

Role of Cross-Allergies to Latex in Clinical Routine of Anesthesia

Helene A. Haeberle, MD,* Daniela Lupic,†
Terumi Midoro-Horiuti, MD PhD,‡
Ralph T. Kiefer, MD,* Torsten H. Schroeder, MD,*
Klaus Unertl, MD,§ Hans-Juergen Dieterich, MD*

Department of Anesthesiology and Intensive Care Medicine, Clinical University Tübingen, Hoppe-Seyler-Str. 3, 72076 Tübingen, Germany and the Department of Pediatrics, University of Texas Medical Branch, Galveston, TX

Study Objective: To determine the applicability and reliability of a screening questionnaire to detect patients at high-risk of latex allergy; to assess the importance of other allergies such as profilin allergies (pollinosis) for presence of latex sensitization; and to determine the clinical effectiveness of preemptive avoidance of latex exposure in high-risk patients.

Design: Prospective, clinical trial.

Setting: Operative theater of a university hospital.

Patients: 95 adult patients.

Interventions: Patients were preoperatively screened and classified for present latex allergy (high-risk and low-risk group) according to a specially designed screening questionnaire. Anesthesia and surgery in the high-risk group were performed strictly avoiding latex-containing materials. The low-risk group (other allergies including pollinosis) received routine treatment, without latex-avoidance. Effects of latex avoidance or exposure were evaluated by measuring specific IgE titers perioperatively.

Measurements and Main Results: According to the questionnaire, 45 patients at high risk were defined. Validity of classification of high-risk patients is supported by significantly higher total IgE and latex and grass profilin specific IgE compared to the low-risk group. There were no significant differences in other profilin-specific IgEs. In one case of severe anaphylactic reaction a drop of latex-specific IgE during surgery could be observed.

Conclusion: The questionnaire allowed the identification of most patients at high risk for latex allergy. In isolated pollinosis no changes in any specific IgE levels were detectable. Strict avoidance of perioperative latex exposure in high-risk patients increases safety during anesthesia and surgery. © 2003 by Elsevier Inc.

Keywords: Latex allergy; anesthesia; profilin; serum antibody.

Introduction

The clinical relevance of latex allergy has been increasingly recognized during the last years. In routine anesthesia practice, muscle relaxants are the major cause for anaphylactic reactions, directly followed by latex (19%).¹ Although latex has been eliminated in many areas, exposure to latex in hospitals still remains a serious problem for sensitized patients. The fast and reliable identification of these patients is important to prevent severe anaphylactic reactions, especially during surgery and therefore would contribute to increased safety in

*Staff Anesthesiologist

†Predoctoral Fellow

‡Assistant Professor of Pediatrics

§Head, Department of Anesthesiology

Address correspondence to Dr. Helene Haeberle at the Department of Anesthesiology and Intensive Care Medicine, Clinical University Hospital Tübingen, Hoppe-Seyler-Str. 3, 72076 Tübingen, Germany. E-mail: helene.haeberle@uni-tuebingen.de

Received for publication June 19, 2002; revised manuscript accepted for publication January 23, 2002.

clinical practice. However, for the anesthesiologist this situation still remains challenging, particularly with respect to the often limited time in routine practice. Although, as suggested by several algorithms, various preoperative diagnostic tests might validly detect patients at high risk for latex allergy, this is not feasible in urgent and emergency clinical case management. Further, based on recent studies describing in latex sensitized patients cross reacting antibodies to pollens and food, patients at risk may also include individuals with other allergies, such as pollinosis. This raises important questions for the anesthesiologist: 1) how can latex allergy be reliably diagnosed/suspected in emergencies without the possibility to perform specific but time-consuming laboratory tests, 2) which cross-reactivities may play a role in latex allergy during daily routine, and 3) how protective is anesthesia in latex-secured operating rooms for sensitized patients.

The risk for developing latex allergy in patients with spina bifida²⁻¹² and other patients with increased frequency of operative procedures during early childhood,¹³⁻¹⁵ as well as the cross-reactivity between latex and bananas, avocados, and kiwis are well described.^{16,17} However recent description of common IgE epitopes between latex and certain pollens^{18,19} and cross-reactivities between latex and certain allergens, such as profilin²⁰ may imply that patients with elevated IgE titers to profilin or with pollinosis may be at increased risk for anaphylactic reactions following latex exposure. Profilin, a 14-kD protein is mainly found in birch trees, grasses, and weeds and is responsible for many cross-reactivities between different pollens and certain food allergies.^{17,21-23} Among rubber-derived allergens, latex profilin (Hev b 8) and latex prohevein (Hev b 6.02) are reported to have cross-reactivity to profilins from other plants and PR-3 and 4 proteins (pathogenesis-related plant protein group 3 and 4, respectively).²⁴ Therefore, these data might imply that patients with pollinosis are at a higher risk for latex allergy.

