Hev b 6.02 Is the Most Important Allergen in Health Care Workers Sensitized Occupationally by Natural Rubber Latex Gloves

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ABSTRACT
Background: Natural rubber latex (NRL) allergy is a common occupational disease in health care workers (HCW). However, few reports have compared the major allergen of HCWs to those in gloves that are routinely used in the hospital. The aim of this study was to evaluate the major NRL allergens in gloves used by HCWs.

Methods: We studied 20 HCWs who were suspected to have latex allergy (LA). We performed a skin prick test (SPT) using NRL allergens. Serological testing was performed using the ImmunoCAP™. The total amount of protein and the antigenic protein concentrations extracted from NRL gloves were measured. Four different types of FITkit™ were used to measure the concentrations of Hev b 1, 3, 5, and 6.02 in the gloves.

Results: A SPT using NRL extract identified 14 cases with positive reactions. The sensitivity and specificity of the SPT scores to the NRL glove extract were 100%. The sensitivity of latex specific IgE was 100% but the specificity was 14.2%. The sensitivity and specificity of rHev b 6.02 specific IgE were 100% in the LA group. The total amounts of protein from the medical gloves for surgery and examination were 265 μg/g and 95 μg/g, respectively. The antigenic protein concentrations in the gloves were 24.9 μg/g and 1.0 μg/g, respectively. The total amounts of the specific four allergens in the NRL gloves were 2.18 μg/g and 0.45 μg/g, respectively.

Conclusions: We concluded that the main allergen of HCWs who have been sensitized occupationally by NRL gloves was Hev b 6.02.

KEY WORDS
allergen, health care workers, latex allergy, latex gloves, skin prick test

INTRODUCTION
Type I allergy to natural rubber latex (NRL) in health care workers (HCWs) is a well-known problem. Between 3% and 17% of HCWs have become sensitized to NRL.1-3 In February 2006, the WHO/IUIS Allergen Nomenclature Committee (www.allergens.org) listed 13 NRL Hev b allergens as molecularly characterized proteins.4-13 Among children with latex allergy (LA), who is often associated with spina bifida (SB), hydrophobic proteins bound to rubber particles, such as Hev b 1 (rubber elongation factor) and Hev b 3 (small rubber particle protein), have been reported to be very important allergens.4,14 On the other hand, in HCWs with LA, hydrophilic proteins, such as Hev b 5 (acidic latex protein) and Hev b 6.02 (hevein), have been reported to be important allergens.7,15 Such differences are attributed to different routes of allergen exposure and different amounts of major allergic proteins eluted from the causable products in these patient groups. In most children with LA, sensitization and induction of LA may occur by direct contact of the internal mucosa with NRL products during surgery to treat SB or congenital disorders, which is repeated many times after birth, or catheterization for the maintenance of excretion routes.14,15 On the
other hand, in HCWs with LA, sensitization and induction of LA may mainly occur by skin contact, such as wearing NRL gloves or by inhaling latex aeroallergens, such as allergic protein-adsorbed powder.\textsuperscript{16-18} No studies have examined the amount of allergic proteins eluted from commercially available NRL products in Japan. The aims of this study were to characterize the major allergens in HCWs occupationally sensitized to latex in and to clarify the difference with the LA observed in children often complicated by SB.

**METHODS**

**SUBJECTS**

We studied 20 HCWs at the Fujita Health University Hospital (Aichi, Japan) in the 1990s who were suspected to have LA. These workers had used the same types of surgical and examination NRL gloves. We performed the skin prick test (SPT) using NRL glove extract, and used these test results to divide the HCWs into allergen-positive and -negative groups (LA group and non-LA group, respectively). The study group consisted of three males and 17 females (mean age, 29.3 years; range, 23–46 years). With regard to the clinical symptoms of LA, three patients had anaphylaxis, three had respiratory symptoms and urticaria, three had generalized urticaria and five had contact urticaria. The LA clinical symptoms ranged from minor indications such as contact urticaria, eye symptoms, facial edema, generalized urticaria, rhinitis, and asthma, to more severe symptoms such as anaphylactic shock. We classified the degree of symptoms into four groups, Stages 1–4, according to the classification of the contact urticaria syndrome described by Krough and Maibach.\textsuperscript{19} The stage descriptions were as follows: Stage 1, localized urticaria, dermatitis, nonspecific symptoms, itching, tingling, burning, etc.; Stage 2, general urticaria and extracutaneous reactions; Stage 3, bronchial asthma, rhinoconjunctivitis, pharyngeal larynx symptoms, and gastrointestinal symptoms; and Stage 4, anaphylactic shock. In the LA group, three patients were Stage 4, three were Stage 3, three were Stage 2, and five were Stage 1 (Fig. 1, Table 1, 2). At the time of diagnosis, five subjects worked as nurses in the intensive care unit or the operating room, nine worked as nurses in the general ward, two were medical technicians, two were nursing assistants in the general ward, and two were doctors. Twelve out of the 20 subjects (60.0%) had complications from other allergic diseases such as atopic dermatitis (AD), allergic rhinitis (AR), allergic conjunctivitis (AC), and bronchial asthma (BA). Three subjects had AD, AR, and BA, two had AD and AR, four had only AD, three had only AR, and one had BA. HCWs were diagnosed with NRL sensitization based on positive SPT results with NRL glove extract or a positive NRL glove use test and clinical symptoms compatible with NRL glove use.

