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Latex-specific proteins causing immediate-type cutaneous, nasal, bronchial, and systemic reactions

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*We examined 70 patients reporting hypersensitivity reactions caused by latex articles. All patients suffered from urticaria, 36 from rhinitis, 31 from conjunctivitis, 22 from dyspnea, and 17 from systemic reactions, and four patients developed severe systemic complications during surgery. By means of inhalative challenge tests with powdered latex gloves, it could be demonstrated that the glove powder (cornstarch) obviously functions as a carrier for latex allergens, which then become airborne. Five of 18 patients undergoing such challenge tests demonstrated a significant increase of specific airway resistance; 17, acute rhinitis and/or conjunctivitis; and two, a systemic reaction. Sixty-two percent of the patients demonstrated specific IgE antibodies to natural latex, 58% to an irradiatively cross-linked, so-called, "hypoallergenic" latex preparation, and 46% to commercial-latex RAST disks (Pharmacia). No specific antibodies to cornstarch or a mixture of rubber chemicals were found. A good correlation (82%) exists between latex IgE RAST and latex skin prick test, as revealed in a subgroup of 45 subjects. By means of sodium dodecyl sulfate-polyacrylamide gel electrophoresis, the latex allergen appears to be a mixture of proteins in a molecular weight range from 10 to 67 kd. (*J ALLERGY CLIN IMMUNOL* 1992;89:759-68.)*

Key words: Latex, rubber gloves, glove powder, latex asthma, immediate-type hypersensitivity, specific IgE antibodies, PAGE, immunoblot, inhalative provocation test

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Abbreviations used

SDS-PAGE:	Sodium dodecyl sulfate-polyacrylamide gel electrophoresis
SPT:	Skin prick test
PBS:	Phosphate-buffered saline
SR:	Systemic reaction
SR _{aw} :	Specific airway resistance

Natural rubber is obtained from *Hevea brasiliensis* (family of Euphorbiaceae), a tree originating from the Amazonian area.^{1, 2} The milky sap of this plant, the so-called "latex," contains about 33% rubber, cis-1,4-polyisoprene, 2% resin, 65% water, and 1.8% protein. During the rubber-manufacturing process, many chemicals are added to the latex, depending on shape, design, and technical requirements of the finished product: vulcanizers (e.g., 4,4'-dithiomorpholine), accelerators (e.g., thiurams, mainly tetramethylthiuramdisulfide, mercaptomixtures, benzothiazoles, diphenylguanide, or thioureas), stabilizers, and antioxidants (zinc oxide, thiocarbamates, paraphenylendiamine or phenole derivatives).³⁻⁷ In addition to synthetic rubber (e.g., cis-1,4-polyisoprene [Neoprene], polybutadiene, or copolymers of styrene/butadiene, chlorobutadiene/chloroprene, acrylonitrile/butadiene, or polyether/diisocyanate), since 1930 natural rubber is increasingly used; the world production is now 6 million tons per year.

Rubber hypersensitivity was often described in recent years but usually as a contact dermatitis caused by chemical rubber additives.^{8, 9} Since the first description by Nutter¹⁰ in 1979, a limited number of patients was also reported demonstrating contact urticaria to latex,¹¹⁻¹⁴ which could be proven to be IgE mediated.^{3, 12, 15} Different explanations have been offered for the nature of the sensitizing allergen: rubber chemicals,^{16, 17} flock,¹⁸⁻²⁰ or even vapors of terpenes.²¹ During the past few years, there was increasing evidence for the causative agents to be water-soluble,²² thermostable,⁶ and trypsin-sensitive¹¹ proteins or glycoproteins from natural latex.^{7, 23, 24} Roe and Ewart²⁵ had already demonstrated the presence of seven electrophoretically distinct protein constituents of the *Hevea brasiliensis* latex. Additional characterizations were somewhat contradictory. Proteins of >30 kd,¹¹ protein peaks of 2, 5, and 30 kd,²² and, finally, protein components of 10, 24, 35, and 100 kd with a predominantly acidic pH⁶ were believed to be allergenic.

At the present time, SRs to latex with rhinitis/conjunctivitis, angioedema, asthma,^{6, 7, 11, 12, 26, 27} hypotension,⁶ or even shock during surgery of latex-allergic patients* have been attributed to direct contact to rel-

evant amounts of latex allergens.^{5, 7, 15, 20, 23, 26} Because of reported symptoms after inhalative exposure to powder of surgical latex gloves, we investigated components of latex articles as possible airborne allergens. Furthermore, latex allergens were characterized by SDS-PAGE and immunoblot.

MATERIAL AND METHODS**Subjects**

We examined 70 patients (21 male and 49 female patients; mean age, 33 ± 9 years) who reported hypersensitivity reactions to latex products; 37% were physicians or medical students, 54% were male or female nurses or technicians, and 8% worked in other professions without latex contact at their workplace. Most of these patients had replied to our announcement in medical papers, some had been recruited from the outpatient group, and nine patients were medical staff from our hospital.

