

Short communication

Frequency of natural rubber latex allergy in adults is increased after multiple operative procedures

Background: It has been shown that immediate-type allergy to natural rubber latex (NRL) affects predominantly health-care workers and infants with malformations requiring repeated medical procedures. Adult patients with multiple invasive procedures are not thought to be at an increased risk of NRL allergy.

Methods: A total of 325 consecutive adult inpatients (54.4 ± 15.6 years; 219 men, 106 women) awaiting surgical or urologic procedures were assessed by questionnaire-based history (atopic diseases, number of previous standard operative or endoscopic procedures, intolerance to rubber products, and adverse reactions during medical care), by skin prick tests with different NRL test solutions, by measurement of NRL-specific IgE in the serum, and, if sensitization to NRL was found, by cutaneous challenge tests with NRL-containing material. Subjects were classified as sensitized to NRL if skin prick test reactions to NRL were positive or if NRL-specific IgE antibodies were found. NRL allergy was defined as NRL sensitization and immediate-type symptoms to NRL.

Results: Thirty-one of 325 (9.5%) subjects were found to be sensitized to NRL, 14/285 (4.9%) by skin prick testing and 23/323 (7.1%) by NRL-specific IgE antibodies in the serum. Four individuals (1.2%) were diagnosed as having clinically manifest NRL allergy, and another 27 (8.3%) were sensitized to NRL without symptoms to date. The frequency of previous invasive procedures was zero in eight patients, up to 10 in 245, 11–20 in 52, 21–30 in seven, and over 30 (up to 83) in 13 patients. No association was found between the number of invasive procedures and NRL sensitization without clinical symptoms. However, 3/4 patients with NRL allergy had undergone more than 30 interventions, and 1/4 had had 11 operations. Frequent invasive procedures (more than 10) were significantly associated with NRL allergy ($P < 0.001$). Allergy or sensitization to NRL was associated with atopy (21/31 vs 87/294) ($P < 0.001$).

Conclusions: A remarkable percentage of unselected adult patients undergoing surgical procedures have allergy or sensitization to NRL. Repeated invasive treatment appears to be a risk factor for NRL allergy.

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Allergy to natural rubber latex (NRL) was reported for the first time more than 70 years ago (1, 2). However, it was not until the 1980s that immediate-type reactions to NRL became an important problem in medical practice. Powdered NRL gloves are the most important source of exposure in the medical environment, as they are used frequently and are particularly rich in allergens.

The major risk factors in sensitization to NRL are intense exposure to NRL allergens, atopy (3–6), and hand eczema (7–9). As gloves and other devices made from NRL are widely used in clinical practice, health-care workers (3, 10, 11) and patients with spina bifida or other urogenital abnormalities (12–19), who need

frequent or continuous medical treatment, have been found to be particularly affected by NRL allergy or sensitization. It has been suggested that the high risk of spina bifida patients to develop NRL allergy might be specifically related to this malformation, and not only to allergen exposure; however, this relation seems unlikely, as the frequency of NRL allergy in such patients without intense contact with NRL allergens also was low (14, 20). Finally, if there was a history of multiple operations in children, NRL allergy was frequent also in such patients without spina bifida (17).

Furthermore, adult patients without spina bifida or urogenital malformations who have undergone multi-

ple medical procedures may be at an increased risk of NRL allergy. However, until now, this issue has not yet been conclusively determined. By a complete allergologic investigation, we evaluated the frequency of NRL allergy or sensitization in a consecutive series of surgical patients in relation to the frequency of previous invasive medical procedures.

Material and methods

Patients

Consecutive inpatients of the departments of urology and surgery of the University of Munich (Germany), in whom an elective operative procedure was planned, were examined over a 6-month period. All patients were evaluated the day before surgery. The exclusion criteria were age below 18 years, pregnancy, severe cardiovascular disease, unstable pulmonary disease, or therapy with β -blocking drugs. The study was approved by the local institutional review board. All patients gave their informed, written consent.

