Diagnostic performance of Food and Drug Administration–cleared serologic assays for natural rubber latex–specific IgE antibody

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Background: In the absence of Food and Drug Administration–approved natural rubber latex skin testing reagents, latex-specific IgE antibody immunoassays are used in the diagnosis of latex allergy. Comparative diagnostic performance of these tests has not been definitively determined.
Objective: We sought to study the predictive value of available Food and Drug Administration (510K)–cleared latex-specific IgE antibody immunoassays in the diagnosis of latex allergy.
Methods: Subjects (n = 312) were classified as having a positive (n = 117) or a negative (n = 195) latex allergy history (Hx) or having a positive (n = 131) or a negative (n = 181) puncture skin test (PST) response (Greer reagent). The 14 subjects with a negative Hx and a positive PST response had negative responses to glove provocation testing and thus were considered sensitized but asymptomatic. Sera from 22 subjects were split to evaluate intra-assay variation. All 334 coded sera were analyzed for latex-specific IgE antibodies in the Diagnostic Products Corporation microplate AlaSTAT, Hycor HY-TEC EIA System, and Pharmacia-UpJohn CAP System. Variance and diagnostic performance parameters of each test were computed with 95% confidence intervals in relation to the subjects' Hx and PST status.
Results: Intra-assay concordance of split sera results was 96.0% for all 3 assays, with coefficients of variation of less than 25% and between-assay coefficients of variation of less than 21%. The diagnostic performance of the CAP and AlaSTAT assays were equivalent in comparison with PST results: sensitivity, CAP 76.3% and ALASTAT 73.3% and specificity, CAP 96.7% and AlaSTAT 97.2% (*P* = NS). The HY-TEC assay was more sensitive (91.6%) and less specific (73.3%) than the CAP and AlaSTAT assays (*P* < .001). From 9% to 25% of the sera were discordant, being positive in at least 1, but not all 3, assays.
Conclusion: The CAP and AlaSTAT assays produce 24% and 27% of false-negative results, respectively, whereas the HY-TEC produces 27% of false-positive results when compared with the PST. (J Allergy Clin Immunol 1999;103:925-30.)

Key words: *Natural rubber latex, IgE anti-latex, diagnosis, serologic testing, human*

The diagnostic algorithm for natural rubber latex allergy begins with a clinical history and often involves a confirmatory test.[1-4] Although the puncture skin test (PST) has been regarded as a primary confirmatory test for the assessment of patients for IgE-mediated disease, the absence of a Food and Drug Administration (FDA)–licensed *Hevea brasiliensis* latex extract in the US has restricted its use in the diagnosis of latex allergy. Serologic tests have therefore become critically important as an alternative diagnostic confirmatory test. Early research has demonstrated good concordance among results of immunoassays that measure latex-specific IgE antibody, despite the use of different assay formats and natural rubber latex allergen reagents.[5] Three manufacturers have currently obtained 510K clearance for their latex (K82) in vitro reagents from the FDA on the basis of the requirements specified in the Safe Medical Devices Act of 1990 (SMDA 1990) and 21 CFR Part 807.92. 510K clearance means that the assay has been shown to perform in a substantially equivalent manner to an existing, previously cleared, or marketed assay that

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The Johns Hopkins University segment of this work was supported by National Institutes of Health grant AI-31867 and Allegiance Healthcare Corporation. The National Institute for Occupational Safety and Health (NIOSH) aspects of this work were supported by an interagency agreement between the NIOSH and the National Institutes of Environmental Health Sciences.

Dr Hamilton and the Johns Hopkins University are entitled to royalties derived from the sale of latex skin testing reagents prepared by Greer Laboratories, Inc, used in the skin testing portion of this study. The terms of this arrangement have been reviewed and approved by the Johns Hopkins University in accordance with its conflict of interest policy.

Mention of a product or company name does not constitute endorsement by the (NIOSH) or Johns Hopkins University.

Received for publication Sept 16, 1998; revised Dec 18, 1998; accepted for publication Dec 23, 1998.

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1/1/96701

Abbreviations used
FDA: Food and Drug Administration
Hx: Clinical history
NIOSH: National Institute for Occupational Safety and Health
PST: Puncture skin test

measures the same analyte. FDA clearance does not guarantee diagnostic performance. To date, there has been no independent assessment of the clinical performance of commercial reagents and assays for the measurement of latex-specific IgE antibody. In this study we use sera from well-characterized subjects who participated in a recent multi-center latex skin testing study[6] to examine the diagnostic performance of these assays in comparison with the subjects' clinical history (Hx) and PST status.

