

LRA by ELISA/ACT® CLINICAL UPDATE # 8

Latex Allergy / Delayed Sensitivity

What makes latex allergenic?

Natural rubber, or latex, is derived from the sap of the *Hevea brasiliensis*, a tree grown in the Amazon^{10,20}. Before being useful commercially, latex must undergo extensive processing to achieve the properties that make it so desirable. In the water soluble fraction of fresh natural latex, a small percentage of this fraction consists of proteins, and these proteins appear to be the primary initiator of the allergic reactions¹⁸. Determining the proteins in latex responsible for the allergic reactions has been extremely important since isolated proteins are necessary for developing specific antigens for diagnostic tests. To date, at least four antigenic proteins have been isolated from raw latex, although the degree of antigenicity among the proteins differs. In general, the non-ammoniated latex extract from untreated sap produces the major antigen, but the ammoniated extract, a standard raw preparation used in the manufacturing process, is an acceptable antigen for *in vitro* diagnostic testing^{14,18}. Work in this area will continue until all antigenic proteins in latex can be identified.

Although several proteins in raw latex are allergenic, it appears that some of the additives also contribute to the symptoms^{3,5,10,19}. During the processing procedures, many small molecular weight chemicals are added to shorten production time, to optimize the quality, and to extend the life-span and utility of rubber products. Rubber additives include accelerators, curing agents, antioxidants, stabilizers, dyes

and, other substances. In particular, the rubber additives thiurams, carbamates, mercaptobenzothiazole, and phenylenediamine have been reported to induce delayed hypersensitivity reactions and contact dermatitis^{14,19}.

What are the manifestation of latex allergy and how does latex invoke an immune response?

The first, recognized presentation of latex allergy was contact dermatitis¹³, but since then other manifestations have been noted, including rhinitis, asthma, angioedema, conjunctivitis, urticaria, tachycardia, and anaphylaxis^{1-5,9,16-19}. The different manifestations clearly indicated that cutaneous contact was not the only mode of presentation. It is now recognized that latex allergy usually develops as prolonged cutaneous exposure to latex antigens, and this is manifested as urticaria, eczema or dermatitis. However, after prolonged exposure and repeated contact with latex products, sensitization occurs^{3,9,16}.

In addition to cutaneous exposure, latex devices/antigens can initiate reactions through a variety of different anatomical sites, including the lungs^{2,18}. Apparently, latex antigens can become aerosolized and provoke responses such as rhinitis, conjunctivitis and asthma in numerous individuals^{2,7,10,16,17,19}. The responsible allergens are easily airborne when gloves are either put on or removed. The aerosolized antigens can cause symptoms in sensitive persons

who are simply in the area where gloves are being used. Finally, sensitization to latex can ultimately result in anaphylaxis. The anaphylaxis observed with latex allergy is, however, believed to be induced by mucosal absorption of latex antigens through disrupted skin barriers¹⁸, primarily the rectum, vagina, and mouth. It has been postulated that contact dermatitis and eczema may be early manifestations of latex allergy, and that sensitization occurs only after latex antigens are absorbed. However, the true clinical picture of latex allergy has not yet been delineated, and it may be that no one picture can account for the multiple presentations.

What immunologic mechanisms are involved in latex allergy?

It is currently believed that allergy to latex may occur by a Type I or Type IV mechanism. That latex could cause a Type IV, contact dermatitis has long been recognized²⁰. Type IV responses are cell-mediated, delayed hypersensitivity

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reactions, wherein T-lymphocytes are activated to recruit and stimulate the proliferation of other cells. The initial phase, including induction and sensitization, usually takes about seven days; thereafter exposure to antigen elicits a response that peaks within 48 hours⁵. Ultimately, the release of cell mediators results in local tissue inflammation and dermatitis.

