

Clinical aspects of allergic disease

Quantification of occupational latex aeroallergens in a medical center

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To determine the quantity, variability, and mean aerodynamic diameter of latex aeroallergens in a large medical center, we collected air samples from work sites by using area and personal breathing zone air samplers, and we measured latex allergens by an inhibition assay with IgE antibodies from latex-sensitive individuals. Latex aeroallergen concentrations in 11 areas where powdered latex gloves were frequently used ranged from 13 to 208 ng/m³, and in areas where powdered latex gloves were never or seldom used, concentrations ranged from 0.3 to 1.8 ng/m³. Installation and use of a laminar flow glove changing station in one work area did not reduce latex aeroallergen levels. Large quantities of allergen were recovered from used laboratory coats and anesthesia scrub suits and from laboratory surfaces. Latex allergen concentrations in personal breathing zone samplers worn by health care workers in areas where powdered gloves were frequently used ranged from 8 to 974 ng/m³. Exposure likely occurs when gloves are changed and as a result of resuspension from reservoirs of powder in the room and clothing. Latex allergens were found in all particle sizes but were predominant in particles greater than 7 µm in mass median aerodynamic diameter. Results of electrophoretic immunoblotting showed that the aeroallergens are primarily the higher molecular mass components of the latex glove proteins. Measures to control exposure can be monitored by both area and personal air sampling with this immunochemical approach. Use of gloves with low allergen content or powder-free gloves appears to be more effective than use of a laminar flow glove changing station in reducing aeroallergen levels. (J ALLERGY CLIN IMMUNOL 1994;94:445-51.)

Key words: Latex allergy, glove sensitivity, latex aeroallergen, occupational latex aeroallergen, latex allergen air sampling

Natural rubber proteins from *Hevea brasiliensis* latex are allergenic. Latex products have caused anaphylaxis during surgical and radiographic procedures in sensitized patients.¹⁻⁴ Immediate contact urticaria from latex gloves and other sources can afflict some surgeons, nurses, and other health care workers.^{5, 6} Tarlo et al.⁷ reported respiratory allergy to latex in workers employed in a plant making latex articles. Jaeger et al.⁸ called attention to the occurrence of respiratory symp-

Abbreviations used

HEPA: High-efficiency particulate air
SDS-PAGE: Sodium dodecylsulfate-polyacrylamide gel electrophoresis

toms in health care workers. During the past 2 years, we have evaluated 49 medical center employees for respiratory allergy, who had symptoms of both rhinitis and asthma while they were working in areas of the institution where latex gloves were used extensively.⁹ Many of these workers have positive skin test responses to extracts prepared from latex, but not to extracts prepared from vinyl gloves or cornstarch. Many had elevated specific IgE antibodies to the latex glove extract. With the use of high-titer sera from some of these patients, it has been possible to develop an immunoassay to measure latex aeroallergens at the work site. The aims of this study were: (1) to deter-

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TABLE 1. Latex aeroallergen levels in various areas within Mayo Medical Center

Air samples	Aeroallergen level (ng/m ³)
Extensive glove use areas	
Urology — Cystoscopy	121.8
In-patient surgical suites (<i>n</i> = 5)	111 ± 25
Orthodontics — Outpatient Surgery	99.8
Mohs Dermatology — Outpatient Surgery	78.5
Blood Bank Drawing Room	46.3
Blood Bank Components — Separation Lab	38.4
Surgical Pathology — Lab	37.4
Venipuncture — Room	29.6
Blood Bank Cross Match — Lab	16.4
Hematopathology — Lab	14.3
Allergy Research — Lab	13.8
Minimal glove use areas	
Allergy Clinic	1.8
Spirometry	0.6
Bone Marrow Transplant*	0.6
Blood Bank — Virus Serology Lab†	0.3
Personal	
Hematopathology Tech	8.4
Venipuncture Tech	25.9
Venipuncture Tech	136.9
Anesthetists (<i>n</i> = 9)	419 ± 292

tech, Technician.

*Powder-free glove use.

†Vinyl glove use.

mine the airborne concentrations of the allergen in various areas of the medical center with varying activities and usage levels of latex gloves, (2) to determine the personal exposure of health care workers to latex allergens during performance of various tasks, (3) to determine the aerodynamic size of the allergen-carrying particles, and (4) to evaluate effectiveness of a laminar flow glove changing station in reducing latex aeroallergen levels.

