

Type I allergy to natural rubber latex and type IV allergy to rubber chemicals in health care workers with glove-related skin symptoms

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Summary

Background It has been established that there are type I and type IV allergens in latex gloves.

Objective The purpose of the study was to establish the prevalence of rubber glove-induced skin symptoms among health care workers in one Italian hospital.

Methods Health care workers ($n = 1584$) were evaluated using a written questionnaire and 295 respondents with glove-induced skin symptoms were tested. We performed: skin prick test with latex glove extract and commercial latex, and environmental and food allergens; glove use test; patch tests with a rubber additive series; and RASTs.

Results Hospital employees who used or had used latex gloves at work were 1294. Three hundred and sixteen (24.4%) reported glove-induced symptoms, namely, cutaneous symptoms in all the cases and non-cutaneous symptoms in 105 subjects (8.1%). Twenty-seven of the 295 symptomatic employees tested (9.1%) were latex sensitive. Thirty-one patients (10.5%) exhibited positive patch test to rubber-related allergens. The most positive readings were obtained from the Thiuram mix and the Carba mix, with 12 and 9 positivities, respectively. The risk factors for latex skin sensitization were: a previous history of atopy and asthma; history of surgery; pre-existing hand dermatitis; work-related symptoms; and positive skin tests to common inhalant and certain foods ($P < 0.05$). Subjects who exhibited positive patch test were significantly more likely to have a prior hand dermatitis ($P < 0.001$). Of the 295 cases, 275 (93.2%) were contact dermatitis (CD), 13 (4.4%) contact urticaria (CU) (including protein CD) and 7 (2.4%) CD associated with CU.

Conclusions Our results show a high prevalence of rubber glove-induced dermatoses among the employees in one Italian hospital. The majority of skin complaints of latex gloves are related to skin irritation rather than to allergy. The immediate allergy to latex and the delayed allergy to rubber chemicals suggest that all the health care workers with glove-related dermatitis should undergo both skin prick test and glove use test to detect type I hypersensitivity to latex, and patch test to detect type IV hypersensitivity to rubber chemicals.

Keywords contact dermatitis, health care workers, latex allergy, latex gloves, rubber chemicals, skin symptoms

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Introduction

Concern about acquired immunodeficiency syndrome (AIDS) and hepatitis B has increased the use of protective gloves among health care workers. The increased use of latex gloves has led to numerous undesirable cutaneous and mucosal effects. IgE-mediated reactions are only one facet of a spectrum of reactions to latex gloves in the health care setting. Indeed, the most common clinical presentation is a non-immunological irritant contact dermatitis (CD). Other immunologically mediated reactions, such as delayed allergic CD, occur probably even more frequently than type I responses [1]. The wide spectrum of IgE-mediated clinical symptoms ranges from mild contact

urticaria (CU), conjunctivitis and rhinitis to generalized urticaria, asthma and anaphylactic shock [2]. Type IV allergens are additives that are used to act as preservatives, vulcanizing agents and accelerators during the processing and subsequent manufacture of rubber products [1].

The only test that clarifies the allergic status of a patient is latex challenge test; in fact, clinical history is often unreliable and IgE tests do not have 100% diagnostic accuracy because of variety of NRL (natural rubber latex) allergens; besides, sometimes SPTs are dangerous [3–5]. The challenge test, which ensures a whole allergenic spectrum of NRL, has been considered to be decisive for the diagnosis of latex allergy [6]. Here, again, reproducibility, standardization and quantification remain the common weaknesses of these tests. The diagnosis of rubber allergic CD is based on patch testing with rubber chemicals. Our aim was to establish the prevalence of rubber glove-induced skin symptoms among health care workers in one Italian hospital.

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Materials and methods

Study questionnaire and subjects

The study was conducted at Bari University Hospital. Hospital workers ($n = 2600$) were asked to complete a questionnaire concerning age, sex, job position, department (surgical, medical, laboratory, radiology, non-clinical), length of current occupation, use of rubber and/or other types of gloves, frequency of latex glove use categorized as daily, weekly and monthly, and agents used during working hours (such as soaps, detergents and disinfectants). The questionnaire also provided data on symptoms related to glove use, history of non-work-related previous hand dermatitis, any atopic condition, and number of previous surgical procedures. Subjects reporting in the questionnaire reactions caused by natural rubber gloves were invited to undergo skin tests (prick, patch and glove use tests) and RAST tests at our Allergologic and Dermatology Unit.

