Can a threshold limit value for natural rubber latex airborne allergens be defined?

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Background: Recent studies have shown that systemic or respiratory occupational responses to latex can be induced by inhalation of latex aeroallergens.
Objective: Our objectives were to study the relationship between exposure to different latex aeroallergen levels and type I allergic reactions in subjects with occupational contact with latex and to assess a threshold value for latex airborne allergens required for sensitization and symptom elicitation.
Methods: We screened 145 subjects working in 32 hospitals or operating rooms with different latex aeroallergen levels. The quantified latex aeroallergen concentrations in the 32 rooms were compared with latex-related allergic symptoms.
Results: Different latex aeroallergen concentrations could be detected in rooms where powdered latex gloves were used and no effective ventilation systems were installed. In environments with latex aeroallergen levels of 0.6 ng/m^3 or greater, the reported workplace-related symptoms were significantly increased ($p < 0.02$). All 22 subjects with latex-specific IgE antibodies worked in rooms contaminated with latex aeroallergens ($p < 0.05$).
Conclusions: Our results demonstrate that symptoms and presence of latex-specific IgE antibodies in subjects are significantly associated with measurable levels of latex aeroallergens. A latex aeroallergen level of 0.6 ng/m^3 is a critical threshold, especially for health care workers who are sensitized to natural rubber latex. (J Allergy Clin Immunol 1998; 101:24-7.)

Key words: *Latex, latex allergy, latex aeroallergen, occupational asthma, threshold value*

Latex hypersensitivity has been recognized as an important occupational risk especially among health care workers.[1-4] Recent studies have shown that skin contact with natural rubber latex (NRL) allergens is associated with the risk of type I allergic reactions, and inhalation of latex aeroallergens carried on the cornstarch powder of latex gloves also causes cutaneous, conjunctival, and/or respiratory responses to latex.[1, 5, 6] By using immune inhibition assays, the concentration of latex aeroallergens in medical facilities can be determined.[7-9] Several studies have shown that individuals working or staying in environments with a high level of latex aeroallergens have more symptoms than those in environments with no detectable latex aeroallergens.[1, 6, 7, 10] The relationship between levels of latex aeroallergens and allergic responses, especially among health care workers, has only been scarcely investigated. The threshold of latex airborne allergens causing sensitization and bringing about symptom elicitation is not known.

Abbreviation used
NRL: Natural rubber latex

Recently, proposals have been made for reducing latex hypersensitivity by elimination of glove powder or by use of synthetic materials.[8-11] However, because of the high cost and the lack of suitable alternative materials, it does not seem possible, at least in Europe, to replace all NRL gloves and other latex products used in medical and dental care with synthetic materials in the near future. As long as powdered latex gloves are in use, the latex allergens will be spread into the air of hospital rooms. Therefore to minimize the occupational exposure to latex aeroallergens, it is of importance to find out whether type I sensitization to latex is correlated with inhalation of latex allergens by hospital staff. In case of a positive correlation, it is necessary to set up a threshold limit value for latex aeroallergen loads in hospital rooms and to require hospitals to purchase powder-free gloves with low allergen content.

In this study we screened 145 persons employed in 32 hospitals or in general practitioner surgery rooms for their workplace-related symptoms, skin prick test responses, and IgE antibodies to NRL. The obtained results were compared with the levels of latex aeroallergens in these rooms. The aim of this study was to evaluate the associations between the potential risk of latex allergy and the detected levels of latex aeroallergens.

METHODS

Air samples were collected in 30 rooms of different hospital units and two physicians' offices where different amounts of powdered latex gloves were used each day. The number of latex gloves used in these rooms varied from two to thirty-five pairs per day. In 16 rooms, continuously working ventilation systems with filters for respirable dust were present. Collection of air samples and quantification of latex aeroallergens in the samples by inhibition immunoassay were performed as previously described[8] and summarized in Table I. All 243 employees working in these 32 rooms were invited to participate in the study. One hundred forty-five gave their consent and filled out a questionnaire designed to determine a history of latex allergy. These

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subjects also underwent skin prick testing and gave blood for antibody testing for latex-specific IgE. A complete history about current and past symptoms related with latex contact was recorded. Specific IgE antibodies against latex proteins in serum were determined by the CAP system (Pharmacia, Freiburg, Germany). The main reasons for the absence of 98 exposed workers in the study included leave of absence, working on the night shift (skin prick testing and personal interviews with physicians were performed only during the day shift), and sick leave. About 20% of workers declined to participate in the study. The air sampling was run in parallel with the screening of workers.