Based on this information, we have assessed the value of a standardized preoperative screening questionnaire to validly predict relevant risk factors for latex hypersensitivity. Once patients at risk were identified, latex- and profilin-specific IgE antibodies were determined. Because it has been described that specific IgE levels drop during anaphylactic reactions,²⁵ we evaluated the efficiency of latex avoidance by determination of total IgE concentrations, latex- and profilin-specific IgE concentrations during surgery in patients with high risk for latex sensitization in a latex-free environment. In patients with isolated pollinosis or no signs of latex allergy, the effect of latex exposure was tested.

Materials and Methods

Patients

After obtaining informed written consent and approval of the ethics committee at our institution, 95 patients were included in the study.

Screening Questionnaire

Questions regarding medications, previous surgeries, previous allergy tests, and anaphylactoid reactions to aspirin were included. Allergic disposition was analyzed by asking for anaphylactic reactions to plastic/polyester material, latex, bananas, other fruits, nuts, vegetables, or pollinosis including birch pollens, grass, and others. Symptoms and season of the occurrence of hay fever and/or asthma were further questioned. Severity and clinical symptoms were categorized by no rash, itching, wheals, exanthem, asthma/wheezing, vomiting, or hemodynamics or cardiovascular problems (*Table 1*). Risk for latex allergy was evaluated preoperatively based on this questionnaire. Patients who described exanthema, conjunctivitis, sneezing and/or bronchoconstriction after contact to balloons, latex gloves, or other rubber and latex equipment or who had banana, kiwi, or avocado allergy were considered at high risk of latex allergy. In cases in which the latex allergy could not be ruled out completely by history, patients were asked to wet their hands and to wear latex gloves, rubbing their hands during the interview. This provocative test was only done in the presence of resuscitation equipment. If symptoms of rash or itching occurred, the procedure was stopped immediately. Patients with a low risk for latex allergy were classified as having no reaction after contact to the latex gloves and had no evidence of allergic reactions to rubber in the past.

Anesthesia

All patients underwent elective operations. The surgical procedure for patients with history of latex allergy was performed at the beginning of the day in a latex-free operating room (OR). Anesthesia was induced with thiopentone or propofol, opioids, and muscle relaxants. Latex-free materials used for such patients included vinyl gloves, infusions in glass bottles (Fresenius, Bad Homburg; B. Braun, Melsungen, Germany), as previously described.²⁶ In patients without latex allergy, anesthesia was conducted in the same way but included latex-containing materials.

Blood Sampling

Blood samples [10 mL in a serum monovette (Sarstedt, Germany)] were drawn before induction of anesthesia, 15 to 20 minutes after the beginning of surgical procedures, and after recovery from the anesthesia. Serum was collected by centrifugation, aliquoted, and frozen at -70°C until analyses were performed.

Laboratory Analyses

Each sample was analyzed for total IgE, latex-specific IgE, and grass profilin-specific IgE, weed profilin-specific IgE, and tree profilin-specific IgE concentration. The incidence of atopic disposition was determined by an allergy screening test, AlaTOP® (DPC-Biermann, Bad Nauheim, Germany). AlaTOP® is an enzyme assay, which tests for

Table 1. Questionnaire for Evaluation of Possible Latex Allergies

1. Please provide following information:
 Initials: (z.B. Josef Mayer J.M.)
 Age: years old
 Gender: Male ☐ Female ☐

2. Profession?.....

3. Do you suffer of one of the following diseases:
 Heart diseases no ☐ yes ☐ :.....
 Lung disease no ☐ yes ☐ :.....
 Disorders of immune system no ☐ yes ☐ :.....
 Vascular disease no ☐ yes ☐ :.....
 Gastrointestinal disorders no ☐ yes ☐ :.....

4. What kind of surgery will be done?

5. Do you take any medication? no ☐ yes ☐

6. Did you have surgeries done before? no ☐ yes ☐
 How many?
 When?

7. Do you have any allergies? no ☐ yes ☐

8. What kind of symptoms do you have during allergic reactions?
 Erythema no ☐ yes ☐
 Itching no ☐ yes ☐
 Exanthem no ☐ yes ☐
 Asthma no ☐ yes ☐
 Dyspnea no ☐ yes ☐

9. Were any allergy tests performed before?
 no ☐ yes ☐ not known ☐
 Kind of Test: Scratch test no ☐ yes ☐ not known ☐
 Prick test no ☐ yes ☐ not known ☐
 Exposure no ☐ yes ☐ not known ☐
 RAST (blood drawn) no ☐ yes ☐ not known ☐
 Result:

10. Do you suffer from hay fever? no ☐ yes ☐
 If yes, in which month?
 To which pollen do you react?

11. Do you suffer from allergic asthma? no ☐ yes ☐
 If yes, what is the causing problem?

12. Please indicate if you react to one of the following agents and if yes characterize the reaction by the following staging:
 No erythema = 0
 Erythema = 1
 Itching = 2
 Exanthema = 3
 Asthma-dyspnea = 4
 Vomiting = 5
 Circulation problems = 6
 Consciousness = 7
 not known = 8
 Others = 9 (please verify below).

