

THE JOURNAL OF Allergy AND Clinical Immunology

July 1994 • Volume 94 • Number 1

A cluster of anaphylactic reactions in children with spina bifida during general anesthesia: Epidemiologic features, risk factors, and latex hypersensitivity

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Abstract

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Background: Anaphylactic reactions (ARs) in high-risk pediatric patients undergoing general anesthesia, especially those with spina bifida, have been attributed to anesthetics, muscle relaxants, antimicrobials, ethylene oxide, and latex.

Methods: To identify risk factors for AR during general anesthesia and to investigate the role of latex allergy, we studied epidemiologic and immunologic characteristics of patients with ARs during general anesthesia during a 13-month cluster of such reactions at Children's Hospital of Wisconsin (case patients). Patients with AR were compared with patients with spina bifida undergoing uneventful general anesthesia during the same period (control patients). For each case patient and control patient, we conducted a chart review; a parental interview; skin prick testing with latex, anesthetics, aeroallergens, and banana extract; ELISA and RAST for latex-specific IgE; a total serum IgE; and an ELISA for IgE antibody to ethylene oxide.

Results: Anaphylactic reactions occurred exclusively in patients with spina bifida ($n = 10$) or patients with a congenital urinary tract anomaly ($n = 1$). Case-patients were more likely than control patients to have a history of asthma ($p = 0.002$), rubber contact allergy ($p = 0.001$), food allergy ($p = 0.001$), rash caused by adhesive tape ($p = 0.05$), daily rectal disimpaction ($p < 0.001$), nine or more prior surgical procedures ($p < 0.002$), latex-specific IgE ($p = 0.027$), or elevated total serum IgE levels ($p = 0.002$). Multivariate analysis identified non-white race, rubber contact allergy, history of food allergy, and nine or more surgical procedures as significant independent risk factors. Logistic model equation identified the predicted probability of AR with a sensitivity, specificity, and positive predictive value of 82%, 97%, and 82%, respectively.

Conclusions: These findings demonstrate that atopy, especially symptomatic latex allergy, is associated with AR during anesthesia in patients with spina bifida. Until a standardized latex test is available, a medical history of immediate rubber contact allergy, non-white race, food allergy, or nine or more prior surgical procedures can identify patients with spina bifida at highest risk for ARs. A complete history, including rubber contact and food allergy, should be compiled on all patients with spina bifida before surgery. (J ALLERGY CLIN IMMUNOL 1994;94:53-61.).

AR	Anaphylactic reaction
CHW	Children's Hospital of Wisconsin
ETO	Ethylene oxide
IU	International units
SPT	Skin prick test

(Click on a term to search this journal for other articles containing that term.)

Key words: [Latex](#), [spina bifida](#), [ethylene oxide](#), [anaphylaxis](#), [general anesthesia](#), [allergy](#)

Anaphylactic reactions (ARs) during surgical procedures have been attributed to anesthetic agents, muscle relaxants, ethylene oxide (ETO), or antimicrobials administered intraoperatively. However, approximately 16% of these reactions are idiopathic. ^{[1](#), [2](#)}

Recently, there have been increased reports of immediate AR presumed to be caused by latex exposure in patients undergoing surgical ^{[3](#), [10](#)} or diagnostic radiographic procedures. ^{[11](#), [13](#)} Hypersensitivity responses to latex products have included rhinitis, bronchospasm, angioedema, urticaria, anaphylaxis, and sudden death. ^{[12](#), [14](#), [15](#)} Persons frequently exposed to latex products, ^{[15](#), [16](#)} such as patients with spina bifida ^{[3](#), [4](#), [8](#)} and health care workers are at greatest risk for developing hypersensitivity reactions. Data on the prevalence of latex sensitization are limited. Previous estimates have been confounded by small sample size and the isolated use of serologic tests with unknown sensitivity. ^{[3](#), [7](#), [8](#), [17](#)}

From January 1990 through January 1991, a cluster of ARs occurred in patients during induction of anesthesia at the Children's Hospital of Wisconsin (CHW). This provided an opportunity to conduct an epidemiologic study to identify risk factors for AR and to evaluate the patients' clinical and immunologic features.

Methods

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Case definitions and ascertainment

An AR was defined as hypotension (a fall of ≥ 30 mm Hg in systolic blood pressure from preinduction blood pressure) and at least one of the following: rash, angioedema (facial and lip swelling), stridor, wheezing, or bronchospasm (increased airway pressure with or without a decrease in arterial oxygen saturation). The study period was defined as January 1989 through January 1991; the precluster period, as January 1989 through December 1989; and the cluster period as January 1990 through January 1991. A case patient was defined as any CHW patient undergoing general anesthesia during the study period who experienced an AR.

