Letters

LATEX AS A SIGNIFICANT SOURCE OF *HEVEA BRASILIENSIS* ALLERGEN EXPOSURE

The prevalence of allergic reactions to *Hevea brasiliensis* natural rubber latex among high-risk health care workers and patients undergoing multiple surgical procedures has diminished from epidemic levels in the mid-1990s. This decrease is attributed to avoidance of powdered latex medical gloves[1] and improved quality control in the manufacturing process. However, sensitization to *Hevea* allergens continues through exposure to less well-established sources. To document this phenomenon, we used 3 standardized methods approved by the American Society for Testing Materials (ASTM) to quantify the total protein (ASTM Standard Test Method for Analysis of Aqueous Extractable Protein in Natural Rubber and Its Products Using the Modified Lowry Method, 2005), *Hevea* antigen (ASTM Standard Test Method for the Immunological Measurement of Antigenic Protein in Natural Rubber and Its Products, 2007), and *Hevea* allergen (ASTM Standard Test Method for Immunological Measurement of Four Principal Allergenic Proteins [*H brasiliensis* 1, 3, 5, and 6.02] in Natural Rubber and Its Products Derived From Latex, 2008 [D7427–08]) content in natural rubber latex toy balloons, dental dams, medical gloves, and nitrile and guayule medical gloves (negative controls). Although previous studies examined allergen/antigen content in rubber medical products,[2–4] this study simultaneously investigated *Hevea* levels in balloons, dental dams, and glove products using the 3-tier ASTM test protocol.

A single extraction method (2 hours at 25°C using saline, 0.1 g/mL, with agitation) was used to facilitate comparisons among the 3 assays. Table 1 lists the commercially available *Hevea* latex toy balloons, dental dams, examination gloves (3 powdered and 4 powder free), powder-free *Hevea* surgical gloves, and nitrile and guayule examination gloves evaluated in the study. The balloons and dental dams had a broad range of total protein, *Hevea* antigen, and *Hevea* allergen levels. ASTM standard specifications (D3577 and D3578) recommend a limit of 200 and 10 $\mu g/dm^2$, respectively, for antigenic protein content on latex surgical and examination gloves. Although limits for *Hevea* allergen levels in rubber products have not yet been established using the new ASTM allergen assay, a health-based *Hevea* allergen threshold of 2 $\mu g/g$ (approximately 2.5 $\mu g/dm^2$) for latex gloves (eg, < 0.5 ng/m^3 of air) has been proposed to minimize hypersensitivity reactions.[5] Two balloon sources and all the natural rubber latex dental dams were at or above the 200 $\mu g/dm^2$ limit, whereas 2 others approached the limit. The balloon with the highest level of total protein (307 $\mu g/dm^2$, balloon 1) had the highest levels of antigen (112 $\mu g/dm^2$) and allergen (27.5 $\mu g/dm^2$).

There was no detectable protein, antigen, or allergen in extracts of nitrile or guayule rubber gloves or synthetic dental dam (negative controls). Guayule (*Parthenium argentatum*) is a shrub that produces a latex with essentially no extractable protein or cross-reactivity to known *Hevea* allergens.[6,7] *Hevea* gloves in this study were segregated into powder-free surgical gloves with the lowest level (range, 0.09–0.62 $\mu g/g$) and powdered examination gloves with the highest level (range, 6.38–13.66 $\mu g/g$) of allergen. Surprisingly, several powder-free *Hevea* examination gloves had unacceptably high levels of *Hevea* allergen (range, 0.03–6.10 $\mu g/g$).

A wide range of *Hevea* allergen was detected in the toy balloon sources (range, 0.21–16.73 $\mu g/g$). Certain manufacturers (eg, B, E, and F in Table 1) produced balloons with consistently low levels of allergen across their different product lines, whereas others (eg, C in Table 1) produced balloons consistently with the highest levels of protein, *Hevea* antigen, and allergen detected. The manufacturing process for natural rubber latex balloons varies among manufacturers in terms of the number of water-leaching steps used and, thus, the level of residual allergenic protein. Previous reports have shown that toy balloons contained significant levels of allergen,[8,9] and our data confirm that toy balloons continue to represent a major unappreciated source of *Hevea* allergen exposure. This is especially troubling because balloons are marketed to the general public, including children. Surprisingly, the *Hevea* product with the highest level of allergen in all 3 assays were the dental dams that are used to isolate teeth for dental procedures. Direct mucosal contact with such high allergen levels can lead to sensitization as a result of repetitive exposure. Allergists should remain vigilant when collecting a clinical history from individuals suspected of being sensitized to natural rubber latex and should ask about possible inadvertent exposures from less obvious sources, such as toy balloons and dental dams.