METHODS

Air sampling

Area air samplers (Quan-Tec-Air, Inc., Rochester, Minn.) or personal breathing zone samplers (SKC, Inc., Eighty-Four, Pa.) were used to collect air samples from various areas in the medical center, including five surgical suites. Area samplers were operated for 4 hours at a flow rate of 3 L/sec, except in the surgical suites, where sequential 1-hour samples were obtained at a flow rate of 1 L/sec. Personal breathing zone air sampling pumps were worn by the individuals during a partial work shift and operated at a flow rate of 5 L/min. Airborne particles were collected onto polytetrafluoroethylene filters (Quan-Tec-Air, Inc.).

To estimate the relative amounts of allergen carried on different size particles, we operated an area sampler fitted with a 5-stage cascade impactor (Andersen model

no. GMW 65000; Andersen Instruments, Inc., Atlanta, Ga.). We also tested the effect of donning and removing gloves in a negative pressure, high-efficiency particulate air (HEPA)-filtered cabinet (Lab Products, Inc., Maywood, N.J.) on the concentration of airborne latex allergens. This apparatus is analogous to a laminar flow hood, but the airflow is reversed to carry particles into the filter. Latex aeroallergens were measured in an orthodontics clinic daily for 2 weeks; the first week served as a control period, then the glove changing station was installed and used during the second week. Compliance with the use of the glove changing station was ascertained by comparing the total number of gloves discarded in the changing station with the total number of gloves dispensed and used.

Recovery of allergen from clothing

A hand-held vacuum with a polytetrafluoroethylene filter installed in the hose was used to collect particles from used lab coats and surgical scrub suits. The surfaces of the protective clothing were vacuumed thoroughly for 1 minute, and the samples were prepared for immunoassay as described below.

Immunoassay for latex aeroallergens

Latex allergens were extracted from the filters in 1 ml of 0.1 mol/L phosphate buffer containing 0.2% bovine serum albumin and 0.01% sodium azide and assayed immunochemically by an inhibition technique. Extracts

TABLE II. Latex aeroallergen concentrations in four surgical suites and a postanesthesia recovery area

Room descriptions			Latex aeroallergen (ng/m ³)		
Room no.*	Volume (m ³)	Air changes/hr	Anesthetist	Table	Room no.
19	127	23	974	208	151
11	127	23	636	118	88
33	185	23	549	96	114
26	128	225	613	130	92
PAR	1051	2-6	—	—	112

PAR, Postanesthesia recovery room.

*Surgical suite number.

TABLE III. Sequential collection and measurement of latex aeroallergens in a surgical suite throughout the day

Time	Latex aeroallergen level (ng/m ³)	
	Area samples (1-hr collections)	Personal samples* (collection duration)
8:00-9:00 AM	162	354 (30 min)
9:00-10:00 AM	59	331 (2 hr)
10:00-11:00 AM	177	282† (10 min)
11:00 AM-12:00 PM	53	8 (2 hr)
12:00-1:00 PM	61	23 (2 hr)
1:00-2:00 PM	89	
2:00-4:30 PM	4	

*Four anesthetists — four procedures.

†Sample changed 10 minutes after donning gloves.

of the filters or a laboratory reference standard extract from latex gloves (Bodyguards, T. K. Glove Products Co., Ltd., Huntington Beach, Calif.) competed with solid-phase reference latex glove allergens for specific IgE antibodies obtained from three sensitized individuals who worked in the medical center. Radioiodinated affinity-purified rabbit anti-IgE was used for detection.¹⁰ The results were calculated with logistic regression and expressed as mass protein per cubic meter of air, based on the glove extract that contained 7 mg of protein per milliliter, as determined by the bicinchoninic acid protein assay and calculated by linear regression, compared with a standard of bovine serum albumin. The sensitivity of the assay was 2 ng, allowing detection of 0.1 ng/m³ in 20 cubic meters of air.

