

Latex Allergy in Polish Nurses

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Background Reports on the studies conducted in Western Europe and North America revealed that from 2.8 to 16.9% of the health care personnel were allergic to latex. No respective data are available from Eastern European countries.

Methods A postal questionnaire inquiring about the history of latex-induced allergic reactions was distributed among 3,750 nurses. The participation rate was 77.3%. To verify the results of the survey, in randomly selected nurses, skin prick tests with latex and tropical fruit allergens, evaluation of total IgE, and specific anti-latex IgE, skin and nasal provocation with latex were performed.

Results Allergic symptoms in the workplace were reported by 1,016 subjects (35%); out of this group 847 (29.2%) persons associated the symptoms with latex exposure. The group of cases with self-reported latex allergy revealed a significantly increased frequency of history of atopy, allergy to β -lactam antibiotics and tropical fruits. Allergy to latex was confirmed in 33.3% of randomly selected nurses with a positive history of occupational allergy. It was found that 18.6% of nurses working at hospital wards were allergic to latex. The 95%CI was estimated to be 13.5–23.6%.

Conclusions Latex allergy is an important health problem among nurses in Poland. Atopy, allergy to β -lactam antibiotics and tropical fruits, are the risk factors for latex allergy. *Am. J. Ind. Med.* 35:413–419, 1999. © 1999 Wiley-Liss, Inc.

KEY WORDS: latex allergy; risk factor; nurses; atopy; occupational exposure

INTRODUCTION

Health care workers are known to be a high-risk group for allergic reactions to latex. Reports on the studies conducted in Western Europe and North America revealed that from 2.8 to 16.9% of the health care personnel were allergic to latex [Arellano et al., 1992; Lagier et al., 1992; Turjanmaa, 1987; Turjanmaa et al., 1995; Vandenplas et al., 1995; Wrangsjö et al., 1994; Yassin et al., 1994]. However, no respective data are available from Eastern European countries. It seems plausible that in view of the specific

economic conditions in these countries, the prevalence and risk factors of latex allergy in medical personnel will be different. The rubber gloves used may be of lower quality and the general conditions of work, including ventilation, may be inferior. On the other hand, however, disposable latex equipment has been in use for a far shorter period of time than in Western Europe.

In view of the above, it seemed necessary to assess the prevalence of latex allergy among health care workers and identify the risk factors. The first stage of the screening was a survey, which is a relatively inexpensive method that can be helpful in a population-wide diagnosis of latex allergy. This was followed by the performance of diagnostic tests to verify the collected data. Accordingly, the present study aimed at evaluating the applicability of the questionnaire for the identification of latex-sensitive individuals.

MATERIALS AND METHODS

Study Design

A postal questionnaire inquiring about the history of and present occupational exposure to latex and incidents of

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allergic reactions was distributed among 3,750 nurses from surgical, internal medicine, and obstetric wards from 7 districts of central and northern Poland. The nurses were identified based on the information provided by regional Boards of Nurses. The study was approved by the local Ethics Committee.

Subject to analysis were 2,899 questionnaires (response rate: 77.3%). The non-respondents were sent a memo requesting the return of the completed questionnaire. However, this has yielded only a slight increase in the participation rate. The comparison of age and seniority distribution in the group of subjects and of the general population of nurses employed in selected districts of central and northern Poland did not reveal significant differences.

The results of the survey were verified by a general medical examination followed by skin prick test (SPT) with latex and tropical fruit allergens, evaluation of total serum IgE and specific anti-latex IgE, and skin and nasal provocation with latex.

For the medical verification of reported symptoms, four subgroups of nurses were distinguished: (1) with a self-reported history of allergic symptoms in the workplace closely related to latex exposure ($n = 847$); (2) other subjects with allergic symptoms in the workplace ($n = 137$); (3) atopic subjects without allergic symptoms in the workplace ($n = 911$); (4) healthy individuals ($n = 972$).

From each of the subgroups, 50 nurses were randomly selected and invited to take part in the medical examination. The final rate of participation was 83.5% despite our intensive efforts to encourage participation among the non-respondents. Written consent to participate was received from the subjects after they had been informed about the purpose of the medical part of the project.

