Latex Allergy: A Path to Prevention

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Natural rubber latex (NRL) is an integral part of today's healthcare environment. In the late 1980s, reports of severe allergic reactions to NRL began to emerge.[1] These preliminary reports of adverse reactions reported to the FDA implicated powdered latex gloves and/or barium enema tips as the medical devices most often associated with these clinical reactions.[2] Up to that time, adverse reactions to glove exposure had only been recognized as irritant or contact dermatitis, some of which were delayed-type allergic responses (type IV) to chemical additives (thiuams, carbamates, mercaptobenzothiazole) used in the processing of rubber products. This new type of rubber allergy was manifested by type I hypersensitivity reactions, including contact urticaria, allergic rhinitis, asthma and anaphylaxis, with some deaths reported. The clinical consequences of latex allergy were reported primarily in two specific risk groups: healthcare workers with significant glove exposure and spina bifida children who had early surgical interventions.[3,4]

Following the early reports, the clinical manifestations of this new type of latex allergy were more clearly defined and were associated with an exponential increase in reports of latex-related illnesses in the 1990s. Numerous laboratory investigations helped identify the factors responsible for latex allergy, the proteins and peptides originating from *Hevea brasiliensis,* a tree that produces natural rubber latex.[5] These proteins represent only a very small percentage of the glove composition. There are an estimated 250 proteins found in NRL, approximately 50 to 60 of which can induce an IgE response.[6] The proteins identified as allergens include structural proteins, housekeeping enzymes, proteins involved in the biosynthesis of polyisoprene rubber and proteins with pathogenesis or defense-related functions. With extensive research, most of the major latex allergens have been identified and characterized. Thirteen (Hev b 1-13) have been cloned and are available in recombinant form. Several of these proteins are pan-allergens with extensive homology to protein families common to many plants.

Diagnosis of Latex Allergy

Because of the complexity and number of allergens in latex, the development of diagnostic tests for latex sensitization remains difficult. Standardized tests for measuring total protein and antigen content of NRL-containing products have been adopted by the American Society for Testing and Materials and have clearly been helpful in the overall reduction of protein levels on NRL gloves. Three commercially-available Food and Drug

Administration (FDA)-licensed in vitro tests for predicting latex sensitization, while helpful, remain problematic with relatively low sensitivity and frequent false negative results. Of greater concern is the lack of a FDA-licensed skin test reagent in the U.S. market. It is hoped that the recombinant proteins provide the potential of improved diagnostic and therapeutic reagents.[7]

Donning Powders: Another Factor for Latex Allergy

The starch powders used as donning lubricants were also factors responsible for NRL allergy. Excess donning powder has long been associated with granuloma formation and increased scarring, but was generally considered a necessary evil required to allow glove donning. Although not allergenic, it was recognized early on that glove powder was responsible for the airborne dispersal of the allergenic latex peptides.[8] The manufacturing process of applying the donning powder as a slurry allowed the latex proteins to solubilize and adsorb to the powder prior to drying on the gloves. Snapping on and off latex gloves is a clear visual example of the allergenic powder release that was one factor responsible for NRL sensitization and the major reason for the development of inhalant latex allergy, rhinitis, and occupational asthma. The latex proteins could reliably be measured using immuno-assays and their level in the healthcare environment was quantitatively similar to that reported for other occupational aeroallergens.

An important lesson was that, with latex allergy, everything was not always readily apparent. The clinical manifestation of contact allergy was thought to be the sole clinical syndrome caused by rubber hypersensitivity. Latex was not previously recognized as being capable of stimulating an IgE-mediated allergic response. The exponential increase in the prevalence of latex allergy in the 1990s was alarming but this epidemic helped us to better understand other types of IgE-mediated allergy. Because of latex allergy, we now clearly recognize that cutaneous allergen exposures can produce specific IgE antibody responses and adverse systemic allergies.[9]

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Related Food Allergies

An interesting development with latex allergy was the emergence of new food allergies, particularly to banana, avocado, kiwi, and chestnut.[10] These allergies, previously rare, increased in frequency with the emergence of NRL allergy. Further studies have confirmed cross-reactivity between *Hevea brasiliensis* defense-related proteins and certain proteins common to these foods. This demonstrated that there are pan-allergens present in seemingly unrelated exposures, and with the development of NRL allergy came the emergence of these new food allergies, some of which caused severe anaphylactic shock. With the relative disappearance of latex allergy, there was a concomitant decline in the incidence of these specific food allergies.

