

Ten years incidence of natural rubber latex sensitization and symptoms in a prospective cohort of health care workers using non-powdered latex gloves 2000–2009

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Abstract

Objectives To assess the incidence of sensitization and gloves-related symptoms in 10-year follow-up in a group of health care workers (9,660 person-years) using non-powdered latex gloves from 2000 to 2009 and to examine related factors.

Materials and methods We studied 2,053 health care workers in Trieste Hospitals by means of skin prick test for latex extract, patch tests and medical examinations. We report the incidence of latex sensitization among workers using non-powdered latex gloves.

Results The incidence of latex sensitization, rhinitis, asthma, urticaria, irritant and allergic contact dermatitis were 1.0; 0.12; 0.21; 0.72; 2.39 and 2.50 cases per 1,000 person-years, respectively. Respiratory symptoms and urticaria were positively related with latex sensitization (OR = 8.0; 95 % CL 1.27–48.6), with common allergic respiratory symptoms (OR = 4.19; 95 % CL 1.04–16.8) and with familial atopy (OR = 4.47; 95 % CL 1.1–17.9).

Conclusion The incidence of latex sensitization and latex-related symptoms were very low but subjects with allergic symptoms related to common allergens are at higher risk. The use of non-latex gloves is suggested for them.

Keywords Occupational exposure · Hypersensitivity · Natural rubber latex · Follow-up incidence · Health care workers

Introduction

Allergy to natural rubber latex (NRL) is an important health concern among health care workers, and the main source of workplace exposure is powdered latex gloves. NRL allergy emerged as an important clinical condition following an increased use of latex gloves for skin protection in the early 80s (Roland and O’Heir 2008). Initially, authors reported cases of contact urticaria (Meding and Fregert 1984), afterward respiratory symptoms (Turijanma 1987; Fiorito et al. 1996; Lagier et al. 1992; Vanderplas et al. 1995; Yassin et al. 1994) and intraoperative anaphylaxis. In 1995, Hunt spoke about an “epidemic of occupational allergy to NRL involving health care workers” and stated the need to prevent NRL sensitization. From 90s, many papers were published on NRL allergy in occupational and non-occupational settings, and NRL became the most common cause of occupational asthma in industrialized countries (Lagier et al. 1992; Grzybowski et al. 1996; Liss et al. 1997; Hadjiliadis et al. 1995; Hamann et al. 1998).

In studies on hospital personnel, latex sensitivity was found to be three to five times higher among nurses and doctors than among workers not involved in patient care (Turijanma 1987; Yassin et al. 1994). It was reported that the prevalence of NRL allergy is influenced by atopy, frequency and years of glove use, previous and current hand dermatitis (Larese et al. 2001; Moneret-Vautrin et al. 1993; Bousquet et al. 2006). In 2006, Larese demonstrated that the sensitization and NRL-related symptoms decreased after 2000 by means of simple measures such as avoiding unnecessary glove use, using non-powdered latex gloves by all workers and using non-latex gloves by sensitized subject. These measures can stop the progression of latex symptoms and can avoid new cases of sensitization.

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Malerich et al. (2008) reported that the changeover to non-powdered NRL gloves was associated with a significant decrease in worker's compensation claims for latex-related illness in USA. Vandenplas reported in 2009 the time trend incidence of latex occupational asthma (OA) in Belgium: the national compensation-based data confirmed that a persistent decline in incidence of OA had occurred since late 90s. This downward trend has been associated with a decreasing usage of powdered NRL gloves and with an increasing usage of latex-free gloves.

Till now, there are no, to our knowledge, data on latex sensitization and symptoms in long-term follow-up of health care workers using non-powdered latex gloves. For that reason, we studied the health care workers in Trieste Hospitals in a prospective cohort from 2000 to 2009 to evaluate the 10-year incidence rate of sensitization and gloves-related symptoms in workers using non-powdered latex gloves.

