Bruno Riou, M.D., Ph.D., Editor

Case Scenario

Perioperative Latex Allergy in Children

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LATEX allergy emerged as a serious health concern in the 1980s when an alarming number of cases of latex anaphylaxis occurred in patients during general anesthesia.[1] In addition, an even greater number of local allergic reactions occurred in health care workers who wore latex gloves. The incidence of latex anaphylaxis increased dramatically through the mid-1990s, affecting three groups of infants and children undergoing general anesthesia: those with spina bifida, those with congenital urological anomalies who required frequent bladder catheterizations, and those who underwent multiple invasive surgeries involving mucosal contact by latex gloves.[1] Despite numerous reviews on the risk factors for latex sensitivity and anaphylaxis in susceptible children, latex is often overlooked as the primary allergen in those who develop anaphylaxis in the perioperative period. We present a case history of an anaphylactic reaction to latex that was attributed to antibiotics and the subsequent follow-up with the parent.

Case Report

A 13-yr-old white boy (58 kg) was scheduled for upper endoscopy and colonoscopy for protracted diarrhea. He was prescribed loratadine for seasonal allergies (allergic rhinitis) associated with wheezing. He was reported to be allergic to ampicillin and had experienced an immediate hypersensitivity reaction to vancomycin (likely Red Man Syndrome).[2] He had four previous anesthetics for ventricular septal defect repair, tethered cord, right club foot repair, and tongue tie. His mother reported that he had experienced no complications during those anesthetics, except for the tethered-cord surgery, 10 yr previously. During that anesthetic, the mother recalled that the anesthesiologist had informed her that her son's airways had narrowed during surgery and that his blood pressure had decreased resulting in a near-fatal reaction while intravenous Ampicillin was infusing. The response was so severe that emergency resuscitation measures were necessary. The anesthesiologist advised that her son never receive Ampicillin again. Her son recovered uneventfully from that anesthetic and surgery.

On the day of endoscopy, the child's vital signs were normal and his physical examination was unremarkable. The child's cardiologist recommended intravenous clindamycin and gentamicin for endocarditis prophylaxis (pre-2007 American Heart Association guidelines). At the end of the history, one of the authors (J.L.) asked the mother to describe what occurs when her son holds a toy balloon to his lips? She expressed surprise at the question because no one had ever asked that before, explaining that her son's lips swell enormously. She was then asked if anything remarkable occurs when the dentist inserts a rubber dam into his mouth? She reported that her son's tongue swells. At that point, the mother was informed that in light of her son's atopic history, multiple surgeries and responses to toy balloons and rubber dams, that his previous intraoperative reaction was most likely an anaphylactic reaction to latex.

All natural rubber latex (NRL) products were removed from the operating room before proceeding with the upper endoscopy and colonoscopy. The anesthetic course was unremarkable. Subsequently, we referred the patient to an allergist for investigation of his purported allergies to Ampicillin and latex. The child was tested with benzylpenicilloyl polylysine (Prepen; Hollister-Stier Laboratories, Spokane, WA), penicillin G, and ampicillin using skin prick and intradermal tests. Minor determinant mixture[3] to determine sensitivity to less frequent haptens was not available for clin-

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ical use at that time. The patient was also tested for latex sensitivity. The results indicated an extremely positive response to latex and completely negative responses to the antibiotics. The child's mother was notified of the diagnosis of latex sensitivity and her son was advised to wear medical alert identification.

During follow-up contact, we discovered that the mother's memory was factually vague concerning the "life-threatening event in the operating room" and my presurgical interview. We then searched the anesthetic record for the original event to verify the original reaction—only to find that no adverse event had been documented. When the anesthesiologist of record was contacted, he, too, failed to recall the reaction. As a result, we have been unable to verify many details of the original reaction. However, this incomplete medical record in no way detracts from our recollection of the mother's report regarding her son's reaction to NRL products in contact with oral mucosa. Moreover, the suspected diagnosis was confirmed by immunologic testing. Subsequent to the supposed "intraoperative event," an antibiotic provocation challenge was not performed to establish the veracity of the negative testing for ampicillin sensitivity as recommended in cases of discordance between clinical history (suggestive of anaphylaxis) and negative skin test results.[4]

Discussion

Important issues to consider in this case include the following:

1. *What Is the Epidemiology of Perioperative Anaphylaxis?*
The incidence of anaphylaxis under anesthesia in adults is estimated to be 1:6,000–20,000,[5,6] with cardiac arrest and fatal outcomes occurring in 0.7–10% of reactions.[5] The most common trigger of anaphylaxis in the perioperative period is neuromuscular blocking drugs (approximately 60% of reactions), followed by latex (12–16% of reactions) and antibiotics (8%).[6] In contrast, the incidence of anaphylaxis in children is 1:7,700, with latex accounting for 76% of the reactions.[7] No pediatric fatalities were reported.[7]

The frequency of latex anaphylactic reactions in children has waned since the mid-1990s for at least three plausible reasons: (1) elimination of NRL-containing material from clinical care, (2) increased awareness of at-risk children, and (3) improved laboratory identification of latex allergy. Furthermore, clinical guidelines have been established to prevent exposure to NRL products—and to direct diagnostic and therapeutic strategies for perioperative reactions.‡[8]

2. *What Is Latex Sensitization and Hypersensitivity?*
Latex sensitization is defined as the presence of immunoglobulin antibodies to NRL products without clinical manifestations. The prevalence of latex hypersensitivity in the general adult population is 1–6.7%, with a similar incidence in the pediatric population, 0.3–4%.[9,10] Sensitization does not always lead to allergy, notwithstanding subsequent NRL contact. It remains unclear why some who are exposed to latex do not develop a latex sensitivity whereas others who do develop this sensitivity do not manifest reactions on contact.

In 2001, a position statement on the nomenclature for allergy diagnoses defined hypersensitivity as an "umbrella term" that causes "objectively reproducible symptoms or signs, initiated by exposure to a defined stimulus at a dose tolerated by normal subjects."[11] Hypersensitivity is either allergic (immunologic based) or nonallergic (nonimmunologic based). Allergic hypersensitivity reactions have an underlying immunologic mechanism, either immunoglobulin E (IgE) (immediate) or non-IgE mediated (delayed).[11] Allergic reactions to NRL products in children in the perioperative period are immediate, IgE-mediated reactions that result in anaphylactic reactions of varying severity.

Of the more than 200 polypeptides that have been identified in NRL as potential immunoreactive allergens for latex, 13 polypeptides (*Hevea brasiliensis* [Hev b]), Hev b 1–13, are recognized as the primary allergens by the International Union of Immunological Societies. The concentrations of these proteins in NRL products vary according to the manufacturing process. For example, flat sheets of latex extruded into products (*e.g.*, catheters, rubber vials, rubber shoes) contain Hev b 1 and 3, whereas molds that are dipped in liquid latex (*e.g.*, gloves, rubber dams, tourniquets, condoms) contain Hev b 2, 4, 6.01, 6.02, 6.03, 7.01, 10, and 13.[12] Other latex proteins (Hev b 5, 7.02, 8, 9, 11) are water-soluble and appear in varying quantities as minor epitopes in both products. NRL products made from molds (*e.g.*, latex gloves) *versus* sheets contain much greater concentrations of uncrosslinked or free proteins that may be sloughed onto mucosal membranes and absorbed, triggering immediate reactions.[12] The major allergens identified in children with spina bifida include Hev b 1 (rubber elongation factor) and Hev b 3 (small rubber particle protein), as well as Hev b 6.01 and 6.02, with minor contributions from Hev b 5, 7, and 13.[12]

3. *Who Are the At - Risk Children?*
Although the prevalence of latex allergy in the general pediatric population is less than 4%, the prevalence in specific at-risk subpopulations may be as great as 71%.[9,13–15] Children at risk for developing latex sensitivity include those with spina bifida; congenital urologic, gastrointestinal, and tracheoesophageal defects; those who have undergone multiple (*i.e.*, more than five) surgeries; and those with a history of atopy.[1,7,9,10,13,14] Atopy is manifested by the symptom complex of rhinoconjunctivitis, asthma, and/or eczema. The most common routes for exposure to latex epitopes in children in the perioperative period are through mucosal and parenteral surfaces (*e.g.*, surgeons wearing latex gloves during intracavity surgery), which may trigger immediate allergic reactions of varying severity.[1]

‡ American Society of Anesthesiologists. Natural Rubber Latex Allergy: Considerations For Anesthesiologists. Available at: http://ecommerce.asahq.org/publicationsAndServices/latexallergy.pdf. Accessed July 18, 2010.

