



Occupational allergies caused by latex

Debra D. Fett Ahmed, MD^{a,b,c}, Steven C. Sobczak, MIS, CIH^c,
John W. Yunginger, MD^{b,*}

^a*Indiana University Dermatology Clinic, 550 North University Boulevard, Suite 3240,
Indianapolis, IN 46202, USA*

^b*Mayo Medical School, 200 First Street SW, Rochester, MN 55905, USA*

^c*Mayo Clinic and Foundation, 200 First Street SW, Rochester, MN 55905, USA*

Natural rubber latex allergy increasingly has been recognized during the past decade [1]. It now is considered to be the most frequent cause of occupational allergy in healthcare workers [2]. Natural rubber products can trigger urticaria, angioedema, and anaphylaxis after cutaneous, mucosal, or visceral exposure, and in the case of disposable medical gloves, latex allergens that are adsorbed to glove-donning powders can trigger rhinoconjunctivitis and asthma [3].

Natural rubber latex

Natural rubber is derived from the cytosol, or latex, of the commercial rubber tree *Hevea brasiliensis* [4]. It is important to distinguish natural rubber from synthetic elastomers, which include butyl rubber (a petroleum-based product), polymers of 2-chlorobutadiene (Neoprene, DuPont Dow Elastomers LLC, Wilmington, DE), and copolymers of butadiene and acrylonitrile [5]. Synthetic rubber products pose no risks to persons who have been sensitized to natural rubber proteins.

Rubber processing

Ammonia is added to natural rubber latex to prevent autocoagulation during harvesting. About 90% of harvested latex is processed by subsequent acid

This article was supported by Mayo Foundation.

* Corresponding author. 1760 Walden Lane SW, Rochester, MN 55902–0908, USA.

E-mail address: yunginger.john@mayo.edu (J.W. Yunginger).

coagulation into dry sheets or crumbled particles for manufacture of vehicle tires, rubber thread products, rubber seals and diaphragms, or other dry rubber products. The remaining 10% of harvested rubber is concentrated to 60% (vol/vol) by centrifugation, after which various compounding materials are added for manufacture of dipped latex products, such as gloves, condoms, or balloons [4]. Dipped latex products are responsible for most allergic reactions to natural rubber latex.

Rubber chemistry

Rubber particles are composed of *cis*-1,4-polyisoprene, which contains an outer layer of protein, lipid, and phospholipid that provides structural integrity [4]. The latex cytosol contains most of the enzymes that are necessary for the conversion of sucrose into *cis*-1,4-polyisoprene. The protein content of raw latex is 10 to 15 mg/mL, about 27% of which is associated with the rubber particles [4].

Natural rubber latex allergens

Several natural rubber proteins are allergenic (Table 1) [6]. These proteins are involved in rubber biosynthesis, disease resistance, or structural or housekeeping activities. Hev b 1 (rubber elongation factor) and Hev b 3 are associated with the polyisoprene particles and, along with Hev b 7, are major allergens for persons

Table 1
Natural rubber latex allergens

Allergen	Molecular weight (kD)	Biologic function
Hev b 1	14.6	Rubber elongation factor; involved in polyisoprene biosynthesis
Hev b 2	35.1	Endo-1,3- β -glucanase; involved in defense against fungal pathogens
Hev b 3	22.3	Involved in polyisoprene biosynthesis
Hev b 4	50–57	Component of microhelix protein complex
Hev b 5	16	Structural protein; partial homology with acidic protein from kiwi fruit and potato
Hev b 6.01	20	—
Hev b 6.02	4.7	Involved in latex coagulation
Hev b 6.03	14	—
Hev b 7	42.9	Patatin-like protein with lipid acylhydrolase and phospholipase A ₂ activity; inhibitor of polyisoprene biosynthesis
Hev b 8	13.9	Profilin; supports actin polymerization
Hev b 9	47.7	Enolase
Hev b 10	22.9	Manganese superoxide dismutase; protection from reactive oxygen species
Hev b 11	33	Class I chitinase; involved in plant-pathogen interaction

Data from Sussman GL, Beezhold DH, Kurup VP. Allergens and natural rubber proteins. J Allergy Clin Immunol 2002;110(Suppl):S33–9.

with myelodysplasia [7,8]. Healthcare workers are more likely than patients with myelodysplasia to be sensitized to Hev b 5, an acidic protein in latex serum, and Hev b 6 [9,10].

Cross-reactive allergens

Clinical associations have been reported between latex allergy and allergy to several fruits and vegetables (Box 1), most commonly bananas, kiwi fruit, chestnut, avocados, papayas, potatoes, and tomatoes [11]. In the clinical history

Box 1. Foods that are cross-reactive with natural rubber latex

Foods that frequently cause clinical allergy in persons with latex allergies

Avocado
Kiwi fruit
Banana
Potato
Tomato
Chestnut
Papaya

By skin testing or immunoassay for specific IgE, persons with latex allergies may be cross-sensitized to the following foods, but clinical allergy is less common

Passion fruit
Fig
Melon
Mango
Pineapple
Peach
Pear
Celery
Pineapple
Cantaloupe
Apple
Cherry
Wheat
Turnip
Spinach

of some patients, the latex allergy has preceded the food allergy, whereas the converse is true in other patients. Structural homologies exist between Hev b 6 and wheat germ agglutinin [12] and between endochitinases in avocado [13] and banana [14].