METHODS

Human sera

The institutional review boards of the 12 participating study sites and the Centers for Disease Control/National Institute for Occupational Safety and Health (NIOSH) Human Subjects Review Board approved the study design. Subjects were randomly recruited as part of an FDA-reviewed multi-center latex skin testing study protocol. After informed consent was obtained, each subject's latex allergy Hx status was reevaluated by using an extensive Hx questionnaire. To be considered for this study, an individual had to use powdered latex gloves and either have a convincing Hx of latex allergy (test group) or no Hx of latex allergy (control group).[6] Factors considered in this Hx classification included any clinical features suggesting latex-induced IgE-mediated immunopathology, the consistency of reactions, and the absence of viable alternative explanations for the symptoms reported. Subjects were excluded if they had a Hx of unstable asthma with an exacerbation within 72 hours of the study; were women who were pregnant or breast feeding; had extensive dermatitis precluding skin testing; used a β-blocker (oral or topical), antihistamine, or tricyclic antidepressant within 3 weeks of the study; or had a PST wheal response induced by 1.8 mg/mL histamine that was less than 3 mm in diameter. Whole blood was collected by venipuncture, clotted for 30 minutes, and centrifuged, and sera were placed in aliquots, coded, and frozen until the time of analysis. All subjects underwent PSTs with saline, histamine (1.8 mg/mL, Allermed), and nonammoniated latex (Greer Laboratories, Lenoir, NC) at 1, 100, and 1000 μg/mL by using a bifurcated needle as described elsewhere.[6,7] A positive PST response was defined as one that produced a greater than 2 mm wheal and greater than 5 mm erythema above that caused by the saline control at 15 minutes after application. Serum in volumes sufficient for analysis in 3 centers was available from 312 subjects. These subjects were classified by their Hx as having a positive latex allergy Hx (n = 117) or a negative latex allergy Hx (n = 195). Of the subjects with a negative Hx, 14 (7.2%) had a negative PST response at 100 μg/mL but a positive PST response at 1 mg/mL. These subjects underwent a 2-stage glove provocation (contact and inhalation) test[8] with highly allergenic powdered latex gloves to examine the significance of the positive PST response. Results of these glove provocation tests were all negative, indicating that the subjects were most probably sensitized (IgE antibody positive) but asymptomatic. When the group was classified according to their PST responses, 131 had positive latex PST responses and 181 had negative PST responses. Performance of the latex-specific IgE antibody assays was therefore analyzed separately in comparison with the subjects' Hx and PST status.

For reproducibility testing, sera from 5 subjects with positive Hx and PST responses and 17 subjects with negative Hx and PST responses were split, recoded, and tested as unknowns to study intra-assay variability. Separate quality control sera containing 1 to 3 IU/mL latex-specific IgE were analyzed in multiple runs of each assay, and coefficients of variation were computed to evaluate intra-assay variation.

Serologic analyses

Total serum IgE was measured by enzyme immunoassay (IMx; Abbott Laboratories, Abbott Park, Ill) to identify any study sera that had elevated IgE that may possibly produce false-positive latex-specific IgE antibody results because of nonspecific adsorption. Natural rubber latex–specific IgE antibody was measured in the following 3 FDA-cleared immunoassays briefly described below by using coded sera in a blinded mode. After submission of the data, an independent investigator at the NIOSH broke the latex allergy Hx and PST codes and provided the data to the statistician (EFK) for analysis.

The CAP System RAST FEIA was performed by the Johns Hopkins DACI Reference Laboratory (Baltimore, Md) according to the manufacturer's instructions by using reagents purchased from Pharmacia-UpJohn Corporation (Uppsala, Sweden). The assay is a solid-phase immunofluorometric assay in which IgE antibody is bound to latex allergosorbent (K82, sponge matrix) and detected with β-galactosidase–labeled rabbit polyclonal anti-human IgE and 4-methylumbelliferyl β–D galactosidase substrate. Results greater than 0.35 kU_A/L were considered positive.