Continued

Table 1. Continued

	0	1	2	3	4	5	6	7	8
Plastic:	☐	☐	☐	☐	☐	☐	☐	☐	☐
LATEX:	☐	☐	☐	☐	☐	☐	☐	☐	☐
Bananas:	☐	☐	☐	☐	☐	☐	☐	☐	☐
Birch pollens:	☐	☐	☐	☐	☐	☐	☐	☐	☐
Other Pollens:	☐	☐	☐	☐	☐	☐	☐	☐	☐
Name Pollens:									
Nuts:	☐	☐	☐	☐	☐	☐	☐	☐	☐
Aspirin:	☐	☐	☐	☐	☐	☐	☐	☐	☐
Other Medications:									
.....	☐	☐	☐	☐	☐	☐	☐	☐	☐
.....	☐	☐	☐	☐	☐	☐	☐	☐	☐
.....	☐	☐	☐	☐	☐	☐	☐	☐	☐
.....	☐	☐	☐	☐	☐	☐	☐	☐	☐
Other reactions:									
.....									

reactivity with frequent allergens, allowing the diagnosis of atopic disease with a sensitivity of 89.57% and specificity of 98.06%.²⁷ The allergy diagnostic system AlaSTAT® (cut-off 0.7 kU/L) (a generous gift of DPC-Bierman) was used for measuring allergen specific IgE concentration, as described elsewhere.²⁸ Total IgE concentration was determined in the same way, except at a lower sample volume (10 µL).

Amino Acid Sequence of Latex and Grass Profilin

Analysis of amino acid sequences reported in the GenBank (Figure 1) showed that the latex profilin sequence had significant homology to other profilins, ranging from 73.1% to 82.4%. The closest homologies to latex profilin were found in Bermuda grass (79.4%), timothy grass (77.9%), birch (76.3%), and sunflower (weed group) (73.1%) profilins.

Statistics

Statistical analyses were done in cooperation with the Institute for Medical Biometry, at the University of Tuebingen, Germany. Because data were not distributed normally, a Wilcoxon test was performed to test for significance between the control group and patients with latex allergy. Therefore, the concentration of latex-specific IgE were ranked and the results are presented as means $\pm$ standard error of the ranks. The ranks were determined by sorting the values from minimum to maximum, after which each sample was given a rank value relative to the other samples. Profilin-specific IgE values are presented as median plus 10%, 25%, 75%, and 90% quantile.

Results

The preoperative screening by a standardized questionnaire, including allergic reactions to latex and fruits such as banana, kiwis, or avocados, allowed us to validly identify most patients at high risk in our study. Forty-five patients

Y15042: <i>Hevea brasiliensis</i> (rubber) profilin, Hev b 8									
AF059616:	<i>Arachis hypogaea</i> (peanut) profilin, Ara h 5								
Y08390:	<i>Cynodon dactylon</i> (Bermuda grass) profilin, Cyn d 12								
X77583:	<i>Phleum pratense</i> (timothy) profilin, Phl p 12								
AF129423:	<i>Apium graveolens</i> (celery) profilin, Api g 4								
M65179:	<i>Betula verrucosa</i> (birch) profilin, Bet v 2								
Y13271:	<i>Mercurialis annua</i> profilin, Mer a 1								
Y15210:	<i>Helianthus annuus</i> (sunflower)profilin, Hel a 2								
Y15042	MSWQTYVDER	LMCEIEGN***HL	TAAAIIGQDG	SVWAQSSNFP	QFKSEEITAI	50			
AF059616	NH	.L.....D***..	SS...L....	G.....H..	...P.....				
Y08390	...A...DH	H***..	.S.....H..	T....AA..	A..P..MAN.				
X77583	H	H***..	AS...L.H..	T....AD..	...P....G.				
AF129423	...A...DH	...V...PGQT.	H..	T..	.I.P...AG.				
M65179	H	...D.D.Q*ASNS	L.S..V.H..	S..	...PQ...G.				
Y13271	DH	...D.D.Q*GQ..	A..S.V.H..	.I....AS..	.L.P....G.				
Y15210	...A....H	...D...*TGQ..	.S...L.L..	T.....AK..	...P..MKG.				
Y15042	MSDFDEPGTL	APTGLHLGGT	KYMVIQGEAG	AVIRGKKGPG	GVTVRKTNQA	100			
AF059616	.N..A...S.	Y....	P.	.I.P.....	...IE.....				
Y08390	.K.....F.	F..P.	P.	S.	...K..G..				
X77583	HH.	...MFVA.A	P.	R.....A.	.I.IK..G..				
AF129423	.K.....H.	Y..A	PN	GS.	...IK..G..				
M65179	.K..E...H.	I	S.	S.	.I.IK..G..				
Y13271	.K.....H.	YIA..	S.	S.	.I.IK..G..				
Y15210	IKE...A...	...MFIA.A	...L...P.	A.	.ICIK..G..				
Y15042	LIIGIYDEPM	TPGQCNMIVE	RLGDYLLEQG	M	Identity	131			
AF059616	K..		DT.	L	82.4 (%)				
Y08390	.V.....	VI.	K.....I...	.	79.4				
X77583	.VV.....	V..	V...	.	77.9				
AF129423	.VF.V....V	V...	ID..	L	77.1				
M65179	.VF...E..V	V..	ID..	L	76.3				
Y13271	.VF...E..V	V..	I...	.	75.6				
Y15210	M.M.....V	A.....V..		.	73.1				