History

A questionnaire-based history was taken, and an examination was carried out by an allergologist for atopic diseases (hay fever, asthma, and atopic eczema), hand eczema, number of preceding invasive medical procedures (conventional, laparoscopic, or endoscopic operation), immediate-type reactions during medical care, hypersensitivity reactions to NRL, occupation, and general medical history.

Skin tests

Skin prick tests were done with two commercially available NRL skin prick test solutions (Abelló, Madrid, Spain; Bencard, SmithKline Beecham, Munich, Germany, 1%), common aeroallergens (grass pollen, house-dust mite, and cat; Bencard, SmithKline Beecham, Munich, Germany), and physiologic saline and histamine dihydrochloride 0.1% as controls. Reactions were evaluated after 20 min and interpreted, according to Ring (21), as positive if there was a wheal of ≥ 2 mm. Skin tests were not considered if there was a reaction to the negative control or no reaction to the positive control.

Specific IgE in the serum

Determination of NRL-specific IgE antibodies in the serum was made by CAP-FEIA (Pharmacia & Upjohn, Freiburg, Germany). If NRL-specific IgE antibodies were found, duplicate tests were carried out, and mean values were taken as results. Test results were available only after surgery.

Challenge tests

In patients who had a positive skin test, challenge tests were performed immediately after the skin test; i.e., before surgery. For patients in whom we found NRL-specific IgE, challenge tests could be done only after surgery. If the patients had already been discharged, they were invited back for a challenge test. Challenge tests were made on the back of a hand by applying a piece of a powdered NRL glove (Sempermed[®], Semperit, Vienna, Austria) fixed with a NRL-free adhesive (Fixomull Stretch, Beiersdorf, Hamburg, Germany). The test material was removed after 30 min, and the test site was read immediately. Patients were informed that a postponed reaction could occur, and if it did, they were advised to inform the physician. A control test was carried out in the same way with NRL-free material (Glovex[®] Neoderm, Beiersdorf, Hamburg,

Germany). If the patient noticed pruritus during the first 30 min, the test material was removed immediately. The challenge test was positive if erythema and pruritus and/or whealing occurred.

NRL allergy

NRL allergy was defined as NRL sensitization (demonstration of NRL-specific IgE antibodies in the serum and/or skin prick test reaction to at least one NRL test solution) and a definite history of immediate-type symptoms to NRL material and/or an immediate-type reaction to NRL-containing material, but not to NRL-free material at the challenge test.

In patients with NRL allergy and in patients in whom skin prick test reactions to NRL were found before surgery, NRL material was avoided during the intervention and also during the subsequent treatment.

Atopy

Atopy was diagnosed if there was a history of any atopic disease (allergic rhinoconjunctivitis, asthma, and atopic eczema) and/or at least one skin prick test reaction to grass pollen, house-dust mite, and/or cat.

Statistics

An elevated risk of NRL allergy was derived from results in children with spina bifida: if there was a history of more than nine (18, 22–24) or 10 (19) operations, patients had an increased risk of NRL allergy. For our study, the patient was classified as a patient with multiple operative procedures if a history of over 10 invasive procedures was stated. Conventional, laparoscopic and endoscopic operative procedures were counted together. Data were analyzed with SPSS (Microsoft). A 95% confidence interval was calculated for categorical variables and compared by the chi-square test. If data were not binominally distributed, Student's *t*-test was used.

Results

From a total of 433 consecutive patients, 325 (75.1%; 219 men, 106 women; aged 18–87 years, mean age 54.4 ± 15.6 years) agreed to participate in the study. Zero to 10 invasive procedures had been performed in 253 patients, and more than 11–83 operations in 72 patients (11–20 in 52, 21–30 in seven, and >31–83 in 13 patients).