The Immunochemical Research Section at NIOSH (Cincinnati, Ohio) performed the AlaSTAT Microplate Assay according to the manufacturer's instructions by using reagents purchased from Diagnostic Products Corporation (Los Angeles, Calif). The assay is a liquid-phase immunoenzymetric assay in which latex allergen (K82) that is coupled to soluble biotin-polymer/copolymer matrix binds antibody. The complex is then bound to biotin-coated microtiter plate wells by the addition of avidin, and bound IgE is detected with peroxidase-labeled murine monoclonal anti-human IgE and 3,3′,5,5′ tetramethyl benzidine substrate in buffered H_2O_2. Results greater than 0.35 kIU/L were defined as positive.

The company laboratory (HYCOR Biomedical, Irvine, Calif) performed the HY-TEC EIA assay System according to the package insert. The assay is an enzyme immunoassay in which IgE antibody binds to latex (K82) cellulose discs and is detected with phosphatase-conjugated mouse anti-human IgE and *p*-nitrophenyl phosophate substrate in diethanolamine buffer. Modified scoring system–derived results greater than 0.05 kIU/L were defined as positive.

Statistical analyses

Statistical analyses were performed separately with SPSS^x (Chicago, Ill) and SAS (Cary, NC) by using the Hx and PST as endpoints. Assay performance was computed by using the following definitions (with TP defined as a true-positive diagnostic test result, TN defined as a true-negative diagnostic test result, FN defined as a false-negative diagnostic test result, and FP defined as a false-positive diagnostic test result). Sensitivity $(TP/[TP + FN] \times 100)$ was defined as the percentage of positive test responses in subjects with a positive latex allergy Hx or latex PST response. Specificity $(TN/[FP + TN] \times 100)$ was defined as the percentage of negative tests in subjects with a negative Hx or PST response. Predictive value for positive test responses $(TP/[TP + FP] \times 100)$ describes the percentage of subjects with a positive test response that had a positive Hx or PST response. Predictive value for negative test responses $(TN/[TN + FN] \times 100)$ is the percentage of subjects with a negative test response that have a negative Hx or PST response. Efficiency

TABLE I. Diagnostic performance of IgE anti-latex assays*

Assay method	Parameter	Based on clinical history	Based on PST
CAP System	Sensitivity	75.2% (67.4%-83.0%)	76.3% (69.1%-83.6%)
	Specificity	90.8% (86.7%-94.3%)	96.7% (94.1%-99.3%)
	Positive predictive value	83.0% (75.9%-90.2%)	94.3% (89.9%-98.7%)
	Negative predictive value	85.9% (81.2%-90.7%)	85.0% (80.0%-89.8%)
	Test efficiency	84.9% (81.0%-88.9%)	88.1% (84.6%-91.7%)
AlaSTAT	Sensitivity	78.6% (71.2%-86.1%)	73.3% (65.7%-80.1%)
	Specificity	95.4%†‖ (92.4%-98.3%)	97.2% (94.9%-99.6%)
	Positive predictive value	91.1%†‖ (85.5%-96.6%)	95.0% (90.8%-99.2%)
	Negative predictive value	91.1% (83.8%-92.5%)	83.4% (78.3%-88.4%)
	Test efficiency	89.1%†‖ (85.6%-92.6%)	87.2% (83.4%-90.9%)
HY-TEC	Sensitivity	89.8%‡¶,§‖ (84.2%-95.2%)	91.6%‡¶,§¶ (86.9%-96.3%)
	Specificity	67.5%‡¶,§¶ (60.9%-74.1%)	73.3%‡¶,§¶ (66.9%-79.8%)
	Positive predictive value	62.5%‡¶,§¶ (55.2%-69.8%)	71.4%‡¶,§¶ (64.6%-78.3%)
	Negative predictive value	91.6%‡¶ (87.1%-96.2%)	92.3%‡¶,§¶ (87.9%-96.7%)
	Test efficiency	75.9%‡¶,§¶ (71.1%-80.6%)	81.0%‡¶,§‖ (76.7%-85.4%)

*Parentheses are 95% confidence limits; n = 312 for CAP System and AlaSTAT and n = 311 for HY-TEC.
†Performance parameters of the AlaSTAT based on Hx only are significantly different than those displayed by the CAP System.
‡Performance parameters displayed by the HY-TEC based on Hx and PST are significantly different than those produced by the CAP assay.
§Performance parameters displayed by the HY-TEC based on Hx and PST are significantly different than those produced by the AlaSTAT assay.
‖$P < .05$.
¶$P < .001$.

