
Clinical and occupational outcomes in health care workers with natural rubber latex allergy

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Background: There is limited information pertaining to clinical outcomes and economic consequences of natural rubber latex (NRL) allergy in health care workers (HCWs).

Objective: To evaluate retrospectively health and economic outcomes in HCWs identified with NRL allergy and percutaneous reactivity to NRL.

Methods: Sixty-seven HCWs with NRL allergy, confirmed by percutaneous reactivity to non-ammoniated latex (NAL) extract, were administered a detailed questionnaire to evaluate clinical and economic outcomes of active work and environmental interventions subsequent to recognition of work-related symptoms associated with NRL gloves.

Results: Diagnoses based on predetermined case definitions associated with direct or indirect exposure to NRL gloves included contact urticaria in 67 (100%); work-related rhinitis in 23; work-related asthma symptoms in 25; and work-related anaphylaxis in 4 workers. Work related symptoms reportedly resolved in 44 of 49 (90%) of NAL skin test-positive workers who had reported skin, respiratory, and/or systematic symptoms and remained in their current work area and who switched to non-NRL gloves. Four of 24 (17%) workers with work-related asthma symptoms were compelled to change employment to NRL-safe workplaces, resulting in a mean 24% reduction in annual income.

Conclusions: Clinical outcomes in this group of HCWs with NRL allergy were favorable after institution of interventions but incurred deleterious consequences in a minority of workers.

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INTRODUCTION

The widespread use of natural rubber latex (NRL) gloves in health care workers (HCWs) has been associated with high prevalences of work-related sensitization to NRL protein allergens.^{1,2} Various estimates of immunoglobulin E-mediated sensitization to NRL allergens have ranged between 5 and 15%.^{3–5} Because of high prevalence rates of NRL sensitization among HCWs combined with substantial workplace exposure to ambient allergens, it has been speculated that NRL allergy could become a major cause of work-related illness and disability.⁶ Although there have been many published studies pertaining to the epidemiology and clinical evaluation of NRL allergy, there are far fewer data pertaining to clinical and economic outcomes of affected HCWs. This paper reports effects on work-related symptoms by workplace interventions instituted in 67 HCWs identified with NRL allergy. Effects of the outcomes resulting from interventions were evaluated in terms of work-related symptoms, changes in occupations and job status as well as the economic impact of job changes.

METHODS

Subjects

Sixty-seven HCWs living in the Greater Cincinnati area were recruited by advertisement for participation in a study evaluating in vivo skin prick test reactivity of purified Hev b proteins that had been isolated from NRL.⁷ Patients were recruited who gave histories of rash or itching associated with direct contact to NRL gloves. Cutaneous symptoms have been reported in more than 90% of HCWs with NRL allergy; thus, despite exclusion of persons without cutaneous complaints, this population was representative.⁸ To qualify, subjects were required to demonstrate a positive skin puncture test to a non-ammoniated NRL (NAL) extract. The NAL extract was provided by Dr. Robert Hamilton and had previously been evaluated in a multicenter study for use as a diagnostic skin test reagent.⁸

Patients who were considered by the physician to have clinically unstable asthma were excluded from skin testing as well as those with a baseline forced expiratory volume in 1 second (FEV₁) of <70% predicted. The latter exclusion was instituted to reduce and prevent potential systemic allergic reactions to skin prick testing with NAL and Hev b proteins. Only one HCW was excluded at screening because of the aforementioned asthma exclusion criteria: an oral surgeon with asthma since early childhood and an FEV₁ of 51% predicted. He reported a skin rash but denied other symptoms associated with wearing NRL gloves. The Centers for Dis-

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ease Control/National Institute for Occupational Safety and Health Human Subjects Review Board approved the study protocol, and all participants had given informed consent before entry.

Questionnaire

A questionnaire was administered to all participants to gather retrospective data on exposure history: clinical symptoms related to NRL glove exposure, specific environmental interventions, and outcomes after interventions. The questionnaire was modified from an instrument used by Liss et al.⁹ Exposure data included previous duration of NRL glove use and general types of gloves used by each HCW. Reliable information was not available pertaining to specific brands of NRL glove products used by HCWs. Information was obtained pertaining to interventions that included personal glove changes by affected HCWs with NRL allergy, as well modifications in glove use of unaffected co-workers. Information was collected pertaining to the status of work-aggravated symptoms after intervention, job changes, and economic impact (ie, change in annual income) attributable to job changes caused by work-related morbidity.

