STUDY

Clinical Presentations of Patients Sensitive to Natural Rubber Latex

Jere D. Guin

Background: **Eczematous reactions to natural rubber latex (NRL) have been associated with both immediate and delayed hypersensitivity.**

Objective: **To determine clinical cases that might require testing for immediate sensitivity or patch testing for delayed hypersensitivity to latex fabric.**

Methods: **Patients with suspected sensitivity to NRL were given in vitro testing by radioallergosorbent test (RAST) or ImmunoCAP test and if negative, were prick-tested. If prick-test results were negative and the patients were still available, patch testing was done with latex glove fabric. Case histories of persons with positive results on RASTs, ImmunoCAP tests, prick tests, and patch tests were reviewed for clinical presentation and relevance.**

Results: **Of 92 persons with positive responses, 26 had positive RAST results, 26 had positive ImmunoCAP test results, 33 had positive prick-test results, and 7 had a positive patch-test result. Presentations included hand urticaria or eczema (46 patients), eyelid dermatitis (14), shoe dermatitis (10), atopic eczema (6), waistband dermatitis (5), clothing dermatitis (3), contact eczema to elastic in a mask (2), urticaria to a phlebotomy tourniquet, and eczema over the elbows and from an elastic bandage used for occlusive dressing therapy. Several other presentations were less likely to be relevant.**

Conclusion: **Persons with putative contact dermatitis in areas that may come into contact with NRL deserve not only to be patch-tested with rubber chemicals but also to be tested for immediate sensitivity and, if results are negative, to be patch-tested with NRL.**

REACTIONS TO NATURAL RUBBER LATEX (NRL) have become all too common in recent years, especially among health care workers[1–8] although this has been questioned.[9] Prevalence in other segments of the general population, such as spina bifida patients,[10–12] may rival or exceed that among health care workers, and increased prevalence has been reported among construction workers[13] and hairdressers.[14,15] It also seems to be a problem in the general population,[16,17] especially among atopic persons[18–22] and those with increased exposure.[22,23] Most of these case histories involve contact urticaria from NRL gloves, but asthma, anaphylaxis, rhinitis, facial edema, generalized urticaria, conjunctivitis,[24,25] and eczema[26,27] are also seen in persons with type I allergy to NRL.[1,6]

Reactions to NRL gloves include urticarial reactions, eczematous reactions, or both.[24,25,28] The urticarial responses are often due to type I allergy to NRL protein but also may be due to glove powder[29] or even to the chemicals used to process rubber.[30–33] Eczematous reactions are normally associated with delayed allergy to rubber chemicals[1] but can also be caused by protein contact dermatitis (PCD)[26,27] or delayed hypersensitivity to rubber protein.[34,35] In a contact dermatitis population, 1.0% of routine patch-test patients had positive patch-test reactions to NRL.[36]

There are scattered reports of presentations other than hand eruptions associated with NRL allergy, including some associated with immediate hypersensitivity and delayed hypersensitivity. These include reactions to an underwear band (tested with elastic itself),[37] footwear, a support bandage,[35] and an eyelid paste;[38] facial eczema;[39] and eyelid dermatitis.[26,27]

To gain perspective on what clinical presentations might deserve testing for both immediate and delayed sensitivity to NRL, I have reviewed the records of 92 patients with NRL allergy for presentations to use as a guide for the inclusion of testing for NRL allergy in the work-up for patients with contact dermatitis.

Methods

Between mid-1997 and mid-2004, in a practice limited to contact dermatitis, radioallergosorbent tests (RASTs) or ImmunoCAP tests (Pharmacia Diagnostics AB, Kalamazoo, MI) were ordered for patients suspected of having

Reprints not available.

immediate hypersensitivity to NRL protein or PCD from NRL protein. The RAST that was used unfortunately often depended on the insurance coverage and was not given in the written reports. If results were negative and an obvious cause was not found, prick testing followed if the patient was still available. This was done with extracts of Safeskin (powder-free) gloves (Safeskin Corp., San Diego, CA) and Medipak (light powder) latex gloves (General Medical Corp., Richmond, VA). More recently, testing has also been done with a latex antigen (Allergy Canada, Ltd., Thornhill, ON, Canada).

If prick-test results were also negative, many patients were then patch-tested with the fabric of an NRL glove that was either untreated or treated with water or petrolatum. Positive results of testing done elsewhere, if documented, were usually accepted, and retesting was not attempted. When the result of any one of the tests was positive, further testing was not done unless the result was questionable or borderline.

Records of persons known to be allergic to NRL through one or more of these tests were reviewed to determine the presentation and possible relevance.