Skin prick test reagents

Glove extracts to be used for skin prick testing were prepared as reported previously [7]. Briefly, 400 mg of latex rubber gloves usually used in the hospital (Le Petit, Grandate, Como, Italy) were incubated for 30 min in 5 mL of sterile physiological saline. The incubation fluid was used as a stock solution for prick testing.

Additional skin prick tests were performed with food and common inhalant allergens, and a commercial extract of non-ammoniated latex (Stallergènes, Paris, France). Food and inhalant extracts (Bayropharm, DHS, Milan, Italy) included avocado, banana, chestnut, kiwi, pineapple, *Dermatophagoides pteronyssinus* and *farinae*, grass pollen, olive pollen, cypress pollen, *Parietaria*, *Artemisia vulgaris*, cat dander, dog dander and *Alternaria Tenuis*. Histamine dihydrochloride (10 mg/mL) was used as positive control, and physiological saline as negative control. A prick test was considered as positive if the weal size was mean diameter 3 mm larger than the weal of the negative control. Atopy was diagnosed by the presence of one or more positive prick tests of common inhalant allergens.

Patch tests

Patients were patch tested to a rubber additive series (Table 1). Patch testing was performed by means of Finn Chambers secured with Scampor tape [8], which were left on the back for 48 h. Readings were taken at days 2 and 4. All reactions were scored in accordance with the recommendations of the International Contact Dermatitis Research Group [9].

Glove provocation tests

The glove use test was performed with the same type of gloves as follows: a fingertip was cut from the suspected glove and placed on one finger for 15–30 min. If the reaction was negative, the whole glove was worn for the same amount of time. One vinyl glove was used as a control. A glove use test was regarded as positive when there was contact urticaria on the finger/hand exposed to latex, rhinitis or asthma.

Latex-specific IgE

The laboratory evaluation included measurements of serum-specific IgE to latex (Pharmacia CAP system, RAST FEIA)

Table 1. List of rubber allergens tested and positive patch test reactions (295 individuals tested)

Rubber allergens	No. positive reactions	(%)
Thiuram mix 1% pet	12	4
Carba mix 3% pet	9	3
Tetramethylthiuram monosulphide 0.25% pet	8	2.7
Mercaptobenzothiazole 2% pet	4	1.3
Mercapto mix 2% pet	4	1.3
N-Cyclohexylbenzothiazyl sulfenamide 0.5% pet	4	1.3
Tetramethylthiuram disulphide 0.25% pet	4	1.3
Hexamethylenetetramine 1% pet	4	1.3
Black rubber mix 0.6% pet	3	1
N-Isopropyl-N-phenyl-4-phenylenediamine 0.1% pet	3	1
1,3-Diphenylguanidine 1% pet	3	1
Tetraethylthiuram disulphide 0.25% pet	3	1
bis(Diethyldithiocarbamate) zinc 1% pet	2	0.7
Dipentamethylenethiuram disulphide 0.25% pet	2	0.7
Diphenylthiourea 1% pet	2	0.7
N-Cyclohexyl-N-phenyl-4-phenylenediamine 0.25% pet	1	0.3
Dibenzothiazyl disulphide 0.5% pet	1	0.3
Morpholinyl mercaptobenzothiazole 0.5% pet	1	0.3
Mercaptobenzothiazole 0.5% pet	1	0.3
Dibutylthiourea 1% pet	1	0.3
Dithiomorpholyn 1% pet	1	0.3
N,N-Diphenyl-4-phenylenediamine 0.25% pet	0	0
2,2,4-Trimethyl-1,2-dihydro-quinoline 1% pet	0	0
Hydroquinone mono-benzylether 1% pet	0	0
bis(Dibutylthiocarbamate) zinc 1% pet	0	0
Zinc dimethyldithiocarbamate 1% pet	0	0
Triethylene-tetramine 1% pet	0	0
Diethylthiourea 1% pet	0	0
Ethylene thiourea 1% pet	0	0
Dodecylmercaptan 0.1% pet	0	0
Phenyl-beta-naphthylamine 1% pet	0	0

Five out of 12 Thiuram mix-positive patients were negative to individual ingredients. Five out of 9 Carba mix-positive patients were negative to individual ingredients. Two patients reacted to an ingredient of the Thiuram mix when tested separately but not to the mix itself.

under standardized conditions, as recommended by the manufacturer. A positive RAST was defined as a value > 0.35 kU/L.

