

Local Anesthetic Cartridges and Latex Allergy: A Literature Review

(Cartouches d'anesthésiques locaux et allergie au latex :
recensement de la littérature)

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S o m m a i r e

But : Évaluer la validité des recommandations visant à éviter l'utilisation de cartouches pour l'administration d'anesthésiques dentaires locaux, chez les patients allergiques au latex.

Méthodologie : Une recherche a été effectuée dans MEDLINE pour la période de 1966 à 2001, et les publications pertinentes ont été examinées afin de relever les données faisant état de réactions allergiques précipitées par le latex contenu dans les flacons de médicaments ou les cartouches d'anesthésiques locaux d'usage dentaire.

Résultats : Douze publications répondant aux critères de sélection sont résumées ici; il s'agit de 4 études de cas, 5 études expérimentales, une mise à jour clinique et 2 lettres au rédacteur en chef.

Conclusion : La littérature médicale fournit certaines données selon lesquelles le latex allergène peut s'introduire dans les solutions pharmaceutiques contenues dans les flacons, soit lors de la pénétration du latex soit par contact direct avec les bouchons en latex naturel. Cependant, aucune étude, ni aucun exposé de cas, ne fait état d'allergie documentée causée par le latex contenu dans les cartouches d'anesthésiques locaux d'usage dentaire.

Mots clés MeSH : anesthetics, local/adverse effects; hypersensitivity, immediate/etiology; latex/adverse effects

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The potential for latex allergy is an increasing clinical concern in dentistry. Numerous items used in dental practice, such as those listed in **Table 1**, contain natural rubber (latex) and therefore are possibly allergenic. One item that may contain a small amount of latex is the local anesthetic cartridge. At one end of the anesthetic cartridge is the stopper, also called the plunger, where either the harpoon penetrates or the flat piston end of a self-aspirating syringe rests (**Fig. 1**). At the other end of the cartridge is the diaphragm, where the needle penetrates. Either of these components may contain latex. Whether the latex present in these cartridges can induce an allergic reaction is unknown.

Latex allergies can lead to type I and type IV hypersensitivity reactions. Type I hypersensitivity manifests as an immediate or anaphylactic reaction with signs and symptoms such as rash, swelling, bronchospasm and hypotension; such reactions can be fatal. In a dental office, immediate hypersensitivity

reactions have been elicited by exposure to rubber gloves, rubber dams and dental prophylaxis cups.¹ Type IV reactions involve delayed hypersensitivity and can be localized to the area of contact. This contact dermatitis is the most common expression of latex allergy.

Although the prevalence of latex allergy is about 1% in the general population,² 3 groups appear to be at higher risk of sensitization: children and adults with spina bifida, those with urogenital abnormalities requiring repeated surgeries involving catheterization and health care workers (who experience high exposure to natural rubber products).³ Additional risk factors for latex allergy include a history of atopy, which may manifest as rhinitis, reactive airway disease or childhood dermatitis; eczema, due to increased invasion of latex proteins through disrupted skin; and allergies to foods with known cross-reactivity with latex allergens, such as avocado, banana, chestnut and kiwi.⁴ Latex allergy is diagnosed from a complete medical

Table 1 Examples of latex sources in dentistry^a

Gloves
Rubber dams
Suction tips
Suction tubing
Prophylaxis cups
Orthodontic elastics
Face masks with latex ties
Mixing bowls
Bite blocks
Anesthetic cartridges

^aThis list is not exhaustive but is representative of commonly used products.

