

A comparative analysis of latex allergy in the healthy versus high-risk pediatric population

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Allergic or hypersensitivity reactions to natural latex have been reported with increasing frequency. Many specific populations have been identified as high risk for latex sensitivity. This research focused on the pediatric surgical population. Previous research had identified children with spina bifida, children requiring bowel or bladder programs, children with a history of atopy, and children with multiple surgical exposures as high risk.

The purposes of this study were to identify the prevalence of latex sensitivity in the healthy pediatric population, to compare the incidence with that of an identified high-risk population, and to determine if a survey of known risk factors for latex sensitivity was predictive of positive serum latex antibody.

This was a prospective, descriptive correlational study utilizing a convenience sample size of 400 pediatric patients aged 1 to 18 years, conducted at Henry Ford Hospital and Children's Hospital of Michigan. Children were identified as high or low risk from the survey results, and all had AlaSTAT latex allergy testing (Diagnostic Products Corporation, Los Angeles, Calif). The survey was not predictive for the positive serum latex antibody. The incidence of latex sensitivity was found to be greater in the high-risk group (17.3%) than in the general pediatric population (8.6%) using the χ^2 test ($P = .01$).

Latex-reduced environments for children likely to have repeated latex exposure may decrease the risk of reaction and more importantly decrease sensitization for them. From an anesthetic standpoint, a fairly standard preoperative question is, "What are the number and types of surgeries a patient has undergone in the past?" This information can alert the healthcare worker to how much exposure the child has had and whether a latex-reduced environment might be required to avert a latex reaction.

Key words: Latex allergy, myelodysplasia, pediatrics, spina bifida.

Introduction

Latex allergy has become an increasingly serious concern for the public and healthcare providers. Nutter first described latex allergy in 1979 as a contact dermatitis.¹ Latex-sensitive individuals have experienced reactions that range from minor contact dermatitis to life-threatening anaphylaxis.

Latex is the milky white liquid produced by the laticifer cells of the *Hevea brasiliensis* tree. Small globules of natural rubber are suspended in this milky liquid. Latex is composed of acetone-soluble material (resins, fatty acid, etc), protein, ash, water, and cis-1,4-polyisoprene, or tiny globules of rubber. During the manufacturing process, various chemicals are added to give rubber many of its desirable qualities. Vulcanization is the process of treating rubber with heat and sulfur, resulting in cross-linkage formation of the polyisoprene molecules and thickening of the material. This gives natural rubber

elasticity, strength, and stability. The final product contains between 2% to 5% protein antigens, which can trigger the IgE-mediated reactions. Individuals who have a latex allergy have developed IgE antibodies specific to many peptides of the *Hevea brasiliensis* tree.²

The added chemicals are considered to be responsible for the contact dermatitis-type reactions seen with exposure to latex. Not until 1987 did Axellsson et al³ report urticaria, asthma, and anaphylaxis to rubber. Means and Rescorla⁴ state that repeated exposure to latex antigens leads to production of specific IgE antibodies that are bound to receptors on mast cells and basophils. With subsequent exposure, latex antigens bind with IgE antibodies, causing mast cell and basophil activation with release of histamine and chemotactic factors of anaphylaxis (leukotrienes, prostaglandins, kinins, and platelet-activating factors).

The reason for the sudden increase in reports of latex reactions is unknown. The institution of universal precautions increased the use of latex gloves, resulting in sensitization of more people. The true incidence of anaphylactic reactions to latex may have been underestimated because mild reactions often go unrecognized, urticaria may not be noticed under the surgical drapes, or providers may fail to include allergy to latex in the differential diagnosis.

This research focused on the pediatric surgical population. Previous research had identified children with histories of spina bifida, bowel or bladder programs, atopy, multiple surgical exposures, and certain food allergies as high risk. Results of a study by Moneret-Vautrin⁵ showed that children with spina bifida who also had a history of atopy demonstrated a greater percentage of positive skin prick tests than the children with spina bifida who were without the atopic history. Frequent exposure to latex increased the likelihood of sensitivity from 0.37% to 6.85% in the nonatopic group and from 9.44% to 36.4% in the atopic group. A history of atopy greatly increased the likelihood of sensitivity to latex, from 6.85% to 36.4% ($P < .001$).