Statistical analyses

The study was approved by the ethical committee and subjects signed an informed consent to participate in the study. The data were input on a database that stored test results and all information from the questionnaire. The statistical analysis included chi-square test (with Yates' correction when necessary) and Fisher's exact test (one-tailed) as appropriate. We compared mean values of continuous variables with *t*-tests. In all instances, a probability value less than 0.05 was considered to be statistically significant.

Results

Study questionnaire results

A total of 1584 workers responded to the survey, representing a participation rate of 60.9%. The results from the questionnaire for workers who ever used latex gloves are shown in Table 2. Out of the workers who used latex gloves, 316 (24.4%) reported

Table 2. Results from the questionnaire in workers who ever used latex gloves

	Number	%	95% confidence intervals
Sex			
Female	677	52.3	49.6–55
Male	617	47.7	45–50.4
Age (yr)			
< 20	1	0.1	0.0–0.2
21–30	178	13.7	11.8–15.6
31–40	523	40.4	37.7–43.1
41–50	436	33.7	31.1–36.3
> 50	156	12.1	10.3–13.9
Mean ($\pm$ SD) age (yr)	40.03 $\pm$ 8.53		(range 19–74)
Work experience, year			
< 5	379	29.3	26.8–31.8
6–10	227	17.5	15.4–19.6
> 11	688	53.2	50.5–55.9
Job title			
Nurse	495	38.3	35.7–40.9
Doctor	276	21.3	19.1–23.5
Cleaner	263	20.3	18.1–22.5
Laboratory technologist	63	4.9	3.7–6.1
Other	197	15.2	13.2–17.2
Department			
Medical	870	67.2	64.7–69.7
Surgical	230	17.8	15.7–19.9
Laboratory	81	6.3	5–7.6
Radiology	43	3.3	2.3–4.3
Non-clinical	70	5.4	4.2–6.6
Current use of latex gloves			
Monthly	189	14.6	12.6–16.6
Weekly	197	15.2	13.2–17.2
Daily	908	70.2	67.7–72.7
Hours per day	3.71		
$\leq$ 4 h	633	48.9	46.2–51.6
> 4 h	275	21.2	19.2–23.2
Mean length of glove usage (yr)	11.7		
History of atopic disease			
At least one disease	359	27.7	25.3–30.1
Rhinoconjunctivitis	274	21.2	19–23.4
Asthma	97	7.5	6.1–8.9
Childhood dermatitis	68	5.2	4–6.4
Prior hand eczema	70	5.4	4.2–6.6
Food allergies	73	5.6	4.4–6.8
Drug allergies	112	8.6	7.1–10.1
Previous surgical procedures	545	42.1	39.4–44.8
Frequent use of soaps, detergents or antiseptics	1092	84.4	82.4–86.4

glove-induced symptoms (Table 3). They were cutaneous symptoms in all cases and non-cutaneous symptoms in 105 cases (33%). The mean duration of daily glove usage in the subjects who reported these reactions was larger than that of those who did not have any symptoms (4.2 h vs. 3.5 h).

Study group

All the persons with undesirable glove reactions reported in the questionnaire were invited to our unit by the preventive

Table 3. Prevalence of symptoms associated with usage of latex gloves in 1294 hospital workers

	Number	%	95% confidence intervals
Skin disorders			
At least one dermatological symptom	316	24.4	
Drying of skin	254	19.6	17.4–21.8
Itching	246	19	16.9–21.1
Redness	208	16.1	14.1–18.1
Eczema	65	5	3.8–6.2
Localized hives	55	4.2	3.1–5.3
Generalized hives and/or facial angioedema	17	1.3	0.7–1.9
Respiratory and conjunctival symptoms			
At least one non-cutaneous symptom	105	8.1	6.6–9.6
Rhinorrea or nasal congestion	65	5	3.8–6.2
Dyspnoea	18	1.4	0.8–2
Lacrimation or conjunctival itching	83	6.4	5.1–7.7

medicine service of Bari University Hospital, but only 295 of them accepted clinical evaluation, skin tests and serum analyses. A standardized interview, the clinical evaluation and allergologic tests suggested that these subjects had suffered from or still had glove-induced dermatoses.