([TP+TN]/[TP + FP + TN + FN] × 100) describes the percentage of subjects correctly classified as having a positive and negative latex allergy Hx or latex PST response. The 95% confidence intervals were calculated from a normal distribution, as previously described by Galen and Peters.[9] McNemar's test was used to assess statistical differences between the sensitivity, specificity, and efficiency of the methods. A *z* test for correlated proportions was used to compare the positive and negative predictive values of the different methods. An averaging method[10] was used to minimize bias in cases in which sera had results below the limits of detection of the assays. Associations between variables were evaluated by using Pearson's correlation coefficient. A mixed model for repeated measures with an unstructured covariance matrix was used to investigate differences in kIU/L levels reported by the different assays. The model was estimated by using restricted maximum likelihood (SAS Proc Mixed).

RESULTS

Reproducibility

Intra-assay agreement was evidenced by 96% concordance of positivity among results of the 22 coded duplicate (split) specimens in all 3 assays. Intra-assay coefficients of variation for the interpolated kIU/L results obtained with the split sera from subjects with positive PST responses were 24.9% (CAP), 16.1% (AlaSTAT), and 15.2% (HY-TEC). Between-assay variation for the 3 assays was 10.5% (n = 36, mean level 0.78 kIU/mL), 12.4% (n = 12, mean level 1.61 kIU/L), and 20.3% (n = 69, mean level 2.41 kIU/mL) for CAP, ALASTAT, and HY-TEC assays, respectively.

Total serum IgE

Total serum IgE levels in the sera ranged from 1 to 2469 IU/mL in the group with negative PST responses and 4 to 15,394 IU/mL in the group with positive PST responses. Five sera from subjects with positive PST responses had IgE levels of greater than 3000 IU/mL (3309, 6367, 6402, 6679, and 15394 IU/mL). These sera had potential to produce false-positive results because of nonspecific adsorption, and they were diluted to 3000 IU/mL before being reanalyzed in the CAP system. When corrected for dilution after interpolation, the predilution positive result remained positive. These 5 sera were not diluted before analysis in the AlaSTAT and HY-TEC assays because of the absence of a written manufacturer policy on this issue. Although all 5 of these sera with high IgE levels were positive for latex-specific IgE in the AlaSTAT and HY-TEC assays, it is unclear whether there was significant nonspecific binding in these assays.

Diagnostic performance

Table I summarizes the diagnostic performance of the CAP, AlaSTAT, and HY-TEC assays for latex-specific IgE antibody on the basis of the subjects' Hx and PST results. Because the bias of the authors has been that the PST more accurately reflects the state of latex sensitization than the Hx,[6,11] we have focused this critique on comparison of performance data to the subjects' PST responses. The observed diagnostic sensitivities of the CAP (76.3%) and AlaSTAT (73.3%) assays were statistically not different from each other when compared against the PST. Importantly, approximately 24% to 27% of subjects with a positive PST response were incorrectly identified with a false-negative latex-specific IgE result by these immunoassays. The diagnostic specificity of the CAP and ALASTAT was similar (96.7% to 97.2%), indicating that approximately 3% of with negative PST responses had a false-positive serology. In contrast, the HY-TEC assay displayed a statistically higher sensitivity (91.6%, $P < .001$) but a statistically lower specificity (73.3%, $P < .001$) than both the CAP and AlaSTAT assays. The HY-TEC assay classified approximately 27% of subjects with negative PST responses incorrectly as being IgE anti-latex positive. The efficien-