All patients answered a standardized questionnaire about common and latex allergies. All patients gave their informed consent to participate in the study.

The first symptoms of latex allergy appeared 3 weeks to 16 years after the beginning of latex exposure (mean, 3 years). Seven patients could not remember repeated latex contact; however, childhood exposure to latex-made articles could not be excluded.

Substances for in vivo and in vitro tests

Two latex samples of the rubber tree, *Hevea brasiliensis*, were supplied by the Kautschuk Co. (Frankfurt, Germany): ammoniated latex (0.7% ammonia) and a recently developed liquid latex that had been cross-linked by irradiation with fast electrons. A vulcanization paste, a mixture of rubber chemicals (tetramethylthiuram, zinc oxide, zinc diethyldithiocarbamate, and sulphur), was also provided by the above company.

Seven different sterile latex gloves were used: Triflex Travenol (Travenol laboratories, Ltd., Thetford and Norfolk, England), Sempermed, hypoallergenic (Semperit, Vienna, Austria), Peha microptic, hypoallergenic (Paul Hartmann AG, Heidenheim/Brenz, Germany), Neutrolon, hypoallergenic (Surgikos, Inc., Johnson & Johnson Co., Arlington, Texas), and Puritee Pur (Medimex Holfeld GmbH, & Co., Hamburg, Germany, produced by the Puritee Medical Co. Ltd., Slough, England). Nonsterile latex gloves used were Glads (Mölnlycke GmbH, Bruchsal, Germany) and disposable latex examination gloves (Malaysia). Latex-free gloves used were Elastyren (Danpren, Albertelund, Denmark), Neolon (Deseret Medical, Inc., Division of Parke-Davis & Co., Sandy, Utah), and Clinhand elastic (Heisig, Clinhand product, Penzberg, Germany). Cornstarch was provided as "absorbable dusting powder according to United States Pharmacopeia XXI (Paul Hartmann AG, used for gloves, "Peha soft" and "Peha taft").

Extracts

Crude latex solutions. Natural latex and latex cross-linked without chemicals were diluted 1:10, 1:100, and

*References 3, 6, 7, 11, 14, 15, 28, and 29.

1:1000 vol/vol in 0.9% NaCl, 0.4% phenol, and 0.1% human serum albumin (skin test solution).

Glove extract. One latex glove (Triflex Travenol) was cut into pieces (5 to 10 cm²), and the pieces were stirred overnight at room temperature in 250 ml of PBS solution (0.02 mol/L of NaPh, 0.15 mol/L of NaCl, and 0.02% of NaN₃, pH 7.3). The solution was lyophilized, and the lyophilisate was dissolved in 4 ml of distilled water and dialyzed overnight against 1000 ml of distilled water. After a second lyophilization, the lyophilisate was dissolved in 0.6 ml of double-distilled water again and filtered through a Millex-FG 0.2 µm filter unit (Millipore SA, Molsheim, France).

Saline latex extract (2% NaCl). Natural latex was diluted with distilled water (65% vol/vol) and, after addition of NaCl up to 2% (wt/vol), stirred overnight and centrifuged for 20 minutes at 2500 g. The aqueous phase (about 2 ml) at the bottom, containing the soluble proteins, was separated from the rubber phase and centrifuged several times in small aliquots in a table centrifuge (centrifuge 5415, Multimed, Wicker & Löscher, Kirchheim, Germany) at 5000 g until no more rubber precipitate formed and finally filtered through a 0.2 µm filter. The protein content of the saline latex extract was 3.5 mg/ml.

Acidic latex extracts. Natural latex, 0.7% ammonia, and irradiatively cross-linked latex were dissolved in distilled water (30% vol/vol) according to the method of Morales et al.⁶ Acetic acid was added stepwise until a rubber precipitate formed. The aqueous phase was neutralized with NaOH, dialyzed against distilled water (cutoff, 3 kd), freeze-dried, and resuspended in 1 ml double distilled water.

Rubber precipitate extract. The rubber precipitates (see under "acidic latex extract" above) were stirred overnight in 30 ml of PBS, pH 7.3. The washing solution was dialyzed against distilled water, freeze dried, and resuspended in 1 ml of distilled water.

Cornstarch or glove-powder solution. Ten milligrams of cornstarch from the manufacturer, the powder used to coat latex gloves, were dissolved in 1 ml of skin test solution. A sample of glove powder recovered from latex gloves (Sempermed) by scraping was prepared in the same way.