Epidemiology

Although latex sensitization can occur in the general population, occupational allergy to latex has been described mainly in persons who manufacture or use disposable latex gloves. Most data concerning the prevalence of latex sensitization are derived from large cross-sectional studies that assess sensitivity and self-reported symptoms. These studies are confounded by the different serologic assays and skin test reagents that are used, concomitant sensitization to cross-reacting fruits and vegetables, differences in latex exposure levels in the study populations, and the unreliability of self-reported symptoms [15].

Prevalence of latex sensitization

General population

The prevalence of latex sensitization in the general population ranges between 5% and 10%. Positive skin tests to latex were noted in 9.5% of 325 consecutive adult hospital inpatients awaiting surgical or urologic procedures [16]. Elevated levels of latex-specific immunoglobulin E (IgE) antibodies were measured in 6.5% of 1000 volunteer blood donors [17] and in 6.7% of 996 ambulatory surgical patients [18].

Manufacturing workers

Occupational asthma that is caused by latex allergy has been reported in workers who manufacture latex gloves. In a Canadian study, the prevalence of positive skin tests to latex were noted in seven of 64 workers (11%), and latex-induced occupational asthma was documented by spirometry and questionnaires in 3 of 81 workers (3.7%) [19]. In contrast, the prevalence of latex sensitization, assessed by prick skin testing, was only 1.3% in latex harvesters and 1.7% in workers from a latex glove factory in Thailand, despite personal mean exposures to latex aeroallergens greater than 1000 ng/m³ [20]. Two of 22 workers in a manufacturing plant that produces latex dolls were noted to have flushing, rhinoconjunctivitis, and wheezing when exposed to sanded doll parts [21]. In a study of 35 current or former workers in a Swedish condom packaging factory, 10 workers reported work-related rhinoconjunctivitis, and 3 workers had occupational asthma [22]. Only one worker had elevated levels of latex-specific IgE antibodies, whereas eight workers were sensitized to *Lycopodium clavatum* (staghorn club moss) spores, which were used to lubricate the rolled condoms. In a cross-sectional survey of 418 greenhouse workers who wore rubber gloves

daily, the prevalence of positive latex prick skin tests was 5%, and the prevalence of elevated levels of latex-specific IgE antibodies was 4% [23].

Healthcare workers

Healthcare workers, particularly those who are atopic, show an increased prevalence of latex sensitization. In surveys involving questionnaires and either latex skin testing or immunoassays for latex-specific IgE antibodies, 0.5% [24], 5.0% [25], and 17% [26,27] of various hospital employee groups were documented as latex sensitive [28]. To compare the prevalence rate of latex sensitization in healthcare workers with the rates in other population groups, Garabrant and colleagues measured latex-specific IgE antibodies that were collected from 5512 adults who participated in the Third National Health and Nutrition Examination Survey (1988–1991) [29]. The prevalence of latex sensitization (latex-specific IgE antibody >0.35 IU/mL) ranged from 9% in secretaries to 18% in healthcare workers to 38% in other machinists. These findings suggest that glove use was not associated with latex sensitization in healthcare workers or in other jobs in which latex glove use was common; however, this study was limited by the relatively low response rate of participants concerning present occupation and glove use, raising issues of reliability and reporting bias [30]. The study also used serologic tests, which significantly overestimate true sensitization rates in low-prevalence populations [31].

Incidence of latex sensitization and latex allergy

In contrast to the many cross-sectional studies of the prevalence of latex sensitization [32], there are few studies on the incidence of latex sensitization or latex allergy. Annual incidence rates for contact urticaria in healthcare workers have been estimated to be 1.9 of 10,000 workers according to a questionnaire survey [33] and between 1.3 and 11.8 of 10,000 workers according to a review of a national registry [34]. Archambault and colleagues prospectively studied 122 dental hygiene students at the beginning and end of their 3-year training period and found a cumulative incidence rate of 6.4% for skin sensitization to latex [35]. This rate was significantly higher than that found in two comparison groups (animal health apprentices, 1.0%; pastry-making apprentices, 1.6%) [36]. Among the dental hygiene students, the cumulative incidence rates were 4.5% for latex-induced occupational asthma and 1.8% for latex-induced rhinoconjunctivitis.

In an incidence study, Sussman and colleagues first determined the baseline prevalence of latex sensitization (12.1%) among 1351 healthcare workers at two hospital sites [37]. At one site, the use of moderate-to-high protein latex gloves was continued, whereas powder-free latex gloves were introduced at the other site, and the cohort members were restudied after 1 year. Only four persons with initially negative latex skin test results converted to positive results after 1 year, two of whom were in the powdered-glove group (1.0% incidence rate) and two of whom were in the powder-free-glove group (0.9% incidence rate); only the former two persons were symptomatic.