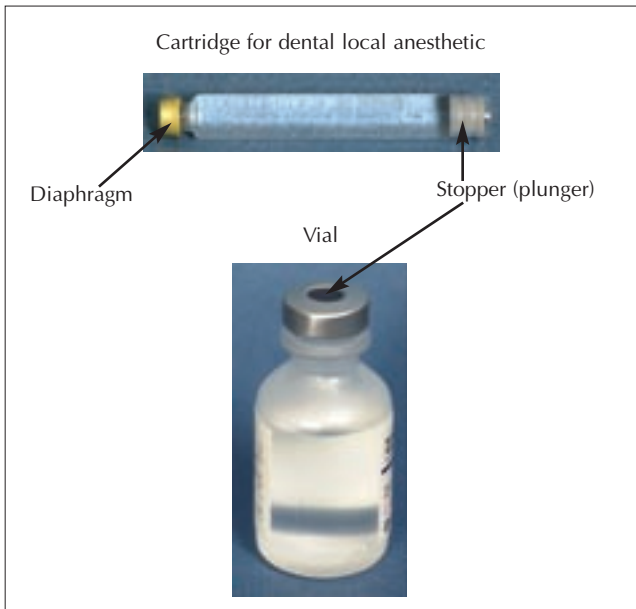


Figure 1: Potential sources of latex

history, a physical examination and diagnostic tests such as the radioallergosorbent test (RAST), skin prick tests, and skin patch tests.⁵

Natural latex is used to make more than 40,000 medical and consumer products that can be classified as either dipped (also known as soft) or moulded (also known as hard or dry).² Dipped rubber products, such as gloves, appear to have a higher content of latex proteins and greater allergic potential, whereas moulded rubber products, such as medication vial stoppers, contain denatured latex proteins and are therefore less antigenic.²

There has been some concern that latex allergen may leach from natural rubber vial stoppers into drug solutions, with the potential of causing an allergic reaction in a person with latex allergy. A commonly used textbook on medical emergencies in dentistry includes the following statement: "When latex allergy exists, the use of local anesthetic cartridges should be avoided. The thin diaphragm through which the needle enters the cartridge is composed of latex. Although unlikely, it is potentially possible for this latex to be injected into the sensitive patient, inducing a serious allergic reaction."⁶ Other

published recommendations have suggested that cartridges for dental local anesthetic can induce allergy and should be avoided in the latex-allergic patient.^{7,8}

Despite these published recommendations that dentists be concerned about using local anesthetic cartridges in patients with an allergy to latex, an important question remains unanswered: Are these recommendations valid? Is there any evidence that an allergic reaction can be induced by the latex present in a cartridge for dental local anesthetic? The purpose of this study was to search for any such reports of latex allergy involving cartridges for dental local anesthetic. In medicine, the analogous product is the vial, so the potential of medical vial stoppers to induce a reaction was also assessed.

Methods

A MEDLINE search was conducted for the period 1966 to 2001 with the following key terms and their combinations: "allergic reaction," "latex allergy," "local anesthetics," "rubber stopper," "medication vials" and "drug contamination." The search was limited to English-language publications. All publications that met these criteria were reviewed.

Results

The literature search yielded 12 relevant publications: 4 case reports, 5 experimental studies, 1 clinical update and 2 letters to the editor. The findings from the case reports and studies are summarized in **Table 2**.

There were no case reports or controlled studies demonstrating that the latex present in the stopper (plunger) or diaphragm of a local anesthetic cartridge can induce an allergic reaction.

There were 4 case reports describing allergic reactions elicited by trace amounts of latex from other medication vial stoppers, intravenous tubing or solution bottles.

The first case report described a 24-year-old laboratory worker with a history of type 1 (insulin-dependent) diabetes who experienced local erythema and pruritus at the insulin injection site within 1 minute after an injection.⁹ Intradermal testing confirmed latex hypersensitivity. The only combination that did not produce a local reaction was the latex-free insulin diluent with a latex-free syringe (insulin packaged in vials without latex components). Even when the latex-containing stopper for the medication vial was removed and the diluent was drawn directly into a latex-free syringe, a local reaction occurred (the diaphragm of the insulin vial was a natural latex rubber product that may have leaked antigens into the solution).

The second case¹⁰ was very similar to the first. A 6-year-old girl with type 1 diabetes experienced local erythema and pruritus at the insulin injection site. Intradermal testing confirmed latex hypersensitivity. However, if the natural rubber septum was removed from the insulin vials before injection, the patient did not react to the injections.¹⁰

These 2 cases suggest that direct contact of a medication with the rubber stopper of the vial⁹ or puncture through the

Table 2 Summary of reports of allergy to drug-related latex

Authors	Study type	Putative allergen source
Towse and others ⁹	Case report	Insulin vial
Hoffman ¹⁰	Case report	Insulin vial
Vassallo and others ¹¹	Case report	Methylprednisolone vial
Schwartz and Zurowski ¹²	Case report	Intravenous tubing
Terrados and others ¹³	Uncontrolled clinical	Penicillin vials
Jones and others ¹⁴	Uncontrolled clinical	Syringe with rubber stopper
Primeau and others ¹⁵	In vitro and clinical	Vial
Thomsen and Burke ¹⁶	In vitro	Vial
Nettis and others ⁴	Clinical (dental patients)	Not from local anesthetic

stopper¹⁰ may release quantities of latex antigens sufficient to elicit local cutaneous reactions in people with latex allergy.