The following case definitions for NRL work-related disorders (Table 1) assigned to HCWs were based upon responses reported on the questionnaires: 1) work-aggravated contact urticaria; 2) work-aggravated rhinitis with contact urticaria; 3) work-aggravated asthma with concurrent contact urticaria; and 4) work-related anaphylaxis. Because work-aggravated asthma was unable to be confirmed by specific challenge studies or monitoring of lung function at work, it is likely that identification of work aggravated asthma by the case definition overestimated the prevalence of occupational asthma (OA).

Skin Testing

An NAL extract, provided by Dr. Robert Hamilton and previously validated in a multicenter clinical study to be a clinically useful diagnostic NRL skin test reagent,⁸ was used to confirm immunoglobulin E-mediated sensitization to NRL. Skin prick testing was performed with a bifurcated needle (Allergy Labs of Ohio, Columbus, OH) using serial 10-fold

dilutions prepared from a starting concentration of 1 mg/mL NAL extract(10⁻⁶ to 1 mg/mL). Skin puncture testing was performed at 15- to 20-minute intervals with increasing concentrations of NAL extract until either no response or a positive skin test reaction was observed (ie, wheal of at least 3 mm > saline). Patients were also tested for atopic status with a panel of 12 aeroallergens (timothy, meadow fescue, American elm, maple, white oak, house-dust mite, ragweed, *Alternaria*, *Cladosporium*, *Helminthosporium*, cat and dog epidermal extracts [ALK America, Wallingford, CT]). Histamine dihydrochloride (10 mg/mL) was used as the positive control and saline was used as the negative control.

RESULTS

Three male and 64 female HCWs (mean age 36.1 years; range 21 to 67) participated in this study. Workers wore NRL gloves for a mean 5.2 years (range 0 to 32) before the onset of work-aggravated NRL glove-associated symptoms. Fifty-five of 62 (89%) workers were atopic and exhibited percutaneous reactivity to at least one common aeroallergen. All subjects exhibited percutaneous sensitization to NAL and 97% of the group reacted at endpoint percutaneous threshold concentrations between 0.001 and 10 µg/mL of NAL extract and two workers reacted to NAL at 1 mg/mL. Participants reported that occupational symptoms persisted for a mean 4.5 years (range 0 to 19) before the initiation of specific interventions.

As mentioned, all participants had work-aggravated urticaria, but only 15 reported contact urticaria as their sole clinical manifestation associated with NRL glove exposure. Among the participants, there were 23 reporting work-aggravated rhinitis, 25 experienced work-aggravated asthma, and 4 who reported anaphylaxis.

Of the 15 workers presenting exclusively with contact urticaria, a glove change was instituted in 13 (Fig 1). Of the 11 who changed to non-NRL gloves, all had complete resolution of work-related hives. Two changed to powder-free NRL gloves, an intervention that was successful in one subject. Contact urticaria persisted in the one worker who continued to use NRL gloves.

Table 1. Case Definitions for NRL Allergy Based on Questionnaire Responses

Latex allergy terminology	Case definition
Work-aggravated contact urticaria	1. Hives with itching occurring during the skin contact with NRL gloves 2. Positive skin puncture test to non-ammoniated latex (NAL) skin test antigen
Work-aggravated rhinitis	1. Sneezing, nasal congestion, and eye itching associated with work exposure to powdered NRL gloves 2. Positive skin puncture test to NAL skin test antigen
Work-aggravated asthma	1. Immediate onset wheezing, shortness of breath, and chest tightness associated with work exposure to powdered NRL gloves 2. Positive skin puncture test to NAL skin test antigen
Work-aggravated anaphylaxis	1. Immediate onset dyspnea, diffuse urticaria, and/or hypotension requiring emergency treatment with epinephrine 2. Positive skin puncture test to NAL skin test antigen

NRL, natural rubber latex.