Nineteen patients reported intolerance of rubber material (mainly gloves). A history of definite immediate-type symptoms due to NRL contact was given by 3/325 patients. Conclusive skin prick test reactions to at least one of the NRL test solutions were found in 14/285 patients (4.9%), eight patients exhibiting reactions to both, and six only to one of the solutions. NRL-specific IgE antibodies were demonstrated in 23/323 patients (7.1%): CAP class 1, nine patients; CAP class 2, 11 patients; CAP class 3, one patient; and CAP class 4, two patients. Six patients had both NRL-specific IgE antibodies in the serum and skin prick test reactions to at least one NRL test solution. Altogether, 31 patients (9.5%) were found to be sensitized by skin prick test and/or assessment of specific IgE in the serum. Challenge

Table 1. Characteristics of patients

	Patients with ≤ 10 surgical procedures	Patients with > 10 surgical procedures	
<i>n</i>	253	72	
Mean age (years)	53.1 (± 15.9)	58.9 (± 13.8)	NS
Men	172 (68.0%)	47 (65.3%)	NS
Atopy	86 (34.0%)	22 (30.6%)	NS
Number of surgical procedures	4.7 (± 2.7)	20.1 (± 12.8)	< 0.001
History of immediate-type symptoms due to NRL	0	3	
Skin prick test reaction to NRL	9 /221 (4.1%)	5/64 (7.8%)	NS
Specific IgE antibodies to NRL			
CAP class 1	7	2	
CAP class 2	11	0	
CAP class 3	1	0	
CAP class 4	1	1	
Any CAP class	20/252 (7.9%)	3/72 (4.2%)	NS
NRL allergy or sensitization	24 (9.5%)	7 (9.8%)	NS
NRL sensitization without symptoms	24 (9.5%)	3 (4.2%)	NS
NRL allergy	0	4 (5.6%)	< 0.001

NS: not significant.

tests could be performed in only 18 patients with NRL sensitization and resulted in a diagnosis of NRL allergy in three patients. In one of the 13 patients who did not have a challenge test, a diagnosis of NRL allergy had already been established before this study; consequently, a challenge test was not done. There was no evidence that one of the remaining 12 patients was allergic to NRL, since all these patients tolerated contact to NRL-containing material (such as gloves etc.).

In our study, four individuals (1.2%) were diagnosed as having manifest NRL allergy, and another 27 (8.3%) were sensitized to NRL without clinical symptoms. Atopy was present in 108/325 patients

(33.2%). Patients with atopy were significantly ($P < 0.001$) more often allergic or sensitized to NRL (21/108; 19.4%) than patients without atopy (10/217; 4.6%). Allergy or sensitization to NRL was not associated with occupation, sex, age, or history of private NRL contact. Data on the patients are given in Table 1.

Among those with NRL allergy, three patients had undergone 30 or more, and one patient 11 operative procedures. Details on these four patients are given in Table 2. A history of immediate-type symptoms to NRL during medical treatment was clear in three patients, and one patient reported no symptoms due to NRL contact during medical treatment or private

Table 2. Clinical data of patients with natural rubber latex allergy

Age (years), sex	Atopy ^a	Occupation	Number of operations	Clinical diagnosis	NRL-specific IgE CAP-class (kU/l)	Skin prick test reaction to test solution from	Reactions due to NRL during medical care	Reaction at challenge test
30, M	Yes	Printer	35	Spina bifida Hydrocephalus Hip joint dysplasia	0	Abelló Bencard	Contact urticaria, nausea, dizziness, vomiting	Yes
37, M	Yes	Formerly farmer, now commercial clerk	34	Bladder carcinoma Duodenal ulcer Knee-joint arthrosis	4 (20.2)	Abelló	No symptoms noticed so far	Yes
60, F	Yes	Formerly saleswoman, now retired	30	Breast cancer Cholecystolithiasis Hysteromyoma Bladder cancer Kidney carcinoma	1 (0.6)	ND ^b	Pruritus, erythema urticaria, rhinitis, asthma, cardiovascular symptoms	ND
23, F	No	Telephone operator	11	Congenital neurogenic atony of bladder	0	Abelló Bencard	Generalized urticaria	Yes

ND: not done.