A third report¹¹ described a 16-year-old girl who became bronchospastic and hypotensive during surgery; an allergic reaction to the surgeon's latex gloves was assumed. However, to investigate the possibility of allergy to latex from a vial, the outer stopper of the 2-compartment methylprednisolone vial was removed so the drug could be drawn up into a glass syringe without the needle passing through the stopper. Several minutes after the drug was injected through the patient's intravenous line, erythema developed. In this case, sensitivity to latex particles in the methylprednisolone vial was presumed. One month later, the patient underwent another procedure in which non-latex supplies and equipment were used; her course was uneventful.

The fourth report described a 32-year-old operating room nurse with a history of systemic reaction to latex who underwent a surgical procedure herself.¹² Before the procedure, intravenous infusion of Ringer's lactate solution was started, with lidocaine for local anesthesia. Within seconds after initiation of the infusion, the patient experienced emesis, facial flushing, hypotension, chest tightness, wheezing and syncope. Skin tests showed no reaction to 1% lidocaine or Ringer's lactate solution. At a later appointment, an intravenous line with normal saline solution was started without a local anesthetic, and a similar systemic reaction occurred. Because the authors suspected that small amounts of latex in the intravenous tubing and bottles were responsible for the allergic reactions, they subsequently administered saline from a glass bottle with a synthetic stopper, with no adverse reactions.

In addition to the 4 case reports, 5 experimental studies were found.

The first of these studies assessed 20 subjects who had good tolerance of penicillin but who also had a history of positive results on skin testing for this drug and a history of latex allergy.¹³ Sixteen of the subjects tested positive to at least one of the penicillin determinants, but when the skin tests were repeated using containers without latex stoppers, the results were negative in most cases. RAST inhibition studies, which are the most successful immunochemical measurements of latex antigens,¹ showed that all of the penicillin determinants contained trace amounts of latex allergens. These results suggest that allergenic proteins released from natural rubber

vial stoppers into aqueous pharmaceuticals may induce allergic reactions in individuals with known latex allergy who receive medications from such vials.

Another study assessing the latex allergen content of glutaraldehyde cross-linked injectable bovine collagen stored in syringes with rubber plungers yielded contradictory results.¹⁴ Extracts of syringe plungers and collagen solutions before and after storage in syringes with natural rubber plungers were tested for latex allergens. No latex proteins were detected with in vitro immunochemical techniques, and only 1 of 39 latex-allergic patients reacted to the skin prick testing with syringe extract and the collagen that had been stored in the syringe. There were no skin reactions to collagen that had had no contact with latex. The authors concluded that the level of latex antigens in injectable collagen is very low. They further concluded that the low prevalence of skin test reactivity in these highly allergic individuals indicates that type I hypersensitivity reactions resulting from latex contamination are unlikely.¹⁴

Another study was carried out to determine whether solutions stored in vials containing natural rubber stoppers release allergenic proteins detectable by skin testing of subjects with latex allergy.¹⁵ The subjects were divided into 2 groups, those with and those without latex allergy. All subjects underwent skin testing with saline solutions from each of 5 vials, 2 with natural rubber stoppers and 3 with synthetic stoppers. These solutions were further divided into those for which the stopper had not been punctured and those for which the stopper had been punctured 40 times with a 21-gauge needle 1 day before testing. In the group without latex allergy, all intradermal skin test responses were negative. Two of the 12 subjects with latex allergy had positive intradermal skin reactions to the solutions from vials with nonpunctured stoppers, whereas 5 had positive reactions to the solutions from vials with punctured stoppers. In vitro inhibition analysis detected trace amounts of latex allergen in extracts of cut stoppers containing natural rubber but not in extracts of synthetic closures. Seven of the 12 individuals with latex allergy did not display positive skin reactions to solutions from vials with natural rubber stoppers. The authors concluded that natural rubber stoppers released (through direct contact) allergenic latex proteins into solutions in sufficient quantities to elicit positive intradermal skin reactions in some individuals with latex

allergy.¹⁵ The higher rate of observed positive skin test responses in this study than in the study by Jones and others¹⁴ was likely due to the greater sensitivity of the intradermal skin test technique, which is 1,000 times more sensitive than skin puncture testing.