**SKIN TEST**

**SPT**

We made extracts from NRL gloves that HCWs had used in the 1990s following the method of Turjanmaa \textit{et al.}\textsuperscript{20} and purchased recombinant (r) allergens (rHev b 1, 3, 5, 6.02, 8, 9, and 11) from BIOMAY, Vienna, Austria. The allergens were diluted to 100 μg/ml in distilled water. As for quality control, all materials were stored at −20°C to avoid repeat freezing/thawing.

One drop of the diluted solution was applied to the skin on the forearm, which was then pierced with a lancet (PRICK-LANCETTER, Ewo Care AB, Sweden)\textsuperscript{20,21}. The drops were removed with a paper towel, and the test was evaluated 15 minutes later. A wheal at least half the size of that caused by histo-
Table 1  List of 14 cases with latex allergy

<table>
<thead>
<tr>
<th>Case No</th>
<th>Sex</th>
<th>Age</th>
<th>Occupation</th>
<th>Clinical symptoms by LA</th>
<th>Severity stage of contact urticaria syndrome by LA</th>
<th>Personal allergic history</th>
<th>IgE RIST (IU/ml)</th>
<th>Latex SPT score</th>
<th>rHev b6.02 SPT score</th>
<th>Latex specific IgE (UA/ml)</th>
<th>rHev b6.02 specific IgE (UA/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>24</td>
<td>Ns of operating room</td>
<td>anaphylaxis</td>
<td>4</td>
<td>AR</td>
<td>78</td>
<td>4</td>
<td>4</td>
<td>1.28</td>
<td>7.32</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>23</td>
<td>Ns of ICU</td>
<td>anaphylaxis</td>
<td>4</td>
<td>(−)</td>
<td>203</td>
<td>4</td>
<td>4</td>
<td>11.4</td>
<td>5.96</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>45</td>
<td>Ns of operating room</td>
<td>anaphylaxis</td>
<td>4</td>
<td>(−)</td>
<td>130</td>
<td>4</td>
<td>4</td>
<td>1.3</td>
<td>10.40</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>25</td>
<td>Ns of ICU</td>
<td>respiratory symptoms and urticaria</td>
<td>3</td>
<td>AD, AR, asthma</td>
<td>320</td>
<td>4</td>
<td>4</td>
<td>13.1</td>
<td>13.90</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>26</td>
<td>Ns of ICU</td>
<td>respiratory symptoms and urticaria</td>
<td>3</td>
<td>AD, AR, asthma</td>
<td>900</td>
<td>4</td>
<td>4</td>
<td>53.7</td>
<td>42.50</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>23</td>
<td>Ns of general ward</td>
<td>respiratory symptoms and urticaria</td>
<td>3</td>
<td>AD</td>
<td>240</td>
<td>3</td>
<td>3</td>
<td>7.23</td>
<td>5.38</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>26</td>
<td>Ns of general ward</td>
<td>generalized urticaria</td>
<td>2</td>
<td>(−)</td>
<td>21</td>
<td>4</td>
<td>4</td>
<td>2.17</td>
<td>8.85</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>26</td>
<td>Dermatologist</td>
<td>generalized urticaria</td>
<td>2</td>
<td>AD</td>
<td>469</td>
<td>2</td>
<td>3</td>
<td>3.25</td>
<td>3.53</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>27</td>
<td>Ns of general ward</td>
<td>generalized urticaria</td>
<td>2</td>
<td>(−)</td>
<td>93</td>
<td>2</td>
<td>2</td>
<td>3.03</td>
<td>4.48</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>30</td>
<td>Medical laboratory technician</td>
<td>contact urticaria</td>
<td>1</td>
<td>AD, AR, asthma</td>
<td>712</td>
<td>3</td>
<td>3</td>
<td>21.3</td>
<td>14.90</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>26</td>
<td>Medical laboratory technician</td>
<td>contact urticaria</td>
<td>1</td>
<td>AD</td>
<td>4089</td>
<td>3</td>
<td>4</td>
<td>25.4</td>
<td>20.50</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>37</td>
<td>Medical assistant</td>
<td>contact urticaria</td>
<td>1</td>
<td>AD</td>
<td>3880</td>
<td>1</td>
<td>3</td>
<td>14.3</td>
<td>24.60</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>41</td>
<td>Ns of general ward</td>
<td>contact urticaria</td>
<td>1</td>
<td>Asthma, SB</td>
<td>39.2</td>
<td>1</td>
<td>3</td>
<td>3.66</td>
<td>1.19</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>25</td>
<td>Ns of general ward</td>
<td>contact urticaria</td>
<td>1</td>
<td>(−)</td>
<td>1620</td>
<td>4</td>
<td>2</td>
<td>38.9</td>
<td>3.25</td>
</tr>
</tbody>
</table>

