SUMMARY
Natural rubber latex is found in numerous medical and dental products. Adverse latex reactions in dental patients and practitioners have significantly increased since the introduction of universal precautions for infection control. These reactions range from contact dermatitis to potentially life-threatening hypersensitivity. Patients with a history of spina bifida, urogenital anomalies, multiple surgical procedures, allergic reactions or atopy, health care personnel and latex production workers are at increased risk of latex allergy. Diagnosis is based on a combination of clinical history and laboratory tests. Identification of latex sources and the avoidance of latex exposure are critical for protecting both dental patients and dental personnel.

Keywords: Latex Allergy; Dental Patient; Dental Personnel; Prevention; Management

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LITERATURE REVIEW (LR)

Introduction

During the last 100 years latex products have become ubiquitous in everyday life. It is estimated that over 40,000 products contain latex rubber; some of them are presented in table 1. The popularity of latex is attributed to its unique biomechanical performance characteristics including strength, elasticity, tear resistance and superior barrier qualities. Latex is found in numerous medical and dental care products1-5 (Tab. 2).

Table 1
Common household products that may contain latex

- Athletic equipment
- Balloons
- Toys
- Infant pacifiers and feeding nipples
- Erasers
- Household gloves
- Elastic fibre diapers
- Elastic bands on clothing
- Condoms
- Shoe soles
- Rubber bands
- Rubber mats
- Computer mouse pads

The long history of the use of rubber dates back to the native populations of South and Central America before the arrival of Columbus in the new world. Commercial applications in Europe began in 1839. By

Table 2
Latex dental care products
- Latex gloves
- Latex bite blocks
- Rubber dams
- Rubber file stops
- Rubber stoppers on local anaesthetic carpules
- Rubber mixing cups
- Amalgam carriers
- Impression material
- Orthodontic elastics
- Face mask retention straps
- Polishing cups
- Polishing points
- Disposable syringes
- Containers with rubber droppers
- Surgical masks, hats and shoe covers
- Elastic wraps
- Nitrous oxide masks
1890 rubber gloves had been introduced into surgical practice by Dr. William Halsted, an American surgeon, to protect hands from the strong antiseptics then in use. In recent years, concern about the transmission of human immunodeficiency virus (HIV) and hepatitis B virus has led to increased glove usage by health care workers throughout the world.

The word “latex” refers to natural rubber latex (NRL), an extract from the rubber tree Hevea Brasiliensis. Although this tree is a native of Brazil, the majority of plantations currently producing commercial latex are located on the Pacific Rim - Malaysia, Indonesia, Thailand, and Vietnam. Latex is a generic term designating a water emulsion, or a liquid dispersed within another liquid. NRL is composed of rubber particles and water, and contains 256 proteins, including 11 being potentially allergens. Although some of chemicals and additives used in latex manufacturing are implicated as being responsible for dermatitis and other irritations, true latex allergies usually occur in response to the naturally occurring proteins found in latex.

Recently, the use of latex has been strongly implicated in the occurrence of latex allergies. A commonly expressed theory about latex allergy is that the increased demand for latex gloves, brought on by more widespread precautions, has led to a decline in the quality and an increase in the average allergen content of gloves. Repeated exposure to latex allergens in dental practice is known to elicit adverse immune responses that limit patient access to dental care. Dental practitioners, like other health care providers, are at increased risk of latex sensitivity and are sometimes forced to change jobs.

The purpose of this article is to review the literature regarding population at risk of latex allergy, as well as etiology, diagnosis, prevention and management of latex allergy, both in patients and dental practitioners.

Population at Risk

The risk of latex allergy in general population is quite low, ranging from 5 to 10%. However, a number of factors are associated with increased risk of latex allergy. Risk factors for latex allergy have been defined as healthcare workers, persons with a history of atopy, children with spina bifida, workers in rubber manufacturing plants and individuals with congenital urinary tract abnormalities and a history of multiple operations.

One of the groups at greatest risk of latex allergy concerns patients with cystic spina bifida. Spina bifida is a congenital neural tube defect that occurs when a portion of the neural tube fails to close or when the neural tube reopens after successful closure. The prevalence of latex allergy in children with spina bifida ranges from 28% to 67%. These patients may become sensitized to latex allergens from mucosal latex exposure during procedures involving the use of latex products (gloves, catheters, blood pressure cuffs). Children with spina bifida and latex sensitivity may present initially with an allergic contact dermatitis reaction. These children are treated as latex allergic when this occurs, and latex precautions are required to prevent sensitivity reactions from progressing to anaphylactic shock.

