Latex allergy revisited: a review

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ABSTRACT

The prevalence of latex allergy has increased because of the increased regular use of natural rubber latex gloves. The increase in sensitisation and allergy has also been linked to the poor quality of glove and condom production to meet the increased demand. However, the prevalence has been decreasing in some Western countries as a result of the implementation of preventive strategies.

Certain individuals such as health care workers and children with spina bifida are at increased risk of sensitisation and development of latex allergy. There are various ways in which sensitisation to latex occurs, including inhalation of airborne latex particles, and mucosal and skin contact.

Household gloves have been found to cause less latex allergy because of their special production techniques, the fact that there is loose contact with hands, and the short period of use.

Diagnosis of latex allergy depends on a good history, clinical symptoms and signs such as irritant dermatitis, allergic contact dermatitis, and type I hypersensitivity reaction. Diagnosis is confirmed by skin-prick test and specific latex IgE. Other diagnostic tests that can be used are nasal provocation tests and the glove use test.

Management strategies are mainly preventive measures and use of symptomatic therapy.

INTRODUCTION

The use of natural rubber latex (NRL) has increased since the start of the HIV/AIDS pandemic because of the realisation that gloves also prevent infection by other infectious diseases including viral hepatitis and influenza.[1] The prevalence of latex allergy has increased worldwide and this has become a public health issue.[1] This increase has been linked to increased use of poorly manufactured rubber gloves and condoms to meet the high demand for protection.[2]

Latex is a natural product from the rubber tree, *Hevia brasiliensis.* Because of allergic reactions to the natural material, allergy to latex rubber has become a growing problem.

This has had serious implications for health care workers (HCWs) and patients. Allergy has a potential to cause serious and fatal reactions for all involved.[3]

In highly developed and industrialised countries such as those of Europe and America, the latex allergy epidemic in HCWs seems to be abating. This is as a result of implementation of preventive measures recommended by the task forces of the European and American allergy associations.[4]

Despite the decrease in latex-related accidents that need emergency hospitalisation, the prevalence is still unnecessarily high, and exposure represents a potentially life-threatening complication of latex allergy.[3] Intraoperatively, latex allergy is second only to reaction to muscle relaxants as a cause of anaphylaxis.[3] The early cutaneous signs of anaphylaxis are missed in theatre because patients are draped. Here we rely on bronchospasm and cardiovascular collapse for the diagnosis of anaphylaxis. It should also be noted that adverse latex reactions during anaesthesia occur 30-60 minutes after induction.[3] To complicate matters, latex is found in medical devices and equipment, toys and some elasticated clothes.[5-7]

EPIDEMIOLOGY AND PREVALENCE

Latex allergy prevalence depends on the population studied. Prevalence in the general population has been reported as being less than 1% in some studies and between 1% and 6.7% in others.[3,5] HCWs, workers in the latex industry and construction workers, to mention but a few categories, have a high prevalence of between 2% and 17%.[5-7]

MECHANISM OF SENSITISATION AND IMPORTANT LATEX ALLERGENS

Development of latex allergy will depend on sensitisation by the latex protein. Different brands of gloves have different latex protein and allergen contents. The range of amount of allergen is between 22 and more than 12 000 units (AU/ml of allergen), depending on the latex brand.[1]

Latex allergy is due to the latex proteins which generally cause a type I immediate hypersensitivity reaction, while chemicals added to latex during processing cause a type IV delayed hypersensitivity reaction. Immunological contact urticaria (from latex protein) and allergic contact eczema (from additives such as thiurams, dithiocarbamates and benzothiazoles) also occur.[8] During the manufacturing process the extent of washing will determine how much allergen the gloves will contain. Cornstarch powder increases the risk of sensitisation and latex hypersensitivity.[1,9] The risk of sensitisation, through inhalation, will also depend on the amount of allergen circulating in the air. These airborne allergens can be measured at levels of between 13 and 208 ng/m^3. The following are mechanisms by which patients at risk can be sensitised:

- Inhalation of airborne latex allergen
- Mucosal contact with latex protein
- Skin contact especially if the exposee wears latex gloves over skin sores or abrasions
- Intranasal exposure from inhalation or when a latex endotracheal tube is used
- Intra-tracheal exposure during intubation
- Intra-peritoneal exposure during surgery
- Subcutaneous exposure during insertion of IV lines.

There are certain high-risk situations for latex sensitisation and subsequent development of latex allergy (Table I).[1]

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Table I. Risk factors for latex sensitisation and allergy

Health care workers
Atopic individuals
Spina bifida patients
Multiple surgeries during early childhood
Multiple urinary tract procedures
Multiple rectal tract procedures
Multiple thecal procedures
A history of multiple surgeries
Cerebral palsy
Mental retardation
Quadriplegia
Other multiple latex-exposing procedures
Allergies to avocado, banana, chestnut, kiwi, papaya, peach or nectarine
Rubber industry workers
Patients with food allergy

A special note worth mentioning is that allergy to household gloves (non-occupational) is a rare event with only four publications documenting research available. The first report was in 1987 and the last in 2006.[8] Table II tabulates the reasons for such a low incidence.