For the purposes of standardization and the investigator's ability to compare other studies to these results, the latex glove extract was compared with a Food and Drug Administration reference raw latex preparation

TABLE IV. Latex aeroallergen levels (in a laboratory environment) associated with airborne particles of varying size*

Latex aeroallergen levels		
Dp50 (μm)	ng/m ³	% Total
14	3.0	67
7	0.6	14
4	0.3	7
2	0.3	6.5
<2	0.3	6.5

*Particle size cutoffs (in microns) at 50% collection efficiency for spherical particles with unity mass density at 25° C and 760 mm Hg are designated Dp50.

(FDA lot E-5 latex) by this RAST inhibition method. With the latex glove extract on the solid phase, the inhibition lines were parallel with 129 ng protein of the glove extract and 1037 ng protein of the E-5 raw latex extract, producing approximately 50% inhibition, respectively. With the E-5 extract on the solid phase, the inhibition lines were also parallel; however, 42 ng of protein of the glove extract corresponded to 120 ng of the E-5 raw latex preparation. All results reported in this study are from the glove extract solid-phase system and glove extract standard.

Immunoblotting

To further characterize the allergenic molecules in the air compared with those of the glove extract, we performed immunoblots of the standard glove extract and of air samples, using different IgE-containing sera from affected individuals. Extracts were run under reducing conditions on 12.5% gels according to the method of Laemmli.¹¹ Gels were stained with Coomassie Brilliant Blue (Sigma Chemical Co., St. Louis, Mo.) and silver stains to better visualize bands of low intensity by Coomassie Brilliant Blue staining. Immunoblots were performed with the method of Towbin et al.¹² Allergens binding IgE antibody were detected by incubation with a radioiodinated affinity-purified rabbit anti-IgE and sub-

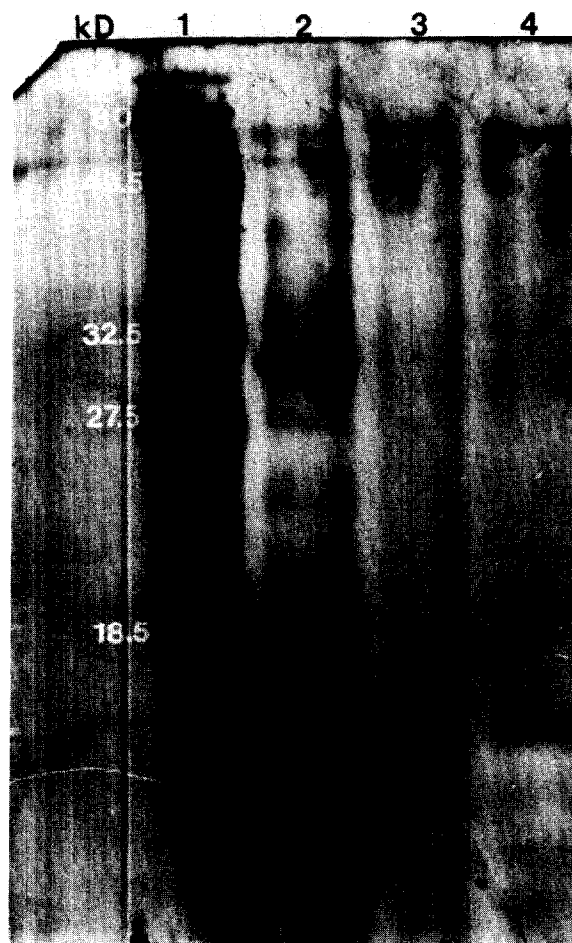


FIG. 1. SDS-PAGE of latex allergens from gloves and air samples stained with silver. *Lane 1*, Molecular weight markers; *lane 2*, latex glove extract; *lane 3*, an air sample of latex gloves snapped deliberately over an air sampler; *lane 4*, air sample of laboratory where latex gloves were used.

sequent washing step; IgE binding components were identified by subsequent autoradiography at -70°C for 24 hours.

RESULTS

Latex aeroallergen levels

The amount of latex allergen captured after snapping gloves over an air sampler was dependent on the number of gloves used. In a second experiment we determined the amount of latex allergen liberated into the air while donning gloves and later while removing them. When a glove brand of high allergen content (15 mg of protein per glove) was used, equal amounts of allergen were captured during donning and removal of 10 gloves (approximately 1700 ng of protein per glove).