To explain the greater prevalence of latex sensitization in children with spina bifida compared with other surgical conditions, a number of factors have been identified, including the age at which first surgeries were performed, the number of surgeries, the frequency of daily bladder catheterizations, atopy, and genetic predisposition. Of all infants who underwent surgery for gastrointestinal or urologic abnormalities within 6 months of birth, 30% developed latex sensitivity and 30% of these had a positive provocation test results, suggesting a clinical response to latex after future contact.[14] Infants who underwent more than eight surgeries were determined to be at significantly greater risk for developing latex sensitivity than those who undergo fewer surgeries.[14] These results are identical to those reported for infants with spina bifida. IgE and Hev b 1 antibodies to latex have been detected in at least 78% of children with spina bifida after 7–9 surgeries in their first year, a three-fold greater incidence than in healthy children after 2–4 surgeries.[15] The prevalence of latex hypersensitivity in children also varies by surgery type; 71% incidence in children with spina bifida, 42% in isolated hydrocephalus, 31% in gastrointestinal malformations, 11% in congenital heart disease, and 6% in malignancies.[13,15] The frequency of daily bladder catheterizations with latex catheters in children with spina bifida has been correlated with latex sensitivity, although the importance of this factor remains unclear. Latex-specific IgE antibodies have been reported in 1–16% of children with atopy who have never had surgery.[9,16] A history of atopy increases the risk of latex sensitivity up to 10-fold.[9,14]

Several candidate genes have been investigated for their role in predisposing children with spina bifida to latex hypersensitivity. Human leukocyte antigen genes have been associated with IgE responses to latex in health care workers, but not in children with spina bifida.[15,17] In adult health care workers who developed latex hypersensitivity, the frequency of single-nucleotide polymorphisms of interleukins 13 and 18 (the former activates B cells to IgE production whereas the latter stimulates interferon production as well as enhancing cytokine and IgE production) was two-fold greater than in controls, suggesting a genetic predisposition to latex allergy.[18] The lack of a similar association between these two polymorphisms and children with spina bifida led to the recent conclusion that environmental factors exerted more influence on the genesis of latex sensitivity in the latter population than did genetics.[19]

Latex Fruit Syndrome. Children who are allergic to certain fruits (*e.g.*, avocado, banana, kiwi, chestnut), vegetables (*e.g.*, tomato, bell pepper, carrot), and the Ficus tree may exhibit evidence of cross-sensitivity to latex. Hev b 2, 6.02, and 7 are the primary allergens responsible for most instances of latex-fruit cross-sensitivity.[12,20] The risk of an allergic reaction to latex in a patient who is allergic to these fruits is 11%—similar to the risk of reaction to these fruit in a patient who is latex sensitive (7%). This cross-sensitivity is most likely the result of similar epitopes found in the fruits and vegetables.[12] It is currently held that latex sensitivity precedes latex fruit sensitivity.

Table 1. Severity Grade for Anaphylaxis

Grade I.	Generalized cutaneous signs: erythema, urticaria with or without angioedema
Grade II.	Moderate multiorgan involvement with cutaneous signs, hypotension and tachycardia, bronchial hyperreactivity (cough, ventilatory impairment)
Grade III.	Severe life-threatening multiorgan involvement that requires specific treatment: collapse, tachycardia, or bradycardia, cardiac arrhythmias, bronchospasm; the cutaneous signs may be absent or occur only after the arterial blood pressure recovers
Grade IV.	Circulatory or respiratory arrest
Grade V.	Death due to a lack of response to cardiorespiratory resuscitation

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Clinical Signs of Perioperative Latex Anaphylaxis

The onset of latex anaphylaxis in the operating room occurs 25–290 min after induction of anesthesia, when latex gloves are in direct contact with large surface areas within a body cavity (*e.g.*, peritoneal, thoracic).[1,7] In our experience, children who develop latex anaphylaxis present with hypotension, tachycardia, bronchospasm with increasing airway pressures during positive pressure ventilation, and, less frequently, cutaneous manifestations.[7] Bradycardia[7] and cardiac arrest[21] rarely occur during these reactions in children, even under anesthesia.