Fig. 1. Amino acid sequences of profilins. Amino acid sequences of profilins are shown in comparison to the latex profilin sequence (*Hevea brasiliensis*; top line). The sequence identities to latex profilin were analyzed and are indicated on the right side.

had a history suggestive of latex allergy (35 females, average age 37 yr; 10 males, average age 27 yr), 50 patients had no history of latex allergy (23 females, average age 43 yr; 27 males, average age 55 yr). Additional factors included atopic disease. Sixty-two percent of patients at high risk (28 patients) and 28% of patients at low risk (14 patients) for latex allergy described atopic disease, indicated by previous diagnostics or by chronically relapsing course of skin lesions including lichenification (atopic dermatitis) and/or allergic asthma after exposure to allergens such as dust mites. Patients with suspected latex allergy had a higher incidence of other allergies, hay fever, asthma, and an

increased frequency of previous surgeries (Table 2). Thirty percent of the patients at high risk for latex allergy versus 2% of the patients at low risk for latex allergy described symptoms such as pruritus of lips and throat, skin irritation, or abdominal pain, cramps, or diarrhea after consumption of kiwis, bananas, or avocados. Provocation test to latex (wearing latex gloves) did not give further information to further define individuals at risk. Clinical signs of allergic reactions to latex included rash (n = 26), itching (n = 24), exanthema (n = 23), asthma or wheezing (n = 6), vomiting (n = 1), heat waves (n = 1), and hemodynamic problems such as hypotension (n = 2). In one case there was a history of

Table 2. Self-reported Prevalence of Allergic Diseases and Risk Factors

Patients	(N)	Tree pollinosis	Grass pollinosis	Food allergy	Allergy to medications	Asthma wheezing	Other allergies	Exposure during work	Previous surgeries
No latex allergy	50	19	5	15	4	3	23	2	40
Latex allergy	45	24	13	37	8	11	47	10	27

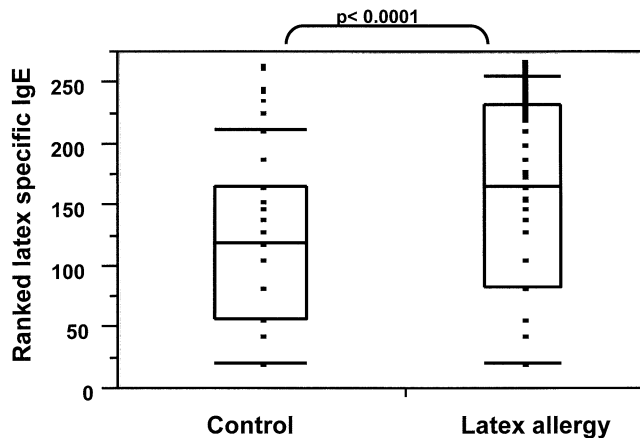


Fig. 2. Levels of latex-specific IgE during anesthesia in patients without and with risk of latex allergy. Patients at high risk of latex allergy had significantly higher concentrations of latex-specific IgE. The lines in the bars show 25% quantile, median, and 75% quantile (from bottom to top); the lower line indicates 10% quantile, the upper line the 90% quantile. Because the data were not normally distributed, they were ranked. The diagram shows the ranked data of latex-specific IgE concentration.

unconsciousness after exposure to latex, but no further information was available.