Questionnaire

The scope of the questionnaire included self-reports of current and past symptoms associated with latex exposure (urticaria, angioedema, conjunctivitis, rhinitis, dyspnea, anaphylaxis); history of atopy and allergic diseases (including diagnosis of hay fever, allergic rhinitis and conjunctivitis, bronchial asthma, atopic dermatitis); medical history (including any current or previous food or drug allergies); family history of atopy; tobacco smoking habit; exposure to pet allergens at home. A detailed work history including past and present work post was also elicited.

The assessment of latex as an etiologic factor of the allergic disease was based on the self-reports of the allergic symptoms closely related to latex exposure. Reported isolated pruritus was not considered a symptom of allergy.

Skin Prick Test and IgE Evaluation

SPT was performed using latex (Stallergen, Paris, France), common allergens and tropical fruit allergens

(Allergopharma, Hamburg, Germany). The negative control was allergen diluent and the positive one, histamine solution. All the tested sites were examined after 20 min: a wheal of 3 mm > control and a flare of 5 mm > control were considered positive.

Total serum IgE and the presence of specific anti-latex IgE (RAST) were determined (Pharmacia, Uppsala, Sweden). The threshold of positivity was set at 0.35 kU/l for RAST.

Pulmonary Function Tests

Bronchial response was assessed by measuring Forced Expiratory Volume in one second (FEV_1) using a spirometer (Vicatest 2A, Mijnhardt, Holland). Histamine challenge was performed according to Cockcroft [Cockcroft, 1977]. Bronchial reversibility test was performed 15–30 min after administration of 200 µg of salbutamol MDI. It was considered positive if the increase in FEV_1 was at least 15% of the initial value.

Provocation Tests

Use test.

The use test started with pulling one finger piece of a glove on a wet finger. If two to three wheals were seen on the contact area after 15 min, the result was considered positive. When a negative result was obtained, the challenge was continued with a whole latex glove pulled on a wet hand and a vinyl glove as the negative control on the other hand to exclude dermatographism [Turjanmaa et al., 1995, 1996].

Nasal challenge test.

The study was designed as a two-stage, cross-over single blind trial. At the first stage the subjects were challenged with placebo. The second stage, allergen challenge, was performed at least 7 days afterwards.

Latex Solution

The latex solution was prepared by washing pieces of latex gloves, catheters, and drains with phosphate-buffered saline (PBS) (Sigma, St. Louis, MO) at 37°C for 2.5 hours. The resulting solution was then decanted, filtered, and lyophilized. Protein content was estimated; it was found to be 100: g/ml (0.01 g/dl) and pH was 7.4.

Nasal Lavage, Provocation Challenge, and Nasal Washings Processing

Nasal lavage and provocation challenge were performed using the “nasal pool” method [Greiff et al., 1990].

Nasal washings processing was performed as described previously [Górski et al., 1998].

Nasal washings total protein content was evaluated according to Lowry et al. [1951]. Albumin concentration was measured using the "rocket" method by Laurell (assay ranged between 20 and 200: g/ml) [Laurell, 1966]. The permeability index, i.e., albumin to total protein ratio was calculated [Raphael et al., 1991].

Nasal concentrations of eosinophil cationic protein (ECP) and tryptase were measured using radioimmunoassay (RIA kits, Pharmacia) according to the manufacturer's protocol. The samples for these assays were collected before and 30 min, 4 and 24 hours after the provocation.

The nasal challenge test was considered positive if a twofold increase in the number of eosinophils, permeability index, and ECP level persisted up to 24 hours after the challenge. The proportion of eosinophils should be at least 5%. The additional criterion of positiveness of the test was the increase in tryptase level immediately after the challenge [Górski et al., 1998].

Diagnostic Criteria of Atopy

Atopic disease was recognized when positive personal and family history of atopy was indicated in the questionnaire. In laboratory tests, positive results of SPT to common allergens and elevated total IgE level were the additional criteria.

Diagnostic Criteria of Urticaria, Allergic Rhinitis, Conjunctivitis, and Bronchial Asthma

Diagnosis of urticaria, allergic rhinitis and conjunctivitis, and bronchial asthma was based on questionnaire responses. In most cases, when a previous diagnosis of allergic disease was reported, additional information was obtained from the patient's medical files. In all patients suffering from asthma, baseline spirometry, reversibility test with β_2 -agonists and, in disputable cases, bronchial responsiveness to histamine, were performed.