Individuals with congenital urinary tract anomalies, or past medical history significant for multiple surgeries or catheterizations seem to be at high risk of latex sensitization. One study has specifically addressed the isolated risk factor of multiple surgical interventions. This study has shown that 6.5% of multiply operated patients were sensitized to latex, whereas individuals without prior surgery or other risk factors were sensitized at a rate of 0.37%.

The risk of developing latex hypersensitivity increases with prolonged and repeated exposure. The frequency of the donning and removal of latex gloves by health care professionals is extremely high, and this high level of exposure to latex gloves and other latex medical products places them in a high-risk group for developing latex allergy. With dental professionals, as with other health care workers, the use of NRL examination gloves has led to an unfortunate trade off between the protection offered by such gloves and the possible adverse reactions associated with latex allergy. Investigations have shown that up to 17% of health care workers are sensitized to NRL allergens. Although many health care workers remain able to continue practicing by switching to synthetic or non-latex gloves, some develop such severe allergic responses, including asthma and anaphylaxis, that they are forced to change careers.

Atopy is a type I hypersensitivity with a genetic predisposition and has an incidence in general population that approaches 20%. Individuals with atopy tend to develop allergic reactions like asthma, allergic rhinitis, dermatitis, hay fever or eczema. An individual with a personal or family medical history of these diseases is at higher risk of experiencing allergic response to latex.

Latex allergies are linked to allergies to fruits and vegetables due to a probable cross-reactivity between latex antigens and those contained in certain foods. The frequency of sensitization ranges from 18% to 32% in patients allergic to latex. The most common cross reacting foods include avocado, banana, chestnut, kiwi, potato and tomato, all of which are antigenically similar to the latex allergen. Not all patients with these food allergies will develop latex allergy. Conversely, not all patients with latex allergies will have adverse reactions to these foods.
Workers in the latex industry are regularly exposed to latex allergens. This frequent exposure is responsible for the heightened risk of latex sensitization in this population group. In one study, 11% of the workers at a latex glove factory had positive allergy skin tests to latex. For people who work directly in production processes involving NRL containing materials, exposure is impossible to avoid, and they usually have to quit their job. Nevertheless, little is known about the prevalence of latex allergy in this group of patients.

Etiology

Penetration of the allergen may occur through many routes, such as the respiratory system, skin or vascular system. Furthermore, high vascularity and a thin epithelium of mucous membranes contribute to increased risk of sensitization on direct contact between the oral mucosa and latex products.

When the protective barrier of the skin is weakened due to contact dermatitis, latex proteins may be easily absorbed. Friction, pressure, heat and perspiration also increase absorption. The respiratory route of exposure occurs mainly through aerosolized powder. The powder covering the gloves absorbs latex allergens. These allergens become airborne when gloves are donned or removed and aerosol concentrations are higher in areas where staff usage of gloves is high. Once aerosolized, the latex protein-carrying starch particles may be inhaled by members of the dental team and patients in the dental surgery. The resulting effect is sensitization and repeated exposure may lead to hypersensitivity reactions.

Clinical Manifestations

Irritant Contact Dermatitis

Irritant contact dermatitis (ICD) is the most common reaction to latex products. It is a non-immunologic local inflammatory reaction of the skin caused by direct damage to the stratum corneum, which is the principal epidermal barrier against most exogenous noxious agents. Damage to the stratum corneum is followed by an increase in penetration of the irritants. Any substance causing chemical or physical damage to cells is an irritant. ICD arises when irritants penetrate the skin, producing an alteration in cells or inducing an inflammatory response.

Scratching, scrubbing, washing, excessive wetness, improper drying, perspiration, and extremes of temperature, all contribute to the reaction. Certain groups are at high risk, including people who work in wet environments (such as health care workers who frequently wash their hands), atopic patients, and individuals with fair skin. ICD occurring on dentists’ hands has been associated with frequent hand washing and occlusion of skin by gloves and glove powders.

Clinical findings include erythema, oedema, dryness, fissuring, chapping, and vesicle formation as a late manifestation. Lesions are sharply demarcated and limited to the area in direct contact with the offending agent. ICD is not considered to be an allergic reaction. However, these inflammatory changes in epidermis can promote penetration of allergens. Treatment is aimed at careful hand-washing and drying of hands, avoidance of extremely hot water, and use of skin emollients.