DAVID KOSTYAL, PHD*
KELLY HORTON, BS*
DONALD BEEZHOLD, PHD†
SUZANNE LOCKWOOD, CST‡
ROBERT G. HAMILTON, PHD§

*Guthrie Foundation for Education and Research
Sayre, Pennsylvania
†National Institute of Occupational Safety and Health
Centers for Disease Control and Prevention
Morgantown, West Virginia
‡American Latex Allergy Association
Slinger, Wisconsin
§Johns Hopkins University School of Medicine
Baltimore, Maryland
kostyal_david@guthrie.org

1. Hamilton RG, Brown RH. Impact of personal avoidance practice on healthcare workers sensitized to natural rubber latex. *J Allergy Clin Immunol.* 2000;105: 839–841.
2. Palosuo T, Alenius H, Turjanmaa K. Quantitation of latex allergens. *Methods.* 2002;27:52–58.
3. Jones RT, Scheppmann DL, Heilman DK, Yunginger JW. Prospective studies of extractable latex allergen contents of disposable medical gloves. *Ann Allergy.* 1994;73:321–325.
4. Beezhold DH, Pugh B, Liss G, Sussman GL. Correlation of protein levels with skin prick reactions in latex allergic patients. *J Allergy Clin Immunol.* 1996;98:1097–1102.
5. Baur X. Are we closer to developing threshold limit values for allergens in the workplace? *Ann Allergy Asthma Immunol.* 2003;90:11–18.
6. Siler DI, Cornish K, Hamilton RG. Absence of cross-reactivity of IgE antibodies

Disclosures: Authors have nothing to disclose.

Funding Sources: This study was funded by Johns Hopkins University School of Medicine.

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

Table 1. Protein, Antigen, and Allergen Levels in Test Products[a]

Source code	Specimen descriptor	Total protein assay 5712–05		Latex antigen assay 6499–07		Latex allergen assay 7427–08		Description of product
		Result in μg/g	Result in μg/dm²	Result in μg/g	Result in μg/dm²	Result in μg/g	Result in μg/dm²	
A	NRL toy balloon A	125	200	6.6	10.5	1.51	2.41	11-in 5300 Fashion Assorted latex balloons
B	NRL toy balloon B	<42	<60	1.6	2.2	0.43	0.62	3- to 5-in round red latex balloons
	NRL toy balloon C	<42	<63	4.3	6.5	0.64	0.97	2 – 14-in white round latex balloons
	NRL toy balloon D	63	112	3.3	5.8	0.21	0.38	3-in Latex balloons
C	NRL toy balloon E	182	307	67.5	112.0	16.73	27.46	3-in Latex balloons
	NRL toy balloon F	160	175	88.0	96.2	4.42	4.84	2- to 12-in blue round latex balloons
D	NRL toy balloon G	<42	<46	1.1	1.2	1.74	1.92	3- to 5-in silver round latex balloons
E	NRL toy balloon H	<42	<66	1.7	2.7	0.21	0.33	1 yellow standard No. 17 latex balloon
F	NRL toy balloon I	85	93	3.2	3.5	0.62	0.68	2 large white round latex balloons
G	NRL toy balloon J	115	192	2.2	3.6	1.83	3.04	3-in latex balloons
				Negative Controls				
H	Guayule glove	<43	<45	<0.2	<0.2	<0.15	<0.16	Guayule powder-free sterile surgical glove
I	Nitrile glove A	<42	<28	<0.2	<0.1	<0.15	<0.10	Nitrile examination glove
J	Nitrile glove B	<42	<30	<0.2	<0.1	<0.15	<0.11	Nitrile examination glove
K	Dental dam	<42	<45	<0.2	<0.2	<0.15	<0.16	Synthetic dental dam
				Positive Controls				
L	NRL dental dam	560	434	122.4	94.7	50.59	38.86	Thin NRL dental dam
M	NRL dental dam	790	475	148.5	89.7	49.77	30.08	Thin NRL dental dam
N	NRL dental dam	390	266	41.7	28.4	36.69	25.05	Thin NRL dental dam
O	NRL dental dam	265	336	295.6	358.9	43.18	54.44	Thin NRL dental dam
P	NRL-PF examination glove 1	<42	<45	0.3	0.3	0.03	0.03	Powder-free latex examination glove
Q	NRL-PF-PC examination glove 2	83	57	2.9	2.0	6.10	4.19	Polymer-coated, powder-free examination glove
R	NRL-PF-CF examination glove 3	58	37	4.9	3.1	3.88	2.46	Powder-free latex examination glove
S	NRL-PF examination glove	85	79	2.5	2.3	1.21	1.12	Supreme powder-free latex
T	NRL-PF surgical glove 1	<42	<43	1.0	1.0	0.31	0.31	Powder-free latex surgical glove, nitrile coating
U	NRL-PF surgical glove 2	<26	<30	0.9	1.0	0.62	0.73	Powder-free latex surgical glove
V	NRL-PF surgical glove 3	<25	<24	0.3	0.3	0.45	0.44	Powder-free eclipse surgical glove
W	NRL-PF surgical glove 4	<42	<43	1.3	1.3	0.092	0.095	Powder-free latex surgical glove
X	NRL-PW examination glove 1	<42	<27	4.3	2.8	6.38	4.21	Powdered examination glove
Y	NRL-PW examination glove 2	310	198	14.5	9.2	13.66	8.70	Powdered examination glove
Z	NRL-PW examination glove 3	110	63	18.2	10.4	8.69	4.96	Powdered examination glove