Clinical manifestations

Cutaneous reactions

Cutaneous reactions to natural rubber latex most often involve dermatitis of the hands, wrists, or forearms [38,39]. These reactions include irritant contact dermatitis, allergic contact dermatitis, protein contact dermatitis, or contact urticaria. Although other latex-containing products may contribute to these problems, most latex-related problems arise from natural rubber latex gloves [38].

Irritant contact dermatitis

Most skin complaints that are associated with wearing gloves are assumed to be caused by skin irritation, but few studies in the literature document this assumption [40]. Irritant contact dermatitis usually is caused by multiple irritants, such as hand washing, moisture trapped inside gloves, occlusion, friction, glove-donning powder, or other irritating chemicals [39,41]. Irritant contact dermatitis is not an immunologic reaction; it results from direct injury of the epidermis [40]. Irritant contact dermatitis most often involves the webbed spaces between the fingers and the dorsal surface of the hand, where the stratum corneum is thinner. Acute irritant dermatitis can occur with a single exposure to a substance that impairs epidermal function, whereas chronic irritant dermatitis occurs after repeated exposures to the same substance or a series of irritants. In the latter case, cumulative damage to the skin may continue after exposure to the irritant ceases [42]. Irritant contact dermatitis may predispose the individual to subsequent allergic reactions to latex [38].

Allergic contact dermatitis

The most common immune-mediated reaction to latex gloves is allergic contact dermatitis, a delayed hypersensitivity reaction to chemical additives that generally occurs 1 to 2 days after exposure, but can occur from several hours to several days after exposure [38]. The most common culprits are accelerators, especially thiurams and carbamates [39,43,44]. The para-phenylenediamine group includes the most common sensitizers for allergic contact dermatitis to industrial rubber (eg, the rubber tire industry) [39]. In a report from the North American Contact Dermatitis Group, carbamate sensitivity was reported more frequently than thiuram sensitivity [44].

Protein contact dermatitis

Protein contact dermatitis is a chronic, recurrent dermatitis that is caused by proteins rather than chemicals [45]. The reaction most often occurs in an occupational setting and can occur with latex. The urticarial or vesicular eruption occurs 30 minutes to 6 hours after contact with the allergenic protein [39,46].

Contact urticaria

Contact urticaria is the most common and often is the only manifestation of IgE-mediated latex allergy in healthcare workers, 60% to 80% of whom report

contact urticaria involving the hands [47,48]. Urticarial lesions occur in the distribution of contact with a latex item within 30 minutes of contact [41].

Respiratory reactions

Inhalation of latex allergen-coated cornstarch particles from powdered gloves can evoke rhinoconjunctivitis and asthma in latex-allergic healthcare workers [49,50]. Occupational asthma has been described in employees at a rubber-glove manufacturing facility [19]. Most individuals with latex allergies are highly atopic and have histories of seasonal allergic rhinitis caused by pollens or allergic asthma caused by house dust mites or animal danders [51]. Of the 29 healthcare workers with latex-induced asthma reported by Hunt and colleagues, however, 14 had no history of asthma, suggesting that latex-induced wheezing may occur as an isolated phenomenon [2].

Anaphylaxis

Latex-allergic persons can experience anaphylaxis in a variety of medical care situations [52]. Anaphylaxis can be triggered by toy balloons [53], squash racquets with rubber handles [54], and latex padding in children's play areas [55]. Fatal latex-induced anaphylaxis has been attributed to a rubber balloon rectal catheter [56], a urethral catheter [57], and a latex-containing hair adhesive [58].

Diagnosis

Patch testing

Patch testing is the diagnostic method of choice for latex-induced allergic contact dermatitis. Various rubber additives are applied to the patient's back for 48 hours, after which the test sites are read at 48 and 96 hours. The thin layer rapid use epicutaneous (T.R.U.E.) test (Kabi Pharmacia Service A/S, Hillerød, Denmark) is a panel of 24 allergens that are most widely available in the United States and includes four rubber screening mixes and mercaptobenzothiazole. More comprehensive rubber allergen series are available worldwide (Box 2). Pieces of latex gloves or ammonia-free natural rubber latex also can be applied for testing.

Measurement of latex-specific IgE antibodies

Skin testing

Skin testing with natural rubber latex is the diagnostic procedure of choice in Europe and Canada, where commercial extracts are available for this purpose. In the United States, no licensed commercial latex extracts are available for diagnostic use. Allergists frequently perform puncture skin testing with extracts of finished rubber products (usually latex gloves), which vary widely in their

Box 2. Materials for diagnostic patch testing for rubber additives

Thiuram mix

Tetramethylthiuram disulfide

Tetramethylthiuram monosulfide

Tetraethylthiuram disulfide

Dipentamethylenethiuram disulfide

Black rubber mix

N-cyclohexyl-N-phenyl-4-phenylenediamine

N,N'-diphenyl-4-phenylenediamine

N-isopropyl-N-phenyl-4-phenylenediamine

Mercapto mix

2,2'-Benzothiazyl disulfide

N-cyclohexylbenzothiazyl sulphenamide

4-Morpholinyl-2-benzothiazyl disulfide

Carba mix

1,3-Diphenylguanidine

Zinc diethyldithiocarbamate

Zinc dibutyldithiocarbamate

Other materials

N,N-di-C-naphtyl-4-phenylenediamine

N-phenyl-2-naphtylamine

Hexamethylenetetramine

Diaminodiphenylmethane

Diphenylthiourea

Dibenzothiazyl disulfide

Zinc dimethyldithiocarbamate

2,2,4-Trimethyl-1,2-dihydroquinoline

Diethylthiourea

Dibutylthiourea

Dodecylmercaptan

N-cyclohexylthiophthalimide

Data from Chemotechnique Diagnostics, Dormer Laboratories, Ontario, Canada.

allergen contents [3,59]. Systemic reactions have been reported with use of these nonstandardized preparations [60]. Skin testing with glove extracts, ammoniated latex, or nonammoniated latex that have standardized protein contents is safe and efficient [61].

