

Allergic reactions to natural rubber latex at home, to rubber products, and to cross-reacting foods

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The prevalence of clinical sensitivity to natural rubber latex (NRL) has increased dramatically in the last 15 years. In the health care setting this has been associated with the increased use of latex gloves. It does not, however, explain the observation that IgE antibodies to NRL are detected in equal rates in both health care workers and the general population, with the numerous reactions occurring in homes and in health care settings in non-health care workers. This increase in NRL sensitivity has occurred at the same time as our observation of an increase in atopy. In addition, atopy is a definite risk factor that has been associated with NRL sensitivity in all studies. Exposure to NRL products outside the health care environment is significant and ubiquitous. Exposure to NRL epitopes also occurs by ingestion of foods, food additives, and pollen. This exposure is sufficient to induce IgE antibodies to both the food and NRL proteins. It is therefore difficult in an individual patient to implicate any single product as the cause of NRL sensitization leading to the development of symptoms. Outside of the health care environment there does not appear to be an increase in exposure to NRL products or to cross-reacting materials. This would suggest that there is an increase in the susceptible population, which clearly appears to be the atopic individual.

A great deal of attention is devoted to reducing exposure to latex gloves in the health care setting, which may be only the visible portion of the iceberg. More attention should be devoted to reducing the antigens present in all NRL products and consideration given to developing vaccines for the food-sensitive individuals. (J Allergy Clin Immunol 2002;110:S107-10.)

Key words: Allergic reactions, natural rubber latex, home, foods

Most reported IgE reactions to natural rubber latex (NRL) have been described in medical settings. It is therefore assumed that the medical environment is the major source of exposure to NRL that accounts for both sensitization and allergic reactions. The number of reactions that occur at home is unknown, but there are numerous cases in the literature in which reactions have occurred at home in individuals who have no occupational exposure to NRL or frequent surgical procedures. The European experience, as reported by Turjanmaa et al,¹ states, "It is clear that although health care workers

Abbreviation used

NRL: Natural rubber latex

compose the largest single risk group for NRL allergy, the majority of NRL allergic patients in European studies are non-health care workers." The same is probably true for the United States.

CASE REPORT

This patient was a 63-year-old female who was referred for evaluation of anaphylaxis to latex paint. The patient felt that she was allergic to the paint because she experienced generalized urticaria, abdominal cramping, and upper and lower respiratory symptoms while she was in the kitchen, which had been painted the previous day. She self-medicated with an albuterol metered-dose inhaler but became faint; when she was examined by the medical emergency workers, she was noted to have a blood pressure of 60/40 mm Hg and a pulse of 160 beats/minute. She was treated with epinephrine and had a good response. In the emergency department, she once again became faint and was treated with epinephrine, corticosteroids, and antihistamines. Her medical history revealed that, as a child, she experienced seasonal allergic rhinitis during the summer, which correlated with the tree, grass, and ragweed pollen seasons. During her teens, she noted wheezing with exercise and upper respiratory infections. As a young adult, she experienced an oral food allergy syndrome to fruits and melons. In her 50s, she had facial urticaria in a dentist's office and was advised by the dentist that she was allergic to latex. Other than the inhalant and food sensitivities, she had no other risk factors (Table I), such as working in a health care environment or multiple surgical procedures or occupational exposure to latex. Additional medical history revealed that she had eaten a kiwi fruit for breakfast. On skin prick test, her test results were positive to a latex glove extract, fresh kiwi fruit, banana, and potato. The patient ate potatoes without difficulty and avoided bananas because of the oral allergy syndrome. She could not recall the last time that she had eaten kiwi fruit.

My conclusions were that this patient's reaction was due to the ingestion of kiwi fruit and that she had the latex-food allergy syndrome. Because the latex paint did not contain NRL, she was reassured that this did not cause her symptoms. In evaluating patients, it is easier to determine the cause of the allergic reaction than to determine the sensitizing agents. Was this patient sensitized by foods because her first reaction was to foods? Was she sensitized by NRL products in her environment? What role did her exposure to grass and ragweed pollen play in the development of the oral allergy syndrome and sensitivity to gloves? This case emphasizes the ubiquitous nature of NRL products in the home and the important role of cross-reacting epitopes that are detected in foods, food additives, and pollen that make it difficult, in an individual patient, to determine the source of sensitization.²

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TABLE I. Risk factors for the development of NRL sensitivity

Health care worker
Rubber industry worker who manufactures latex products
Spinal cord abnormalities
Multiple surgical procedures
Multiple catheterizations
Atopy
Food allergy

TABLE II. NRL products that are present in homes

Bandages
Baby bottle nipples
Balloons
Carpet backing
Condoms
Diaphragms
Douche bulbs
Elastic in clothing and disposable diapers
Erasers
Eye dropper bulbs
Hot water bottles
Rubber balls
Pacifiers
Paints (some waterproofing paints)
Rubber hand grips on racquets, bicycles, garden tools, etc.
Rubber bands
Rubber clothing (such as rain coats)
Rubber gloves
Rubber toys
Shoes