Diagnosis of Latex Allergy

In nurses subject to clinical verification, latex allergy was diagnosed in persons with allergic symptoms in the workplace if at least one of the following tests: SPT, RAST, nasal challenge, use test, was positive. Nurses with only positive results of the above tests were regarded as sensitized to latex.

Statistical Analysis

To evaluate the risk factors of latex allergy, based on the survey data, the odds ratios (ORs) and their 95% confidence

intervals (CI) were calculated. The analysis covered a group of cases: 847 nurses reporting allergy to latex and the controls; 2,020 nurses free from such symptoms. Logistic regression model, using SPSS package, was applied to examine the relationship between the risk of latex allergy and the risk factors under study. The *P* value less than 0.05 was adopted as reference for the selection of significant risk factors.

The prevalence of allergy to latex in the population of Polish nurses was estimated based on the examined samples of groups 1–4 using the statistical methods proposed by Cochran [Cochran, 1991].

RESULTS

Questionnaire

The mean age of the responding nurses was 34.8 ± 10.3 years, mean seniority 17.8 ± 8.9 years. Latex allergy based on questionnaire data was diagnosed in 879 nurses (30.3%). The majority of cases ($n = 847$) related their symptoms to latex exposure at the workplace (29.2% of the respondents). No influence was found of either the subject's age or seniority on the prevalence of latex allergy.

At least one episode of allergy during lifetime was reported by 1,927 respondents (66.5/100). The most prevalent symptoms were skin allergy, rhinitis and/or conjunctivitis; the respective rates being 48.7/100 and 51/100. Episodes of dyspnea were experienced by 388 subjects (13.4/100).

Allergic symptoms at the workplace were reported by 1,016 subjects (35/100); out of this group 847 (29.2/100) persons associated their symptoms with latex exposure.

Moreover, 93 subjects (3.2/100) reported symptoms of allergy to tropical fruits: urticaria, 70 (2.4/100); conjunctivitis, 17 (0.6/100); rhinitis, 17 (0.6/100); dyspnea, 9 (0.3%); and food intolerance symptoms, 29 (1/100).

Family history of atopy was declared by 406 nurses (14/100). Among the responding nurses, 1,029 subjects (35.5%) were current smokers and 409 (14.1%) past smokers. All the subjects could be regarded as being exposed to environmental tobacco smoke (ETS).

Considering the results of the case-control univariate analysis, the group of cases with self-reported latex allergy presented a statistically significant increase in the frequency of allergic symptoms of the skin, eye, and respiratory system. Tobacco smoking as the risk factor was also considered, with the non-smokers as the reference group. The analysis revealed that the history of latex allergy was more frequently reported by active smokers.

All the variables found to be significant risk factors in the univariate analysis were included in the logistic regression model. Rhinitis and skin symptoms, allergy to tropical fruits and beta-lactam antibiotics were found to be significant predictors of a positive history of latex allergy (Table I).

TABLE I. Factors of Self-Reported Latex Allergy in the Group of 2,867 Nurses According to Survey Data: Multiple Logistic Regression Analysis, Poland 1998*

Factor (according to questionnaire data)	Group with self-reported latex allergy		Control group		Multivariate analysis (OR 95% CI)
	n	Rate/100	n	Rate/100	
Skin symptoms	721	85.0	691	34.2	1.27 (0.95–1.70)
Rhinitis symptoms	592	69.9	825	40.8	1.98 (1.61– 2.46)
Allergy to β -lactam antibiotics	402	47.5	356	17.6	1.51 (1.19–1.78)
Allergy to tropical fruit	67	7.9	27	1.3	3.48 (2.14–5.68)
Family history of atopy	172	20.3	236	11.7	1.07 (0.84–1.38)
Active smoking	448	52.9	721	35.68	1.00 (0.85–1.26)
Past smoking	123	14.5	286	14.19	0.77 (0.59–1.01)
N	847		2,020		

*Significant values of OR 95% CI in boldface.

