

Allergy to latex

Levy DA, Charpin D, Pecquet C, Leynadier F, Vervloet D. Allergy to latex.

Allergy 1992; 47: 579–587. © Munksgaard 1992

D. A. Levy¹, D. Charpin², C. Pecquet²,
F. Leynadier¹, D. Vervloet²

¹ Service de Médecine Interne, Centre d'Allergie, Hôpital Rothschild, 75012 Paris, France, and ² Département des Maladies Respiratoires, Hôpital Sainte-Marguerite, B.P. 29, 13274 Marseille, France

Key words: Allergy; adverse effects; latex; rubber.

Prof. D. Vervloet
Département des Maladies Respiratoires
Hôpital Sainte-Marguerite
B.P. 29, 13274 Marseille
France

The first reported case of an immediate hypersensitivity reaction to latex was described by Nutter in 1979 (52), although this allergy had certainly occurred before that date. During the past 5 years, allergic reactions to products made of natural rubber latex have been reported with increasing frequency, especially in health care personnel and their patients. This phenomenon has been attributed to the recent dramatic rise in the use of latex gloves by medical, dental and auxiliary personnel for protection against the AIDS and hepatitis viruses, although not all authors agree (74), and it might not explain the apparently increased incidence in children with spina bifida and in the general population. It is likely that the increased incidence of allergy to latex among hospital personnel and their patients is related to changes in the manufacturing of gloves and/or to the change from reusable, steam-sterilized to single-use gloves that followed the increased demand for these products. In addition it might be related to better recognition of the clinical problem by the medical community.

In this review, we will consider, successively, the epidemiology of allergy to latex including its prevalence and the risk factors for its development, its clinical manifestations, the nature of latex allergens, immunologic mechanisms of latex allergy, diagnostic methods, and the prevention of allergic reactions to products made of natural rubber latex.

Epidemiology of latex allergy

Repeated exposure to natural rubber latex is obviously essential for the development of sensitivity to

latex. The variety of articles containing latex is considerable. Among the more important, we can cite medical equipment (including, of course, surgical and examination gloves but also tubes and catheters, face masks and other anesthesia equipment, tourniquets, adhesive tape, and elastic bandages), household and electrician's gloves, balloons and balls, condoms, footwear, adhesives (for example, on stamps and envelopes), stretch fabrics, baby pacifiers, carpets and mats, and sports equipment. Since exposure to rubber products is so widespread, it would be of interest to determine the prevalence of latex allergy in the general population; however, this information is not available.

In fact, more than half the reported cases have occurred in health care workers and in patients undergoing surgical procedures or internal examinations, both these groups having frequent contact with natural rubber products. In 1987, Turjanmaa reported the prevalence of allergy to latex (as defined by a positive skin test) in a group of 512 hospital personnel (74). Of the 145 subjects working in different operating units (surgery, ophthalmology, ORL, gynecology and obstetrics), 6.2% were allergic to latex, in contrast to only 1.6% of the 367 persons working in laboratory units. This difference is not surprising, given that the concentration of airborne latex allergens in areas where surgical gloves are frequently used has been found to be 10–100 times higher than in areas where gloves are never or seldom used (71). Beaudouin et al. reported a lower rate of sensitization (2.5%) in hospital employees, but they did not specify how many operating-room (OR) nurses were included in the population they

studied (7). We conducted a study of the prevalence of latex sensitivity in 268 OR nurses in several hospitals in Marseille (35). Of the total target population, 248 (96%) answered a questionnaire, and 197 (73.1%) were skin tested with a latex extract. Symptoms associated with wearing gloves were acknowledged by 41% of the nurses, significantly more often by those who were atopic, whereas the latex skin test was positive in only 21 (10.7%) of these OR nurses tested. Among the 102 nurses complaining of local symptoms, most often itching and/or urticaria, only 19 (18.6%) had a positive latex skin test. The results of our study therefore suggest that latex allergy is probably more common in OR nurses than previously recognized, especially among those who are atopic. Moreover, it appears that in an epidemiologic survey a questionnaire alone is unreliable for the detection of latex sensitivity. To make a definitive diagnosis, a questionnaire must be complemented by a latex skin test. Of course, OR nurses are not the only category of hospital personnel affected by latex allergy: among a group of 31 latex-sensitive hospital employees seen in consultation by one of us (56) were seven nurse's aides, seven doctors (including four surgeons), and two anesthesiologists; 37% of the 70 patients seen by Jaeger et al. were physicians or medical students, while 54% were male or female nurses or technicians (26). Other professions at risk include dentists and other health care workers, cleaners, restaurant workers, gardeners, and painters.

Because many children with spina bifida require multiple surgical procedures, they are at risk of developing allergy to latex. Thus, a number of investigators have found a strong association between spina bifida (with meningocele) and anaphylactic reactions during general anesthesia (25, 29, 44, 51, 55, 59, 63, 85). In a study of 187 families, Meeropol et al. found that up to 28% of spina bifida children are allergic to latex (46). Slater et al. reported that as many as 34% of such children have evidence of latex-specific IgE antibodies (detectable by RAST), and they found a strong correlation between a positive RAST and the number of prior operations, providing evidence that repeated exposure during surgical procedures can induce sensitization to latex (66).

Not surprisingly, workers in glove-manufacturing plants are also at risk of developing latex allergy. Tarlo et al. examined 81 workers in one plant for evidence of allergy to latex (72). Sixty-seven workers completed a questionnaire to assess work-related respiratory symptoms, 63 underwent skin prick tests to latex, and 50 underwent work-shift spirometry. A positive skin test to latex occurred in (7 (11%) of the workers tested. Three of the 50 (6%) who underwent work-shift spirometry were consid-

ered to have latex-related occupational asthma. All these findings indicate that latex is now an important cause of occupational allergy, especially among health care workers. Although it has not been reported, it would be interesting to know the prevalence of latex allergy among workers on rubber tree farms in latex-processing facilities.