NRL AT HOME

NRL products are ubiquitous in modern society. There are an estimated 40,000 consumer products that contain NRL.² Exposure to NRL starts at birth and continues through adulthood. Table II lists the types of products that one can be exposed to at home. Two recent reports continue to emphasize the ubiquitous presence of NRL in our environment. Sanchez-Lopez et al³ reported that the normal handling of food with latex gloves by food handlers was capable of transferring sufficient NRL antigen to the food to produce a positive skin prick test reaction in latex-sensitive individuals. Fiocchi et al⁴ reported 2 cases of severe anaphylaxis that were induced by NRL from a play pit liner that had contaminated the plastic balls that were present in a ball pit in the recreational area of a fast food outlet. The ability to be sensitized outside of a health care environment and to have severe anaphylaxis and death in a health care environment was demonstrated in the series reported by Ownby et al.⁵ In their report of 6 patients with severe anaphylaxis (including 1 patient who died), the only risk factor noted was atopy. Five of the 6 patients had hay fever or asthma, and 3 patients also had symptomatic atopic dermatitis. The sixth patient had 1 previous surgical procedure and a history of adverse reactions to medications. Of the 15 deaths that were associated with barium enemas, only 2 deaths have occurred in individuals with the first 5 risk factors that are listed in Table I. Although death caused by NRL

exposure is rare, when it does occur, it is more likely to occur in an atopic individual with no other risk factors. The implication from these severe cases that occur in health care environments is that sensitization is occurring at home from NRL products or from cross-reacting substances, such as pollen,^{6,7} food,⁸⁻¹⁴ or food additives.¹⁵

The ability to be sensitized and to experience reactions at home is not a new observation. The early literature concerning NRL allergy indicated that reactions occurred in both health care and non-health care workers. The very first case was reported in the German literature in 1927.¹⁶ That report concerned a 48-year-old housewife who experienced generalized urticaria and oral angioedema in association with a dental prosthesis. Symptoms resolved when the prosthesis was removed and recurred when it was reintroduced into her mouth. The 2 cases of documented NRL reactions that were described in 1979, which stimulated interest in NRL IgE allergic reactions, occurred in a nurse at work¹⁷ and a housewife at home.¹⁸ Both individuals had atopic dermatitis and contact urticaria to gloves. These early cases are supported by more recent observations that indicate that the NRL products we are exposed to from birth are both capable of sensitizing and inducing the allergic reactions (Table III). As emphasized elsewhere in this supplement, only NRL products that are produced by dipping contain the antigens that are capable of both sensitizing and causing allergic reactions. This would exclude rubber tire dust. The NRL antigens that have been detected in dust are derived from pollen.¹⁹

ALLERGIC REACTIONS TO FOODS

Allergic reactions to foods in individuals who are allergic to latex²⁰ and allergic reactions to latex in individuals who are allergic to foods²¹ have received growing attention and have been called the *latex-food allergy syndrome*. Clinical reports have described allergic reactions to an increasing number of fruits and vegetables from phylogenetically different sources in patients who are allergic to latex.^{9,22} NRL epitopes have also been detected in an increasing number of ingestants and substances without clinical sensitivity by more sensitive assays, such as immunoblotting and monoclonal antibodies. On the basis of a number of reports, it appears that approximately 50% of patients who are allergic to NRL have evidence of concomitant food allergies.¹ The range in different studies is from 30% to 80%. This wide range depends on the population that was studied (such as atopic vs nonatopic individuals) and the definition of food allergies. If food allergy is defined by the presence of IgE antibody without clinical symptoms on ingestion of food, the prevalence will be higher than if symptoms are required. The first reports of the latex food allergy syndrome and the most common associations are with banana, avocado, kiwi fruit, and chestnuts. In addition to these, clinical or serologic sensitivity has been demonstrated to almond, apple, beets, buckwheat, wheat flour, celery, citrus fruits, figs, grapefruit, hazelnut, lettuce, peach, peanut, pear,

spinach, strawberry, sweet pepper, tomato, walnut, watermelon, passion fruit, and a number of spices. The enzymes papain and bromelain that are present in papaya and pineapple also have epitopes that are present in NRL.¹⁵ The symptoms that are experienced by individuals who have the latex-food allergy syndrome on ingestion of foods are similar to those symptoms that occur when the individual is exposed to latex. The symptoms consist of anaphylactic shock, itching of the throat, eyes, or ears, worsening of asthma or eczema, gastrointestinal disorders, and oral or facial swelling.²⁰