^a History of any atopic disease (allergic rhinoconjunctivitis, asthma, and atopic eczema) and/or at least one skin prick test reaction to grass pollen, house-dust mite, and/or cat.^b Skin prick test reactions to NRL known from previous diagnostic tests.

or occupational NRL exposures. In three of these four patients, NRL allergy had not been diagnosed before this investigation.

The frequency of NRL allergy and sensitization together was similar in patients with 0–10 (24/253; 9.5%) or more than 10 operative procedures (7/72; 9.7%) (Table 1). NRL allergy was not found among 253 patients who had a history of up to 10 operations, but 4/72 patients (5.6%) with a history of more than 10 operations were allergic to NRL ($P < 0.001$). Thus, frequent invasive procedures were associated with allergy, but not with sensitization to NRL without clinical symptoms.

Discussion

Among unselected patients scheduled to undergo operative procedures, 1.2% had manifest NRL allergy and another 8.3% NRL sensitization without clinical symptoms. In three of four patients with NRL allergy, the diagnosis had not been made prior to this study. Interestingly, despite previous immediate-type symptoms during surgery, we found NRL allergy undiagnosed in two patients with urogenital malformations, which are known risk factors. The frequency of allergy or sensitization to NRL was surprisingly high, and allergy was found only in patients who had undergone more than 10 operative procedures. The frequency of NRL allergy in this patient group (5.6%) was significantly higher than in patients who had undergone fewer than 10 invasive procedures (0%) ($P < 0.001$).

Until now, predominantly children with spina bifida were known to be at increased risk of NRL allergy due to operative procedures. Only a few studies have investigated the frequency of NRL allergy in other patients with multiple operations. Porri et al. (17) found that children with a history of multiple operations also had an increased frequency of NRL allergy irrespective of the underlying disease.

Several studies have examined the frequency of NRL sensitization in adult surgical patients in the past (25–28). One study similar to our investigation examined 996 adult outpatients by questionnaire-based history and determination of NRL-specific IgE in the serum by the AlaSTAT method (25). However, skin prick tests or challenge tests were not carried out in this investigation. In 67 of the 996 patients (6.7%), NRL-specific IgE antibodies were found. This frequency is in accordance with our findings. In part, sensitization seemed to be of clinical relevance, as suggested by the occurrence of intolerance reactions (rash, wheezing, or conjunctivitis) during medical care and/or a history of intolerance to rubber products. In a study from Spain (27), skin prick tests were performed in 1000 patients with a history of drug

allergy or atopy prior to operative procedures; NRL sensitization was present in 0.8%. No further diagnostic tests were applied in this investigation. A study from Finland found NRL allergy in one of 804 unselected adults (0.12%) prick-tested before surgery (28). However, none of the above studies examined a potential correlation between the number of previous surgical procedures and NRL sensitization.

Golden et al. (26) investigated the frequency of NRL sensitization among 829 surgical patients who had undergone 0–20 previous operations. In this study, no indication of sensitization or allergy to NRL was found. A questionnaire-based history did not reveal previous immediate-type reactions during medical care; NRL-specific IgE in the serum was determined in some of the patients, but no such antibodies were found in 34 atopic patients with a history of four or five surgical procedures or in 62 patients with a history of more than six surgical procedures. Incomplete use of diagnostic tools may have led to an unrealistically low diagnosis of allergy or sensitization to NRL in the above studies.

Skin prick test reactions in patients with NRL allergy may be discrepant with different NRL preparations due to variations in allergen content and/or composition. Thus, we recommend that skin prick tests be performed with at least two skin prick test solutions. Specific IgE antibodies to NRL are demonstrable with the CAP-FEIA only in from 76% (29) to 92% (30) of patients with NRL allergy. Challenge tests with glove material are only poorly standardized. It cannot be excluded that results are false negative in some cases. Moreover, due to incomplete skin or *in vitro* testing in 39 patients, we may have missed single patients with NRL sensitization. Challenge tests could not be performed in 12 patients with NRL sensitization. Therefore, our results represent minimal numbers of NRL allergy or sensitization in surgical patients.