In the 295 cases evaluated, the glove-induced skin symptoms were diagnosed as CD in 275 (93.2%) cases (28 ACD and 247 ICD, respectively) and as CU (including protein contact dermatitis) in 13 (4.4%) cases; seven (2.4%) subjects had concomitantly latex CU and CD to rubber chemicals (three ACD and four ICD). The lesions were located on the hands in 279 workers, on the wrists in 18, and on the forearms in 19.

IgE tests and challenge tests results

Only 27 (9.1%) subjects presented positive skin prick tests to latex glove extract. Out of them, 24 (88.9%) had also a positive response to commercial extract, while 13 (48.1%) had a positive blood test to latex with titres varying between 0.6 and 85.1 kU/L. Latex challenge was positive only in 20/27 (74.1%) (all positive latex workers). By definition, 20/27 subjects could be considered as latex allergic, while 7/27 were only sensitized. The main characteristics concerning glove use test negative patients are shown in Table 4.

None of the participants experienced adverse reaction to the latex SPT procedure; on the contrary, during the first step of challenge test two patients with latex allergy experienced generalized urticaria and asthma which subsided quickly after adequate therapy. The first patient had a history of asthma, rhinorrea and conjunctival itching on latex exposure and RAST value was 44.5 kU/L. The other one had a history of contact urticaria on latex exposure and RAST value was 85.1 kU/L. At the time of glove use test both subjects suffered from an active mild hand dermatitis.

Atopy and food sensitivity

Of 295 prick-tested subjects, 72 (24.4%) showed one or more positive SPT to common inhalant and were considered atopic. SPT reactions to one or more food allergens were seen in 22 (7.4%) workers.

Table 4. Main characteristics concerning glove use test negative patients

No.	Sex	Age	History of atopic diseases*	Latex gloves-attributed symptoms†	SPT with latex glove eluate	SPT with latex commercial extract	Latex RAST	SPT with common inhalant allergens‡	SPT with latex cross-reacting foods
1	F	39	Neg.	C-DS-E-I-R-RE	Pos.	Neg.	Neg.	Neg.	Banana-chestnut
2	F	35	Neg.	DS-E-I-RE	Pos.	Pos.	Neg.	G-P	Neg.
3	F	33	Neg.	C-DS-I-LU-RE	Pos.	Pos.	Neg.	A-P	Neg.
4	F	43	Neg.	I	Pos.	Pos.	Neg.	CD	Neg.
5	F	57	A-R	C-D-DS-E-I-LU-R-RE	Pos.	Pos.	Neg.	Neg.	Kiwi
6	F	44	Neg.	C-DS-E-I-LU-R-RE	Pos.	Pos.	Pos.	Neg.	Neg.
7	F	31	R	C-DS-E-I-LU-R-RE	Pos.	Pos.	Pos.	A-G-O-P	Neg.

*A = Asthma; R = rhinoconjunctivitis. †DS = drying of skin; I = itching; RE = redness; E = eczema; LU = localized urticaria; R = rhinorrhea; D = dyspnoea; C = conjunctivitis. ‡O = olive pollen; G = grass pollen; A = *Artemisia vulgaris*; P = *Parietaria*; CD = cat dander. Neg. = negative; Pos. = positive.

Patch tests results

Patch tests with rubber-related antigens were positive in 31 (10.5%) of the 295 individuals tested (Table 1). In view of the clinical situation all were felt to be of current relevance. Positive test results for the Thiuram mix and the Carba mix were found more frequently (12 and 9, respectively).

Risk factors for latex sensitization and rubber chemicals allergy

Demographic, exposure characteristics, personal history, symptoms on exposure to latex gloves, and skin test results, were compared between those with and without a positive response to latex on prick testing (Tables 5 and 6). Participants who were positive for SPTs to latex were significantly more likely to have a history of atopy and surgery, significantly more likely to work as nurses and doctors in the surgical departments, and significantly more likely to have positive skin tests to one or more of the tested common inhalants or foods. They were clearly more likely to report contact and generalized urticaria, asthma, rhinitis or conjunctivitis symptoms on exposure to latex products.