Immunoassays for latex-specific IgE antibodies

Three FDA-licensed immunoassays for latex-specific IgE antibodies are available from diagnostic reference laboratories. When skin tests and immunoassays are performed in the same patient groups, only 50% to 90% of persons with positive skin test results have latex-specific IgE antibodies that are measurable by immunoassay [62]. The sensitivity of these immunoassays can be improved by spiking latex with recombinant latex proteins [63].

Challenge studies

A fitted face shield and hood system has been developed to perform graded inhalation challenge studies with latex allergen-coated cornstarch particles [64]. The allergenicity of powdered gloves has been tested by having patients don and remove powdered gloves inside a small provocation chamber [65]. Nasal and bronchial inhalation challenge tests have been used to document the allergenicity of crude latex or individual latex proteins [7,66,67].

Latex allergy can be confirmed by the use test, in which the fingers of latex gloves are cut off and applied to the wet fingers of persons with suspected contact urticaria to rubber [25]. After 30 minutes (sooner if intense itching occurs), the glove finger is removed, and the reaction is graded. If the finger challenge test is negative, a further challenge can be conducted using the whole glove. The usefulness of this test is limited by the widely varying allergen contents of gloves from different manufacturers or from different lots [59].

Management of workers with latex allergies

Workers with possible occupational allergy to latex should receive a complete medical, occupational, and allergy history; should receive a physical examination; and should undergo appropriate laboratory studies to confirm the diagnosis. The magnitude of latex aeroallergen exposure can be measured using high-volume air samplers (3 L/s) or personal breathing-zone samplers (4 L/min) that are equipped with polytetrafluoroethylene (Teflon E.I. DuPont de Nemours and Co., Wilmington, DE) filters [68]. Exposed filters are extracted with small volumes of buffer, and latex allergens in the extracts are measured by inhibition immunoassay using pooled, IgE antibody-containing sera from several latex-sensitized healthcare workers. Alternatively, an inhibition immunoassay that uses polyclonal rabbit antiserum [69] or a monoclonal, antibody-based ELISA for individual latex proteins [70] can be used to measure latex aeroallergens or the latex allergen contents of finished rubber products. Such assays are vital to

objectively assess baseline exposure levels to latex aeroallergens, to evaluate the results of subsequent environmental changes that have been designed to reduce workplace aeroallergen exposures, and to select latex products with low allergen content when no substitute synthetic elastomer product is available.

Latex-safe environments for healthcare workers and patients

Because most IgE-mediated reactions to rubber have been described in healthcare workers or in latex-sensitive individuals undergoing medical or dental procedures, emphasis has been placed on providing latex-safe clinics and hospitals [71]. In addition to reducing or eliminating use of powdered latex gloves, cleaning of carpets and upholstered furniture can eliminate reservoirs of latex allergens [72]. A cost-analysis study suggested that healthcare facilities are likely to benefit from becoming latex-safe, even if latex-related disability rates among employees are low [73].

A team approach is critical to implementing environments for medical care delivery that are latex-safe [47,74]. Such teams should include industrial hygienists, who are trained to deal with work-related illnesses and injuries [75]. High-risk work areas, where large quantities of latex gloves are used, can be identified by review of purchasing and stockroom records or by review of worker compensation or Occupational Safety and Health Administration injury records. The goals of the team should include: (1) identification and elimination of powdered gloves with high allergen content, (2) definition and labeling of latex-safe areas within the medical center, (3) establishment of a mechanism for periodic retesting of purchased latex products to ensure that they are safe, (4) selection and introduction of latex alternatives into the medical center. Whereas some latex-sensitive workers, such as food service workers, safely can use non-latex gloves without an increased risk for infection or disease transmission, the superior barrier protection of natural rubber latex may dictate that workers such as nurses or emergency medical technicians use low-protein, powder-free latex gloves [76]. Internal policies should be established for latex-sensitive employees and patients. These policies should address: (1) the responsibilities of management and employees in identifying the signs and symptoms of latex allergy, (2) the provision and maintenance of latex-safe carts for patients with latex allergies, (3) requirements for testing new latex products, and (4) goals for staff and patient education. Establishment of early intervention protocols may reduce lost-time and medical claims for latex-sensitized workers [77].