Occupational urticaria (n=15) Interventions and outcomes

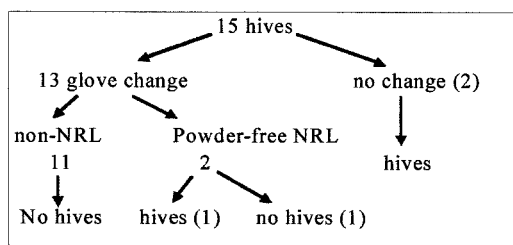


Figure 1. Results of interventions among 15 HCWs presenting exclusively with work-related urticaria.

Twenty-two of 23 workers with work-related rhinitis and contact urticaria made a glove change. Contact urticaria and rhinitis resolved in 15 of 18 (83%) subjects who changed to non-NRL gloves. Three of the 18 who changed to non-NRL gloves reported no subsequent skin symptoms but did report persistent symptoms of work-related rhinitis. Symptoms of work-related rhinitis and urticaria persisted in four HCWs who were specifically changed to powder-free NRL gloves.

Workplace interventions were initiated in 20 of 25 subjects reporting symptoms consistent with work-aggravated asthma (Fig 2). Without exception all had concurrent symptoms of work-related urticaria and rhinitis. Nineteen workers were switched to non-NRL gloves and 18 reported resolution of all symptoms despite the fact that 12 of 18 (66%) continued to work with fellow employees who were using powdered NRL gloves. Another HCW had a job change that resulted in resolution of both contact urticaria and asthma, although

rhinitis symptoms persisted. Four workers in the asthma group left their jobs because of persistence of occupational symptoms before specific interventions were initiated. One HCW continued to work in the same health care facility without intervention, and all NRL-associated symptoms persisted. The mean FEV₁ was 94% of predicted at the time of evaluation, which occurred a mean 3.9 years after workplace interventions were initiated. Two of the latter group were being treated with daily asthma medications, one with inhaled nedocromil and another with fluticasone dipropionate.

There were four subjects who reported systemic anaphylactic symptoms associated with NRL-glove exposure. Three were moved to NRL-free environments in the same health care facility and had no further NRL-related symptoms. The remaining subject stayed at the same job and changed to personal use of non-NRL gloves. Although the latter HCW experienced work-aggravated rhinitis and asthma symptoms, there were no further reports of anaphylaxis.

There were 4 of 24 (17%) workers, classified with work-related asthma, who changed jobs because of NRL allergy. Job changes led to resolution of work-related symptoms but also resulted in a mean 24% reduction in income (14 to 41%) in this group. Two workers changed from inpatient to outpatient health care settings, whereas two others moved to non-health care vocations. One patient applied for and received workers' compensation.

DISCUSSION

This study explored clinical and job outcomes in a group of 67 HCWs with NRL allergy who presented with a variety of NRL-triggered allergic symptoms. This survey uniquely focused on HCWs with NRL allergy who reported work-related cutaneous, rhinitis, asthmatic, and systemic symptoms rather than strictly concentrating on OA.^{10,11} Allergic sensitization to NRL was confirmed by a positive skin prick test with a previously validated NAL skin test reagent.⁸ Fifteen patients who experienced exclusively contact urticaria related to use of NRL gloves reported that minimal interventions (ie, personal glove changes to non-NRL gloves) were effective in reducing cutaneous symptoms. Thus, not surprisingly, a switch to non-NRL gloves was reported to be successful in reducing cutaneous symptoms associated with NRL allergy. A switch to non-NRL gloves was also adequate in controlling work aggravated rhinitis symptoms in the majority (83%) of HCWs who reported them. Although information on the specific NRL gloves used by co-workers was not available, it is likely that the persistent rhinitis reported by the remaining workers resulted from continued ambient exposure to powdered-NRL gloves used by fellow employees. It was not unexpected that symptoms persisted in NRL-sensitized workers who changed to non-powdered NRL gloves.