ICU, intensive care unit; Ns, nurse; AD, atopic dermatitis; AR, allergic rhinitis; SB, spina bifida.
Table 2  List of 6 cases without latex allergy

<table>
<thead>
<tr>
<th>Case No</th>
<th>Sex</th>
<th>Age</th>
<th>Occupation</th>
<th>Personal allergic history</th>
<th>IgE RIST (IU/ml)</th>
<th>Latex skin prick test score</th>
<th>rHev b 6.02 skin prick test score</th>
<th>NRL glove use test</th>
<th>Latex specific IgE (UA/ml)</th>
<th>rHev b 6.02 specific IgE (UA/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>23</td>
<td>Ns of general ward</td>
<td>AD, AR</td>
<td>1020</td>
<td>negative</td>
<td>ND</td>
<td>negative</td>
<td>0.77</td>
<td>&lt; 0.35</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>23</td>
<td>Ns of general ward</td>
<td>AR</td>
<td>87.8</td>
<td>negative</td>
<td>ND</td>
<td>negative</td>
<td>0</td>
<td>&lt; 0.35</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>23</td>
<td>Ns of general ward</td>
<td>AD, AR</td>
<td>250</td>
<td>negative</td>
<td>ND</td>
<td>negative</td>
<td>3.01</td>
<td>&lt; 0.35</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>38</td>
<td>Medical assistant</td>
<td>AR</td>
<td>135</td>
<td>negative</td>
<td>ND</td>
<td>negative</td>
<td>2.01</td>
<td>&lt; 0.35</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>32</td>
<td>Ns of general ward</td>
<td>(—)</td>
<td>78</td>
<td>negative</td>
<td>ND</td>
<td>negative</td>
<td>1.51</td>
<td>&lt; 0.35</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>43</td>
<td>Radiologist</td>
<td>(—)</td>
<td>1100</td>
<td>negative</td>
<td>ND</td>
<td>negative</td>
<td>4.22</td>
<td>&lt; 0.35</td>
</tr>
</tbody>
</table>

ND, Not done.

Fig. 2  Prevalence percent of LA group exhibiting positive SPT responses to *Hevea brasiliensis* proteins.

mine dihydrochloride (10 mg/ml) was considered a positive reaction. PS was used as a negative control, and the scores were assigned as follows: 2+, between half to the same size (as that caused by histamine); 3+, the same size; and 4+, a larger size. Scores of 2+ or greater were considered positive.

**NRL Glove Use Test**

The subject who showed a negative reaction in SPTs wore a NRL glove on one finger, which was wetted with water, and a control chloroprene glove on the opposite finger for 15 minutes.\(^{20,21}\) If subjects showed no symptoms, they wore the NRL glove on the whole hand and the chloroprene glove on the opposite hand.

**IMMUNOGLOBULIN E ANTIBODY ANALYSES**

Serological testing was performed using the ImmunoCAP\textsuperscript{TM} system (Phadia, Uppsala, Sweden). All sera were analyzed for latex specific IgE. The LA group was analyzed with rHev b 1, 3, 5, 6.01, 6.02, 8, 9, and 11.