RESULTS

Latex aeroallergens were present in all 16 rooms without ventilation systems and in four of the 16 rooms with ventilation systems and a fresh air supply. The concentration of latex aeroallergens ranged from 0.4 to 205 ng/m^3. Interestingly, a relationship between total dust and latex aeroallergen concentration, on the basis of an investigation of 30 rooms, was not detectable (Fig. 1). Similarly, we found that the aeroallergen levels in the rooms did not always reflect total glove use. Rooms with well-functioning ventilation systems and a fresh air supply were found to have no or a much lower concentration of latex aeroallergens, even though more gloves were used each day.

Data about the duration of exposure were also obtained and evaluated. The geometric mean time of exposure was 6.2 years (range, 0.1 to 25.5 years). However, our preliminary results showed no significant association between the duration of exposure and latex-related symptoms and the prevalence of seropositive IgE antibodies to latex.

Of 145 subjects who participated in the study, 22 (15%) showed positive latex-specific IgE antibodies and positive skin responses to latex proteins. Workplace-related, self-reported symptoms included 17 cases of conjunctivitis, 19 cases of rhinitis, and 5 cases of dyspnea. It is remarkable that all the respiratory and conjunctival symptoms were reported exclusively in rooms where a concentration of at least 0.6 ng/m^3 latex aeroallergens had been measured. Furthermore, all 22 persons with latex-specific IgE antibodies worked in rooms contaminated by these allergens. The occurrence of latex-associated symptoms and the prevalence of seropositivity for latex-specific IgE in subjects working in rooms with different latex aeroallergen levels are shown in Table II. All but three of 22 subjects with latex-specific IgE antibodies reported symptoms associated with latex contact.

The degree of latex skin contact in subjects studied varied because of a different use frequency of latex gloves in each hospital unit. Furthermore, the number of gloves used by individuals, often also by the same person, varied every day according to the means and types of work. We also found that subjects who used more gloves per day did not always have a higher degree of exposure to latex; persons who had to wear latex gloves for a long time during their work shift often had a longer time of contact with latex. In addition, in most hospital units at least four brands of latex gloves with different protein and allergen contents and other vinyl gloves have been used at the same time, and subjects with any reactions to latex gloves were found to be more likely to use non-latex gloves. All these confounders made it impossible for us to get an objective statistical analysis, and we assume that the numbers of glove uses alone does not reflect the real degree of exposure to latex in individuals. However, the finding that latex-specific IgE antibodies were present only in staff working in rooms where latex aeroallergens could be detected suggests that continuous latex aeroallergen exposure of the mucosa covering the upper and lower respiratory tract may play an important role in the induction of immediate-type sensitization.

TABLE I. Collection of air samples and quantification of latex aeroallergens

Air sampling	
Sampler 1 (area sampler VC 25)	
Flow rate	22.5 m^3/h
Collection duration	18 h
Volume	405 m^3
Sampler 2 (area sampler Wazau)	
Flow rate	2.8 m^3/h
Collection duration	ca. 20 h
Volume	56 m^3
Quantification	Inhibition immunoassay
Reference allergen*	Latex sap extract (7.5 mg/ml)
IgE source	Pooled serum from 4 subjects
Standard calculation	CAP system Fluorescence
Solid-phase antigen	Latex ImmunoCAP
Sensitivity (assay)	0.2 ng in 14 m^3 of air

*Reference allergen contains both C-serum and particle-bound protein such as Hev b 1.

DISCUSSION

Our results (shown in Table II) demonstrate that NRL allergy–related symptoms in subjects are significantly associated with latex aeroallergen concentrations in their work areas. It appears likely that symptoms were induced when allergen levels exceeded a threshold value (i.e., 0.6 ng/m^3) as shown in our results. This effect was confirmed by our additional clinical observations: five of our patients allergic to latex developed conjunctivitis, rhinitis, and/or asthma (asthma in two patients) when they entered an above-mentioned hospital unit where 28 ng NRL allergen per m^3 air could be detected. This corresponds to a recently published case report[7] in which a technician who was hypersensitive to latex allergen, and who showed no symptoms in the laboratory when no allergen was detectable in air samples, reported an asthma episode on a day when the latex allergen concentration was 12 ng/m^3. An additional case report[6]