Clinical Verification

Clinical verification of the survey results was performed in 39 nurses from group 1, 42 from group 2, 33 from group 3, and 36 from group 4. The subjects' characteristics and obtained data are presented in Table II. Latex allergy was confirmed only in 13 subjects from group 1 (33.3%). All of them suffered from urticaria and most of them from angioedema (N = 9). Allergy to latex was also recognized in 14 cases from group 2 (33.3%). It manifested mainly as an allergic reaction of the respiratory system (N = 11), bronchial asthma (N = 8) and/or rhinitis. In that group, only 3 nurses reported latex-induced urticaria. Table III summarizes laboratory results and clinical characteristics of nurses with confirmed latex allergy. Seven subjects from group 1, with latex allergy, reported a progression of the symptoms from urticaria (N = 4) or rhinitis (N = 4) to angioedema (N = 4), dyspnea (N = 6) and anaphylaxis (N = 2). Anaphylactic shock was reported in two cases and occurred outside the workplace; in one case it was induced by blowing up a balloon, in the other, by inhalation challenge with latex. In group 2, only one nurse noted the progression of symptoms, from rhinitis to dyspnea. Moreover, 7 cases from group 1 and 3 from group 2 reported contact dermatitis.

In 4 subjects from group 3, the SPT with latex gave positive results. Three of them suffered from hay fever and the fourth one from molds-induced allergic rhinitis. All of them were considered as sensitized to latex.

No subject from group 4 presented positive laboratory results nor symptoms of latex allergy.

Prevalence of Latex Allergy in the Population of Polish Nurses

The nurses with clinical examinations in each of the four groups were treated as random samples of relevant

TABLE II. Characteristics of the Examined Groups of Nurses Randomly Selected for the Clinical Verification*

	Group 1	Group 2	Group 3	Group 4
Number (N)	39	42	33	36
Age (years $\pm$ SD)	41.2 $\pm$ 9.4	38.7 $\pm$ 8.1	42.4 $\pm$ 8.0	42.4 $\pm$ 8.0
Seniority (years $\pm$ SD)	22.4 $\pm$ 7.8	19.1 $\pm$ 6.9	23.2 $\pm$ 5.8	23.2 $\pm$ 5.8
Positive SPT to common allergens (N, % of the group)	13 (33.3%)	17 (40.5%)	33 (100%)	1 (2.8%)
Elevated total IgE level >100 ku/l	9 (23.0%)	18 (42.9%)	24	0
Positive SPT to latex (N, % of the group)	11 (28.2%)	10 (23.8%)	4 (12.1%)	0
Positive SPT to tropical fruit (N, % of the group)	1 (2.6%)	2 (4.8%)	0	0
Specific anti-latex IgE (N, % of the group)	6 (15.4%)	5 (11.9%)	0	0
Positive use test (N, % of the group)	12 (30.8%)	3 (7.1%)	0	0
Performed nasal challenge with latex	12	15	18	9
Positive result of nasal challenge with latex	7	9	1	0
Diagnosis of latex allergy	13 (33.3%)	14 (33.3%)	1 ? ^a	0

*Group 1, with a self-reported history of allergic symptoms in workplace closely related to latex exposure; Group 2, other subjects with allergic symptoms in workplace; Group 3, atopic subjects without allergic symptoms in workplace; and Group 4, healthy individuals.

^aPositive result of SPT and specific nasal challenge to latex was found in 1 person from groups.

subpopulations. Based on these samples, the proportion of persons with clinically verified allergy and 95%CI was calculated (Table IV). It was found that 18.6 % of nurses

TABLE III. Characteristics of Cases With Confirmed Latex Allergy From Group 1 (With a self-reported history of allergic symptoms in workplace closely related to latex exposure) and Group 2 (Other nurses with allergic symptoms in workplace), Poland 1998

	Group 1	Group 2	All
Number (N)	13	14	27
Age (years $\pm$ SD)	40.2 $\pm$ 9.4	39.3 $\pm$ 9.4	39.7 $\pm$ 9.2
Seniority (years $\pm$ SD)	21.3 $\pm$ 7.9	19.4 $\pm$ 7.5	20.8 $\pm$ 6.4
Positive SPT to common allergens (N, % of the group)	9	9	18
Elevated total IgE level >100 ku/l	5	8	13
History of contact dermatitis	7	3	10
Duration of latex allergy (years $\pm$ SD)	5.9 $\pm$ 8.2	3.6 $\pm$ 2.8	4.7 $\pm$ 6.0
Urticaria	13	3	16
Rhinitis	13	8	21
Angioedema	9	3	12
Bronchial asthma	5	8	13
Anaphylaxis	2	0	2

working in the surgical, internal medicine, and obstetric wards in Poland might be affected by allergy to latex. The 95%CI was estimated to be 13.5–23.6%.