Meeropol et al⁶ compared 185 patients with spina bifida with a control group of 87 patients with orthopedic or other neuromuscular conditions. The results demonstrated that children in the spina bifida group exhibited a higher incidence of latex allergy (20.4%) than those in the control group (1.1%). Gold⁷ identified 15 children with either spina bifida or congenital urologic abnormalities who had intraoperative anaphylaxis. All

were exposed to rubber products since infancy as part of their medical management. All had positive skin tests and a positive radioallergosorbent test (RAST) to latex allergen. Gold concluded that this group was at risk when they were exposed to latex intraoperatively because of their history of frequent exposure to these materials. Porri et al⁸ compared a group of patients with spina bifida with a group of patients without spina bifida who had undergone multiple surgical procedures, and a control group who had undergone zero or 1 surgical procedure. It was concluded that the amount of exposure to latex was implicated in latex sensitization, not spina bifida.

One problem encountered with the in vitro and in vivo testing has been the crossreactivity between latex and foods such as bananas, avocados, chestnuts, and kiwi. Ross et al⁹ reported that 10 of 12 sera that had a banana-specific IgE also demonstrated a positive enzyme-linked immunosorbent assay (ELISA) for latex-specific IgE. The crossreactive antibodies are not clearly understood, but it is speculated that an individual with crossreactive IgE antibodies will react to any of the allergens upon exposure. Blanco et al¹⁰ performed a prospective study to determine the clinical features of latex-allergic patients and latex-associated food hypersensitivities. Twenty-five patients with latex allergies were asked about history of allergies, and total and specific IgE antigens were obtained through RAST inhibition and Pharmacia Immucap/RAST (Pharmacia Diagnostics, Sweden) methods. Fifty two percent displayed immediate hypersensitivity to foods. The most common hypersensitivities were avocados, chestnuts, bananas, kiwi, and papaya.

Identification of children with latex sensitivity as either high or low risk in this study was obtained via the AlaSTAT assay (Diagnostic Products Corporation, Los Angeles, Calif). The assay uses a soluble allergen matrix to absorb the allergen-specific IgE, which once bound is insolubilized by streptavidin bridging between biotin coupled to the matrix and biotin coating the assay tubes. A comparison study by Ownby and McCullough¹¹ tested 52 sera using AlaSTAT, ELISA, and RAST. With the AlaSTAT, preproduction lots manufactured using the Food and Drug Administration latex extract E2 were used. Two lots were used, one with the latex extract coupled with hydroxyl linkages and the other coupled with amino linkages. Of the 52 sera, 50 or 96% were positive for latex-specific IgE using the amino-coupled matrix and 69% positive in the hydroxyl-

coupled matrix. RAST identified 26 of the 52 or 50% positive, and ELISA identified 13 of the 52 or 25% positive. It also is important to note that the presence of IgE antibodies, or a positive test result, only shows that sensitization has occurred, therefore, a reaction may or may not occur upon exposure. Stuckey et al¹² estimated that approximately 8.5% of known latex-sensitive individuals reacted with exposure.

The purposes of this study were 2-fold: (1) to determine the incidence of latex sensitivity in the general pediatric population and compare this with pediatric patients who are considered high risk, and (2) to determine whether a survey of known risk factors for latex sensitivity would predict positive serum latex antibody results.

Methods and materials

This study was approved by Henry Ford Hospital and Children's Hospital of Michigan institutional review boards. Four hundred children were enlisted after written informed consent was obtained from the parents and, if at an appropriate age, the child. All participants were between the ages of 1 and 18 years and were scheduled for surgery.

The parents and children were interviewed using the pediatric latex survey designed for the study (Figure 1). Routine anesthetic care was provided unless a child was predetermined to be latex sensitive and was provided a latex-free environment. Blood samples were obtained preoperatively or after induction, depending on the age and psychological presentation of the child. Each sample was transferred to Henry Ford Hospital Allergy Research Laboratory for IgE determination using the AlaSTAT latex allergy test.

