Latex Allergy: Where Are We Now and How Did We Get There?

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Latex allergy emerged as an epidemic of anaphylaxis, occupational asthma, and clinical dilemmas in the 1980s. A systematic recognition, investigation, discovery, epidemiology, and prevention strategy followed. International attention and collaborations of investigators, government agencies, manufacturing, and health policy resulted in near elimination of a global epidemic. This article summarizes nearly 4 decades of work in control of this epidemic and focuses attention on future problems that still require resolution. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;5:1212-6)

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Nearly 4 decades have passed since the first modern case of IgE-mediated natural rubber latex (NRL) allergy was reported.[1] Subsequently, a worldwide epidemic of allergy and anaphylactic reactions to NRL proteins emerged, was systematically investigated, and nearly eliminated. Persistent sensitization is observed, and occasional new sensitization occurs as well.

Epidemics are frequently first recognized by astute clinicians who recognize a new constellation of signs and symptoms in patients that are not explained by known exposures or vectors. Latex allergy resolution represents a notable collaboration of medical clinicians, researchers, manufacturers, the Centers for Disease Control and Prevention, the National Institute of Occupational Safety and Health (NIOSH), and the Food and Drug Administration to control an epidemic. This global collaboration of multiple research groups proceeded with synergy between the United Kingdom, Europe, Scandinavia, Canada, the United States, Southeast Asia, Japan, Australia, and South America. At its peak, up to 17% of health care workers (HCWs) had become sensitized to latex, compromising their ability to work in the health care industry,[2] as had 70% of all patients with spina bifida[3] who were at risk of death during surgical operations and daily care of their medical conditions. Today, we see less than 1% of the population developing latex allergy.[4-6]

THE EPIDEMIC

During the 1980s to 1990s, the risk of sensitization to NRL became very high for HCWs, patients with spina bifida, genitalurinary tract anomalies, and neurologic defects, patients requiring multiple surgeries, atopic individuals, and workers in industries that manufactured rubber products.[7-18]

In 1927, a single case of chronic urticaria from rubber prosthetics was reported in Germany.[19] Fifty years passed until a second case of latex allergy was confirmed by dermatitis, urticaria, and pruritus in a homemaker to rubber gloves.[1] In the 1980s, latex allergy—induced rhinitis, asthma, and ocular symptoms in HCWs were identified by various authors in Europe. The growing prevalence of sensitization to latex in 2.9% of HCWs was confirmed in Finland. Indeed, operating room personnel were found to have the highest prevalence at 6.2% with a very strong association with atopic predisposition.[20]

In the same year, 5 individuals were reported with systemic reactions to latex gloves, but only 1 was an HCW.[21] It was not until 1989 that the first cases of occupational asthma to latex were reported.[22] Until that time, mucosal reactions of conjunctival irritation and rhinitis were believed to have come from direct allergen transfer. These sentinel case reports started to confirm an understanding that the environment was being contaminated by allergen-carrying glove powder.

In 1989, 2 children with spina bifida suffered anaphylactic reactions during surgery. Following an evaluation that excluded other causes and confirmed the presence of latex-specific IgE, these reactions were attributed to intraoperative latex exposure.[23] It was not until 1991 that investigators in the United States working with the Centers for Disease Control and Prevention identified a marked increase in anaphylactic reactions during surgical procedures.[24] This identification took place in Canada as well as the United States with distinctly different clinical scenarios.[25] In one case series, all the children had developed allergic reactions during the induction of anesthesia, whereas in the other case series mucosal contact with rubber gloves occurred intraoperatively.[3] The episodes of anaphylaxis in the operating room reached a heightened level in 1991 in the United States when in one hospital 1 out of every 8 patients with spina bifida developed anaphylaxis during induction of anesthesia, representing a 500-fold higher rate of anaphylaxis than expected from general

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anesthesia. The study identified that 100% of these patients had latex allergy.

A subsequent follow-up study of the prevalence of latex allergy found that nearly 70% of all patients with spina bifida in one center were skin test positive to latex allergens; skin prick testing with a glove extract caused not only local reactions, but some systemic reactions as well.[7] The risk factors identified during this period of time for sensitization to latex included atopy, multiple surgeries, rectal mucosal contact from latex gloves for bowel disimpaction, and skin test reactivity to some fresh fruits.