Results

Ninety-two persons had positive reactions to NRL or NRL glove fabric. There were 26 positive RAST results (8 were class 1, 8 were class 2, 4 were class 3, 3 were class 4, 2 were class 5, and 1 was class 6). There were 26 positive ImmunoCAP (CapRAST) test results (18 were class 1, 6 were class 2, 1 was class 3, and 1 was class 4). Thirty-three persons had positive prick-test results (16 were +, 15 were ++, 1 was +++, and 1 was ++++). Seven persons had positive patch-test results, but of these, only two were ++ reactions. All but one of the patients with positive patch-test results were health care workers, and the exception worked in an industrial laboratory and wore gloves. Two of these seven patients had eczema in other areas; one broke out under her bra, and the other had eyelid dermatitis. Ages ranged from 16 to 80 years, with a mean of 48 years and a median of 49.5 years. There were 66 women and 26 men. Of the 92 patients, 33 worked in health care. Twelve patients had atopic eczema or a history of atopic eczema.

Of the 92 patients with NRL sensitivity, 46 (4 of whom had a second, different presentation) presented ostensibly with an eruption of the hands or had a history of the same, and 10 had shoe dermatitis (2 of these had a second presentation). Of 14 patients with eyelid dermatitis, 2 patients had a second presentation and 2 patients were not included in two previous reports.[26,27] Six patients (one of whom had a second presentation) presented with atopic eczema, 5 presented with waistband dermatitis, 3 had clothing dermatitis, and one patient broke out from NRL gloves and a tourniquet when blood was drawn in a hospital laboratory. One person reacted to an elastic bandage, and another person reacted to protective gear on the legs. Two persons broke out from contact with masks (a sleep mask in one case and a surgical mask in the second case, in which the rash was also accompanied by eyelid dermatitis). One patient had swelling following joint surgery, one had stasis dermatitis, one had pruritus, and one presented with contact dermatitis from a sunscreen. Two patients had psoriasis, one had eczema over the elbows and leg, and one had sore mouth.

Most of those with hand involvement were health care workers or persons who wore NRL gloves in their work. Some were clear at the initial visit as they had identified NRL gloves as a problem and had avoided them. However, none of those patients with presentations at locations other than on the hands had associated their problem with NRL. In some cases, relevance was only possible, such as the case of a nurse whose psoriasis of the hands may have been aggravated by exposure. Reactions of dermatitis or pruritus under the elastic in an undergarment were considered probably relevant, especially after improvement followed avoidance. Cases of shoe dermatitis were all possibly or probably relevant. The reaction of the person with elbow eczema was probably relevant. In those with atopic eczema, NRL sensitivity may have been a possible trigger, but none of the patients identified it before test results were available. Relevance was doubtful in the patient with swelling following joint surgery, as well as in the patients with stasis dermatitis and sore mouth.

Discussion

Contact allergy to rubber products traditionally has been associated with chemicals used in the processing of rubber.[1] In fact, almost all of the standard series of patch-test antigens contain numerous rubber chemicals, especially mercaptobenzothiazole, mercapto mix, thiuram mix, carba mix, and either an isopropylphenyl-p-phenylenediamine as a single antigen or a mixture of p-phenylenediamine derivatives. Contact urticaria is associated with immediate sensitivity. Details can be found in more lengthy reviews of the subject,[1,6] but briefly, NRL allergy has been associated with a variety of presentations, including contact urticaria, conjunctivitis, rhinitis, facial edema, asthma, generalized urticaria, and anaphylaxis.[24,25] However, hand eczema is

also a common finding,[24,25] and there are reports of involvement of other areas with eczema.[26,27]

In 1976, Hjorth and Roed-Petersen[40] described PCD in a group of food service employees. These patients, referred because of a putative occupational dermatitis of the hands, had type I reactions to various foods, including both meats and vegetables. The investigators used several testing procedures, including patch testing read at 20 minutes and at 48 hours. These workers were scratch-tested to the foods with which they worked, and many were tested with RASTs as well. While some of these patients had positive patch-tests reactions to the foods to which they were allergic, the apparent PCD was felt to be related to immediate hypersensitivity. Interestingly, many of the patients in that series were not atopic. PCD, associated with immediate sensitivity to NRL, can be seen with eyelid dermatitis,[26,27] atopic eczema, and reactions to NRL gloves.

There are also persons who react to NRL on patch testing.[34,35,41] Some are felt to have delayed hypersensitivity to NRL protein as patch-tests results were positive with NRL protein ostensibly without additives.[34,35] Reactions to glove fabric may be caused by other allergies, including allergy to chemicals used in manufacturing, such as Lowinox or butylated hydroxyanisole (BHA).[42] NRL gloves may contain a variety of chemical constituents not found in most test series, including different accelerators, accelerator activators, degradants, antioxidants, antiozonants, fillers, vulcanizing agents, pigments, odorants, flavorings, processing aids, and blowing agents.[1] Some investigators have found positive patch-tests reactions to NRL that is said to be chemical free.[34,35] However, almost any source of NRL is likely to contain chemicals because chemicals are added to the container used to collect the NRL unless it is deliberately collected in an unused container without additives.