Data based on the questionnaire were supported by measurements of more specific parameters, such as antigen-specific IgE titers. Patients at high risk of latex allergy had significantly higher titers of latex-specific IgE than the low-risk group ($p < 0.0001$; Figure 2). There was no relation or connection observed between clinical signs and levels of latex-specific IgE levels. Latex avoidance was sufficient for prevention of severe anaphylactic reactions because the IgE concentration did not change significantly in the high-risk group during anesthesia (high-risk group: preoperative: 158 ± 3 kU/L; intraoperative: 158 ± 4 kU/L; postoperative: 155 ± 3 kU/L). Patients with isolated pollinosis or other allergies also did not show any changes in IgE levels during anesthesia (low-risk: preoperative: 120 ± 3 kU/L; intraoperative: 119 ± 3 kU/L; postoperative: 112 ± 3 kU/L). In patients at high risk for latex allergy, the serum concentration of total IgE was significantly increased and did not change during anesthesia in either patient group (low-risk: preoperative: 70 ± 29 kU/L; intraoperative: 69 ± 29 kU/L; postoperative: 62 ± 29 kU/L; high-risk: preoperative: 226 ± 31 kU/L; intraoperative: 220 ± 33 kU/L; postoperative: 241 ± 33 kU/L; $p < 0.0001$).

By avoiding contact to latex, anesthesia was performed without any anaphylactic reaction in patients at high risk for latex allergy. After surgery, those patients who had undergone previous anesthesia with latex material, described during the postoperative interview less anxiety and fewer clinical problems than before (respiratory problems, itching, exanthema; $n = 5$).

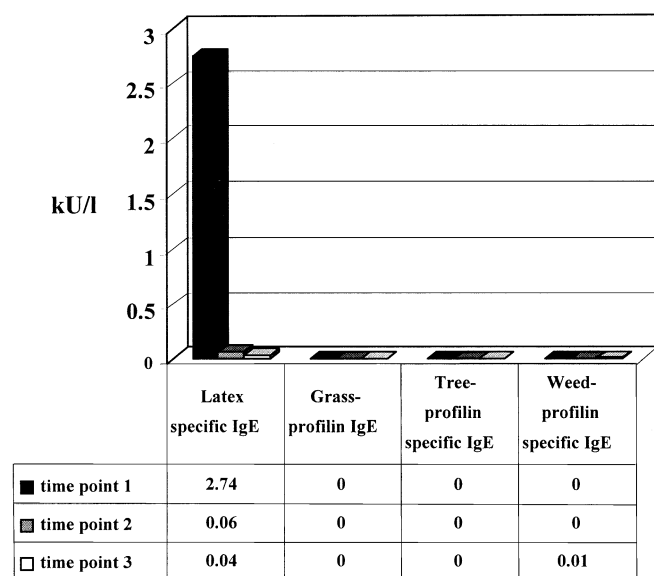
In one female patient (33 yr of age) with Crohn's disease, latex allergy was not identified by the question-

naire or by exposure to latex gloves. In the preoperative interview, she had described allergic reactions to tapes and antibiotics. Because of her Crohn's disease she had undergone multiple surgeries ($n = 10$). During induction of anesthesia (including latex), a flush around her mouth in the shape of the mask was noticed. This was immediately followed by severe bronchoconstriction, complicating mechanical ventilation and severe hypotension. The symptoms were treated with cortisone (1g Solu-Decortin®, Merck KGaA, Germany), vasoconstrictor (Akrinor®: 200 mg cafedrine hydrochloride, 10 mg theopinehrine hydrochloride in 2 mL solution, Astra Medica AG, Germany, a short-acting pressor amine commonly used in Germany) and immediate volume expansion, which stabilized the patient's condition. After the surgery, on repeated inquiry, she remembered that she had exanthema after contact to rubber gloves before. Of note, in her case the screening test for atopic disorders was negative. Afterward her latex allergy was confirmed by a dermatologist. In this patient, the latex-specific IgE concentration dropped from 2.74 kU/L before anesthesia induction to 0.06 kU/L and 0.04 kU/L after anesthesia. Total IgE titers increased slightly and profilin-specific IgE titers were low and did not change during the event (Figure 3).

