

Effect of reduced exposure on natural rubber latex sensitization in health care workers

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Background: Knowledge about the long-term course of allergy or sensitization to natural rubber latex (NRL) is insufficient.

Objective: To investigate the long-term effect of preventive measures on sensitization variables in health care workers who had been diagnosed as having NRL allergy (NRLA) or NRL sensitization (NRLS) without clinical symptoms.

Methods: Repeated follow-up investigations, skin prick tests, and NRL specific IgE serum antibodies were performed in 88 health care workers—33 with NRLA and 55 with NRLS. All workers had been instructed to avoid NRL exposure. At the workplace, powder-free NRL gloves for all other employees were gradually introduced. Re-evaluations were done at 14 ± 3.7 (N = 86) and 38 ± 4.0 (N = 78) months after the first examination.

Results: At the last follow-up, a loss of skin prick test reactivity to NRL was observed in 1 of 29 subjects with NRLA (3.4%) and 16 of 35 with NRLS (45.7%) with previous skin test reactions ($P < .001$). Among those subjects who demonstrated a kU/L level (CAP class) equal to or greater than class 1 to NRL at the initial examination, NRL-specific IgE was absent at the last follow-up in 8 (32.0%) of 25 subjects with NRLA and 14 (38.9%) of 36 with NRLS. At the final examination, we could no longer demonstrate sensitization to NRL by any method in 24 (27.3%) of 88 health care workers. Complete loss of NRL sensitization was less frequent in subjects with NRLA than in those with NRLS (1 of 33 or 3.0% vs 23 of 55 or 41.8%; $P < .001$).

Conclusions: Implementation of simple preventive measures lowers markers of sensitization to NRL quickly in many health care workers with NRLA or NRLS.

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INTRODUCTION

Immediate-type hypersensitivity to natural rubber latex (NRL) was first reported in 1926.¹ Not until the 1980s, however, did IgE-mediated reactions to NRL become an important issue. In addition to intense exposure to material containing NRL allergens, the main risk factors for sensitization to NRL are atopy^{2–4} and hand eczema.^{5–7} Because of frequent use of gloves and contact with many other items made from NRL in the medical field, NRL allergy (NRLA) is found in up to 17% of health care workers^{8–12} and in up to 70% of patients needing frequent or continuous care, particularly those with spina bifida.^{13–21}

The most important measure in the management of allergic disease is strict avoidance of allergen contact. Adequate secondary prevention also allows health care workers with NRLA to remain at their jobs.^{22–25} Allergen avoidance should not only diminish allergic disease but also reduce sensitization, since the permanent booster of repeated allergen contact is removed. Heretofore, the efficacy of allergen avoidance has been investigated only in small and selected groups of health care workers with NRLA. These studies found clinical improvement and also a decrease in factors reflective of NRL sensitization (NRLS), in part.^{23–27} Despite continuous exposure, not all health care workers with skin test reactions or specific IgE antibodies in the serum to NRL ultimately man-

ifest allergic disease (ie, NRLA).^{9,28} Thus far, investigators do not know whether NRLS in these subjects would also decline if measures for allergen avoidance were introduced.

In 1997, we initiated a prospective long-term epidemiologic study involving 759 employees from a university hospital in Bavaria, 107 (14.1%) of whom were found to have NRLA or NRLS.¹² After the introduction of NRL avoidance measures, the future course of these employees was evaluated relative to clinical symptoms and features of sensitization.

SUBJECTS AND METHODS

Overall Study Design

In a prospective longitudinal study,¹² employees of the Klinikum der Universität München, a university hospital, were scheduled for evaluation for NRLA or NRLS. An initial examination performed between July 1997 and August 1998 aimed to diagnose symptomatic NRLA or NRLS without clinical symptoms in a large cohort of health care workers.

After these examinations were initiated, the use of powder-free gloves was introduced for all employees. Subsequently, universal use of powder-free gloves could be achieved in direct association with this study. Concurrently, all workers with NRLA or NRLS but without symptoms were advised to use only NRL-free gloves and to avoid other exposure to NRL.

