
Atopic status and latex sensitization in a cohort of 1,628 students of health care faculties

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A B S T R A C T

Background: Atopic diseases have increased since the second half of the previous century. Atopic workers are at higher risk to be sensitized to latex, and the first years of exposure are supposed to be especially risky.

Objective: To assess atopic status and rate of latex sensitization in health care students starting their exposure to latex gloves.

Methods: We analyzed medical surveillance data from 1,628 health care students from 2010 to 2016. Students completed a questionnaire focused on their previous and current latex exposure and personal and family histories of allergic diseases; underwent skin prick testing with common allergens and latex extract (and/or total and latex-specific immunoglobulin E in serum); and underwent a medical examination.

Results: Skin prick test results for common inhalant allergens showed that 807 of 1,628 students (49.6%) had atopy. Atopy by skin prick testing was associated with male sex (odds ratio 1.49, 95% confidence interval 1.18–1.86), a personal history of oculorhinitis or asthma (odds ratio 10.22, 95% confidence interval 7.4–14.13), and atopic eczema (odds ratio 1.87, 95% confidence interval 1.05–3.36) at multivariate regression analysis. Eleven students (0.7% of total population) were found to be sensitized to latex and all had atopy.

Conclusion: Despite the high prevalence of atopy in health care students of Trieste, the latex sensitization rate is very low and comparable to general population. This is reasonably due to the low exposure to latex gloves at the time of the evaluation and to low latex release from the gloves currently used in our hospital.

Introduction

Latex sensitization and allergic symptoms are crucial aspects for health care workers who can be exposed to latex gloves and can develop skin, respiratory, and systemic allergic symptoms.^{1,2} The introduction of non-powdered latex gloves, with low allergen release, and non-latex gloves in all public hospitals of the Friuli Venezia Giulia region of Italy have lowered the prevalence and incidence of latex allergy and symptoms in health care workers.^{3–5} Preventive measures can be used to decrease latex sensitization and to avoid latex exposure in individuals with allergic symptoms who can be considered at higher risk to develop latex allergy.⁵

Latex allergy has increased in the recent past with the widespread use of latex gloves after the 1980s to prevent blood-transmissible diseases. Latex allergy causes cutaneous and respiratory allergic diseases in health care workers, with a reaction mediated by immunoglobulin E (IgE). The rate of latex sensitization has been estimated at approximately 1% in the general population and 5% to 12% in those with occupational latex exposure.^{1,2,6}

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Of health care workers of the University Hospital of Trieste, approximately 6% were detected as having positivity to latex by skin prick tests (SPTs) from 1997 through 1999,⁴ and glove-related symptoms were present in 21.8% of the cohort, probably in part ascribable to mild nonspecific reactions to gloves or delayed hypersensitivity reactions to rubber-related haptens. The use of powder-free latex gloves decreases the latex release from the glove and avoids air contamination. Their use contributes to preventing new latex sensitizations and decreases cutaneous symptoms in workers, proving to be a necessary primary prevention measure.⁷

Students attending health care courses can be exposed to latex. Therefore, extension of the preventive protocol is of crucial importance to identify individuals at risk of sensitization or already sensitized to latex, with the aim of avoiding exposure at an early stage.⁵ Moreover, younger individuals could be at higher risk to develop latex sensitization and symptoms. According to the importance of the first years of occupational exposure to allergens at work in developing sensitization and allergic symptoms, Gautrin et al⁸ reported a higher incidence of sensitization to high-molecular-weight allergens during apprenticeship than at a subsequent retesting of the same cohort while working (7.3–1.3 cases/100 person-years). The first year is crucial for the development of sensitization, and symptoms occur during the second or third year.