Cases were identified by review of anesthesia quality assurance records. Because all suspected cases that were initially identified were in children who had either spina bifida or a congenital genitourinary anomaly, the medical records of all patients with these two diagnoses who had general anesthesia during the cluster period were reviewed.

Latex sensitivity was defined as at least one positive serum or skin prick test (SPT) result for latex-specific IgE.

Epidemiologic studies

To assess potential risk factors for AR, we compared case patients with all other patients with spina bifida who had undergone procedures requiring general anesthesia during the cluster period (control patients). For each control patient, the surgical procedure chosen for comparison with the case surgical procedure was the last general anesthesia procedure performed during the study period.

Case- and control-patient medical records were reviewed for age, gender, race/ethnicity, date and day of surgery, history of allergy, asthma, history and duration of clean intermittent catheterization, preoperative medications, surgical procedure, type of anesthesia induction, intraoperative medications and anesthetic gases, surgery and anesthesiology personnel, operating room nurses, history of intraoperative urinary catheterization and type of catheter used, number of previous general anesthesia procedures, and the presence of hypotension, bronchospasm, rash angioedema, and stridor. Preoperative and intraoperative patient routines and operating room equipment cleaning and maintenance procedures were extensively reviewed during the cluster period by the physician from the Centers for Disease Control.

The parents of all case and control patients were contacted during clinic visits, through the mail, or by telephone and asked to complete a questionnaire. The questionnaire inquired about a history of asthma, wheezing, rhinitis, allergy to foods or drugs, allergic reactions, hypersensitivity to latex products, bladder catheterization, manual rectal disimpaction, and total number of surgical procedures.

Immunologic evaluation

This study was approved by the Human Research Review Committee of the Medical College of Wisconsin and CHW. Consenting case and control patients (60 of 75) had immunologic evaluations that included SPTs, intradermal testing, and serologic evaluation. Intradermal and skin prick tests were performed with anesthetics (case patients only), muscle relaxants (case patients only) (i.e., thiopental sodium, pancuronium bromide, vecuronium, and fentanyl), crude extracts of high ammoniated raw latex or nonpowdered glove latex, and common inhalant aeroallergens (i.e., ragweed, grass, tree, mite, dog, cat, and *Alternaria* and *Cladosporium* species).¹⁸ In addition, because of the demonstrated cross-reactivity between banana and latex, patients had SPTs with banana extract (Greer Laboratories,* ■

- *Use of trade names and commercial sources is for identification only and does not imply endorsement by the Public Health Service or the Department of Health and Human Services.

Lenoir, N.C.)

Case patients and control patients were tested by the Multi-test (Lincoln Diagnostics Inc., Decatur, Ill.) prick technique with raw latex antigen obtained from Canada (ammoniated Nicaraguan latex) and nonpowdered latex glove extract (Perry, Smith & Nephew, Massillon, Ohio)²⁰ (0.1 mg/ml) diluted 1:1000 to 1:1,000,000 in phosphate-buffered saline. Patients with a history of anaphylaxis were initially tested with concentrations of 1:100,000 to 1:1,000,000, and control patients, with concentrations of 1:1000 to 1:10,000 of latex antigen. All sites were examined and graded as previously described.²⁰ After preliminary studies demonstrated that all patients who reacted to the 1:1000 concentration of raw latex also reacted to the glove extract, we tested the remaining patients only with the glove extract.

Serum latex-specific IgE antibodies were measured by RAST (ammoniated crude latex) and by ELISA (0.5% formalin-preserved crude latex and Perry latex glove extract).^{21 22} Serum IgE antibodies against ETO-human serum albumin conjugates were measured by ELISA as previously described.^{23 24} Latex sensitivity was defined as one or more positive test results (ELISA, RAST, or SPT). Quantitative serum IgE levels were measured by means of the total IgE II FAST test (3M Diagnostic Systems, Santa Clara, Calif.). An IgE level of greater than 84 international units (IU) (200 ng/ml) exceeded the normal range.

Statistical analysis

All data were collected on standardized forms, entered into a microcomputer, and analyzed with PC-SAS version 6.04 (SAS Institute, Cary, N.C.). Risk ratios and 95% confidence intervals were calculated for categorical variables and compared by using the chi square or Fisher's exact test. Continuous variables were compared by using the Wilcoxon test. Multivariate analysis with logistic regression was also performed.