Repeated follow-up examinations involved all available employees with NRLA or NRLS identified at the first investigation. The objectives of the follow-up investigations were to determine the further clinical course and to evaluate the persistence of or change in features of sensitization to NRL—that is, skin prick test reactivity and concentration of NRL-

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specific IgE antibodies in the serum. A first follow-up investigation was done a mean of 14 ± 3.7 months (January–November 1999) and a second follow-up took place a mean of 38 ± 4.0 months (August 2000–May 2001) after the initial examination. The individual health care worker's last follow-up was denoted as the final examination.

Study Population

Of 823 employees from various representative hospital areas chosen for this investigation, 759 (92.2%) were available for the initial examination. The study was approved by the local Institutional Review Board (Ethikkommission der Medizinischen Fakultät der Ludwig-Maximilians-Universität München, Munich, Germany). Informed, written consent was obtained from all study participants.

History

A questionnaire-based history was elicited with regard to atopic diseases (allergic rhinoconjunctivitis, allergic asthma, and atopic eczema), hand eczema, previous and current occupation, glove use (powdered or unpowdered NRL gloves as well as NRL-free gloves), contact with NRL outside the work setting, and immediate-type reactions attributable to contact with NRL.

Skin Tests

Skin prick tests were performed with a commercial NRL test solution (1%; Bencard, Munich, Germany), a raw ammoniated NRL milk (Hartmann, Heidenheim, Germany), and a glove extract (1-g glove/1-mL physiologic saline, shaken 1 hour at room temperature) from powdered NRL gloves (Sempermed; Semperit, Vienna, Austria). At the follow-up examinations, an additional NRL test extract [100 HEP (histamine equivalent potency); ALK-Scherax, Hamburg, Germany] was also used. The sensitivity and specificity of skin prick test preparations had been previously evaluated.^{29–32} In subjects reporting immediate-type symptoms from exposure to NRL, tests were begun with the 1% NRL test solution and continued only if no reaction or only a weak reaction occurred to this solution. At the initial examination, subjects were considered sensitized to NRL only if a reaction occurred to the 1% NRL test solution or to both of the other preparations. At follow-up, a loss of skin prick test reactivity was stated only if no reactions were seen to any of the NRL test preparations, including the additionally tested 100-HEP extract. Additional skin prick tests were performed with common aeroallergens (grass pollen, *Dermatophagoides pteronyssinus*, and cat; Bencard). Reactions were evaluated after 20 minutes and interpreted as positive if a wheal 2 mm or larger in diameter was present.³³ Physiologic saline and 0.1% histamine dihydrochloride served as negative and positive controls, respectively. Results of skin tests were disregarded if a subject had a reaction to the negative control or no reaction to the positive control. Exclusion criteria for skin prick tests were pregnancy, severe cardiovascular disease, unstable pulmonary disease, or therapy with a β -adrenergic blocking agent.

NRL-Specific Serum IgE

NRL-specific IgE antibodies in the serum were determined by Pharmacia CAP-fluorescence enzyme immunoassay, a commercial kit detecting NRL allergens not additionally spiked with Hev b 5 or Hev b 12 (Pharmacia AB, Uppsala, Sweden). Results are reported as kU/L or CAP class. If specific IgE antibodies were present at the initial examination or if previously demonstrable NRL-specific IgE antibodies had changed by at least one CAP class at follow-up, duplicate measurement was done, and mean values were recorded as the results.

Challenge Tests

Challenge tests were performed on the back of a subject's hand by applying a piece of powdered NRL glove (Sempermed) fixed with an NRL-free adhesive (Fixomull stretch; Beiersdorf, Hamburg, Germany). The test material was removed after 30 minutes, and the test site was evaluated immediately (or later in the case of a postponed reaction). A control test was performed in the same way with NRL-free glove material (Glovex Neoderm; Beiersdorf). The challenge test result was considered positive if whealing occurred. In addition to the aforementioned exclusion criteria for the skin prick test, subjects were excluded from challenge tests if they had a history of previous severe anaphylactic reactions to NRL exposure. In subjects with NRLA, challenge tests were not reapplied at the follow-up examinations.

NRLA or NRLS

NRLA was diagnosed if the subject had NRLS (demonstration of skin prick test reactivity to NRL, NRL-specific IgE antibodies in the serum, or both) and a definite history of immediate-type symptoms to NRL material or a positive challenge test result to NRL (or both).