Knowledge of individual risk factors in addition to those cited above might allow better identification of subjects susceptible to sensitization. Among adults, latex allergy occurs predominantly in women, but this is not surprising, as most published reports concern hospital personnel, and, as is well known, women are overrepresented among health care workers. Thus, 80% of the cases reported by Wrangsjö et al. were female (84); Beaudouin et al. reported that all 24 latex-sensitive subjects they studied were female (7); 70% of those reported by Jaeger et al. were female (26); and 79% of Pecquet's patients were female (56). In the Marseille study on OR nurses, of which only 13% were male, only one of the 21 latex skin test-positive subjects was a man (35). The overrepresentation of women in these populations is certainly linked to greater exposure to latex gloves in their work.

With respect to age as a risk factor, it is not surprising that latex allergy appears to cluster in younger people, being reported most often in health care personnel and in children requiring multiple operations. Thus, in the series reported by Jaeger et al., the mean age was 33 years (26), and in the series reported by one of us (56), it was 32 years. In addition to being related to heavy latex exposure, this age clustering might also be related to the age dependence of IgE responses in general (5).

Many reports of latex allergy concern atopic individuals. In those cited above, there was a positive association between atopic status and the risk of latex allergy (7, 35, 56, 74, 84). For example, Turjanmaa reported that 67% of the 15 latex-allergic patients in her survey were atopic (defined as having a positive skin prick test to major aeroallergens), as opposed to only 23.9% of the 497 who were not allergic to latex (74). Among the group of OR nurses studied in Marseille, those with a history of allergic rhinitis and/or asthma had a 4.4-fold higher risk if being allergic to latex (35).

Interestingly, an association between allergy to latex and allergy to a variety of fruits, most often banana and avocado, has been noted (13, 18, 37, 39, 50, 62, 84, 86). Nearly half the patients seen by Pecquet reported having had an allergic reaction to a fruit, the most frequently mentioned being banana (34%), avocado (25%), and kiwi (20%) (56). Less frequently noted were apricot, chestnut, grape, passion fruit, and pineapple.

Pre-existing contact dermatitis on the hands, fre-

quently caused by the nonlatex components in rubber gloves (20), is thought by some authors to promote sensitization to latex. In a Finnish survey, 60% of the latex-sensitive persons had a history of hand eczema, whereas only 17.4% of nonsensitized persons had such a history (74). In contrast, the rate of skin test positivity to latex among subjects with a history of hand eczema was not higher in the Marseille survey (35), and contact dermatitis caused by latex was rarely present in the latex-sensitive patients seen in consultation by Pecquet (56). Obviously, this might be a treatable risk factor and it should be investigated further.

Clinical manifestations

The clinical manifestations of immediate hypersensitivity to latex usually arise from direct contact with a natural rubber product but may also result from inhalation of airborne latex allergens, such as that which is attached to the cornstarch powder used to lubricate surgical gloves. The symptoms and signs may be localized or generalized, consisting of local, regional, or generalized urticaria, angioedema, rhinitis, conjunctivitis, asthma, tachycardia, and/or anaphylactic shock. Of the 70 patients described by Jaeger et al. 100% had experienced urticaria, 51% rhinitis, 44% conjunctivitis, 31% dyspnea, and 24% a systemic reaction (including angioedema of the lips and face), and four patients had developed a severe reaction during surgery or delivery (26). In some cases, gloves worn by colleagues in the same room were sufficient to cause symptoms. Among the 80 patients seen by Pecquet, 92% had contact urticaria as the primary manifestation of their allergy, this reaction having first occurred from 6 months to 20 years earlier (56). Pruritus was often noted within 5 min after contact with a latex product, household or surgical gloves in most cases, and the eruption lasted 30–60 min after the gloves were removed. The reaction was usually localized to the zone of contact, but local and/or regional extension occurred in some patients. Anaphylactic shock had occurred in two cases, one of which had resulted from prolonged wearing of gloves.

Certain aspects of each type of reaction deserve special comment.

Contact urticaria

A growing number of cases of contact urticaria to natural rubber latex are being reported (12, 21, 23, 24, 30, 45, 52, 57, 83, to cite just a few). Local or regional urticaria is often the only manifestation of latex allergy, and its occurrence is highly correlated with this allergy, especially in atopic persons, where its predictive value approaches 70% (35). In con-

trast, pruritus alone is usually not predictive of latex allergy: in our Marseille study, only one of the 25 nurses who complained only of itching when wearing surgical gloves had a positive skin test to latex (35). Similarly, Turjanmaa found that only 13% of nurses with this complaint were actually allergic to latex (74).

Respiratory symptoms

Acute rhinitis, asthma, or both may be part of a generalized reaction following contact with latex, or they may occur as a result of the inhalation of allergen. Challenge testing by handling boxes gloves can induce immediate sneezing, rhinorrhea, and wheezing in latex-sensitive persons (6, 34, 60). Turjanmaa et al. have demonstrated latex allergens associated with glove powder (78). Glove powder obtained by gentle rubbing of surgical gloves is contaminated with the same proteins that are present in ammoniated latex and in eluates from the same surgical gloves. It was recently reported that the concentration of airborne latex allergens in hospital areas where gloves are frequently used ranges from 13 to 121 ng/m³, whereas in areas where gloves are seldom or never used it ranges from 0.3 to 1.8 ng/m³ (71). The concentration in the personal breathing zone of health care workers in high glove-use areas ranges from 8 to 136 ng/m³. Thus, it is not surprising that allergic OR personnel can have respiratory symptoms at work.