Nevertheless, we found a fairly high frequency of NRL allergy in our study. The main reason seems to be patient selection, since numerous subjects with a history of multiple surgical procedures were included. However, the frequency of allergy or sensitization to NRL also differs largely among patients from known risk groups and evidently depends on the geographic origin of the individuals investigated. Among patients with spina bifida, NRL sensitization was found in Venezuela in only 4.3% (14), but in the USA in up to 64.5% of subjects (12). The frequency of NRL allergy in patients with spina bifida was up to 72.2% in the USA (15), whereas in Europe it was found in only 11.5% in Germany (16) and 15.0% in Spain (31).

Three out of four patients with NRL allergy reported symptoms occurring during medical treatment that were probably related to NRL exposure. One NRL-allergic patient had not previously noticed

symptoms. Despite typical symptoms of NRL allergy, the diagnosis had not been made in two of three allergic patients prior to our study.

Symptoms of NRL allergy during medical care in our patients included contact urticaria, rhinoconjunctivitis, shortness of breath, and cardiovascular reactions. Most patients who experienced severe cardiovascular symptoms or full anaphylactic shock due to NRL were affected during invasive procedures (19, 22, 32–35). As invasive treatment is associated with the highest risk of severe reactions, NRL allergy must be considered in all patients in whom NRL contact occurs in the course of therapy.

In our study, atopy was a risk factor for NRL allergy or sensitization: 19.4% of the atopic patients were allergic or sensitized to NRL compared with 4.6% of those without atopy. Evidently, NRL sensitization is common in the population, particularly among atopic individuals. The frequency of sensitization to NRL has been assessed among patients presenting for evaluation of different allergic diseases in allergy units, and was found to range from 1.7% (36) to 27.2% (37). NRL-specific IgE antibodies were found in the sera of 3.5% of blood donors in Italy (38) and up to 7.9% in the UK (39). The generally high prevalence of NRL sensitization would explain the high frequency of NRL sensitization found in our study group which was not related to the number of invasive procedures.

Occupational NRL exposure or a history of eczema

did not correlate with NRL allergy or sensitization. The number of patients at risk may have been too small in our study to allow the detection of a significant association. Hand eczema is considered a risk factor in subjects who acquire their NRL allergy at the workplace (7–9).

All in all, repeated operative procedures seem to be a risk factor for NRL allergy, but not for NRL sensitization without symptoms in adults. As such procedures often include other diagnostic tests or treatment before and after surgery, this procedure-related frequency probably reflects total exposure to the health-care environment. It is advisable to put in practice measures of primary prevention of NRL allergy for all patients, particularly through the use of material with no or at least low allergen content. The possibility of NRL allergy should be considered for all patients, especially for those from high-risk groups, which evidently also includes patients who have undergone a large number of previous invasive interventions. A complete series of preoperative allergologic investigations might be advantageous in order to prevent life-threatening allergic reactions by exposure to NRL during further treatment.