Results

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Eleven patients, who experienced 12 ARs, met the case definition. Nine cases were preliminarily reported by the Centers for Disease Control in 1991.¹⁸ The rate of ARs (number of ARs per number of procedures) during the cluster period was significantly greater than that during the precluster period (12 of 7386 vs 0 of 5925 procedures; $p = 0.003$). ARs occurred only in patients with spina bifida (11 ARs in 10 patients) or congenital urinary tract anomalies (1 AR). During the cluster period, 74 patients with spina bifida (patient AR rate, 10 of 74; 13.5%) had a total of 152 general anesthesia procedures (procedure AR rate, 11 of 152; 7.2%). The ARs were characterized by hypotension (100%), bronchospasm (83%), wheezing (55%), rash (50%), stridor (8%), and angioedema (8%). The mean decrease in systolic blood pressure was 55 mm Hg, and the mean increase in peak inspiratory airway pressure was 18 mm Hg. The ARs occurred at a mean of 13 minutes (range, 5 to 30 minutes) after the start of anesthesia. No case patient had a surgical incision begun when the AR occurred. No AR resulted in death, but all case patients with AR were treated with epinephrine, intravenously administered fluids, corticosteroids, antihistamines, and — except for two patients — admission to the intensive care unit and cancellation of the planned surgery.

Case and control patients were similar in age, gender, race/ethnicity, history or duration of clean intermittent catheterization, history of eczema, rhinitis, and drug allergy (■ Table I). Case and control procedures were similar with respect to day of surgery, operating room, anesthesiology personnel, preoperative medications, type of anesthesia induction, anesthetic gas used, surgical procedure, intraoperative antimicrobial agents, and use of intraoperative urinary catheterization (data not shown). The only new product was an intravenous buretrol and tubing system (Dosifix Burette Set; Burron Medical Inc., Bethlehem, Pa.) containing two internal latex valves, which was introduced into general use in the operating rooms 1 month before the first episode of anaphylaxis occurred. Protein extracted in phosphate-buffered saline and measured by the Lowry method revealed protein extraction of 0.1% of dry weight of the disk valve and back-check valve.

TABLE I. Comparison of potential risk factors for ARs among case and control patients, CHW, January 1, 1990 to January 31, 1991

	Case patients (n=11)	Control patients (n=64)	Odds ratio (95% CI)	p Value
Age (yr) (mean ± SD)	7.8 ± 3.3	5.6 ± 4.5		>0.1
Sex (M : F)	6 : 5	28 : 36		>0.1
Race				
White	8 (73%)	52 (81%)		>0.1
Black	2 (18%)	8 (12.5%)		
Other	1 (9%)	4 (6.5%)		
CIC	7 (64%)	42 (66%)	1.0 (0.6, 1.6)	>0.1
Duration CIC-years (mean ± SD)	3.4 ± 3.1	3.0 ± 3.9		>0.1
Rhinitis	5 (45%)	12 (18%)	2.4 (1.0, 5.4)	>0.1
Eczema	0 (0%)	6 (9%)	NC	>0.1
Tracheostomy	2 (18%)	5 (8%)	2.3 (0.5, 10.5)	>0.1
Prior surgeries (number ± SD)	12.1 ± 5.9	7.2 ± 4.8		0.008
≥ 9 Surgical procedures	9 (82%)	19 (30%)	2.8 (1.7, 4.4)	0.002
Midazolam given intraoperatively	4 (36%)	6 (9%)	3.9 (1.3, 11.6)	0.045
History of anaphylaxis	11 (100%)	4 (6%)	16.0 (6.2, 41.3)	<0.001
Asthma	7 (64%)	10 (16%)	4.1 (1.98, 8.4)	0.002
Rubber contact allergy*	6 (55%)	3 (5%)	11.6 (3.4, 39.8)	<0.001
Food allergy	5 (45%)	1 (2%)	29.1 (3.8, 226)	<0.001

Rash from adhesive tape	5 (45%)	11 (17%)	2.6 (1.1, 6.1)	0.05
Daily rectal disimpaction	6 (55%)	5 (8%)	7.0 (2.6, 19.0)	<0.001
Drug allergy history	5 (45%)	14 (22%)	2.1 (0.9, 4.6)	<0.1

C/C, Clean intermittent catheterization; NC, not calculable.
 *Urticaria, angioedema, wheezing, or anaphylaxis.