Prick tests

Latex SPTs were performed with 45 patients with natural latex milk, cornstarch, or latex glove-powder solutions (1:1000, 1:100, 1:10, vol/vol) and histamine hydrochloride at a concentration of 0.1% in 0.9% NaCl, 0.4% phenole, and 0.1% human serum albumin. A wheal reaction of at least 3 mm surrounded by an erythema was regarded as a positive reaction. SPT results and case histories of 66 patients concerning common allergies were available.

Protein concentration

The protein concentration of the saline-latex extract was determined according to the method of Lowry et al.³⁰ with bovine serum albumin as a standard.

Total serum IgE

Total IgE concentration in sera of 66 patients was determined with a Phadebas IgE PRIST (Pharmacia, Uppsala, Sweden) with a polyclonal rabbit anti-IgE antibody.

Specific IgE antibodies

To determine the presence of allergen-specific IgE, CNBr-activated paper disks were coupled with crude latex solutions from natural latex, irradiatively cross-linked latex, and a mixture of rubber chemicals at a concentration of 1:10 and cornstarch at a concentration of 1 mg/ml (diluted in 0.1 mol/L of NaHCO₃). The solutions were stirred overnight at room temperature and centrifuged at 1500 g for 20 minutes; 125 mg of CNBr-activated disks were added to 5 ml of supernatant and stirred gently during 5 hours. Then disks were washed once for 10 minutes in 0.5 mol/L of NaHCO₃, pH 8.4, twice for 10 minutes in 0.1 mol/L of ethanolamine-0.1 mol/L of NaHCO₃, and, after disks were left overnight at 4° C in this solution, washed twice for 2 minutes in 0.5 mol/L of NaHCO₃, once for 2 minutes in 0.1 mol/L of Na-acetate, pH 4.0. After incubation of 30 minutes in the last solution, disks were washed twice for 2 minutes in a Tween buffer (50 mmol/L of Na₂HPO₄, 0.15 mol/L of NaCl, 0.1% of NaN₃, and 1% of Tween 20, pH 7.4 to 7.6). In addition, we used disks from Pharmacia for latex, and we punched disks from washed latex gloves for IgE RAST. RAST was performed according to the instructions of Pharmacia, and the results were expressed in Phadebas RAST units per milliliter of serum and scored from 0 to 5.

SDS-PAGE and immunoblot

SDS-PAGE was performed in a vertical electrophoresis system (Bio-Rad Laboratories, Richmond, Calif.) with an acrylamide gradient from 7.5% (top) to 15% (bottom) 50 to 100 µl of saline extract of natural latex, glove extract, and acidic-latex extracts, and rubber-precipitate extracts were applied to the gel. Gels were stained for proteins with 0.1% Serva blue G (Serva Biochemics, Heidelberg, Germany) in 50% methanol, 10% acetic acid vol/vol; 800 µl of saline-latex extract (2.8 mg of protein) was then applied to one gel for immunoblotting. Proteins resolved by SDS-PAGE were electrotransferred onto nitrocellulose sheets (Bio-Rad Laboratories) overnight, applying 0.1 A at room temperature. The nitrocellulose paper was cut into 3 mm strips and incubated with 2.5 ml of latex IgE-positive serum or control sera, diluted 1:10 vol/vol with PBS-Tween (0.05 mol/L Na₂HPO₄/NaH₂PO₄, 0.9% NaCl, and 0.1% Tween 20, pH 7.4 to 7.6) plus 38% bovine serum albumin. The bound latex IgE antibodies were detected with ¹²⁵I-labeled anti-IgE (Pharmacia) at an activity between 40,000 and 80,000 cpm per lane.

Glove-exposure test

A glove-exposure test with one original and one washed latex glove (stirred during two days and nights in 0.9% NaCl) on the right and left hand, respectively, was performed for 30 minutes. Differences of symptoms and skin reactions were noted.

Seven patients sensitized to latex were tested with six different gloves (Triflex Travenol [powdered latex glove], Peha microptic [concentration of accelerators reduced], Neulon [inner coating of polyurethane], Neolon [Neoprene], Puritee [accelerator free], and Elastyren [polymer of styrol/butadiene]).

TABLE I. List of articles containing latex that caused hypersensitivity reactions in 70 patients and corresponding specific IgE antibodies

	No. of patients	Latex IgE+ % patients
Latex gloves (surgical household)	69	43 (62)
Balloons	8	6 (75)
Sticking plaster	11	9 (82)
Rubber contraceptives	5	3
Bracers	6	5
Masks (anesthetic/diving)	3	3
Stretch textiles	3	2
Shoes	3	2
Hot-water bottle	1	0
Air mattress	1	1
Baby pacifier	1	0
Shower curtain	1	0
Sailing equipment	1	1
Door/window isolations	2	1
Stamps	1	1
Colors	1	1

Inhalative provocation test

Eighteen patients with latex-specific IgE antibodies and symptoms of rhinitis, conjunctivitis, or dyspnea underwent an inhalative provocation test with latex gloves. First, the patients were tested with 20 pairs of plastic gloves powdered with cornstarch for 30 minutes in a small provocation chamber. Then, patients were tested with increasing numbers of powdered latex gloves (maximum 20 pairs) in the same way. The patients were not informed about the material of the gloves or the nature of the powder. The SR_{aw} and intrathoracic gas volume values were determined at regular time intervals until 5 hours after the last step of a maximum provocation with latex gloves of 60 minutes. To prevent local penetration of latex antigens, latex-free gloves had to be worn throughout the test.