Another reason it is important to identify students at risk is the fact that young people are more allergic than older people. It is well known that a global epidemic of allergic diseases, such as asthma, allergic rhinitis, and eczema, occurred in the second half of the previous century, especially until 1990, in children.⁹ The “hygiene hypothesis”¹⁰ was formulated to explain this phenomenon suggesting that a lower exposure to bacterial endotoxins and less frequent infections in early life are related to a higher risk of developing atopic diseases and asthma. After 1990, the prevalence pattern of asthma showed opposite trends in different industrialized countries, although the prevalence of allergic rhinitis still seemed to be increasing.⁹ In Italy, 3 multicenter cross-sectional surveys on respiratory diseases were carried out in young adults from 1991 through 2010 (the Italian arm of the European Community Respiratory Health Survey, the Italian Study on Asthma in Young Adults, and Gene-Environment Interactions in Respiratory Disease [GEIRD]). These studies reported an increase in the national median prevalence of asthma and rhinitis from 4.6% to 6.6% and from 19.4% to 25.8%, respectively, during the past 10 years, with a similar trend in men and women and higher asthma prevalence in the Mediterranean area than in the subcontinental area of the country.¹¹ Focusing on a young population, a cross-sectional study carried out in Brescia from 2002 to 2003 in primary school children found that 49% of the studied population had atopy by SPT (although approximately half these children were asymptomatic for asthma or allergic rhinitis) and 10.2% of the population had physician-diagnosed asthma, with higher rates in boys.¹²

With the aim of evaluating students at risk for developing latex allergy or already sensitized to this allergen, we examined students attending the health care faculties at the University of Trieste to assess the atopic status of this young adult population and to define the rate of latex sensitization occurring during the first years of occupational exposure to latex gloves. Our final aim was to suggest preventive measures and the avoidance of latex gloves in individuals already sensitized or with allergic respiratory symptoms.

Methods

Study Population

The study population consisted of 1,628 students attending the health care faculties of the University of Trieste from 2010 through 2016, specifically the faculties of obstetrics, nursing, laboratory technicians, physiotherapy, radiology technicians, odontology, dental hygienists, medicine, biology and medical residents. In accord with the medical surveillance protocol of the hospital, at the beginning of their apprenticeships in the wards, the students completed a questionnaire providing descriptive data about their previous and current latex exposure and atopic status. They also underwent SPT with common allergens and latex extract and underwent a medical examination. The medical surveillance examination occurred during the first year of study in 77.5% of the population, the second year in 16.1%, the third year in 11.7%, and later in 2.4% of the student population, depending on the time of beginning the apprenticeship during the specific degree course. A written informed consent was obtained from each student before SPT. All data analyzed in this study were collected during compulsory medical surveillance examinations in accord with the protocol of the hospital and Italian law for the prevention of occupational diseases. Therefore, no specific consent for data collection was needed and no institutional review board approval was required.

Questionnaire

Before SPT, all students completed a self-reported standardized questionnaire to collect demographic data (age, sex, course of

study), exposure data (use of gloves at work, number of gloves used per day, hours of use, kind of gloves), and information about family and personal histories of allergic disorders (asthma, hay fever, food allergies, atopic dermatitis), use of medicines for allergic diseases, and symptoms related to glove use and current or previous hand dermatitis.

Atopy was defined as a positive SPT result or specific IgE to at least 1 common allergen. Asthma was defined as the presence of attacks of cough, wheezing, and dyspnea that required pharmacologic treatment (bronchodilators, inhaled corticosteroids, or their combination). Rhinitis was defined as the presence of sneezing and/or itchy, runny nose. Atopic eczema was defined as an itchy dermatitis in the flexures during childhood or currently. Latex glove-related symptoms were defined as erythema or itching; contact urticaria (self-reported wheal and flare reactions at the site of glove contact that appear within 10–15 minutes of usage); contact dermatitis (self-reported erythematous-papulous persistent eruption that appears on the skin after 2–3 days of contact with latex gloves); and rhinitis or asthma when using latex gloves.

Familial atopy was defined as allergic rhinitis, asthma, or atopic eczema reported in parents.

Skin Prick Testing

Before SPT, an interview with a trained physician was performed to identify and exclude students at risk for severe adverse reactions to SPTs. The criteria for exclusion were a severe asthma attack in the past year or a history of anaphylactic shock or severe reaction to latex. For these subjects and for students taking antihistamine medication at that time, SPTs were not performed and serum was tested for total and latex-specific IgE (radioallergosorbent test; Pharmacia, Boulder, Colorado). Nineteen subjects did not undergo SPT but total and latex-specific IgE levels in serum were measured.