Atopy

Atopy was diagnosed if the subject had a history of any atopic disease (allergic rhinoconjunctivitis, allergic asthma, or atopic eczema) or at least one positive skin prick test reaction to grass pollen, *D pteronyssinus*, or cat.

Statistical Analysis

The statistical software SPSS for Windows (SPSS, Inc, Chicago, IL) was used. Categorical variables were compared with use of the χ^2 test. For comparison of continuous variables, analysis of variance was used. Independence of categorical variables was tested by Pearson χ^2 test. We used Wilcoxon test for 2-paired samples and the Friedman test for 3 samples to analyze the change of the concentration of NRL-specific IgE during the observation period. $P < .05$ was considered statistically significant.

RESULTS

Characteristics of Study Population

At the initial examination of the 759 employees, 107 (14.1%; 70 women and 37 men) were sensitized to NRL. Conclusive skin prick test reactions were found in 57 (55.3%) of 103

subjects, and NRL-specific IgE antibodies were demonstrable in 74 (69.2%) of 107 subjects. No systemic anaphylactic symptoms occurred at skin prick testing. The sensitivity of the 1% test extract was 65.7% (corresponding specificity, 97.5%), of the glove extract was 80.6% (specificity, 96.9%), and of the NRL milk was 97.1% (specificity, 89.1%). Challenge tests were done in 29 of 38 subjects later diagnosed as having NRLA. Erythema and pruritus developed at the test site in 9 subjects, and localized urticaria occurred in 20 subjects, 2 of whom also had mild respiratory symptoms at the time of the challenge test. On the basis of the history or challenge tests with NRL (or both), 38 (5.0%) of 759 were diagnosed as having NRLA, and 69 (9.1%) had NRLS without clinical symptoms on NRL contact. Of these 107 subjects, 88 participated in the follow-up investigations, 86 in the first, and 78 in the second re-examination. Details of these 88 participating subjects at the initial investigation are shown in Table 1.

One office worker with NRLA had undergone repeated surgical and medical procedures and obviously had acquired NRLA at some place other than the workplace. No other subjects with NRLA or NRLS had a history of repeated invasive procedures. At the first follow-up investigation, 8 subjects had retired from their former occupation, as had 7 subjects at the second follow-up examination. Only 1 study subject had retired from his occupation as a physician because of his NRLA. All other subjects who had changed their job function at one of the follow-up examinations had left the hospital permanently or temporarily because of motherhood, retirement, or private reasons.

Symptoms of NRLA

At the initial investigation, all 33 subjects with NRLA had reported previous symptoms attributable to exposure to NRL.

At the first follow-up re-evaluation, further reactions had occurred in 14 (42.4%) of the 33 subjects (Table 2). Symptoms had occurred only in private life in 3 subjects, only at the workplace in 7, and in both settings in 4. At the second follow-up, only 4 (12.9%) of 31 subjects reported having symptoms of NRLA during the second observation period (Table 2). Despite receiving detailed information about preventive measures for medical procedures, 6 subjects had experienced symptoms during dental treatment, anesthesia, or gynecologic examinations.

At both follow-up examinations, no allergic symptoms to NRL were reported by any of the 55 health care workers with NRLS diagnosed at the initial examination. Challenge tests were performed at the second examination in 52 of 53 subjects and at the third examination in 23 of 47 subjects who had demonstrated NRLS. No specific symptoms were elicited.

Skin Prick Tests With NRL

The results of the skin prick tests are summarized in Tables 3 and 4. At the initial examination, study subjects with NRLA (31 of 31, or 100%) exhibited skin prick test reactions to at least 1 NRL test extract more frequently than did study subjects with NRLS (35 of 54, or 64.8%; $P < .001$). This same pattern prevailed and was statistically significant at both the first ($P < .001$) and the second ($P < .001$) follow-up. Only 1 (3.4%) of 29 subjects with NRLA previously reactive to skin prick testing had lost skin prick test reactivity to NRL by the time of the final examination, whereas this change occurred in 16 (45.7%) of 35 subjects with NRLS ($P < .001$). Study subjects without atopy lost skin reactivity to NRL more often than did those with atopy (6 of 15, or 40.0%, vs 11 of 68, or 16.2%), and skin test reactivity to NRL only at the final examination but not at the first examination was found in 7