The values obtained ranged from Classes 1 to 6. IgE levels more than 0.70 IU/ml (Class 2) were considered positive.

**GLOVE ANALYSIS**

**Glove Collection**

The Fujita Health University provided two brands of medical gloves for surgery and examinations used in the 1990s. The surgical glove was a powdered one (Micro-Touch Surgical Gloves, Johnson & Johnson, NJ, USA), and the examination glove was a non powdered one (Glovex Eco Latex Exam Gloves, Termo Beiersdorf, Tokyo, Japan).

**Extraction of Latex Allergens**

The NRL gloves were cut into small pieces which were mixed carefully. Subsequently, 1 g of the mixture was weighed and extracted in 5 ml of phosphate-buffered saline, pH 7.2.

**Measurements of Total Amounts of Proteins and Allergens**

The total amount of protein in each extract was measured by the ASTM D5712-95 method (modified Lowry method), and the antigenic protein concentra-
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Fig. 3 The correlation of the severity and SPT scores of NRL glove extract in LA group.

Fig. 4 The correlation of the severity and SPT scores of rHev b 6.02 in LA group.

Quantification of Individual Allergens

Four different allergens with FTKit™ (FIT Biotech Ltd, Tampere, Finland) were used to measure the concentrations of Hev b 1, Hev b 3, Hev b 5 and Hev b 6.02 in the NRL glove extracts. The detection limits of FTKit™ for allergens are as follows: Hev b 1, 50 ng/g; Hev b 3, 50 ng/g; Hev b 5, 25 ng/g; Hev b 6.02, 25 ng/g. Values below these detection limits were denoted as zero. The sum of the four allergens in the NRL glove extracts was denoted as the allergen sum (μg/g).

STATISTICS

Fisher’s exact test was performed to examine the sensitivity and specificity of the SPT score and serum specific IgE analysis.

The correlation between individual SPT scores or the serum IgE antibody levels and the severities of the LA group was assessed by a non-parametric Spearman’s r-test.

ETHICAL CONSIDERATION

We obtained informed consent from each subject to perform the examination and to publish the final results.

RESULTS

First, we performed a SPT on 20 subjects using NRL extract and identified 14 cases with positive reactions and six cases with negative reactions. Then, we performed a SPT using recombinant allergens in the 14 cases that reacted positively to the NRL extract.
In the SPT-negative subjects, we performed the glove use test.

SKIN TEST RESULTS

SPT Results

The sensitivity and specificity of the SPT scores to the NRL glove extract were 100%. The positive ratios of SPT for latex extract and rHev b 6.02 in the LA group were 100%, while those for rHev b 5, rHev b 8, and rHev b 11 were 42.8%, 14.2%, and 7.1%, respectively (Fig. 2). There were significant correlations between the severity stage and the SPT scores for the NRL glove extract or rHev b 6.02 in the LA group (Spearman’s rank correlation coefficient; r = 0.615; P < 0.01 and r = 0.724; P < 0.01, respectively) (Fig. 3, 4).

Glove Use Test Results

We performed a glove use test in the six cases with a negative SPT reaction to NRL gloves. All of them reacted negatively in the use test (Fig. 1, Table 2).

SERUM SPECIFIC IgE RESULTS

The sensitivity of latex specific IgE was 100%, whereas the specificity was 14.2%. The latex specific IgEs were not significantly different in the LA group compared to the non-LA group (Table 1, 2). The positive ratios of serum specific IgE for latex, rHev b 6.01, and 6.02 in the LA group were 100%, while those for rHev b 5, rHev b 8, and rHev b 11 were 42.8%, 14.2%, and 7.1%, respectively (Fig. 5). rHev b 6.02 specific IgE had the highest frequency of positive reaction in comparison with the other allergen proteins in HCWs.

There were no significant correlations between the severity stages and serum specific IgEs against latex or rHev b 6.02 in the LA group.

GLOVE ANALYSIS RESULTS

The results of the total protein, antigenic protein concentration, and each specific NRL glove allergen are summarized in Table 3.

1. The total amounts of protein of the surgery and examination NRL gloves were 265 μg/g and 95 μg/g, respectively.
2. The antigenic protein concentrations of the surgery and examination NRL gloves were 24.9 μg/g and 1.0 μg/g, respectively.
3. The total amounts of the four specific allergens in the surgery and examination NRL gloves were 2.18 μg/g and 0.45 μg/g, respectively.