The first report of immediate hypersensitivity, or Type I, reactions to latex was in 1979¹³; the response was contact urticaria. In 1987, anaphylaxis to latex was first reported¹, and since then over 10 people have died from latex anaphylaxis³. Moreover, in the past few years, immediate hypersensitivity reactions have been reported with increasing frequency^{2,5,18,20}. Although it has been suggested that the increased frequency of latex allergy reflects greater awareness and the failure to connect latex to allergic reactions in the past, this is unlikely. A more reasonable explanation is the increased need for, and hence more regular exposure to latex products due to the acquired immunodeficiency syndrome/HIV epidemic. This epidemic has resulted in a dramatic increase in precautionary measures, in particular the use of latex gloves, by both medical and paramedical personnel. Chronic latex exposure may impair the immune system through an underlying, persistent Type IV response, which in turn could cause sensitization,

and ultimately, anaphylaxis. Furthermore, a change in the manufacturing process could have altered proteins or added new chemicals that could lead to increased antigenicity. Whatever the reason, latex allergy is a reality that must be dealt with accordingly.

What populations are at greatest risk, and what commercial products are responsible for inducing latex allergy?

Both occupational and non-occupational latex allergy has been identified^{6,19}, with occupational exposure accounting for 55% of all latex allergy¹⁹. Most occupational latex allergy occurs in health care workers, with those in the medical and dental professions¹⁵ at greatest risk. In fact, recent studies have shown that the incidence of latex allergy (both Types I and IV) may be as high as 10% among surgeons, radiologists, and anesthesiologists¹⁶. The prevalence among nurses in operating units was reported to range from 5.6 to 12.5%¹⁸. Of medical care workers reporting contact dermatitis, rubber gloves worn at work were the main source of sensitization in 84%¹⁹. Other occupations associated with risk for latex allergy are jobs in industry, in particular, workers in metal, ceramic/glass, textile, plastic processing, and building industries¹⁹. To date, it appears

that most people acquire occupational latex allergy from wearing gloves.

Non-occupational latex allergy has also been noted. At highest risk are children with spina bifida, children who have received multiple operations such as congenital urologic abnormalities^{8,11}, and persons with prolonged use of latex products in the home. It has been reported that 32% of latex allergic patients are of non-occupational origin¹⁹.

Interestingly, among persons with latex allergy, concomitant atopic disease (53 to 74%) and food allergies (56 to 76%) are common. In fact, a cross-allergenicity between some latex proteins and tropical fruits, particularly bananas, has been reported¹². However, further confirmation of these reports is needed.

Populations at greatest risk for anaphylactic reactions to latex are persons undergoing surgery (abdominal, genitourinary, cesarean section, or dental), or medical procedures (barium enema). The use of latex products during these procedures may result in mucosal absorption, which subsequently triggers anaphylactic shock. In addition, persons with hand eczema who are exposed to latex gloves may be at risk for anaphylaxis²¹. It is believed that natural skin barriers are compromised in persons with eczema, and as such, latex antigens are better able to gain access and challenge immunocompetent cells in the epidermis. This access would increase the possibility for sensitization and anaphylaxis.

Latex is very popular and its unusual properties make it very desirable in many products. It has been estimated to be used in over 40,000 products, especially medical products. For example, latex is found in surgical/medical exam gloves, catheters, intubation tubes, medication stoppers, dental dams, and adhesives. On the non-medical side, rubber/latex is found in balloons, numerous children's toys, pacifiers, shoes, household cleaning gloves, hot water bottles, shower curtains, sporting equipments, and contraceptive condoms and diaphragms,

Reported frequency of latex sensitivity

- **Nurses in operating rooms:** **6-12%**
- **Surgeons, radiologists, anesthesiologists:** **5-10%**
- **Contact dermatitis in medical care workers:** **>80%**
- **Atopic disease in latex-sensitive people:** **>50%**
- **Food/chemical sensitivities in latex sensitives:**



to name a few. Clearly, getting rid of products that contain latex is not going to be easy, especially if suitable alternatives are not found.

How can latex allergy be diagnosed, and what treatments or preventive measures are currently available?