Case patients were more likely than control patients to have a history of asthma, rubber contact allergy symptoms (urticaria, angioedema, or wheezing with latex contact), food allergy, rash at the site of adhesive tape use, daily rectal disimpaction, or more prior surgical procedures; case patients were also more likely to have received midazolam before surgery. Case patients who required daily rectal disimpaction had more surgical procedures than patients who did not (mean, 12.1 vs 7.1; $p = 0.003$).

Immunologic studies

No case patient had evidence of immediate hypersensitivity to anesthetic or muscle relaxant agents. Case and control patients did not differ significantly in reactivity to ETO, aeroallergens, or banana. In contrast, the mean total serum IgE was significantly higher in case patients than in control patients; seven of nine case patients had total serum IgE greater than 84 IU (200 ng/ml). Case patients were more likely than control patients to have latex-specific IgE as determined by SPT, ELISA, or RAST (11 of 11 vs 33 of 49; $p = 0.027$) (■Table II). Fifteen sera that were reactive to both ETO and latex were tested by ELISA inhibition for cross-reactivity. Latex-reactive sera could be inhibited to 85% by preincubation with latex in the latex ELISA but could not be inhibited by pretreatment with ETO. Similarly, latex pretreatment did not inhibit the ETO ELISA with ETO-reactive sera at any concentration of latex antigen tested, but the sera could be inhibited by pretreatment with ETO–human serum albumin conjugate. A comparison of the immunologic tests (SPT, ELISA, and RAST) (■Table III) showed the RAST test to be the most specific in detection of latex hypersensitivity, whereas the ELISA was most sensitive overall. No SPT was performed at a dilution of less than 1:1000, and this may account for the lower sensitivity.

TABLE II. A comparison of immunologic evaluation of case and control patients, CHW, January 1, 1990 to January 1, 1991

Test	Case patients			Control patients			<i>p</i> Value
	No. positive	No. tested	%	No. positive	No. tested	%	
Latex SPT	10	10	100	19	39	46	0.01
Latex ELISA	10	10	100	27	42	62	0.02
Latex RAST	10	10	100	21	41	51	0.017
Latex sensitivity*	11	11	100	33	49	67	0.027
ETO	3	9	33	15	44	34	>0.1

Aeroallergen SPT	3	8	38	9	33	27	>0.1
Banana SPT	2	8	25	5	33	15	>0.1
IgE > 84 IU	7	9	78	9	44	20	0.002
IgE mean IU + SD	476 ± 606 IU			75 ± 155 IU			<0.001

*Latex sensitivity = any one of the following positive: latex SPT, latex ELISA, or latex RAST.

TABLE III. Comparison of SPT, RAST, and ELISA for detection of latex hypersensitivity

Latex tests	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
SPT vs ELISA or RAST	77	82	92	50
ELISA vs SPT or RAST	87	68	83	73
RAST vs SPT or ELISA	82	100	100	60

Risk factor assessment

Univariate analysis

Sixty patients (11 of 11 case patients and 49 of 64 control patients) had positive latex SPT, latex-specific IgE ELISA, or RAST test results; 45 patients had two or more positive test results. The 15 patients not tested were from out of the state and refused testing or had died.¹ Sensitive but not specific variables for identifying case patients included the following (either alone or in combination): latex sensitivity, a history of asthma, rubber contact urticaria, food allergy, or rash caused by adhesive tape (■Table IV). In addition, there was no risk of AR in patients who were not latex-sensitive or who did not have a positive history of latex allergy (negative predictive value = 100%).

TABLE IV. Comparison of clinical and immunologic tests as predictors of ARs among pediatric patients with spina bifida during general anesthesia procedures, CHW, January 1, 1990 to January 31, 1991

Variables or combination of variables	Odds ratio* (95% CI)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Latex sensitivity†	∞	100	33	25	100

Positive history†	∞	100	72	39	100
Daily rectal disimpaction	7.0 (2.6, 19.0)	55	92	55	92
≥ 9 Prior surgeries	7.6 (1.8, 32.5)	82	70	32	96
IgE > 84 IU	7.4 (1.7, 32.0)	78	77	41	94
Latex sensitivity & positive history	∞	100	76	48	100
Latex sensitivity & daily rectal disimpaction	5.4 (2.0, 14.4)	55	90	55	90
Latex sensitivity & IgE > 84 IU	8.9 (2.1, 37.9)	78	82	47	95
Latex sensitivity & positive history & daily rectal disimpaction	6.8 (2.6, 17.6)	55	94	67	90
Latex sensitivity & positive history & IgE > 84 IU	13.4 (3.2, 55.5)	78	91	64	95
Positive history & IgE > 84 IU	13.4 (3.2, 55.5)	78	91	64	95

*The reference population is patients with spina bifida undergoing a surgical procedure during the epidemic period without developing an anaphylactic reaction.