Systemic manifestations

Angioedema, generalized urticaria, or anaphylactic shock caused by latex allergy may occur under a variety of circumstances; however, most reported cases have occurred in the OR. While serious reactions have occurred in OR personnel, the great majority have occurred intraoperatively in patients, some of whom are, of course, nurses. Anaphylaxis has been induced in patients by contact with a surgeon's gloves, as in an intra-abdominal operation (25, 38, 39, 54, 56, 63, 73, 87). In some cases, it occurred after contact with a rubber face mask or rubber tubing, for example, following tracheal intubation or after insertion of a catheter. Many of the reported cases have occurred during gynecologic or obstetric procedures, for example, during Caesarean section (41, 80) or vaginal delivery (36), and even after vaginal examination with a latex finger cot (4). Some patients have experienced more than one episode of this type during surgery, the cause of the first episode not having been recognized (56). As the signs of latex-induced anaphylaxis – pruritus, generalized urticaria, bronchospasm, tachycardia, and cardiovascular collapse – are generally delayed in

onset, appearing more than 30 min after the induction of anesthesia (25), and as they become worse progressively, anesthetic drugs – especially thiopental (9) – can usually be excluded as being the cause of the reaction; further evidence can be obtained by negative skin tests with the drugs.

Anaphylaxis caused by latex has occurred during barium enema and rectal manometry. Ownby et al. reported six cases of anaphylaxis that had occurred during a barium enema examination; one of these patients died as a consequence (53). All the patients were female, and four of them were atopic; none had had a previous reaction to latex, and only one had had previous surgery. All the procedures were performed with a rectal catheter having a latex cuff. Latex allergens were detected in an extract of the catheter used to instill the enemas, and latex-specific IgE antibody was detected in the serum of five of the patients. One case of systemic anaphylaxis occurred during rectal manometry in which a latex balloon was used (68).

Allergic reactions to latex have also arisen during leisure activities. Beuers et al. reported the case of a 25-year-old woman who was admitted to an emergency unit in severe anaphylaxis after a game of squash (8). Allergy skin tests were positive to an extract of the handle cover of the patient's squash racket as well as to extracts of latex and latex gloves. Axelsson et al. described angioedema and anaphylaxis caused by the rubber in toy balloons among children allergic to latex (3). Eleven percent of the cases of latex allergy reported by Jaeger et al. were due to contact with balloons, and 16% to adhesive bandages (26). Among the rare causes of latex allergy reported by these same authors were stretch textiles, a hot-water bottle, a baby pacifier, a diving mask, sailing equipment, shower curtains, an air mattress, stamps, and window insulation.

As noted above, local or systemic allergic reactions can be induced by contact with condoms and dental dams. Leynadier et al. reported a case of vaginal urticaria induced by contact with a latex condom (40). Wrangsjö et al. described three cases of contraceptive-induced localized urticaria, associated in one case with mild distant symptoms and in another with a systemic reaction; all three patients had a history of personal atopy (84). Turjanmaa & Renälä reported that 7 of 29 women (24%) allergic to latex gloves had experienced localized vaginal pruritus and/or edema during or after intercourse (76). Generalized urticaria shortly after protected intercourse was reported in a latex-sensitive woman (19). Anaphylactic shock following vaginal contact with a rubber condom in a latex-sensitive woman has also been reported (56). A number of authors have reported the occurrence of allergic symptoms, for example, edema of the lips and face, following

contact with a latex dam during dental surgery (4, 26, 84).

Immunologic mechanisms

Allergy to latex is a typical example of an immunologically-mediated immediate hypersensitivity reaction: it is induced by allergenic proteins from a naturally occurring substance, mediated by IgE antibodies and expressed through sensitized mast cells and basophils. Nutter (52) demonstrated the presence of an immediate skin test reaction to a 5% aqueous solution of natural latex in a patient with contact urticaria. Köpman & Hannuksela (31) were the first to provide direct evidence of the IgE mechanism when they passively transferred the reaction with serum from a latex-sensitive patient to the skin of a nonsensitized person. Since then, there have been many reports on the presence of IgE antibodies in the serum of latex-sensitive persons, leaving no doubt about its central role in this problem. However, as stated by Alenius et al. (1), while it appears that there is a correlation between high levels of IgE antibody and severe allergic reactions, the natural course of the IgE antibody response in these patients remains unknown. One thing is certain, however: most latex-sensitive patients have an atopic background (7, 35, 56, 70, 74, 84).

IgG4 antibodies have also been detected in the serum of a few latex-sensitive persons, possibly as a result of lengthy exposure to latex antigens (1).

Sensitization is acquired by repeated contact with latex, a substance found in a very wide variety of common, manufactured products. This explains the high prevalence of latex allergy among workers in factories manufacturing rubber products (72), in nurses and doctors (7, 35, 74), and in children who have undergone multiple operations (46, 63). The duration of exposure to rubber before the onset of the allergic reaction has been reported to vary from 0.5 to 15 years (84). The precise mode of sensitization has not been demonstrated, but must certainly include both cutaneous and mucosal (including respiratory) routes.

Latex allergens

Natural latex, an emulsion of rubber particles in an aqueous serum, is the sap of the rubber tree, *Hevea brasiliensis*. The rubber particles consist mainly of long-chain polymers of *cis*-1,4-polyisoprene which are surrounded by a thin phospholipoprotein coat. After addition of preservative (usually ammonia) and concentration (to increase its rubber content to at least 60%), liquid latex is delivered in tanks or drums to the consuming factories, where it is stored before

use. Various chemical agents are added to give it specific characteristics. The final rubber product, cross-linked (vulcanized) through sulfur bonds by heating, contains 93–95% polyisoprene and up to 3% protein by weight.

Natural rubber latex contains many different proteins, lipids, nucleotides, and other organic substances (16). The protein concentration of a native latex sap was reported to be 16.53 mg/ml (11). Gel electrophoresis of this sap revealed at least 16 protein bands, the most abundant ranging in molecular weight from 14 to 17 kDa (2). On isoelectric focusing, most of the protein bands migrated into the pH zone between 4 and 6.5 (27).