Reduction or prevention of latex sensitization

In 36 latex-sensitive workers with well-documented occupational asthma who reduced or avoided latex exposure, significant lessening of asthma and decreased bronchial hyperreactivity were noted after a median follow-up of 56 months [78]. Latex-specific IgE levels decreased in six of seven healthcare workers who avoided use of powdered latex gloves for 12 months [79]. Twenty latex-

sensitized anesthesiologists (12 symptomatic, 8 asymptomatic) who avoided use of latex gloves for 10 to 15 months became asymptomatic, and 16 of these doctors had decreased levels of latex-specific IgE [80]. Latex skin test titration endpoints did not change appreciably, however, suggesting that a longer period of avoidance of latex gloves or tighter environmental-control measures may be necessary to achieve maximal immunologic improvement. In a long-term follow-up study of 71 healthcare workers and 89 non-healthcare workers with well-documented latex allergy (primarily hand eczema), the use of latex gloves with low allergen content or non-latex gloves substantially reduced the prevalence of hand eczema [81]. All of the healthcare workers and 98% of the non-healthcare workers continued working. In two cross-sectional surveys of dental students and staff at one medical school that were performed 5 years apart and after the school began purchasing low-protein, powder-free latex gloves, latex-related symptoms and positive latex skin test responses were reduced significantly in the second survey [82].

After active efforts to reduce workplace exposure to latex allergens and to increase use of non-latex gloves and powder-free, low-protein latex gloves, workers compensation claims resulting from latex-induced asthma have declined in Ontario, Canada, since 1994 [83]. During the same period, the number of new cases of occupational allergy to latex declined substantially at two large teaching hospitals in Toronto that have approximately 8000 employees [84]. The publication of guidelines to prevent latex allergy and the subsequent increased use of powder-free latex surgical and examination gloves in German acute care hospitals was associated with significant declines in the numbers of occupational allergy and asthma cases reported to the agency responsible for accident insurance and worker's compensation measures [85].

Summary

Allergy to natural rubber latex is an important cause of occupational allergy in healthcare workers. Disposable medical gloves are the major reservoir of latex allergens, particularly powdered gloves, in healthcare delivery settings. Diagnosis of latex allergy requires a history of exacerbation of cutaneous, respiratory, ocular, or systemic signs and symptoms after exposure to natural rubber latex products; and evidence of sensitization by patch testing, skin testing, measurement of latex-specific IgE antibodies, or challenge testing. Optimal management of latex allergy involves education concerning cross-reacting allergens, reduction of cutaneous or mucosal contact with dipped rubber products, and minimization of exposure to latex aeroallergens in work environments.

References

- [1] Ownby DR. A history of latex allergy. *J Allergy Clin Immunol* 2002;110:S27–32.
- [2] Hunt LW, Fransway AF, Reed CE, Miller LK, Jones RT, Swanson MC, et al. An epidemic of

- occupational allergy to latex involving health care workers. *J Occup Environ Med* 1995;37:1204–9.
- [3] Jaeger D, Kleinhans D, Czuppon AB, Baur X. Latex-specific proteins causing immediate-type cutaneous, nasal, bronchial, and systemic reactions. *J Allergy Clin Immunol* 1992;89:759–68.
- [4] Yip E, Cacioli P. The manufacture of gloves from natural rubber latex. *J Allergy Clin Immunol* 2002;110:S3–14.
- [5] Renaud MY. Composition of synthetic latexes used for manufacturing gloves by dipping processes. *Clin Rev Allergy* 1993;11:363–70.
- [6] Sussman GL, Beezhold DH, Kurup VP. Allergens and natural rubber proteins. *J Allergy Clin Immunol* 2002;110:S33–9.
- [7] Czuppon AB, Chen Z, Rennert S, Engelke T, Meyer HE, Heber M, et al. The rubber elongation factor of rubber trees (*Hevea brasiliensis*) is the major allergen in latex. *J Allergy Clin Immunol* 1993;92:690–7.
- [8] Wagner B, Buck D, Hafner C, Sowka S, Niggemann B, Scheiner O, et al. Hev b 7 is a *Hevea brasiliensis* protein associated with latex allergy in children with spina bifida. *J Allergy Clin Immunol* 2001;108:621–7.
- [9] Akasawa A, Hsieh LS, Martin BM, Liu T, Lin Y. A novel acidic allergen, Hev b 5, in latex: purification, cloning, and characterization. *J Biol Chem* 1996;271:25389–93.
- [10] Slater JE, Vedvick T, Arthur-Smith A, Trybul DE, Kekwick RG. Identification, cloning, and sequence of a major allergen (Hev b 5) from natural rubber latex (*Hevea brasiliensis*). *J Biol Chem* 1996;271:25394–9.
- [11] Beezhold DH, Sussman GL, Liss GM, Chang NS. Latex allergy can induce clinical reactions to specific foods. *Clin Exp Allergy* 1996;26:416–22.
- [12] Wright HT, Brooks DM, Wright CS. Evolution of the multidomain protein wheat germ agglutinin. *J Mol Evol* 1985;21:133–8.
- [13] Chen Z, Posch A, Cremer R, Raulf-Heimsoth M, Baur X. Identification of hevein (Hev b 6.02) in *Hevea* latex as a major cross-reacting allergen with avocado fruit in patients with latex allergy. *J Allergy Clin Immunol* 1998;102:476–81.
- [14] Mikkola JH, Alenius H, Kalkkinen N, Turjanmaa K, Palosuo T, Reunala T. Hevein-like protein domains as a possible cause for allergen cross-reactivity between latex and banana. *J Allergy Clin Immunol* 1998;102:1005–12.
- [15] Fish JE. Occupational asthma and rhinoconjunctivitis induced by natural rubber latex exposure. *J Allergy Clin Immunol* 2002;110:S75–81.
- [16] Ruëff F, Kienitz A, Schöpf P, Hartl WH, Andre H-J, Zaak D, et al. Frequency of natural rubber latex allergy in adults is increased after multiple operative procedures. *Allergy* 2001;56:889–94.
- [17] Ownby DR, Ownby HE, McCullough JA, Shafer AW. The prevalence of anti-latex IgE antibodies in 1000 volunteer blood donors. *J Allergy Clin Immunol* 1996;97:1188–92.
- [18] Lebenbom-Mansour MH, Oesterle JR, Ownby DR, Jennett MK, Post SK, Zaglaniczy K. The incidence of latex sensitivity in ambulatory surgical patients: a correlation of historical factors with positive serum immunoglobulin E levels. *Anesth Analg* 1997;85:44–9.
- [19] Tarlo SM, Wong L, Roos J, Booth N. Occupational asthma caused by latex in a surgical glove manufacturing plant. *J Allergy Clin Immunol* 1990;85:626–31.
- [20] Chaiear N, Sadhra S, Jones M, Cullinan P, Foulds IS, Burge PS. Sensitisation to natural rubber latex: an epidemiological study of workers exposed during tapping and glove manufacture in Thailand. *Occup Environ Med* 2001;58:386–91.
- [21] Orfan NA, Reed R, Dykewicz MS, Ganz M, Kolski GB. Occupational asthma in a latex doll manufacturing plant. *J Allergy Clin Immunol* 1994;94:826–30.
- [22] Rask-Andersen A, Boman J, Grängsjö A, Silverdahl M, Lindberg M, Lundberg M, et al. Asthma, skin symptoms, and allergy in a condom factory. *Allergy* 2000;55:836–41.
- [23] Carrillo T, Blanco C, Quirarte J, Castillo R, Cuevas M, Rodríguez de Castro F. Prevalence of latex allergy among greenhouse workers. *J Allergy Clin Immunol* 1995;96:699–701.
- [24] Poole CJ, Nagendran V. Low prevalence of clinical latex allergy in UK health care workers: a cross-sectional study. *Occup Med* 2001;51:510–2.