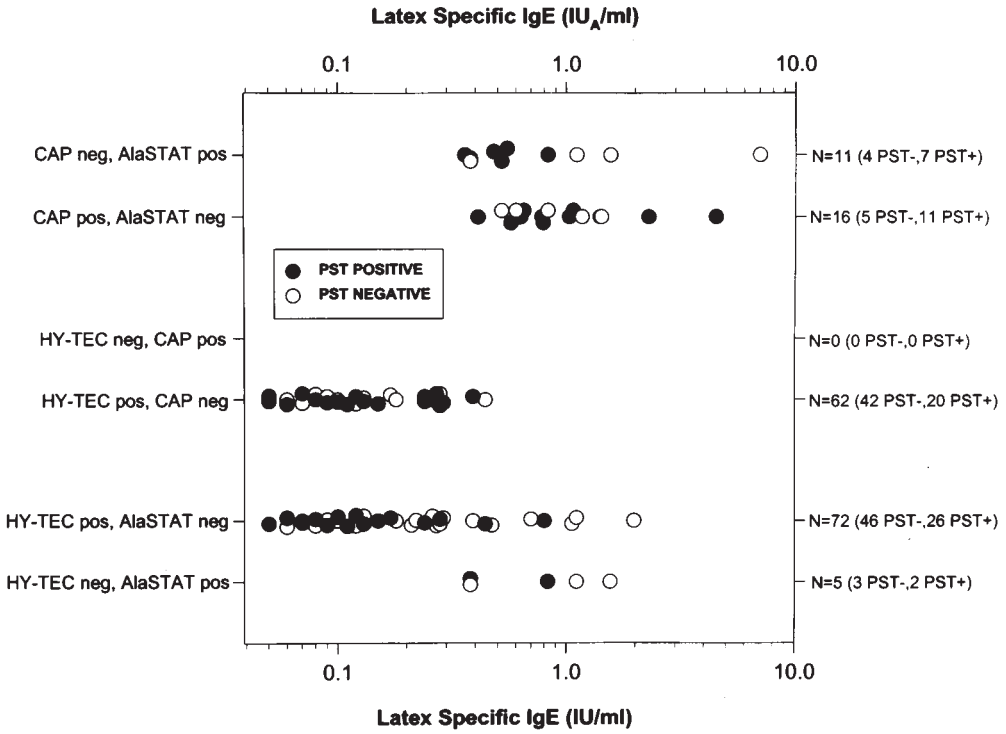

FIG 1. Scattergram of discordant IgE anti-latex results obtained in the analysis of 312 sera in the Pharmacia-UpJohn CAP System, Diagnostic Products Corporation's AlaSTAT, and Hycor HY-TEC assays. Sera that were detected in 1 or 2 but not all of the 3 assays were equivalently distributed (P = NS) among subjects with positive PST responses *(filled circles)* and negative PST responses *(open circles)*. The total number of sera producing discordant IgE antibody results and the number of positive and negative PST responses are denoted on the right Y-axis in parentheses. IgE anti-latex results are presented in international units of allergen-specific IgE per milliliter (CAP; *top axis*) or international units per milliliter (AlaSTAT and HY-TEC; *bottom axis*).

cy or measure of the percentage of subjects that had concordant IgE anti-latex serology and PST results was comparable for the CAP System and AlaSTAT (87.2% to 88.1%) and statistically lower for the HY-TEC assay (81.0%, $P < .05$).

Differences in IgE antibody detection among methods

Fig 1 presents the number of sera that had discordant positive or negative IgE anti-latex results among the CAP System, AlaSTAT, and HY-TEC assays. The CAP System, for instance, detected 0.41 to 4.5 kIU$_a$/L latex-specific IgE in the serum from 16 individuals (11 with positive PST results) who all had negative AlaSTAT results. In contrast, the AlaSTAT detected 0.36 to 7.01 kIU/L of IgE anti-latex in the serum from 11 subjects (7 with positive PST results) who all had negative results to the CAP System and 0.38 to 1.56 kIU/L in the serum of 5 subjects (3 with positive PST results) who had negative results to the HY-TEC assay. Overall, the CAP System and AlaSTAT assays displayed 9% discordance among latex-specific IgE results, whereas the HY-TEC assay displayed a 20% and 25% discordance with the CAP and AlaSTAT assays, respectively (Fig 1). Interestingly, the percentage of discordant results that were positive on PST were not different from those that were negative on PST.

Direct comparison of all the quantitative IgE antibody results (n = 312) generated in the CAP, AlaSTAT, and HY-TEC assays was performed by using a mixed-model analysis for repeated measures. The resultant mean (± SEM) latex-specific IgE antibody levels (2.63 ± 0.43 kIUa/L [Pharmacia CAP], 3.39 ± 0.62 kIU/L [AlaSTAT], and 1.02 ± 0.17 kIU/L [HY-TEC]) were significantly different between all 3 assays ($P < .05$). When data were analyzed only from individuals with positive latex-specific IgE antibody results, the AlaSTAT results (6.95 ± 1.50 kIU/L, n = 101) were significantly different from those produced by the HY-TEC assay (1.84 ± 0.30 kIU/L, n = 168) ($P = .0003$). The CAP results (5.11 ± 0.91 kIUa/L, n = 106) were also significantly different from those generated by the HY-TEC assay ($P = .0001$) but not different from the AlaSTAT results ($P = .09$).