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References

1. STERN G. Überempfindlichkeit gegen Kautschuk als Ursache von Urticaria und Quinckeschem Ödem. *Klin Wochenschr* 1927;**6**:1096–1097.
2. GRIMM. Überempfindlichkeit gegen Kautschuk als Ursache von Urticaria und Quinckeschem Ödem. *Klin Wochenschr* 1927;**6**:1479.
3. TURJANMAA K. Incidence of immediate allergy to latex gloves in hospital personnel. *Contact Dermatitis* 1987;**17**:270–275.
4. MONERET-VAUTRIN D-A, BEAUDOUIN E, WIDMER S, et al. Prospective study of risk factors in natural rubber latex hypersensitivity. *J Allergy Clin Immunol* 1993;**92**:668–677.
5. PORRI F, LEMIERE C, BIRNBAUM I, et al. Prevalence of latex allergy in atopic and nonatopic subjects from the general population. *J Allergy Clin Immunol* 1995;**95**:154.
6. BEEZHOLD DH, SUSSMAN GL, LISS GM, CHANG N-S. Latex allergy can induce clinical reactions to specific foods. *Clin Exp Allergy* 1996;**26**:416–422.
7. WRANGSJÖ K, WAHLBERG JE, AXELSSON IGK. IgE-mediated allergy to natural rubber in 30 patients with contact urticaria. *Contact Dermatitis* 1988;**19**:264–271.
8. CHAROUS BL, HAMILTON RG, YUNGINGER JW. Occupational latex exposure: characteristics of contact and systemic reactions in 47 workers. *J Allergy Clin Immunol* 1994;**94**:12–18.
9. TAYLOR JS, PRADITSUWAN P. Latex allergy. *Arch Dermatol* 1996;**132**:265–271.
10. LAGIER F, VERVLOET D, LHERMET I, POYEN D, CHARPIN D. Prevalence of latex allergy in operating room nurses. *J Allergy Clin Immunol* 1992;**90**:319–322.
11. WRANGSJÖ K, OSTERMAN K, VAN HAGE-HAMSTEN M. Glove-related skin symptoms among operating theatre and dental care unit personnel. II. Clinical examination, tests, and laboratory findings indicating latex allergy. *Contact Dermatitis* 1994;**30**:139–143.
12. YASSIN MS, SANYURAH S, LIERL MB, et al. Evaluation of latex allergy in patients with meningomyelocele. *Ann Allergy* 1992;**69**:207–211.
13. KELLY KJ, KURUP V, ZACHARISEN M, RESNICK A, FINK JN. Skin and serologic testing in the diagnosis of latex allergy. *J Allergy Clin Immunol* 1993;**91**:1140–1145.
14. CAPRILES-HULETT A, SÁNCHEZ-BORGES M, VON-SCANZONI C, MEDINA JR. Very low frequency of latex and fruit allergy in patients with spina bifida from Venezuela: influence of socioeconomic factors. *Ann Allergy* 1995;**75**:62–64.
15. KONZ KR, CHIA JK, KURUP VP, RESNICK A, KELLY KJ, FINK JN. Comparison of latex hypersensitivity among patients with neurologic defects. *J Allergy Clin Immunol* 1995;**95**:950–954.
16. MICHAEL T, NIGGEMANN B, MOERS A, SEIDEL U, WAHN U, SCHEFFNER D. Risk factors for latex allergy in patients with spina bifida. *Clin Exp Allergy* 1996;**26**:934–939.
17. PORRI F, PRADAL M, LEMIERE C, et al. Association between latex sensitization and repeated latex exposure in children. *Anesthesiology* 1997;**86**:599–602.