Allergic Contact Dermatitis

Allergic contact dermatitis (ACD) is delayed type IV hypersensitivity. It is a specific allergic reaction mediated by T cells. The allergens in ACD are usually small-molecular-weight-molecules or haptons that conjugate with proteins in the skin and induce activated epidermal keratinocytes to release pro-inflammatory cytokines. The Langerhans cells endocytose the process, and combine specific hapten peptides with HLA class I molecule and then activate and sensitize T-cells. Activated T cells then proliferate and generate clones of hapten-specific CD4+,CD25+ regulatory and CD8+ effector cells, which become either memory or effector cells. This is known as the afferent limb of the immune reaction. The CD4+ regulatory/effector and CD8+ effector cells then return to the original skin site and there function as the efferent limb of the immune response. Both CD4+ and CD8+ sensitized effector cells release pro-inflammatory cytokines. These cytokines, especially interferon-γ (IFN-γ), tumour necrosis factor (TNF), and migration inhibitory factor (MIF), are mainly responsible for inflammatory events during the development of a delayed hypersensitivity reaction, causing vasodilatation and accumulation of lymphocytes and macrophages at the site of allergic challenge. Memory lymphocytes are retained for long periods of time at the original ACD sites, accounting for the prolonged latent period (anamnesis) on subsequent exposure. ACD principally is caused by cutaneous or mucous contact with the offending agent. Accelerators and antioxidants used in latex manufacturing are commonly implicated agents. Allergic contact dermatitis, however, can be secondary to any of the chemicals used in latex manufacturing.

Clinical findings are similar to those of irritant contact dermatitis and include pruritus, erythema, scales, crusts, scabs, papules, and vesicles. They appear 48 to 96 hours after exposure and are initially located on the site of contact with the allergen. Lesions can persist for weeks and may ultimately spread peripherally. The development of a type IV hypersensitivity allergic response may occur...
even after years of contact with a substance. The patient will remain sensitized, and a reaction will recur if the individual comes into contact with products containing the same allergen4,16,39.

ACD and ICD frequently overlap because many allergens at high enough concentrations can also act as irritants36,41. Impairment of the epidermal barrier layer, such as fissuring, can increase allergen entry into the epidermis16,36,39.

Immediate Type I Reaction

Although less prevalent, Immediate type I reaction (type I hypersensitivity) is the most serious response. Immunoglobulin E (IgE) mediated type I responses to latex proteins result in adverse reactions within minutes to hours of exposure, ranging from mild irritation to loss of life9,12,35. Immediate type I reaction is IgE-mediated and is secondary to the proteins present in NRL. IgE antibodies are formed and bind to mast cells with the initial latex contact. Secondary exposure causes cross-linking of the IgE molecules on the surface of the mast cells, with resultant degranulation and histamine release. This mast cell degranulation and histamine release is responsible for clinical manifestations of immediate type I hypersensitivity4,12,31.

These symptoms include immediate pruritus and stinging, with erythema, oedema and a wheal and flare reaction occurring minutes later. After this initial reaction, rhinoconjunctivitis, generalized urticaria, dyspnoea, palpitations, dizziness, laryngeal oedema, bronchospasm, anaphylaxis, vasodilatation, gastrointestinal cramping, vomiting, hypotension and even death may result4,9,26,31,35,45. In some cases, general anaesthetics or surgical drapes may mask the early signs of more severe allergic reactions, and hypotension or oxygen desaturation may be the first signs of anaphylaxis4,31.

Diagnosis

Clinical history is the first step in the diagnosis of latex allergy46-49. Patients who have positive histories for latex allergy are treated with latex avoidance. Persons with a very high risk of latex allergy, such as patients with spina bifida, should be considered latex-allergic4,50. Such a patient is treated with latex avoidance and should be referred to an allergist for definitive testing. Individuals in other high-risk categories should be questioned thoroughly about latex hypersensitivity. Patient complaints often begin with a spectrum of allergic symptoms - skin, upper and lower airway symptoms - that are associated with exposure to natural rubber latex products. The temporal association between latex exposure and allergic symptoms may be strengthened by the disappearance and reappearance of allergic symptoms after concurrent separation from, and reintroduction of the individual to a known latex allergen source46,48,49. The suspected latex-allergic individual should be questioned about a number of issues: atopy, hand dermatitis and allergies to certain foods are established risk factors associated with latex allergy9,12.