Skin prick tests included common inhalant allergens, perennial (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* and dog and cat dander), and pollens (*Gramineae*, *Parietaria* species, *Betulaceae*, and *Oleaceae*). Extracts of common allergens and of latex were supplied by Lofarma Allergeni (Milan, Italy). The protein concentration of this latex extract was 12.5 mg/mL.³ The positive control was 1% histamine dihydrogen chloride solution and the negative control was 1% glycerinate solution. SPTs were performed by trained registered nurses. Skin test sites were clearly marked, a drop of extract was placed on the skin, and this spot of skin was pricked with commercially available skin test lancets (Hollister Stier Laboratory, Spokane, Washington). All tests were read and recorded after 15 minutes, and a wheal of at least 3 mm was considered a positive result. A single positive response to an inhalant allergen was considered the determining criterion for atopy (by SPT). One case of a false positive SPT result occurred (in subject with a wheal reaction to the negative control solution) and his serum was tested for total and latex-specific IgE levels. No adverse reaction to SPT was recorded.

Students sensitized to latex obviously must avoid latex gloves. Students with atopy and common allergic symptoms were asked to avoid latex gloves as a preventive measure. Non-latex gloves are available for all students.

Statistical Analyses

Data analysis was performed with STATA 13.0 (STATA Corp, College Station, Texas). Continuous data were summarized as mean and SD. The difference between mean values was tested by Student *t* test. Categorical data were analyzed by the likelihood χ^2 test with Yates correction, as indicated by the data. Fisher exact test was used if the expected number of observations in any cell was smaller than 5. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated after adjusting for confounding factors (sex, age)

Table 1
Characteristics of Analyzed Population

Total population, N	1,628
Sex, n (%)	
Men	581 (35.7)
Women	1,047 (64.3)
Smoke, n (%)	
Yes	331 (20.3)
No	1,229 (75.5)
Former	68 (4.2)
Age (y), mean ± SD	23.45 ± 5.3
Course of study, n (%)	
Obstetrics	80 (4.9)
Nursing	564 (34.6)
Laboratory technicians	96 (5.9)
Physiotherapy	180 (11.1)
Radiology technicians	4 (0.2)
Odontology	129 (7.9)
Dental hygienists	100 (6.1)
Residents	247 (15.2)
Medicine	205 (12.6)
Biology	23 (1.4)
Glove use at work, n (%)	
Daily	470 (28.9)
Occasionally	420 (25.8)
Not yet	738 (45.3)

through multiple logistic regression analysis. For all statistical analyses, a .05 level of significance was used, and all *P* values were 2-sided.

Results

The study population had a mean age of 23.5 years (SD 5.3) and included more female students ($n = 1,047$; 64.3%) than male students. Their distribution among the different courses of study is presented in Table 1. Most students were nursing students (34.6%) and medical students and residents (12.6% and 15.2%, respectively). SPT results to common inhalant allergens or total IgE levels in serum showed that 807 of 1,628 students (49.6%) had atopy, with a higher prevalence of atopic men (55.2%) than women (46.4%) in this population. Considering the specific allergens, 587 subjects (36.1%) showed positivity for *D pteronyssinus* and/or *D farinae*, 442 (27.1%) for *Gramineae*, 344 (21.1%) for *Oleaceae*, and 233 (14.3%) for dog and cat dander. According to personal history of allergic diseases, 19.7% of students reported oculorhinitis, 6.6% reported asthma, and 4.8% reported a history of atopic dermatitis. Prevalence of oculorhinitis was a slightly higher in men than in women (21.7% vs 18.5%) and asthma was reported by 7% of women vs 5.9% of men (Table 2), but without a statistically significant difference between women and men (oculorhinitis in women, OR 0.83, 95% CI 0.65–1.08; asthma in women, OR 1.23, 95% CI 0.8–1.8). Latex glove-related symptoms were reported by 53 students (3.2%): 3.8% of women reported itching and erythema vs 1.4% of men ($P < .05$), 4 subjects reported contact urticaria, and 7 reported contact dermatitis (mainly women).