RESULTS

Symptoms

In our group of patients, symptoms of latex hypersensitivity were caused predominantly by rubber gloves. Balloons, sticking plaster, rubber contraceptives, stretch textiles, or rubber shoes were less frequent. Hypersensitivity caused by other articles, like shower curtains or sailing equipment, were rare (Table I).

All patients suffered from local urticaria to latex articles, 36 complained of rhinitis, 31 complained of conjunctivitis, and 22 complained of a reaction of the lower respiratory tract (Table II). Additional SRs of 17 patients were edema of lips, eyes, or face after

contact to balloons or gloves in nine cases, lips or facial edema at the dentists in three cases, and anaphylactoid reactions in four cases (glove contact, gynecologic examination, use of condoms, and squash match with rubber-coated racket). Four patients had experienced severe complications with bronchospasm, generalized urticaria, hypotension, or shock during surgery or delivery. In some cases, even indirect contact to latex gloves was reported to be sufficient to cause the symptoms, that is, colleagues wearing gloves in the same room.

Measurement of total and specific IgE antibodies

Latex-specific IgE antibodies to natural latex could be detected in the sera of 62% of all patients. Additional symptoms of the eyes, nose, bronchi, or SRs were connected with an increased frequency of specific IgE antibodies (71% to 82%) and with higher RAST scores (Table II). Severe complications during surgery or delivery were always associated with the presence of latex-specific IgE in our study population. In general, the concentration of latex-specific IgE antibodies was independent from duration or intensity of latex exposure, as obtained from the case histories.

IgE antibodies to the latex cross-linked without chemicals were positive in 58% of the patients. The RAST score was lower at least 1 score in 22 cases and higher in two cases compared with that of natural latex. IgE antibodies to the commercial latex RAST disks from Pharmacia were found in 46% of the patients, that is, 16% reacted only with the disks prepared in our laboratory (Fig. 1). No specific IgE antibodies were detectable against cornstarch or rubber chemicals, although sufficient binding of these substances to the disks is uncertain.

The sera of 12 patients with IgE antibodies to natural latex were tested with punched disks from washed gloves. Only five sera with very high antibody levels against natural latex revealed a positive reaction.

Total IgE was elevated (>120 IU/ml) in 42 of a subgroup of 66 patients, in 50% of the latex IgE-positive patients and in 23% of the latex IgE-negative patients. There was no clear correlation between total IgE and specific IgE concentrations. Patients with common allergies (positive skin test or RAST to one or more allergen and history of allergic symptoms; $N = 24$) demonstrated an increased total IgE in 58% of the cases. Only 14% of a group of patients without any common allergy ($N = 21$) had elevated IgE levels (data not presented).

We also compared latex allergy, common allergies (positive prick or RAST test with one or more allergen and corresponding symptoms), and signs of food in-

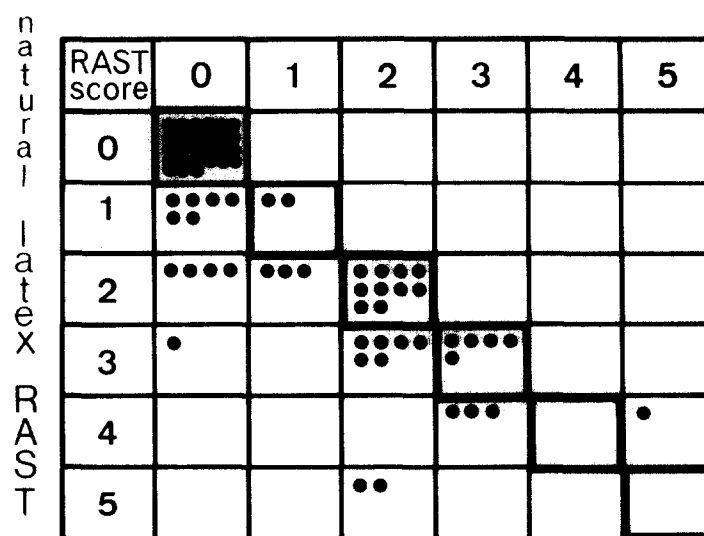


FIG. 1. Comparison between specific IgE antibodies with commercial and self-coupled latex disks. In 16% of latex-allergic patients, specific IgE antibodies were not detectable with commercial RAST.