- [25] Turjanmaa K. Incidence of immediate allergy to rubber gloves in hospital personnel. *Contact Dermatitis* 1987;17:270–5.
- [26] Yassin MS, Lierl MB, Fischer TJ, O'Brien K, Cross J, Steinmetz C. Latex allergy in hospital employees. *Ann Allergy* 1994;72:245–9.
- [27] Liss GM, Sussman GL, Deal K, Brown S, Cividino M, Siu S, et al. Latex allergy: epidemiological study of 1351 hospital workers. *Occup Environ Med* 1997;54:335–42.
- [28] Vandenplas O, Charous BL, Tarlo SM. Latex allergy. In: Bernstein IL, Chan-Yeung M, Malo J-L, Bernstein DI, editors. *Asthma in the workplace*. 2nd edition. New York: Marcel Dekker; 1999. p. 425–44.
- [29] Garabrant DH, Roth HD, Parsad R, Ying G-S, Weiss J. Latex sensitization in health care workers and in the US general population. *Am J Epidemiol* 2001;153:515–22.
- [30] Wartenberg D, Buckler G. Invited commentary: Assessing latex sensitization using data from the NHANES III. *Am J Epidemiol* 2001;153:523–6.
- [31] Yeang H. Prevalence of latex allergy may be vastly overestimated when determined by in vitro assays. *Ann Allergy Asthma Immunol* 2000;84:628–32.
- [32] Garabrant DH, Schweitzer S. Epidemiology of latex sensitization and allergies in health care workers. *J Allergy Clin Immunol* 2002;110:S82–95.
- [33] Salkie ML. The prevalence of atopy and hypersensitivity to latex in medical laboratory technologists. *Arch Pathol Lab Med* 1993;117:897–9.
- [34] Jolanki R, Estlander T, Alanko K, Savela A, Kanerva L. Incidence rates of occupational contact urticaria caused by natural rubber latex. *Contact Dermatitis* 1999;40:329–31.
- [35] Archambault S, Malo J-L, Infante-Rivard C, Ghezzo H, Gautrin D. Incidence of sensitization, symptoms, and probable occupational rhinoconjunctivitis and asthma in apprentices starting exposure to latex. *J Allergy Clin Immunol* 2001;107:921–3.
- [36] Gautrin D, Ghezzo H, Infante-Rivard C, Malo J-L. Incidence and determinants of IgE-mediated sensitization in apprentices: a prospective study. *Am J Respir Crit Care Med* 2000;162:1222–8.
- [37] Sussman GL, Liss GM, Deal K, Brown S, Cividino M, Siu S, et al. Incidence of latex sensitization among latex glove users. *J Allergy Clin Immunol* 1998;101:171–8.
- [38] Zak HN, Kaste LM, Schwarzenberger K, Barry MJ, Galbraith GMP. Health-care workers and latex allergy. *Arch Environ Health* 2000;55:336–46.
- [39] Heese A, van Hintzenstern J, Peters KP, Koch HU, Hornstein OP. Allergic and irritant reactions to rubber gloves in medical health services: spectrum, diagnostic approach, and therapy. *J Am Acad Dermatol* 1991;25:831–9.
- [40] Nettis E, Assennato G, Ferrannini A, Tursi A. Type I allergy to natural rubber latex and type IV allergy to rubber chemicals in health care workers with glove-related skin symptoms. *Clin Exp Allergy* 2002;32:441–7.
- [41] Toraason M, Sussman G, Biagini R, Meade J, Beezhold D, Germolec D. Latex allergy in the workplace. *Toxicol Sci* 2000;58:5–14.
- [42] White IR. Occupational dermatitis. *BMJ* 1996;313:487–9.
- [43] Taylor JS, Praditsuvan P. Latex allergy: review of 44 cases including outcome and frequent association with allergic hand eczema. *Arch Dermatol* 1996;132:265–71.
- [44] Marks Jr JG, Belsito DV, De Leo VA, Fowler Jr JF, Fransway AF, Maibach HI, et al. North American Contact Dermatitis Group patch test results, 1996–1998. *Arch Dermatol* 2000;136:272–3.
- [45] Janssens V, Morren M, Dooms-Goossens A, Degreef H. Protein contact dermatitis: myth or reality? *Br J Dermatol* 1995;132:1–6.
- [46] Parry EJ, Beck MH. Acute anaphylaxis resulting from routine patch testing with latex. *Contact Dermatitis* 1999;41:236–7.
- [47] Hunt LW, Boone-Orke JL, Fransway AF, Fremstad CE, Jones RT, Swanson MC, et al. A medical center-wide, multidisciplinary approach to the problem of natural rubber latex allergy. *J Occup Environ Med* 1996;38:765–70.
- [48] Charous BL, Hamilton RG, Yunginger JW. Occupational latex exposure: characteristics of contact and systemic reactions in 47 workers. *J Allergy Clin Immunol* 1994;94:12–8.