Materials and methods

Study population

The study population consisted of 1,040 medical, surgical and laboratory nurses in Trieste Hospitals (90 % of exposed subjects in departments considered) who started working before 2000 (Larese Filon and Radman 2006) and 1,013 new employers who started to work in the hospital between 2000 and 2009 (93.1 % of eligibles). No differences in age, sex distribution and seniority of work were found between participants and eligibles (data are not shown). At the first control, all participants underwent physical examination and completed a questionnaire providing descriptive data about their past and current health status, NRL exposure and atopy evaluation. All were prick-tested with common allergens and latex (Lofarma allergeni-Milano). Since 2000, the workers used non-powdered NRL gloves with low protein release. Non-latex gloves were available for all workers, and their use was compulsory for symptomatic or latex-sensitized subjects. Before 2000, the other workers used latex gloves every day. Every 2 years, the participants underwent a new medical examination and completed the questionnaire again. New symptomatic subjects were prick-tested with the same latex extract.

Nurses with gloves-related symptoms can require a medical control in allergy department with a free access to the specialist anytime. Symptomatic workers underwent physical examination and all of them completed a questionnaire providing descriptive data about current health status, symptoms and latex exposure. They were prick-tested again with latex extract, and they were patch-tested

with European Standard Series and NRL gloves if symptoms would be suggestive for allergic contact dermatitis. Sensitized and symptomatic subjects were immediately provided with non-latex gloves at work. In case of respiratory symptoms, workers were relocated in a latex-free workplace.

Questionnaire

Before skin testing, a screening questionnaire was administered to exclude workers with serious systemic reactions to the latex-extract skin test (Spaner et al. 1989). The criteria for exclusion were either a severe asthma attack or a severe reaction to latex which had required medical intervention in the past year (Liss et al. 1997). The standardized questionnaire collected demographic data (age, sex, job title, seniority of work, exposure data, task description, number of gloves used per day, hours of use and kind of gloves) and information about family and personal history of allergic disorders (asthma, hay fever, allergies, eczema), as well as about symptoms related to glove use (Larese et al. 1996).

NRL-related lower respiratory symptoms were defined as presence of attacks of cough, wheezing and dyspnoea which appeared only at work or became significantly worse at work and needed pharmacological treatment. Work-related rhinitis was defined as the presence of sneezing and/or itchy, runny nose during working hours. Contact urticaria related to latex use was defined as a self-reported weal and flare reactions at the site of glove contact that appear within 10–15 min of usage; generalized urticaria was defined as a self-reported weal and flare reaction appearing in several skin sites. Contact dermatitis (CD) was defined as a self-reported erythematous-papulous-persistent eruption that appears on the skin after 2–3 days of contact with latex gloves: irritant (ICD) if negative to patch test, allergic (ACD) if positive to patch test to rubber additives (carba mix 3 % pet; thiuram mix 1 % pet, mercapto mix 2 %, PPD mix), to NRL gloves (patch test) or to cobalt chloride (0.5 %). Itching and erythema were defined as discomfort using gloves with itchy and/or erythema that disappear immediately after glove's removal. Personal atopy was defined as reported symptoms of allergic rhinitis and/or asthma in the past not related to latex exposure, while familial atopy was defined as the same symptoms present in parents or children.

Skin testing

Workers were skin tested with common inhalant allergens including perennial allergens (*Dermatophagoides farinae* and *pteronyssinus*, dog and cat danders and *Alternaria* spp.) and pollens (Gramineae, *Parietaria* spp., Betulaceae,

Colylaceae, Oleaceae). The extract of common allergens and latex were supplied by Lofarma Allergeni (Milan, Italy). The protein concentration of this latex extract was 12.5 µg/ml. The positive control was 1 % histamine dihydrogen chloride solution, and the negative control was 1 % glycerinate solution. Skin prick tests were performed by trained registered nurses. Skin test sites were clearly marked, a drop of extract was placed on the skin, and this was pricked with commercially available skin test lancets (Hollister Stier Laboratory, Ontario, Canada).

All tests were read and recorded after 15 min, and a weal of ≥ 3 mm was considered positive. A single positive response to an inhalant allergen was considered the determining criterion for atopy (by prick test). Prick test in subjects who had no reaction to positive control or who had a positive reaction to negative control were repeated after two months. No one was excluded as false positive or negative to skin prick test.

The serum of subjects with positive skin prick tests to NRL, or who had NRL-related symptoms, was tested for specific IgE (RAST-Pharmacia) for NRL extract.