Table 1. Characteristics of Study Subjects with Natural Rubber Latex Allergy or Sensitization at Initial Investigation*

Factor	NRLA (n = 33)	NRLS (n = 55)	Total group (N = 88)	P value
Demographic or clinical feature				
Age, y, range (mean)	21–62 (33.6)	21–62 (34.1)	21–62 (33.9)	.788†
Male subjects	12 (36.4)	18 (32.7)	30 (34.1)	.728‡
Atopy	29 (87.9)	44 (80.0)	73 (83.0)	.34‡
History of hand eczema	16 (48.5)	11 (20.0)	27 (30.7)	.014‡
Occupation				
Nurse	12 (36.4)	24 (43.6)	36 (40.9)	
Physician	16 (48.5)	17 (30.9)	33 (37.5)	.458‡
Laboratory technician	4 (12.1)	8 (14.6)	12 (13.6)	
Office worker	1 (3.0)	6 (10.9)	7 (8.0)	
Skin prick test reaction to NRL				
NRL-specific IgE (CAP class)				ND
Positive	0	8 (24.2)	18 (32.7)	26 (29.5)
Negative	≥1	16 (29.1)	16 (18.2)	
Positive	≥1	23 (69.7)	20 (36.4)	43 (48.9)
ND	≥1	2 (6.1)	1 (1.8)	3 (3.4)

Abbreviations: ND, not done; NRL, natural rubber latex; NRLA, natural rubber latex allergy; NRLS, natural rubber latex sensitization.

* Except for age, data are shown as number of subjects (%).

† Analysis of variance.

‡ χ^2 test.

Table 2. Symptoms Attributable to Natural Rubber Latex Allergy*

Symptom	Initial examination (I) (N = 33)	First follow-up (II) (N = 33)	Second follow-up (III) (N = 31)
Contact urticaria	33 (100.0)	14 (42.4)	4 (12.9)
Rhinoconjunctivitis	14 (42.4)	5 (15.2)	2 (6.5)
Asthma	8 (24.2)	4 (12.1)	1 (3.2)
Cardiovascular symptoms	2 (6.1)	1 (3.0)	0
Any	33 (100.0)	14 (42.4)	4 (12.9)

* Data are shown as number of subjects (%). P values (χ^2 test): 0 vs I, < .001; 0 vs II, < .001; I vs II, .002.

Table 3. Skin Prick Test Reactions to Natural Rubber Latex in 33 Subjects with Natural Rubber Latex Allergy*

Factor	Initial examination	First follow-up	Second follow-up	Final examination
Any test reaction/tested subjects	31/31 (100)	26/27 (96.3)	27/28 (96.4)	29/30 (96.7)
No test reaction	...	1/27 (3.7)	1/28 (3.6)	1/30 (3.3)
No test reaction in previously prick test-positive subjects	...	1/27 (3.7)	1/28 (3.6)	1/29 (3.4)
Not done/total group	2/33 (6.1)	6/33 (18.2)	3/31 (9.7)	3/33 (9.1)

* Data are shown as number of subjects/total number (%).

Table 4. Skin Prick Test Reactions to Natural Rubber Latex in 55 Subjects with Natural Rubber Latex Sensitization*

Factor	Initial examination	First follow-up	Second follow-up	Final examination
Any test reaction/tested subjects	35/54 (64.8)	28/50 (56.0)	19/42 (45.2)	26/54 (48.1)
No test reaction	19/54 (35.2)	22/50 (44.0)	23/42 (54.8)	28/54 (51.9)
No test reaction in previously prick test-positive subjects	...	10/32 (31.2)	14/28 (50.0)	16/35 (45.7)
Not done/total group	1/55 (1.8)	3/53 (5.7)	5/47 (10.6)	1/55 (1.8)

* Data are shown as number of subjects/total number (%).

subjects with atopy but in no study subjects without atopy ($P = .05$).