When analyzing factors associated with atopy by SPT, women had less atopy than men (OR 0.70, 95% CI 0.57–0.86). A strong association was found between atopy by SPT and a personal history of oculorhinitis (OR 12.4, 95% CI 8.6–18.0) and asthma (OR 5.7, 95% CI 3.4–9.5). A personal history of atopic dermatitis (OR 2.3, 95% CI 1.4–3.9), oral allergy syndrome (OR 2.3, 95% CI 1.3–4.2), and familial atopy (OR 1.5, 95% CI 1.2–1.9) also were factors associated with atopy by SPT, whereas latex glove-related symptoms were not significantly related to atopy (Table 3).

Factors associated to atopy by SPT were evaluated using multivariate regression analysis (Table 4) that confirmed the increased risk for men (OR 1.49, 95% CI 1.18–1.86), for subjects with

Table 2
Atopic Status, SPT Results, and Allergic Symptoms in Students

	Total population (N = 1,628), n (%)	Men (n = 581), n (%)	Women (n = 1,047), n (%)
Atopy by SPT or RAST	807 (49.6)	321 (55.2) ^a	486 (46.4)
Prick test positivity			
<i>Dermatophagoides pteronyssinus</i> and/or <i>Dermatophagoides farinae</i>	587 (36.1)	234 (40.2) ^a	353 (33.7)
<i>Gramineae</i>	442 (27.1)	192 (33.0) ^a	250 (23.9)
<i>Oleaceae</i>	344 (21.1)	146 (25.1) ^a	198 (19.0)
Dog or cat dander	233 (14.3)	94 (16.2) ^a	139 (13.3)
<i>Betulaceae</i>	205 (12.6)	91 (15.7) ^a	114 (10.9)
<i>Parietaria</i> sp	111 (6.8)	42 (7.2)	69 (6.6)
Latex	11 (0.7)	3 (0.5)	8 (0.7)
Allergic symptoms			
Oculorhinitis	320 (19.7)	126 (21.7)	194 (18.5)
Asthma	107 (6.6)	34 (5.9)	73 (7.0)
Urticaria	43 (2.6)	12 (2.1)	31 (3.0)
OAS	51 (3.1)	13 (2.2)	38 (3.6)
Contact dermatitis in past year	68 (4.2)	28 (4.8)	40 (3.8)
Atopic dermatitis	78 (4.8)	32 (5.5)	46 (4.3)
Other allergic symptoms	23 (1.4)	12 (2.1)	11 (1.1)
Glove-related symptoms			
Itching or erythema	48 (2.9)	8 (1.4)	40 (3.8) ^a
Contact urticaria	4 (0.24)	1 (0.17)	3 (0.28)
Contact dermatitis	7 (0.43)	1 (0.17)	6 (0.57) ^a
Familial atopy	467 (28.7)	145 (25)	322 (30.8)

Abbreviations: OAS, oral allergy syndrome; RAST, radioallergosorbent test; SPT, skin prick test.

^a $P < .05$.

oculorhinitis or asthma (OR 10.22, 95% CI 7.4–14.13), and for subjects with atopic eczema (OR 1.87, 95% CI 1.05–3.38).

According to latex exposure at work, most students (71.1%) were not using gloves at work or were using them less than daily at the time of medical surveillance (preventive medical examination), whereas 28.9% reported using gloves daily at work at this time (Table 1).

Of 1,628 students, 11 (0.7% of total population) were found to be sensitized to latex: 10 showed positivity by SPT, whereas 1 student did not undergo SPT but had a high level of latex-specific IgE (by radioallergosorbent test). Of the 10 students with latex positivity by SPT, 5 also were tested for latex-specific IgE but only 1 (20%) had specific IgE in serum (Table 5). According to symptoms of latex allergy, 3 of 11 students reported cutaneous symptoms related to latex gloves or latex articles: 2 had erythema and/or itching skin and 1 described a contact urticaria. There were no cases of oculorhinitis or asthma related to latex exposure. Of the 3 symptomatic students, 2 showed positivity by latex-specific IgE and 1 was not tested for it. All students who were sensitized to latex had a personal history of allergic diseases (oculorhinitis, asthma, oral allergy

Table 3
Association Between Atopic Status and Allergic Symptoms Evaluated Using Mantel-Haenszel OR (95% CI) Adjusted for Sex