A number of allergenic proteins have recently been detected in latex sap, ammoniated latex, and extracts of rubber gloves. Carillo et al. demonstrated a trypsin-sensitive allergen with a molecular weight somewhat higher than 30 kDa in natural latex (12). Using a pool of patients' serum in immunoblotting, Morales et al. observed binding of IgE antibody to proteins with molecular weights of 10, 24, 35, and 100 kDa in ammoniated latex (49). Slater reported that on immunoblotting of an extract prepared from nonammoniated latex, 14/14 RAST-positive sera from children with spina bifida bound to a 14-kDa protein band, 6/14 bound to a 20-kDa band, and 5/14 bound to a 23-kDa band (64). Warpinski et al. examined a latex extract with sera from three adults and found IgE binding to proteins with molecular weights of 30 and 66 kDa (83). Mathew et al. detected IgE reactivity to protein bands of 10 and 14 kDa in an aqueous latex extract (44). Chambeyron et al. examined soluble natural latex and ammoniated latex by immunoblotting with sera from eight latex-sensitive persons and found IgE-binding bands with molecular weights of 10, 15, 18, 20, 25, 30, 35, and 60 kDa (14). Alenius et al. performed immunoblotting with serum from five different patients and identified 10 allergenic proteins in natural rubber sap and nine in ammoniated latex, with molecular weights ranging from 14 to 70 kDa (2). Significantly, only two of these proteins – an 11 kDa protein and a 26-Da protein – were seen in a surgical glove extract, suggesting that they might be modified rubber proteins formed during the manufacturing process. Recently, Slater & Trybl reported that they have partially purified latex allergens by affinity chromatography, using an antilatel monoclonal antibody (67). Regarding the charge of latex allergens, Boyle et al. (11) recently reported that IgE in serum from one latex-sensitive patient bound to at least four bands at pHs between 8.0 and 4.5. Obviously, further work is needed fully to identify the major and minor latex allergens, to isolate the most important ones, and to determine their structure, in order to develop better diagnostic methods, to conduct ge-

netic studies, and to control the allergenicity of rubber products.

On the basis of M'Raihi et al.'s observation of a case of allergy to latex gloves in a nurse allergic to banana (50), we studied the possible cross reactivity of banana extract with latex allergens by RAST inhibition and found a dose-dependent inhibition with increasing concentrations of banana extracts, strongly suggesting the presence of a common allergen in the two substances. This observation has recently been confirmed (43). As with some other shared allergens, the basis for this cross reactivity may not be strictly botanic, as the rubber tree and the banana tree (*Musa sapientum*) belong to phylogenetically dissimilar classes, Magnoliopsida and Liliopsida, respectively. It would be interesting to know if latex shares allergens with other foods that cause allergic reactions in latex-sensitive persons.

Diagnosis

Skin testing and other challenge tests

The first step in the diagnosis of latex allergy is obviously to obtain an adequate clinical history (65), but, as noted above, this must be supplemented by skin testing. In spite of the fact that the allergens of *Hevea brasiliensis* are not yet fully characterized, skin tests with latex and extracts of latex products are considered to be very specific, since persons not allergic to latex have negative reactions. At the same time, skin tests are very sensitive, since 100% of subjects seen in consultation for an allergic reaction to latex have been found to have a positive reaction to latex or latex glove extract (44, 79, 84). A latex preparation is available from Stallergènes S.A. for skin testing; however, there is as yet no general agreement concerning the material to use in skin testing. Most investigators have used either latex itself (usually ammoniated and centrifuged latex), an extract of latex, or an extract of surgical gloves for skin testing. Nutter obtained a positive skin test with a 5% aqueous solution of natural rubber latex that had been shaken and left to stand for 24 h (52). Turjanmaa et al. compared several latex-containing materials to determine the most reliable for use in diagnosis and to investigate coexistent sensitivity to glove powder and chemical additives (79). Skin prick tests with latex itself were positive in 12/15 latex-sensitive subjects. A scratch-chamber test using crushed rubber tree leaves was positive in 13/15. Prick tests with a glove extract were positive in all 15 subjects. A latex glove-use test was positive in 12/13 subjects, whereas tests with cornstarch and talcum glove powders were negative. No immediate skin reactions were detected with the various chemical additives.

Wrangsjö et al., investigating 30 patients with con-

tact urticaria, obtained positive skin tests with a solution of rubber latex that had been extracted in saline (1:9, w/v), centrifuged, sterilized by filtration, and diluted 1:100 w/v in saline containing 0.03% human serum albumin (84).

Turjanmaa et al. performed skin prick tests in 40 latex-allergic subjects with extracts of 19 brands of latex surgical and cleaning gloves (75). Twenty-six of the subjects had been sensitized by surgical gloves, and the remaining 14 by cleaning gloves. The results confirm that allergenic proteins persist in various sorts of latex gloves after being manufactured from natural rubber latex and that these allergens can cause contact urticaria. However, the frequency of positive test reactions varied from 8 to 100%, depending on the source of the extract, indicating that there are differences in the quality or the amount of latex allergens eluting from different brands of gloves. It should be noted that methods of extracting gloves vary considerably from one report to another; the method undoubtedly influences the quality and quantity of allergens that are extracted.

Turjanmaa's group also performed skin prick tests with extracts of 16 different brands of condoms and showed that four brands caused a positive reaction in 52–67% of patients allergic to latex (75). The remaining 12 brands were not as allergenic, and the extract of one brand was totally negative on skin testing. These latter results indicate that patients with contact urticaria caused by latex gloves may have reactions with latex condoms.

Provocation tests have been done by having patients with contact urticaria wear latex gloves (79, 84), and by having patients with respiratory symptoms inhale powder from latex gloves (26). Turjanmaa et al. reported that a provocation test in which a latex glove was worn on a dampened hand for 15 min gave positive results in 12/13 cases; the thirteenth patient, who had not worn latex gloves during the previous 4 years, had a positive response only after wearing the glove for 4 h (79). None of these allergic patients reacted to contact with a vinyl glove, and control employees without contact urticaria did not react to the latex glove. Two highly allergic hospital employees were not tested by these investigators, who considered that provocation testing of such persons might induce an anaphylactic reaction. In contrast, Wrangsjö et al. tested 10 patients with a history of systemic symptoms by placing 1 cm² pieces of surgical glove latex material moistened with saline on the skin of the forearm, or by having them wear one glove finger, for 20 min (84). A positive reaction was observed in 9/10 patients, two of whom experienced only distant symptoms (conjunctivitis, rhinitis, dyspnea, facial redness) during the test. Jaeger et al. tested seven patients allergic to latex gloves with six different brands of sterile gloves, including

three "hypoallergenic" brands and two latex-free brands (26). The latex-free gloves were well tolerated, but the "hypoallergenic" gloves were not. Wrangsjö et al. caution that the risk of eliciting systemic reactions must be taken into account when performing provocation tests (84), and we believe that they should be done only in very special cases. These authors also point out that it is difficult to standardize provocation tests because of different reports from patients and the unknown allergen content in rubber materials, as well as differences in the penetration of allergens into the skin.