Airborne allergen concentrations in 11 areas of the medical center where latex gloves were fre-

quently used varied from 13 to 121 ng/m^3 (Table I). Conversely, in four areas where latex gloves were never or seldom used or where powder-free latex or vinyl gloves were used, allergen levels varied from 0.3 to 1.8 ng/m^3 . Personal breathing zone concentrations of latex allergens for workers in areas where gloves were frequently used varied from 8 to 978 ng/m^3 . The highest average values were obtained from anesthesia personnel (mean, 411 ng/m^3 ; range, 8 to 978 ng/m^3). It was evident that the exposure of different individuals with the same job could vary considerably.

Two automated area air samplers were placed at opposite ends of a clinical immunology laboratory. A technician sensitive to latex allergens worked in the laboratory and kept a symptom diary. Samples were taken over a 9-hour period each day for 2 weeks. Most air samples assayed demonstrated no detectable allergen, and no symptoms were reported. However, the technician did report an asthma episode on a day when the latex allergen concentration was 12 ng/m^3 . Although airborne allergen was not always detectable, reservoirs of settled dust were identified. Allergen, in excess of 1 mg, was recovered from a laboratory coat that had been used for a week. Swabs of upper surfaces in the room also contained large amounts of allergen.

Surgical suites

Interestingly, latex aeroallergen levels were similar in an operating room with high laminar flow air exchange rate (225 times per hour) compared with an operating room with conventional air exchange rates (25 times per hour) (Table II). Individual personal breathing zone samples of operating room personnel varied as much as 100-fold depending on the invasiveness of the procedure and frequency of changing gloves. These values were often higher than concentrations measured at different points in the same room by area sampling. In one operating room where area samples were obtained sequentially at hourly intervals for 8 hours, allergen was present every hour while the room was being used for surgical procedures. However, within 2.5 hours after the operations were completed, the allergen levels fell to 4% of the previous average hourly value (Table III). Substantial allergen could also be recovered from used surgical scrub suits (approximately 200 μg).

Particle size

The Andersen cascade impactor was operated in a laboratory where technicians were experi-



FIG. 2. IgE immunoblots of Fig. 1 with three sera from individuals sensitive to latex. Lanes as in Fig. 1.

TABLE V. Effect of a negative pressure HEPA-filtered glove changing station on the concentration of airborne latex allergens in an orthodontics clinic

Day	Week 1			Week 2		
	Date	Patients	Latex (ng/m ³)	Date	Patients	Latex (ng/m ³)
Wed	11/13	47	11.2	11/20*	67	7.2
Thu	11/14	49	9.6	11/21*	60	8.3
Fri	11/15	33	2.8	11/22*	61	5.7
Sat	11/16	0	<0.3	11/23	0	<0.3
Sun	11/17	0	<0.3	11/24	0	<0.3
Mon	11/18	72	9.6	11/25*	69	9.3
Tue	11/19	69	10.3	11/26*	61	13.2
Total no. of patients		270			313	
Mean latex allergen $\pm$ SD			8.7 $\pm$ 3.4			8.7 $\pm$ 2.8
Total glove use		ND			800	
Gloves in changing station					452	
Compliance with use of changing station					57%	

ND, Not determined.

*Glove changing station in use.

encing symptoms of allergy (Table IV). Latex allergen was distributed throughout all particle size ranges, and the majority of recovered allergen (>80%) was associated with particles greater than 7 μ m in mass median aerodynamic diameter.

Immunoblotting

Sodium dodecylsulfate–polyacrylamide gel electrophoresis (SDS-PAGE) demonstrated several proteins common to extracts of air filters and latex gloves. Faint protein staining bands at 60 to 80 kd were evident in both extracts. Several bands at approximately 30 kd and below 18 kd were also present (Fig. 1). Immunoblots with IgE antibody–

containing sera demonstrated diversity in the human allergic response to these proteins. Each of the three sera tested showed a different pattern of IgE reactivity with staining of at least nine bands, ranging in molecular weight from approximately 10 to 100 kd (Fig. 2). A radiostaining band at approximately 30 kd appears to be an important allergen in gloves, being reactive with all three sera tested. It appears that the most abundant allergens in the air are in the 70 to 100 kd range and stain poorly with Coomassie Brilliant Blue or silver stain. This is in contrast to the glove extract in which the most intense binding was associated with proteins of 10 to 60 kd (Figs. 1 and 2).