Table II. Reasons for low latex allergy sensitisation to household gloves

Special production techniques with inner surfaces containing cotton linings. These reduce skin contact with latex allergens
Special production techniques, such as leaching, reduce the allergen content of the gloves
Decrease in the allergen content with repeated wearing of the same gloves
Gloves are loose fitting which reduces skin contact and allows for ventilation and water evaporation
Household gloves are used for a short time per day, for less than 1 hour in most instances
Household gloves release a lower amount of thiurams and carbamates with a significantly smaller number of positive patch reactions than surgical gloves.[8]

There are 13 officially accepted latex allergens at the present time.[4] The following is a brief note on the allergens:

Hev b 1, also called a heat elongation factor, is a major allergen and cause of latex allergy in patients with spina bifida (SB).

Hev b 2 (beta-1, 3-glucanase) has recently been observed at a molecular level.[4] This allergen cross-reacted with a homologus protein of bell pepper. This observation suggests that Hev b 2 is one of the latex allergens operational in the latex-fruit syndrome.

Hev b 3 is mainly associated with latex allergy in SB patients. It is also found in a smaller percentage of HCWs. Owing to similaries in prevalence data for Hev 3 and Hev 1, there is a suggestion that these proteins have similar IgE epitopes.[4]

Hev b 4 (cyanogenic glucosidase) is an important allergen in HCWs and SB patients.

Hev b 5 has been shown to be one of the most important allergens of *Hevia latex* and for the diagnosis of latex allergy. This was demonstrated by a lower sensitivity of the Pharmacia Diagnostics ImmunoCAP when Hev b 5 was excluded and a stronger reaction (and some sera that had tested negative becoming positive) on adding recombinant Hev b 5.[4]

Hev b 6 has a precursor **(prohavein)** which is also a major latex allergen for HCWs and SB patients. Hev b 6.02 has shown sequence identities of more than 50% to the Havea domains of class I chitinases in fruits. Wagner and Breitender[4] have documented the cross-reactivity of Hev b 6.02 with fruits such as avocado and banana.

Hev b 7 (patatin-like protein) has been shown to have some effect as a latex allergen in SB patients and HCWs. There is cross-reactivity between latex and potato and tomato due to this allergen.

Hev b 8 (profilin), caused by one of the plant profilins, has been described as an important pan-allergen. It is involved in the latex-fruit syndrome since cross-reactivity to profilin has been demonstrated from celery tuber, banana, pineapple and bell pepper.[4]

Hev b 9 (enolase) has not been shown to be an important allergen in both HCWs and SB patients.

Hev b 10 (manganese superoxide dismutase) demonstrates low prevalence in allergic patients.

Hev b 11 (class I chitinase) has been described as the most important pan-allergen by Wagner and Breitenender.[4] It is associated with the latex-fruit syndrome.[4]

Hev b 12 (lipid transfer protein) and Hev b 13 (early nodule-specific protein) do not seem to play an important role in latex allergy or cross-reactivity.

CLINICAL PRESENTATION AND INVESTIGATIONS FOR LATEX ALLERGY

The diagnosis of latex allergy, as with any other allergic condition depends on a good history. In some patients symptoms and signs may no longer be evident at the time the patient consults a health care practitioner. In this history, cross-reactivity between latex and fruits and vegetables should be borne in mind. Confirmation of the diagnosis is made by specific laboratory tests. These tests are:

- Skin-prick test, which is the most useful test for allergy
- Detection of specific IgE to latex protein (radioallergosorbent test (RAST)).

Because neither of the tests mentioned have 100% sensitivity and positive predictive value, studies are currently being conducted to assess the effectiveness of using a nasal provocation test for confirmation of the allergy diagnosis.[10] A 'glove use test' may also be useful.[10]

The clinical signs and symptoms are protean. Latex allergy can present as irritant dermatitis, allergic contact dermatitis and a type I hypersensitivity reaction to NRL, the true latex allergy (Table III).

LABORATORY TESTS FOR LATEX ALLERGY

Skin-prick test

This test is done on the volar aspect of the arm or back since these areas have a higher concentration of mast cells. It documents a type I hypersensitivity reaction. Normal saline is used as a negative control and histamine as a positive control. Small drops of each of these controls, and that of a commercial latex test, are applied to the area chosen. A skin prick is performed by making a small scratch, without drawing blood. The test is started by pricking into the saline drop, then the

Table III. Clinical symptoms and signs associated with latex allergy and allergic reactions

Irritant dermatitis

This is a contact dermatitis and non-allergic and as a result does not have inflammation as a cause. It results from hand washing, insufficient rinsing, and glove powder. Clinical signs include fissures, dryness, redness, red raised bumps, sore and horizontal cracks on the skin exposed to the latex gloves. The skin might itch. It results from mechanical friction and drying caused by dry powder particles. It accounts for the majority of latex-induced skin rashes and is not immune-mediated.