Other patients with urologic, neurologic defects, or multiple surgeries

In addition to patients with spina bifida, individuals who had other multiple surgeries,[8] especially those with cloacal anomalies, were experiencing anaphylactic reactions in the operating room. In addition, children with other congenital anomalies such as esophageal atresia, gastroschisis, omphalocoele, and neurologic disease such as cerebral palsy may have a higher prevalence of latex allergy.[8] Patients with spinal cord injuries became the natural control group to study to see whether they were also at risk for developing latex allergies. Conflicting results, probably because of small study size, demonstrated that other neurologic injuries, such as spinal cord injury, were not a significant risk for the development of latex allergy.[12] However, a second study found approximately 15% sensitization rate, but a 4% clinical reaction rate.[13]

Health care workers

Clinical manifestations of latex allergy in HCWs were unique. Most were found to have an irritant or contact hand dermatitis when they wore gloves, with this predicting symptoms of latex allergy 11 times more frequently than those who did not have dermatitis.[26] In 1 hospital 17% of HCWs were found to be sensitized to latex and 50% of these individuals appeared to have respiratory asthma like symptoms from exposure to gloves in their work environment.[2] In fact, many individuals were having clinical reactions on entering the operating room or other medical parts of the facility without specifically donning latex gloves for personal use.

Patients with type 1 diabetes mellitus

Another group of patients described with latex allergy were type 1 diabetics using rubber-topped insulin bottles. These were punctured repetitively and some patients developed latex allergy. These observations resulted in concerns about medications delivered to latex-allergic individuals.[27-31]

General populations

To confirm that the risk groups were limited to the subsets of the patients, prevalence studies were undertaken in the general population. Approximately 1% (range, 0.7%-1.1%) were found to have sensitization to latex.[4,5] Interestingly, in the early 1980s, another epidemic of anaphylaxis occurred with up to 148 episodes of anaphylaxis and 9 deaths associated with rectal mucosal exposure to an air contrast barium enema catheters that had a latex-tipped balloon.[32] Only in retrospect does it appear that these were patients sensitized to latex who were exposed to rectal balloons through manometry or barium retention enemas.[33] It appears that many of those subjects were not HCWs and did not have specific risk factors. There is a risk, albeit not a high prevalence risk, in the general population for the development of latex allergy in some individuals.

Why did the epidemic occur and how was it controlled?

The emergence of the latex allergy epidemic resulted from a confluence of several changes in health care delivery. The emergence of human-to-human transmission of infectious pathogens such as hepatitis C and HIV resulted, in 1987, in the promotion of Universal Precautions to protect workers from acquisition of disease. These precautions have now become known as "Standard Precautions" but resulted in a massive increase in the use of latex examination gloves in health care and other industries (eg, food handling). Before the implementation of these precautions, approximately 300 million units of examination gloves were sold in the United States but by the end of the 1990s, this had risen to approximately 36 billion units of examination gloves for a more than 100-fold rise in volume.[34]

In addition, a change to the use of cornstarch donning powder from talc inadvertently may have created an extremely efficient carrier of latex allergens to skin and airborne environments.

Additional speculation suggested that before the implementation of standard precautions, NRL harvested at rubber tree plantations was stored for up to 6 months before being used in the manufacturing process. That prolonged storage may have resulted in degradation of protein allergens. With purchasing pressure for latex gloves in the health care industry, that storage time may have declined to as little as 2 weeks, resulting in a possible higher content of allergen entering the finished latex product.[34]

Regardless of the other contributing causes, increased exposure to NRL glove allergens was the common factor that paralleled the rise in the prevalence of the disease. Sentinel occupational work in Germany by Allmers et al,[35] latex avoidance from birth for patients with spina bifida,[36] and 2 critical incidence studies from Canada[15] and the United States[37] resulted in the identification of powdered latex examination gloves as the causative agent for the epidemic. A change to nonpowdered latex and synthetic examination gloves dramatically reduced sensitization. More importantly, the US study from Wisconsin demonstrated that 25% of sensitized HCWs lost evidence of skin test reactivity after occupational avoidance of powdered latex gloves.

Simultaneously, latex precautions[36] promoted by the American Academy of Asthma, Allergy & Immunology, the American College of Asthma, Allergy & Immunology, and the Association of Operating Room Nurses in the United States resulted in safer care of patients with latex allergy. NIOSH also adopted these measures and produced an alert for use by health care professionals in 1998.[38] However, it was the scientific and epidemiology work across the globe that resulted in a final understanding that the latex allergen content of gloves and environmental contamination through the air of allergen carried by cornstarch powder was the cause of the epidemic. This finally resulted in the Food and Drug Administration banning the sale of powdered surgeon gloves, powdered patient examination gloves, and absorbable powder for lubrication of surgeons gloves in the United States in January 2017 that should keep this disease under control.