Finally, we examined the characteristics of the people positive and negative for patch tests to rubber-related allergens. The prevalence of positivity did not vary by sex and history of allergies. Subjects who exhibited positive patch test were significantly more likely to have a prior hand dermatitis. Most of them had a contact dermatitis characterized by erythematous squamous eczema, prevalently located on the dorsal surface of the hands.

Discussion

The increased use of latex glove has brought to light the problem of both allergic and non-allergic reactions to these products. Contact with latex gloves may cause irritant dermatitis, delayed hypersensitivity and immediate hypersensitivity reactions [1]. Although these reactions are a particular problem for hospital employees who have to wear gloves, non-allergic dermal and mucosal irritation is only briefly mentioned in recent medical literature [1,10]. In the present study, the prevalence of skin symptoms in hands associated with the usage of latex gloves was evaluated. Our study, carried out in health care workers of an Italian hospital, shows that natural rubber latex gloves are a common cause of occupational skin disorders (24.4%).

We found a positive association between the mean length of daily glove usage and the presence of skin symptoms. In previous studies, the prevalence of self-reported glove irritation had varied from 14% in dental staff [11] to 56% in hospital personnel [12]. Many of these workers might understandably conclude that they have latex allergy; however, non-immunological irritant dermatitis accounted for a large portion of contact symptoms. We observed that the prevalence of latex sensitization based on skin prick tests with latex glove extracts was 9.1% of the symptomatic subjects, with a prevalence of 8.1% using a commercially available latex skin test reagent. Furthermore, specific serum antibodies to latex were demonstrated in 13 of these subjects. Finally, latex challenge was positive in 20/27 (74.1%) latex SPT-positive participants. Depending on examined cohort, the prevalence of sensitization to latex ranges from 3 to 12% in hospital workers [13].

There have been only a few reports of a clinical relevant allergy to latex without SPTs to glove extracts [2,14]. In health care workers, skin testing with glove extract should be preferred to testing with a commercial extract because, given the variety of latex proteins involved in the aetiology of latex allergy, only the allergens that could have sensitized the workers would be used [15]. However, today the allergenicity of latex gloves is getting lower and lower and to find good test gloves is becoming difficult; therefore, commercial, standardized preparations in combination to glove eluates are preferred to detect latex sensitization with skin testing. In studies comparing skin tests with latex and CAP with latex, SPTs were usually reported to be more sensitive than *in vitro* latex-specific IgE assays [16].

The main problem in detecting latex allergy with common procedures (SPT, CAP, challenge test) is that the antigenic molecule profiles differ among the products used and also between the finished products and the raw material. In addition, the specificity of the anti-latex IgE antibodies has varied among the sensitized persons; therefore, the evaluation of latex sensitivity and specificity is strongly limited to the extract used [17]. We did not observe systemic reactions due to SPTs with the latex preparation in our study; however, such reactions have been previously reported [3–5]. Probably these differences are due to the variable extract used; in fact, the material used by Kelly et al. [3] was self-made dilution of raw latex and the lancets used were Multitest lancets (six peaks of 2 mm length each), while usually one-peak lancets of 1 mm length are used.

Table 5. Characteristics of non latex-sensitized (–) and sensitized (+) subjects. Sensitization was defined on a positive skin test with glove extract