Abbreviations: CF, chlorine free; NRL, natural rubber latex; PC, polymer coated; PF, powder free; PW, powdered.

[a] The manufacturers of the latex toy balloons and dental dams evaluated in the study include the following: A, Bellatex, Betallic, St Louis, Missouri; B, Maple City Rubber Company, Norwalk, Ohio; C, Party City Balloons, Park City Corp, Rockaway, New Jersey; D, Pioneer Balloon Company, Wichita, Kansas; E, Standard Mexican Balloons, Unknown Location; F, Unique Industries, Philadelphia, Pennsylvania; G, WalMart Brand Toy Balloons, Bentonville, Arkansas; H, Yulex Corporation, Maricopa, Arizona; I, Kimberly Clark Corporation, Roswell, Georgia; J, Microflex Corporation, Reno, Nevada; K, Hygenic-Non Latex, Akron, Ohio; L, Henry Schein, Melville, New York; M, Isolate, Endodontic Technologies, Great Britain; N, Hygenic (NRL), Akron; O, Coltene/Wholedent, Cuyahoga Falls, Ohio; P, Digitcare, Los Angeles, California; Q, Cypress Medical, McHenry, Illinois; R, SGMP Corporation, Amphur Rattaphum, Thailand; S, Siam Sempermed, Pathong Hatyai, Thailand; T, Cardinal Health, Dublin, Ohio; U and V, Biogel USA, Norcross, Georgia; W, Fabrica De Artefatos, Sao Roque, Brazil; X, Unknown; Y, Siam Sempermed; Z, SGMP Corporation. The formal names of the assays used are as follows: D5712–05, ASTM Standard Test Method for Analysis of Aqueous Extractable Protein in Natural Rubber and Its Products Using the Modified Lowry Method, 2005; 6499–07, ASTM Standard Test Method for the Immunological Measurement of Antigenic Protein in Natural Rubber and Its Products; and 7427–08, ASTM Standard Test Method for Immunological Measurement of Four Principal Allergenic Proteins (H brasiliensis 1, 3, 5, and 6.02) in Natural Rubber and Its Products Derived From Latex, 2008.

from *Hevea brasiliensis* latex allergic subjects with a new source of natural rubber latex from guayule (*Parthenium argentatum*). *J Allergy Clin Immunol.* 1996;98:895–902.
7. Carey AB, Cornish K, Schrank P, et al. Cross-reactivity of alternate plant sources of latex in subjects with systemic IgE mediated sensitivity to *Hevea brasiliensis* latex. *Ann Allergy Asthma Immunol.* 1995;74:317–320.
8. Yunginger JW, Jones RT, Fansway AF, Kelso JM, Warner MA, Hunt LW. Extractable latex allergens and proteins in disposable medical gloves and other rubber products. *J Allergy Clin Immunol.* 1994;93:836–842.
9. Crippa M, Belleri L, Mistrello G, Tedoldi C, Alessio L. Prevention of latex allergy among health care workers and in the general population: latex protein content in devices commonly used in hospitals and general practice. *Int Arch Occup Environ Health.* 2006;79:550–557.