Occupational information helps identify repetitive uses of natural rubber products, which can increase the individual’s frequency and magnitude of latex allergen exposure48-52. The individual should also be asked about the time course and magnitude of any localized or systemic allergic symptoms that might be associated with latex exposure. Dermatitis, swelling, redness, and irritation confined to the area of skin-rubber contact are particularly useful in discriminating between type IV and type I hypersensitivity. Information about the frequency and type of reactions to latex and the number of operations the individual has had with general anaesthesia may determine a positive latex allergy history.

Once the clinician has concluded that there is a high degree of suspicion concerning IgE antibody-mediated latex allergy, a confirmatory test for latex-specific IgE antibody should be performed to obtain support for this doubt. Definitive testing for latex allergy is completed with either in vitro or in vivo tests.

In vitro serologic tests measure the serum level of latex-specific IgE. The most common IgE assay method used is the radio-allergosorbent test (RAST), which has been shown to be of doubtful accuracy as an indicator of latex allergy4,20,48,49,53-55. Although less sensitive than skin testing, RAST has the advantage of avoiding concern about an untoward reaction that exists during skin testing4,5.

In vivo tests are more sensitive than in vitro tests and are clinically more relevant. The most reliable and sensitive test for latex allergy is a skin patch test1,4,5,35. The skin patch test (SPT) involves placing of a piece of latex glove in sterile saline for up to 24 hours. This allows adequate time to elute antigens from the latex into the solution. A drop of the solution is then placed on the patient’s arm, and a skin patch is made. Test results are interpreted in 20 minutes. A flare and wheal constitute a positive reaction. The scratch test involves making a 5-mm scratch on the patient’s arm. A patch of a latex glove is then placed on the scratch. The method of interpretation is similar to the SPT. The wear test differs from the previous 2 tests in that a latex glove with the finger portion removed is worn by the patient. Interpretation is otherwise similar to the other 2 tests. The SPT is most sensitive and has the least likelihood of causing anaphylaxis. Reports indicate that life threatening anaphylactic reactions have occurred during skin testing48,49,56. Intradermal testing is especially dangerous. Commercially available latex extracts are used in Europe and Canada, but are not approved by the Food and Drug Administration for use in the United States5,48.
Prevention

Avoidance is the cornerstone of latex allergy prevention\(^4,5,57,58\). In one study, when measures were taken to minimize latex exposure during dental treatment, 81% of latex allergic patients did not suffer adverse reactions\(^5,59\).

As far as gloves are concerned, latex alternatives - vinyl, nitrile or silicone - should be used in the dental clinic to prevent sensitization of patients and personnel. A number of studies have confirmed that a wide range of NRL proteins leach out of latex gloves and bind to surgical glove powders, so powder free gloves are also recommended\(^13,44,60-62\). Recommendations to use powder-free, low-protein NRL gloves or non-NRL gloves have been issued by the Occupational Safety and Health Administration in the United States and organizations in many other countries\(^77,63\). However, only reports at the level of the individual patient or hospital have shown that these recommendations are successful\(^54,47,64\).

A thorough patient history, including spina bifida, surgery congenital abnormalities, atopy and latex hypersensitivity, should be taken during treatment planning appointments. At-risk patients should be identified and referred for latex allergy testing. Patients with risk factors or confirmed latex hypersensitivity should be scheduled at the beginning of the office workday, when the level of aerosolized latex proteins in the treatment area is at a minimum to prevent exposure to aerosolized allergens\(^4,5,63,65,66\). A thorough wipe down of office equipment before the patient’s appointment is also recommended\(^65,66\).

In addition, latex-sensitive patients should be treated in a latex-safe environment. A latex-safe environment is one in which no latex gloves are used by any personnel and latex-free supplies are used instead of latex materials throughout the patient’s care\(^9,16,57,67-70\) (Tab. 3). A barrier protection is necessary in order to avoid direct contact with any latex item that cannot be removed\(^16,67\).