DISCUSSION

The estimated prevalence of latex allergy among auxiliary medical staff in Poland 18.5% (95% CI 13.5–23.6%) approximates the values obtained from epidemiological studies in other European countries (2.8–10.7%) [Beaduin et al., 1990; Lagier et al., 1992; Turjanmaa, 1987; Vandenplas et al., 1995; Wrangsjö et al., 1994]. It is difficult to assess what kind of bias may have resulted from the response rate lower than 100%. We may assume that most of the non-respondents were free from the symptoms and, consequently, they ignored our survey. Should they have participated, they would be included in the group of healthy individuals. However, we must admit that we did not have at our disposal any data that would support or contradict this assumption. Another explanation of such a high prevalence rate of latex allergy might be profound clinical analysis of random samples. False-positive results of the different diagnostic tests used might have also influenced the final estimation of the prevalence. However, the methods employed in our study are thought to be highly specific.

In the countries at a lower level of socioeconomic development, incidents of latex allergy in some of the risk groups were reported less frequently [Capriles-Hulett et al., 1995; Leung et al., 1997]. At first they had been associated with the race factor, but then it was proved that the presence of specific anti-latex IgE is more closely associated with the non-white race so the race factor could no longer be

regarded as the explanation [Grzybowski et al., 1996]. Poland has been undergoing deep socioeconomic transformations, many of which have had an impact on numerous environmental and dietary factors. The reason for the appearance of latex allergy and its increasing prevalence remains unknown though cumulative effect of multitude of factors has been postulated [Truscott, 1995]. On the other hand, the evaluation of allergen exposure in Polish hospital wards might be helpful in elucidating the particularly high prevalence of latex allergy among nurses; high concentrations of latex aerosol may enhance sensitization. Our questionnaire did not include questions concerning the type of gloves used and the frequency of use of a particular brand. Polish hospitals are supplied with medical equipment by various manufacturers and the quality of delivered goods may vary as well. The level of latex exposure in Polish hospitals has not been measured.

The data obtained from our study confirmed the previously reported associations between atopy, allergy to tropical fruit and latex allergy [Arellano et al., 1992; Blanco et al., 1994; Lavaud et al., 1995; Mäkinen-Kiljunen, 1994; Moneret-Vautrin et al., 1993; Turjanmaa, 1987; Wrangsjö et al., 1994]. In addition to repeated exposure to natural rubber latex, through latex gloves, atopy seems to be the principal determinant of the development of NRL sensitization. In agreement with this, in NRL-allergic health care workers, the frequency of atopy was found to be 2.2–4.2 times higher than in their coworkers without NRL allergy [Arellano et al., 1992; Moneret-Vautrin et al., 1993; Turjanmaa, 1987; Vandenplas et al., 1995; Wrangsjö et al., 1994]. According to some authors, about half of the NRL-allergic patients have experienced allergic response after eating a banana and 35% had positive skin prick test with the banana allergen [Blanco et al., 1994; Mäkinen-Kiljunen, 1994].

A significant association between tropical fruit allergy and latex allergy was also found in our study but the prevalence of tropical fruit allergy (positive history and positive results of SPT) was much lower than in other studies [Blanco et al., 1994; Grzybowski et al., 1996; Lavaud et al., 1995; Mäkinen-Kiljunen, 1994]. We presume this difference may be attributed to the dietary habits, i.e., a lower level of tropical fruit consumption in Poland.

Grzybowski et al. [1996] found an association between anti-latex IgE and self-reported allergy to penicillin. This finding is particularly interesting as atopy is not considered a risk factor for drug hypersensitivity [Sullivan and Wedner, 1992]. Our study also revealed an association between self-reported occupational allergy to beta-lactam antibiotics and latex allergy. This could be explained by using latex gloves when handling beta-lactam antibiotics or by the storage of the drugs in containers with rubber stoppers, but no relationships of this kind was found for other drugs that were handled by the nurses participating in our project. Beta-lactam antibiotics may be of importance as occupational allergens, but the relationship between latex allergy