Factor	Atopy by SPT, n (%)	OR (95% CI)
Sex	Women, 486 (60.2) Men, 321 (39.8)	0.70 (0.6–0.9)
Oculorhinitis ^a	Yes, 283 (37.2%)	12.4 (8.6–18.0)
Asthma ^a	Yes, 88 (11.6)	5.7 (3.4–9.5)
OAS ^a	Yes, 34 (4.5)	2.3 (1.3–4.2)
Atopic dermatitis ^a	Yes, 47 (5.8)	2.3 (1.4–3.9)
Urticaria ^a	Yes, 25 (3.3)	1.5 (0.8–2.8)
Familial atopy ^a	Yes, 264 (32.7)	1.5 (1.2–1.9)
Glove-related symptoms	Yes, 31 (3.8)	1.2 (0.5–2.7)

Abbreviations: CI, confidence interval; OAS, oral allergy syndrome; OR, odds ratio; SPT, skin prick test.

^aAdjusted for sex.

Table 4
Factors Associated With Atopy (by Skin Prick Test) Evaluated Using Multivariate Regression Analysis

Factor	Exp(B)	95% CI
Male sex	1.49	1.18–1.86
Atopic dermatitis	1.87	1.05–3.38
Familial atopy	1.08	0.84–1.38
Oculorhinitis or asthma	10.22	7.4–14.13

Abbreviation: CI, confidence interval.

syndrome, or atopic dermatitis) and all who underwent SPT (10 of 11) showed positivity to at least 1 of common allergen.

No difference in order of a more frequent use in latex gloves in sensitized students compared with the total analyzed population was found (OR 0.35, 95% CI 0.1–1.8). Factors associated to latex sensitization are listed in Table 6. Oculorhinitis (OR 8.9, 95% CI 2.4–33.8), asthma (OR 8.8, 95% CI 2.5–31.1), and atopic dermatitis (OR 9.2, 95% CI 2.4–33.8) were strongly related to latex sensitization.

Discussion

This cross-sectional study analyzed latex sensitization and symptoms and atopic status in one of the largest group of health care students in Europe. Despite the high level of atopy detected by SPT, we found a very low prevalence of latex sensitization (0.7%), comparable to the latex sensitization rate in the general population. This is likely due to a low and sporadic exposure to latex gloves at the time of the preventive medical examination: in fact, only 28.9% of students reported using gloves daily at the workplace at that time. Moreover, since 2000 in our hospital, powdered latex gloves have been replaced with powder-free alternatives, which have avoided air contamination¹³ and decreased the latex release from gloves, helping to prevent new cases of sensitization.^{4,5} Only 3 students with latex sensitivity met the definition of latex allergy, with mild and localized cutaneous symptoms. Of the symptomatic students, 2 also had high levels of latex-specific IgE in serum and the third did not undergo testing. No cases of latex-related respiratory symptoms were reported. Overall, the SPT latex detection rate was higher than the latex-specific IgE detection rate, as reported in other studies,¹⁴ confirming that latex SPTs are more sensitive.

Latex allergy and latex sensitization were strongly associated with a personal history of atopy and atopy by SPT, because all cases of latex positivity in this population had atopy. This evidence confirms that avoiding the unnecessary use of latex gloves is an important primary prevention measure in patients with atopy who are starting to work in the health care industry. Furthermore, a poor awareness of the kind of gloves used at work (latex, nitrile, vinyl) emerged from the questionnaires (data not shown), suggesting the need for additional education focused on the different materials and characteristics of these gloves.

Table 5
Latex Sensitization and Latex Glove-related Symptoms

	Latex SPT ⁺ (n = 10)			Latex no SPT (n = 1) RAST ⁺ + no SPT
	SPT ⁺ + RAST ⁺	SPT ⁺ + RAST ⁻	SPT ⁺ + no RAST	
Latex sensitization (n = 11, 0.7% of total population)	1	4	5	1
Symptomatic (n 3 / n 11)				
Contact urticaria	0	0	1	0
Itching or erythema	1	0	0	1

RAST⁻, negative radioallergosorbent test result; RAST⁺, positive radioallergosorbent test result; SPT⁺, positive skin prick test result.