TABLE II. Symptoms of 70 patients caused by latex articles and corresponding latex-specific IgE antibodies

	No.	Latex-specific IgE antibodies RAST score						1-5 +	%
		0	1	2	3	4	5		
Urticaria	70	27	8	17	12	4	2	43	62
Rhinitis	36	7	5	11	8	3	2	29	81
Conjunctivitis	31	7	4	7	8	3	2	24	77
Dyspnea	22	3	2	5	6	3	2	18	82
Systemic reactions (including angioedema of lips or face)	17	5	2	4	4	1	1	12	71
Surgery or delivery compli- cations	4	0	1	0	2	1	0	4	100

tolerance in 56 patients. Common allergies were more frequent in the group with latex IgE antibodies (21/36) than in the group with negative latex RAST (7/20). Symptoms of food intolerance did not predominate in the latex-allergic subgroup.

SPT

Latex prick test data with natural latex milk were available from 45 subjects. These data corresponded well with the RAST data (82%) with the natural latex disks; 31 patients were positive in SPTs and RAST, and six patients were negative in both tests. One patient with latex IgE antibodies in serum did not demonstrate a reaction of the skin; seven patients with a

wheel-and-flare reaction to latex milk were RAST negative.

SPTs with pure cornstarch from a glove manufacturer were always negative. Additional SPTs with glove powder, obtained from latex gloves by scraping, were performed in 24 patients. Of 21 latex RAST-positive patients, 18 demonstrated an immediate skin reaction with the glove powder (as strong as with natural latex).

Glove-exposure test

Fifteen patients with skin hypersensitivity to latex gloves wore a washed and an original latex glove during 30 minutes of testing; 12 of the patients were

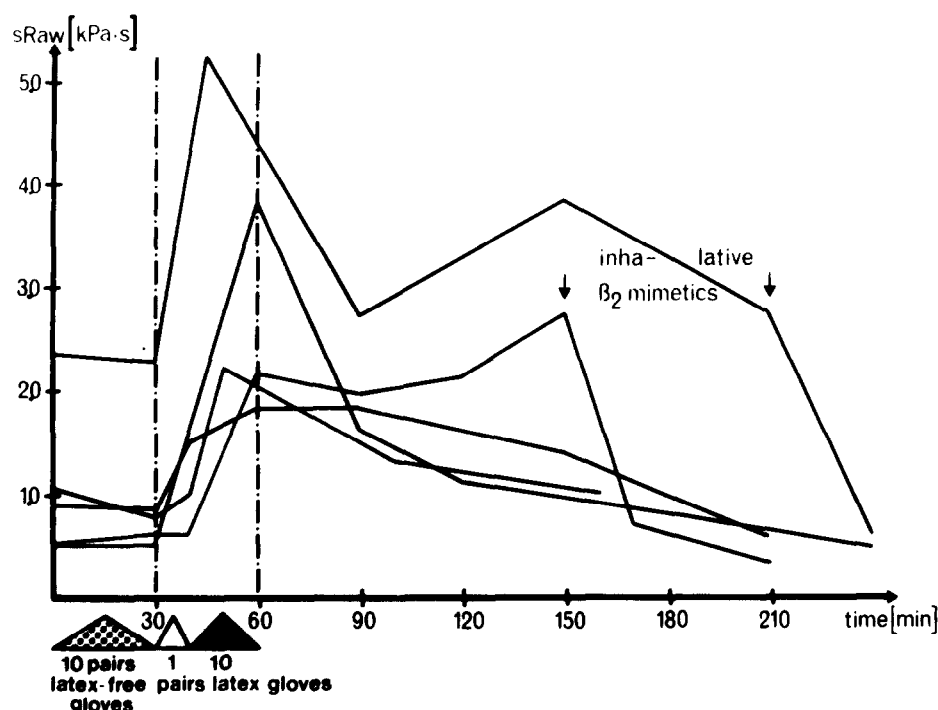


FIG. 2. SR_{aw} of five patients during an inhalative challenge test with powdered latex gloves. To prevent local penetration of allergens, the patients wore additional plastic gloves under latex gloves.

TABLE III. Result of a comparative glove test of seven patients under workplace conditions

Type of glove	Tolerated	Not tolerated
Triflex Travenol	1	6
Neutalon	1	6
Peha microptic	2	5
Puritee Pur	5	2
Neolon*	7	0
Elastyren*	6	1

*Most comfortable (latex-free) gloves worn.

latex IgE positive. Four patients demonstrated an identical reaction with both gloves, six had a stronger reaction with the original, and five patients had a stronger reaction with the washed glove.