	Latex negative (<i>n</i> = 268)		Latex positive (<i>n</i> = 27)		
	<i>n</i>	%	<i>n</i>	%	<i>P</i> -value
<i>Personal characteristics</i>					
Mean (± SD) age (yr)	37.57 ± 7.6		35.44 ± 8.2		NS‡
Sex (female)	201	75	24	88.9	NS*
<i>History of atopic disease</i>					
At least one disease	103	38.4	16	59.2	< 0.05*
Rhinoconjunctivitis	86	32.1	13	48.1	NS*
Asthma	24	8.9	6	22.2	< 0.05†
Childhood dermatitis	18	6.7	2	7.4	NS†
Prior hand eczema	28	10.4	7	25.9	< 0.05†
Food allergies	20	7.5	6	22.2	< 0.05†
Drug allergies	32	11.9	2	7.4	NS†
Previous number (mean ± SD) of SP	133	43.6	20	74.1	0.01*
	0.8 ± 1.05		1.3 ± 1.17		< 0.05‡
<i>Work characteristics</i>					
Work experience, year (mean ± SD)	11.28 ± 8.1		8.44 ± 7		NS‡
Department					< 0.05*
Medical (nurses and doctors)	142	53	10	37	
Surgical (nurses and doctors)	37	23.8	9	33.3	
Job title					NS*
Nurse	143	53.3	17	63	
Doctor	36	13.4	2	7.4	
Cleaner	30	11.2	3	11.1	
Laboratory technologist	13	4.9	2	7.4	
Other	46	17.2	3	11.1	
<i>Current use of latex gloves</i>					
Weekly	22	8.2	1	3.7	
Monthly	28	10.5	1	3.7	
Daily	218	81.3	25	92.6	
Hours per day (mean ± SD)	4.1 ± 2.2		4.6 ± 1.9		NS‡
Period of glove latex usage, year (mean ± SD)	10.9 ± 6.7		9.2 ± 6.3		NS‡
Frequent use of soaps, detergents and antiseptics	232	86.6	21	77.8	NS*
<i>Symptoms on exposure to latex</i>					
Localized hives	34	12.7	19	70.4	< 0.001*
Generalized hives	8	3	6	22.2	< 0.001†
Conjunctivitis	60	22.4	18	66.7	< 0.001*
Rhinitis	47	17.5	15	55.6	< 0.001*
Dyspnoea	5	1.9	12	44.4	< 0.001†
At least one symptom	94	35.1	22	21.5	< 0.001*

SP = surgical procedures; NS = not significant. **P*-value determined by chi-square test. †*P*-value determined by one sided Fisher's exact test. ‡*P*-value determined by Student's *t* test.

Systemic reactions due to SPTs with glove eluates are not common despite these tests being widely performed. This could be attributed to different allergenic qualities of latex gloves, the different methods in preparing the glove eluates and, perhaps, different individual sensitivity. For this reason, several studies have been performed to verify the possibility of carrying out safer extracts, for example by shortening the extraction time or using extracts with known total protein content [18,19].

Therefore, clinical assessment in combination with commercially available RAST assay, notwithstanding the acknowledged limits of the latter, must represent the first step to diagnose latex allergy, particularly in subjects 'at risk' for reaction.

We reported two generalized positive reactions to glove challenge. Glove use test has significant limitations, despite only challenge tests being used to diagnose latex allergy. In fact,

because they are not standardized, they have to be performed with caution, especially in patients with a previous history of NRL-related anaphylaxis when SPT or latex RAST are positive and in patients with active hand dermatitis because the challenge dose adsorbed increases [20].

The risk factors for latex skin sensitization in this study are similar to those previously reported [13,21–23]. These include: a previous history of atopy and asthma; pre-existing hand dermatitis; work-related symptoms; and positive skin tests to common inhalants and certain foods. The association between latex and food allergy is partly due to common epitopes in fruit and latex [24]. We have evaluated the role of previous surgical operations in latex sensitization rate. Repeated latex exposure in children with spina bifida who have to undergo multiple surgery treatments is a cause of latex sensitization [25–27]. Our results showed a high rate of history of previous surgery in sensitized

Table 6. Statistical comparison of positive SPT responses to various aeroallergens and food allergens and positive patch test among non-latex-sensitized (–) and sensitized (+) subjects

	Latex negative (n = 268)	Latex positive (n = 27)	P-value
<i>D. pteronyssinus</i>	20	5	NS†
<i>D. farinae</i>	26	5	NS†
Grass pollen	13	5	NS†
<i>Parietaria</i>	10	6	< 0.01†
Olive pollen	10	5	< 0.01†
Cypress pollen	14	8	< 0.01†
<i>Artemisia vulgaris</i>	8	4	< 0.05†
<i>Aspergillus</i>	0	1	NS†
Cat dander	5	3	< 0.05†
Dog dander	6	0	NS†
At least one of inhalant (atopy)	55	17	< 0.001*
Kiwi	2	7	< 0.001†
Avocado	0	3	< 0.001†
Banana	1	8	< 0.001†
Chestnut	2	5	< 0.001†
Pineapple	2	0	NS†
At least one of food	6	16	< 0.001†
Patch test positivity	27	4‡	NS†