Diagnosing latex as the epitope responsible for an anaphylactic reaction during general anesthesia may be difficult because there are no characteristics that uniquely identify latex as the cause. However, the combination of susceptibility (*e.g.*, atopy), surgical predisposition (*e.g.*, spina bifida) and surgical onset of anaphylaxis (*e.g.*, bronchospasm, circulatory instability) strongly supports latex as the cause of the reaction. Cutaneous manifestations of anaphylaxis may be absent or masked by surgical drapes. In addition, circulatory instability may be attributed to anesthesia and surgery, but the diagnosis of latex anaphylaxis should remain at the top of the differential list.

The clinical severity of immediate hypersensitivity reactions in the perioperative period have been graded (table 1).[8] Although most immediate reactions to latex in the perioperative period are grade 2 or higher, a grade 4 reaction is rarely observed in children. The grading table has been used to guide the treatment of anaphylaxis in children and adults.

4. *How to Treat an Anaphylactic Reaction?*

When a latex reaction is suspected, all latex-containing products should be removed from contact with the child. The ABCs of resuscitation should be instituted, and strat-

Table 2. Management of an Anaphylactic Reaction to Latex in Children

Primary Management
1. Remove latex and maintain anesthesia, if necessary.
2. Notify the surgical team and complete surgery as quickly as possible.
3. Call for help.
4. Secure the airway (tracheal intubation) and ventilate with 100% oxygen.
5. Special handling for severe reactions:

Grade 3 Reaction

a. Hypotension
   Using Trendelenburg position, administer balanced salt or colloid (preferably hydroxyethyl starch) solution in 20 ml/kg bolus doses with parenteral intravenous bolus doses 1–10 μg/kg epinephrine, depending on the severity of the hypotension.
b. Bronchospasm (in association with hypotension)
   Parenteral intravenous boluses doses 1–10 μg/kg epinephrine, depending on the severity of the bronchospasm, and β_2 agonists *via* metered-dose inhaler or nebulized solution (the latter every 20 min).

Grade 4 Reaction

As required, repeated intravenous bolus doses of 10 $\mu g \cdot kg^{-1}$ epinephrine. Consider preparing an infusion beginning at 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ increasing up to 1 $\mu g \cdot kg^{-1} \cdot min^{-1}$.

Secondary Management*
1. Consider alternate vasopressors (titrate to effect), including glucagon (20–30 $\mu g \cdot kg^{-1}$ bolus then 5–15 $\mu g \cdot min^{-1}$ [1 mg maximum]), phenylephrine (0.1–1 $\mu g \cdot kg^{-1} \cdot min^{-1}$), noradrenaline (0.01–2 $\mu g \cdot kg^{-1} \cdot min^{-1}$), or vasopressin (0.3–3 mU $\cdot kg^{-1} \cdot min^{-1}$).
2. Corticosteroids methylprednisolone or hydrocortisone 1–2 μg/kg IV.
3. Antihistamines diphenhydramine (1.0–2.0 mg $\cdot kg^{-1}$ [50 mg maximum]) or ranitidine (1–2 $\mu g \cdot kg^{-1}$) IV or per os.
4. Bronchodilators–Metered-dose inhaler or nebulized β_2 agonists (salbutamol).

Investigation and Follow-up
1. Admit patients with grade 3 and grade 4 reactions to the intensive care unit until stable.
2. Collect blood for mast cell tryptase at 0, 2, and 24 h postreaction (peaks at 1–2 h).
3. Add signage noting "latex allergy" or "latex alert" on all relevant areas of patient care, including notes and databases.
4. Inform pharmacy and central supply of patient latex sensitivity so that latex can be eliminated from all preparations.
5. Refer child to allergist/immunologist for follow-up and testing.
6. Advise the parents of need for medical alert bracelet for child for latex allergy/anaphylaxis after diagnosis is confirmed.

Refer to table 1 for formal description of graded reactions.[8]

* Secondary management is required for grade 3 and 4 reactions in which hypotension is refractory to epinephrine and above measures. Although such reactions are unreported in children, they have occurred in adults who were β-blocked and in whom epinephrine treatment was delayed.

egies to restore cardiorespiratory homeostasis should be implemented (table 2). If the airway has not been secured, the trachea should be intubated with a cuffed endotracheal tube and the lungs ventilated. Anesthesia may be continued as tolerated while surgery is completed as quickly as possible, using an inhalational agent in 100% oxygen for bronchodilation. Anesthesia should then be discontinued.