DISCUSSION

Although a careful Hx that takes risk factors and symptoms into consideration is a necessary component of a diagnostic work-up of latex allergy, it is not sufficient.[1-3] In a recent study 15% of the 304 adult subjects studied with a well-documented questionnaire provided a false-positive latex allergy Hx.[6] These subjects had negative results on both skin tests and glove challenges. Therefore

a confirmatory test is needed to make the definitive diagnosis. PSTs are extensively performed in Europe by using a characterized latex PST reagent.[12] In the US a candidate nonammoniated latex PST reagent that has shown 96% sensitivity and 100% specificity in adults in a multicenter clinical study[6] is pending FDA licensing. However, in the absence of an FDA-licensed latex skin testing extract, allergists must rely on results from either skin tests performed with home-brew extracts or in vitro serologic assays that detect latex-specific IgE antibody.

A variety of in vitro assays have been used to detect latex-specific IgE antibody in blood. These include basophil histamine release, flow cytometry, cellular proliferation, immunoblot analysis, and enzyme immunoassays.[13-17] However, the need for fresh cells and a general lack of standardization has limited their use in diagnosis. Alternatively, bronchial, nasal, and skin contact provocation procedures[2,8] have been used clinically to evaluate patients for a possible sensitivity to latex. These tests are considered unsafe and too poorly standardized to be used as primary diagnostic tests. Therefore allergists have relied on the results of 1 of the 3 FDA (510K)-cleared diagnostic assays for latex-specific IgE in serum: the CAP System, microplate AlaSTAT, or HY-TEC assays.

In this study we have examined the diagnostic performance of 3 latex-specific IgE antibody immunoassays by using sera from 312 of 324 qualified subjects participating in a multicenter latex skin testing study.[6] Quantities of serum from 12 of the study subjects were insufficient to be analyzed in 3 laboratories. Results of the initial Hx and subsequent PSTs with the Greer nonammoniated latex reagent were used to define the latex allergy status of these subjects. The clinical significance of mismatched Hx and PST responses was clarified with a 2-stage glove provocation test. Within-assay concordance between the positive/negative responses from the 22 split serum specimens was acceptable (96%) for all 3 assays. The overall sensitivity, specificity, positive and negative predictive value, and efficiency of the CAP and AlaSTAT microplate assays were not statistically different from each other when compared with skin test results (Table I). Both assays missed about a quarter of the subjects with positive PST responses, classifying them as anti-latex IgE negative. The HY-TEC assay, however, displayed a significantly higher sensitivity and lower specificity, most likely as a result of the use of a modified scoring system.[18] Data from this study demonstrate that under the best of circumstances, the CAP and AlaSTAT (microplate assay) both produce a substantial number of false-negative IgE antibody results. The HY-TEC assay, in contrast, produced false-positive IgE anti-latex results in 28% of subjects who had a negative latex Hx and a negative PST response. Causes for the observed misclassification of a quarter of the test subjects may relate to either limited analytical sensitivity of the assays in comparison with PSTs with the Greer reagent and/or the use of allergen-containing reagents that need optimization.

The strength of this study relates to the careful characterization of the latex allergy status of the subjects in a multicenter skin testing study and the use of coded sera in a blinded manner to assess assay performance. In contrast, an early 1995 open study performed by Alemohammad et al[19] involved the testing of 104 sera by using the Hycor RAST assay and ELISA (the HY-TEC predecessor). They reported a sensitivity and specificity for the latex-paper disc–based RAST and ELISA approaching 100%. The highly selected nature of the sera evaluated, and the fact that subjects were not skin tested with qualified reagents, essentially invalidates the conclusions of their study.