- [49] Seaton A, Cherrie B, Turnbull J. Rubber glove asthma. *BMJ* 1988;296:531–2.
- [50] Baur X, Jäger D. Airborne antigens from latex gloves [letter]. *Lancet* 1990;335:912.
- [51] Bubak ME, Reed CE, Fransway AF, Yunginger JW, Jones RT, Carlson CA, et al. Allergic reactions to latex among health-care workers. *Mayo Clin Proc* 1992;67:1075–9.
- [52] Yunginger JW. Latex-associated anaphylaxis. *Immunol Allergy Clin North Am* 2001;21:669–77.
- [53] Axelsson IG, Eriksson M, Wrangsjö K. Anaphylaxis and angioedema due to rubber allergy in children. *Acta Paediatr Scand* 1988;77:314–6.
- [54] Beuers U, Baur X, Schraudolph M, Rickter WO. Anaphylactic shock after game of squash in atopic woman with latex allergy [letter]. *Lancet* 1990;335:1095.
- [55] Fiocchi A, Restani P, Ballabio C, Bouygue GR, Serra A, Travaini M, et al. Severe anaphylaxis induced by latex as a contaminant of plastic balls in play pits. *J Allergy Clin Immunol* 2001;108:298–300.
- [56] Ownby DR, Tomlanovich M, Sammons M, McCullough J. Anaphylaxis associated with latex allergy during barium enema examination. *AJR Am J Roentgenol* 1991;156:903–8.
- [57] Martinez Jabaloyas JM, Broseta Rico E, Ruiz Cerda JL, Sanz Chinesta S, Osca Garcia JM, Jimenez Cruz JF. Extracorporeal shockwave lithotripsy in patients with urinary diversion. *Actas Urol Esp* 1995;19:143–7.
- [58] Pumphrey RSH, Duddridge M, Norton J. Fatal latex allergy [letter]. *J Allergy Clin Immunol* 2001;107:558.
- [59] Yunginger JW, Jones RT, Fransway AF, Kelso JM, Warner MA, Hunt LW. Extractable latex allergens and proteins in disposable medical gloves and other rubber products. *J Allergy Clin Immunol* 1994;93:836–42.
- [60] Kelly KJ, Kurup VP, Zacharisen M, Resnick A, Fink JN. Skin and serologic testing in the diagnosis of latex allergy. *J Allergy Clin Immunol* 1993;91:1140–5.
- [61] Hamilton RG, Adkinson Jr NF. Natural rubber latex skin testing reagents: safety and diagnostic accuracy of nonammoniated latex, ammoniated latex, and latex rubber glove extracts. *J Allergy Clin Immunol* 1996;98:872–83.
- [62] Hamilton RG, Biagini RE, Krieg EF. Diagnostic performance of Food and Drug Administration-cleared serologic assays for natural rubber latex-specific IgE antibody: the Multi-Center Latex Skin Testing Study Task Force. *J Allergy Clin Immunol* 1999;103:925–30.
- [63] Lundberg M, Chen Z, Rihs H-P, Wrangsjö K. Recombinant spiked allergen extract. *Allergy* 2001;56:794–5.
- [64] Kurtz KM, Hamilton RG, Schaefer JA, Primeau M-N, Adkinson Jr NF. Repeated latex aero-allergen challenges employing a hooded exposure chamber: safety and reproducibility. *Allergy* 2001;56:857–61.
- [65] Laoprasert N, Swanson MC, Jones RT, Schroeder DR, Yunginger JW. Inhalation challenge testing of latex-sensitive health care workers and the effectiveness of laminar flow HEPA-filtered helmets in reducing rhinoconjunctival and asthmatic reactions. *J Allergy Clin Immunol* 1998;102:998–1004.
- [66] Marcos C, Lázaro M, Fraj J, Quirce S, de la Hoz B, Fernandez-Rivas M, et al. Occupational asthma due to latex gloves. *Ann Allergy* 1991;67:319–23.
- [67] Pisati G, Baruffini A, Bernabeo F, Stanizzi R. Bronchial provocation testing in the diagnosis of occupational asthma due to latex surgical gloves. *Eur Respir J* 1994;7:332–6.
- [68] Reed CE, Swanson MC, Li JT. Environmental monitoring of protein aeroallergens. In: Bernstein IL, Chan-Yeung M, Malo J-L, Bernstein DI, editors. *Asthma in the workplace*. 2nd edition. New York: Marcel Dekker; 1999. p. 235–55.
- [69] ASTM D6499. Standard test method for the immunological measurement of antigenic protein in natural rubber and its products. *Annual Book of ASTM Standards* 2000;9.02:219–24.
- [70] Palosuo T, Ovod V, Kärkkäinen T, Kalkinen N, Kulomaa M, Reunala T, et al. The major latex allergens Hev b 6.02 (hevein) and Hev b 5 are regularly detected in medical gloves with moderate or high allergen content [abstract]. *J Allergy Clin Immunol* 2001;107:S321.
- [71] Task Force on Allergic Reactions to Latex. Committee report. *J Allergy Clin Immunol* 1993;92:16–8.