As mentioned above, inhalation provocation tests have been done with latex to confirm the presence of respiratory symptoms induced by contact with latex or airborne latex particles. Jaeger et al. performed such tests with 18 patients who had experienced dyspnea or rhinitis/conjunctivitis related to latex contact (26). Inhalation of cornstarch from latex gloves in a small inhalation chamber during 5–60 min induced reactions in all 18 patients tested. The most frequent reactions during the test were rhinitis, cough, and conjunctivitis. A significant increase in airway resistance was seen in five cases. One patient developed severe facial angioedema and hypotension; another complained of generalized malaise. These symptoms were not induced by handling of cornstarch-powdered, latex-free gloves.

In vitro tests

A latex radioallergosorbent test (RAST) is available commercially for the *in vitro* detection of latex IgE antibodies (Latex, k82, Pharmacia Diagnostics), but, as expected, it is less sensitive than skin tests and provocation challenge, detecting these antibodies in only about 50–70% of skin-test-positive, latex-allergic patients (4, 22, 26, 79, 84). Jaeger et al. found that in 16% of their latex-allergic patients, specific IgE antibodies were detected by RAST only when the test was made with latex-coupled disks prepared in their laboratory (26).

Sandberg et al. recently reported that 39% of a group of 31 children in a spina bifida clinic had a positive RAST (59). Three of these children had had an allergic reaction to latex, whereas no child with a negative test had a clinical history of hypersensitivity. These authors concluded that the value of rubber-specific IgE awaits prospective studies.

A new latex-specific fluorescent enzyme immunoassay for the detection of latex-specific IgE (Pharmacia CAP System, PCS) was recently evaluated by Dolen et al. (17). Mathew et al. obtained a positive result with this assay in 4/10 skin-test positive, latex-sensitive spina bifida patients (44). Kwitken et al. have developed a flow cytometric assay (FCA) for antilatax IgE antibodies and report an excellent cor-

relation between FCA and RAST, and between FCA and ELISA values (33).

In some cases, it is necessary to rule out sensitivity to such rubber additives as accelerators and antioxidants, especially thiurams, which cause delayed hypersensitivity (24), but also ethylene oxide (48) and, rarely, cornstarch powder (61). It must be remembered that immediate and delayed hypersensitivity may coexist in the same patient (77, 81). Finally, when allergic reactions occur during surgery, allergy to muscle relaxants and other drugs used during general anesthesia must be considered (9, 10, 82).

Prevention

Primary prevention of sensitization to latex means avoidance of exposure to latex, which is virtually impossible, given the large number of latex products we encounter from childhood. Nevertheless, since atopy is a risk factor for latex allergy, persons with a history of allergy who must use rubber products in their work, for example, operating-room personnel, might be advised to substitute synthetic rubber alternatives for natural rubber products whenever possible.

Secondary prevention, the principal therapeutic approach, consists of avoiding exposure to latex by sensitized persons, a method which likewise may be difficult because of the ubiquity of latex products and their similarity to nonallergenic synthetic rubber products.

Health professionals who are required to wear surgical or examination gloves and other latex-allergic persons who use rubber gloves can avoid latex in several ways: 1) Wear plastic or cotton undergloves inside latex gloves. 2) Wear gloves made of synthetic nonlatex polymers, such as styrol-butadiene polymers (Elastyren[®], Danpren), polyvinyl chloride (Ethiparat[®] vinyl glove, Johnson and Johnson; Triflex polyvinyl[®], Travenol Laboratories), or Neoprene (Neolon[®], Becton-Dickinson; Dermaprene[®], Ansell, Inc.), or Tactylon (Tactylon[®], Tactyl Technologies). 3) Use liquid "gloves" made of a foam including stearate, glycol-propylene, glycerol, and sorbitol (Marlyskin[®], Farmitalia-Carlo Erba); these "gloves" provide protection against acids, bases, and salts for 4 h. 4) Use gloves coated on their internal surface with polyurethane (Neutralon[®], Johnson and Johnson). 5) Wear "hypoallergenic" latex gloves (for example, "Low-powdered" Travenol Laboratories; Ansell Gammex[®], Ansell, Inc.; Baxter Triple-Washed[®], Baxter Pharmaseal). The protective effect of some of these gloves has been disputed (22, 26), and some are unacceptable to surgeons (63) because nonlatex gloves generally do not have the same mechanical characteristics as

latex gloves and therefore do not give surgeons an accurate touch. In addition, they may not be watertight and thus could be permeable to the *Herpes simplex* virus (32). In any case, a "use test" should be carried out by affected persons to determine their tolerance to a particular brand of glove.

Patients with a history of allergy to latex or to any of the foods mentioned above; patients with a history of a serious allergic reaction during a prior surgical, medical, or dental procedure; and patients with spina bifida and others who have undergone multiple operations must be considered at risk of developing anaphylaxis during surgery or Caesarean or normal delivery and following medical examination with latex gloves. Health professionals should use nonlatex gloves and equipment when in contact with these patients.

It has been suggested that preoperative skin testing may help avoid a serious allergic reaction in patients at risk (47). However, we certainly do not believe that preoperative skin testing should be done routinely in all surgical patients.