AlaSTAT is a liquid phase immunoassay for the detection of circulating latex IgE antibodies. Each sample was measured and recorded in International Units according to Table. Repeat testing was done on all positive and questionable results. Children whose test results demonstrated the presence of latex IgE antibodies were placed in class I or greater, and those with the absence of IgE antibodies were placed in class 0. In the event of a positive test, a notification letter was sent to the parents.

Children were placed in high- or low-risk groups based on information obtained from the survey before laboratory analysis. Based on literature review, children were considered high risk if they reported history of myelodysplasia, congenital urological problems, 3 or more previous

Figure 1. Pediatric survey for latex allergy

Age: _____	Weight: _____
Male/Female: _____	
Address: _____	City: _____
Zip code: _____	Level of education: _____
Are there any known allergies to any of the following?	
Medications	Yes/No
Rubber or latex	Yes/No
Pollen, dust, grass, or other environmental allergens	Yes/No
Does your child have eczema?	Yes/No
Does your child have asthma?	Yes/No
Does your child get a rash, watery eyes, itching, or swelling after eating any of the following?	
Bananas:	Yes/No
Kiwi:	Yes/No
Papaya:	Yes/No
Chestnuts:	Yes/No
Avocado:	Yes/No
Does any family member have a rubber or latex allergy?	Yes/No
Does any family member have a history of other allergies?	Yes/No
Was your child born early?	Yes/No
If so, how many weeks early? _____	
Was your child hospitalized overnight?	Yes/No
If so, how many days? _____	
Has your child undergone any surgeries?	Yes/No
If so, how many? _____	
Does your child require catheterization for urine?	Yes/No
If so, how many times per day? _____	
Does your child have any of the following problems?	
Myelomeningocele/meningocele/myelodysplasia	Yes/No
Bladder or bowel problems	Yes/No
History of shunt insertion	Yes/No
Cerebral palsy	Yes/No
Spinal cord injury	Yes/No
Cleft lip and/or palate	Yes/No

surgical procedures, asthma, atopy, or previous reactions to latex.

The χ^2 test was used to determine if a statistically significant difference in the incidence of

Table. AlaSTAT Interpretation

Class	IU/mL	Interpretation
0	0.000-0.29	Negative for latex allergen
0/I	0.30-0.34	Equivocal
I	0.35-1.49	Positive for latex allergen
II	1.50-2.99	Strongly positive
III	3.00-14.99	Strongly positive
IV	15.0 and over	Strongly positive

AlaSTAT results were computed in international units per milliliter of blood. A positive result was classified as 0.35 or greater IU/mL as depicted on the table.

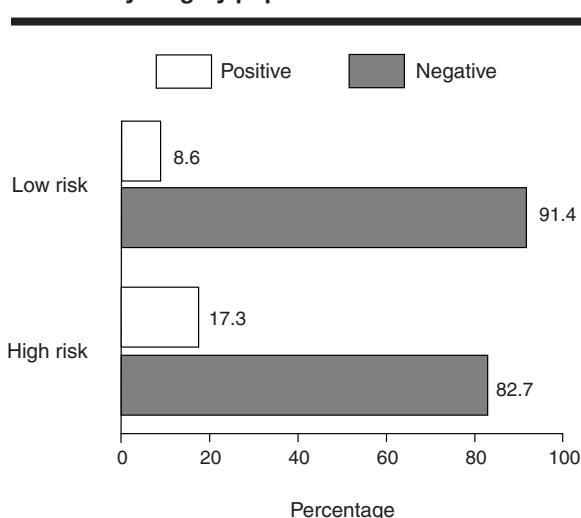
latex allergy existed between the 2 groups. The χ^2 test was used to compare the groups on sex, and the groups were compared on age and weight using the Student *t* test. Based on a review of the literature, risk factors or variables were identified that would most likely predict latex sensitivity.^{6,10,13,14} These were then used to develop the survey. To determine the ability of the survey to predict latex sensitivity, as confirmed by the AlaSTAT results, a logistic regression was performed. These risk factors also were analyzed using Fisher exact and Student *t* tests. SPSS/Windows 6.0 (SPSS, Inc., Chicago, Ill) and Number Cruncher Statistical System (NCSS Software, Kaysville, Utah) statistical software were used to aid in the statistical computation.