Grade 2 reactions usually respond to intravenous bolus doses of balanced salt solutions (20 ml/kg during 10–20 min) and placing the child in the Trendelenburg position. If these measures are not completely effective in restoring circulatory homeostasis, bronchospasm occurs or the reaction progresses to grade 3 severity. Then, intravenous epinephrine should be administered.

The primary treatment for anaphylaxis is intravenous epinephrine along with intravenous fluids.[7,8,22] The dose of epinephrine should follow a sliding scale from 1–10 μg/kg, where the dose is proportional to the severity of the bronchospasm and/or hypotension. A dose of 10 μg/kg is reserved for grade 4 reactions or cardiac arrest. Repeated intravenous doses of epinephrine may be required if recrudescence occurs. If multiple bolus doses of epinephrine are required to control the reaction, then an intravenous infusion of epinephrine should be commenced beginning at 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and increasing up to 1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ until cardiorespiratory homeostasis is achieved.

In our experience, although children uniformly respond to epinephrine alone,[8,22] none have responded to other vasopressors, including methoxamine and phenylephrine. Although epinephrine is the only first-line vasopressor for anaphylaxis, several other vasopressors—including noradrenaline, vasopressin, and glucagon—have been recommended as second-line treatments for anaphylaxis in adults who were β-blocked and in whom anaphylaxis was refractory to epinephrine.[8,23]

Intravenous fluid boluses of balanced salt solutions (10–20 ml/kg) or colloid solutions should be adminis-

tered as necessary to supplement epinephrine.[8,22] The preferred colloid volume expander is hydroxyethyl starch because it is less likely to trigger allergic reactions than gelatin-based colloids. Bronchospasm that occurs as a part of an anaphylactic reaction should be treated with intravenous epinephrine.[8,22]

However, if isolated bronchospasm occurs, suggesting an acute asthmatic episode (as opposed to anaphylaxis), primary treatments should include β_2 inhaled agents and methylprednisolone.[8,22] The addition of a potent inhaled anesthetic such as sevoflurane, may further attenuate bronchospasm.

Secondary treatments for latex anaphylaxis have not been established in children.[8,22] There is no clear evidence that either H_1- or H_2-blocking drugs (1–2 mg/kg diphenhydramine or ranitidine) alter anaphylaxic outcomes in children although these medications continue to be recommended and administered.[22] Although their role in anaphylaxis remains unclear, intravenous steroids (1–2 mg/kg methylprednisolone or hydrocortisone) may attenuate bronchospasm as well as angioedema.[22]

If an allergic reaction is suspected, blood should be collected for serum tryptase concentrations as soon as possible, 1–2 h after the start of the reaction and 24 h later or during convalescence. For a complete description of the management of anaphylactic reactions, please refer to the British§ and Scandinavian[8] guidelines.

All children who develop latex reactions should be referred to an immunologist or allergist to confirm the diagnosis, lest a presumptive and potentially erroneous diagnosis of an allergic reaction to an innocent medication is documented instead of latex allergy. A letter in which the anesthesiologist outlines the severity of the anaphylactic reaction, the intervention required, and the outcome should be transmitted to the allergist or immunologist. Additional details regarding follow-up are outlined in table 2.

Preventing Latex Anaphylaxis

The key to preventing latex reactions is to avoid exposure to latex products from birth. Although many hospitals have become latex-free,[24] others continue to stock latex gloves and other NRL products in operating rooms. The quantity of latex aeroallergens measured in the operating room after using latex *versus* nonlatex gloves follows the order: powdered latex gloves > powderless latex gloves > nonlatex gloves, where the substitution of powderless for powdered latex gloves reduced the aeroallergen concentration of latex by 10–20-fold.[25]

It is noteworthy that the concentration of extractable latex proteins from powdered latex gloves from 10 manufacturers varies up to 3,000-fold. Since the mid-1990s, steps have been introduced to reduce the concentration of latex proteins in gloves during the manufacturing process (*e.g.*, aggressive washing), although even powderless latex gloves may cause latex hypersensitivity.[24,25] Less appreciated is the fact that cornstarch, the powder on medical gloves, may be directly harmful to patients.[26]

All surgical equipment should be prepared using nonlatex gloves. Before the child arrives in the operating room, signs that warn of latex allergy should be displayed on all doors that lead to the operating room. Despite implementing these precautions, latex reactions have occurred in the perioperative period, often as a result of breeches in latex precautions. To further protect susceptible children from latex reactions, some experts recommend pharmacologic prophylaxis with steroids and antihistamines (H_1- and H_2-blocking agents). However, allergic reactions have been reported despite these measures as well.[1] Accordingly, we do not recommend pharmacologic prophylaxis for latex hypersensitivity.