NRL-Specific Serum IgE

If only the results of the initial examination and the last follow-up (final examination) were considered, data sets from 33 subjects with NRLA and from 54 subjects with NRLS were available for evaluation. In 25 of 33 subjects with NRLA and 36 of 54 subjects with NRLS, NRL-specific IgE antibodies were detected at the first examination. At the final examination in subjects with NRLA, NRL-specific IgE could no longer be demonstrated in 8 (32.0%) of the 25 subjects, had declined by one or more CAP classes in 9 (36.0%) of the 25, and had remained within the same CAP class in 8 (32.0%) of the 25. In 6 subjects with NRLA, NRL-specific IgE antibodies were not demonstrable at the initial examination and remained negative at the final examination. Among those with NRLS, NRL-specific IgE could no longer be demonstrated at the final examination in 14 (38.9%) of the 36 subjects, had declined by one or more CAP classes in 11 (30.6%) of the 36, and had remained within the same CAP class in 11 (30.6%) of the 36. In 17 of 18 subjects with NRLS who had not exhibited NRL-specific IgE at the initial examination, NRL-specific IgE was also not demonstrable at the final exam-

ination. In 1 subject, however, NRL-specific IgE (CAP class 2) was demonstrable only at the second follow-up.

The mean value for NRL-specific IgE concentration in study subjects with NRLA declined significantly at both follow-up examinations (Table 5). In subjects with NRLS, a significant decline of the NRL-specific IgE was found only between the initial examination and the first follow-up.

With respect to the loss or decline of NRL-specific IgE, no remarkable differences were noted between subjects with NRLA (18 of 25, or 72.0%) and those with NRLS (25 of 36, or 69.4%). A loss of previously demonstrable NRL-specific IgE was more often found in subjects without atopy than in those with atopy (4 of 7, or 57.1%, vs 18 of 54, or 33.3%; $P = .025$).

NRLA or NRLS

Overall, at the individual worker's final examination, 24 (27.3%) of 88 subjects with previous skin prick test reactions to NRL, NRL-specific IgE antibodies, or both no longer demonstrated sensitization to NRL by any test (Tables 6 and 7). One (3.0%) of 33 subjects with previously diagnosed NRLA and 23 (41.8%) of 55 subjects with NRLS had lost sensitization to NRL ($P < .001$). The NRL-allergic subject who had lost NRLS also reported tolerance of NRL contact, an indication that NRLA had completely subsided. One sub-

Table 5. Natural Rubber Latex-Specific Serum IgE Antibodies, Stratified by Study Group*

Study group	NRL-specific IgE (kU/L)		
	Initial examination	First follow-up	Second follow-up
	A	B	C
Subjects with NRLA	N = 33	N = 33	N = 30
Mean $\pm$ SD	6.7 $\pm$ 15.2	3.8 $\pm$ 9.4	3.2 $\pm$ 10.1
Range (median)	0–62.0 (1.2)	0–40.6 (0.7)	0–53.6 (0.4)
	D	E	F
Subjects with NRLS	N = 55	N = 52	N = 45
Mean $\pm$ SD	1.4 $\pm$ 2.4	0.8 $\pm$ 1.3	0.5 $\pm$ 1.0
Range (median)	0–13.5 (0.6)	0–7.8 (0.0)	0–5.8 (0.0)

Abbreviations: NRL, natural rubber latex; NRLA, natural rubber latex allergy; NRLS, natural rubber latex sensitization.

* In subjects with NRLA, the NRL-specific IgE declined significantly (Wilcoxon test for 2 paired samples) between the initial examination and the first follow-up (A vs B, $P < .001$) and between the first and the second follow-up (B vs C, $P < .001$). The corresponding statistical analysis of the results in subjects with NRLS showed a significant difference between the initial examination and the first follow-up (D vs E, $P < .001$) but no significant difference between the first and the second follow-up (E vs F, $P = .073$). Over the total observation period, the concentration of NRL-specific IgE (Friedman test for 3 samples) significantly decreased both in subjects with NRLA (A vs B vs C, $P < .001$) and in subjects with NRLS (D vs E vs F, $P < .001$).