- [72] Charous BL, Schuenemann PJ, Swanson MC. Passive dispersion of latex aeroallergen in a healthcare facility. *Ann Allergy Asthma Immunol* 2000;85:285–90.
- [73] Phillips VL, Goodrich M, Sullivan TJ. Health care worker disability due to latex allergy and asthma: a cost analysis. *Am J Public Health* 1999;89:1024–8.
- [74] Bollinger ME, Mudd K, Keible LA, Hess BL, Bascom R, Hamilton RG. A hospital-based screening program for latex allergy. *Ann Allergy Asthma Immunol* 2002;88:560–7.
- [75] Reiter JE. Latex sensitivity: An industrial hygiene perspective. *J Allergy Clin Immunol* 2002;110:S121–8.
- [76] Korniewicz DM, Kirwin M, Cresci K, Larson E. Leakage of latex and vinyl exam gloves in high and low risk clinical settings. *Am Ind Hyg Assoc J* 1993;54:22–6.
- [77] Tyler D. Disability and medical management of natural latex sensitivity claims. *J Allergy Clin Immunol* 2002;110:S129–36.
- [78] Vandenplas O, Jamart J, Delwiche J-P, Evrard G, Larbanois A. Occupational asthma caused by natural rubber latex: outcome according to cessation or reduction of exposure. *J Allergy Clin Immunol* 2002;109:125–30.
- [79] Allmers H, Brehler R, Chen Z, Raulf-Heimsoth M, Fels H, Baur X. Reduction of latex aeroallergens and latex-specific IgE antibodies in sensitized workers after removal of powdered natural rubber gloves in a hospital. *J Allergy Clin Immunol* 1998;102:841–6.
- [80] Hamilton RG, Brown RH. Impact of personal avoidance practices on health care workers sensitized to natural rubber latex. *J Allergy Clin Immunol* 2000;105:839–41.
- [81] Turjanmaa K, Kanto M, Kautianen H, Reunala T, Palosuo T. Long-term outcome of 160 adult patients with natural rubber allergy. *J Allergy Clin Immunol* 2002;110:S70–4.
- [82] Saary MJ, Kanani A, Alghadeer H, Holness DL, Tarlo SM. Changes in rates of natural rubber latex sensitivity among dental school students and staff members after changes in latex gloves. *J Allergy Clin Immunol* 2002;109:131–5.
- [83] Liss GM, Tarlo SM. Natural rubber latex-related occupational asthma: association with interventions and glove changes over time. *Am J Ind Med* 2001;40:347–53.
- [84] Tarlo SM, Easty A, Eubanks K, Parsons CR, Min F, Juvet S, et al. Outcomes of a natural rubber latex control program in an Ontario teaching hospital. *J Allergy Clin Immunol* 2001;108:628–33.
- [85] Allmers H, Schmengler J, Skudlik C. Primary prevention of natural rubber latex allergy in the German health care system through education and intervention. *J Allergy Clin Immunol* 2002;110:318–23.