Results

In the study sample, the incidence for latex-specific IgE antibodies in the general pediatric population was 8.6%, compared to the high-risk group in which the incidence was 17.3% ($P = .01$). A comparison of the groups is depicted in Figure 2. The 2 groups did not differ in sex ($P = .88$), age ($P = .13$), or weight ($P = .50$).

Survey questions that were previously shown to be associated with a higher incidence of latex allergy also were analyzed in this study.^{6,10,13,14} A known allergy to latex, a history of 3 or more surgeries, a history of bowel and/or bladder problems, and a history of spina bifida all showed a significantly greater incidence of latex allergy than the group that was negative for these factors ($P < .01$). Children with a history of asthma did not show a greater incidence of latex allergy ($P = .69$).

To determine the ability of the survey to predict latex sensitivity, as confirmed by the AlaSTAT results, a logistic regression was per-

Figure 2. Incidence of latex sensitivity in the ambulatory surgery population

formed. A model was constructed specifying a combination of independent (predictor) variables significantly related to the likelihood of a positive blood test for latex allergy ($P < .0001$ for the model). The model included the predictor variables (all *yes* or *no* type variables): sex, medication allergy, rubber allergy, environmental allergy, eczema, asthma, balloon allergy, family allergy, family rubber allergy, prematurity, spina bifida, bladder program, shunt insertion, cerebral palsy, cleft lip, and 3 or more surgeries. The survey correctly classified 79.6% of the patients testing positive and 69.3% testing negative ($P < .0001$).

Two variables from the regression achieved statistical significance. A positive blood test was 3.7 times more likely if that patient had a family history of latex allergy ($P < .03$). Patients with cerebral palsy were 5.34 times more likely to have a positive blood test for latex allergy ($P < .003$).

Discussion

Children who were classified as high risk by the survey were shown to have a higher incidence of latex sensitivity than the general pediatric population. A previous study in the same institution demonstrated a lower incidence of latex allergy in the adult outpatient surgical population, 67 of 1,000 subjects (6.8%),¹⁴ while another study by Ownby et al showed a 6.4% incidence in 1,000 volunteer blood donors.¹⁵

Although these earlier studies demonstrated that younger patients were more likely to test positive for latex allergy, neither Lebenbom-

Mansour et al¹³ or Ownby et al¹⁵ speculated as to why this was found. The higher incidence within the pediatric population suggests that younger patients are more likely to test positive than adult patients. Healthcare workers are facing a growing population of latex-positive individuals. Future studies might examine the sources and amount of latex exposure people are receiving, since identifying and limiting latex exposure theoretically should help control the increasing incidence of latex sensitivity.

Predictors of sensitivity to latex included the following variables: sex, medication allergy, rubber allergy, environmental allergy, eczema, asthma, balloon allergy, family allergy, family rubber allergy, prematurity, spina bifida, bladder program, shunt insertion, cerebral palsy, cleft lip, and 3 or more surgeries. The regression analysis showed that the survey correctly classified 79.6% of the children with positive results and 69.3% of the children with negative results. Two of the variables in the model showed independent significance: a history of cerebral palsy and a family history of latex allergy. Overall, the survey was not a significant predictor of positive latex antibody results.

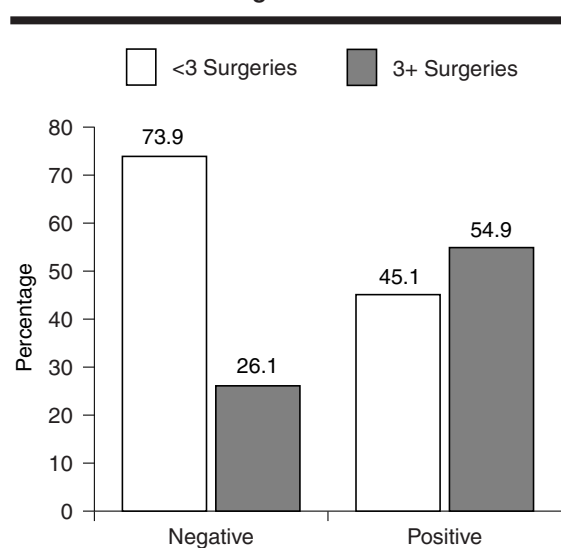
A history of allergy to latex was a significant finding in this study. If a child already is known to have an allergy to latex, it makes sense that the child has antibodies present and will have a positive blood test. This also supports the findings by Lebenbom-Mansour et al,¹³ who also found a history of latex allergy to be a significant predictor.