DISCUSSION

As in other western countries, in Japan the number of LA patients increased rapidly from 1990 to 2000. In Japan, various preventative procedures were quickly implemented, such as low-protein processing of NRL products, developing NRL free products, and creating LA guidelines, and as a result, the prevalence of LA has been decreasing. However preventative procedures for HCWs with LA have not been well-established.

We believe that it is important to identify the source allergens by serologic and skin tests and to examine the amount of protein allergens in NRL.
products. The results will provide a better understanding of the features of LA in Japan and find the most efficient diagnostic procedures for diagnosis of LA in HCWs. It was previously reported that HCWs with LA were sensitized to LA by contact with NRL products, such as NRL gloves, or inhalation of airborne NRL allergens.16-18 Although it was reported that HCWs with LA were mainly sensitized by NRL gloves, no report has examined whether Japanese HCWs are sensitized to the main extracted allergens in NRL gloves. In this study, we examined 20 HCWs who had worked at the Fujita Health University Hospital in the 1990s and used the same NRL glove brands. Although they worked in different hospital settings, they used the same brands of NRL gloves in the hospital. Therefore, we considered that these HCWs had been sensitized to the same allergens in NRL gloves.

The purpose of this study was to investigate the sensitized allergens of these patients. First, we performed a SPT with NRL glove extract in 20 HCWs who had clinical symptoms, such as itchiness and erythema, due to wearing NRL gloves at the Fujita Health University Hospital in the 1990s. From the results, we identified 14 cases as the LA group and six cases as the non-LA group. We considered that the symptoms associated with NRL gloves in the non-LA group were irritations and dank.

Both the sensitivity and specificity of the SPT with NRL extract in the LA group were 100%. These results were similar to previously published results.30 We also performed SPTs with recombinant allergens in the LA group. The positive ratios of SPT scores to NRL glove extract, rHev b 6.01, and rHev b 6.02 in the LA group were 100%. There were significant correlations between the severity stages and SPT scores to NRL glove extract or rHev b 6.02 in the LA group (Spearman’s rank correlation coefficient; r = 0.615; P < 0.01 and r = 0.724; P < 0.01, respectively) (Fig. 2, 3). These results suggested that the SPT reflected the clinical symptoms of LA and was a useful tool to diagnose LA. These results also suggested that among the LA allergens, rHev b 6.02 reflected LA clinical symptoms better than NRL extract in the SPT. Bernstein et al. performed a SPT with 7 native proteins purified from nonammoniated latex (Hev b 1, 2, 3, 4, 6.01, 7.01, and 13) and rHev b 5 in HCWs.31 They reported positive ratios of Hev b 2, 5, 6.01, and 13 greater than 60%. Our positive ratio of rHev b 6.01 was consistent with their results. Sussman et al. also reported that using a combination of recombinant latex allergens Hev b 5, 6, and 7 could identify LA with 93% sensitivity and 100% specificity.32 They reported that the results of SPTs using recombinant allergens were comparable to the results of SPTs using NRL extract.

It has been reported that the diagnostic sensitivity of latex specific IgE is 23–83%,32 ImmunoCAP™, the EIA with fluorescent substrate (FEIA) from Pharmacia Diagnostics, uses a non-ammoniated latex allergen preparation with at least 10 different protein components. Because of the possibility of mistakes in identifying the most responsible antigen, use of recombinant allergens may therefore be of great value. Rihs H-P et al. reported the IgE-binding prevalence of the allergens as follows, the prevalence of rHev b 1 for SB was 81%, while HCWs was 52%. The prevalence of rHev b 3 for SB was 76–78%, while HCWs was 13–20%. The prevalence of rHev b 6.02 for HCWs was 75%, while SB was 27%.33 Based on these results, we considered that it was useful to measure recombinant allergens of LA in the specific IgE rather than crude LA allergen.

We measured the serum specific IgE for latex and recombinant latex allergens in the LA group (n = 14). The positive ratios of serum specific IgE for latex, rHev b 6.01, and 6.02 in the LA group were 100%, while those of rHev b 5, rHev b 8, and rHev b 11 were 42.8%, 14.2%, and 7.1%, respectively. We considered that Hev b 6.02 mainly contributed to LA sensitization. Although five of the six cases in the non-LA group showed positive reactions for latex specific IgE, all cases showed negative reactions for rHev b 6.02 specific IgE. This suggested that false positive reactions occurred with latex specific IgE when using latex extract. In this study, the sensitivity of latex specific IgE was high but the specificity was low, while both the sensitivity and the specificity of rHev b 6.02 specific IgE were high. Therefore, we concluded that rHev b 6.02 specific IgE was more useful than latex specific IgE for diagnosing LA.