†Latex sensitivity is defined as positive latex test, RAST, or ELISA result.

‡Positive history is defined as any one of the following: balloon contact urticaria, glove contact urticaria, food allergy, adhesive tape rash, or asthma.

The need for daily rectal disimpaction, despite being less sensitive, was the most specific variable for identifying case patients. A combination of three variables (latex sensitivity, positive history, and daily rectal disimpaction) was most specific with the best predictive value for identifying patients with AR. The specificity of a positive history in identifying patients with AR was markedly improved with addition of a serum test for total IgE greater than 84 IU (200 ng/ml). Patients with a positive clinical history and total IgE greater than 84 IU had a 13.4-fold greater risk of AR than other patients with spina bifida.

Multivariate analysis

To identify the independent risk factors for AR, we assessed the potential association of AR with all variables by forward selection logistic regression analysis (■Table V). Because many patients did not have all three tests (SPT, RAST, and ELISA) performed, the model including these variables

was based on data from only 31 patients (model 1, ■Table V). This model identified allergy symptoms with rubber contact and non-white race as significant predictors of anaphylaxis. Despite inclusion in the list of variables entered into the model, none of the specific tests for latex sensitivity were independent risk factors for AR. Because of this, the latex-specific test variables were excluded from the model building scheme, and patients who did not have these tests were included in model 2. In this model history of food allergy, non-white race, daily rectal disimpaction, and total IgE greater than 84 IU were identified as the most important predictors of anaphylaxis. Because IgE tests were not performed in 22 patients, this variable was excluded from the variables available for inclusion in the analysis resulting in model 3. In this model race, history of allergy symptoms with rubber contact, food allergy, and nine or more previous surgical procedures were identified as the most important predictors of anaphylaxis.

TABLE V. Logistic regression models predicting risk of anaphylaxis in patients with spina bifida at CHW, January 3, 1990 to January 1, 1991

No. of patients	Model chi square (degrees of freedom)*	Area under the ROC curve†	Significant risk factors‡	Parameter estimates	Standard error	Odds ratio	95% CI
Model 1							
31	18.5 (2)	0.84	Race	1.03	0.59	2.8	0.89, 8.83
			Allergy symptoms with rubber contact	3.7	0.95	40.4	6.3, 260
Model 2							
53	35.7 (4)	0.99	Race	2.57	1.4	13.1	0.84, 203.9
			Food allergy	6.34	2.69	567	2.9, 110441
			Daily rectal disimpaction	3.65	1.62	38.3	1.6, 919
			IgE > 84 IU	4.81	2.35	122	1.2, 12121
Model 3							
75	45.2 (4)	0.96	Race	2.16	0.98	8.6	1.3, 58.8
			Allergy symptoms with	5.80	1.91	331	7.8, 14132
			rubber contact	6.08	2.10	437.1	7.1, 26938

Food allergy				
≥ 9 prior				
surgical				
procedures	3.32	1.43	27.6	1.7, 450.7

*Calculated with -2 • log likelihood statistic.²⁹
†The area under the receiver operating characteristic (ROC) curve is a measure of how well the model is able to predict outcome.³⁰
‡Determined with the use of forward selection logistic regression in PC-SAS.

Discussion

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In this study 10 of 74 (13.7%) children with spina bifida who underwent 151 procedures experienced 11 episodes of anaphylaxis during induction of anesthesia before surgical intervention. In contrast, during the same period, only one patient experienced anaphylaxis during induction of anesthesia in over 7500 procedures performed on patients who did not have spina bifida; this patient had congenital posterior urethral valves requiring frequent urinary tract catheterization. Thus the risk of AR in the operating room was greater than 500-fold in patients with spina bifida when compared with the population without spina bifida. In contrast to other reports in which anaphylaxis presumed to be caused by latex occurred between 40 to 225 minutes into a procedure, each AR in this study occurred during anethesia induction and before surgical incision.^{3 25} This earlier occurrence of AR is similar to that observed in AR attributed to latex sensitivity, in which presumably latex proteins in balloon-tipped barium enema catheters are contacted and absorbed rapidly across rectal mucosa.¹¹

During anesthesia induction, patients may have multiple exposures to latex gloves worn by personnel; latex injection ports in intravenous lines, tubing, and bags; latex plungers on syringes used to administer medication intravenously; and latex tops on medication vials. Because the internal components of anesthesia machines are made of natural rubber devices, delivery of oxygen and anesthetic gases may also be a potential source of latex exposure. These exposures may account for the early onset of anaphylaxis, occuring within 30 minutes of the induction of anesthesia. Because of these multiple potential exposures, we could not identify the source of latex antigen, although the intravenous buretrol system may be implicated.