Several methods are currently used to confirm or diagnose latex allergy. The most common method, as well as the most sensitive, easiest to perform, and most inexpensive, is the skin prick test. Several latex antigens and latex additives are available for this skin test. When the skin test is performed, positive (histamine) and negative (saline) controls should also be performed. No false positives have been observed in over 200 patients, and 100% of patients with previous responses to latex have been positive to the prick test^{5,9,10}. Scratch-chamber tests and patch test have also been used, but are less specific, and yield a high incidence of false positive results^{5,10,19}. Another test commonly used, especially when anaphylaxis has been documented, is the specific latex radioallergosorbent test (RAST)^{5,10,16-18}. However, this test is much more expensive, and less sensitive than the skin prick test. This is not unexpected, given that the RAST is specific for immunoglobulin E (IgE) or Type I allergies. Basophil histamine release and basophil degranulation tests have also been used, but again, the low sensitivity and specificity of these tests, as well as their expense, make them less desirable than the skin prick test^{5,10,18}. Finally, intradermal skin tests have also been performed, but are currently not recommended, as they may be dangerous when anaphylaxis is suspected.

Recently, a latex antigen has been developed for the ELISA/ACT[®] LRA test. This new antigen can be ordered alone or in combination with other antigens. It is unique in that it will be the only diagnostic test available that can detect Types II through IV allergies in blood cells. This is a breakthrough given that many persons with latex allergy have negative IgE RAST values. Fuchs

Latex: Common sources of contact

- **Contraceptive condoms, diaphragms, and cervical caps**
- **Intravenous infusion tubing**
- **Surgical and barrier gloves**
- **‘Elastic’ patches for bandages and transdermals**
- **‘Stretchable’ protective laundry and kitchen gloves**
- **Surgically implanted shunts and reservoirs**
- **Intubation devices**
- **Dental barriers and dams**
- **Textiles (synthetic); pacifiers, children’s toys, balloons**
- **Building materials (pressboard other & composites)**

et al³ reported that of 27 patients positive to scratch tests with latex gloves, 59.2% were negative when tested by RAST with latex³. Bubak et al² reported that only 54% of their patients were RAST positive, and all of these had positive skin tests. Others have reported that the RAST is positive in about 65% of patients with latex hypersensitivity⁵. This clearly points to mechanisms other than those that are IgE-mediated. With the LRA by ELISA/ACT[®] technology, the hypothesis that latex allergy extends beyond the previous boundaries of Type I and Type IV reactions can now be evaluated.

What preventive & treatment measures are currently available?

Both prevention and treatment of latex allergy should be considered. For prevention, the allergenic components of latex must be identified and removed from raw latex in the processing, but this is much easier to say than to do! Another possibility is to use products in which latex substitutes have been used. For example, medical gloves without latex are available. Two synthetic gloves have been tested and appear to be tolerated by those with latex allergy: Neolon and Elastyren. They were also the most comfortable of the latex-free gloves. However, these gloves do contain carbamates which may be allergenic to

some people. Unfortunately, the synthetic rubber gloves are quite expensive, and many of those available already have their own unique set of both undesirable and allergenic properties.

Latex allergy is currently treated by diagnosing or confirming an allergic response, and then managed by avoidance of latex products. Decreasing exposure is critical but not always successful, given that latex can be aerosolized. Importantly, once a latex allergy has been confirmed, the person should be instructed to inform medical professionals about their allergy, wear a medical alert identification tag, and in patients with severe reactions, instruction should be given to possibly carry non-latex gloves with them for emergencies. Furthermore, those persons with severe or anaphylactic reactivity to latex should carry and know how to use an epinephrine-containing emergency kit. Finally, educating health care workers about the potential problems with latex allergy is critical. In particular, atopic individuals and persons exposed chronically to latex products should probably be screened for latex allergy prior to anesthesia and surgery.

In sum, latex allergy is of concern because it affects a growing number of physicians, nurses, and other medical personnel, as well as other populations requiring long-term use of medical



devices. Much work remains before a complete understanding of the etiology and epidemiology of latex allergy is understood, but medical professionals should begin to recognize and respond to any indication of a potential latex allergy.

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As part of the *Complete* and the *Environmental Chemicals* LRA by ELISA/ACT test panels, latex sensitivity is tested. This is the first and only delayed sensitivity latex test clinically available. EAB, your CLIA-certified lab for delayed sensitivity testing, is pleased to make this advanced testing method available to you.