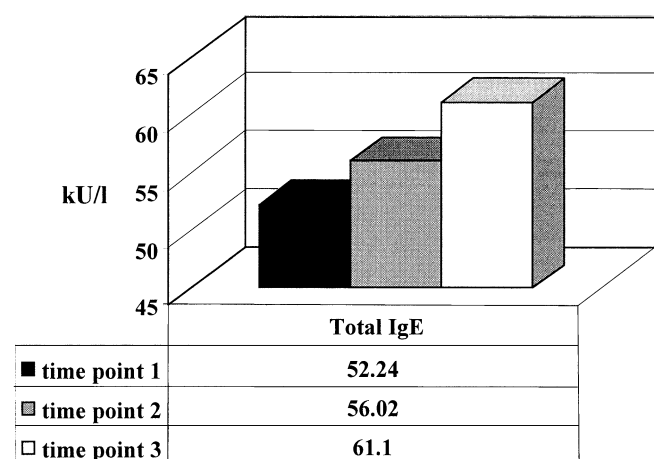
Profilin-specific IgE titers were barely detectable in all patients. The concentration of tree and weed profilin were not significantly different between the two groups. The titers of grass profilin-specific IgE were significantly higher in patients at high risk for latex allergy (Table 3; $p < 0.05$). Patients with isolated hay fever ($n = 24$) or elevation of grass profilin-specific IgE concentrations did not show any symptoms of anaphylactic reactions perioperatively, although they were exposed to latex. No correlation was found between latex-specific IgE and any profilin-specific IgE.

Discussion

Latex allergy represents a frequent problem for clinicians, especially for anesthesiologists, because the incidence of latex allergy has increased consistently from previous years.²⁹ Although recent studies have shown that elimination of latex exposure reduces the risk of latex allergies in high-risk patients,^{30,31} latex still is not eliminated completely. For sensitized patients, exposure to even low amounts of latex-containing particles is sufficient to induce severe anaphylactic reactions. This problem needs to be considered during the preoperative evaluation of the patient and also in the emergency room. We have shown that a focused screening of patients for cross allergies to certain fruits, frequency of previous surgeries and atopic disease, allowed the identification of most patients at high risk for latex allergy, followed by prevention of perioperative anaphylactic reactions to latex. Although cross allergies to proteins in pollens have been described,¹⁸ thus strongly suggesting a potentially increased risk of latex-induced anaphylactic reactions, we were not able to confirm this assumption in patients with pollinosis. Further, we were able to demonstrate that a latex-free environment during surgical procedures most effectively protected pa-



A



B

Fig. 3. Concentration of latex-specific IgE, grass-, tree-, and weed-specific profilin IgE (A) and total IgE (B) (kU/L) during anesthesia in a patient who had an anaphylactic reaction during induction of anesthesia. Blood samples were drawn before anesthesia induction (time point 1), 20 minutes after anaphylactic reaction (time point 2), and after recovery (time point 3).

tients from anaphylactic reactions, reflected by stable levels of latex-specific IgE perioperatively in these patients. In patients with hay fever but no signs of latex sensitization, no symptoms or significant decreases in specific IgE levels during surgery could be observed. Based on our data and that from other studies, a detailed interview is very important, focusing on preexisting allergies, especially any history of reactions (wheals, exanthema, or wheezing) to rubber products, such as rubber gloves and balloons. However, in some cases the differentiation between con-

tact dermatitis and an allergic reaction was difficult. The differentiation occurred along with questioning the relation between exposure and skin irritation, area of involvement, and additional allergies. Equally important are information about reactions to bananas, avocados, and kiwis and other fruits such as pineapples because of the described cross allergies (Table 3).³²⁻³⁵ One of several allergens responsible for cross-reactivity between latex and food is Hev b 6.02. This allergen belongs to the pathogenesis-related (PR) plant protein group 3, including chitinase from chestnut, Pers a 1 from avocado, 32-kD banana allergen, and Bra r 2 from turnip root.³⁶ PR-proteins are produced in plants that are under stress, including drought, fungal and bacterial infections, ozone, and ultraviolet B light and represent an important cause of cross-reactivity between latex allergen and other proteins^{21,24,36} (Table 4). However, milder food allergies are mostly unknown or unrecognized by patients or can not be related to one kind of food and should be pointed out to the patients.

Although in our study, as in other work³ there was no difference in frequencies of previous surgeries between the two groups (high-risk group: average 3.7 surgeries; low-risk group: average 3.5 surgeries), other studies described frequency of previous surgeries as an additional risk factor.^{4,13,37} However, we and others have observed a higher incidence of atopic disorders in patients with latex allergy, including atopic dermatitis and asthma.^{38,39}

Our data also show that the elimination of latex from the environment of patients at high-risk is effective to prevent any IgE-induced reactions (IgE consumption), because the perioperative concentration of specific IgE was stable throughout the whole procedure. Only one patient in our study with preoperatively undetected latex allergy showed a severe allergic reaction including flush, bronchospasm and hypotension. During this event, latex-specific IgE levels dropped drastically (Figure 3). This is in accordance with reports of declined levels of specific IgE after severe anaphylactic reactions.^{25,40} Therefore single determination of circulating IgE concentration may not be effective for diagnosis of any allergy but may be used as a diagnostic tool for suspected anaphylactic reactions during surgery, if IgE concentrations can be evaluated from preoperative serum samples.

