

Natural rubber latex allergy

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Summary

Rubber is an important industrial and consumer product encountered in many household items and medical devices. Whereas the chemical additives used in its manufacture are well recognized as a cause of delayed-type hypersensitivity (allergic contact dermatitis), it is only during the past decade that immediate-type allergy to natural rubber latex (NRL) proteins (latex allergy) has emerged as a serious health issue. Frequent, prolonged wearing of NRL gloves, especially amongst health care workers, is a major risk factor for such sensitization. Latex allergy is now an important medical, occupational, medico-legal and financial problem, and it is essential that policies are developed to reduce it. Undiagnosed latex allergy is potentially very serious for patients. This article briefly overviews latex allergy with emphasis on the practical issues of diagnosis and management.

Latex production and nomenclature

Natural latex is the sap of the tropical rubber tree *Hevea brasiliensis*. It is a colloidal dispersion of rubber particles (*cis*-1,4 polyisoprene) in water, and contains a complex mixture of organic substances including many proteins of varying molecular weight which comprise about 1–2% of the natural product. The term 'NRL' refers to items made directly from a latex emulsion rather than from dried rubber latex sheets (for example gloves, condoms, balloons) and it is primarily this form of natural rubber which causes immediate-type hypersensitivity reactions. Many chemicals are added during processing, including accelerators (vulcanizing agents). Leachable chemicals and water-soluble proteins are removed later during a series of water bath washes, which are crucial in determining the residual protein and chemical content.¹

Epidemiology

NRL was first reported to cause glove-related contact urticaria in 1979,² and the IgE-mediated nature of this reaction was soon established. Systemic allergic reactions including anaphylaxis,³ were recognized later, and awareness increased after reports of fatal reactions to latex enema tips.⁴ In response to the HIV and viral hepatitis pandemic, there was an exponential rise in production of NRL gloves and their use amongst

health care workers; many of these gloves were poorly manufactured with high levels of residual protein. This is thought to have fuelled an epidemic in sensitization to latex in the late 1980s.

The highest rate of latex allergy is amongst patients with spina bifida (Table 1), whose risk of intraoperative anaphylaxis to latex is increased approximately 500-fold.⁵ This is probably due to frequent exposure to NRL-containing medical devices such as catheters, and repeated surgical procedures. The reported prevalence of latex allergy in health care workers has varied widely according to study populations and diagnostic criteria. Rates of sensitization range from $\approx$ 2% to 17% of asymptomatic employees,⁶ to more than two-thirds of those with symptoms.⁷ Regular glove wearers in other occupations such as pharmaceutical, electronic, cosmetic industries and glove manufacturers are also at increased risk. The use of skin protection creams may favour the uptake of allergens and increase the rate of allergic responses.⁸ The occurrence of latex allergy in the general population has not been systematically surveyed, but the prevalence appears to be less than 1%.⁹

Pre-existing hand eczema is an important risk factor for latex allergy, and there is also an association with delayed-type hypersensitivity to rubber chemicals.¹⁰ This presumably reflects an increased opportunity for sensitization, to both type I and type IV allergens which arises when the epidermal barrier is disrupted. Latex

Table 1 Risk factors associated with latex allergy

Multiple surgical procedures – especially in spina bifida
Frequent or prolonged wearing of NRL gloves
Pre-existing hand eczema
Atopy
Fruit allergy
Female gender

allergy is strongly associated with a personal history of atopy, and affected individuals may also show immediate-type hypersensitivity to a wide range of fruits, especially avocado, banana, chestnut and kiwi.¹¹ There is also an association with female sex, but this probably reflects increased exposure rather than an enhanced tendency to sensitization.

Clinical features

The most common manifestation of latex allergy (see Table 2) is localized contact urticaria, presenting with pruritus, erythema and urticarial wheals, which usually develop within minutes of contact. This may be associated with localized eczema in some cases,^{10,12} similar to a so-called 'type 1 protein contact dermatitis'.¹³ It is important to enquire about immediate symptoms on contact with NRL items in patients with hand dermatitis, as these may be easily overlooked by both patient and doctor, or simply attributed to irritation. Rhino-conjunctivitis and asthma are frequent, and occur principally due to airborne spread of NRL proteins on glove powder. Systemic reactions, including generalized urticaria, and anaphylactic shock, are uncommon, and are usually precipitated by direct contact with mucosae or abraded skin. A diagnosis of latex allergy should be considered in the evaluation of patients with peri-operative anaphylactoid reactions.¹⁴