Table 6
Factors Associated With Latex Sensitization Evaluated Using Mantel-Haenszel OR (95% CI) Adjusted for Sex

Factor	Sensitized to latex, n (%)	OR (95% CI)
Sex	women, 8 (0.8) men, 3 (0.5)	1.46 (0.39–5.6)
Atopy by prick	yes, 11 (100)	∞
Personal atopy ^{a,b}	yes, 9 (81.8)	8.8 (6.5–11.8)
Oculorhinitis ^a	yes, 7 (66.6)	8.9 (2.4–33.8)
Asthma ^a	yes, 4 (36.4)	8.8 (2.5–31.1)
OAS ^a	yes, 1 (9)	3 (0.4–23.4)
Atopic dermatitis ^a	yes, 3 (27.3)	9.2 (2.4–33.8)
Urticaria ^a	yes, 0	—
Familial atopy ^a	yes, 4 (36.7)	1.39 (1.2–1.9)
Use of latex gloves	yes, 2 (18)	0.35 (0.1–1.8)

Abbreviations: CI, confidence interval; OAS, oral allergy syndrome; OR, odds ratio.

^aAdjusted for sex.

^bOculorhinitis, asthma, and atopic dermatitis.

This study showed a high prevalence of atopy by SPT in the general population (49.6%) in our geographic area and suggests that men are more susceptible to atopy than women. Many studies in the literature have evaluated atopic status in pediatric populations: 49% of primary school children were found to have atopy by SPT in Brescia in 2002 to 2003¹² and Fiocchi et al¹⁵ reported a prevalence of 50.2% of atopy by specific IgE levels in Italian and Spanish children younger than 15 years with at least 1 allergy-like symptom. They also reported a prevalence of boys among children with atopy, an increase in the number of sensitizations with age, and a more marked sensitization to inhalant allergens than to food allergens in children who were older than 6 years. A population-based study on Belgian children also found boys had atopy more often than girls when tested with SPTs for inhalant allergens.¹⁶ Our study suggests that men continue to have atopy more often than women in later years of life, although no statistically significant difference in prevalence of allergic diseases was found between women and men. Nevertheless, asthma was found to be slightly more frequent in women than in men (7% vs 5.9%), which could be in line with the hypothesis of a switch at puberty in the gender susceptibility to develop asthma, perhaps because of hormonal changes.¹⁷

According to allergic symptoms, asthma prevalence was 6.6% in our population, in line with data on the subcontinental area of Italy from the GEIRD study (2007–2010), whereas the prevalence of oculorhinitis was slightly lower in our population (19.7% vs 24.2%, respectively; GEIRD study). The most frequent cause of sensitization in health care students of Trieste was house dust mites, followed by *Gramineae* and *Oleaceae* pollens and cat and dog dander. *Parietaria* pollens, a recurrent cause of sensitization especially in southern Italy,¹⁸ were only secondarily involved in allergic sensitization in our geographic area (6.8% of students).

When analyzing the relation between atopy by SPT and a personal history of allergic diseases, we found that oculorhinitis and asthma were strongly associated with atopy status by SPTs in our

population, whereas the association with other allergic diseases such as oral allergy syndrome and atopic dermatitis was moderate. However, the association between atopy by SPT and asthma was weaker than the association with oculorhinitis. This might be ascribable to the lack of discrimination between cases of allergic and nonallergic asthma in our study.

Our results also confirm that a family history of allergic disease is a risk factor for atopy, but the force of the association could be underestimated in our study because of potential recall bias about a family history of allergies that could have led to underreporting.

To our knowledge, this study is the first Italian study to analyze a large group of health care students to investigate atopic status, allergic symptoms, and latex allergy. Despite the high prevalence of atopy by SPT, the sensitization rate to latex was similar to or lower than that in the general population, confirming that the preventive measures suggested and the avoidance of unnecessary use of latex gloves are useful in preventing latex sensitization and symptoms in most of our students. Moreover, the presence of very few symptomatic cases suggests the need to continue the monitoring of students, increasing their knowledge on latex risk, and suggesting the avoidance of these gloves in symptomatic and/or sensitized students and in those who have allergic respiratory symptoms.

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