Table 6. Skin Prick Test Reactions to NRL and NRL-Specific Serum IgE Antibodies in 33 Subjects with NRL Allergy*

Skin prick test reaction to NRL	NRL-specific IgE (CAP class)	Initial examination (N = 33)	First follow-up (N = 33)	Second follow-up (N = 31)	Final examination (N = 33)
Negative	0	...	1 (3.0)	1 (3.2)	1 (3.0)
Not done	0	...	2 (6.1)	1 (3.2)	1 (3.0)
Negative	≥ 1	...	...	...	...
Positive	0	8 (24.2)	10 (30.3)	12 (38.7)	14 (42.4)
Positive	≥ 1	23 (69.7)	16 (48.5)	15 (48.4)	15 (45.5)
Not done	≥ 1	2 (6.1)	4 (12.1)	1 (3.2)	2 (6.1)
Not done	Not done	...	...	1 (3.2)	...

Abbreviation: NRL, natural rubber latex.

* Data are shown as number of subjects (%).

Table 7. Skin Prick Test Reactions to NRL and NRL-Specific Serum IgE Antibodies in 55 Subjects With NRL Sensitization*

Skin prick test reaction to NRL	NRL-specific IgE (CAP class)	Initial examination (N = 55)	First follow-up (N = 53)	Second follow-up (N = 47)	Final examination (N = 55)
Negative	0	...	15 (28.3)	18 (38.3)	23 (41.8)
Not done	0	...	1 (1.9)	2 (4.3)	...
Negative	Not done	...	1 (1.9)	1 (2.1)	1 (1.8)
Negative	≥ 1	16 (29.1)	6 (11.3)	4 (8.5)	4 (7.3)
Positive	0	18 (32.7)	11 (20.7)	7 (14.9)	8 (14.6)
Positive	≥ 1	20 (36.4)	17 (32.1)	12 (25.5)	18 (32.7)
Not done	≥ 1	1 (1.8)	2 (3.8)	2 (4.3)	1 (1.8)
Not done	Not done	...	...	1 (2.1)	...

Abbreviation: NRL, natural rubber latex.

* Data are shown as number of subjects (%).

ject with NRLS consented only to skin prick testing, and 1 subject with NRLA consented only to blood sampling. These 2 subjects had negative test results.

DISCUSSION

In a longitudinal study, 33 health care workers with NRLA and 55 with NRLS without clinical symptoms underwent

re-evaluations up to a mean of 38 months after a first examination. During this follow-up period, we had introduced individual preventive measures for subjects with NRLA or NRLS and had replaced powdered NRL gloves with powder-free NRL gloves for all workers. The key finding of this study is that, at follow-up, 27% of these 88 health care workers no longer showed signs of sensitization. Nevertheless, whereas

42% of subjects with NRLS had lost markers for sensitization to NRL completely, only 1 subject (3%) with NRLA demonstrated a comparable improvement.

In the subjects with NRLA, however, at least the occurrence of clinical symptoms significantly declined during the observation period. Thus, at the first follow-up, more than half of the subjects with NRLA reported to have become free of allergic symptoms at work, and this portion increased to nearly 90% after approximately 2 more years. Because challenge tests with NRL were not performed on these subjects at the follow-up examinations, this improvement does not necessarily indicate loss of clinical reactivity but may simply reflect successful avoidance of NRL allergens. Only 1 subject with previous NRLA was definitely able to tolerate exposure to NRL and was also found to have lost sensitization to NRL.

A decrease in NRL-allergic symptoms after introduction of preventive measures has also been found in other studies of health care workers.^{23–27} Preventive measures that differed between and also within these studies—maintenance of an overall NRL-free environment,²⁴ only avoidance of direct contact with NRL,²⁴ use of powder-free NRL gloves,^{25,26} or use of low-allergenic, powdered NRL gloves²³—were variably imposed for prevention. Irrespective of the nature of these measures, however, some preventive effect was found with all interventions. Compared with previous studies, our current study is the largest investigation of the effect of a standardized and uniform introduction of preventive measures on the clinical course of NRLA and NRLS.

Because the sensitivity of skin tests with various NRL preparations differs,^{29–32} the use of more than 1 NRL extract can improve the sensitivity of the procedure. At the beginning of our study, the criteria used to declare a skin prick test to NRL positive were restricted. Therefore, we hoped to minimize the inclusion of subjects judged to be sensitized only on the basis of a skin prick test reaction to NRL milk, which can frequently elicit nonspecific reactions. Furthermore, a finding of skin prick test reactions to very specific NRL test preparations or NRL-specific IgE antibodies does not necessarily indicate clinically evident disease (that is, NRLA). “Positive” test results in this case might be considered “falsely positive” with regard to clinical reactivity. Because these tests disclose only an immunologic sensitization, however, they must be considered clinically irrelevant but not “false.” Many other allergens have also been shown to induce immunologic sensitization without correlating clinical symptoms.^{34–36} Interestingly, of 17 subjects with NRLS who had only NRL-specific IgE at the initial examination, 7 reacted to a more sensitive skin prick test extract at follow-up. A loss of skin prick test reactivity to NRL was significantly more frequent in subjects with NRLS than in those with NRLA; it was also associated with the absence of atopy.