18. DE SWERT LFA, VAN LAER KMIA, VERPOORTEN CMA, VAN HOEYVELD EM, CADOT P, STEVENS EAM. Determination of independent risk factors and comparative analysis of diagnostic methods for immediate-type latex allergy in spina bifida patients. *Clin Exp Allergy* 1997;**27**:1067–1076.
19. MAZÓN A, NIETO A, ESTORNELL F, NIETO A, REIG C, GARCÍA-IBARRA F. Factors that influence the presence of symptoms caused by latex allergy in children with spina bifida. *J Allergy Clin Immunol* 1997;**99**:600–604.
20. CREMER R, KLEINE-DIEPENBRUCK U, HOPPE A, BLÄKER F. Latex allergy in spina bifida patients – prevention by primary prophylaxis. *Allergy* 1998;**53**:709–711.
21. RING J. *Angewandte Allergologie*. München: MMV Medizin Verlag, 1995.
22. KELLY KJ, PEARSON ML, KURUP VP, et al. A cluster of anaphylactic reactions in children with spina bifida during general anesthesia: epidemiologic features, risk factors, and latex hypersensitivity. *J Allergy Clin Immunol* 1994;**94**:53–61.
23. NIGGEMANN B, BUCK D, MICHAEL T, WAHN U. Latex provocation tests in patients with spina bifida: who is at risk of becoming symptomatic? *J Allergy Clin Immunol* 1998;**102**:665–670.
24. PEARSON ML, COLE JS, JARVIS WR. How common is latex allergy? A survey of children with myelodysplasia. *Dev Med Child Neurol* 1994;**36**:64–69.
25. LEBENBOM-MANSOUR MH, OESTERLE JR, OWNBY DR, JENNER MK, POST SK, ZAGLANICZY K. The incidence of latex sensitivity in ambulatory surgical patients: a correlation of historical factors with positive serum immunoglobulin E levels. *Anesth Analg* 1997;**85**:44–49.
26. GOLDEN DBK, HAMILTON RG, BIRENBERG A, KRESHTOOL B, HAGLAUER C, ADKINSON NF Jr. Latex sensitization in surgical patients. *J Allergy Clin Immunol* 1995;**95**:157.
27. SÁNCHEZ-FERNÁNDEZ C, QUIRCE S, SÁNCHEZ-CANO M. Preoperative screening for general anesthesia. *Allergy* 1998;**53**:542–543.
28. TURJANMAA K, MÄKINEN-KILJUNEN S, REUNALA T, ALENUS H, PALOSUO T. Natural rubber latex allergy – the European experience. *Immunol Allergy Clin North Am* 1995;**15**:71–88.
29. NIETO A, ESTORNELL F, MAZÓN A, REIG C, NIETO A, GARCÍA-IBARRA F. Allergy to latex in spina bifida: a multivariate study of associated factors in 100 consecutive patients. *J Allergy Clin Immunol* 1996;**98**:501–507.
30. BLANCO C, CARRILLO T, CASTILLO R, QUIRALTE J, CUEVAS M. Latex allergy: clinical features and cross-reactivity with fruits. *Ann Allergy* 1994;**73**:309–314.
31. HAMILTON RG, BIAGINI RE, KRIEG EF. Diagnostic performance of Food and Drug Administration-cleared serologic analysis for natural rubber latex-specific IgE antibody. *J Allergy Clin Immunol* 1999;**102**:925–930.
32. GERBER AC, JÖRG W, ZBINDEN S, SEGER RA, DANGEL PH. Severe intraoperative anaphylaxis to surgical gloves: latex allergy, an unfamiliar condition. *Anesthesiology* 1989;**71**:800–802.
33. GELFAND DW. Barium enemas, latex balloons, and anaphylactic reactions. *AJR Am J Roentgenol* 1991;**156**:1–2.
34. OWNBY DR, TOMLANOVICH M, SAMMONS N, MCCULLOUGH J. Anaphylaxis associated with latex allergy during barium enema examinations. *AJR Am J Roentgenol* 1991;**156**:903–908.
35. SLATER JE, MOSTELLO LA, SHAER C. Rubber-specific IgE in children with spina bifida. *J Urol* 1991;**146**:578–579.
36. YLITALO L, TURJANMAA K, PALOSUO T, REUNALA T. Natural rubber latex allergy in children who had not undergone surgery and children who had undergone multiple operations. *J Allergy Clin Immunol* 1997;**100**:606–612.
37. RUËFF F, THOMAS P, REIBIG G, PRZYBILLA B. Natural rubber-latex allergy in patients not intensely exposed. *Allergy* 1998;**53**:445–449.
38. SENNA GE, CROCCO I, ROATA C, et al. Prevalence of latex-specific IgE in blood donors: an Italian survey. *Allergy* 1999;**55**:80–81.
39. MERRETT TG, MERRETT J, KEKWICK R. The prevalence of immunoglobulin E antibodies to the proteins of rubber (*Hevea brasiliensis*) latex and grass (*Phleum pratense*) pollen in sera of British blood donors. *Clin Exp Allergy* 1999;**29**:1572–1578.