An alternative approach to identify patients with an allergy to latex before surgery would be to determine latex-specific IgE in serum in combination with other tests such as pinprick tests⁴¹. These tests should be performed in patients at high risk for latex allergy before admission. Indeed, several algorithms have been described but cannot always be performed in anesthesia because of the lack of time in emergencies. In our study, a significant increased level of latex-specific IgE was noted in patients identified as potentially at high risk for latex allergy. However, recent studies show that the specificity and sensitivity of these tests not only differ between the different commercially available assays, but also between the patient groups investigated.^{11,42,43} According to these studies, the combination of total IgE, latex-specific IgE measurements, immunoblots, and pinprick tests allow the best

Table 3. Titers of Profilin-specific IgE (kU/L) in Patients with or without a History of Latex Allergy

	Min.	25% quantile	Median	75% quantile	Max.	Stat.Sign.
Gras profilin-specific IgE						
Patients without latex allergy	0	0.01	0.03	0.15	0.24	p < 0.05
Patients with latex allergy	0	0.02	0.06	0.215	3.47	
Tree profilin-specific IgE						
Patients without latex allergy	0	0.015	0.02	0.19	0.19	p = 0.6
Patients with latex allergy	0	0.01	0.02	0.06	0.77	
Weed profilin-specific IgE						
Patients without latex allergy	0	0.01	0.03	0.17	0.2	p = 0.05
Patients with latex allergy	0	0.02	0.04	0.17	0.75	

sensitivity and specificity. It has to be considered, however, that the evaluation of the prick test is dependent on the experience of the investigator and not all of the 30 latex allergens contained in natural rubber latex are characterized yet.^{41,44} Elevated total IgE titers allow identification of some patients with atopic disorders. However, we also observed many patients with elevated IgE concentrations, but with no clinical symptoms. Patients with other allergies, parasite infections, and certain disorders have elevated concentrations of total IgE in their serum, therefore, total IgE titers alone may not be useful to screen for high-risk patients.⁴⁵ Further, routine performance of all these tests for all patients at risk may be expensive (assay) and time-consuming. The results may depend on the experience of the investigator (prick test) and finally are not helpful in fast decisions. In this study, we used a nonstandardized allergy test,⁴⁶ which did not help to further identify patients at risk. The reliability of the latex glove wearing test depends on the test protocol and the protein concentration of the gloves used.⁴⁷ Increased sensitivity of exposure tests has been obtained by puncturing the skin before contact with the latex glove. However, many patients would refuse this invasive, unpleasant procedure in clinical routine before surgery. In addition to the test protocol, undefined allergens in natural rubber

latex may play an important role. Recently, 34 relevant latex allergens have been described containing more than a dozen relevant proteins, which are not completely defined yet.⁴⁴ Furthermore, the protein content of different latex allergens vary between latex gloves. Specifically, the content of one allergen has been shown to be unpredictable even in gloves with low total protein.⁴⁸

Although we and others⁴⁹ have found higher grass profilin-specific IgE levels in patients with latex allergy, we do not consider this an additional risk factor, because only 5 of 45 patients had IgE levels greater than 0.7 kU/L, which is a concentration that is predictive of an allergy to grass⁴² (although allergic reactions may take place even at lower levels of specific IgE). In our study, patients with no history of latex allergy but with pollinosis (n = 20) did not develop clinically relevant problems or any decrease in specific IgE concentration after exposure to latex. These findings are in accordance with the clinical study of Drouet *et al.*,⁵⁰ reporting no pollen polysensitization in patients with clinical history for latex allergy and *vice versa*. The incidence of higher grass profilin-specific IgE titers may be a result of the close homology of the two antigens. Sequence analysis showed higher identity of grass profilins to latex profilin than tree and weed profilins (*Figure 1*), which may also cause false-positive test results.

Table 4. Most Important Latex Allergens and Described Cross-Allergies³⁶

Allergen source	Allergen designation	Molecular weight	Cross allergies
Hevea brasiliensis (rubber)	Hev b 1; elongation factor	14,6/58	Birch pollen
	Hev b 2; β 1,3-glucanases	34/36	
	Hev b 3;	24	
	Hev b 4; component of microhelix protein complex	50/100/110/115	
	Hev b 5	16	Kiwifruit
	Hev b 6: Prohevein	20	
	Hev b 6. 01; hevein precursor	20	Chestnut, banana
	Hev b 6. 02; hevein	5	
	Hev b 6. 03; C-terminal fragment of hevein	14	Ficus benjamina
	Hev b 7; patatin homologue	46	Potato
	Hev b 8; profilin	14	Pollen, vegetables
	Hev b 9; enolase	51	Fruits
	Hev b 10; Mn-superoxide dismutase	26	Mold