Seven patients with positive IgE antibodies to latex tested six different pairs of gloves. All seven patients were free of symptoms with Neolon, six with Elastyren (itching and redness in one case), and five patients with Puritee (itching in two cases). Only one patient could work with Triflex Travenol, two with Peha microptic, and also only one with Neutalon. One surgeon could wear Neutalon longer (1 hour) than Triflex Travenol or Peha microptic (5 minutes). The five other patients could not detect any advantage

TABLE IV. Results of the inhalative provocation test with latex gloves during 5 to 60 minutes (N = 18)

Rhinitis	16
Cough	8
Conjunctivitis	8
Dyspnea	7
Bronchial obstruction	5
Facial edema	1
Systemic reaction	2

To prevent dermal penetration of latex allergens, the patients wore latex-free gloves under latex gloves.

of Neutalon compared with the other latex gloves (Table III).

Inhalative provocation tests with latex-free and latex gloves

Inhalative provocation tests with latex gloves were performed with 18 patients with dyspnea or rhinitis/conjunctivitis related to latex contact. The most frequent reactions during the test were rhinitis, cough, and conjunctivitis (Table IV). A significant increase of the SR_{aw} (an increase of SR_{aw} of $\geq 100\%$ reaching at least 2 kPa · s) was found in five cases (Fig. 2). One nurse developed a severe facial angioedema and hypotension; another nurse, already resigned from

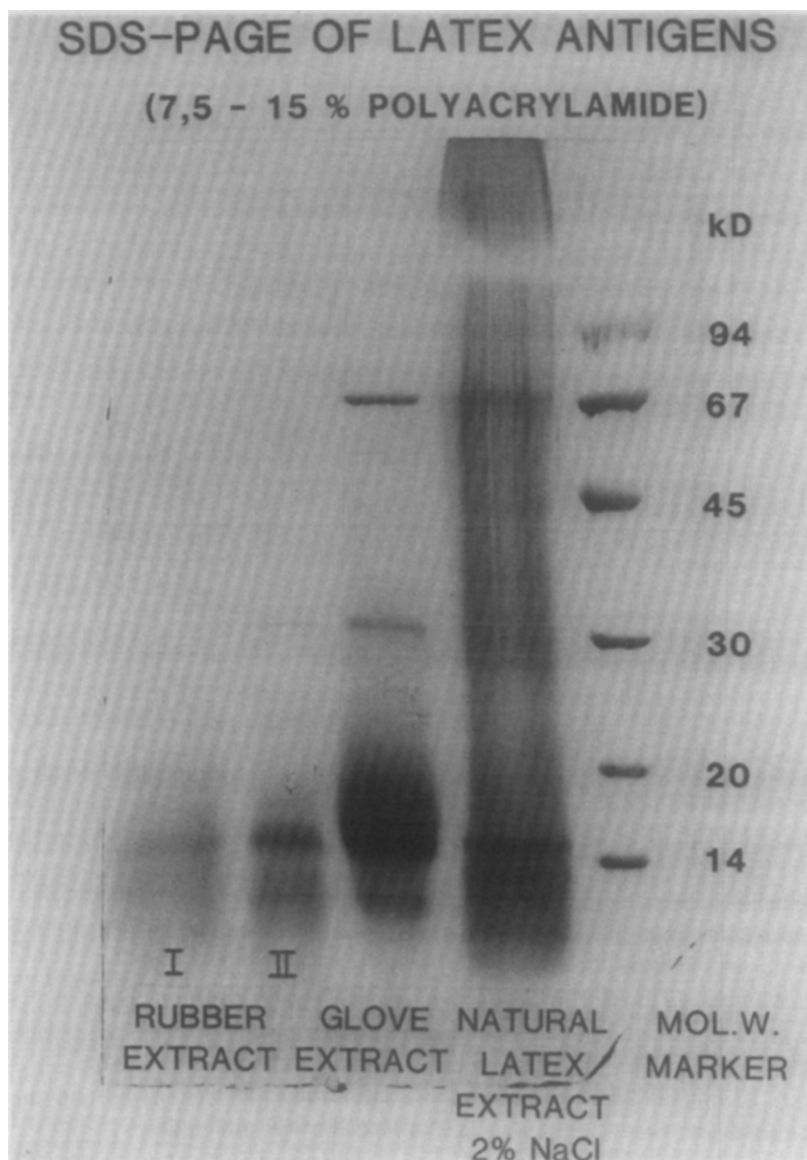


FIG. 3. SDS-PAGE of latex extracts with a gradient of 7.5% to 15% acrylamide. Saline extract of natural latex milk resolved into seven distinct protein bands. Rubber extract I is from polymerized irradiatively cross-linked latex; rubber extract II, polymerized natural latex milk. Strong protein component was found in common for latex milk and glove extract.

her profession for 1 year, demonstrated general malaise. The handling of the cornstarch-powdered latex-free gloves (negative control) only caused mild sneezing in three patients. Patients demonstrating a reaction of the lower respiratory tract in this test did not generally have higher specific IgE antibody concentrations than patients who exclusively had skin, eye, or nose reactivity.