Subjects with contact dermatitis underwent patch test with the European baseline series using Finn[®] chambers on Scanpor[®] tape. The tested allergens (FIRMA—Firenze) included thiuram mix (1 %), balsam of Peru (25 %), carbamates (carba mix 3 %), potassium dichromate (0.5 %), 4-paraphenylenediamine (1 %), anhydrous lanolin (c.t.), colophony (20 %), neomycin sulfate (20 %), IPPD (*N*-Isopropyl-*N*-phenyl-4-phenylenediamine 0.1 %), ethylenediamine dihydrochloride (1 %), epoxy resins (1 %), 2-mercaptobenzothiazole (1 %), formaldehyde (1 % H₂O), disperse yellow 3 (1 %), cobalt chloride (1 %), fragrance mix (8 %), benzocaine (5 %), nickel sulfate (5 %), disperse blue 124 (1 %), quinoline mix (6 %), quaternium-15 (1 %), diaminodiphenylmethane (0.5 %), methyl-*di*-bromoglutaronitrile and 2-phenoxy-ethanol (MDBGN) (1.5 %), thimerosal (0.1 %), primine (0.01 %), methyl-chloroisothiazolinone and methylisothiazolinone (MCI/MI) (0.01 % H₂O).

All haptens were applied on the upper back and removed after 48 h. The sites were examined on removal and 72/96 h after application, according to the International Contact Dermatitis Research Group (ICDRG) guidelines (Wilkinson et al. 1970).

Statistical procedure

Data analysis was performed with the SPSS program for Windows, release 9.0 (SPSS Inc, Chicago, IL, USA). Continuous data were summarized as means and standard deviation (SD). The difference between means was tested by Student's *t* test. Categorical data were analyzed by the likelihood χ^2 techniques with Yates's correction was

indicated by the data. Fisher's exact test was used if the expected number of observations in any cell was <5 . Odds ratios (OR) and 95 % confidence limits (CL) were calculated adjusting for confounding factors (sex, age) through multiple logistic regression analysis. We did weighted regression analyses using duration of follow-up as weights to account for the increased risk of developing the outcomes associated with a longer follow-up.

Incidence was calculated considering exposed subject in person-years and new symptomatic cases registered in each year of the follow-up. For all statistical analyses, a 0.05 level of significance was used, and all *p* values were two-sided.

Results

The characteristics of the population exposed to latex in Trieste Hospitals are reported in Table 1. The total number of participants at the follow-up was 2,053 with a mean age (SD) between 32.1 (8.0) and 38.2 (8.5) years. The majority was female (range 66–89.7 %).

Gloves-related symptoms and skin prick test sensitization to NRL at the first control are reported in the Fig. 1 that shows a progressive decrease in NRL sensitization and symptoms.

Before 2000, gloves-related symptoms were over 20 %, and latex sensitization was present in more than 5 % of workers. Workers that started working from 2000 to 2009 showed a decrease in latex sensitization from 2001 to 2005, a peak of sensitization in 2006 and no sensitization at all in 2007 and 2008. This trend is related to the changeover of

Table 1 Characteristics of the population studied

Start of work in hospital	Eligibles <i>n</i>	Studied <i>n</i> (%)	Age (years) Mean (SD)	Female %	Retired <i>n</i>
Before 2000	1,155	1,040 (90.0)	36.8 (9.1)	72.5	–
2000	86	85 (98.8)	34.2 (6.7)	77.6	260
2001	53	53 (100.0)	32.1 (8.0)	77.3	148
2002	51	51 (100.0)	33.3 (8.5)	76.5	123
2003	256	250 (97.6)	35.4 (8.7)	75.2	112
2004	171	152 (88.9)	35.2 (8.5)	80.3	111
2005	44	39 (88.6)	38.2 (8.5)	89.7	81
2006	72	70 (97.2)	32.8 (8.8)	75.7	42
2007	102	90 (88.2)	36.4 (8.7)	75.5	63
2008	101	91 (90.1)	35.0 (8.6)	66	53
2009	151	132 (87.4)	32.4 (8.3)	70.2	52
Total	2,242	2,053 (95.5)			1,045