Given that allergenic proteins are certainly eluted from latex gloves on contact with the moist skin and mucous membranes, and by soaking in aqueous solutions, it is not surprising that Morales et al. were able to diminish this water-soluble allergenic material by washing gloves (49). Moreover, Jones et al. found that triple-washed, powder-free latex gloves contained several thousand times less allergen than typical latex surgical gloves (28). Leynadier et al. showed that increasing the time of washing latex gloves during the manufacturing process decreased the protein content and the allergenicity of the gloves but not sufficiently to eliminate a potential allergic reaction (42). Supplemental steam sterilization of the gloves further decreased their protein content to undetectable levels and the allergenicity at least sevenfold. Investigators at the Malaysian Rubber Producers Research Association, Hertford, UK, are attempting to find practical ways to reduce the extractable protein level of rubber gloves (15). They report that the "extractable protein" is on the surface of latex films and is easily removed by washing: approximately 90% is removed in the first of a series of washes in water, and running or stirred water is more effective than a static water bath. According to these investigators, modifications in current manufacturing processes can provide truly "hypoallergenic" (a term we find difficult to define) latex gloves. It is recognized, however, that there is as yet no established method for determining the allergenic potential of rubber goods, or have standards been established by regulatory agencies. Accordingly, given the apparently increasing incidence of allergy to latex, much more work remains to be done.

References

1. ALENUS H, REUNALA T, TURJANMAA K, PALOSUO T. Detection of IgG4 and IgE antibodies to rubber proteins by immunoblotting in latex allergy. *Allergy Proc* 1992; 13: 75-7.
2. ALENUS H, TURJANMAA K, PALOSUO T, MAKINEN-KILJUNEN S, REUNALA T. Surgical latex glove allergy: characterization of rubber protein allergens by immunoblotting. *Int Arch Allergy Appl Immunol* (in press).
3. AXELSSON IGK, ERIKSSON M, WRANGSJO K. Anaphylaxis and angioedema due to rubber allergy in children. *Acta Paediatr Scand* 1988; 77: 314-16.
4. AXELSSON JGK, JOHANSSON SGO, WRANGSJO K. IgE-mediated anaphylactoid reactions to rubber. *Allergy* 1987; 42: 46-50.
5. BARBEE RA, HALONEN M, LEBOWITZ M, BURROWS B. Distribution of IgE in a community population sample: correlations with age, sex, and allergen skin test reactivity. *J Allergy Clin Immunol* 1981; 68: 106-11.
6. BAUR X, JAEGER D. Airborne antigens from latex gloves. *Lancet* 1990; 335: 912.
7. BEAUDOUIN E, PUPIL P, JACSON F, LAXENAIRE MC, MONERET-VAUTRIN DA. Allergie professionnelle au latex. *Rev Fr Allergol* 1990; 30: 157-67.
8. BEUERS U, BAUR X, SCHRANDOLPH M, RICHTER W. Anaphylactic shock after a game of squash in an atopic woman with latex allergy. *Lancet* 1990; 335: 1095.
9. BINKLEY K, CHEEMA A, SUSSMAN G, et al. Generalized allergic reactions during anesthesia. *J Allergy Clin Immunol* 1992; 89: 768-74.
10. BIRNBAUM J, VERVLOET D. Allergy to muscle relaxants. *Clin Rev Allergy* 1991; 9: 281-93.
11. BOYLE KT, ANDERSON MC, KENIMER JG. Specific IgE to latex extracts [Abstract]. *J Allergy Clin Immunol* 1992; 89: 224.
12. CARILLO T, CUEVAS M, MUNOZ T, HINOJOSA M, MONEO I. Contact urticaria and rhinitis from latex surgical gloves. *Contact Dermatitis* 1986; 15: 69-72.
13. CEUPPENS JL, VAN DURME P, DOOMS-GOSENS A. Latex allergy in patient with allergy to fruit. *Lancet* 1992; 339: 493.
14. CHAMBEYRON C, DRY J, LEYNADIER F, PECQUET C, TRAN XT. Study of the allergenic fractions of latex. *Allergy* 1992; 47: 92-7.
15. DALRYMPLE SJ, AUDLEY BG. Protein allergies in latex products. Presented at Seminar on "Latex Technology and Processing", Rubber Consultants, Brickendonbury, Hertford, UK, 21 May 1992.
16. D'AUZAC J, JACOB JL, CHRISTIN H, eds. *Physiology of rubber tree latex*. Boca Raton, FL: CRC Press, 1989.
17. DOLEN WK, WILLIAMS PB, KOEPEK GW, SELNER JC. Laboratory evaluation of a commercial immunoassay for latex-specific IgE [Abstract]. *J Allergy Clin Immunol* 1992; 89: 224.