Recently, a reduction of skin prick test reactivity to NRL 6 months after the onset of preventive measures was found in 8 of 23 health care workers with NRLA.²⁴ This effect was more pronounced in 6 subjects who had changed to a completely NRL-free environment than in those who avoided personal

contact with NRL only but who remained in an NRL-contaminated environment.

At the first examination, 24% of our study subjects with NRLA and 33% of those with NRLS had no demonstrable NRL-specific serum IgE. Other studies have shown that up to 25% of subjects with NRLA do not exhibit NRL-specific IgE antibodies.^{29–31} Little information is available on the occurrence of skin prick test reactions to NRL and NRL-specific IgE antibodies in subjects with NRLS.^{1,6,28,37} In our study, 32% of health care workers with NRLA and 39% of those with NRLS who had initially been found to have NRL-specific serum IgE had lost these antibodies at the last follow-up examination. In 36% of the subjects with NRLA and in 31% of those with NRLS, NRL-specific IgE was still demonstrable but had declined by at least one CAP class. Only 1 of the 26 subjects with initially negative results for NRL-specific IgE had positive results at follow-up. A loss or decline of NRL-specific IgE antibodies was found more often in workers without atopy than in those with atopy. In subjects with NRLA and those with NRLS, however, the changes in NRL-specific serum IgE concentrations over time were not similar.

Data on the course of NRL-specific serum IgE after the introduction of preventive measures are somewhat controversial. Studies of health care workers with NRLA found a decline of NRL-specific serum IgE concentrations within 1 year,²⁵ 2.5 years,²⁷ and up to 7 years³⁸ after the onset of individual prevention. Subsequent to the introduction of NRL-free medical procedures, the mean of NRL-specific IgE concentrations had declined in NRL-allergic children with spina bifida after 5 years.^{21,39} In contrast to these studies, no decrease of NRL-specific serum IgE was noted after a mean of 2.8 years in 32 children with NRLA⁴⁰ or in 38 adults, including health care workers, 0.5 to 24 years after diagnosis,²³ although all subjects had received a thorough education regarding preventive measures. No previously published studies have examined the change of markers of sensitization over time in subjects who were only sensitized but not symptomatic, nor have they compared such changes with those in subjects with NRLA. Therefore, the explanation of our findings in subjects with NRLS will remain somewhat hypothetical until further information is available.

Primary prevention of NRLS or NRLA can be achieved by avoidance of allergen exposure. In 1986, 3% of hospital employees in Finland were shown to be allergic to NRL²; after introduction of gloves with a reduced NRL-allergen content in 1990, this rate declined to only 1% in 1999.²⁶ Powdered NRL gloves pose particular risks because of their high allergen content, and the powder is known to act as an allergen carrier.^{41–43} Indeed, *de novo* sensitization was less frequent when powder-free rather than powdered NRL gloves were used.⁴⁴ In Germany, use of powdered NRL gloves in the workplace was banned in December 1997 by legal regulations. Subsequently, the incidence of suspected occupational disease due to NRLA has steadily declined.⁴⁵

CONCLUSION

When health care workers with NRLA or NRLS underwent reassessment up to approximately 3 years after the introduction of preventive measures, we found a decrease of markers of sensitization in many of them, whereas a loss of sensitization almost exclusively occurred in subjects with NRLS. Concomitantly, most study subjects with NRLA became symptom-free, and clinically evident NRLA had developed in no subjects with asymptomatic NRLS. Health care workers with NRLA or NRLS benefit within a short period from simple preventive measures. Nevertheless, these preventive measures are unlikely to "cure" all subjects, particularly those with NRLA. Longer observation periods and new strategies to treat NRLA are needed.

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