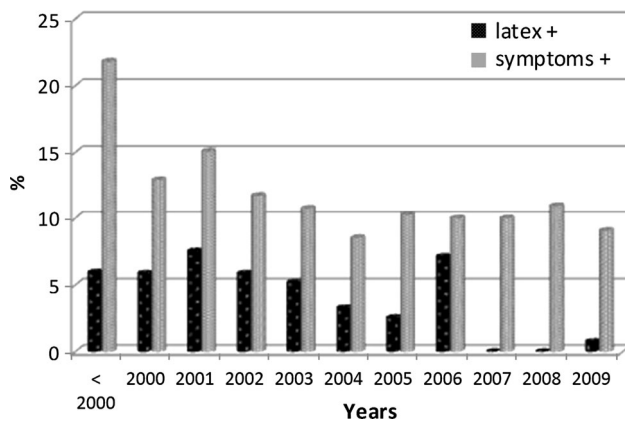


Fig. 1 Gloves-related symptoms and skin prick test sensitization to latex in workers employed before 2000 and in new employed workers

Table 2 Characteristics of workers at the first control and prevalence of allergic symptoms and sensitization before and after 2000

	Before 2000 (n = 1,040) ^a	After 2000 (n = 1,013)	p
Females	749 (72)	765 (75.5)	0.07
Familial atopy	209 (20.1)	200 (19.7)	0.8
Personal atopy	215 (20.7)	201 (19.8)	0.6
Sensitization to common allergens	405 (38.8)	418 (41.2)	0.3
Skin prick test + to latex	62 (6.0)	37 (3.6)	0.01
IgE latex+	54 (5.2)	32 (3.2)	0.01
Gloves-related symptoms	227 (21.8)	107 (10.6)	0.001
Itching-erythema	181 (17.4)	88 (8.7)	0.001
Contact dermatitis	26 (2.5)	16 (1.5)	0.1
Contact urticaria	38 (3.6)	2 (0.2) ^b	0.001
Rhinitis	21 (2.0)	2 (0.2) ^b	0.001
Asthma	3 (0.3)	2 (0.2) ^c	0.6

Data are reported as number (%) unless otherwise noted

^a Larese Filon and Radman (2006)

^b Latex negative

^c In 2000 and 2001, latex + in atopics with allergic symptoms with inhalant allergens

latex gloves in professional schools (later than in our hospitals) and can be explained by lower previous latex exposure and latex sensitization in new employed workers. Gloves-related symptoms decreased in years reaching a value around 10 % from 2004 till 2009.

The Table 2 reports the characteristics of the population studied before 2000 and of new workers employed from 2000 to 2009. The groups are similar for familial, personal atopy and sensitization to common allergens. Sensitization and symptoms related to latex gloves were significantly higher in the older group vs new employers: the prevalence

of all symptoms was 21.8 versus 10.6 % ($p = 0.001$), itching-erythema 17.4 versus 8.7 % ($p = 0.001$), contact urticaria 3.6 versus 0.2 % ($p = 0.001$), rhinitis 2 versus 0.2 % ($p = 0.001$). No differences were shown for contact dermatitis and asthma prevalence.

Incidence of gloves-related symptoms is reported in Table 3: person-years were calculated considering workers exposed to latex without symptoms for a total of 9,660 person-years. Latex sensitivity is reported as ⁺. The incidence of irritant contact dermatitis ranged between 0 and 6.20 per 1,000 person-years with a cumulative incidence of 2.39 cases per 1,000 person-years. Allergic contact dermatitis ranged from 0 to 5.70 per 1,000 person-years with 24 cases: 3 sensitized to latex (by skin prick test), 2 with NRL glove's sensitization (by patch test), 12 to rubber additives and 7 to cobalt. Urticaria incidence was very low with 0.72 cases per 1,000 person-years (7 cases). Incidence cases of respiratory symptoms were sporadic: one rhinitis and one asthma (with rhinitis) in 2 workers sensitized to NRL with allergic respiratory symptoms to common allergens and one asthma NRL negative. After 2004, no new cases of respiratory symptoms occurred in our cohort.

Ten symptomatic subjects developed a skin sensitivity to latex with an overall incidence rate of 1.0 cases per 1,000 person-years. It is noteworthy that 2 workers with irritant contact dermatitis and 3 workers with allergic contact dermatitis are sensitized to latex (by prick test).