<table>
<thead>
<tr>
<th>Product</th>
<th>Alternative</th>
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</thead>
<tbody>
<tr>
<td>Latex gloves</td>
<td>Vinyl/Nitrile/Silicone gloves</td>
</tr>
<tr>
<td>Rubber dams</td>
<td>Non-latex (Polyvinyl Chloride) dams</td>
</tr>
<tr>
<td>Latex bite blocks</td>
<td>Metallic/Silicone mouth props</td>
</tr>
<tr>
<td>Rubber file stops</td>
<td>Wax file stops</td>
</tr>
<tr>
<td>Injectable ampules (rubber plungers in syringe)</td>
<td>Injectable vials</td>
</tr>
<tr>
<td>Orthodontic elastics used for oral fixation</td>
<td>Sterile wire to secure arch bars</td>
</tr>
<tr>
<td>Polishing cups</td>
<td>Non-latex toothbrushes</td>
</tr>
<tr>
<td>Rubber mixing cups</td>
<td>Silicone mixing cups</td>
</tr>
<tr>
<td>Penrose latex surgical drains</td>
<td>Silicone/Polyvinyl Chloride surgical drains</td>
</tr>
<tr>
<td>Containers with rubber droppers</td>
<td>Containers without rubber droppers</td>
</tr>
<tr>
<td>Instrument bands, impression material, polishing wheels</td>
<td>Non-latex alternatives from dental manufacturers</td>
</tr>
</tbody>
</table>

Because it is impossible to remove all latex-containing materials from the dental office, patients with an extreme sensitivity to latex or rubber should consult their physician regarding premedication with antihistamines and corticosteroids\(^64\). Premedication may reduce the severity of an allergic response; however, it should not be considered an alternative to latex avoidance\(^65,64,71-73\).

With respect to endodontics, the potential for immunological cross-reactivity between the gutta-percha used in endodontics and NRL has been the subject of some controversy\(^74\). Chemically, gutta-percha and NRL appear as isomers\(^66,73-76\). Several studies have suggested that gutta-percha may release proteins that induce reactions in latex-allergic individual\(^64,76-78\). These studies, however, have not proven cross reactivity between NRL and gutta-percha\(^73\). However, manufacturers of gutta-percha products should be encouraged to avoid the addition of any gutta-balata in their formulation, as gutta-balata releases proteins that can cross-react with NRL\(^73\). Moreover, the clinician should avoid gutta-percha extension beyond the apex of the tooth root that exposes the gutta-percha to a blood supply, inflammatory tissue and surrounding bone, and may increase the risk for allergic reactions\(^65,78\).

Health care providers who have contact dermatitis to latex products should be appropriately investigated to identify the implicated antigen. This can then be avoided by changing to a different brand of glove. Cotton liners and barrier creams also may be effective. Personnel with type I sensitivities to latex proteins should completely avoid the offensive allergens. Sometimes occupational asthma or rhino-conjunctivitis may force health workers to leave their workplace\(^12,16,29,65,79\).
Management

Knowledge of signs and symptoms and management protocols for allergic reactions are essential. The treatment of latex reactions is based on severity and sometimes additional medical intervention is necessary. In all cases, the first step is removal of the allergen\(^4,9,31,65,80\).

Contact dermatitis and type IV allergy may be managed with topical corticosteroids. Mild type I reactions without respiratory distress can be treated with topical steroids and antihistamines (50 mg diphenhydramine, 4 times a day until swelling resolves). Severe type I hypersensitivity with respiratory distress, swelling of the tongue, larynx or pharynx, and anaphylaxis requires assessment of ABCs (airway, breathing and circulation) and activation of emergency medical services. Drugs needed for management of an anaphylactic reaction should be readily available for high-risk patients. In this case, latex-free resuscitation carts are used to administer high-flow oxygen and deliver 0.3-0.5 ml intramuscular or subcutaneous doses of 1:1000 epinephrine (0.1 ml/kg every 5 minutes for children). Vital signs and ABCs should be continually checked. After stabilization, antihistamines, such as diphenhydramine, and corticosteroids should be prescribed\(^4,5,9,65,79\).

Conclusions

Reactions to latex products are reportedly occurring with an increased frequency, both in patients and in health care providers. Dental practitioners should consider the potential health risks that are associated with the use of Natural Rubber Latex in dental practice.

Patients with a history of spina bifida, urogenital anomalies, multiple surgical procedures, allergic reactions or atopy, health care personnel and latex production workers are at increased risk of latex allergy.

Adverse reactions following exposure to latex products may be categorized as irritant contact dermatitis, delayed (Type IV) and immediate (type I) hypersensitivity reactions.

Diagnosis is based on a patient’s history, but several \(\textit{in vitro}\) and \(\textit{in vivo}\) tests can be very useful as well. The most reliable and sensitive test for latex allergy is the skin patch test.

For patients with confirmed latex allergy, or those at risk of hypersensitivity, it is critical for dental personnel to be familiar with the range of possibilities for latex exposure and to employ appropriate preventive procedures.

References


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