Glove changing station

The results from the experiments involving the HEPA-filtered glove changing station are shown in Table V. During days on which patients were being seen, latex aeroallergen levels ranged from 2.8 to 13.2 ng/m³; when the area was not occupied on weekends, the aeroallergen levels were undetectable. Virtually no reduction in latex aeroallergen concentration was achieved during the week that the glove changing station was in operation. However, only 57% of the gloves used were disposed of in the changing station.

DISCUSSION

The air sampling methods and aeroallergen assay established here provide objective methods for assessment of airborne latex allergen concentrations and the effects of various allergen abatement efforts. Not surprisingly, the latex aeroallergen concentrations in the air were higher in areas of the medical center where the staff used many gloves per person. It seems likely that most of the latex allergen initially becomes airborne when the gloves are donned or removed, but resuspension from clothing or settled dust also contributes to the allergen in the air of a room where gloves are used. Allergen particles of the size those from latex gloves will settle rapidly. This is consistent with the absence of measurable latex allergen in the air at the end of workdays and on weekends when the rooms were not in use. Also, the fact that only a small portion of the allergen is carried on particles below 7 μ m in mean mass aerodynamic diameter is consistent with the observation that most of the subjects had symptoms of rhinitis and conjunctivitis and only some had asthma.⁹

Our results with IgE immunoblot autoradiography of electrophoretically separated latex glove extracts confirm the observations of Jaeger et al.,⁸ Chambeyron et al.,¹³ and Slater et al.¹⁴ that almost all allergenic protein molecules and some additional components not visible by Coomassie Brilliant Blue or silver staining can persist through the manufacturing process and can be readily extracted from the gloves. Our results also confirm that various individuals' IgE may be directed to different allergenic molecules. Results of SDS-PAGE immunoblots suggest that the quantitative distribution of specific latex allergen molecules varies between airborne particles and direct contact with gloves. The most abundant allergens in the air appear to be high molecular mass molecules, which stain poorly with protein stains. In this context, direct measurement of allergen may

in principle be a more reliable means of evaluating exposure to latex than total protein because some of the allergens do not stain with Coomassie Brilliant Blue or silver stain. These patients did not react to allergens in cornstarch alone. However, the extractable proteins in latex adsorb to cornstarch powders used as lubricants on gloves. It is interesting to note that no interaction was observed with calcium carbonate powder.¹⁵ Calcium carbonate is often used as a mandrel release agent in the manufacture of gloves.

In the single experiment conducted in the orthodontic clinic, which involved the glove changing station, the latex aeroallergen levels were not significantly reduced. However, the workers changed only about half of their gloves in the protected area, and no special efforts were made to clean the area to prevent resuspension of particles already present. It is possible that with greater compliance over a longer period of time, a significant reduction in latex aeroallergen levels could be achieved. However, subsequent measurements in the same area indicated that after personnel began using a brand of gloves that contained only small amounts of allergen, airborne exposure fell from 100 to 10 ng/m³.

It is interesting that these latex aeroallergen concentrations are of the same order of magnitude (10 to 1000 ng/m³) as many other allergens such as papain, laboratory animal urinary proteins, insect particles, soybean dust, *Alternaria* species, and grass and ragweed pollens.^{16, 17}

From these results we conclude that many of the proteins in latex are allergenic, but each individual's unique IgE response to latex allergens, as with most allergens, complicates the issue. Latex allergen becomes adsorbed to cornstarch powder, which becomes airborne when gloves are donned or removed. Although the heaviest exposure probably occurs at these times, there is a reservoir of settled allergenic dust on surfaces, surgical gowns, and coats, which can become resuspended and cause secondary exposure. The majority of particles carrying allergen are 7 μ m or larger and therefore likely to cause upper respiratory tract symptoms. However, 20% of the particles are respirable and capable of causing asthma. Higher molecular weight molecules in the range of 80 kd are overrepresented in the airborne particles compared with glove extract. Control of exposure by changing to powder-free or low allergen-containing gloves appears more effective than trying to contain airborne allergens with a glove changing station.

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