The characteristics associated with incidence of gloves-related symptoms are reported in Table 4 divided by IgE-type symptoms (urticaria, rhinitis and asthma) and contact dermatitis symptoms. Logistic regression analysis adjusted for age, gender and weighted for duration of follow-up showed a different pattern for the two kinds of symptoms: IgE-related symptoms were significantly associated with familial and personal atopy, while contact dermatitis were associated with female sex but not with atopy. Sensitization to latex was significantly associated with IgE-related symptoms (OR = 8.0, 95 % CL 1.27–48.6). Surgical workers and subjects who used gloves for more than 4 h a day showed higher risk to have IgE-mediated symptoms with OR = 4.7 (95 % CL 1.0–28.4) and OR = 5.15 (95 % CL 1.2–31), respectively, and higher risk to have contact dermatitis with OR = 2.3 (95 % CL 1.0–4.0) and OR = 6.32 (95 % CL 3.2–13.0), respectively.

Discussion

Our study is the first long-term follow-up of health care workers exposed to non-powdered latex gloves followed for 10 years. In a previous study (Larese Filon and Radman 2006), we investigated the effects of the changeover from powdered to non-powdered latex gloves, and in the present

Table 3 Incidence of gloves-related symptoms from 2000 to 2009 (cases per 1,000 person-years)

Years	Exposed	Person-years	Irritant contact dermatitis		Allergic contact dermatitis		Urticaria		Rhinitis		Asthma	
			<i>n</i>	‰	<i>n</i>	‰	<i>n</i>	‰	<i>n</i>	‰	<i>n</i>	‰
2000	981	743	3	4.00	4	5.40	0	0.00	0	0.00	0	0.00
2001	886	878	1 ⁺	1.10	5	5.70	0	0.00	0	0.00	0	0.00
2002	814	808	5	6.20	3	3.71	1	1.23	1 ⁺	1.23	1	1.23
2003	958	931	5	5.37	2	2.14	1 ⁺	0.00	0	0.00	0	0.00
2004	1,018	1,005	0	1.68	2 ⁺	1.99	1	0.84	0	0.00	1 ⁺	0.84
2005	981	977	1 ⁺	1.02	2 ⁺	2.04	1	1.02	0	0.00	0	0.00
2006	1,011	1,004	2	1.99	2	1.99	1 ⁺	0.99	0	0.00	0	0.00
2007	1,050	1,041	1	0.96	0	0.00	1 ⁺	0.96	0	0.00	0	0.00
2008	1,158	1,088	0	0.00	1 ⁺	0.91	1	0.91	0	0.00	0	0.00
2009	1,197	1,185	4	3.37	3	2.53	0	0.00	0	0.00	0	0.00
Incidence		9,660	22	2.39	24	2.50	7	0.72	1	0.12	2	0.21

In superscript latex sensitization

study, we investigated the long-term effect of exposure to non-powdered latex gloves considering all workers who enter in our cohort in the period considered. This is an important aspect because it is known that the first three years of exposure are crucial for the development of IgE-type allergy (Gautrin et al. 2008).

The changeover to a powder-free environment in 2000 caused a significant decrease in gloves-related symptoms with no new cases of sensitization in 2-year-follow-up (Larese Filon and Radman 2006). After 2000, all new employees exposed to latex were skin prick tested with common allergens and latex founding a progressive decrease in latex sensitization from 5.9 % in 2000 to 0 in 2007 and 2008 and a decrease in gloves-related symptoms from 12.9 % in 2000 to 9.1 % in 2009 with only sporadic cases of urticaria (2 cases), rhinitis (2 cases) and asthma (2 cases). The decreased sensitizations and symptoms in new employees could be explained by the use of better gloves than before (non-powdered latex gloves and vinyl gloves) in the professional school for health care operators.

These data are consistent with other studies that demonstrated a decrease in latex symptoms and sensitization after the introduction of non-powdered latex gloves and the diffusion of vinyl or nitrile gloves (Malerich et al. 2008; Vandenplas et al. 2009; Edelstam et al. 2002; Saary et al. 2002; Merget et al. 2010; Allmers et al. 2005). The banning of powdered latex gloves in Germany caused a reduction in latex-related symptoms (Allmers et al. 2005).

The sensitization to NRL in workers starting to work in our hospitals from 2000 is lower respect to other studies: 3.6 % on average vs more than 6 % in all studies (Bousquet et al. 2006) to confirm the positive effect of preventive measures implemented in professional and training schools in our region since 2000.

The evaluation of incidence cases of gloves-related symptoms in 10 years revealed very low figures for urticaria (0.72 cases per 1,000 person-years) and for respiratory symptoms (0.12 cases per 1,000 person-years for rhinitis and 0.21 per 1,000 person-years for asthma).