The Elimination of Latex Allergy

The practical application resulting from the latex allergy research was that, by identification and study of the factors responsible for NRL allergy, came the knowledge of how to deal with and eliminate latex sensitization. Latex allergy appeared with the implementation

of universal precautions, important measures to reduce the risk of blood-borne pathogen exposure, but which resulted in greater latex allergen exposure and subsequent development of NRL allergy. Following the identification of these factors and understanding the causes, government policies and hospital guidelines were developed and nationwide educational initiatives

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and support groups promoted the use of only low-protein, powder-free gloves and the elimination of unnecessary latex exposure. An important contributing factor involved industry voluntarily lowering the protein content and thus exposure to the NRL allergens. Significant research and

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development work by manufacturers resulted in a choice for gloves made with new synthetic polymers that do not have naturally-occurring proteins associated with them. Together these major interventions were responsible for the significant decline in exposure and reduction in NRL allergy in recent years.[11]

Today, most latex-sensitized healthcare workers can be accommodated in the "new" latex-allergen-safe environment. Low-protein, powder-free gloves dominate the market and have drastically reduced exposure in the healthcare setting. Early intervention promoted by the Spina Bifida Association with the complete elimination of latex exposure for children requiring multiple surgeries from birth has resulted in these children no longer developing latex allergies. Studies that were done to document and measure sources of aerosilized latex exposure identified the high-risk areas as operating rooms, intensive care units and emergency units. Hospital personnel had to grapple with the problem of adapting to new types of disposable medical gloves. Non-powdered gloves were different and often surgeons found it difficult to change. However, with the removal of the glove powder and lowering the protein levels on latex gloves came the opportunity to remove a significant exposure and offer hospital workers and patients a latex-safe environment.

The use of the low-protein, powder-free latex gloves has had a very significant impact on latex sensitization.[11] The ability to identify and understand the needs of latex-allergic patients prior to surgery has allowed the use of latex-safe precautions. These primarily involve the use of non-latex gloves, and removal of any latex device with significant patient contact from the operating room. It is necessary for allergic healthcare workers to only wear non-latex gloves. There remains a high risk for anaphylactic reactions in patients with unrecognized latex allergy who have surgery. It is important for all surgical personnel to recognize latex allergy and identify patients at risk to prevent these potentially fatal consequences of allergic reactions.

Lessons learned in latex allergy start from the early recognition of at-risk individuals, significant allergen identification and reduction

interventions. Further cooperative studies will enable us to better understand the problem. Strategies to deal with the major factors responsible have allowed us to control and maybe eliminate latex allergy. However, we should not let our guard down. We have to be vigilant in identifying other new sources of exposures and deal with these. For example, the widespread use of latex gloves by food handlers has to be stopped.

Conclusion

Latex allergy has influenced everyday medical practice, healthcare policy decisions and industry modifications, which were necessary to deal with this rapidly growing disease. A recent study of latex-allergic patients clearly demonstrated a decline in latex sensitization. This was partly due to the decline in levels of the allergenic proteins on gloves. However, in some patients, latex allergy disappeared with a conversion to a negative in-vivo- and in-vitro-specific IgE test. This is another area where latex allergy research can enter into an area of the unknown. The natural history of allergic diseases is largely unknown. With the removal of the major source of sensitization, the next decade may witness the continued decline and disappearance of latex allergy. However, it must be stressed that present-day avoidance precautions are still mandatory in all latex allergic patients.

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The findings in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

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