5. *How Do We Establish the Diagnosis of Latex Hypersensitivity?*

A diagnosis of latex hypersensitivity requires a focused history of the clinical signs and symptoms that are consistent with an allergic reaction to latex and evidence of latex-specific sensitization based on skin (*in vivo*) and/or serum (*in vitro*) tests. In Europe, latex hypersensitivity is investigated using skin prick testing with standardized commercial latex extracts whereas in the United States, it is based mainly on *in vitro* testing, although some also use skin prick tests through latex gloves.

The skin-prick test involves depositing small and diluted aliquots of latex protein solution on the skin and pricking the skin below the solution to observe the response. In the United States, the skin prick test is conducted through a latex glove. This test is usually performed 4–6 weeks after the reaction. If the child is allergic to latex, a small, raised area surrounded by redness appears at the test site within approximately 15 min. The specificity and sensitivity of this test is close to 100%.[27]

Four commercially available serum tests—AlaSTAT EIA (Diagnostic Products Corporation, Los Angeles, CA), IMMULITE 2000 (Diagnostic Products Corporation), Pharmacia CAP (Pharmacia-Upjohn Diagnostics Inc., Kalamazoo, MI), and HY-TEC EIA (HYOCOR Biomedical, Irvine, CA)—make use of technologies such as RAST (radioallergosorbent test) or EAST (enzyme allergo-sorbent test) and are approved for detecting latex-specific immunoglobulin IgE. The sensitivity of these tests is 60%, with a false negative rate of 30% or less.[28]

6. *How Do We Prepare for the Child Sensitized or Allergic to Latex?*

A facility-wide strategy and commitment is necessary to establish a latex-free health care environment. A multidisciplinary latex-allergy task force should include broad representation from hospital staff and should have policies and protocols for the management of the latex-sensitive child, including educational programs for all health care workers.

§ Association of Anaesthetists of Great Britain and Ireland. Management of a Patient with Suspected Anaphylaxis during Anaesthesia: Safety Drill. 2009. Available at: http://www.aagbi.org/publications/guidelines/docs/ana_laminate_2009.pdf. Accessed December 7, 2010.

The management strategy recommended by the American Society of Anesthesiology consists of a complete medical history and questionnaire (from the parents), application for a medical alert bracelet, a latex-free cart, a list of latex-free devices and alternatives, signage on the patient's medical records that highlights his/her latex allergy, and "Latex Allergy" signs in the perioperative area.‡

Although some parents may not realize their children are sensitive to latex, inquiring about their child's responses to touching a toy balloon to their lips or inserting a rubber dam in their mouths during dental surgery, as well as a history of atopy, the number of previous surgeries, and any coexisting medical conditions (including spina bifida and congenital urological abnormalities) should be included in preoperative assessment. Children with latex allergy should be scheduled as either the first case of the day or 2.5 h after room latex exposure because the concentration of aerosolized latex particles (*i.e.*, after using powdered latex gloves) after that hiatus decreases to 4% of the average room concentration of latex.[29] To reduce latex exposure and the risk of reactions, many institutions currently use either latex-free or powder-free latex gloves in operating rooms,[24,25] thus rendering the timing of surgery of lesser importance. Many of the new anesthetic machines, ventilators, and equipment, including masks and tubes, are NRL-free. However, if the internal components of an anesthetic machine contain latex, then a filter (BB25; Pall Corporation, Port Washington, NY) may be inserted into the breathing circuit to reduce the risk of exposing the child to NRL during mechanical ventilation.[30]