Electrophoresis/immunoblot

SDS-PAGE was performed with the saline natural latex extract, glove extract, acidic latex milk extracts, and rubber precipitate extracts. Acidic latex milk ex-

tracts did not resolve into distinct bands. As many as seven different protein components were detectable in the other extracts of a molecular weight about 14 kD, between 30 and 45 kD, and about 67 kD (Fig. 3). A marked difference of the protein pattern was found between the extract of natural latex milk (Fig. 3, right) and the glove and rubber precipitate extracts (*rubber extract I*, polymerized irradiatively cross-linked latex; *rubber extract II*, polymerized natural latex). The rubber precipitate extracts and the glove extract revealed very similar bands. A strong protein component of 67 kD could be demonstrated to be in common for natural latex milk extract and glove extract.

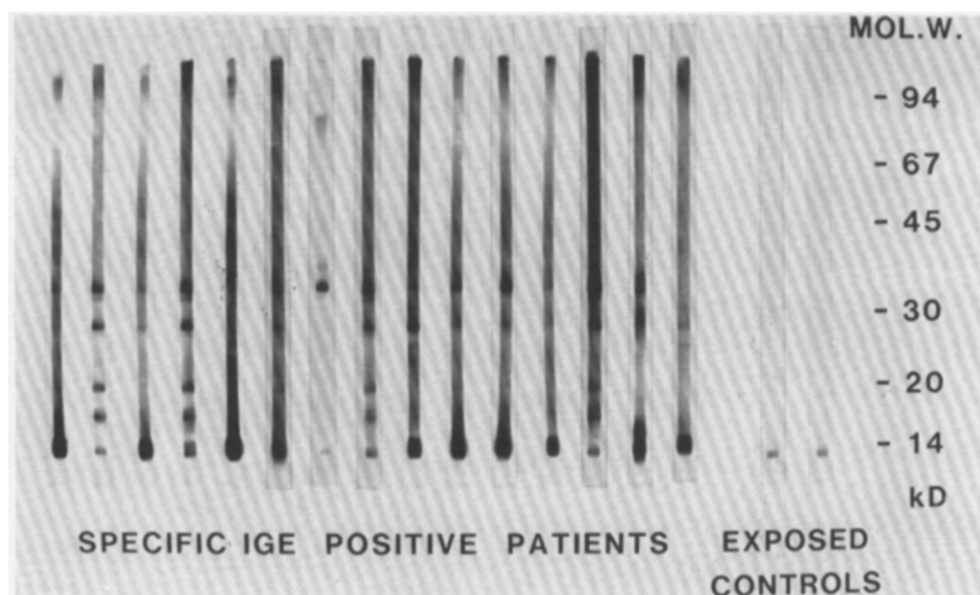


FIG. 4. Immunoblot of 15 latex IgE-positive patients with protein components of saline extract of natural latex without chemicals except 0.7% ammonia.

In immunoblot studies (Fig. 4), the sera of 15 latex IgE-positive patients reacted with protein components found electrophoretically all over the molecular weight range. In many cases the reaction was so strong that almost no single bands were distinguishable. Most sera revealed a similar reaction pattern with the strongest bands about 14 kD and between 30 and 45 kD. Some patients demonstrated antibodies only against one or two components. We did not find a correlation between specific antibody concentration and reaction pattern or intensity in the immunoblot.

DISCUSSION

Many studies about asthmatic or anaphylactoid reactions in addition to local urticaria to latex articles* underline the increasing importance of latex as an inhalative occupational health hazard. Meanwhile, there is convincing evidence that the chemical additives are not responsible for type I hypersensitivity to latex,^{6, 7, 23, 32} although there are some studies about immediate-type reactions to accelerators.^{17, 31, 33} In agreement with our SPT results, Geier and Fuchs³¹ and Turjanmaa et al.³⁴ reported only negative results using cornstarch or talcum in eight and 15 patients, respectively.

In the sera of 43 of 70 patients with immediate hypersensitivity to latex articles, specific IgE antibodies against natural latex milk could be demonstrated. IgE-mediated allergy must therefore be di-

rected against components of the native latex itself. In agreement with many other authors,^{6, 7, 11, 15, 22-24} the protein nature of these allergens could be proven by PAGE and immunoblot. The use of self-coupled latex disks in a RAST was superior to the use of commercial latex disks³⁴ or punched disks from washed rubber gloves^{12, 26} in our study.

In contrast to Wrangsjö et al.²⁰ who did not find a clear relationship between severity of symptoms and latex IgE levels, we demonstrated a positive correlation between symptoms and the concentration of specific IgE antibodies.