18. EHL W, HARTJEN A, THIEL CL, AULEPP H, FUCHS E. Latex-Allergien als IgE-vermittelte Sofortreaktionen. *Allergologia* 1988; 11: 182-7.
19. ESPIN M, DIDIER A, PEREZ T, CARRE P, LEOPHONTE P. Manifestations anaphylactiques au cours d'un rapport sexuel protégé révélant une allergie au latex. *Rev Med Interne* 1991; 12: 447-8.
20. FISHER AA. *Contact dermatitis*, 3rd ed. Philadelphia: Lea & Febiger, 1986.
21. FORSTROM L. Contact urticaria from latex surgical gloves. *Contact Dermatitis* 1980; 6: 33-4.
22. FROSCH PJ, WAHL R, BAHMER FA, MAASCH HJ. Contact urticaria to rubber gloves is IgE-mediated. *Contact Dermatitis* 1986; 14: 241-5.
23. GERBER AC, JORG W, ZINDEN S, SEGER RA, DANGEL PH. Severe intraoperative anaphylaxis to surgical gloves: latex allergy, an unfamiliar condition. *Anaesthesiology* 1989; 71: 800-2.
24. GOH CL. Contact allergy to surgeons' gloves in their patients. *Contact Dermatitis* 1989; 20: 223.
25. GOLD M, BRAUDE BM, SWARTZ JS, DOLOVICH J, SHANDLING B. Intraoperative anaphylaxis: an association with latex sensitivity [Abstract]. *J Allergy Clin Immunol* 1991; 87: 268.
26. 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.
27. JOGUET MN, THAN XT. Etudes des fractions allergéniques du latex d'*Hevea brasiliensis*. In: *Allergies et caoutchouc: aspects médicaux et industriels*. Proc d'une Table Ronde, Faculté de Médecine Saint-Antoine, Centre d'Allergie de l'Hôpital Rothschild, Paris, 27 December 1991: 101-11.
28. JONES RT, BUBAK ME, GOSSELIN VA, YUNGUNGER JW. Relative latex allergen contents of several commercial latex gloves [Abstract]. *J Allergy Clin Immunol* 1992; 89: 225.
29. KELLY KJ, KURUP VP, RESNICK A, et al. A case control study of hypersensitivity to latex (L), ethylene oxide (ETO) and allergic factors predicting anaphylaxis in pediatric patients undergoing general anesthesia [Abstract]. *J Allergy Clin Immunol* 1992; 89: 226.
30. KLEINHANS D. Contact urticaria to rubber gloves. *Contact Dermatitis* 1984; 10: 124-5.
31. KOPMAN A, HANNUKSELA M, KUMIN Aihentama Kosketusurtokari. *Duodecim* 1983; 99: 221-4.
32. KOTILAINEN H, BRINKER J, AVATO J, GANTZ N. Latex and vinyl examination gloves. *Ann Intern Med* 1989; 149: 2749-53.
33. KWITTEN PL, PAWLOWSKI NA, DOUGLAS SD, CAMPBELL DE. Measurement of human IgE to natural latex proteins: comparison of flow cytometry and enzyme-linked immunosorbent assays (ELISA) [Abstract]. *J Allergy Clin Immunol* 1992; 89: 225.
34. LAGIER F, BADIER M, MARTIGNY J, CHARPIN D, VERVLOET D. Latex as aero-allergen. *Lancet* 1990; 336: 516-17.
35. LAGIER F, VERVLOET D, LHERMET I, POYEN D, CHARPIN D. Prevalence of latex allergy in operating room nurses. *J Allergy Clin Immunol* (in press).
36. LAURENT J, MALET R, SMIEJAN JM, MADELENAT P, HERMAN D. Latex hypersensitivity after natural delivery. *J Allergy Clin Immunol* 1992; 89: 779-80.
37. LAUVAUD F, COSSART C, REITER V, BERNARD J, DELTOUR G, HOLMQUIST I. Latex allergy in a patient with allergy to fruit. *Lancet* 1992; 339: 492-3.
38. LEYNADIER F, PECQUET C, DRY J. Choc anaphylactique périopératoire au latex des gants chirurgicaux. *Presse Médicale*, Paris: 1988; 17: 390-1.
39. LEYNADIER F, PECQUET C, DRY J. Choc anaphylactique périopératoire au latex. *Rev Fr Allergol* 1989; 29: 98-9.
40. LEYNADIER F, PECQUET C, DRY J. Allergie vaginale au latex d'un préservatif masculin. *Rev Fr Allergol* 1989; 29: 99.
41. LEYNADIER F, PECQUET C, DRY J. Anaphylaxis to latex during surgery. *Anaesthesiology* 1989; 44: 547-50.
42. LEYNADIER F, TRAN XUAN T, DRY J. Allergenicity suppression of natural latex surgical gloves. *Allergy* 1992; 46: 619-25.
43. MAKINEN-KILJUNEN S, TURJANMAA K, PALOSUO T, REUNALA T. Latex and banana: structurally similar antigens and allergens [Abstract]. Presented at the XVth European Congress of Allergy and Clinical Immunology, Paris, 12 May 1992.
44. MATHWEN SN, MELTON A, WAGNER W, BATTISTO JR. Latex hypersensitivity: prevalence among children with spina bifida and immunoblotting identification of latex proteins [Abstract]. *J Allergy Clin Immunol* 1992; 89: 225.