When SPT was compared with specific IgE for diagnosis, we considered that SPT with latex allergen was most relevant for diagnosis of LA in HCWs compared to measurement in specific IgE. We have further shown that the accuracy of the examinations would increase by using the recombinant allergen, especially rHev b 6.02, for HCWs with LA. Hamilton et al. also reported that in vitro assays possess suboptimal diagnostic sensitivity compared to SPTs in identifying HCWs with LA.34

We measured the total amount of proteins and allergens in each NRL glove that had been used in our hospital. The total amounts of proteins were 265 μg/g in the surgery glove and 95 μg/g in the examination glove. The antigenic protein concentrations were 24.9 μg/g and 1.0 μg/g in each respective glove. Our results of allergen levels with the gloves were low compared with the NRL gloves used in Europe and the US.23

Children with neural tube defects such as SB have a particularly high prevalence of LA. Latex-sensitive persons with SB reacted preferentially to Hev b 1 and Hev b 3 proteins, whereas latex-sensitive HCWs are more apt to be sensitized to Hev b 5 and Hev b 6. Such differences are considered due to the different...
amounts of major allergic proteins eluted from causative products in patient groups. In our research, the allergens of the NRL gloves were only Hev b 5 and Hev b 6.02. We consider that those results have reflected the clinical conditions of HCWs. Yip et al. have reported that the allergenicity of NRL products can be estimated only by measuring the levels of four allergens: Hev b 1, Hev b 3, Hev b 5, and Hev b 6.02. They performed similar examinations in Singapore HCWs and reported that NRL allergen levels (Hev b 1, Hev b 3, Hev b 5, and Hev b 6.02) are present in the majority of examination gloves at sufficiently high levels to cause LA among sensitized persons. They concluded that their research provides evidence that could require manufacturers to produce gloves with low NRL allergen levels and to report allergen levels in the glove product information. Therefore, in this study we analyzed these four allergens in NRL gloves. Yeang et al. suggested that Hev b 5 and Hev b 13 played important roles in determining the allergenicity of NRL gloves. In this study, we did not estimate the amount of Hev b 13 because it was difficult to prepare native Hev b 13 with sufficient purity. On the other hand, Palosuo et al. quantified four NRL allergens (Hev b 1, 3, 5, and 6.02) in all medical glove brands marketed in Finland in 1999, 2001, and 2003 by a capture enzyme immunoassay. They concluded that when the sum of these four allergens was 0.15 μg/g, these gloves could be distinguished as ‘low allergenic’. In our examinations, the sum of four allergens was 2.18 μg/g in the surgery glove and 0.45 μg/g in the examination glove, suggesting that these gloves had high allergenicity. Hev b 5 and Hev b 6.02 were detected in the surgery glove, and Hev b 6.02 was detected in the examination glove. The allergenicity results in the NRL gloves were the same as the SPT results and specific IgE antibodies in HCWs sensitized occupationally by NRL gloves were Hev b 6.02. We consider that those results have reflected the clinical conditions of HCWs. Yip et al. performed similar examinations in Singapore HCWs and reported that NRL allergen levels (Hev b 1, Hev b 3, Hev b 5, and Hev b 6.02) are present in the majority of examination gloves at sufficiently high levels to cause LA among sensitized persons. The guideline for LA was made in 2006. The guideline includes many educational suggestions. It is very useful for HCWs and hospital managers. However, because of the limitation due to data derived from only retrospective studies, Bousquet et al. reported that the effect of these interventions could not be assessed with powder-free NRL gloves. The effect of powder-free gloves was examined only in one prospective cohort study, which failed to show a protective effect of powder-free NRL gloves for LA. Further studies are needed to investigate this point. In this study, we characterized the most important allergen in HCWs sensitized occupationally by NRL gloves. We concluded that the main allergen in HCWs sensitized occupationally by NRL gloves was Hev b 6.02. More measurements for LA are needed in hospital settings. In addition, hospitals will have to continue to be cautious about latex exposure and be particularly mindful of the amounts of Hev b 5 or Hev b 6.02 in latex gloves.

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