The absence of latex-specific IgE antibodies in the sera of five of 17 patients with SRs and three of 22 patients with dyspnea may be explained by, for example, C1 esterase-inhibitor deficiency, unspecific bronchial hyperreactivity, misinterpretation of symptoms, or very low antibody concentrations. Local hypersensitivity symptoms to gloves without corresponding IgE antibodies (27/70) may be due to contact dermatitis to rubber chemicals,³⁵ for example, thiurams,^{4, 5} which can act as haptens,¹⁵ unspecific contact urticaria, or eczema from local humidity, pressure of tight gloves, or irritative effects of cornstarch or disinfectants.⁵ A coexistence of type I allergy to latex and type IV allergy to chemicals has also been described.^{14, 32, 36} According to our data, neither cross-linkage of latex with irradiation instead of vulcanization introduced by one manufacturer nor exhaustive washing of latex gloves⁶ prevents type I latex allergy. This finding is understandable since the latex allergen

*References 3, 6, 7, 11, 12, 14, 15, 26, 27, and 31.

is a natural ingredient of rubber and cannot, at the present time, be separated from the rubber polymer.

Our data confirm previous results about a positive correlation between latex allergy and elevated total IgE^{3, 20} and atopy.^{3, 14-16, 22, 26} A generally higher sensitivity of atopic individuals to all kinds of allergens is discussed.³ However, a higher incidence of food-related allergies (fish, nuts, tomatoes, apples, and spices) among latex-allergic patients^{3, 20, 26} could not be demonstrated in the present study.

The lower sensitivity of latex RAST compared with SPTs or exposure tests is in agreement with the findings of other authors.^{12, 15, 20, 29, 34} The lower sensitivity might be caused by structural changes of the allergen during the fixation to the solid phase or too low protein concentrations of the allergen solution. "False positive" reactions of the (sometimes eczematous) skin may be due to unspecific reactions to unstandardized mixtures of rubber components, chemicals, and glove powder.

The positive SPTs with glove powder obtained from latex gloves by scraping in contrast to negative results with the native powder indicate that allergenic protein components of the rubber must bind to the powder. Wrangsjö et al.^{20, 24} have already studied the possibility of latex allergens being absorbed from glove powder.

This finding could be substantiated for the first time in an inhalative provocation test with powdered latex gloves in our study in which symptoms from the eyes, nose, bronchial system, or SRs were reproducible without direct skin contact to latex. This finding would mean that latex-allergic patients are not only threatened by cutaneous absorption of latex allergens⁵ but also by inhalation of allergen-loaded airborne glove powder. This finding also explains fewer symptoms of some latex-allergic patients using powder-free latex gloves.

The glove-exposure test with six different brands of gloves revealed that latex-free gloves, for example, Elastyren or Neolon, are the best alternative for patients with latex IgE antibodies.³¹

SDS-PAGE demonstrated the best results when the saline extract of natural latex containing 0.7% ammonia was used. We found protein components about 10 to 14 kD, 30 to 45 kD, and about 67 kD, comparable with the results of Morales et al.⁶ Our immunoblot data demonstrated that many latex protein components from natural latex milk are reactive with the latex-specific IgE-antibodies of latex-allergic patients. Recently, in a glove-washing extract, only one main allergenic component with a molecular weight of 58 kD could be identified.³⁷

Discrepancies of reported molecular weights of protein components^{6, 11, 22} may be due to different latex

sources and extraction methods that modify the proteins by degradation or polymerization.

To the best of our knowledge, we could, for the first time, demonstrate differences in the reaction pattern of 15 latex-allergic patients with protein components of latex in the range of 10 to 45 kD predominantly. At the present time, we are working on the biochemic and immunologic characterization of a major inhalative latex allergen.

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Generalized allergic reactions during anesthesia

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Twenty-eight adults with a history of a generalized allergic reaction during anesthesia were investigated. The reactions were systemic in 23 adults, urticaria/angioedema in four, and bronchial obstruction in one adult. The study population and an additional 35 subjects with a history of use of thiopental during anesthesia but without reactions were investigated by methods including thiopental skin test, succinylcholine skin test, and IgE RAST for antibodies to thiopental, succinylcholine, or latex. Among the 28 patients with reactions, 17 had positive thiopental skin tests; 14/28 reactors and 1/35 of the control group had an IgE thiopental RAST value >2 SD above the mean for control sera from ragweed-allergic subjects. The one control subject with a positive thiopental RAST also was the only control subject with a positive thiopental skin test. IgE succinylcholine RAST was negative in all 23 reactor sera tested. The IgE latex RAST was strongly positive in one reactor. In conclusion, evidence of allergy, particularly allergy to thiopental as a possible basis for the reactions, was obtained in >50% of the patients who were investigated. No allergy to succinylcholine was found. (J ALLERGY CLIN IMMUNOL 1992;89:768-74.)

Key words: Anesthesia, anaphylaxis, thiopental, succinylcholine, latex skin tests, RAST

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