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Latex allergy—What do we know?

In the last few years, immediate hypersensitivity to latex has been accepted by much of the North American medical community as a legitimate and serious medical problem. (European physicians have been aware of it since 1979.) A broad consensus exists on the pathobiologic features of this phenomenon, which is typical of other type I reactions. Patients may exhibit a full range of reactions from contact urticaria to anaphylaxis, during which mast cell mediators may be detected in increased levels in the serum. Life-threatening reactions are typically preceded by mucosal or parenteral exposure, whereas cutaneous exposure leads to localized reactions. Antigen-specific IgE has been identified in patients by in vivo and in vitro methods. Peptide antigens have been identified in raw and processed latex, presumably originating in the rubber tree *Hevea brasiliensis*, to which patient IgE can be shown to bind, and which can elicit antibody responses in laboratory animals. The stringent elimination of latex from the operating room can protect the sensitive patient from immunologic disaster. Such protection is not conferred by premedication with histamine antagonists and glucocorticoids alone.

In this month's JOURNAL, two groups with significant experience in the investigation of latex allergy present some of their observations on this problem. Lagier et al. have examined the prevalence of latex allergy among operating room nurses using question-

naires, epicutaneous testing with raw latex, and the determination of serum IgE specific for antigens in raw latex. They found that 102 of 248 nurses reported itching, redness, or urticaria associated with latex glove use, but positive latex skin tests were found in only 21 nurses, among whom two had no complaint of reactions associated with gloves. They noted that urticaria was a much better predictor of a positive skin test than redness and itching. Finally, they found that in vitro testing was positive in only 3 of 13 patients with positive skin tests. Their report highlights the high risk of latex allergy among health care workers and the discordance among clinical history, skin tests, and currently available serologic screens in making the diagnosis.

Also in this issue of the JOURNAL, Ross et al. confirm and expand the prior observations that banana and latex antigens appear to be at least partially cross-reactive. Prior reports have documented the coexistence of latex and banana allergy in several patients. This study demonstrates, in patients with hypersensitivity to latex or banana, that crossed inhibition of specific IgE binding occurs in a significant number of sera. As yet, no epidemiologic data support the inclusion of patients who are allergic to banana as a risk group for latex allergy, but these serologic data certainly suggest the need for further study.

These two studies are but the latest in a series of efforts to define the risk and delineate the proper management of this newly identified and important disorder. Several questions regarding latex allergy arise often enough to warrant direct, albeit in some cases incomplete, answers.

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Who is at risk for latex allergy?

So far, children with spina bifida or severe urogenital defects, health care workers, and rubber industry workers appear to be at greater risk than the general public. However, other people have experienced serious, even fatal latex reactions. Presumably, other risk factors have yet to be identified. The most likely source of risk is a high level of exposure, and the pediatric experience suggests that the bladder and rectal mucosa are the routes of exposure associated with the greatest likelihood of sensitization. Recent anecdotal reports and cross-reactivity studies, like those of Ross et al., suggest an association between latex allergy and allergies to banana, chestnut, and avocado.¹⁻⁴ Several of these reported patients were already members of an established high-risk group for latex allergy. Whether patients with certain fruit allergies constitute an independent risk group remains to be answered.

Is latex allergy a new phenomenon?

The first reported case of type I latex allergy appeared in 1979. Before that article, even the occupational medical literature is devoid of articles suggesting this type of problem. Did patients allergic to latex systematically avoid medical care? This is rather unlikely, since chronically ill children and health care workers constitute the major risk groups. Were physicians unable or unwilling to recognize this allergic reaction? This is unlikely as well, especially since the literature has examples of latex allergy reports in North America *after* 1979 but *before* the reporting physicians understood the origin of the reactions that they were reporting.^{5,6} In these incomplete and, at the time, unsatisfying reports, the investigators have provided us with valuable records of these reactions. We have no reason to believe that physicians before 1979 were any less observant or less willing to record unexplained phenomena.

If latex allergy is a new phenomenon, why is it happening now? Many speculative explanations exist. It is most likely that changes in latex manufacturing methods or usage patterns have been important factors. If so, then occupational health officials, epidemiologists, allergists, and basic scientists have a unique opportunity to collaborate in the study of the evolution of this disorder. The lessons that we learn may help us to prevent future outbreaks of hypersensitivity to materials that we currently consider to be biologically inert.

How do you test for latex allergy?

In vitro tests are now available from several commercial laboratories and in some academic centers.

Although no approved skin test reagent is available in the United States, extracts have been made from raw latex as well as finished rubber products. Numerous investigations support the observations of Lagier et al. that skin tests are more sensitive than available serologic tests among health care workers allergic to latex. Both types of tests are sensitive (but not particularly specific) among children with spina bifida. Systemic reactions to epicutaneous tests have been reported among children with spina bifida as well as patients with prior histories of anaphylaxis to latex. Although such reactions may occur with any allergen skin tests, these reactions highlight the care that must be taken when performing skin tests with uncharacterized extracts.

Who should be tested?

At present, any patient at high risk should be tested. Testing methods are insufficiently predictive to recommend for others.

Who should avoid latex?

Prudence would suggest that any patient with either a history of latex allergy *or* a positive test for latex-specific IgE should avoid latex. It should be admitted that this relatively nonselective approach will lead to much effort at providing latex-free environments unnecessarily. When some form of latex allergy testing is demonstrated to have a high negative predictive value in these target populations, we will be in a position to be more selective. Children with spina bifida are at such high risk of sensitization that many centers have recommended that latex products be avoided entirely in this group.

How should latex be avoided?

Broad consensus exists that, at a minimum, direct contact with latex implements and toys should be avoided. The spread of latex antigens by adsorption to cornstarch particles is also well documented,⁷ suggesting that latex glove packets should not be opened in the same "breathing space" as the sensitive patient, and that health care providers who care for patients allergic to latex should wash their hands of any latex glove powder before patient contact. However, some investigations have indicated that latex antigen may be delivered to the patient from the injection sites on intravenous tubing and the stoppers on multidose drug vials. The necessary and sufficient features of latex avoidance await further clarification.

The avoidance of latex products has been severely hampered by inadequate and, at times, misleading product labeling. Mandatory labeling of the natural rubber content of medical devices should be imple-

mented without delay. When the current efforts of medical investigators to detect and quantify relevant latex antigens are validated with clinical studies, labeling may be modified to incorporate these data. Until then, we must assume that there are no "hypoallergenic" latex-containing devices, and must insist that information regarding the latex content of the materials to which we expose our patients be readily available.

Can latex products be made safe for use by individuals allergic to latex?

Current efforts in industry and the Food and Drug Administration are aimed at reducing the antigenicity of medical products made of natural rubber. The antigens are clearly elutable from gloves and condoms under relatively mild conditions, although it is doubtful that any natural rubber product can be made 100% antigen free. If our experience with casein hydrolysate formulas is any indication, a few patients allergic to latex will be unable to tolerate any *Hevea* rubber. On the other hand, many truly hypersensitive patients report that they can tolerate some latex products; these, presumably, contain less bioavailable antigen.^{8, 9} If medical investigators, industry representatives and federal regulators can agree on methods to reduce the antigen content of rubber, and on ways to measure that reduction, then the incidence of reactions and, more importantly, of sensitization may decrease.

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