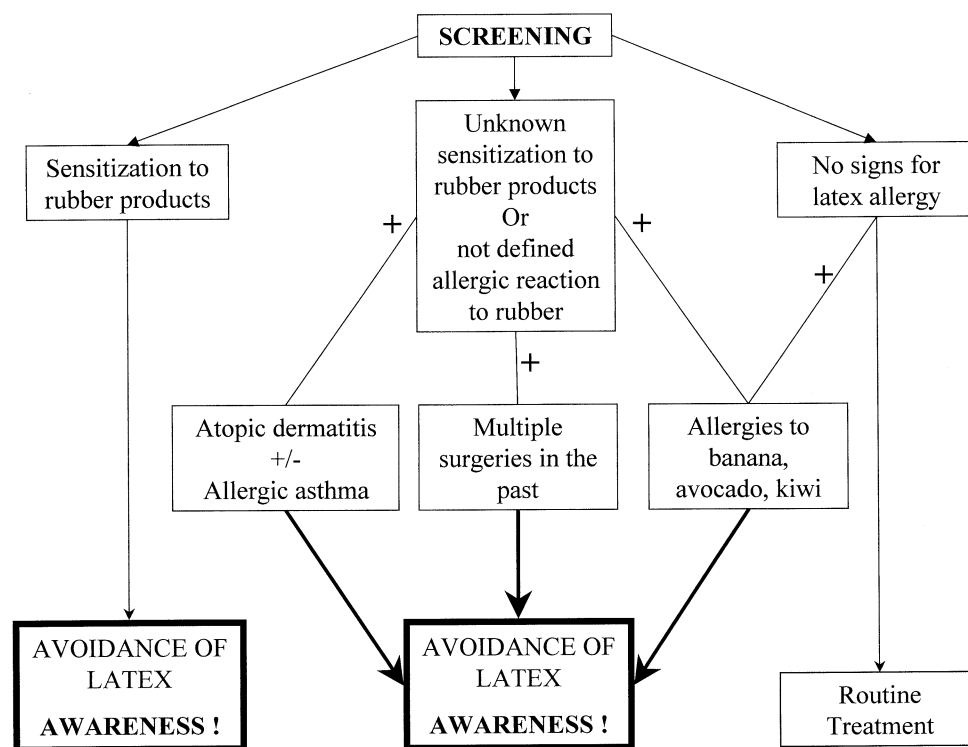


Fig. 4. Suggested algorithm to identify and preemptively treat patients at high risk for sensitization to latex.

The gold standard for the diagnostic of latex allergy is not defined yet. Especially for the anesthesiologist, it is impossible to diagnose or exclude a latex allergy positively in all patients, however, it is the responsibility of the anesthesiologist to provide a safe environment for patients with allergies.

Even if the diagnosis of latex allergy is assured, there may still be a problem in protecting the patient during anesthesia. Stable perioperative levels of specific IgE determined in this study emphasize once again that eliminating of latex from the environment of the patient is the best form of protection and prevention. Latex-specific IgE levels and total IgE titers were stable during the operative procedure in both groups. Although powdered gloves are mostly eliminated, it is still recommended to treat sensitized patients at a high risk for latex allergy in an operating room that has not been used during the last 6 hours to ensure low latex particle concentration in the air.^{31,51} In any suspected case of latex allergy, all latex-containing equipment in the operating room has to be eliminated to reliably avoid any contact with latex. Latex-free equipment should be prepared in advance for different operative procedures and the emergency room. Because latex has been eliminated in most equipment, it is important to indicate materials that still contain latex and these materials should be stored separately. It has to be considered that currently there are no latex-free pulmonary artery catheters available. In addition, an interdisciplinary approach to avoid latex before, during, and after anesthesia

should be a further goal. A latex-free environment not only protects patients, it also prevents and decreases sensitization, especially in children^{30,52,53} and health care workers.

In our department, patients are categorized as high or low risk according to the presented data. Powdered gloves were totally eliminated as were most latex-containing materials to avoid latex contamination of the environment and sensitization. In patients at high risk for latex allergy, latex material is avoided, including tapes that contain latex. The incidence of anaphylactic reactions could be decreased by this management.

We conclude that, for the preoperative evaluation of risk factors for latex sensitization, information about fruit allergies, atopic disorders, and number of surgeries (*Figure 4*) but not pollinosis are essential. This screening system represents now the fastest, most reliable and easiest procedure to 1) identify patients at risk for latex sensitization and 2) to prevent severe anaphylactic reactions in anesthesia.

Acknowledgments

Special thanks to DPC-Biermann for the support to establish the assay in our laboratory. The authors thank Dr. Randy Goldblum for his assistance in English grammar and for critical review of this publication and Alice Mager for the excellent technical assistance. This work was supported by grant F 1211030.2 of the Fortune Program of the University of Tübingen, Germany.

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