NS = statistically not significant. *P-value determined by chi-square test. †P-value determined by one sided Fisher's exact test. ‡Three of them suffering from a concomitant contact urticaria to latex.

workers, in contrast to Liss [13] who found no difference in the prevalence of reported past surgical procedures between health care workers who were positive and those who were negative for skin prick tests to latex. A possible explanation of our findings, according to Porri et al. [26], is that it is the number of surgical procedures rather than spina bifida *per se* [25] that is related to sensitization to latex.

Previous studies on latex allergy in health care workers have largely been reported with little detailed information on concomitant hand eczema and contact allergy or on outcome. We examined 295 employees in whom the diagnosis of contact dermatitis and/or contact urticaria was established on objective signs at the time of examination, the history and the results of skin and serological tests. Our findings support the assumption that the majority of skin complaints from gloves were caused by skin irritation rather than by allergy. In fact, the most frequent undesirable effect was ICD (85.1%), followed by ACD (10.5%) and CU (6.8%). ICD is a direct injury to the superficial layers of the skin, similar to a burn or an abrasion, usually caused by friction and exposure to chemicals within the glove [1]: bacterial endotoxin [28], ethylene oxide [29] and cornstarch powder [30]. Ethylene oxide, used in the sterilization of disposable gloves, can also cause IgE-mediated allergy [31]. Furthermore, occlusion increases the water content of the stratum corneum (by preventing evaporation), with consequent enhanced percutaneous absorption of irritant and allergic water soluble substances.

ACD due to rubber chemicals in patients with hand dermatitis has been reported [32,33]. Beck et al. [32] summarized data on 2112 patients referred to his clinic with hand dermatitis. Of these, 7.2% were diagnosed to have an ACD to an allergen present in rubber gloves. De Groot et al. [33] found a positive patch test with rubber additives in 16% of laboratory workers with glove-related dermatitis. Our data were in accordance with these studies and demonstrated that the most common sensitizers were thiuram mix and carba mix. These compounds are

known to cause delayed hypersensitivity reactions in health care workers [33] and in patients with latex allergy [34]. The positive patch test results were relevant to coexisting hand eczema in all our patients.

Associated or pre-existing hand eczema has been previously identified as a risk factor for experiencing latex allergy but patch test results were infrequently reported [20,35]. In our study, a prior hand dermatitis increases the risk of latex allergy and ACD to rubber chemicals, maybe due to the easier penetration of allergens through the damaged skin. Some studies investigated the prevalence of type IV and type I allergy to natural rubber latex [27,33,34]. The prevalence of positive patch tests to rubber chemicals, at 14.8% of our 27 latex sensitive health care workers, is similar to the 13% reported in 83 patients with latex allergy [34]. In our previous study we demonstrated that type I and type IV hypersensitivity are independent [27]. This could depend on both the cellular clones and pathogenic mechanism involved in type I and type IV reactions. In fact, in allergic contact dermatitis Langerhans cells (APC) deliver the allergen to the lymph nodes and sensitize Th1 cells. They release their inflammatory mediators, which produce the clinical eczematous pictures.

The allergens responsible for type I hypersensitivity, instead, induce production of specific IgE by B lymphocytes, followed by degranulation of mast cells and release of mediators. Although this co existence is not common [33], in subjects in risk groups for exposure to rubber products (i.e. health care workers), it is suitable to evaluate both latex and rubber chemicals hypersensitivity.

In conclusion, our results show a high prevalence of rubber glove-induced dermatoses among the employees in one Italian hospital. The majority of skin complaints related to latex gloves are caused by skin irritation rather than by allergy. The immediate allergy to latex and the delayed allergy to rubber chemicals suggest that all health care workers with glove-related dermatitis should undergo both skin prick test and glove use test to

detect type I hypersensitivity to latex, and patch test to detect type IV hypersensitivity to rubber chemicals. The high cost and the lack of suitable alternative materials will prevent the replacement of all latex gloves with synthetic materials in the near future. Therefore, it will be desirable to reduce the allergen content of latex gloves and to use powder-free latex gloves.

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