To understand the significance of the incidence of NRL allergy in occupational populations such as health care workers and patients with spina bifida, one must know the prevalence of NRL allergy in the general population. To determine the significance of atopy and food allergy in the development of sensitivity to NRL, studies concerning prevalence have been performed in allergy clinics where one can assess the relationship between NRL and food sensitivity by skin prick tests. Liebke et al²³ noted latex positive reactions in 20.8% of children with food allergy. Novembre et al,²⁴ in an unselected population of atopic children, detected positive reactions in 3%, one half of whom were clinically sensitive to latex. In an unselected population, Bernardini et al²⁵ noted that only 8 subjects (0.7%) experienced positive skin prick test results to latex; none of whom were felt to be clinically sensitive to latex. All 8 patients, however, were atopic with positive skin tests to aeroallergens, foods, or both. Turjanmaa et al¹ reported that, in 26 children with latex allergy, risk factors included 5 children with spina bifida, 2 children with multiple allergies, and the remainder of the children were allergic to foods. These data would suggest that sensitization to NRL is occurring early in life, at home, and in atopic children, especially children with food allergy.

IDENTIFICATION AND CHARACTERIZATION OF NRL ALLERGENS

NRL contains more than 200 proteins.²⁶ Ten of these proteins bind IgE of individuals who are allergic to latex and have been recognized by the International Union of Immunological Societies as being relevant to latex allergy. These are labeled Hevea brasiliensis latex protein allergens (HEV b 1 through 10). Immunochemical studies that detected the presence of IgE antibody to these allergens have been performed on health care workers, sensitized individuals with spina bifida, and individuals who are allergic to foods.^{22,27} The summary of these results would indicate that the allergens that are recognized by health care workers, patients with spina bifida, children with allergy only to latex, and subjects with food allergy who are sensitive to latex are different (Table IV). Children with allergy only to latex recognize only 1 of the allergens (which is present in avocado, chestnut and banana) that are recognized by the health care workers. Individuals with the latex-food allergy syndrome recognize allergens that are recognized by the health care

TABLE III. Allergic reactions to NRL products

Barium enema catheters (death)
Bladder catheters
Rubber gloves
Condoms
Rubber dental dams
Sports equipment (rubber hand grips)
Toys (balloons, rubber balls)
Dental prophylaxis cups
Diaphragms

TABLE IV. Sensitizing antigens in NRL (HEVb 1–7)

Spina bifida (1, 2, 3)
Health workers (1, 5, 6)
Children (6)
Kiwi (5)
Potato/tomato (7)
Avocado, chestnut, banana (6)

HEVb, Hevea brasiliensis latex protein allergen.

workers. The differences in the allergens that are recognized by health care workers and children with spina bifida are most likely due to the method of sensitization. The health care workers are exposed to airborne allergens or contact with latex gloves. The antigens to which they are sensitive are water soluble. The children with spina bifida recognize hydrophobic proteins, which are tightly bound on other particles. The children with allergy only to latex may be sensitized by NRL products at home or by foods to which they are not clinically sensitive. The individuals with latex allergy who are allergic to foods are most likely sensitized by foods. The ability to be sensitized by foods is supported by Yeang et al,²⁷ who determined the allergen IgE specificity of individuals with allergy to latex gloves. They observed, in some subjects with glove sensitivity, a close association of IgE antibodies to HEVB5 and HEVB7C, which are found in kiwi fruit, potato, and tomato. He felt that, in these individuals with latex glove allergy, the linkage of sensitivity to these 2 proteins may have been acquired from sources other than the latex gloves.

CONCLUSION

NRL allergens are ubiquitous and can be detected in NRL products, foods, spices, pollen, and plants, which raises the possibility that sensitization can occur from multiple sources and be difficult to determine in individual patients. Clinical observations of patients who experience symptoms to foods and pollen before demonstrating sensitivity to NRL products would suggest that sensitization may have occurred with these nonrubber products. These observations have been supported by immunochemical studies that indicate that the individual with latex-food allergy may be uniquely sensitized to the antigens that are present in the food, while clinically demonstrating reactions to both the food and to the NRL products. This same limited IgE response to antigens that are

present in foods in individuals with latex-only allergy also suggests that sensitization may have occurred from foods but that sensitization to NRL products cannot be ruled out. NRL products are also ubiquitous, and case reports have documented allergic reactions to these products at home. There are also numerous case reports of individuals who experienced their first allergic response to NRL products, such as gloves, who subsequently experienced sensitivity to foods at home. These observations are important because patients who are sensitive to foods that contain NRL allergens should be informed that there is a risk of the development of sensitivity to NRL products, such as gloves. In addition, patients who are sensitive to NRL products should be made aware of the foods that are capable of causing symptoms or be evaluated for food sensitivity by skin prick test to fresh foods. The sequence of sensitization to symptom production to foods and NRL will depend on sequential studies of children who are known to have positive reaction to NRL and/or foods by skin prick test and who are asymptomatic to 1 or both.

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