A history of asthma was not a significant predictor in this study. This differs from a previous study at our institution.¹³ In that study, asthma was found to be a significant predictor, as asthmatics were 2 times more likely to have a positive blood test for latex allergy.

Pediatric patients with histories of 3 or more surgeries are significantly more likely to demonstrate a positive AlaSTAT result ($P < .01$). A total of 54.9% of those with 3 or more surgeries tested positive, while 26.1% with less than 3 surgeries tested positive (Figure 3). Descriptively, those children in the high-risk group had a mean of 5.6 surgeries, while those who tested negative had a mean of 0.4 surgeries. This supports the finding of Porri and associates.⁸ However, Lebenbom-Mansour et al did not find the number of surgeries to be a significant predictor. The mean number of surgeries for patients who had positive AlaSTAT results was 3.5 plus or minus 3.1, and the mean number for those with negative AlaSTAT results was 3.3 plus or minus 3.7.¹³

A history of spina bifida (myelomeningocele,

Figure 3. AlaSTAT results for children with or without 3 or more surgeries



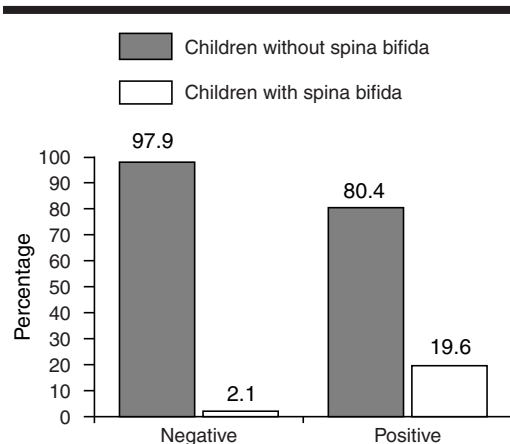
Out of the children who demonstrated a positive AlaSTAT result, 54.9% had 3 or more surgeries, while of those who tested negative, 26.1% had 3 or more surgeries.

meningocele, myelodysplasia) was shown to be a significant predictor (Figure 4), confirming research by Meeropol et al.⁶ Comparing children born with spina bifida who are placed on latex precautions from birth with those who are not placed on latex precautions could determine whether the disease process or the amount of latex exposure is the cause of latex sensitivity. However, since exposure is most likely the cause of sensitization, the standard of care for these patients may soon be latex precautions at all times.

A history of bowel/bladder problems was found to be a significant predictor in this study. Lebenbom-Mansour et al¹³ found that there was no significance shown for the development of latex sensitization from urinary tract abnormalities, self-catheterization, the number of surgical procedures, or on-the-job exposure. This is a surprising finding that suggests further studies are needed to compare the amounts of exposure with the incidence of latex sensitivity.

The majority of research on latex allergy has been conducted in the adult population. This research focused on the pediatric population. A significant incidence was demonstrated in both high- and low-risk pediatric patients. Identification of a reaction needs to be immediate, followed by prompt treatment.

Figure 4. AlaSTAT results for children with or without spina bifida



In the children who tested positive for latex sensitivity, 19.6% did have spina bifida as compared with the children who tested negative, 2.1% had spina bifida.

Latex reactions can be life threatening, making enhanced awareness essential. In addition to monitoring for an unannounced reaction, the healthcare worker must be alert for significant variables in a child's history. Previous latex allergic reaction, spina bifida, cerebral palsy, multiple surgical procedures, and a positive latex allergy in the family were associated with latex sensitivity. Latex-free environments may prevent latex allergic reactions and decrease the rate of sensitization of patients who have not yet developed an allergy. Critical analysis of standards of care may lead to the elimination of latex from the healthcare environment.

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