45. MEDING B, FREGERTS S. Contact urticaria from natural latex gloves. *Contact Dermatitis* 1984; 10: 52-3.
46. MEEROPOL E, KELLEHER R, BELL S, LEGER R. Allergic reactions to rubber in patients with myelodysplasia. *N Engl J Med* 1990; 323: 1072.
47. MERGUERIAN PA, KLEIN RB, GRAVEN MA, ROZYCKI AA. Intraoperative anaphylactic reaction due to latex hypersensitivity. *Urology* 1991; 38: 301-4.
48. MONERET-VAUTRIN DA, MATA E, GUEANT JL, TURGEAN D, LAXENAIRE MC. High risk of anaphylactic shock during surgery for spina bifida. *Lancet* 1990; 335: 865-6.
49. MORALES C, BASOMBA A, CARREIRA J, SASTRE A. Anaphylaxis produced by rubber glove contact. Case reports and immunological identification of the antigens involved. *Clin Exp Allergy* 1989; 19: 425-30.
50. M'RAHAI ML, CHARPIN D, PONS A, BONGRAND P, VERVLOET D. Cross reactivity between latex and banana. *J Allergy Clin Immunol* 1991; 87: 129-30.
51. N'GUEN D, BURNS M, SHAPIRO G, MAYO M, MURREY M, MITCHELL M. Intraoperative cardiovascular collapse secondary to latex allergy. *J Urol* 1991; 146: 571-4.
52. NUTTER AF. Contact urticaria to rubber. *Br J Dermatol* 1979; 101: 597-8.
53. OWNBY DR, TOMLANOVICH M, SAMMONS N, McCULLOUGH J. Anaphylaxis associated with latex allergy during barium enema examinations. *Am J Radiol* 1991; 156: 903-8.
54. PARAT S, DASSIEU G, PECQUET C, BRUNET B, LE BOURGEOIS M, SCHEINMANN P. Allergie au gants de latex. Une cause de choc peropératoire. *Arch Fr Pediatr* 1990; 47: 129-30.
55. PEARSON ML, BYRD R, KELLY KJ, et al. Anaphylactic reactions during general anesthesia in pediatric patients [Abstract]. *J Allergy Clin Immunol* 1992; 89: 226.
56. PECQUET C. IgE-mediated allergy to latex in 80 patients. Presented at the XVth European Congress of Allergy and Clinical Immunology, Paris, 12 May 1992.
57. PECQUET C, LEYNADIER F, DRY J. Contact urticaria and anaphylaxis to natural latex. *J Am Acad Dermatol* 1990; 22: 631-3.
58. RING J, SCHULTE C, VIELUF D. Anaphylaxis during anesthesia due to latex allergy. *ACI News* 1989; 74-5.
59. SANDBERG ET, SLATER JE, ROTH DR, ABRAMSON SL. Rubber-specific IgE in children enrolled in a spina bifida clinic [Abstract]. *J Allergy Clin Immunol* 1992; 89: 221.
60. SEATON A, CHERRIE B, TURNBULL J. Rubber glove asthma. *BMJ* 1988; 296: 531-2.
61. SEGGEV JS, MAWHINNEY TP, YUNGINGER JW, BRAUN SR. Anaphylaxis due to cornstarch surgical glove powder. *Ann Allergy* 1990; 65: 152-5.
62. SEIFERT HU, SEIFERT B, WAHL R, VOCKS E, BORELLI S, MAASCH HJ. Immunoglobulin E-vermittelte Kontaktallergie bzw. Asthma bronchiale durch Latex-enthaltende Hauschallgummihandschuhe: drei Fallberichte. *Derm Beruf Umwelt* 1987; 35: 137-9.
63. SLATER JE. Rubber anaphylaxis. *N Engl J Med* 1989; 27: 1126-30.
64. SLATER JE. Latex antigens [Abstract]. *J Allergy Clin Immunol* 1991; 87: 268.
65. SLATER JE, MOSTELLO LA, SHAER C, HONSINGER RW. Type I hypersensitivity to rubber. *Ann Allergy* 1990; 65: 411-14.
66. SLATER J, MOSTELLO L, SHAER C. Rubber specific IgE in children with spina bifida. *J Urol* 1991; 146: 578-9.
67. SLATER JE, TRYBUL DE. Affinity purification of latex (I) antigens [Abstract]. *J Allergy Clin Immunol* 1992; 89: 226.
68. SONDHEIMER JM, PEARLMAN DS, BAILEY WC. Systemic anaphylaxis during rectal manometry with a latex balloon. *Am J Gastroenterol* 1989; 84: 975-7.
69. SPANER D, DOLOVICH J, TARLO S, SUSSMAN G, BUTTOO K. Hypersensitivity to natural latex. *J Allergy Clin Immunol* 1989; 83: 1135-7.
70. SUSSMAN GL, TARLO S, DOLOVICH J. The spectrum of IgE-mediated responses to latex. *JAMA* 1991; 265: 2844-7.
71. SWANSON MC, BUBAK ME, HUNT LW, REED CE. Occupational respiratory allergic disease from latex [Abstract]. *J Allergy Clin Immunol* 1992; 89: 227.
72. 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.
73. TURJANMAA K, REUNALA T, TUIMALA R, KARKKAINEN T. Severe IgE-mediated allergy to surgical gloves [Abstract]. *Allergy* 1984; 39 (Suppl. 2): 35.
74. TURJANMAA K. Incidence of immediate allergy to latex gloves in hospital personnel. *Contact Dermatitis* 1987; 17: 270-5.
75. TURJANMAA K, LAURILA K, MAKINEN-KILJUNEN S, REUNALA T. Rubber contact urticaria. Allergenic properties of 19 brands of latex gloves. *Contact Dermatitis* 1988; 19: 362-7.
76. TURJANMAA K, REUNALA T. Condoms as a source of latex allergen and cause of contact urticaria. *Contact Dermatitis* 1989; 20: 360-4.
77. TURJANMAA K, REUNALA T. Latex contact urticaria associated with delayed allergy to rubber chemicals. In: FROSC PJ, DOOMS-GOOSSENS A, LACHAPPELLE R, et al., eds. Current topics in contact dermatitis. Berlin: Springer-Verlag, 1989: 460-4.
78. TURJANMAA K, REUNALA T, ALENHUS H, BRUMMER-KORVENKONTIO H, PALUSUO T. Allergens in latex surgical gloves and glove powder. *Lancet* 1990; 336: 1588.
79. TURJANMAA K, REUNALA T, RASANEN L. Comparison of diagnostic methods in latex surgical glove contact urticaria. *Contact Dermatitis* 1988; 19: 241-7.
80. TURJANMAA K, REUNALA T, TUIMALA R, KARKKAINEN T. Allergy to latex gloves: unusual complication during delivery. *BMJ* 1988; 297: 1029.
81. VAN KETEL WG. Contact dermatitis from rubber gloves after dermatitis from thiurams. *Contact Dermatitis* 1984; 11: 323-4.
82. VERVLOET D. Allergy to muscle relaxants and related compounds. *Clin Allergy* 1985; 15: 501-8.
83. WARPINSKI JR, FOLGERT JF, COHEN M, BUSH RK. Allergic reactions to latex: a risk factor for unsuspected anaphylaxis. *Allergy Proc* 1991; 12: 95-102.
84. WRANGSJO K, WAHLBERG JE, AXELSSON IGK. IgE-mediated allergy to natural rubber in 30 patients with contact urticaria. *Contact Dermatitis* 1988; 19: 264-71.
85. YASSIN MS, SANYURAH S, LIERL MB, et al. Evaluation of latex allergy in patients with meningomyelocele [Abstract]. *J Allergy Clin Immunol* 1992; 89: 224.
86. YOUNG MC, OSLEEB C, SLATER JE. Latex and banana anaphylaxis [Abstract]. *J Allergy Clin Immunol* 1992; 89: 226.
87. ZENAROLA P. Rubber Latex Allergy: Unusual complication during surgery. *Contact Dermatitis* 1989; 21: 197-8.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.