus* (27% of individuals tested), grass pollen (25%), cat dander (20%) and tree pollen

(15%). Glove-related rhinoconjunctivitis was reported by 15% ($n=10$) of the participants; in 5/10 cases Type I allergy for latex gloves was confirmed by prick testing, in 3/10 by latex RAST. All 5 individuals were atopic for inhalant allergens, but unaware of the cause of the glove-associated complaints. The correlation of inhalant atopy to the diagnosis of NRL allergy is summarized in Table 4. None reported symptoms of dyspnoea or wheezing, although in 2 individuals, we measured lung function (17) and showed, in 1 case, bronchial hyperreactivity, suggesting asymptomatic occupational asthma. This was reported earlier by Vandenas, who found a positive bronchial response to latex inhalation challenge in nurses without a history of occupational asthma (8).

As shown in Table 3, “hypo-allergenic” gloves also caused strong positive skin reactions in 4/5 NRL atopic cases. Therefore, these gloves are no alternative for NRL atopic individuals, in accordance with previous research (18). Non-latex glove extract and glove powder extract were negative in all cases in patch tests and prick tests. Patch tests with rubber additives, like thiuram mix and carba mix, were also negative in all NRL-atopic persons and had no predictive value for Type I allergy. This was confirmed by the case history: all 5 cases with Type I NRL allergy had complaints of itching and/or redness of the skin within 30 min of glove use. Only 1 individual reported chronic hand eczema (with negative patch test results for rubber additives).

In summary, we found, in accordance with previous investigations in other countries, a high prevalence of glove-related symptoms and NRL Type I and Type IV allergy in laboratory workers exposed to rubber gloves. Furthermore, we showed that regular contact with NRL gloves resulted in 2 distinct disease groups: a Type I allergic population, all atopics and with a high prevalence of co-existing tropical fruit allergy; and a Type IV allergic population without evidence of Type I allergic reactions to inhalant allergens, fruit or NRL. Most individuals were not aware of the existence of latex allergy. Therefore, we conclude that there is a compelling need for education and active search for patients in at-risk populations like health care workers. In this way, we can prevent further sensitization to latex allergens and worsening of atopic complaints by means of individual as well as work-related measures (19, 20).

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References

1. Turjanmaa K, Alenius H, Makinen-Kiljunen S, Reunala T, Palosuo T. Natural rubber latex allergy. *Allergy* 1996; 51: 593–602.
2. Van der Meeren H L M, Boezeman J B M, Rampen F H R. Contacteczem door operatiehandschoenen. *N T v G* 1988; 132: 963–965.
3. Dreborg S, Frew A. Allergen standardization and skin tests. Position paper EAACI. *Allergy* 1993; 48: suppl 14: 1.
4. Kurup V P, Kelly K J, Turjanmaa K, Alenius H, Reunala T, Palosuo T. Immunoglobulin E reactivity to latex antigens in the sera of patients from Finland and the United States. *J Allergy Clin Immunol* 1993; 91: 1128–1134.
5. Watanabe N, Kamei S, Onkubo A et al. Urinary protein as measured with pyrogallol red molybdate complex, manually and in Hitachi 726 automated analyser. *Clin Chem* 1986; 32: 1551–1554.
6. Safadi G S, Corey E C, Taylor J S, Wagner W O, Pien L C, Melton Jr AL. Latex hypersensitivity in emergency medical service providers. *Ann Allergy Asthma Immunol* 1996; 77: 39–42.
7. Turjanmaa K. Incidence of immediate allergy to latex gloves in hospital personnel. *Contact Dermatitis* 1987; 17: 270–275.
8. Vandenplas O, Delwiche J-P, Evrard G, Aimont P, Van der Brempt X, Jamart J, Delaunoy L. Prevalence of occupational asthma due to latex among hospital personnel. *Am J Respir Crit Care Med* 1995; 151: 54–60.
9. Yassin M S, Lierl M B, Fischer T J, O'Brien K, Cross J, Steinmetz C. Latex allergy in hospital employees. *Ann Allergy* 1994; 72: 245–249.
10. Kibby T, Akl M. Prevalence of latex sensitization in a hospital employee population. *Ann Allergy Asthma Immunol* 1997; 78: 41–44.
11. Iacobelli A M, McCullough J A, Ownby D R. The prevalence of latex allergy in high risk medical personnel. *J Allergy Clin Immunol* 1993; 91: 216.
12. Lagier F, Vervloet D, Lhermet I, Poyen D, Charpin D. Prevalence of latex allergy in operating room nurses. *J Allergy Clin Immunol* 1992; 90: 319–322.
13. Mace S, Sussman G, Stark D F, Thompson R, Kelly K, Beezhold D. Latex allergy in operating room nurses. *J Allergy Clin Immunol* 1996; 97: 322.
14. Turjanmaa K, Cacioli P, Thompson R L, Simlote P, Lopez M. Frequency of natural rubber latex allergy among US operating room nurses using skin prick testing. *J Allergy Clin Immunol* 1995; 95: 214.
15. Wrangsjo K, Osterman K, Van Hage-Hamsten M. Glove-related skin symptoms among operating theatre and dental care unit personnel. *Contact Dermatitis* 1994; 30: 139–143.
16. Arellano R, Bradley J, Sussman G. Prevalence of latex sensitization among hospital physicians occupationally exposed to latex gloves. *Anesthesiology* 1992; 77: 905–908.
17. Hargreave F E, Ryan G, Thomson N C et al. Bronchial responsiveness to histamine or methacholine in asthma: measurements and clinical significance. *J Allergy Clin Immunol* 1981; 68: 347–355.
18. Vandenplas O, Delwiche J-P, Depelchin S, Sibille Y, Vande Weyer R, Delaunoy L. Latex gloves with a lower protein content reduce bronchial reactions in subjects with occupational asthma caused by latex. *Am J Respir Crit Care Med* 1995; 151: 887–991.
19. Task Force on Allergic Reactions to Latex, Committee report from the American Academy of Allergy and Immunology. *J Allergy Clin Immunol* 1993; 92: 16–18.
20. Kelly K J, Sussman G, Fink J N. Stop the sensitization. *J Allergy Clin Immunol* 1996; 98: 857–858.

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