Univariate and multivariate analysis indicated that general allergic phenomena (asthma, food allergy, and elevated total IgE) and specific allergic reactivity (allergy symptoms with rubber contact) were independent risk factors identifying patients with spina bifida at highest risk for AR. Furthermore, all patients who experienced anaphylaxis had demonstrable latex-specific IgE antibodies and did not have IgE-mediated reactivity to anesthetics or muscle relaxants used in general anesthesia induction. Despite its high prevalence, ETO-specific IgE was not associated with AR.

Consistent with results of other studies,^{7 26} this study has documented that patients with spina bifida in whom ARs develop are more likely to have elevated total serum IgE levels. Elevated total serum IgE may be a marker of heightened immune responses in this population and appears to be a reasonably sensitive and specific means of identifying patients with spina bifida at risk for AR. In

addition, other factors (daily rectal disimpaction and nine or more prior surgical procedures) also identify those patients at highest risk for AR. These two variables may help identify the route of sensitization to latex or may indicate that the patients in whom ARs develop have a more severe involvement of spina bifida (abnormal gastrointestinal motility and repetitive surgical procedures) than patients in whom ARs do not develop. The high prevalence of multiple allergies (to latex, ETO, and aeroallergens) may indicate that patients with spina bifida tend to form IgE antibody preferentially when in contact with environmental antigens.

The prevalence of latex-specific IgE reactivity among this study's population with spina bifida was 73% (44 of 60). Using different immunologic tests, other investigators have detected latex-specific IgE antibodies in 18% to 34% of patients with spina bifida.^{8 27} Although SPT, ELISA, or RAST identified all patients who experienced ARs, we do not recommend routine testing of all patients with spina bifida because these tests lack specificity for predicting ARs (■Table IV), although they are specific for identifying sensitization to latex (■Table III).^{9 25} Furthermore, standardized antigens are not available, and severe ARs can occur during SPTs.²⁰ Our data show that compared with latex-specific IgE antibodies in SPTs, clinical history in combination with total serum IgE is a more sensitive and specific predictor of patients at risk for AR (■Table IV). Physicians caring for patients with spina bifida should carefully question them about these risk factors so that those at risk for AR can be identified and preventive measures can be instituted.

Preventive measures should include avoidance of latex products for all patients with spina bifida during surgical and diagnostic radiologic procedures by substitution of nonlatex gloves, catheters, tubing, and other instruments. Patients with spina bifida who have symptomatic latex allergy, food allergy, IgE greater than 84 IU, nine or more prior surgical procedures, or require daily rectal disimpaction may benefit from preoperative prophylaxis with corticosteroids, antihistamines, and possibly ephedrine. It is likely that these measures will decrease the number and/or severity of ARs and perhaps decrease the development of sensitization among patients with spina bifida. However, these measures may not be protective in IgE-mediated reactions.

This study highlights the potential risk of latex sensitization which has become a significant health hazard,^{3 12 14 28} especially because latex is ubiquitous in the home and in medical settings.

Latex sensitivity is a factor in life-threatening ARs occurring in the operating room. The recent increase in adverse reactions caused by latex raises questions concerning its source, collection, processing, and manufacture. The reason for the abrupt outbreak of ARs is unclear but is likely due to increasing sensitization and intensive exposure to latex in the operating room. Cooperation among scientific, regulatory, and manufacturing communities is needed to solve this problem and prevent attendant severe morbidity and deaths.

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- Received for publication July 30, 1993.
- Revised Jan. 4, 1994;
- Accepted for publication Feb. 2, 1994.
- Reprint requests: Kevin J. Kelly, MD, Allergy-Immunology Division Department of Pediatrics, Medical College of Wisconsin, 8700 West Wisconsin Ave., Milwaukee, WI 53226
- Copyright © 1994 by Mosby-Year Book, Inc.
- 0091-674/94 \$3.00 + 0 **1/1/55431**

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