Diagnosis

The most sensitive and preferred current diagnostic method is the skin prick test. Many studies have used a

home-made solution obtained from the eluate of a high protein NRL glove. One method is to incubate 1 g of small pieces of latex glove in 15 mL of sterile physiological saline, and remove the latex pieces after 15 min.⁹ The residual solution stock solution can be refrigerated and replaced monthly,⁹ and diluted further if necessary. Our own practice is to use a freshly prepared concentrated solution, obtained by adding ≈ 0.5 mL of water to a few cm² of small strips from a high-protein powdered NRL glove. Eluates should also be made from the patients' gloves, and saline and histamine dihydrochloride (10 mg/mL) used as negative and positive controls. Commercial extracts are available, and some may have a high degree of sensitivity (93%) and specificity (100%).¹⁵ Attempts are being made to standardize these for protein and allergen content. Although the anaphylactic risk associated with prick testing is small, resuscitation drugs and equipment should always be available. Measurement of latex-specific IgE by radio-allergosorbent test (RAST) may be useful when prick testing is contraindicated or shows equivocal results, but the sensitivity is lower than that of skin testing.¹⁶ It should be emphasized that these tests do not detect all cases of latex allergy: if they are negative in patients with a suggestive history, further evaluation by a use test or bronchial challenge should be undertaken. A use test involves wearing a finger of a NRL glove on wet skin for 15 min, with a vinyl glove finger as a control. If this fails to elicit urticarial wheals, a whole glove can be used, and exposure time lengthened. This however, carries a higher risk of anaphylaxis. Scratch-chamber tests are not generally advocated, as they are associated with false-positive reactions.¹⁷

The importance of NRL as a delayed-type allergen is unclear. Positive patch tests to additive-free latex have been reported in 1.2% of a routine patch tested population,¹⁸ and a higher rate (6%) amongst patients with hand dermatitis.¹⁹ However, latex patch test reactions are difficult to interpret, and this requires further evaluation.²⁰

Latex allergens

Major latex antigens have been identified,²¹ including soluble hevein in latex-allergic health care workers^{22,23} and particle-bound rubber elongation factor (hev b1) in spina bifida patients.²⁴ Other antigens have been reported, and many more peptides bind IgE, but characterization of these has proved difficult. Some antigens share sequence homology²⁵ and cross-reacting epitopes with fruit,²⁶ and this may underlie the association of latex and food allergy. The cornstarch used as glove

Table 2 Rubber allergy

	Type 1 hypersensitivity	Type IV hypersensitivity
Allergens	Natural latex proteins: Multiple peptides	Chemical additives: Thiurams, carbamates mercaptobenzothiazoles
Clinical features	Contact/generalized urticaria Rhino-conjunctivitis/asthma Anaphylaxis (contact dermatitis)	Contact dermatitis
Diagnosis	Prick tests/RAST	Patch tests

powder does not itself cause allergy, but adsorbs NRL allergens, rendering them airborne. It can cause significant and long-lasting contamination of the atmosphere by latex antigens, sufficient to elicit symptoms in presensitized individuals,²⁷ and the UK Medical Devices Agency has advised against its use.²⁸ The total protein and allergenicity varies widely between different brands of rubber glove,²⁹ and according to the method of assay. In order to minimize the risk of occupational sensitization to NRL, gloves with a low extractable protein content (<50 µg/g) should be used. This has financial implications, as powder-free low protein gloves are more expensive to produce.

Management of latex allergic patients and staff

Individuals demonstrated to be allergic to latex should inform their medical and dental attendants before any procedure is undertaken, especially those involving contact with mucosal surfaces or the abdominal cavity, including gynaecological and obstetric procedures. They should be advised to carry an alert card or bracelet, and clear documentation made in their clinical records. Non-latex gloves and devices should be available for use in such patients, and any items of NRL or dry rubber latex should not come into direct contact with the patient. This may require considerable effort and planning. 'Hypoallergenic' NRL gloves have a reduced chemical content, and are not a suitable alternative. Clinical staff must be made fully aware of the problems associated with latex allergy and the necessary precautions for dealing with hypersensitive individuals (see Table 3). Attempts to prevent allergic reactions with prophylactic antihistamines and corticosteroids have failed.³⁰

Latex is recognized as a substance hazardous to health (as defined by the Control of Substances Hazardous to Health Regulations (COSHH 1994), and employers have a legal obligation to take measures which ensure the safety of their employees. Employees allergic to NRL may be able to tolerate gloves with very low protein residues, but otherwise should use gloves made from an

alternative material, e.g. neoprene (polychloroprene) or elastyrene (styrene butadiene).

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Table 3 Key aspects in the management of NRL allergy

- Non-powdered gloves
to protect allergic individuals from airborne allergens
- Low protein (low allergen) gloves
to reduce sensitization in at risk populations
- Education of healthcare workers
to identify and protect allergic patients

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Key Points

- NRL allergy is an important occupational disease amongst health care workers.
- Atopic individuals with hand eczema, and glove wearers are at risk.
- NRL-allergic patients may suffer severe allergic reactions on mucosal contact.
- Prick testing with a glove eluate is a rapid, reliable and economical diagnostic test.
- Low protein, powder-free gloves should be used to diminish occupational sensitization.