More recently, Kibby and Akl[20] evaluated 135 hospital employees for possible latex allergy by using a questionnaire, PSTs, and serology. Of their study group, 7 were symptomatic (positive Hx), 11 (8.2% [95% confidence interval, 3.4-13%]) had positive skin test responses, and 9 (6.7%) were classified as having latex-specific IgE antibody in sera with a class II or higher AlaSTAT result (≥1.50 IU/mL). The authors reported a 63.6% diagnostic sensitivity and 98.4% specificity for the AlaSTAT in comparison with PST positivity. In a similar study by Kim et al,[21] 49 of 207 subjects were classified as having a positive Hx for latex allergy. These authors reported a combined CAP/AlaSTAT sensitivity (positive result in one or both assays) of 49% and specificity of 93% in comparison with PST positivity. Several issues, however, make it difficult to compare the data from these previous studies to the assay performance data obtained in the present study. First, the authors used skin testing extracts that were not immunochemically characterized or clinically validated. Second, the authors did not specify whether they used the microplate or tube version of the AlaSTAT in their studies. The performance characteristics of these 2 assays are not equivalent. Third, there was no confirmatory provocation test used in either study to clarify the latex allergy status of individuals who had a discordant history and PST result.

Data in this study (Fig 1) provide support for a proposed hypothesis in a 1998 National Committee on Clinical Laboratory Standards guideline[22] that different IgE antibody assays detect different subsets of IgE antibody of a given specificity, probably as a result of differential specificities on their allergen-containing reagents. There are several possible reasons for this. First, natural rubber latex contains more than 250 polypeptides, with approximately 60 that show IgE-binding epitopes.[23,24] Different batches of source latex are known to vary up to 25-fold in their total allergen content, as assessed by RAST inhibition, simply as a result of normal seasonal variation among the *Hevea brasiliensis* trees.[25] Second, sensitized individuals produce specific IgE antibody to at least 8 potent *Hevea* allergens, Hev b 1 to Hev b 8. Each of these allergens differs in its structure, size, net charge (isoelectric point), relative allergenicity, and abundance in natural rubber latex. Hevein (Hev b 6.02), for instance, is the most abundant soluble protein in latex, constituting approximately 22% of the total soluble latex protein.[23,26] It is often present as its 20-kd prohevein molecule (Hev b 6.01) or as mature hevein, the

N-terminal domain of prohevein (Hev b 6.02, 4.7 to 5.0 kd). IgE antibody epitope mapping of prohevein indicates that 2 epitopes are present on N-terminus hevein (Hev b 6.02) and 4 on the 14-kd C-terminus (Hev b 6.03).[26] The relative percentage of Hev b 6.01, 6.02, and 6.03 in a starting and final processed allergen determines the extent to which an in vitro assay allergen reagent detects antibodies to these various regions of prohevein. Moreover, aqueous latex extracts vary widely in their relative content of rubber particle–associated proteins (Hev b 1 or rubber elongation factor [14.6 kd or 58 kd tetramer] and Hev b 3 or prenyltransferase or small rubber particle protein [23 to 27 kd]). The relative content of Hev b 1 and Hev b 3 in the final allergen preparation is important because they are important allergens for detecting IgE antibody in sera from children with spina bifida and adults with atopic dermatitis who are extensively exposed to rubber through direct mucosal contact or open wounds.[24,27] Other potential causes of allergen-containing reagent heterogeneity include variable stability during storage and variable binding of allergen to labels (eg, biotinylated copolymer in AlaSTAT) or solid supports (sponge in CAP; cellulose disc in HY-TEC).[22] One may attempt to compare qualitative (positive/negative) IgE antibody results across assays, but quantitative data interpolated from dose-response curves should be compared cautiously.[22]

In conclusion, clinicians and researchers should view commercially available latex-specific IgE assays as useful tests for general confirmation of latex sensitization. However, care should be exercised when interpreting negative IgE antibody results from the CAP and AlaSTAT assays because these assays appear to misclassify approximately a quarter of subjects who have positive skin test responses as IgE antibody negative or false negative. Care should also be exercised when interpreting positive IgE antibody results from the HY-TEC assay because this assay misclassifies approximately 25% of subjects with negative PST results as being IgE antibody positive or false positive. Finally, latex allergen–specific IgE antibody results from different assays should not be directly compared because each assay may detect a different subset of antibodies, presumably to different latex allergen epitopes on their respective allergen-containing reagents.

We thank Dr Doug Sharpnack, Deputy Director, DBBS, for proctoring the data for this study. We also thank Mrs S. Robertson, Mrs D. Viers, Ms B. MacKenzie, and Mr J. Wisenauer for their excellent technical assistance. Finally, we extend our appreciation to Drs Hull, Petsonk, Meade, Lewis, Stettler, and Dunn at NIOSH for their critical review of this paper.

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