Interventions were effective in all 19 HCWs with work-related asthma symptoms who remained in their workplace. As noted, 12 of 19 workers who reported resolution of asthma-like symptoms after interventions were instituted were still passively exposed to NRL via powdered gloves

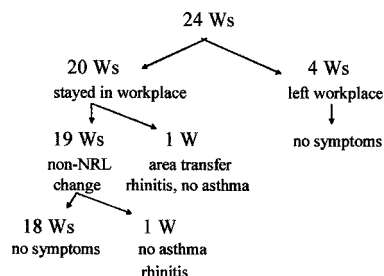


Figure 2. Interventions and outcomes in 24 of 25 workers who reported asthma symptoms. One worker, not shown in the figure and for whom no intervention was initiated, remained in the work environment and had persistent work-related asthma symptoms.

worn by co-workers. These unexpected favorable outcomes after apparently inadequate interventions could be explained in several ways. It is quite possible that, despite asthma-like symptoms and a positive skin test to NRL, an unknown number of these workers did not have OA. This hypothesis is supported by a previous report of Vandenplas et al,¹² in which 25% of workers presenting with percutaneous sensitization to NRL and work-related asthma symptoms had negative responses after NRL-specific inhalation challenge. It is also possible that favorable outcomes in HCWs reporting improvement in asthma symptoms could be attributable to significant reductions in ambient NRL exposures in their respective work areas resulting from NRL glove changes (eg, low-allergen gloves) in co-workers. Such an intervention was found to be effective by Tarlo et al¹³ who recently reported that an institutional change to powder-free NRL and/or low-protein NRL gloves in an Ontario hospital resulted in resolution of work-related symptoms in 2 of 3 workers with asthma and anaphylaxis. In the present study, the favorable outcomes after minimal interventions in those classified with work-aggravated asthma could be attributed to a mild baseline asthma severity status; this was reflected by the fact that only 2 of 25 workers required long-term daily asthma medications. Theoretically, remaining in a health care environment where intermittent ambient exposure to NRL allergens persists could raise concern that asthma severity could progress. However, similar to our experience, Vandenplas et al¹⁰ reported that asthma symptoms and histamine PC₂₀ improved in a group of HCWs with NRL-induced asthma after NRL exposure was reduced but not eliminated. These outcomes were identical to those achieved in another group of workers in whom complete cessation of exposure to NRL had been instituted.¹⁰

Five of 24 HCWs (21%) reporting asthma symptoms were compelled to either leave their work area or terminate employment in their current health care facility because of persistent symptoms (Fig 2). Because this group required more definitive intervention measures (ie, changing jobs), it is likely (although unproven) that this subset of HCWs experienced more severe work-related asthma symptoms. Spirometry studies performed in 24 HCWs with asthma symptoms were normal and only 2 workers had chronic persistent asthma necessitating long-term treatment with inhaled anti-inflammatory agents. Thus, at 4 years after initiation of interventions, this group of HCWs with NRL allergy and asthma symptoms did not exhibit evidence of long-term impairment based upon FEV₁ and asthma medication requirements.

It is unlikely that the latter outcomes are attributable to selection bias in workers identified with work-related asthma. Only one HCW with severe airways obstruction was not invited to participate. It can be argued that exclusion of workers without a history of skin rash associated with the use of NRL gloves could have added selection bias to our study population. This is unlikely to have a major effect because nearly all symptomatic NRL-skin test-positive workers had either rash and/or urticaria. Yassin et al¹⁴ reported that, of 38

workers with positive skin tests, 84% complained of itching or rash and 68% reported a rash associated with using gloves. Hamilton and Adkinson⁸ reported that hives, rash, swelling, and/or itching were reported by 116 of 124 (93%) adult HCWs with NRL-skin test positivity. Thus, although a small number of workers without skin symptoms may have been excluded on this basis, the study population was generally representative of HCWs with confirmed NRL allergy.

Phillips et al¹⁵ estimated that costs of interventions required to achieve an NRL-safe environment are less than costs incurred by cases awarded permanent total disability for which no attempt was made to modify the work environment. In Finland, a questionnaire survey¹⁶ was conducted that evaluated "work ability index" and found that 32 female HCWs with NRL allergy had reduced work ability index when compared with nonallergic co-workers; 10 (31%) changed jobs after development of NRL allergy.

In our study, a mean 24% reduction in income was realized by four workers reporting asthma symptoms (6% of all workers evaluated) that forced them to change their jobs. In those reporting an income loss, only one filed a claim and subsequently received workers' compensation. All were gainfully employed at the time of the survey. No cases of permanent disability resulting from NRL allergy were identified. It was noteworthy that nearly all of the HCWs who had NRL allergy adapted quickly to impositions caused by their condition. The exceptions to this were the four workers forced to change jobs, two of whom were unable to return to any health care facility. Because only one worker filed workers' compensation, the potential costs of NRL allergy were avoided.