Allergic contact dermatitis to rubber chemicals

This is a type IV delayed hypersensitivity reaction usually caused by chemical accelerators such as carbamates, thiurams and benzothiazoles. It is a cell-mediated immune response which develops 24-48 hours after exposure to latex. The dermatitis may predispose patients to further sensitisation. Clinical signs and symptoms include red, raised bumps, sores and horizontal cracks, which may extend up to the forearm. The signs may be persistent for days.

Type I hypersensitivity reaction to NRL (latex allergy)

This results from exposure to proteins in latex suspended in the air. It is the most serious form of latex allergy, but fortunately the least common presentation of latex allergic reactions. Symptoms usually present within minutes of exposure. Clinical signs and symptoms include wheal and flare responses under gloves. It may be difficult to differentiate this from irritant and allergic contact dermatitis. It may, however, present in the most severe way as facial swelling, generalised urticaria, respiratory distress and anaphylaxis.

latex and finally a prick into the histamine drop. Histamine is tested last in order to avoid contamination with histamine. The results are read after 10-15 minutes. The test is deemed positive if the tested allergen expresses a wheal 3 mm greater than the negative control. Skin-prick testing is more sensitive than RAST testing.

Specific ImmunoCAP radioallergosorbent test (RAST)

This test measures the serum level of specific latex IgE. Blood is collected in a clotted blood tube and sent to the laboratory for analysis. It is less sensitive than the skin-prick test, and may miss 10-40% of skin-prick-test-positive patients.[3] It has the advantages though, of not producing anaphylaxis, the patient does not have to stop taking antihistamines before the test, and it can be used even in patients with generalised dermatitis.

Cellular antigen stimulation test (CAST)

This test is a specific test of release of sulphido-leukotrienes from primed basophils exposed to 'allergens'. It has been suggested that the CAST may be useful in evaluating patients with clinical latex sensitivity who are skin-test and RAST-negative.[11] This test is undergoing study by Professor Paul Potter at the Allergy Diagnostic and Clinical Research Unit (ADCRU) at the University of Cape Town.

Nasal provocation test

The test is not routinely used, but is conducted to examine the response of a target organ, such as the nasal mucosa, to allergens. It can be performed with an NRL-specific vaccine that is used for sublingual immunotherapy. The results are interpreted by the production of nasal symptoms such as sneezing, rhinorrhoea, and others.

Glove use test

This test is also not routinely used. It can however be used to determine contact urticaria symptoms associated with NRL. Patients are asked to put one hand in a powdered latex glove after the hands have been placed in water to dampen them. The other hand is inserted into a non-latex vinyl glove. The gloves are removed after 15 minutes and symptoms and findings are recorded after 15-60 minutes.

The nasal provocation test has been shown to have a sensitivity of 96%, specificity of 100%, a negative predictive value of 98% and a positive predictive value of 100%.[10] The sensitivity and specificity of the glove use test are lower, but the test remains useful.

These last two tests, especially the nasal provocation test, should be considered if a patient with suspected latex allergy has negative skin-prick and RASTs while the diagnosis is strongly suspected, and the the patient needs to be removed from a latex environment, such as in an occupational labour dispute.

MANAGEMENT AND PREVENTIVE STRATEGIES

The management of the condition can be divided into treatment of associated reactions and general or preventive measures. A detailed management plan is beyond the scope of this article, but a summary follows.

Management of symptoms

Irritant dermatitis: Avoidance or removal of the irritant. It is also advisable to use non-petropleum-based moisturising creams.

Allergic contact dermatitis: The patient should avoid latex and use moisturising creams that are not petroleum-based.

Latex allergy: Management depends on the severity of the reaction. Remove the patient from the latex environment and treat anaphylaxis according to management protocols.

Preventive measures

Elimination of latex in the environment is the most certain way to prevent latex allergy, but this solution is seldom possible.[6] The most important preventive measure is patient and HCW education in avoidance of contact with latex. Allergic patients should wear a Medic Alert disk and should be informed that they are at particular risk when they are hospitalised, undergo surgical procedures or visit a dentist.[12]

Hospitals should strive to maintain a latex-free environment, use latex-free gloves (such as nitrile gloves) and perform operations on patients at risk in latex-free theatres. In cases where there are limited numbers of theatres, such as in rural hospitals, patients at risk should be the first on the list. If not possible, such as in an emergency, there should be a gap of 90 minutes after the previous case in order to decrease aerolised latex antigen.[3] At times an HCW might have to be transferred to another working environment.

Despite the fact that latex allergy has been around for a long time, specific immunotherapy is still an experimental mode of treatment.[4]

CONCLUSION

Latex allergy remains a problem in South Africa and the challenge is getting the message across to HCWs and patients. Some of the problems we face include the fact that many health care facilities are struggling to cope with the burden of disease and as a result latex allergy becomes less of a priority. The HIV/AIDS pandemic has

also shifted attention away from allergic diseases. It is hoped that with the recognition of allergology as a subspeciality, medical schools in the country will include allergy topics in their training. This has been realised at the University of Pretoria.

Declaration of conflict of interest

Dr Sam Risenga is an executive committee member of ALLSA. Speakers bureau: GlaxoSmithKline.

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