The use of rubber-stopper multidose vials for children with latex hypersensitivity remains a controversial issue. Solid NRL products, such as stoppers, are extruded from sheets of latex, which contain fewer free proteins than NRL products from molds.[22] The composition of these stoppers has shifted in recent years, from predominantly NRL to synthetic materials that do not induce latex reactions.[31] However, there is evidence that latex proteins may leach from NRL stoppers into drug solutions when vials are stored in the inverted position, even if the stopper has not been punctured.[31] Despite this evidence, anaphylactic reactions in children immediately after intravenous administration of drugs from multidose vials are exceedingly rare.[21] It is very difficult to establish the composition of the stoppers in every multidose vial to determine whether they present a substantive risk of latex anaphylaxis to susceptible children. As a result, we hold the view that, given the rarity of anaphylactic reactions at induction of anesthesia combined with the shift away from NRL stoppers, the risk of inducing an anaphylactic reaction in a susceptible child by using a new multidose vial as a drug source is vanishingly small in 2011.

‖ Philadelphia Personal Injury Lawyer; Silverman & Fodera. Latex protein toxic syndrome: The newest toxic exposure. Defective Products. September 8, 2010. Available at: http://www.civilrights.com/defective-products/latex-protein-toxic-syndrome. Accessed December 7, 2010.

Latex-free Environment and the Future

Recent studies have demonstrated that adopting latex-free strategies in health care facilities has reduced the prevalence of latex sensitization and allergy in children with spina bifida (26.7 to 4.5%), myelomeningocele (4 to 1.2%), and a history of multiple surgeries (42 to 7%).[32] One pediatric hospital that adopted a latex-free environment recently reported zero incidence of allergic reactions in 25,000 anesthetic incidents for children.[32] These encouraging results suggest that a latex-free hospital environment may be a key strategy to eliminating latex allergy and anaphylaxis in the operating room. However, we must note that this action alone will not eradicate latex hypersensitivity from children because latex products are ubiquitous outside health care facilities.

If patients continue to be exposed to latex products outside health care facilities, then latex sensitivity will continue to occur. Investigators have focused on hypoallergenic latex immunotherapy including new drugs, desensitization, and vaccines (based on plant epitopes) to reduce latex response in susceptible individuals.[33]

7. *Is it Cost Effective to Convert to a Latex- free Work Environment?*

Conversion to a latex-free hospital environment incurs an initial capital cost. However, ongoing operating costs should not differ substantively from a latex setting. In addition, it may be more cost effective to avoid latex-containing products than to incur the additional costs of diagnosing, treating, and paying for disabilities incurred—as well as any fatalities due to anaphylaxis, however rare they may be—although there is no clear evidence to support this position. Some researchers[34] have suggested that the estimated costs to treat severe drug-related anaphylaxis have been chronically underestimated. Several studies have argued that it is cost effective to have a latex-free work environment, suggesting that institutions, regardless of size, benefit financially from instituting a latex-safe environment, even if latex-related disability levels remain extremely small.[35] We also anticipate that the cost of latex-free equipment will diminish with time. Currently, it seems prudent for institutions to undertake a financial impact analysis to determine the optimal approach to reduce latex exposure for their patients and employees.

8. *What Are the Legal Considerations of Latex Allergy?*

Failure to comply with evolving federal regulations to decrease latex exposure may lead to adverse outcomes and litigation.‖ Common errors in managing latex-susceptible patients include a failure to elicit a history of latex allergy, failure to ensure latex-free equipment is available when latex allergic patients are present, and discharging patients from the hospital without appropriate education and planned follow-up.

Knowledge Gap

Numerous advances in our understanding of the epidemiology of latex sensitivity in children have not been adequately

disseminated to practicing clinicians. Understanding which surgical conditions predispose individuals to latex sensitivity, the importance of the number of previous surgeries, and history of atopy are key features in appreciating the risk of latex hypersensitivity. Although history alone cannot confirm latex sensitivity, inquiring after the child's responses to contact with toy balloons or a dentist's rubber dam may help to clarify the child's susceptibility to latex.

Anaphylaxis is an infrequent event in the operating room, but, when it occurs, it may be life-threatening. To learn how to manage such a reaction, trainees should be encouraged to attend educational programs, such as simulator-based anaphylactic reactions, to acquire the necessary skill sets. Although the current evidence does not demonstrate a link between genetics and latex hypersensitivity in children with spina bifida, there are many untested potential genetic variants that warrant further consideration.

Finally, it remains unclear why some who are exposed to NRL and latex fruit allergens develop hypersensitivity and others do not. These issues should become the foci of future investigations if we are to further understand latex susceptibility in children.

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