Vandenplas et al¹⁰ reported an outcomes study of workers identified with NRL-induced OA confirmed by specific inhalation challenge for a median duration of 56 months. He observed that complete cessation of NRL glove exposure (and leaving the job) was associated with much greater frequencies of work disability and income loss than in those with OA who remained in the work setting where exposure modification had been initiated. The authors concluded that reduction of exposure to NRL gloves appears to be more cost-effective than complete removal from exposure.

CONCLUSION

Despite the widespread availability of substitute glove products at the time of this survey, HCWs continued to experience work-related symptoms associated with exposure to powdered NRL gloves. It appeared that many (but not all) health care facilities were reluctant to accommodate some NRL-allergic workers, particularly those with work-related asthma symptoms. Despite concern that the most severely affected workers were not adequately accommodated, interventions limited primarily to glove changes in affected HCWs and/or their co-workers were adequate in remediating work-related urticarial, nasal, and asthmatic symptoms caused in the vast majority of workers with NRL allergy.

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REFERENCES

1. Ross DJ, Keynes HL, McDonald JC. SWORD '97: surveillance of work-related and occupational respiratory disease in the UK. *Occup Med* 1998;48:481–485.
2. Liss GM, Sussman GL. Latex sensitization: occupational versus general population prevalence rates. *Am J Ind Med* 1999;35:196–200.
3. Poley GE Jr, Slater JE. Latex allergy. *J Allergy Clin Immunol* 2000;105:1054–1062.
4. Toraason M, Sussman G, Biagini R, et al. Latex allergy in the workplace. *Toxicol Sci* 2000;58:5–14.
5. Mace SR, Sussman GL, Liss G, et al. Latex allergy in operating room nurses. *Ann Allergy Asthma Immunol* 1998;80:252–256.
6. Kelly KJ, Walsh-Kelly CM. Latex allergy: a patient and health care system emergency. *Ann Emerg Med* 1998;32:723–729.
7. Yeang HY, Chow KS, Yusof F, et al. Appraisal of latex glove proteins in the induction of sensitivity to multiple latex allergens. *J Investig Allergol Clin Immunol* 2000;10:215–222.
8. Hamilton RG, Adkinson NF Jr. Diagnosis of natural rubber latex allergy: multicenter latex skin testing efficacy study. Multicenter Latex Skin Testing Study Task Force. *J Allergy Clin Immunol* 1998;102:482–490.
9. Liss GM, Sussman GL, Deal K, et al. Latex allergy: epidemiological study of 1351 hospital workers. *Occup Environ Med* 1997;54:335–342.
10. Vandenplas O, Jamart J, Delwiche JP, et al. Occupational asthma caused by natural rubber latex: outcome according to cessation or reduction of exposure. *J Allergy Clin Immunol* 2002;109:125–130.
11. Liss GM, Tarlo SM. Natural rubber latex-related occupational asthma: association with interventions and glove changes over time. *Am J Ind Med* 2001;40:347–353.
12. Vandenplas O, Binard-Van Cangh F, Brumagne A, et al. Occupational asthma in symptomatic workers exposed to natural rubber latex: evaluation of diagnostic procedures. *J Allergy Clin Immunol* 2001;107:542–547.
13. Tarlo SM, Easty A, Eubanks K, et al. Outcomes of a natural rubber latex control program in an Ontario teaching hospital. *J Allergy Clin Immunol* 2001;108:628–633.
14. Yassin MS, Lierl MB, Fischer TJ, et al. Latex allergy in hospital employees. *Ann Allergy* 1994;72:245–249.
15. Phillips VL, Goodrich MA, Sullivan TJ. Health care worker disability due to latex allergy and asthma: a cost analysis. *Am J Public Health* 1999;89:1024–1028.
16. Kujala VM, Karvonen J, Laara E, et al. Postal questionnaire study of disability associated with latex allergy among health care workers in Finland. *Am J Ind Med* 1997;32:197–204.

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