Could this ''delayed hypersensitivity'' be due to PCD? In one study,[34] 1 of 4 patients with a delayed response had positive prick-test results, suggesting PCD, and half the patients had positive prick-test reactions with another series.[35] Apparently there are those with delayed eczematous reactions who do not show evidence of immediate hypersensitivity.[34,35] To be sure, both testing for immediate sensitivity and 20-minute readings are needed.

Reported reactions to NRL more often involve the hands, where they present with a history of contact urticaria or (in many cases) hand eczema. In this series, most of the patients with a history of contact urticaria or eczema of the hands were health care workers. However, one patient was a cafeteria worker, one worked in the laboratory of a manufacturing facility, one was a tool repairman, and one was a hair stylist. Three of these individuals had widespread atopic eczema, and the contribution of NRL sensitivity to their eruption is unclear, but avoidance was obviously required.

Patch-testing patients who have been exposed to protein antigens with standard series will miss most patients with this type of sensitivity. The work-up of individuals presenting with contact dermatitis of the eyelids, hands, and other locations exposed to NRL protein should include a RAST or an ImmunoCAP test and (if these test results are negative) prick testing. Some data suggest that immunoblots[43] and the enzyme-linked immunosorbent assay[44] are more sensitive than other in vitro methods (but not the prick test),[43] but this needs confirmation. If all test results are negative, patch testing could be done with a source containing NRL protein, such as the fabric of an examination glove.

In this series, 46 of 92 patients presented with either contact urticaria or eczema of the hands, and most were health care workers. This is not unexpected as prevalence in health care workers is usually considered to be high[2,45–47] (although this is controversial),[9,48] especially when there is an atopic background[9,19,21,48–50] or increased glove usage.[45,49]

The mechanism responsible for positive patch-test reactions to NRL fabric is unclear. It has been widely attributed to delayed hypersensitivity to NRL protein,[51] which can sometimes be confirmed by testing with NRL that is free of chemicals.[34] However, the meaning of a positive patch-test reaction to NRL glove fabric has been challenged because test results are often quite mild and questionable[52] and because NRL glove fabric may cause allergic contact dermatitis to chemical components that are not in the standard test series. I have tested with NRL fabric for more than 25 years now because this is sometimes the only way one can establish the cause of what clinically looks like glove dermatitis when reactions to all rubber antigens in RASTs and prick tests are negative. However, because of the potential for severe reactions, I now order patch testing with NRL glove fabric only after results of in vitro and prick tests are negative or borderline. This position has also been adopted in a position paper for the American Academy of Dermatology.[53]

Results with eyelid dermatitis have been previously published.[26,27] Several of the case histories were relatively unusual. The patients with shoe dermatitis did not show sensitivity to the rubber chemicals in their patch test series. Those patients experiencing eczematous eruptions on the legs included one patient with a reaction to NRL in

an elastic bandage that she had used with a corticosteroid for occlusive dressing therapy. Another patient presented with dermatitis from athletic shoes as well as dermatitis over her knees where she had worn kneepads containing sponge rubber when playing basketball. Another reacted to the NRL in protective gear worn over the feet and ankles. Of the five patients with waistband dermatitis, four were patch-tested and were found to be negative for bleached-rubber syndrome and to have negative reactions to the five rubber antigens in the patch test series. In the patient with sore mouth, NRL was certainly not the only factor (if a factor at all).

There were two patients with psoriasis of the hands. With one of these patients, NRL was considered to be a trigger factor aggravating the condition. The other patient had pustular psoriasis on the palms and was also NRL sensitive. This was thought to be due to her wearing NRL examination gloves to protect her hands, and I could not elicit a history of aggravation at the time of exposure.

On the basis of the experience in this series, testing for NRL sensitivity seems to be appropriate not only for contact urticaria but whenever there is exposure that might explain the presenting putative allergic contact dermatitis. This would be especially true for glove dermatitis, eyelid dermatitis, shoe dermatitis, waistband dermatitis, and reactions under NRL in clothing, surgical and shower caps, elastic bandages, and other articles containing NRL. Omission of this type of testing may well result in failure to identify the principal cause of the problem or an important aggravating factor. NRL sensitivity seems to be more common in persons with atopic eczema, and it may also be an additional trigger that requires avoidance. However, more data are needed before this assumption can be made.

Many of the + prick-test reactions and class 1 in vitro test results showed relevance. This should not be surprising as we often see persons with ++ prick-test reactions who have totally negative reactions in the in vitro tests and to three of four sources of NRL with which they are prick-tested. The best explanation for this may be the 60 or so potential protein antigens in NRL and the effect that processing has on the antigen content.[1]

Conclusion

The presentation of many of these 92 patients was contact urticaria, but many others had what was ostensibly contact dermatitis. Patch testing alone would have missed the cause with many of these patients. Testing for immediate (and in some cases, delayed) hypersensitivity to latex can be beneficial in the work-up of persons with possible contact dermatitis from rubber materials.

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