To our knowledge, there are no other incidence data on health care workers on that topic: Gautrin et al. (2008) found an incidence of 1.3, 1.7 and 0.7 cases/100 person-years for sensitization, rhinoconjunctival and chest symptoms, respectively, studying apprentices exposed to high-molecular weight agents. Sussman (1998) reported an incidence of latex symptoms of 1 % in nurses exposed to powdered latex gloves followed for 1 year and of 0.9 % of prick conversion without symptoms in nurses wearing non-powdered latex gloves.

Our data showed lower incidences. This could be explained by some considerations: (1) our cohort are constituted by older workers that completed the apprenticeship years ago, and we know that the first 3 years of exposure are at higher risk of sensitization (Gautrin et al. 2008); (2) this could be the result of the introduction of preventive measures: non-powdered latex gloves with low-latex release for all workers and vinyl or nitrile gloves for sensitized and symptomatic subjects; (3) this could be the result of health-worker effect with symptomatic subjects that could have decided to leave the work in hospital going out from the cohort. This aspect should be considered but, generally in Italy, this is unlikely to occur because workers with occupational latex-related diseases can claim for compensation and can ask for job task without latex exposure inside public hospitals.

The low incidence of IgE symptoms is the result of a good glove policy, but there is a need to improve our prevention measures to avoid completely the onset of these symptoms. Considering our 10 incidence cases, we confirm

Table 4 Characteristics associated with incident latex-related allergic symptoms (IgE symptoms = urticaria, rhinitis and asthma) and dermatitis symptoms (CD) at follow-up in subjects who have ever held a gloves-related symptoms

	Referents ^a	IgE symptoms incident cases	OR (95 % CL)	CD incidence cases	OR (95 % CL)
Numbers	1,121	10	–	46	–
Females	821 (73.2)	9 (90.0)	3.29 (0.45–69.7)	39 (84.7)	2.38 (0.98–6.93)
Familiar atopy	205 (18.3)	5 (50.0)	4.47 (1.1–17.9)	10 (21.7)	1.28 (0.55–2.68)
Personal atopy	216 (19.2)	5 (50.0)	4.19 (1.04–16.8)	9 (19.6)	1.05 (0.44–2.26)
Sensitized to common allergens	418 (37.2)	8 (80.0)	3.94 (0.92–19.3)	17 (37.0)	1.02 (0.52–1.96)
Surgical workers	140 (12.5)	4 (40)	4.7 (1.0–28.4)	11 (23.9)	2.3 (1.0–4.0)
More than 4 h/day	325 (29.0)	7 (70)	5.15 (1.2–31.0)	32 (69.6)	6.35 (3.23–13)
Sensitized to latex	–	5 (50)	8.0 (1.27–48.6) ^b	5 (10.9)	

^a Referents are those who never developed the outcome considered in 2009. Logistic regression analysis adjusted for age, gender and weighed for duration of follow-up. Data are reported as number (%)

^b OR for NLR sensitization are calculated considering CD as reference category

that the use of non-powdered latex gloves with low protein release can be considered safe for the majority of workers, nevertheless the workers with common allergic symptoms or with skin prick test positivity are at higher risk. For them, the use of non-latex gloves is suggested.

The incidence of irritant and contact dermatitis is low in our cohort and seems to be stable in years with 1–7 new cases every year and a cumulative incidence of irritant and allergic contact dermatitis of 2.39 and 2.50 cases per 1,000 person-years, respectively. It is known that contact dermatitis can be a risk factor to develop IgE sensitization to latex (Bousquet et al. 2006), so affected workers must avoid the use of latex gloves. The altered skin barrier in subjects affected by contact dermatitis can cause an increased risk to develop a latex sensitization.

Our study demonstrated that the introduction of non-powdered latex gloves for all workers and non-latex gloves for symptomatic or sensitized people can determine a significant reduction in incidence cases of gloves-related symptoms. Nevertheless, we identified subjects at higher risk (subjects with familial or personal atopy, with a skin prick test positive to common allergens and with contact dermatitis).

Our follow-up confirmed the decrease in latex allergy incidence due to glove policy and permitted to identify factors that must be considered in the future for a better prevention.

Conflict of interest The authors declare that they have no conflict of interest.

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