TABLE IV. The Prevalence of Diagnosed Latex Sensitization Among Examined Nurses Based on the Data From the Survey and Medical Examination, Poland 1998*

Study group	Number of respondents	Sample size	Examined	Latex-sensitized nurses	Fraction of all examined (%)	95% CI
Group 1	847	50	39	13	33.3	18.7–48.0
Group 2	137	50	42	14	33.3	21.2–45.4
Group 3	911	50	33	4	8.0	0.6–15.3
Group 4	972	50	36	0	0	0
Total	2,867	200	167	31	18.6	13.5–23.6

*Group 1, with a self-reported history of allergic symptoms in workplace clearly related to latex exposure; Group 2, other subjects with allergic symptoms in workplace; Group 3, atopic subjects without allergic symptoms in workplace; Group 4, healthy individuals.

and beta-lactam hypersensitivity remains unclear [Coutts et al., 1981; Davies et al., 1974; Jakubowski et al., 1997].

The association between latex allergy and tobacco smoking has not been reported so far, but the potential, facilitating effect of exposure to tobacco smoke on the development of allergy has been postulated. Some studies have shown that smoking workers are at an increased risk of developing allergic sensitivity to certain occupational allergens [Venables et al., 1985; Zetterström et al., 1981].

In our study, smoking was found to be a risk factor of latex allergy in the univariate analysis but this was not confirmed in the multivariate one.

The diagnosis of latex allergy should be confirmed by in vitro or in vivo tests [Levy et al., 1992; Ownby and McCullough, 1993; Turjanmaa, 1988]. Many investigators consider the skin prick test the best method [Hadjiliadis, et al., 1995; Turjanmaa et al., 1995]. In order to achieve maximum sensitivity, we used both a standardized allergen solution (Stallergen) and the self-derived extract from the latex equipment used in Poland. The results confirm the high sensitivity and specificity of SPT.

RAST, although a highly specific test, is believed by many authors to have low sensitivity [Wrangsjö et al., 1994]. Our data also confirm this finding. In order to obtain high reliability of allergy diagnosis, we performed the use test that is very helpful in the assessment of skin allergy to latex [Turjanmaa et al., 1988, 1995, 1996]. Our findings indicated that nasal provocation combined with the lavage technique, along with morphological and biochemical analysis of the nasal washings, was a useful and safe method for the differential diagnosis of occupational airway sensitization [Bascom et al., 1988; Górski et al., 1997; Pałczyński et al., 1996; Uliński et al., 1996]. Studies of mediator release during nasal-allergen challenge indicate that the increase in tryptase concentration is the most specific marker of mast cell activation during the immediate allergic response [Nacleario et al., 1983; Rasp and Hochstrasser, 1993]. The nasal challenge enables one to distinguish between specific, allergic, and non-specific, irritant, reactions [Górski et al.,

1997; Pazdrak et al., 1993]. It is also much safer than the bronchial challenge [Górski et al., 1997; Pałczyński et al., 1996]. During the course of the study, we did not observe any serious complications, including anaphylaxis, after nasal provocation.

Clinical verification revealed that all subjects with confirmed latex allergy and with the history of allergic symptoms clearly related to latex, complained of urticaria, and almost all, of angioedema and rhinitis. This group also reported the typical progression of symptoms and previous contact dermatitis. It is worth noting that the presence of the skin symptoms enabled the subject to recognize latex as a sensitizer.

The nurses with occupational allergy, which they did not relate to latex exposure, usually suffered from the respiratory symptoms. Urticaria, typical progression of symptoms, and contact dermatitis were rare in that group. Atopic subjects with positive SPT with latex did not report any symptoms of allergic reaction, so there was no reason to diagnose an occupational disease. However, they require special attention as, according to other authors, in 30–60% of health care workers, the clinical symptoms of latex allergy were preceded by positive SPT with that allergen [Turjanmaa et al., 1996].

The survey proved to be a method of insufficient sensitivity and specificity to detect subjects sensitized to latex. Our findings indicate that in any case of suspected occupational allergy in health care personnel, it is necessary to perform detailed diagnostics towards latex-induced allergy.

The results of the present study have revealed that latex allergy is an important health problem among nurses in Poland. In view of the high estimates of the prevalence of this allergy in our country, prophylactic diagnostic examinations should be performed and appropriate measures undertaken to reduce the exposure to latex.

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