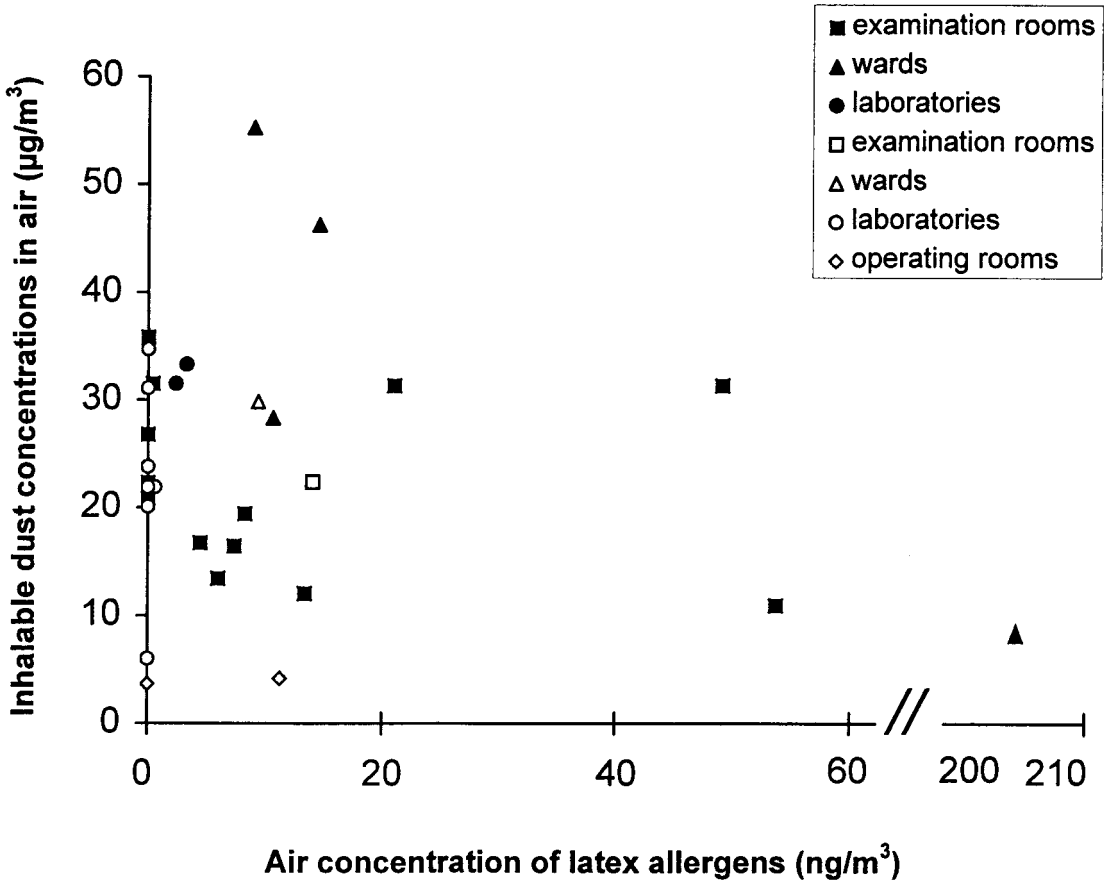

FIG. 1. Distribution of inhalable dust and latex allergen concentrations in hospital rooms with *(open symbols)* and without *(filled symbols)* ventilation systems.

TABLE II. Association between latex aeroallergen level and frequency of latex sensitization or respiratory complaints

Level of latex aeroallergens (ng/m³)	ND	0.4	0.6 to 205	*p* Value*
Ratio of latex-sensitized/exposed subjects	0/22	0/1	22-122	<0.02
Ratio of subjects with respiratory symptoms/exposed subjects	0/22	0/1	19†-122	<0.05
No. of examined rooms	12	1	19	

ND, Not detectable.

*One-sided Fisher's exact test. Data from subjects in rooms with latex aeroallergen compared with those in rooms with no detectable latex aeroallergen.

†Two additional subjects with conjunctivitis only were not taken into account.

showed that allergen levels of latex in the range of 39 to 311 ng/m³ were associated with latex-related anaphylaxis and asthma.

In summary, handling powdered NRL gloves regularly results in a detectable contamination of room air with latex allergens. The latex aeroallergen concentration can be greater than 200 ng/m³.[7, 8] Swanson et al.[7] even measured concentrations up to almost 1000 ng/m³. Our results demonstrate that latex levels of 0.6 ng/m³ or greater are associated with the development of latex-specific IgE antibodies, as well as with occupational respiratory allergic responses (e.g., conjunctivitis, rhinitis, and asthma). Therefore one of the measures shown to be effective in the elimination, reduction, or both of latex sensitization, especially in those health care workers already sensitized,[11] is to control the spread of latex aeroallergens in the working environment. This can be achieved by using powder-free latex gloves. Definition of a legally binding threshold limit value of NRL allergens in the working environment will be the first step needed to reach this goal. According to our results, the threshold level of latex aeroallergens should be lower than 0.6 ng/m³ air.

It should be mentioned, however, that at the moment, because of the use of different methods and reference standard extracts used for allergen detection, different results concerning the latex aeroallergen concentration may be obtained from the same air sample. Therefore an international standardization of quantification of NRL allergens is urgently needed.

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