Does puncturing the rubber stopper increase the release of allergenic latex proteins and lead to a higher incidence of allergic reactions in susceptible patients? To answer this question, latex-containing stoppers for 20 vials were punctured with an 18-gauge needle attached to a latex-free syringe and the contents were withdrawn for comparison with samples taken from vials from which the stoppers had been removed.¹⁶ There was no difference in the concentration of latex allergens in the 2 sets of samples. The authors concluded that the latex allergen content of solutions was not reduced by removing the dry rubber stoppers from vials (instead of puncturing them).¹⁶

In the single dental study that was identified, 21 subjects with a history of an immediate allergic reaction in the dental environment were compared with a control group of 24 healthy individuals.⁴ All subjects were assessed by means of several tests; all 21 patients in the test group and none of those in the control group were determined to be allergic to latex. Seven of the 21 subjects with adverse reactions had experienced their symptoms after the administration of local anesthesia. To eliminate the possibility of an allergy to the local anesthetic, the incremental challenge test with mepivacaine without epinephrine was performed as described previously.¹⁷ The results were negative in all cases, consistent with lack of allergenicity of the local anesthetic and its cartridge.

A clinical update provided recommendations for dentists regarding latex allergy.⁷ This article identified the potential risk due to the latex in dental cartridges, but mentioned no reports of this problem having actually occurred. This article led to 2 letters to the editor discussing the relative amounts of latex in dental cartridges.^{8,18}

Discussion

This literature review found no articles documenting an allergic reaction to latex from local anesthetic cartridges. The 4 case reports found in the review suggested that patients might have an allergic reaction to the latex found in medication vials with rubber stoppers or intravenous tubing. The 5 studies suggested that latex allergens might be released by the rubber stoppers in drug vials.

How this information is incorporated into dental practice depends on the conclusions drawn from the evidence, and 2 different decisions are possible. The finding of no reports of allergic reactions to latex in the local anesthetic cartridge suggests that it might be acceptable to use such cartridges in patients with a history of latex allergy. Yet the lack of reports to date does not rule out the possibility of an allergic reaction some time in the future, especially given the reported allergic reactions to medical sources of drug-associated latex, such as vials and intravenous tubing. The American Academy of Allergy and Immunology Task Force on Allergic Reactions to Latex has a suggested protocol for all patients in whom latex

exposure is anticipated. The protocol includes the following statement: "Medications stored under latex closures should not be used if a substitute is available in a nonlatex-covered storage vial."³ This approach is consistent with the recommendation to use glass ampule-based local anesthetics for patients with known latex hypersensitivity.⁸ Nevertheless, even if such measures are taken, it cannot be assured that no latex allergens are present within the anesthetic solution, since the ubiquitous nature of latex in health care makes it extremely difficult to avoid this allergen entirely. The situation may be analogous to the preparation of foods for those with peanut allergies: certain food manufacturers warn that they cannot guarantee their products to be entirely free of peanuts, even though no peanuts have knowingly been added.

There is a trend to reducing the use of latex in health care products, including cartridges for dental local anesthetic. Today most stoppers are made of materials other than latex, but the main concern is with the diaphragm, which is pierced by the needle. The diaphragm often has a nonlatex coating, even if its centre is hard latex. The future will likely see a complete avoidance of latex in these products.

Until such time, what should be done about local anesthesia for patients with known latex hypersensitivity? Dentists should follow standard protocols for these patients, as described elsewhere,^{6,7,15} to reduce the likelihood of latex exposure. For high-risk patients who require treatment in a hospital setting, it may be prudent to use glass-enclosed ampules of local anesthetic, if they can be obtained, even though the evidence supporting this recommendation is equivocal at best. Numerous items used daily in dentistry have the potential to induce an allergic reaction in a patient with latex hypersensitivity (**Table 1**), but the evidence suggests that it is very unlikely that the local anesthetic cartridge is one of them. ♦

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